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ISSN 1823-6782
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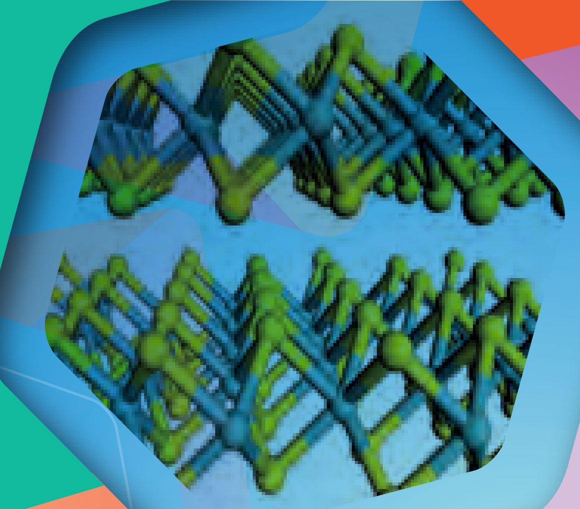
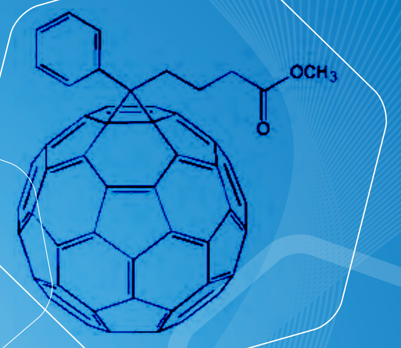
ASM Science Journal 7(2) 2013

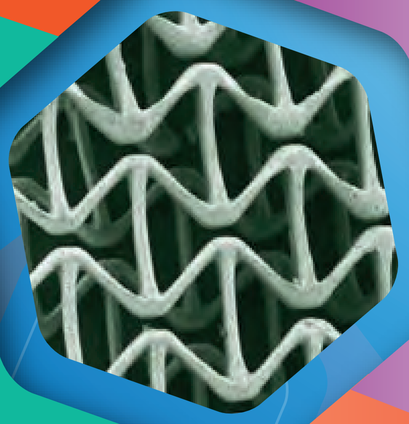
ASM Science JOURNAL

In Pursuit of Excellence in Science

Vol. 7, No. 2, December 2013 • ISSN : 1823-6782







Price (2 Issues)

Malaysia: RM100 (*Individual*)
RM200 (*Institution*)

Other Countries: USD50 (*Individual*)
USD100 (*Institution*)

ASM Science JOURNAL

Cover:

It has been said that Chemistry is arguably the most central of the natural sciences, framing much of our understanding of the natural world and continuing to deliver technologies that impact almost every aspect of our lives. In this issue in an article entitled *Global Trends in Chemistry Research and the Challenge for Malaysian Scientists: A Perspective Review* (pp. 173−220), the author takes the reader into the challenging new frontiers of chemistry research that will be worked globally over the next few decades, offering just the right level of detail for the uninitiated to follow the increasingly interdisciplinary trend of the topics being worked. Researchers across the spectrum of academia and industry as much as research grant committees will find the article a welcome read that gives a comprehensive coverage of key research in contemporary areas like energy, catalysis and chemical synthesis, materials science and biological chemistry. Value addition to the article has also come in the way of recommendations towards forging strong research collaborations between the universities, public research institutes and the industry which are seen as vital in providing cross-cutting chemical solutions throughout the value chains and to the success of technologies identified as critical to the nation.

The cover of this issue shows three figures in the hexagons taken from the above review article: The uppermost figures—on the right (section of *Figure 3*, pp. 178) depicts the PCBM acceptor molecule; and on the left (*Figure 12*, pp. 198) molybdenum disulphide structures of 2D material. The image (*Figure 13*, pp. 204) in the lower-left section of the cover shows optical images of polyethylene glycol scaffolds expanding in response to stretching—result of research by scientists from the University of California (San Diego) in the discovery of a new biomaterial which closely mimics human tissue.

Three examples of sea cucumbers from the genus *Stichopus* which look very similar in their outer morphology is shown in the centre of the cover—pictured (*Figure 1*, pp. 168) in an article where researchers from the Marine Science Laboratory, School of Biological Sciences, Universiti Sains Malaysia concluded that management and conservation of marine organisms was not possible without the ability to identify and classify them taxonomically.

ASM Science Journal is listed and indexed in Scopus.

Published by the Academy of Sciences Malaysia

The Academy of Sciences Malaysia (ASM)

The Academy of Sciences Malaysia (ASM) was established, under the *Academy of Sciences Act 1994* which came into force on 1 February 1995, with the ultimate aim to pursue excellence in science. Thus the mission enshrined is to pursue, encourage and enhance excellence in the field of science, engineering and technology for the development of the nation and the benefit of mankind.

The functions of the Academy are as follows:

- To promote and foster the development of science, engineering and technology
- To provide a forum for the interchange of ideas among scientists, engineers and technologists
- To promote national awareness, understanding and appreciation of the role of science, engineering and technology in human progress
- To promote creativity among scientists, engineers and technologists
- To promote national self-reliance in the field of science, engineering and technology
- To act as a forum for maintaining awareness on the part of the Government of the significance of the role of science, engineering and technology in the development process of the nation and for bringing national development needs to the attention of the scientists, engineers and technologists
- To analyse particular national problems and identify where science, engineering and technology can contribute to their solution and accordingly to make recommendations to the Government
- To keep in touch with developments in science, engineering and technology and identify those developments which are relevant to national needs to bring such developments to the attention of the Government
- To prepare reports, papers or other documents relating to the national science, engineering and technology policy and make the necessary recommendations to the Government
- To initiate and sponsor multi-disciplinary studies related to and necessary for the better understanding of the social and economic implications of science, engineering and technology
- To encourage research and development and education and training of the appropriate scientific, engineering and technical man power
- To establish and maintain relations between the Academy and overseas bodies having the same or almost similar objectives in science, engineering and technology as the Academy
- To advise on matters related to science, engineering and technology as may be requested by the Government from time to time; and
- To carry out such other actions that are consistent with the *1994 Academy of Sciences Act* as may be required in order to facilitate the advancement of science, engineering and technology in Malaysia, and the well being and status of the Academy.

The Academy is governed by a Council. Various Working Committees and Task Forces are charged with developing strategies, plans and programmes in line with the Academy's objectives and functions.

The functions of the Council are:

- To formulate policy relating to the functions of the Academy
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- To appoint such officers or servants of the Academy as are necessary for the due administration of the Academy
- To supervise and control its officers and servants
- To administer the Fund; and
- To convene general meetings of the Academy to decide on matters which under this Act are required to be decided by the Academy.

The Academy has Fellows and Honorary Fellows. The Fellows comprise Foundation Fellows and Elected Fellows. The Academy Fellows are selected from the ranks of eminent Malaysian scientists, engineers and technocrats in the fields of medical sciences, engineering sciences, biological sciences, mathematical and physical sciences, chemical sciences, information technology and science and technology development and industry.

The Future

Creativity and innovation are recognised the world over as the key measure of the competitiveness of a nation. Within the context of K-Economy and the framework of National Innovation System (NIS), ASM will continue to spearhead efforts that will take innovation and creativity to new heights in the fields of sciences, engineering and technology and work towards making Malaysia an intellectual force to be reckoned with.

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Distribution of Disease and Pest Resistance Markers in Malaysian Rice Varieties

W. Wilonita[1], R. Nurliyana[1], D.D. Asma[1], M. Noorazizah[1] and M.Y. Hirzun[1]*

Molecular markers have been intensively used in assisting breeding to reduce the time taken by conventional breeding as well as helping introgression of specific traits. Baseline analysis of known markers is crucial in developing a genetic database on disease and pest resistance for local rice germplasm which does not yet exist. In this study seven local rice varieties, including the popular MR219 and MRQ 74 and MRQ 76 (newly developed aromatic rice varieties), together with a foreign variety, Intani-2, were screened for genetic markers related to pest and disease resistance. One hundred and twenty-two type-related markers (SSR, STS, InDel and Allele-specific) for genes resistant to bacterial leaf blight, blast and brown planthopper were screened using PCR amplification and validated by sequencing. It was found that each variety had its own pattern of resistance. Using allele-specific markers namely pBPH9, pTA248 and Pisbdom were found to be the most efficient way to screen for the targeted genes. Of the seven varieties, MR219 and MR232 were found to have the highest distribution of markers for resistance genes against pest and diseases studied..

Key words: Simple sequence repeat; resistance gene; *Bph1*; *Magnaporthe grisea*; MR 219; MR232; breeding; genetic database; MRQ 74; MRQ 76; bacterial leaf blight; brown planthopper; allele-specific markers;

Rice (*Oryza sativa* L.) is the staple food to more than half of the world's population and is produced and consumed particularly in Asia (Chakravarthi & Naravaneni 2006). The projected increase in global population to nine billion by 2050 and predicted increase in water scarcity and decrease in arable land, the constant battle against new emerging pathogens and pests, and possible adverse effects from climate change present great challenges for rice breeders and agricultural scientists. Although the Malaysian elite variety, MR219, has been cultivated in Malaysia for many years, FAO warns of increasing constraints and issues including brown plant hopper (BPH), stem borers, blast, rice tungro virus, sheath blight and other abiotic and biotic stresses.

Marker-assisted selection (MAS) can be a useful tool for expediting the rice breeding programme which aims to overcome all these challenges. MAS refers to the use of DNA based markers, such as SSR, that are tightly linked to target loci as a substitute or to aid phenotypic screening. Determination of the allele of the DNA marker, allows identification of plants that possess particular genes or quantitative traits loci in terms of their genotype rather than their phenotype (Mackill 2007).

The wild rice species are valuable resources of genes for resistance against major diseases and insects and have been used widely as donor strains (He 2007). According to Gowda *et al*. (2003), four hundred and fifty genes have been identified in rice genomes that are related to abiotic stresses, quality traits as well as pest and disease resistance. BPH, *Nilaparvata lugens*, is one of the most serious insect pests throughout the rice growing areas in Asia. BPH causes direct damage to crops and indirect damage by acting as a vector for viral diseases. Normal practice for controlling these pests are by chemical treatment that is expensive and harmful to the environment (Kim & Sohn 2005). Jena and Kim (2010) have reported that host plant resistance is the most effective way of controlling pests including BPH. To date, researchers have discovered up to twenty-one BPH genes (Jena & Kim 2010) related to rice brown planthopper resistance.

A common disease affecting rice production in Asia is bacterial leaf blight (BLB), which is caused by the rod-shaped bacterium, *Xanthomonas oryzae*. This disease has taken on new importance since the introduction and widespread cultivation of high yielding but susceptible rice varieties, and is especially prevalent in irrigated and rainfed

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lowland areas (Davierwala *et al*. 2001). MAS molecular breeding is important to develop resistant varieties. So far, thirty genes including *Xa21*, *Xa2*, *Xa13*, and *Xa27* have been identified to be related to bacterial leaf blight resistance. Most established markers (e.g. RM122, RM13, and RM224) which specifically detect one or more BLB resistance genes are available online (<www.gramene.com>).

Rice blast is one of the most important diseases of rice crops worldwide. It is caused by the fungus, *Magnaporthe grisea* which can attack the aerial parts of the rice plant at any stage of growth (Babujee & Gnanamanickam 2000). Controlling rice blast by planting rice varieties that are resistant is both most practical and economical. Forty genes have been discovered to be related to blast resistance in rice. Some of the genes which can be detected by established markers (*e.g.* RG64) are *Pi-2, Pi- 40*, and *Pi-ta*. In this research, we studied the pest and disease genotypes as well as marker distribution for eight of the rice varieties. All eight were screened with one hundred and twenty two public domain markers related to resistance genes against brown plant hopper, blast and bacterial leaf blight. Study scopes include detecting gene presence using various types of markers, analysis, validation, and development of a basic genetic database for our local varieties.

MATERIALS AND METHODS

Seeds and Varieties

Most of the *indica* rice varieties showed higher expression level compared to *japonica* species, hence widely used as control varieties. In this study, we used *indica* varieties namely IR 36 that showed durable resistance towards blast, *Pi-ta* gene and IR24 that resistance to blast *Pi-20* gene. Both Nipponbare and CO39 were used as negative control as both are highly susceptible to *Bph1* gene and blast, respectively. Besides, through MAS technology several genes had been successfully pyramided, bacterial blight resistance (Zhang 2007) and were also used as control, e.g. IRBB 61 (*Xa4+xa5+Xa7*), IRBB 54 (*xa5+Xa21*), IRBB 66 (*Xa4+xa5+Xa7+xa13+Xa21*). All the seeds of control varieties were provided by IRRI while seeds of the tested varieties MR219, MR220, MR211, MR232, MRQ76, MRQ74, and MRQ50 together with a foreign variety Intani-2 were provided by MARDI Genebank, Seberang Perai, Pulau Pinang.

Sampling and DNA Preparation

Seeds of all tested varieties including the controls were planted in a greenhouse. Three to four fresh young leaves were collected when the plants were fifteen to twenty one days old. DNA extraction and purification were conducted using the CTAB (hexadecyl trimethyl ammonium bromide) method. DNA pellets were collected and dissolved using TE (Tris Cl and EDTA) buffer. The concentration and molecular weight of DNA were checked by spectrophotometer and agarose gel electrophoresis, respectively. Extracts were stored at –20ºC until further analysis.

Analysis of Samples

One hundred and twenty-two markers related to pest and diseases (BPH, BLB, and Blast) resistance were screened on the seven local varieties. The PCR component was prepared using 1X PCR buffer, 2.5 mM of MgCl2, 0.5 mM of both forward and reverse primers, 0.2 mM of dNTPs and 2U of Taq polymerase along with 100 ng/µl of genomic DNA. The PCR amplification programme consisted of an initial denaturation of 5 min at 94ºC followed by 35 cycles of the polymerization reaction, consisting of denaturation for 30 s at 94ºC, annealing for 30 s at 55ºC and an extension step for 2 minutes at 72ºC. A final extension was programmed for 5 min to 10 min at 72ºC for the various markers. The PCR products were resolved on 1.8%–2.0 % of agarose gels in 1X TAE buffer, stained with GelRed to detect the amplicons.

Sequencing and Data analysis

The PCR products was ligated and cloned into competent cell containing plasmid (pGEM-T Easy Vector from Promega Corporation, Madison) after which the plasmid was extracted and sequenced. Sequencing data were analyzed using NCBI's BLAST (<http://blast.ncbi.nlm.nih.gov/Blast.cgi>) and GRAMENE BLAST (<http://www.gramene.org/multi/blastview>) for confirmation.

RESULTS AND DISCUSSION

Screening with Brown Planthopper Markers

Out of the twenty-one BPH resistance genes, eighteen have been mapped on specific regions of different chromosomes (Jena & Kim 2010). Chromosome 12 of rice is a very important chromosome because of the abundance of genes clustered along its short and long arms: *Bph1*, *bph2, Bph9, Bph10, Bph18 (t)* and *Bph21 (t)* (Brar *et al*. 2008). A total of thirty public domain markers including SSR (Jirapong *et al*. 2007), RFLP, STS co-segregated, and CAPS markers (Murai *et al*. 2001), that are related to brown plant hopper resistance genes were screened for and validated on all seven local varieties tested. Out of the thirty markers screened, only twenty were amplifiable for these local varieties.

Referring to Cha *et al*. (2008), *Bph1* gene is dominant and linked to pBPH9 STS co-segregated markers which can discriminate between resistant and susceptible lines. However this marker was developed for specific crosses of

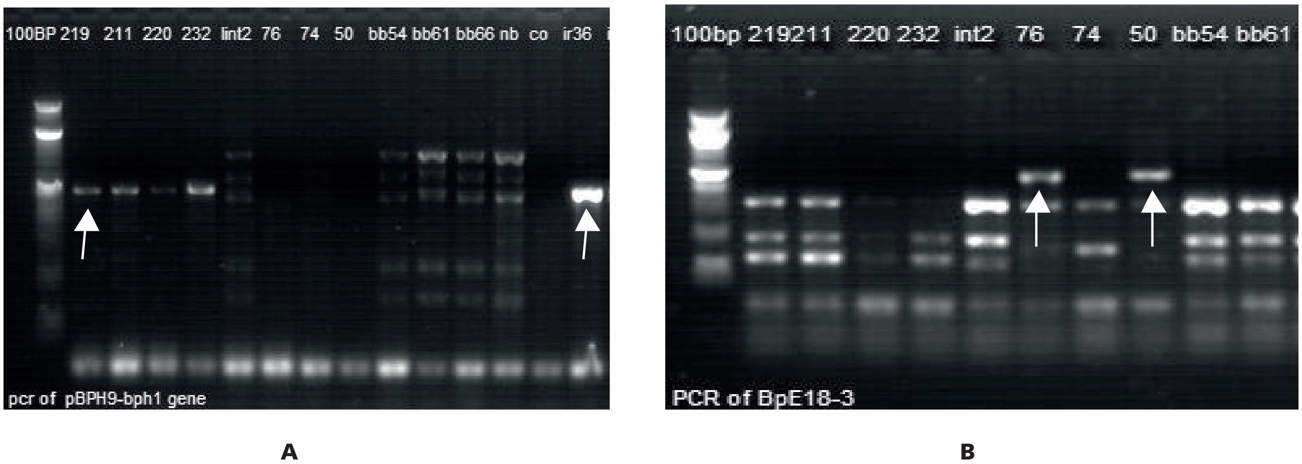
Korean varieties. The pBPH9 had been used in screening and from the result, MR219, MR211, MR220, and MR232 showed a resistant band of approximately 536 bp while a susceptible band was present at 773 bp for the other varieties tested including Nipponbare (susceptible to *Bph1*, control variety), (Figure 1A). Further analysis on MR232 and IR36 (control variety) found to be 95.34% similar with *Oryza sativa japonica* species, chromosome 12 with complete sequences at the AL935070 locus. The sequence length of MR232 and IR36 were detected at 535bp hence pBPH9 STS co-segregated marker was validated and it could be used in screening of local varieties.

The STS-marker, BpE18-3 yielded a polymorphic banding pattern when tested and only aromatic varieties, the MRQ76 and MRQ50 showed the expected size, approximately 536 bp (Figure 1B). BLAST analysis of the MRQ50 fragment of this marker showed a 91% similarity with *Oryza sativa japonica* species, chromosome 12, BAC OJ1112_F01 of variety Nipponbare of spp. *Japonica* and the complete sequence is located at the locus AL732381 with sequence length at 518 bp. The marker could be used for screening of the local rice even though it was developed based on the Japonica rice. The *Bph1* gene was also mapped at a distance of 3.9cM from the said marker. Both pBPH9 and BpE18-3 markers tested here showed different banding patterns that might cause by various sources of donors and different pedigree background of each variety. The BpE18-3 band depends on the resistance source which in all the cultivars detected TKM6 as the resistance source (Kim & Sohn 2005) in comparing to pBPH9 marker that will only amplify a fragment in varieties harbouring the *Bph1* gene from such sources as Mudgo, TKM6, and Samgangbyeo.

Bph1 and *bph2* genes are the two common genes against the rice insect pest that had been initiated in almost all East Asia countries including Japan and Korea. A previous study found that *bph2* gene might be allelic or closely linked to *Bph1* (Sun *et al.* 2006). Hence, research has also concentrated on screening for the presence of *bph2* genes. Associations in local varieties towards resistance and susceptibility of *bph2* gene were identified using four STS markers that were previously converted from AFLP markers, KPM1, KPM3, KPM4 and KPM8. Susceptible plants can be detected using the KPM1 marker at a single fragment of 341 bp while resistance-associated markers, KPM3, KPM4 and KPM8 produced single band at 116 bp, 300 bp, and 149 bp, respectively (Sharma *et al*. 2004). Our study found that only IR64 showed the same pattern of resistance as reported. Most of the *Bph1* and *bph2* resistance-associated markers were present in MR232 as shown in Table 1. This variety also produced a resistance band when screened with the pBPH9 marker hence it could be a strong evidence that MR232 possessed a resistant towards both gene *Bph1* and *bph2*, said to be closely linked.

Screening with Bacterial Leaf Blight Resistance Markers

As mentioned by Goto *et al*. (2009), more than thirty genes which confer resistance to various *Xoo* strains have been identified and are used for genetic improvement of rice for resistance to *Xoo* in Asia. Currently, seventeen bacterial leaf blight R-genes have been mapped on rice chromosomes and used for transferring and pyramiding in marker assisted selection (MAS). In particular, six R-genes, *Xa1*, *xa5*, *xa13*, *Xa21*, *Xa26* and *Xa27*, were cloned by map-based



A **B**

Figure 1. PCR amplification of STS-marker related to *Bph1* gene in local varieties. **A**. pBPH9 co-segregated marker produced a 536 bp band for resistant varieties and a 773 bp of polymorphic band for susceptible varieties; **B**. BpE18-3 marker showed a resistant band at 536 bp in lanes 7 and 9 related to *Bph1*. Arrows indicate resistance to *Bph1*. Lane 1: 100 bp DNA ladder; Lanes 2–9: Local varieties tested; Other lanes: Control varieties.

Table 1. Distribution of BPH associated-markers namely KPM1 (341 bp), KPM3 (116bp), KPM4 (300 bp), and KPM8 (149 bp) in seven local varieties. Mudgo, IR64 IR50 and Taichung Native1 were used as control varieties. KPM3 (116 bp) marker was not amplifiable in all cultivars.

Accession	KPM1 (S-associated)	KPM3 (R-associated)	KPM4 (R-associated)	KPM8 (R-associated)
MR 219	+	NA	–	+
MR211	+	NA	–	+
MR220	+	NA	+	–
MR232	+	NA	+	+
MRQ76	–	NA	–	–
MRQ74	–	NA	–	+
MRQ50	–	NA	–	–
Mudgo	+	NA	+	–
IR64	+	NA	–	+
IR50	+	NA	–	+
Taichung Native 1	–	NA	–	–

+: Resistant type variety, –: Susceptible type variety, NA: Not amplifiable.

cloning. Twenty-eight markers of SSR, STMS and gene/allele specific (Iyer & Mc Couch 2004) related to bacterial leaf blight resistance were screened for via PCR, analyzed and validated by sequencing and sequence analysis. All of the local varieties were screened with two gene-specific markers, pTA248 and MP1+MP2. Each of the markers was developed for screening the presence of the bacterial leaf blight dominant genes, *Xa21* and *Xa4*.

Amplification with the pTA248 marker, located at 0–1cM from *Xa21* on chromosome 11 (Ramalingam *et al*. 2002) produced two band sizes, 1018 bp and ~900–950 bp. None of the seven varieties was found to produce a 1018 bp band similar to the control varieties of IRBB54 and IRBB66, while neither MR232 nor MRQ74 produced any bands at all (Figure 2A). Their sequences were found to have 100% similarity with the *Oryza sativa* linked *Xa21* gene. An analysis of MR219, MRQ76, MR220, MR211 and MRQ54 produced bands within the range of ~900–950 bp, and also showed that the sequences had 92%–97% similarity with the *Oryza sativa* linked *Xa21* gene. Thus, pTA248 was validated as a gene specific marker for *Xa21* gene in the screening of local varieties (Figures 3A and 3B). It could also be concluded that MR219, MRQ76, MR220, MR211 and MRQ50 might contain *Xa21* gene.

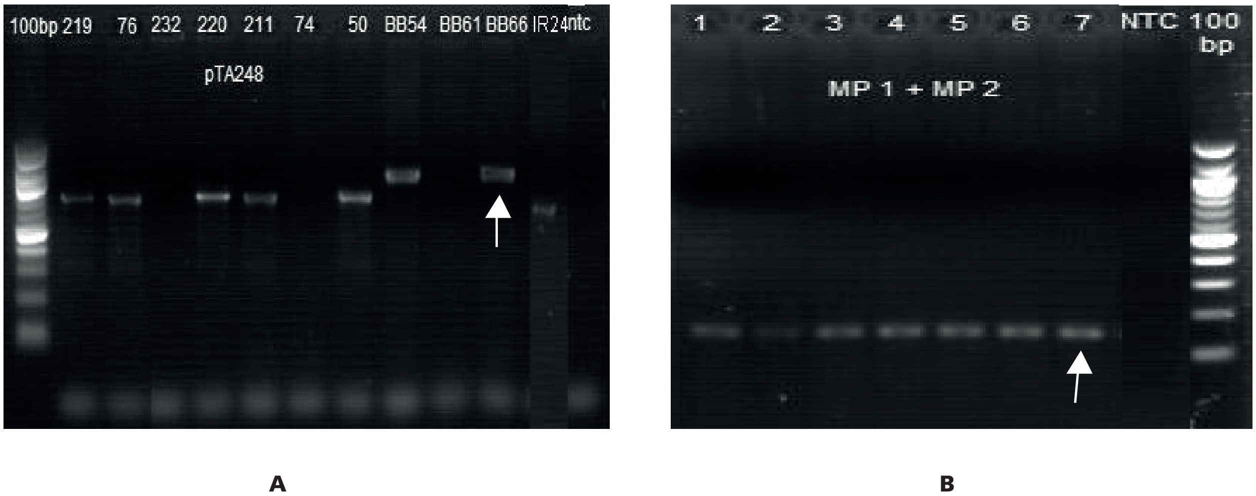


Figure 2. PCR amplification of gene-specific markers for resistance genes *Xa21* and *Xa4* to bacteria leaf blight. **A**. pTA248 marker produced two band sizes, 1018 bp and ~900–950 bp for resistant and susceptible varieties to *Xa21* gene. Lane 1: DNA ladder; Lanes 2–9: Local varieties tested; Other lanes: Control varieties. **B**. MP1+MP2 gene specific marker produced an approximately 175–200 bp singular band for all varieties tested; Lanes 1–7: MR219, MRQ76, MR232, MR220, MR211, MRQ74, MRQ50; Lane 9: 100 bp DNA ladder. Arrows indicate resistance to *Xa21* and *Xa4*.

A

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B

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Strand=Plus/Minus

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Query  294  CAAATCGACCAAAAGGaaaaaaaaaGAAGAAGTAAACGCCTGCGAAAATGGTCAAGGTTG  353
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Sbjct  692  CAAATCGACCAAAAGGAAAAAAAAAGAAGAAGTAAACGCCTGCGAAAATGGTCAAGGTTG  633
Query  354  TGTTCGGCATTGCTGGTTCCCATCCTCTCCCCCTCGTTTTCTGCGCGCACGCTTTTCAAA  413
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  632  TGTTCGGCATTGCTGGTTCCCATCCTCTCCCCCTCGTTTTCTGCGCGCACGCTTTTCAAA  573
Query  414  CTGCTAAACAATGTGTTTTTTGCAAAAAGTTTCTATACGAAAGTTGCTTAAAAAATTATA  473
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  572  CTGCTAAACAATGTGTTTTTTGCAAAAAGTTTCTATACGAAAGTTGCTTAAAAAATTATA  513
Query  474  TTAATCCATTTTTGCaaaaaaaaGCAAATACTTAATTAATCACGCGCTAATGGACTGCTT  533
            |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Sbjct  512  TTAATCCATTTTTGCAAAAAAAAGCAAATACTTAATTAATCACGCGCTAATGAACTGCTT  453
Query  534  CGTTTTCCGTGCGCACATCATGTGCTGGGAAGATTGGCTTCCGAACGCACCCTAAGGCCA  593
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  452  CGTTTTCCGTGCGCACATCATGTGCTGGGAAGATTGGCTTCCGAACGCACCCTAAGGCCA  393
Query  594  CCTCAGGATAACAAACAGTGGCATACCTATTTCTTTTCCACAGATGGACCAAAAGGAAAA  653
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  392  CCTCAGGATAACAAACAGTGGCATACCTATTTCTTTTCCACAGATGGACCAAAAGGAAAA  333
Query  654  CAAGAGTAAACTCCTGCCAAAATGGCTAAGGCCACCTCGGGATAACAAACTGTGGCGGAC  713
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  332  CAAGAGTAAACTCCTGCCAAAATGGCTAAGGCCACCTCGGGATAACAAACTGTGGCGGAC  273
Query  714  CC-AGGATTTAGCCACTATCCAAGCTTGTGTACCCCATACCACAATAGGCAAGACTAAAA  772
            || |||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  272  CCCAGGATTTAGCCACTATCCAAGCTTGTGTACCCCATACCACAATAGGCAAGACTAAAA  213
Query  773  GTAAGACATAAAACTAATCATACTATGACATAGAAGTAAAATACATTTTAAAGTCGGGTT  832
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  212  GTAAGACATAAAACTAATCATACTATGACATAGAAGTAAAATACATTTTAAAGTCGGGTT  153
Query  833  GGCTCTTTTCAAGCCTATAGGAAAAGATATTTACATAATCATATATTAAATATGTTGATa  892
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  152  GGCTCTTTTCAAGCCTATAGGAAAAGATATTTACATAATCATATATTAAATATGTTGATA  93
Query  893  aaaaaaaCAAATTTAATACTAAGTAAATTTCATAACAAGAAGATAAAATTGCAATTACAA  952
            |||||| |||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  92   AAAAAA-CAAATTTAATACTAAGTAAATTTCATAACAAGAAGATAAAATTGCAATTACAA  34
Query  953  AAAAGTAG  960
            ||| ||||
Sbjct  33   AAA-GTAG  27
```

Figure 3. Sequence analysis of fragments amplified by pTA248, gene-specific marker using NCBI's BLAST. **A**. Alignment and comparison of the MR219 fragment showed 92% similarity to *Oryza sativa* wanderer mobile element linked to *Xa21* Length = 995 bp. **B**. Alignment and comparison of control variety, IRBB66 fragment showed 97% similarity to *Oryza sativa* wanderer mobile element linked to *Xa21* Length=995bp.

Qi Ming *et al.* (2006) have noted that *Xa4*, one of the genes related to bacterial leaf blight, can confer resistance to several races of *Xanthomonas*. MP1+MP2 was cloned and developed to screening for the presence of the *Xa4* gene on chromosome 4; it is incompletely dominant and located 5.3cM from the *Xa4*. Screening with the marker, produced bright bands within the expected size (~120–175 bp) for all of the varieties tested (Figure 2B). All of the sequences showed high similarity, 92%–93% with the protein coding region of chromosome 4 where *Xa4* is located. Thus, the marker MP1+MP2 was validated as a gene-specific primer for *Xa4* in local varieties.

Screening with Blast Resistance Markers

More than seventy genes and three hundred and forty-seven quantitative trait loci (QTLs) have been detected to be related to blast resistance. Out of these, nine of the resistance genes (*Pib*, *Pita*, *Pik-h*, *Pi9*, *Pi2*, *Piz-t*, *Pid2*, *Pi36* and *Pi37*) have been isolated and cloned using map-based cloning strategies (Koide *et al*. 2009). Many reports mention that the genes affecting blast resistance are co-localized on chromosomes 6, 11 and 12. On chromosome 6, fourteen genes have been mapped in the region near the centromere, with nine genes on chromosome 11 and 17 genes on chromosome 12.

Sixty-four markers were used to screen for blast resistance genes in all the varieties. Gene-specific markers, SSR as well as InDel markers of the desired resistance genes were validated on selected local varieties. Screening of the local varieties with InDel marker, TA3 showed that all of the varieties produced bright bands of the expected size 173 bp (Figure 4A). The results obtained indicated that all of these varieties might contain *Pi-ta/Pi-ta2*. This InDel marker is located close to the gene on chromosome 12 (Hayashi *et al.* 2006). All of the sequences analyzed showed 100% similarity with the *Pi-ta/Pi-ta2* cds region on chromosome 12. These lie across many different cultivars which have been analyzed. TA3, a SNP/InDel marker, is validated for screening for the presence of the *Pi-ta/Pi-ta(2)* gene.

The *Pi-b* gene which is reported as one of the blast dominant genes that can be screened with several markers such as RM166 and RM208 for SSR, or co-segregate markers, b2 as an InDel marker, and also with Pisbdom, a gene specific marker. Pisbdom was evaluated by Fjellstrom *et al*. (2004) as a gene-specific marker and is located exactly at the *Pi-b* gene location on chromosome 2. Amplification of the Pisbdom markers on all seven local varieties showed that only MRQ74 and MRQ50 did not produce any bands at all. In contrast, the hybrid variety, Intani-2 and the other varieties, MR219, MRQ76, MR232, MR220 and MR211 produced bands which were not of the expected size (~365 bp) as reported to be present in Te-Qing variety. Intani-2 produced two bands, one at 365 bp while the other was slightly below 600 bp. Based on the sequences analysis, the local varieties did not show any similarities with the *Pi-b* gene sequences at all. However, analysis of the 365 bp fragment of Intani-2 showed an identical sequence with the *Pi-b* gene. It could be concluded that Pisbdom could be used as a gene specific marker for the *Pi-b* gene, and that only Intani-2 might contain the said gene.

A total of eighty-eight markers was successfully amplified and yielded reproducible results although

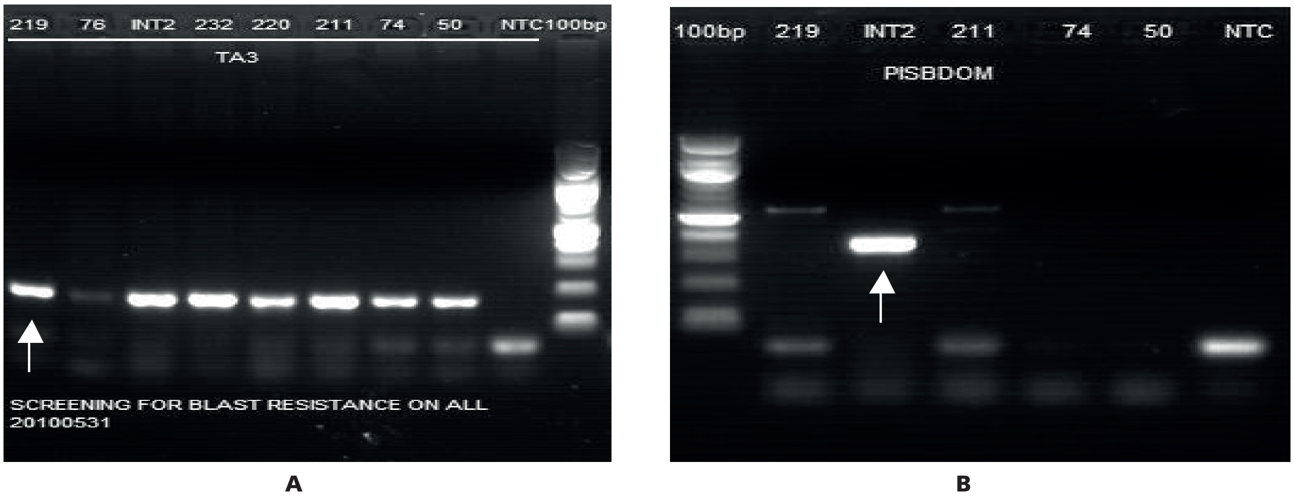

Figure 4. PCR amplification of blast related markers. **A**. TA3, InDel markers for the *Pi-ta/Pi-ta2* gene showed all varieties produced bands at 173 bp. Lanes 1–8: MR219, MRQ76, MR232, MR220, MR211, MRQ74, MRQ50; Lane 10: 100 bp DNA ladder. **B**. Pisbdom, a gene-specific marker amplified a fragment of approximately 365 bp. Lane 1: 100 bp DNA ladder; Lanes 2–6: MR219, Intani-2, MR211, MRQ74, MRQ50. Arrows indicate the expected band size.

Table 2. Resistant gene's distribution on local rice varieties, MR 219, MR220, MR211, MR232, MRQ76, MRQ74, MRQ50 and foreign varieties, Intani-2 tested on gene/allele specific markers.

Rice variety	Variety		Pest and Diseases	
		Brown Planthopper	Blast	Bacteria Blight (BLB)
Local varieties	MR219	*bph2*	*Pi-21, Pi-ta, Pi-ta2, Pi-km*	*Xa4, xa21, Xa1*
	MR220		*Pi-km*	*Xa1, Xa11, Xa21*
	MR211		*Pi-ta2 , Pi-km*	*Xa21*
	MR232	*Bph1, bph2*	*Pi-b, Pi-ta, Pi-ta2, Pi-gm(t)*	*Xa4, xa21*
	MRQ76	*Bph 1, Bph13(t)*	*Pi-ta*	*Xa11, Xa21*
	MRQ74		*Pi-ta*	
	MRQ50	*Bph1*	*Pi-ta2, Pi-km*	*Xa1, Xa21*
Foreign varieties	Intani-2		*Pi-b, Pi-ta, Pi-ta2*	*Xa1, Xa21*

some public domain markers were developed for specific background. The gene distribution in all varieties tested can be summarized as shown in Table 2 however only based on gene/allele-specific markers tested. Study provides basic information on local rice varieties and further works can be conducted to further characterize genes in depth to improve the elite lines.

CONCLUSION

Seven local varieties were successfully screened with one hundred and twenty-two type-related markers for brown planthopper, bacterial leaf blight and blast resistance. MR219 and MR232 were found to possess highest distribution of the resistance markers as compared with the other five varieties. On the other hand, MRQ76, MRQ74 and MRQ50 (high quality aromatic rice) that have been reported to be resistant to blast and bacteria blight were found to have fewer markers distributed compared to MR219 and MR232. Our work provided useful data of markers distribution in local rice varieties that could be utilized by plant breeders for the screening of disease and pests resistance. This utility of the markers would allow plant breeders to reduce the number of progeny that are needed to be experimentally tested by deploying molecular assisted selection approach. However a large population and different crosses are needed in order to further validate these markers, hence assisting in a breeding programme in order to shorten the time consumed by conventional selection.

ACKNOWLEDGEMENTS

This research was funded by Sime Darby Technology Centre Sdn Bhd (Research) and special acknowledgement is accorded to MARDI for providing the seeds.

Date of submission: February 2012
Date of acceptance: March 2013

REFERENCES

Altschul, SF, Gish, W, Miller, W, Myers, EW & Lipman, DJ 1990, 'Basic local alignment search tool', viewed 25 November 2011, <http://blast.ncbi.nlm.nih.gov/Blast.cgi>.

Babujee, L & Gnanamanickam, SS 2000, 'Molecular tools for characterization of rice blast pathogen (*Magnaporthe grisea*) population and molecular marker-assisted breeding for disease resistance', *Current Science*, vol. 78, pp. 248–257.

Brar, DS, Virk, PS, Jena, KK & Khush, GS 2009, *Breeding for resistance to planthoppers in rice*, International Rice Research Institute, Los Banos, The Philippines.

Cha, YC, Ji, H, Yun, DW, Ahn, BO, Lee, MC, Suh, SC, Lee, CS, Ahn, EK, Jeon, YH, Jin, ID, Sohn, JK, Koh, HJ & Eun, MY 2008, 'Fine mapping of the Rice *Bph1* Gene, which confers resistance to the brown planthopper (*Nilaparvata lugens* Stal), and development of STS markers for marker-assisted selection', *Molecular Cells*, vol. 26, pp. 146–151.

Chakravarthi, BK & Naravaneni, R 2006, 'SSR marker based DNA fingerprinting and diversity study in rice (*Oryza sativa* L)', *African Journal of Biotechnology*, vol. 5, no. 9, pp. 684–688.

Davierwala, AP, Reddy, APK, Lagu, MD, Ranjekar, PK & Gupta, VS 2001, 'Marker assisted selection of bacterial blight resistance genes in rice', *Biochemical Genetics*, vol. 39, pp. 261–278.

Fjellstrom, R, Conaway-Bormans, CA, McClung, AM, Marhetti, MA, Shank, AR & Park, WD 2004, 'Development of DNA markers suitable for marker assisted selection of three *Pi* genes conferring resistance to multiple *Pyricularia grisea* Pathotypes', *Crop Science*, vol. 44, pp.1790–1798.

Goto, T, Matsumoto, T, Furuya, N, Tsuchiya, K & Yoshimura, A 2009, 'Mapping of bacterial blight resistance gene *Xa11* on rice chromosome 3', Japan Agricultural Research Quarterly, vol. 43, no. 3, pp. 221–225.

Gowda, M, Venu, RC, Roopalakshmi, K, Sreerekha, MV & Kulkarni, RS 2003, 'Advances in rice breeding, genetics and genomics', *Molecular Breeding*, vol. 11, pp. 337–352.

Hayashi, K, Yoshida, H & Ashikawa, I 2006, 'Development of PCR-based allele-specific and InDel marker sets for nine rice blast resistance genes', *Theoretical Applied Genetics*, doi 10.1007/s00122-006-0290-6.

He, GC 2007 ‘Brown planthopper resistance genes in rices: from germplasm to breeding’, *Molecular Plant Breeding*, vol. 5, pp.175–176.

Iyer, AS & McCouch, SR 2004, ‘The rice bacterial blight resistance gene *xa5* encodes a novel form of disease resistance’, *Molecular Plant- Microbe Interactions*, vol. 17, no. 12, pp. 1348–1354.

Jairin, J, Phengrat, K, Teangdeerith, S, Vanavichit, A & Toojinda, T 2007, ‘Mapping of a broad-spectrum brown planthopper resistance gene, *Bph3*, on rice chromosome 6’, *Molecular Breeding*, vol. 9, pp. 35–44.

Jaiswal, P, Ni, J, Yap, I, Ware, D, Spooner, W, Youens-Clark, K, Ren, L, Liang, C, Zhao, W, Ratnapu, K, Faga, B, Canaran, P, Fogleman, M, Hebbard, C, Avraham, S, Schmidt, S, Casstevens TM, Buckler, ES, Stein, L & McCouch, S 2006, '*Gramene database*', viewed on 8 February 2012, <http://www.gramene.org/multi/blastview>.

Jena, KK & Kim, SM 2010, '*Current status of brown planthopper (BPH) resistance and genetic*', Rice, doi 10.1007.

Kim, SM & Sohn, JK 2005, ‘Identification of a rice gene *(Bph1)* conferring resistance to brown planthopper (*Nilaparvata lugens* Stal) using STS markers’, *Mol. Cells*, vol. 20, pp. 30–34.

Koide, Y, Kobayashi, N, Xu, D & Fukuta, Y 2009, ‘Resistance genes and selection DNA markers for blast disease in rice (*Oryza sativa* L.)’, *Japan Agricultural Research Quarterly*, vol. 43, no. 4, pp. 255–280.

Mackill, DJ 2007, ‘Molecular markers and marker-assisted selection in rice', in *Genomics-assisted crop improvement*‘, eds RK Varshney & R Tuberosa, *Genomics Applications in Crops*. vol. 2, pp. 147–168.

Murai, H, Hashimoto, Z, Sharma, P, Shimizu, T, Murata, K, Takumi, S, Mori, N, Kawasaki, S & Nakamura, C 2001, ‘Construction of a high-resolution linkage map of a rice brown planthopper (*Nilaparvata lugens* Stal) resistance gene *bph2*’, *Theoretical Applied Genetics*, vol. 103, pp. 526–532.

Qi-ming, D, Shi-quan, W, Ai-ping, Z, Hong-yu, Z & Ping, L 2006, ‘Breeding rice restorer lines with high resistance to bacterial blight by using molecular marker-assisted selection’, *Rice Science*, vol. 13, no. 1, pp. 22–28.

Ramalingam, J, Basharat, HS & Zhang, G 2002, ‘STS and microsatellite marker-assisted selection for bacterial blight resistance and waxy genes in rice, *Oryza sativa* L’, *Euphytica*, vol. 127, pp. 255–260.

Sharma, PN, Torii, A, Takumi, S, Mori, N & Nakamura, C 2004, ‘Marker-assisted pyramiding of brown planthopper (*Nilaparvata lugens* Stal) resistance genes *Bph1* and *bph2* on rice chromosome 12’, *Hereditas*, vol. 140, pp. 61–69.

Sun, LH, Wang, CM, Su, CC, Liu, YQ, Zhai, HQ & Wan, JM 2006, ‘Mapping and marker-assisted selection of a brown planthopper resistance gene *bph2* in rice (*Oryza sativa* L.)’, *Acta Genetica Sinica*, vol. 33, no. 8, pp. 717–723.

Zhang, Q 2007, ‘Strategies for developing Green Super Rice’, Inaugural Articles by Members of National Academy of Sciences.

ASM Sci. J., **7(2)**, 113–117

A Review on Materials Waste Quantification and Management in Construction Activities

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Nowadays, construction and demolition waste has become a major issue to environmental problems faced by many countries. This concern comes from the inefficiencies of waste management which includes the waste generated from construction and demolition activities. In Malaysia, there is a lack of database records on construction waste and this has affected proper management planning of the waste. As there is a lack of policy on construction waste management, control on construction waste disposal is very hazy and this has aggravated environmental problems and exhausted landfill usage and increased illegal dumping. This paper reviews the critical issues on construction waste management and also discusses several estimation models on construction waste generation from several countries. Based on the review, most of the countries faced problems regarding construction waste management and the models developed were considered as one of the methods which could be adopted for better management of construction wastes.

Key words: Construction waste; waste management; planning; quantification model; construction industry; models; estimation

The construction industry is one of the most booming activities in the world especially in the developing countries where construction is considered as a continuous activity. Malaysia as one of the developing countries which faces rapid growth in industries which contributes to the Malaysian economy. The former second Finance Minister of Malaysia, enlightened this at a press conference. He mentioned that the Malaysian construction industry registered a growth of 1.1% in the first quarter of 2009 and improved to 2.8% in the second quarter of *The Star* (2009).

The Malaysian construction industry can generally be separated into two areas (Malaysia-German Chamber of Commerce 2010). The first area is general construction which comprises residential construction, non-residential construction and civil engineering construction. While the second area is special trade works which include activities of metal works, electrical, plumbing, sewerage and sanitary, refrigeration and air-conditioning, painting, carpentry, tiling and flooring, and glass.

It was estimated about 709 400 units of residential building will be constructed based on the 9th Malaysian Plan. The state of Selangor announced in 2005 that it embraced the highest percentage of this number which is 19.2%, followed by Johor (12.9%), Sarawak (9.4%) and Perak (8.2%). Presently, sustainable development has become a worldwide issue of several countries. This concern is augmented by the inefficiencies of waste management including the waste generated from construction and demolition activities. Based on the research done by Hendriks and Pietersen (2000) showed that the construction industry generated about 35% of the industrial waste in the world.

In Malaysia, data on the current composition of construction waste flows from the source of generation, types of waste, intermediate and final disposal and the amount of waste reduced at source, reused or recycled on site or off-site composition of waste are not readily available (Begum *et al*. 2006; Tang & Larsen 2004; Kofoworolo & Gheewala 2009). According to a previous study (Nasir *et al.* 1998), it showed that the percentage of industrial and construction waste was placed in third ranking with 28.34% below the household waste and market and commercial waste.

Due to lack of markets for construction waste recycling in Malaysia, all construction wastes are disposed at landfills either legally or illegally except for metals, glass, plastic, paper and cardboards, since these materials could be transformed into various degrees of materials (Pereira 2007). As a result, there will be major problems in disposal activities when landfills are exhausted and also because of illegal dumping.

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This article is intended to obtain some findings on waste quantification from the various models developed which perhaps might not only contribute to the better waste management but also solve the problems arising from waste generated in Malaysia.

REVIEW ON CONSTRUCTION WASTE MANAGEMENT

The construction industry is one of the major activities affecting the environment and this has affected sustainable development which has become a hot issue discussed for several years (DETR 2000). Sustainable development is defined as activities that meet the needs that will deliver social progress, protect the environment, contribute to better resource use, economic growth and employment.

In many countries, the volume of construction waste is very little known and quantifying the waste is very hard because of the lack of record by construction companies on the qualitative and quantitative characteristics of the waste they generate (Begum *et al*. 2006). Some problems were also found concerning solid waste management system in a developing country which includes low collection coverage and irregular collection services; crude open dumping and burning without air and water pollution control; the breeding of flies and vermin; and the handling and control of informal waste picking or scavenging activities (Ogawa 1996). These problems are caused by various factors classified as technical, financial, institutional, economic, and social constraints.

In Spain, the government has proposed a regulation on the production and management of construction and demolition waste. This new regulation required the project developer to include a construction and demolition (C&D) management study in the construction projects and compels the contractor to design a C&D waste management plan for the construction site. Two important aspects of control obtained from the study and plan are waste quantities and treatment costs (Solis-Guzman *et al*. 2009).

In Thailand, the method for the management of construction waste involves manual collections left on the floor which are then cleared out from the site by main contractors or sub-contractors (Kofoworola & Gheewala 2009). Also a survey cited by Chanchorn (2002) revealed that 69% of the construction companies in Bangkok manage the construction waste themselves, while another 31% award this task to sub-contractors or other individuals (Kofoworola & Gheewala 2009).

The Chairman of CIDB Malaysia has stated that there are seven consequences of construction on the environment (Nazirah 2010). The effects are: it contributes about 40% of global house gases (GHG); affects 70% of citys GHG; contributes to the loss of biodiversity ecosystem; occurs in hazard prone geographies; consumes 30% of world resources; deposits 40% of the waste to landfills; and consumes 12% of the world's water (Nazirah 2010).

In Malaysia, 16 000 tonnes of solid waste are produced in the country every day (Yeang 2003) and there are about 230 landfills in Malaysia and it is estimated that there are also three times as many illegal dumps. From these quantities of landfills, 80% of them have been estimated to remain for a lifetime of only 2 years (Agumuthu 2001). Solid waste is managed by Local Authorities and on 6 September 1995, the Federal Cabinet (of Malaysia) decided that the responsibilities of the Local Authorities in these areas had to be privatized. As a precondition to total privatization, the Federal Cabinet again in 1998 decided that the privatization of solid waste management in the country to be conducted on a short-term basis. Solid waste management has been privatized from 48 local authorities to two concession companies e.g. Alam Flora at the central region of the country, and Southern Waste for the southern region (National Solid Waste Management Department 2010).

ESTIMATION MODELS OF WASTE GENERATION

Models which have been developed previously were classified as in Table 1 and the details are discussed below.

A Novel Methodology to Estimate the Evolution of Construction Waste in Construction Sites

A methodology developed (Katz & Baum 2010) evaluated the accumulation of waste generated from construction activities in medium to large residential construction sites and from start to end of the project. By estimating the construction waste generation, it will help project managers to manage their sites, estimate the flow of outgoing materials of the site and cost estimation on waste management.

The authors found that the best method to evaluate the construction waste was by isolating the different construction activities and monitor each activity to record the waste generated. Three phases of construction activities were divided into structural frame, early finishing and late finishing where the amount of waste generated during the sampling period were collected from the accounting book for each site. Ten different sites with an area more than 5000 m^2 with different phase of work were selected. It could be concluded that concrete and steel generated over 50% during structural framework and reduced to 15% – 20% during overlapping stages of structural and early finishing work.

Table 1. Estimation models on construction waste.

No	Estimation model	Factors used	Authors and countries
1	$\Psi(\tau) = 0.52\,\tau^{1.6}$	Time	(Katz & Baum 2010) Country: Israel
2	$C_w = M \times W_c$ $D_w = M - C_w$	Amount of materials purchased and discarded	(Cochran & Townsend 2010) Country: US
3	$R_{build} = \Sigma\,(Rc_i + RR_i + RD_i)$ $= \Sigma\,(Cc.Sc_i + CR.SR_i + CD\,.\,SD_i)$	Amount of waste and area	(Lage *et al.* 2010) Country: Spain
4	$Q_x = A \times G_{av} \times P$	Area, composition of waste, average waste generation rate	Kofoworola & Gheewala 2009). Country: Thailand
5	$VAC_i = Qi\,.\,CC_i$ $VAD_i = VACi.CT_i$ $VAR_i = VAC_i.CR_i$	Quantity of waste	Solis-Guzman *et al*. 2009 Country: Spanish
6	$W = a \times g$ or $W = (c/b) \times g$	Area and cost	(Franklin Associates, US EPA 1998)

1. $\Psi(\tau)$ — Amount of waste at various point of time per m^2; τ — Normalized time.
2. Cw — Materials discard during construction and installation phase of renovation (Mg); M — Amount materials purchased (Mg/yr); Wc —Portion discard during construction (%); D_w — Demolition waste (Mg).
3. R_{build} is C&D waste generated in a year; Rci —Waste generated from new construction; RR_i — Waste generated from renovation activity; RD_i — Waste generated from demolition activities; Sc_i, SR_i, SD_i — Total surface area of construction, renovation or demolition activities; Cc , CR , CD — Quantity of waste generated per unit of surface in construction, renovation or demolition activities.
4. Q_x — Quantity of construction waste material, tons; A — Area of building construct, m^2; G_{av} — Average waste generation rate; P — Average composition of waste material %.
5. VAC_i — Apparent constructed volume in m^3/m^2 for item i; VAD_i — Apparent Demolished Volume in m^3/m^2 for item i; VAR_i — Apparent Wreckage Waste Volume in m^3/m^2 for item i; Qi — Quantity of the item i in its specific unit (m, m^2, m^3, kg or unity); CC_i — Conversion ratio of the amount of item i in m^3/Qi specific unit.; CT_i — Coefficient of transformation of VAC in VAD (dimensionless); CR_i — Cefficient of transformation of VAC in VAR (dimensionless); CC_i , CT_i , CR_i, — Estimated from Andalusian Construction Costs Database (2008).
6. W — Total waste; a — Area of building construct; g — Average waste generation per building area (kg/m^2); c — Cost of project; b — Average cost of construction per building area.

An empirical model developed is used to evaluate the amount of waste generated at different times, from start to end of the project construction. The model was validated by comparing the predicted with the collected value of waste (Katz & Baum 2010) which was about two-third of the amount of waste accumulated during the end finishing of construction activities. The quantity of waste increased towards the end of the project life, whilst the amount of recyclable material was found to be decreased due to the type of waste generated in this phase which is more on packaging. It could also be concluded that there was no correlation between the construction method and the amount of waste generated.

Estimating Construction and Demolition Debris Generation Using Materials Flow Analysis Approach

A study by Cochran and Townsernd (2010) presented an evaluation of materials waste flow analysis as an approach for estimating construction and demolition debris generation and composition for a large region in the US. The major construction materials considered in this study were concrete, wood, metal, drywall and other gypsum products, bricks and other clay products, asphalt concrete and asphalt roofing materials. Data for materials used per year could be gathered from industry association and federal agencies. The equation produced was to predict the total amount of waste from construction and demolition without excluding the waste reused or recycled on or off the site.

Estimation of the Annual Production and Composition of C&D Debris in Galicia (Spain)

The first step towards the correct management of the construction and demolition debris is to determine the volume of the waste Martinez *et al*. 2010; and Solis-Guzman *et al*. (2009) stated that the early estimation of waste would be to generate and allow the calculation of the deposit that the building developer might have to pay to manage the waste and the control of the disposal of this waste.

Martinez Lage and co-researchers in 2010 showed the procedure to calculate construction waste production in a year in any region of Spain. The total waste generated in the year is determined by summing the waste generated from new construction, renovation and demolition activities. There are four assumptions made by the authors to calculate the building related C&D Debris, viz:

- The number of construction, renovation and demolition works might be adjusted to a theoretical function over a time;
- The distribution of construction activities was assumed to be the same every year throughout the whole region;
- The surface area of construction, renovation and demolition project was also adjusted for a variable function over time; and
- The quantity of waste generated per unit surface area was assumed to be the same for each type of construction.

The assumption made might cause a lack of accuracy in wastage estimation since the different wastes would be generated from difference construction activities such as residential, commercial, industrial, religious building, etc.

Estimation of Construction Waste Generation and Management in Thailand

Kofoworola and Gheewala (2009) estimated the quantities of construction waste generated in Thailand from 2002 to 2005; it was carried out as an incentive for the development of an integrated waste management system and implementation of policies for managing construction waste in Thailand.

Due to a lack in qualitative and quantitative report of waste generated, all the data were collected from the National Statistics Organization of Thailand. The quantity of construction waste by material and construction type was obtained by using the equation developed as in Table 1. The same equation was also used to estimate the average quantity of the materials from the demolition of buildings and in determining waste materials generated from new constructions. The infrastructure building, maintenance and demolition activities were excluded due to the lack of data available for these activities. Data collected, indicated that approximately 12 kg of construction waste per capita in 2002 was generated and it increased to 18 kg/capita in 2003 and 22 kg/capita in 2003 and 2004, respectively. The amount of construction waste per capita calculated was considered as a part of the municipal solid waste in Thailand.

Two assumptions were made by HQ Air Force Centre for Environmental Excellence (2006) in order to evaluate the construction waste generation. They are:

(i) New residential building activities generated 21.38 kg/m^2 of waste; and
(ii) New non-residential buildings generated 18.99 kg/m^2 of waste.

In order to obtain the estimated amount of construction waste, the two assumptions stated were multiplied to the area of the construction project.

A Spanish Model for Quantification and Management of Construction Waste

The Alcores model discussed in this paper (Solis-Guzman 2009) was introduced since 2008 to estimate the volume of waste that was expected to be generated at building sites. The model was based on the principle described in the national construction and demolition waste plan 2001–2006 and the concept of the model were tested in Seville which stated that the waste generated should be managed in a correct disposal manner by the concerned parties which produced the waste.

Construction waste was classified into three sources: demolished (due to demolition process); wreckage (due to losses, off-cuts and breakage of materials during work completion) and packaging waste (materials wrapping, cans etc.). The first step in developing this model was to classify the waste item based on the division of budget. This classification characterises the similar materials with the same measurement unit.

The quantity of each item was obtained from 100 surveyed projects selected from bill by following five main characteristics:

- New construction or demolition projects
- From 1 to 10 floors, 1 or 2 basement levels and stores or offices at ground level
- Pile, reinforced concrete slab, reinforced concrete trench or pads of foundation
- Reinforced concrete or brick walls structure; and
- Inclined or horizontal ceiling.

The construction volume of waste is calculated by multiplying the quantity of waste measured from the survey and the conversion ratio estimated from Andalusian Construction Costs Database and from expert team guidelines.

CONCLUSION

Construction waste forms a significant portion of the total waste based on the percentage of the waste embraced by this industry. Hence, proper management of this waste is required in order to avoid the environmental effects such as illegal dumping, open burning, exhaustion of landfill areas and many more. Poor records of construction waste data is one of the issues; the amount of construction waste is hard to find in order to improve better waste management (Kaurmpanis *et al*. 2008).

Previous models developed to estimate construction waste was consider as one of the methods for better management of construction waste. This makes sense since the wastes from building materials was found to be far higher than the nominal figures assumed by the companies and furthermore, the amount of wastage was predicted based on the experience of the person involved (Formoso *et al*. 1999).

Since, there is a lack of quantification and segregation of construction waste in Malaysia, some of the models could be referred to in quantifying the quantity of waste for better management of construction wastes. However, further study should be done to ensure that the models suit the conditions in Malaysia.

ACKNOWLEDGEMENT

This study was funded by the Fundamental Research Grant Scheme (FRGS). It was also carried out as part of a research project entitled “Model Development for Estimating Materials Waste Generated from Building Projects” as a fulfillment of the Master's desertation in Civil Engineering at the Faculty of Civil Engineering, University Technology MARA, Malaysia.

Date of submission: May 2011
Date of acceptance: March 2013

REFERENCES

13 November 2009, *The Star* (Malaysia), 'Construction industry to see 3.5% growth'.

Agumuthu, P 2001, *Solid waste: principles and management*, Universiti Malaya, Kuala Lumpur.

Begum, RA, Siwar, C, Pereira, JJ & Jaafar, AH 2006, 'A benefit-cost analysis on the economic feasibility of construction waste minimisation: the case of Malaysia', *Resources, Conservation and Recycling*, vol. 48, pp. 86–98.

Cochran, KM & Townsend, TG 2010, 'Estimating Construction and demolition debris generation using a materials flow analysis approach', *Waste Management*, vol. 30, no. 11, pp. 2247–2254.

Department of Environment, Transports and the Regions (DETR) 2000, *Building a better quality of life — a strategy for more sustainable construction, London*.

Formoso, CT, Isatto, EL & Hirota, EH 1999, 'Method for waste control in the building industry', in *Proceedings IGLC-7*, University of California, Berkeley, CA, USA.

Franklin Associates 1998, *Characterization of building-related construction and demolition debris in United States*, U.S. Environmnetal Protection Agency.

Hendriks, CF & Pietersen, HS 2000, *Sustainable raw materials: construction and demolition waste*, RILEM Publication, Cachan Cedex, France.

Katz, A & H Baum 2010, 'A novel methodology to estimate the evolution of construction waste in construction sites', *Waste Management*, vol. 31, pp. 91–100.

KLPos.com Malaysia 2007, *12.7 Juta dijangka tinggal di Selangor pada tahun 2020*.

Kofoworola, OF & Gheewala, SH 2009, 'Estimation of construction waste generation and management in Thailand', *Waste Management*, vol. 29, pp. 731–738.

Kourmpanis, B, Papadopoulos, A, Moustakas, K, Stylianou, M, Haralambous, KJ & Loizidou, M 2008, 'Preliminary study for the management of the construction and demolition waste', *Waste Management & Research*, vol. 26, pp. 267–275.

Lage, IM, Abella, FM, Herrero, CV & JLP Ordonez 2010, ‘Estimation of the annual production and composition of C&D debris in Galacia (Spain), *Waste Management*, vol. 30, pp. 636–645.

Malaysia-German Chamber of Commerce 2010, *Market watch Malaysia 2010: construction industry*.

Nasir, MH, Rakmi, AR, Yusoff, MK & Sulaiman, WNA 1998, 'Issues and problems of solid waste management in Malaysia', in *Proceeding on National Review on Environmental Quality Management in Malaysia: Towards the Next Two Decades*.

National Solid Waste Management Department 2010, *Overview of solid waste management in Malaysia*.

Nazirah, ZA 2010, 'Sustainable construction in Malaysia — developers’ awareness', *International Journal of Human and Social Science*, vol. 5, no. 2, pp. 122–129.

Ogawa, H 1996, 'Sustainable solid waste management in developing countries', in *7th ISWA international Congress and Exhibition*.

Pereira, JJ 2007, 'Waste Management in the construction industry-issues and challenges', in *Managing construction waste in Malaysia*, eds JJ Pereira, MD Jantan & G Sundaraj, Malaysia: Institute for Environment and Development (LESTARI).

Solis-Guzman, J, Marrero, M, Maria Victoria, M-D & Ramirez-de-Arellano, A 2009, 'A Spanish model for quantification and management of construction waste', *Waste Management*, vol. 29, pp. 2542–2548.

Tang, HH & Larsen, IB 2004, 'Managing construction waste — a Sarawak experience', DANIDA / Sarawak Government UEMS Project, Natural Resources and Environmental Board (NREB).

Yeang, SC 2003, 'No quick answers to burning issues', *News Strait Times*, Malaysia, 6 April.

ASM Sci. J., **7(2)**, 118–128

Photoinhibition and Development of Stress Proteins in Macroalgae Irradiated with Ultraviolet Radiation

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The response of five marine macroalgae from the temperate region against ultraviolet radiation (UVR) was determined in this study. The algae were exposed to a 35 Wm^{-2} –38 Wm^{-2} UVA, 1.2 Wm^{-2} – 1.7 Wm^{-2} UVB and 129 Wm^{-2} – 148 Wm^{-2} photosynthetically active radiation under four different lights/UV conditions for 5 h in a sun simulator. After 5 h of light stress, the algae were transferred to dim light for an 18 h recovery period. The maximum quantum yield (F_v/F_m) of the algae was measured to determine the degree of photoinhibition. In addition, the content of stress proteins (i.e. hsp60 and hsp70) was also determined as an indicator for the presence of protective mechanisms. In general, F_v/F_m of the algae dramatically declined indicating that the algae experienced high photoinhibitory stress. Induction of both the stress proteins was observed in the irradiated algae especially under the presence of UVB. The induction of hsp70 was stronger than hsp60 in most of the algae. However, after 18 h under dim light, the values for F_v/F_m and stress proteins slowly recovered to the level before the irradiation treatment. UVB seemed to have an ameliorating effect on *Dictyota dichotoma*. Induction of stress proteins might have helped to minimize and repair the damage caused by UVR. Hence, the algae were able to survive under the high UVR.

Key words: F_v/F_m; hsp60; hsp70; macroalgae; photoinhibition; PAR; UVA; UVB; simulation

Although light for photoautotrophs, like marine macroalgae, is vital; it has also the potential to cause damage to the organisms. Absorption of too much energy in the form of high photosynthetically active radiation (PAR, 400 mm – 700 nm) and even low energy amount of ultraviolet radiation (UVR, 280 nm – 400 nm) both part of the natural sun radiation, inhibit photosynthesis and in case of UVR, it can also negatively affect important biomolecules such as DNA, proteins and lipids leading to many untold consequences (see Pessoa 2012 for review). However, the stratospheric ozone layer shields the earth from most of the harmful UVR. In fact, the atmosphere with its ozone layer completely absorbs UVC (100 nm – 280 nm) and permits only a smaller amount of UVB (280 nm – 320 nm) to pass through but allows free passage of UVA (320 nm – 400 nm). Hence, the depletion of ozone layer can become an environmental crisis since it will increase UVB fluence rate at the earth's surface. Since its first discovery in 1970s, the depletion of the ozone layer at the poles has been documented all over the world (Helmig *et al*. 2007; Kane 2008). Generally, each 1% reduction in ozone causes an increase of 1.3%–1.8% in UVB radiation reaching the biosphere (Hollósy 2002). A recent study by Manney *et al*. (2011) demonstrates that the ozone loss in the Arctic is still going on and even reaching the dimensions of that in Antarctica.

Excessively absorbed energy may cause damage to the photosynthetic apparatus when photoprotective mechanisms fail, leading to a phenomenon known as photoinhibition (Powles 1984; Hanelt *et al*. 1996). Photoinhibition has been proposed as a mechanism that is triggered within plants in response to the high irradiance (Osmond 1994; Hanelt 1996) which is mostly related to the degree and extent of damage and recovery of the photosynthetic apparatus. When rate of photodamage

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exceeds that of the rate of repair mechanism, damaged photosystem II (PSII) centres accumulate leading to a reduction in cellular photosynthesis. According to Powles (1984), photoinhibition can be induced either by PAR, UVR or interactions between PAR and UVR. The extent of photoinhibition, however, may differ between these wavelength ranges.

The changes in the quality and quantity of the solar radiation may affect photosynthetic organisms incuding macroalgae or seaweeds. The loss of these important biomass producers of the aquatic ecosystem may disrupt the primary productivity and the whole ecosystem integrity. In addition to their ecological and economical importance, they can also be used as biological bioindicators of environmental changes (Torres *et al*. 2008). Macroalgae are sessile organisms which are not able to avoid harmful irradiation by moving to deeper water regions or shaded locations. Therefore, they have developed various protective mechanisms to avoid or cope with the harmful UVR. For instance, algae may alter their morphology to reduce the area exposed to radiation (Navarro *et al*. 2010). In some algae, they can minimize the occurrence of oxidative damage by secreting excess H_2O_2 into the surrounding medium (Shiu & Lee 2005). Some algae synthesized enzymatic and non-enzymatic antioxidants to scavenge UV-induced oxygen radicals (Aguilera *et al*. 2002; Schmidt *et al*. 2012). Mycosporine-like amino acids (MAAs) are synthesized in red algae as UV-screening pigments, absorbing UVB and UVA but allow other wavelengths to pass through (Helbling *et al*. 2004). In addition, polyamines, compounds which play a critical role in protecting photosynthetic apparatus from high light and UV damage in higher plants were also observed to be synthesized in red algae (Schweikert *et al*. 2011). Non-photochemical mechanisms are activated in some of the photosynthetic organisms to quench singlet-excited chlorophyll and harmlessly dissipate excess excitation energy as heat (Müller *et al*. 2001). Heat shock proteins (hsp) or stress proteins can also be induced in response to proteotoxic stressors including UVR to protect or repair damaged proteins (Häkkinen *et al.* 2004). Among known hsps, hsp70 and hsp60 have been used as biomarkers in various aquatic organisms including algae (Ireland *et al.* 2004; Zhang *et al.* 2011). Transcription of hsp70, for example, was found to be up-regulated by UVR (Zhang *et al*. 2011). In a study by Bischof *et al*. (2002), elevated concentrations of chaperonin 60, a homolog of hsp60 were observed within the canopies of *Ulva* sp. exposed under filtered PAR and UV but not under unfiltered solar radiation.

In this study, we report about the photosynthetic responses of five marine macroalgae from the temperate region against the simulated high UVR and PAR irradiances using a sun simulator. Generally, effects of UVR are investigated under low PAR conditions, as the fluorescence lamps (e.g. Q-Panel or Philips TL12) used, do not or emit little visible light. These conditions are rather unnatural, as high UVR is always accompanied by strong PAR in nature. Photoautotroph organisms react to high irradiances and the response can be different when only irradiated to high UVR under low white light (Hanelt & Roleda 2009). Photosynthetic responses were determined by measuring the maximum quantum yield (F_v/F_m) and the content of stress proteins (i.e. hsp60 and hsp70).

MATERIALS AND METHODS

Algal Materials

The macroalgae examined were: the Rhodophytes, *Solieria chordalis* and *Palmaria palmata*; the Phaeophytes, *Laminaria digitata* and *Dictyota dichotoma*; and, the Chlorophyte, *Ulva lactuca*. The algal samples were collected along the shore of the island of Helgoland or at the coast of Brittany (Roscoff). The algae were grown in a temperature-controlled laboratory under white light (1–32 µmol m^{-2} s^{-1}) in a light-dark cycle (10:14 for *S.chordalis* and 16:8 for other algal species) at 12.5 ± 0.5ºC in aerated beakers filled with nutrient-enriched seawater after Provasoli (1968) with modifications. The algal samples were acclimatized to these conditions for at least a week prior to treatments.

Irradiation Treatment

The sun simulator (SonSi, iSiTEC GmbH, Germany) was used as described by Hanelt *et al*. (2006). The samples were positioned in small plastic beakers filled with culture medium and were mounted on a rotating plate within a double-walled, water-filled glass jar. The temperature of the jar was kept at 12.5 ± 0.5ºC by a thermostated water jacket. To ensure that all samples received a constant fluence within the slightly inhomogeneous light field, the plate was rotated at 5 rph. The algal samples were irradiated for 5 h in the sun simulator. The irradiance of the sun simulator received by the samples are listed in Table 1. For each experimental setups, the samples were covered with four different cut-off filters (Schott, Germany) in order to set three different light/UV conditions: GG400 ($\lambda \geq 400$ nm; i.e. PAR alone, PAR), WG320 ($\lambda \geq 320$ nm, i.e. PAR+UVA, PA), WG295 ($\lambda \geq 295$ nm, i.e. PAR+UVA+UVB, PAB) or UG5 ($\lambda < 400$ nm, i.e. UVA+UVB, AB). After the irradiation treatment, the samples were transferred under dim light for an 18 h recovery period. Algae were the controls before the treatment (i.e. at time 0 h). All treatments including controls were carried out in triplicates.

Determination of the Maximum Quantum Yield

The maximum quantum yield (i.e. F_v/F_m) of the samples was measured by a portable chlorophyll fluorometer, PAM-2100 (Heinz Walz GmbH, Germany) according to Hanelt (1998) and Bischof *et al*. (2000). At the start of the measurement, samples were subjected to a 5-s far-red pulse (~30 µmol m^{-2} s^{-1} at 735 nm) to fully oxidise the electron transport chain and the samples were then kept in darkness for about 5 min to exclude energy-dependent fluorescence quenching (*qE*) and quenching by state transitions (*qT*). After the 5 min darkness, a short, red, actinic pulse (8 µmol m^{-2} s^{-1} at 655 nm) was given for 5 s to ensure a stabilized fluorescence emission during the following F_m measurement. Then F_o was measured with a pulsed, red measuring light (~0.3 µmol m^{-2} s^{-1}, 650 nm), and F_m was determined with a 0.6–0.8 s, saturating white light pulse (~9200 µmol m^{-2} s^{-1}). The maximum quantum yield was calculated as $(F_m – F_o)/F_m$.

Crude Extract Preparation and Proteins Extraction

The crude extracts were prepared by grinding frozen alga material to a fine powder and transferring it into test tubes containing ice-cold extraction buffer (Bischof *et al*. 2000): 0.1M Tris-HCl, 2 mM EDTA, 10 mM $MgCl_2$, 20% glycerol, 2% Triton X-100, 50 mM DTT, 100 mM Na-ascorbate and 10 mM $NaHCO_3$ at pH 7.6. For extraction in the brown algae, 2% polyvinylpolypyrrolidone was included in the extraction buffer. The extracts were then incubated in ice for 30 min before centrifugation at 16 000 xg and 4ºC for 2 min. The crude extracts were stored at –40ºC. Total soluble protein content in the crude extracts was determined using the Bradford method (Bradford 1976), measuring absorbance at 595 nm and calculating the concentration of proteins according to a calibration curve prepared from 1 mg/ml of bovine serum albumin (A2153, Sigma).

SDS-PAGE and Western Blotting for Stress Proteins Detection

The crude extracts were incubated on ice at least 30 min prior to electrophoresis. Proteins in the extracts were separated by SDS-PAGE following the methods of Laemmli (1970). Protein standards and crude extracts of the samples (i.e. 10 µg – 20 µg of protein) were loaded into a 10-well precast polyacrylamide SDS gel (161–1160 Ready Gel Tris-HCl gels, BioRad Lab) with a 10%–20% linear gradient resolving gel and 4% stacking gel. Electrophoresis was performed at 200V constant. Afterwards, proteins from the gels were transferred to nitrocellulose membranes (162-0113 0.45 µm nitrocellulose membranes, BioRad Lab) for Western blotting. The gels were blotted onto nitrocellulose membranes overnight at 30 V or 90 mA. The list of primary (1º) and secondary (2º) antibodies used for detection of each of the stress proteins, hsp60 and hsp70 is shown in Table 2. The amount of proteins analyzed were determined using an image processing and analysis software, ImageJ (National Institutes of Health, USA) based on integrated densitometry and the values were normalized to the control samples that was set to 100%.

Statistical Analysis

Values of F_v/F_m and the stress protein content were standardized to 100% of controls for better comparison. Mean values and standard deviation (SD) were determined from three replicates of each treatment (n = 3). The statistical significance of differences among means was calculated according to ANOVA followed by Fischer's least significance difference (LSD) or Student-Neumann-

Table 1. Irradiances of the different spectral ranges of the sun simulator applied in the experiments.

Species	PAR (µmol m^{-2} s^{-1})	PAR (W m^{-2})	UVA (W m^{-2})	UVB (W m^{-2})
S. chordalis	704	148	37.9	1.72
P. palmata	648	136	35.2	1.35
L. digitata	677	143	36.4	1.59
D. dichotoma	611	129	35.7	1.22
U. lactuca	669	141	37.2	1.71

Table 2. List of primary (1º) and secondary (2º) antibodies used to detect the stress proteins of interest in Western blotting.

Proteins detected	1º antibody	2º antibody
hsp60	1:4000 Anti-HSP60 antibody (AM01345PU-L, Acris Antibodies)	1:4000 Rabbit anti-mouse IgG (H&L) (AP) antibody (R1253AP, Acris antibodies)
hsp70	1:10 000 Anti-HSP70 global antibody (AS08 371, Agrisera)	1:3000 Goat polyclonal to rabbit IgG H&L (HRP) antibody (ab6721, Abcam plc)

Keuls (SNK) *post hoc* testing. A probability level of $p<0.05$ was applied.

RESULTS

The Maximum Quantum Yield, F_v/F_m

The F_v/F_m of the algae before the treatments is listed in Table 3. After the treatment, however, the F_v/F_m of the algae was strongly affected with values reduced to below than 40% (Figure 1a). Several trends in the F_v/F_m changes could be observed. Firstly, *S. chordalis* and *U. lactuca*, were significantly less affected by AB while for the remaining algal species, the least effect was under PAR. Secondly, PA caused the strongest effect in *S. chordalis, D. dichotoma* and *U. lactuca* while PAB caused the strongest effect in *P. palmata* and *L. digitata*. In *D. dichotoma*, PAB caused significantly lower effect (i.e. 86% reduction) than PA (i.e. 90% reduction). Photosynthesis of all algae recovered to a certain extent in the subsequent dim light period (Figure 1b). In most of the algae, recovery was the fastest for PAR which increased to 82% in *S. chordalis*, 77% in *P. palmata*, 63% in *L. digitata* and 67% in *D. dichotoma*. There was a delay in recovery in *U. lactuca* treated with AB (i.e. increased to 68%), which was still higher than in the other species. In the rest of the treatments of *Ulva*, recovery was nearly completed. There was also a delay in recovery of PAB-treated *S. chordalis* and *L. digitata* (i.e. increased to 45% and 24%, respectively) compared to that of PA-treated algae (i.e. increased to 43% and 42%, respectively). In contrast, no recovery was observed in AB-treated *L. digitata*. Furthermore, PAB-treated *D. dichotoma* (i.e. increased to 41%) showed a faster recovery than PA-treated algae (i.e. increased to 23%).

Content of the Stress Proteins

The content of the stress protein hsp60 increased after the irradiation treatments in all the algal species (Figure 2a) but decreased again after the recovery period (Figure 2b). The induction in hsp60 after the irradiation treatment varied among the algal species but followed several trends (Figure 2a). Hsp60 of *U. lactuca* increased to values more than double of before the treatments under all light/UV conditions which were the highest among the algal species. The highest increase among the light/UV conditions in most of the algal species was observed either under PAB as in *S. chordalis* and *U. lactuca* or in PA as in *P. palmata* or AB as in *L. digitata* while the lowest under AB with a significant value of 46% observed in *D. dichotoma*. However, in *L. digitata* the lowest increase was observed under PAR with a significant value of 43%. In most of the recovered algae, the fastest decline of hsp60 was observed in PAR notably in *L. digitata* (i.e. reduced to 115%) and *D. dichotoma* (i.e. reduced to 118%) while *S. chordalis* decline to the values before strong irradiation treatment (Figure 2b). Exception, however, was observed in *U. lactuca* with the fastest decline after AB irradiation. A delay was observed in PAB as shown by *S. chordalis* and *U. lactuca* while in *P. palmata* and *D. dichotoma*, the decline was slightly slower in PA than PAB.

Comparatively, the content of hsp70 in all algae after the irradiation treatments increased more than two-fold of that before the treatments (Figure 3a). The increase in hsp70 was the lowest under PAR in *S. chordalis* (i.e. with a significant 132% increase), *L. digitata* and *U. lactuca* or under AB in *P. palmata*. The highest increase in most of the algae was observed under PAR+UVR treatments. This trend was particularly noticeable in *U. lactuca* with more than 170% increase. Hsp70 of *L. digitata* was strongly affected by PAB while in *P. palmata* and *D. dichotoma*, the highest increase was under PA but not significant. In addition, the highest increase of hsp70 in *S. chordalis* and *P. palmata* was measured under AB. At the end of the recovery period, hsp70 degraded the fastest in PAR notably in *D. dichotoma* (i.e. content reduced to 181%) but with exception observed in *U. lactuca* (Figure 3b). In *U. lactuca*, AB showed the fastest recovery of hsp70 (i.e. concentration reduced to a significant value of 157%). A delay in the decline was observed either in *S. chordalis, L. digitata* and *D. dichotoma* treated with AB or in *P. palmata* treated with PA or in *U. lactuca* treated with PAB.

DISCUSSION

The maximum quantum yield (F_v/F_m) has been frequently used to monitor plant's health (Maxwell & Johnson 2000). A reduction in F_v/F_m usually indicates that the plants are under stress or experiencing photoinhibition (Cordi *et al.*

Table 3. F_v/F_m of the macroalgae before the treatments. Data are mean±SD of n=3.

Algal species	F_v/F_m (rel. unit)
S. chordalis	0.636 ± 0.02
P. palmata	0.553 ± 0.04
L. digitata	0.749 ± 0.01
D. dichotoma	0.689 ± 0.02
U. lactuca	0.741 ± 0.01

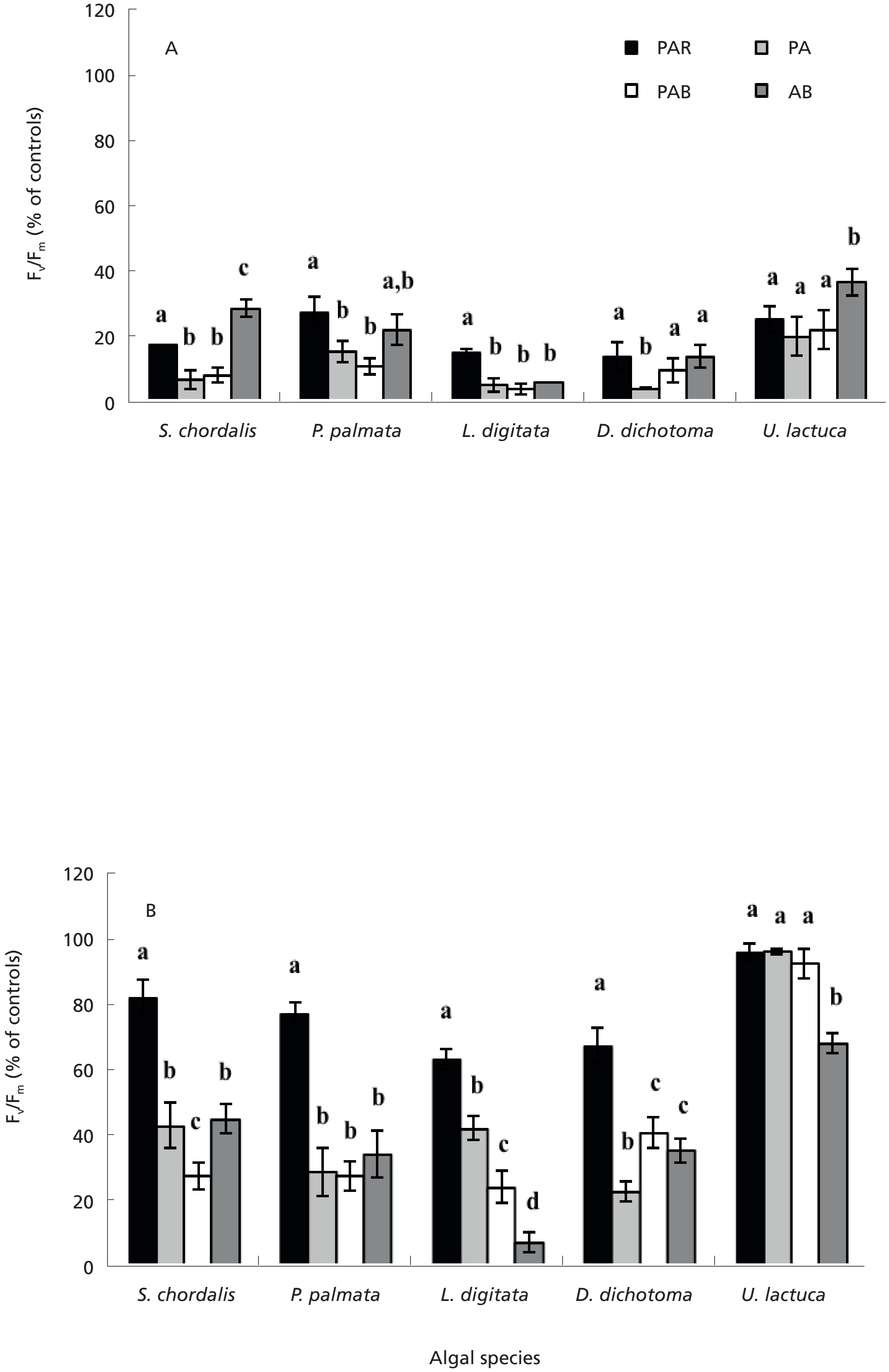

Figure 1. The maximum quantum yield (Fv/Fm) of the five macroalgal species (A) after treatments with PAR alone (i.e. PAR), PAR+UVA (i.e. PA), PAR+UVA+UVB (i.e. PAB) and UVA+UVB (i.e. AB) for 5 h and (B) after the recovery period under dim light for 18 h. Different letters above bars indicate statistically significant differences among light treatments within similar species (ANOVA, Fischer's LSD test, p<0.05, n=3).

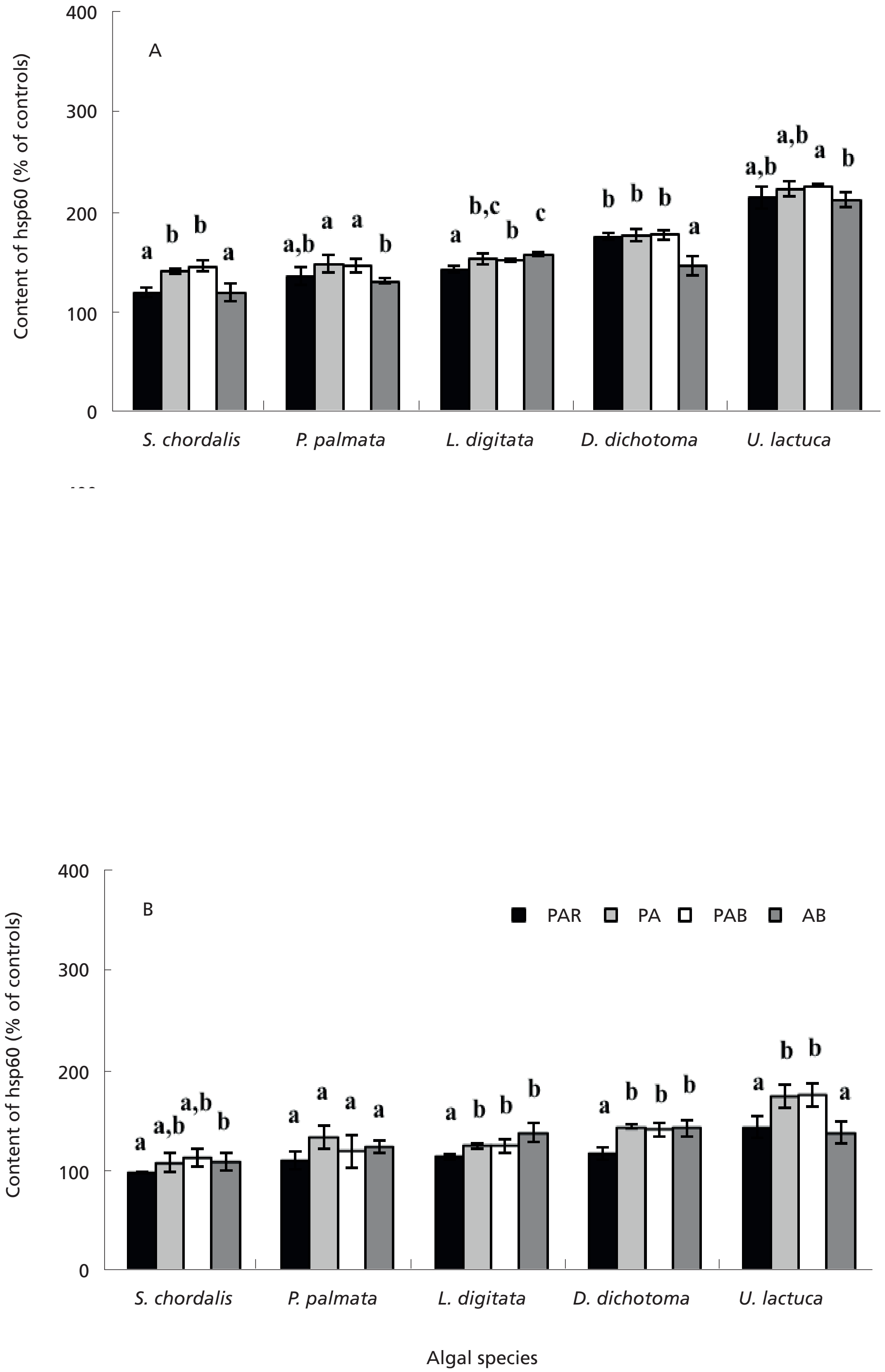

Figure 2: The content of stress protein hsp60 of the five macroalgal species (A) after treatments with PAR alone (i.e. PAR), PAR+UVA (i.e. PA), PAR+UVA+UVB (i.e. PAB) and UVA+UVB (i.e. AB) for 5 h and (B) after the recovery period under dim light for 18 h. Different letters above bars indicate statistically significant differences among light treatments within similar species (ANOVA, Fischer's LSD test, p<0.05, n=3).

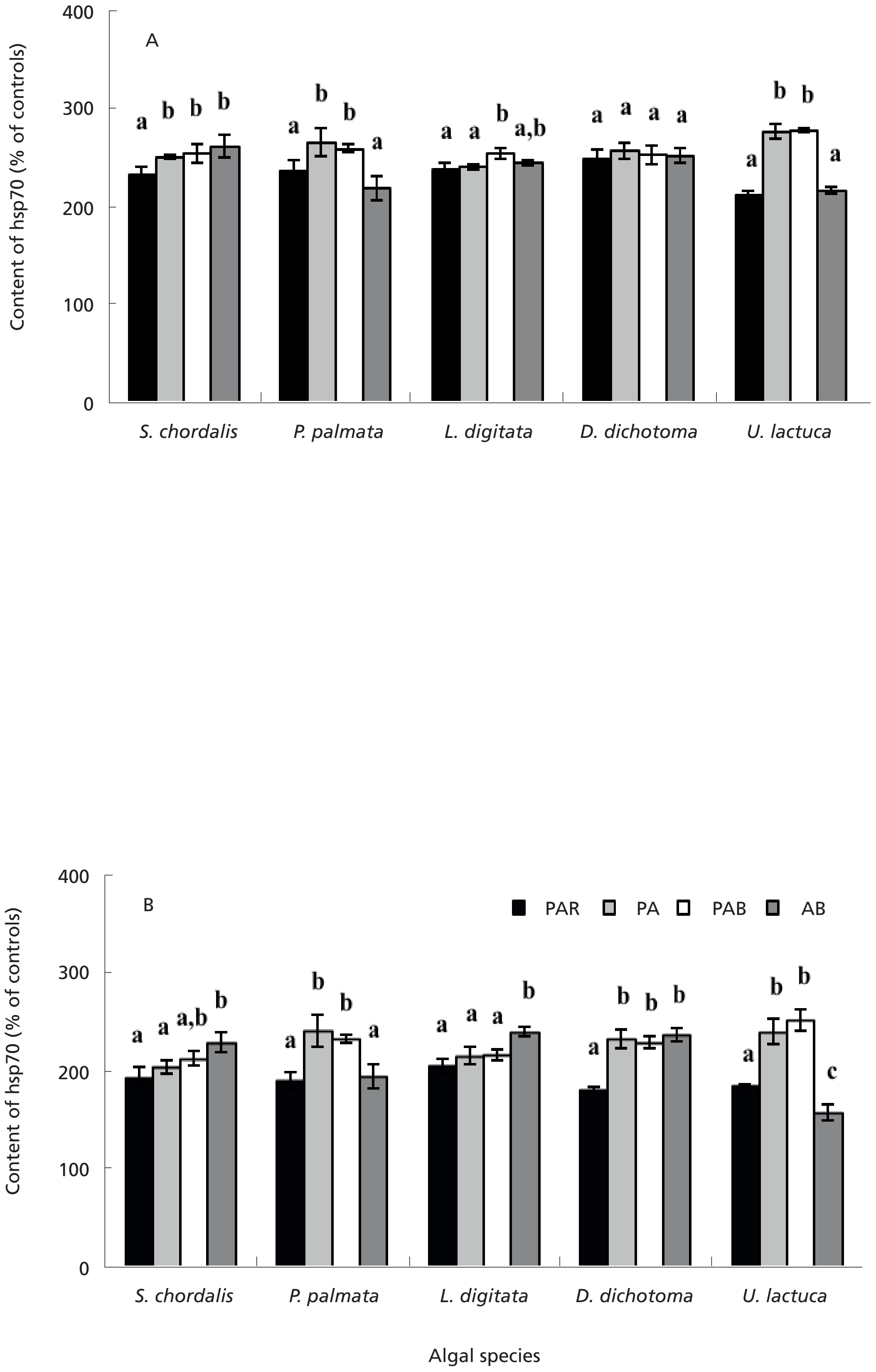

Figure 3: The content of stress protein hsp70 of the five macroalgal species (A) after treatments with PAR alone (i.e. PAR), PAR+UVA (i.e. PA), PAR+UVA+UVB (i.e. PAB) and UVA+UVB (i.e. AB) for 5 h and (B) after the recovery period under dim light for 18 h. Different letters above bars indicate statistically significant differences among light treatments within similar species (ANOVA, Fischer's LSD test, p<0.05, n=3).

1997). In this study, a dramatic decline in F_v/F_m after the irradiation treatments (Figure 1a) indicates that the algae are strongly photoinhibited by the photoinhibitory quenching mechanisms (*qI*) which is not similar to photoregulation as the algae were measured in darkness without the occurrence of energy-dependent quenching (*qE*). A large fraction of photoinhibition in macroalgae comes from the high PAR, whereas a considerable fraction is due to short wavelength solar UV (Cordi *et al.* 1997; Hanelt 1998). Hence, F_v/F_m was greatly declined under PAR alone with further decline observed in the presence of UVR and in some algae, the decline under PAR is more than under AB (Figure 1a). The effects of UVR take a longer time to be reversed than those involving PAR (Hanelt 1998, Häder *et al*. 2001) since UVR-induced photoinhibition seems to be caused by direct damage of proteins or DNA while photoinhibition induced by PAR is more related to the down-regulation process of PSII (Franklin and Forster 1997). Due to this reason, recovery in UVR treated algae requires additional protein synthesis and this process is slow (Franklin and Forster 1997). Therefore, it took a longer time for the UVR-treated algae to recover compared to the PAR-treated algae (Figure 1b). Furthermore, there is a necessity for PAR to be present in the repair and recovery mechanisms (Aguilera *et al*. 2008). PAR and PAR+UVR treated algae show a faster recovery than the AB treated algae for some species (Figure 1b). These results are more conclusive compared to the many other studies done with only low PAR but high UV irradiances (e.g. Häder *et al*. 2001), as the photoprotective regulation of PSII to natural high light conditions has occurred (Hanelt & Roleda 2009).

A slow or delay in recovery may also indicate photo damage (i.e. chronic photoinhibition) while fast recovery indicates photoprotection (i.e. dynamic photoinhibition) (Hanelt *et al.* 1997). Chronic photoinhibition leads to inactivation or damage to D1 protein of PSII in which recovery and repair mechanisms may take many hours or days (Osmond 1994). Dynamic photoinhibition, on the other hand, is regarded as a mechanism for protecting photosynthesis under conditions of high PAR and UV (Hanelt *et al*. 1997) and is defined as an internal down-regulation process of PSII in order to increase the dissipation of excess absorbed energy allowing the recovery of photosynthetic activity when the excess energy is removed (Osmond 1994). The data obtained from this study shows that most of the algal species are photoregulated against high PAR and UVR by dynamic photoinhibition while *L. digitata* is photoregulated against high UVR by chronic photoinhibition since there is no significant change in F_v/F_m of AB-treated algae even after the recovery period (Figure 1).

In the case for *U. lactuca*, its photosynthetic apparatus was downregulated by photoprotection because the alga can still recover from the UV stress. This can be observed where the F_v/F_m is reduced by PA and PAB but has almost fully recovered after the recovery treatment (Figure 1). In fact, in our separate study, *U. lactuca* shows that it is well adapted to high levels of PAR (data not shown). Similar or slightly higher rates of photoinhibition as observed in samples exposed under only PA, for example, in *S. chordalis, D. dichotoma* and *U. lactuca* compares to that of PAB (Figure 1a) can be of ecological relevance since the intensity of UVA spectral range in the natural sunlight is at least 10 times more than UVB and, UVA cannot be attenuated by the ozone layer (Holm-Hansen *et al.* 1993). A study performed with Antarctic phytoplankton has demonstrated that at least half of the damage caused by solar radiation between 290 nm and 400 nm is induced by the UVA range (Holm-Hansen *et al.* 1993). Furthermore, Cullen *et al.* (1992) stated that even under strong ozone depletion, UV damage is dominated by the UVA range (40%–50% inhibition) with only a small effect induced by UVB (10% inhibition). Thus, UVA can be damaging to the algae as that of UVB. However, UVA irradiation, which fully inactivates PSII in a minute, does not induce significant damage to DNA and other cellular components (Zsiros *et al.* 2006). In fact, UVA and blue light had the capability of reversing the damage of DNA and hence can contribute to the fast recovery of the algae from DNA damage. UVA being less energetic than UVB is less likely to be absorbed by the proteins as well (Davies 2003). Hence, a faster recovery was observed under PA-affected algae than that of PAB in most of the temperate algae with one exception in this study (Figure 1b).

This exceptional phenomenon can be observed in *D. dichotoma* (Figure 1a). Here, PA causes more pronounced photoinhibition than PAB and after PAB recovery was significantly rapid than after PA. The results suggest that UVB seems to cause an ameliorating effect on this alga under certain conditions. According to Hanelt and Roleda (2009), the UVB ameliorating effect is demonstrated by the lower F_v/F_m recovery kinetics under PA in comparison to that of PAB. Similar observations in *D. dichotoma* obtained in *in situ* studies had been reported by Flores-Moya *et al*. (1999) and in *Dictyota* spp. by Hanelt and Roleda (2009). In both studies, a stronger photoinhibition was observed under PA and PAB than under PAR but recovery was delayed when UVB was filtered out from the full spectrum radiation. Moreover, in *Dictyota* spp., PAB or PA caused a stronger effect than the sum of the effects of each waveband alone (Hanelt & Roleda 2009) which also coincide with the results in this study (Figure 1a). In addition to *Dictyota* spp., an ameliorating effect of UVB was observed in the green alga *Halimeda discoidea* and in the brown alga *Turbinaria turbinata* by Hanelt and Roleda (2009); and, in several aquatic freshwater plants of New Zealand lakes (Hanelt *et al*. 2006) as well. All photoautotrophs showing this phenomenon were living in a natural high light environment with a high share of UVR. This phenomenon is quite interesting since UVB compared to UVA is regarded as being more energetic and is known to cause damage to many important biological macromolecules. Kinetic studies show that photoprotective processes and recovery of photosynthesis occur concomitantly during the inhibition phase so that an increase or better induction of this process may cause a decrease in the level of photoinhibition (Osmond 1994; Hanelt 1998). Therefore, it seems that UVB has induced or even is involved in the repair mechanism during the irradiation. Recovery would be better under full solar radiation (i.e. PAB) if UVB supports repair or photoprotective processes (Sicora *et al.* 2003).

Oxidative stress created by the build-up of reactive oxygen species (ROS) concentration is usually observed in plants under stress and this physiological phenomenon has been known to cause damage in proteins (Davies 2003). The build-up of ROS may be caused by the impairment of PSII centres (Hideg *et al*. 2000). Accumulation of damaged or abnormal proteins may in turn activate the stress protein genes (Bierkens 2000). Thus, induction of the stress proteins is observed in all algae studied indicating an accumulation of damaged proteins (Figures 2a and 3a). In fact, it is observed that there is a reduction in the D_1 protein, some enzymes activity as well as the total soluble proteins in the algae in concomitant with the induction of stress proteins (data not shown). Under normal conditions, the stress proteins are present in low concentrations and play essential roles in cellular protein homeostasis by acting as molecular chaperones (Sharkey & Schrader 2006). Under stress conditions, however, the stress proteins take on additional but related functions to molecular chaperones, by preventing the denaturation of proteins and holding them in the state of folding or assembly to facilitate repair and promoting the degradation of abnormal proteins (Bierkens 2000). This is a reason why after photoinhibition the content of hsp60 (Figure 2a) and especially of hsp70 (Figure 3a) has strongly increased. Moreover, induction of hsp70 is found to be much higher than hsp60 (ANOVA, SNK test, $p<0.001$).

The expression of hsps in response to abiotic stresses has been reported by many studies. Tominaga *et al*. (2012), for example, identified two hsps, Uphsp90 and Uphsp60, from sterile *Ulva pertusa* which were involved in algal tolerance to thermal and heavy metals stresses. These two hsps have similar proteins as the cytoplasmic hsp90 and mitochondrial hsp60. Hsp70 and hsp90 members were found to be the most abundant hsps overexpressed in heat-shocked *Fucus serratus*, desiccated *F. serratus*, and desiccated *F. vesiculosus* indicating the importance of these two hsps in the algal tolerance against heat and desiccation (Pearson *et al.* 2010).

During the recovery period, however, the protein content started to decline. The reduction was higher for hsp60 (Figure 2b) than for hsp70 (Figure 3b) which may mean a different relevance of the two proteins. This will help in repairing the denatured proteins and protecting others from damage allowing the cells to recover and survive under the stress. Hence, recovery of the algae from photoinhibition is observed in all the algae indicating an efficient protective mechanism is triggered within the algae. In *U. lactuca* for example, higher concentration of stress proteins compared to the other algal species (Figures 2a and 3a) helps the alga to recover faster as shown by almost a full recovery of F_v/F_m (Figure 1b). Role of hsp70 and hsp60 and their homologs in the function and protecting the photosynthetic machinery from UV and high light irradiance had been reported by several studies. Schroda *et al*. (2001) observed that overexpression of hsp70b in response to light stress reduces photoinactivation of PSII and enhances recovery in *Chlamydomonas reindhartii*. In addition, binding of hsp70b to an exposed hydrophobic regions of photodamaged D_1 protein resulted in the formation of PSII repair intermediates (Yokthongwattana *et al*. 2001). Hsp60, on the other hand, was involved in the *in vitro* reassembly of UVB-induced denaturation of ribulose-1,5-bisphosphate carboxylase-oxygenase (RuBisCO) enzyme subunits into holoenzyme (Yong *et al*. 2006). Moreover, hsp60 may also aids in the refolding of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) enzyme during UV damaging effects (Naletova *et al*. 2006).

In conclusion, the algae were strongly affected by the presence of high UVR in combination with high irradiance of PAR. This was evident from the high reduction of F_v/F_m of the algae (Figure 1a). However, the algae were able to protect their photosynthetic apparatus by the induction of stress proteins (Figures 2a and 3a). This protective mechanism helped the algae to reduce photodamage to their photosynthetic apparatus and might help in the recovery of the damaged proteins, hence, the algae could recover from the stress impinging on them.

Date of submission: May 2012
Date of acceptance: March 2013

REFERENCES

Aguilera, J, Dummermuth, A, Karsten, U, Schriek, R & Wiencke, C 2002, 'Enzymatic defenses against photooxidative stress induced by ultraviolet radiation in Arctic marine macroalgae', *Polar Biology*, vol. 25, pp. 432–441.

Aguilera, J, Figueroa, FL, Häder, D-P & Jiménez, C 2008, 'Photoinhibition and photosynthetic pigment reorganisation dynamics in light/darkness cycles as photoprotective mechanisms of Porphyra umbilicalis against damaging effects of UV radiation', *Scientia Marina*, vol. 72, pp. 87–97.

Bierkens, JGEA 2000, 'Applications and pitfalls of stress-proteins in biomonitoring', *Toxicology*, vol. 153, pp. 61–72.

Bischof, K, Hanelt, D & Wiencke, C 2000, 'Effects of ultraviolet radiation on photosynthesis and related enzymes reactions of marine macroalgae', *Planta*, vol. 211, pp. 555–562.

Bischof, K, Peralta, G, Kräbs, G, van de Poll, WH, Pérez-Lloréns, JL & Breeman, AM 2002, 'Effects of solar UVB radiation on canopy structure of *Ulva* communities from southern Spain', *Journal of Experimental Botany*, vol. 53, pp. 2411–2421.

Bradford, MM 1976, 'Rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding', *Analytical Biochemistry*, vol. 72, pp. 248–254.

Cullen, JJ, Neale, P & Lesser, MP 1992, 'Biological weighting function for the inhibition of phytoplankton photosynthesis by ultraviolet radiation', *Science*, vol. 258, pp. 646–650.

Cordi, B, Depledge, MH, Price, DN, Salter, LF & Donkin, ME 1997, 'Evaluation of chlorophyll fluorescence, *in vivo* spectrophotometric pigment absorption and ion leakage as biomarkers of UV-B exposure in marine macroalgae', *Marine Biology*, vol. 130, pp. 41–49.

Davies, MJ 2003, 'Singlet oxygen-mediated damage to proteins and its consequences', *Biochemical and Biophysical Research Communications*, vol. 305, pp. 761–770.

Flores-Moya, A, Hanelt, D, Figueroa, F-L, Altamirano, M, Viñegla, B & Salles, S 1999, 'Involvement of solar UV-B radiation in recovery of inhibited photosynthesis in the brown alga *Dictyota dichotoma* (Hudson) Lamouroux', *Journal of Photochemistry and Photobiology B: Biology*, vol. 49, pp. 129–135.

Franklin, LA & Forster, RM 1997, 'The changing irradiance environment: consequences for marine macrophyte physiology, productivity and ecology', *European Journal of Phycology*, vol. 32, pp. 207–232.

Häder, D-P, Porst, M & Lebert, M 2001, 'Photosynthetic performance of the Atlantic brown macroalgae, *Cystoseira abies-marina, Dictyota dichotoma* and *Sargassum vulgare*, measured in Gran Canaria on site', *Environmental and Experimental Botany*, vol. 45, pp. 21–32.

Häkkinen, J, Vehniäinen, E & Oikari, A 2004, 'High sensitivity of northern pike larvae to UVB but no UV-photoinduced toxicity of retene', *Aquatic Toxicology*, vol. 66, pp. 393–404.

Hanelt, D & Roleda, MY 2009, 'UVB radiation may ameliorate photoinhibition in specific shallow-water tropical marine macrophytes', *Aquatic Botany,* vol. 91, pp. 6–12.

Hanelt, D 1996, 'Photoinhibition of photosynthesis in marine macroalgae', *Scientia Marina*, vol. 60, Suppl. 1, pp. 243–248.

Hanelt, D 1998, 'Capability of dynamic photoinhibition in Arctic macroalgae is related to their depth distribution', *Marine Biology*, vol. 131, pp. 361–369.

Hanelt, D, Hawes, I & Rae, R 2006, 'Reduction of UV-B radiation causes an enhancement of photoinhibition in high light stressed aquatic plants from New Zealand lakes', *Journal of Photochemistry and Photobiology B: Biology*, vol. 84, pp. 89–102.

Hanelt, D, Wiencke, C & Nultsch, W 1996, 'The influence of UV radiation on the photosynthesis of Arctic macroalgae in the field', *Journal of Photochemistry and Photobiology B Biology*, vol. 38, pp. 40–47.

Hanelt, D, Wiencke, C & Nultsch, W 1997, 'Influence of UV radiation on the photosynthesis of Arctic macroalgae in the field', *Journal of Photochemistry and Photobiology B: Biology*, vol. 38, pp. 40–47.

Helbling, EW, Barbieri, ES, Sinha, RP, Villafañe, VE & Häder, D-P 2004, 'Dynamics of potentially protective compounds in Rhodophyta species from Patagonia (Argentina) exposed to solar radiation', *Journal of Photochemistry and Photobiology B: Biology*, vol. 75, pp. 63–71.

Helmig, D, Oltmans, SJ, Carlson, D, Lamarque, J-F, Jones, A, Labuschagne, C, Anlauf, K & Hayden, K 2007, 'A review of surface ozone in the polar regions', *Atmospheric Environment*, vol 41, pp. 5138–5161.

Hideg, E, Kálai, T, Hideg, K & Vass, I 2000, 'Do oxidative stress conditions impairing photosynthesis in the light manifest as photoinhibition?', *Philosophical Transactions of the Royal Society B*, vol. 355, pp. 1511–1516.

Hollósy, F 2002, 'Effects of ultraviolet radiation on plant cells', *Micron*, vol. 33, pp. 179–197.

Holm-Hansen, O, Lubin, D & Helbling, EW 1993, 'Ultraviolet radiation and its effects on organisms in aquatic environments', in *Environmental UV Photobiology*, eds AR Young, LO Bjorn, J Moan & W Nultsch, Plenum, New York, USA, pp. 379–425.

Ireland, HE, Harding, SJ, Bonwick, GA, Jones, M, Smith, CJ & Williams, JH. 2004. 'Evaluation of heat shock protein 70 as a biomarker of environmental stress in *Fucus serratus* and *Lemna minor*', *Biomarkers,* vol. 9, pp. 139–155.

Kane, RP 2008, 'Is ozone depletion really recovering?', *Journal of Atmospheric and Solar-Terrestrial Physics,* vol. 70, pp. 1455–1459.

Laemmli, UK 1970, 'Cleavage of structural proteins during assembly of the head of bacteriophage T4', *Nature*, vol. 227, pp. 680–685.

Manney, GL, Santee, ML, Rex, M. *et al.* 2011, 'Unprecedented Arctic ozone loss in 2011', *Nature*, vol. 478, pp. 469–475.

Maxwell, K & Johnson, GN 2000, 'Chlorophyll fluorescence — a practical guide', *Journal of Experimental Botany*, vol. 51, pp. 659–668.

Müller, P, Li, X-P & Niyogi, KK 2001, 'Non-photochemical quenching. A response to excess light energy', *Plant Physiology*, vol. 125, pp. 1558–1566.

Naletova, IN, Muronetz, VI & Schmalhausen, EV 2006, 'Unfolded, oxidized, and thermoinactivated forms of glyceraldehyde-3-phosphate dehydrogenase interact with the chaperonin GroEL in different ways', *Biochimica et Biophysica Acta*, vol. 1764, pp. 831–838.

Navarro, NP, Palacios, M, Mansilla, A & Jofre J 2010, 'Morphological and growth alterations on early development stages of *Iridaea cordata* (Rhodophyta) under different intensities of UVB radiation', *Review of Biological Marine and Oceanography*, vol. 45, pp. 255–265.

Osmond, CB 1994, 'What is photoinhibition? Some insights from comparisons of shade and sun plants', in *Photoinhihition of photosynthesis: from molecular mechanisms to the field*, eds NR Baker & JR Bowyer, BIOS Scientific Publishers Ltd, Oxford, pp.1–24.

Pearson, GA, Hoarau G, Lago-Leston A, Coyer JA, Kube M, Reinhardt R, Henckel K, Serrão ET, Corre E & Olsen JL 2010, 'An expressed sequence tag analysis of the intertidal brown seaweeds *Fucus serratus* (L.) and *F. vesiculosus* (L.) (Heterokontophyta, Phaeophyceae) in response to abiotic stressors', *Marine Biotechnology*, vol. 12, pp.195–213.

Pessoa, MF 2012, 'Harmful effects of UV radiation in algae and aquatic macrophytes — a review', *Emirates Journal of Food and Agriculture*, vol. 24, pp. 510–526.

Powles, SB 1984, 'Photoinhibition of photosynthesis induced by visible light', *Annual Review of Plant Physiology*, vol. 35, pp. 15–44.

Provasoli, L 1968, 'Media and prospects for the cultivation of marine algae', in *Cultures and Collections of Algae: Proceedings of the U.S.-Japan Conference in Hakone, Japan, September 1966*, eds A Watanabe & A Hattori, The Japanese Society of Plant Physiologists.

Schmidt, ÉC, Pereira, B, dos Santos, RW, Gouveia, C, Costa, GB, Faria, GSM, Scherner, F, Horta, PA, Martins, RP, Latini, A, Ramlov, F, Maraschin M & Bouzon, ZL 2012, 'Responses of the macroalgae *Hypnea musciformis* after *in vitro* exposure to UV-B', *Aquatic Botany*, vol. 100, pp.8–17.

Schroda, M, Kropat, J, Oster, U, Rüdiger, W, Vallon, O, Wollman, F-A & Beck, CF 2001, 'Possible role for molecular chaperones in assembly and repair of photosystem II', *Biochemical Society Transactions*, vol. 29, pp. 413–418.

Schweikert, K, Sutherland, JES, Hurd, CL & Burritt, DJ 2011, 'UV-B radiation induces changes in polyamine metabolism in the red seawedd *Porphyra cinnamomea*.', *Plant Growth Regulation*, vol. 65, pp. 389–399.

Sharkey, TD & Schrader, SM 2006, 'High temperature stress', in *Physiology and molecular biology of stress tolerance in plants*, eds KVM Rao, AS Raghavendra & KJ Reddy, Springer, The Netherlands, pp. 101–129.

Shiu, C-T & Lee, T-M 2005, 'Ultraviolet-B-induced oxidative stress and responses of the ascorbate–glutathione cycle in a marine macroalga *Ulva fasciata', Journal of Experimental Botany*, vol. 56, pp. 2851–2865.

Sicora, C, Máté, Z & Vass, I 2003, 'The interaction of visible and UV-B light during photodamage and repair of photosystem II', *Photosynthesis Research*, vol. 75, pp. 127–137.

Tominaga, H, Coury, DA, Amano, H, Miki, W & Kakinuma, M 2010, 'cDNA cloning and expression analysis of two heat shock protein genes, Hsp90 and Hsp60, from a sterile *Ulva pertusa* (Ulvales, Chlorophyta)', *Fisheries Science*, vol. 78, pp. 415–429.

Yokthongwattana, K, Chrost, B, Behrman, S, Casper-Lindley, C & Melis, A 2001, 'Photosystem II damage and repair cycle in the green alga *Dunaliella salina*: Involvement of a chloroplast-localized HSP70', *Plant and Cell Physiology*, vol. 42, pp. 1389–1397.

Yong, ZH, Chen, GY, Shi, JN & Xu, DQ 2006, '*In vitro* reassembly of tobacco ribulose-1,5-bisphosphate carboxylase/oxygenase from fully denatured subunits', *Acta Biochimica et Biophysica Sinica*, vol. 38, pp. 737–45.

Zhang, H, Li, W, Li, J, Fu, W, Yao, J & Duan, D 2011, 'Characterization and expression analysis of hsp70 gene from *Ulva prolifera* J. Agardh (Chlorophycophyta, Cholophyceae)', *Marine Genomics*, vol. 5, pp. 53–58.

Zsiros, O, Allakhverdiev, SI, Higashi, S, Watanabe, M, Nishiyama, Y & Murata, N 2006, 'Very strong UV-A light temporally separates the photoinhibition of photosystem II into light-induced inactivation and repair', *Biochimica et Biophysica Acta*, vol. 1757, pp. 123–129.

ASM Sci. J., **7(2)**, 129–138

Risk Assessment for Living Modified Organisms

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The paper seeks to assuage the fears and worries over living modified organisms (LMOs). It describes how any research carried out on LMOs as well as any release activity on LMOs for public use in Malaysia is controlled by the *Biosafety Act 2007*. Stringent risk assessment of the LMO and its product/s is carried out to eradicate or minimize the negative effects of these on animal and human health, and to biological diversity and the environment. In contrast, no such risk assessment is carried out on introduced exotic species, or on the products of other types of technology, with the exception of pharmaceuticals. Examples are given comparing risk assessment on LMOs and exotic species.

Key words: Living modified organisms, risk assessment, exotic species; biosafety; animal/human health; biological diversity; environment

Living modified organisms (LMOs), also known as genetically modified organisms (GMO) are the products of modern biotechnology. The term modern biotechnology is adopted by international convention to refer to biotechnological techniques for the manipulation of genetic material and the fusion of cells beyond normal breeding barriers. The most obvious example is genetic engineering to create genetically modified/engineered organisms through ‘transgenic technology’ involving the insertion or deletion of genes (IAASTD 2008).

Rightly or wrongly, many people are still apprehensive when they are told that the food they eat is sourced from LMOs. Perhaps, it is a fear of the unknown, or trepidation arising from too little understanding of the subject matter. After all, there is an adage that “A little knowledge is a dangerous thing”.

The truth of the matter is that these products of modern biotechnology are probably more thoroughly tested for possible risks to human and animal health, as well as to the environment, than the products of any other technology, barring pharmaceuticals. The procedure for screening and evaluating risks is called risk assessment. If we were to turn back the clock and assume that a number of plant and animal species were being newly introduced into Malaysia, and we were to subject these to the same risk assessment used for LMOs, there is a good possibility that these organisms would not have been allowed to be grown/reared for food, or introduced and released into the environment.

This paper sets out to attempt to explain in simple terms the process of risk assessment and to draw parallels by using the process in assessing the risks of a few conventional species currently used as food, or has been released into the environment.

THE MALAYSIAN *BIOSAFETY ACT 2007*

The *Malaysian Biosafety Act* was passed in Parliament and gazetted on 28 August 2007. To quote, the Act seeks “to establish the National Biosafety Board” which will “regulate the release, importation, exportation and contained use of living modified organisms, and the release of products of such organisms, with the objectives of protecting human, plant and animal health, the environment and biological diversity”. “Where there are threats of irreversible damage, lack of full scientific evidence may not be used as a reason not to take action to prevent such damage; and to provide for matters connected therewith” (*Biosafety Act 2007*). Thus, it may be seen from the last sentence, the Precautionary Principle is in place to make sure that when and where there is room for doubt, it is better to practise the maxim “Better be safe than sorry”.

The Act also defines what is covered by modern biotechnology, *viz*. “the application of:

(a) *In vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and

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direct injection of the nucleic acid into cells or organelles; or

(b) Fusion of cells beyond the taxonomic family,"

both of which "overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection" (*Biosafety Act 2007, Section 3*).

The National Biosafety Board (a composite body with representatives from six relevant ministries and not more than four additional experts), set up as a result of the Act, resides in the Ministry of Natural Resources and Environment, and tasks a Genetic Modification Advisory Committee (GMAC) to carry out risk assessment on all LMOs on which R&D is to be carried out in Malaysia, as well as all LMOs and/or their products which are to be introduced into the country for the purpose of release (see Appendix 1). GMAC will then recommend to the Board on whether or not a particular activity associated with an LMO or its product should be approved, rejected, or approved with terms and conditions.

It may be seen therefore that there is a law in place which makes it mandatory to notify the National Biosafety Board of all R&D involving LMOs, and to seek approval from the Board when there is an intention for release activities as defined in Appendix 1. Failure to do so is an offence and would result in a fine not exceeding RM250 000 or imprisonment for not more than five years, or both, for an individual. In the case of a continuing offence, a further fine not exceeding RM10 000 per day will apply during which the offence continues after conviction. Where the offender is a body corporate, the fine not exceeding RM500 000 will apply, and in the case of a continuing offence, the further fine will be not exceeding RM20 000 per day during which the offence continues after conviction (*Biosafety Act 2007, Sections 12* and *22*).

RISK ASSESSMENT

To understand risk assessment, we have first to understand the difference between a hazard and a risk. A hazard is anything, including a situation or state, that has the potential to cause harm or an adverse effect. If there is no exposure to a hazard, there is no risk. Exposure may be defined as contact or occurrence of a potential hazard with a living organism or an environmental entity of value. Thus, risk is a function of hazard and exposure, i.e.

$$\text{Risk} = f\ (\text{Hazard, exposure})$$

Let us make a simple analogy: An electric kettle of boiling water is a hazard but not a risk if it is located in a locked room. It becomes a risk when the door is unlocked and there a toddler wandering about. The risk becomes even greater when the kettle is within direct reach of the child, or the electrical cord is left dangling down.

For every notification or application for approval of an LMO or its product, GMAC has to carry out a risk assessment of the activity to be carried out. In conducting a risk assessment, several steps need to be followed:

(i) Problem formulation, including hazard identification
(ii) Hazard and exposure characterization
(iii) Risk characterization
(iv) Risk management strategies; and
(v) Overall risk evaluation and conclusions.

From this point a risk determination matrix is drawn up, typically looking something like what is shown in Table 1. With the risk determination matrix in hand, the next step will be to decide whether the risk is acceptable or not, and risk management strategies will be proposed for any residual risk identified.

How Risk Assessment Works with LMOs

The important thing to remember is that risk is assessed in relation to any harm the activity involving LMO (or its product), henceforth, any mention of an LMO in the text also includes its product/s. may cause to animal and human health, and the environment including biodiversity. The assessment is science-based and specific to the activity, following established and internationally recognized protocols for LMOs (for more details, please refer to *Ad Hoc* Technical Expert Group AHTEG) on Risk Assessment and Risk Management).

In the case of R&D involving LMOs being carried out in a contained facility, i.e. a laboratory, greenhouse, glasshouse or similar, the risks are associated with:

(i) Any harm the R&D activity may inflict on the personnel working with the LMO; and
(ii) Any accidental release of the LMO from the research facility, or of the biohazardous wastes (comprising solid, liquid or gaseous materials which had been in contact with the LMO), into the environment.

To address the first problem, safety procedures are in place to exclude direct contact of the LMO with the personnel working on it. One example is the mandatory wearing of personal protective equipment (PPE) such as laboratory coats, goggles and gloves. Another is the strict compliance to good laboratory practices, such as no consumption of food or drinks in the contained facility, no smoking, removal of PPE and washing of hands before leaving the facility. The procedures become more stringent as the biosafety level of the facility increases.

Table 1. Risk determination matrix.

		Likelihood of exposure			
		4 Highly likely	3 Likely	2 Unlikely	1 Highly unlikely
Consequence	4 Major	High	High	Moderate	Moderate
	3 Intermediate	High	Moderate	Moderate	Low
	2 Minor	Moderate	Low	Low	Negligible
	1 Marginal	Low	Low	Negligible	Negligible

Risk estimate	Score
Negligible	1
Low	2
Moderate	3
High	4

For the second source of risk, contained R&D work on LMOs is governed by strict protocols or standard operating procedures for the safe disposal of the LMO and its wastes at the end of the experiments. In the event of accidental spillage and other actions which lead to the release of the LMO without first rendering it biologically inactive, an emergency response plan (ERP) must be in place so that personnel can take corrective action immediately to limit exposure to the LMO. An effective ERP can only be drawn up with a thorough risk assessment to cover all eventualities.

All these ensure that there is very minimal risk of actual release of the LMO into the environment or exposure of it to life forms outside the contained facility.

For release activities involving LMOs (as defined by the *Biosafety Act 2007*, and shown in Appendix 1), careful and all-encompassing risk assessments are required to protect animal and human health, and the environment, and to remove threats to biodiversity. Taking the example of genetically modified (GM) plants, a first step is to gauge their substantive equivalence compared to the unmodified parent plants. Questions that need to be answered include:

1. How similar is the GM plant compared to the parent plant (discounting the modified trait)? This is assessed by molecular characterization, compositional analyses and agronomic features.
2. Has the parent plant a history of safe use? If the parent plant produces an allergenic effect, this may be amplified in the GM version. Likewise, the transgene from a donor plant with a known allergen (e.g. Brazil nut) should be regarded as being especially risky. Novel proteins in the GM plant can be checked against a database of known allergens and toxins to identify any ‘suspicious’ protein/s.
3. Has the parent plant shown any tendency towards weediness? If yes, there is a risk of the GM plant showing stronger weediness. Such a character has strong implications of its persistence in the environment which may lead to a selective advantage over native species, i.e. a threat to biodiversity.

Further details on risk assessment are given in a series of publications by the Department of Biosafety, Ministry of Natural Resources and the Environment, and the reader is urged to refer to them (Appendix 2).

The reader should note that in contrast very little or no risk assessment of the kind described for LMOs is carried out when an exotic plant species is introduced and released in many parts of the world. To demonstrate this further, a few examples of GM and exotic non-GM species are given below.

Example 1. The Release of a New Plant Species (Table 2)

Consider the introduction for cultivation of:

- GM herbicide-resistant corn (*Zea mays*)
- Exotic water hyacinth (*Eichhornia crassipes*)

The example uses only a limited list of identified potential risks but serves to prove the point, namely, if water hyacinth had been risk-assessed as stringently as the GM corn, it would not have been introduced into Malaysia as an ornamental aquatic species. Using the template given in Table 1, it may be seen that the risk estimates for GM corn are largely negligible, except for the risk to animal and human health which is moderate. The latter is not due to the GM corn itself but to the herbicide (glyphosate) use. Data on this are still preliminary (Séralini *et al*. 2012) and not entirely conclusive (EFSA 2012).

Table 2. Introduction of (A) herbicide-resistant corn and (B) water hyacinth for cultivation in Malaysia.

Identification of potential risk	Comments on likelihood	Likelihood of risk	Comments on consequence	Consequence of risk
(A) Herbicide-resistant corn				
1. Environment Increased weediness	Corn has a long history of cultivation and is highly domesticated. GM corn is thus unlikely to become more weedy.	1	In the unlikely event of GM corn becoming weedy, it can be easily eradicated using weedicides other than glyphosate.	1
2. Environment Loss of biodiversity	Corn is an introduced species in Malaysia, and has no wild relatives. It is unlikely that the GM trait can be transferred to other wild species and cause their extinction.	1	Extremely low because of the absence of wild relatives as Malaysia is not a centre of origin and diversity for corn.	1
3. Animal and human health Toxicity	Corn has a long history of safe use as an animal feedstuff and for human food. GM corn is unlikely to cause toxic effects to animals or humans (Ronald 2011).	2		2
	Nevertheless, some recent reports indicate some harmful effects in rats from glyphosate used in the cultivation of GM corn.		In view of the recent studies, the judicious use of glyphosate should be ensured to avoid over-use. Monitoring of glyphosate residual levels is required in the harvested corn. Further studies are required to substantiate the reported results.	

Table 2 (cont.). Introduction of (A) herbicide-resistant corn and (B) water hyacinth for cultivation in Malaysia.

Identification of potential risk	Comments on likelihood	Likelihood of risk	Comments on consequence	Consequence of risk
(B) Water hyacinth (*Eichhornia crassipes*)				
1. Environment Increased weediness	Water hyacinth is a non-indigenous species, with no prior history of cultivation in Malaysia. Being very fast-growing, it has shown extreme weediness and invasiveness in other countries (e.g. Australia, USA) where it has been introduced.	4	It has been shown to be difficult to eradicate once it takes hold and can seriously block waterways, shade off and eradicate native aquatic plants. This has serious repercussions on native fauna dependent on such species for food and shelter. The thick mats it forms can limit sunlight penetration into the water body, reducing water quality from the increased biomass to be decomposed.	4
2. Environment Loss of biodiversity	It is highly likely that native aquatic flora will be suppressed as well as native fauna populations dependent on these species for food and shelter will be reduced.	4	There may be eradication of native aquatic flora and fauna in the long term.	4
3. Animal and human health Toxicity	Water hyacinth has been used as an animal feedstuff (for pigs) without harmful effects. It is also eaten as a vegetable in Taiwan and in Java without toxic and other harmful effects.	1	No toxic effects have been reported when eaten by animals or humans.	1
4. Animal and human health Habitat for harmful organisms	The plants can create an ideal habitat for mosquitoes to breed and for water snails which are hosts to parasitic flatworms to flourish.	4	Animals and people living around water bodies covered by water hyacinth can suffer mosquito-borne diseases and schistosomiasis (snail fever).	4

The risk estimates for water hyacinth, on the other hand, are mostly high, except for a negligible risk to animal and human health from its consumption. These high risks would have been basis enough to reject an application to introduce the water hyacinth …IF exotic species introduction and release underwent the same risk assessment as GM plant species. Seeing the difficulties in managing this aggressively invasive species faced today (Lim 1992; Fatimah & Gopinath 1995; Kua 2001) that might not have been a bad thing at all.

Example 2. The Release of a new Arthropod Species (Table 3)

Consider the release of the following:

- RIDL male mosquitoes (*Aedes aegypti*)
- oil palm pollinating weevils (*Elaeidobious kamerunicus*)

The Release of insects carrying a dominant lethal (RIDL) mosquito was developed by Oxitec. Basically the male mosquito contains a genetic modification that causes its offspring to die, but the insect can live and reproduce normally when it is fed a diet containing tetracycline. Release of the RIDL male *Ae. aegypti* is aimed at reducing the population of this mosquito species which carries the virus for dengue fever. By mating with the wild type female, the progeny which inherits the dominant lethal gene will die in the absence of tetracycline before reaching adulthood. The risk assessment carried out is for the scenario of large-scale regular releases of the RIDL males. (It should be noted that in the case of Malaysia, Institute for Medical Research (IMR) has thus far only applied for limited releases for Mark-release-recapture (MRR) studies, and this has been carried out in an uninhabited area). The risk estimates for the identified potential risks (list not exhaustive) are all negligible.

In the case of the oil palm pollinating weevil, assume that a similar risk assessment was conducted before its introduction from Cameroon in 1981 (Anon 2005). With so many unknowns, and practicing the Precautionary Principle, most of the risk estimates are rated as high and only one moderate. In this case, it may be seen on hindsight that being overcautious, the oil palm pollinating weevil would not have been introduced into Malaysia at all, and that would have resulted in high hand pollination costs and much lower oil palm yields than what Malaysia enjoys today! Perhaps, the move to introduce the weevil was a lucky break (as the weevil has proved to be harmless to other flora and fauna) but it should be stressed that more studies and data should be available to guide a decision for any exotic species to be introduced into a country.

Things can go horribly wrong, as exemplified by the following (but a few) cases:

1. The rabbit (kept as a food animal) was first brought by British sailors to Australia in the 18th century. Twenty-four animals were purposely released in 1859 for hunting. From this small number, the rabbit has become a serious mammalian pest and invasive species. In addition to being partially blamed for the extinction of almost one eighth of the mammal species in Australia, rabbits cause great damage to crops and serious soil problems (Anon 2011).
2. Introduction of the Asian carp into USA where they have become invasive, threatening endangered native mussels and snails, and displacing local fish species (Anon 2000).
3. Introduction of the Burmese python into Florida for the pet trade, with the subsequent release or escape of the snakes into the Everglades. It is estimated there are between 5000 and 180 000 pythons there! They eat amphibians, reptiles (even the occasional alligator!), birds, and mammals (from small rodents to deer). By preying on native wildlife and competing with other native predators, the pythons are seriously impacting the ecological communities of south Florida (NPS 2012).
4. Introduction of the African honey bee into Brazil for interbreeding with the European honey bee in the hopes of getting a hybrid bee which would produce more honey and be better adapted to tropical conditions. Twenty-six African queen bees were accidentally released in 1957. These mated with the local domesticated bees resulting in Africanized honey bees (also known as killer bees for their aggressive defensive behaviour), and they have spread throughout the Americas (Hall *et al*. 2010).

These examples only cover the large species; there are untold numbers of non-GM plant, arthropod and microbial species which have been introduced without proper risk assessment (to be fair) at a time when there were no such procedures in place. Indeed, some countries (e.g. Australia, Belgium, Germany/Austria, Ireland, Norway, Switzerland, United Kingdom and United States/Canada/Mexico) have now developed risk assessment protocols for exotic species (Verbrugge *et al*. 2010) to prevent such catastrophes from recurring.

CONCLUSION

LMOs are possibly the most stringently risk assessed living organisms compared with any other organisms bred or propagated by natural means. ‘Natural’ in this

Table 3. Release of (A) RIDL *Aedes aegyptii* male mosquito and (B) oil palm pollinating weevil in Malaysia.

Identification of potential risk	Comments on likelihood	Likelihood of risk	Comments on consequence	Consequence of risk
(A) RIDL *Aedes aegyptii* male mosquito				
1. Environment Persistence of the transgene	The transgene can only persist in the environment in the unlikely possibility that the male GM mosquitoes survived longer than normal, or that its progenies survive and continue to reproduce. Studies show that the male GM mosquitoes do not have a longer lifespan than the wild type. The GM mosquitoes have been designed such that their larvae die in the absence of tetracycline (Lacroix *et al*. 2012).	1	Release of the mosquitoes should only take place in areas free of tetracycline use. There should be post-release monitoring for the persistence of GM mosquitoes.	2
2. Environment Loss of biodiversity	Genetic modification was not targeted to change the behaviour of the male mosquito making it a predator to other species. Thus, release of GM mosquitoes is unlikely to cause other species to become less abundant.	1	If this ever happens, the GM mosquitoes can be controlled or reduced by fogging with insecticides.	1
3. Environment Horizontal transfer of transgene to other mosquito genera	Reproductive isolation mechanisms exist, preventing cross-species mating, e.g. with *Anopheles*	1	Very low risk because of the natural reproductive isolation mechanisms that exist.	1
4. Human health More efficient transmission of dengue and chikungunya disease	Only male GM mosquitoes will be released and males do not bite, i.e. feed on human blood. The modification does not affect efficiency of disease transmission.	1	Very low risk because the released male GM mosquitoes do not feed on blood and transmit disease.	1

Table 3 (cont.). Release of (A) RIDL *Aedes aegyptii* male mosquito and (B) oil palm pollinating weevil in Malaysia.

Identification of potential risk	Comments on likelihood	Likelihood of risk	Comments on consequence	Consequence of risk
(B) Oil palm pollinating weevil (*Elaeidobious kamerunicus*)				
1. Environment Harm to non-target plant species	As a new species, there is no data to ensure that the oil palm pollinating weevil does not cause damage to other cultivated and non-cultivated plant species by the feeding behaviour of its larvae	3	Feeding on the pollen of plant species which have limited pollen production can lead to poor fruit and seed set, and reduce the species populations.	4
2. Environment Loss of biodiversity	With lower seed set, the poorer reproduction rate of affected species may lead to their extinction — either directly or through ecological succession by other more competitive species.	3	Eradication of affected plant species is a possibility.	4
3. Environment Harm to oil palm	There is no study to show that the weevil to be introduced will not cause economic damage to the oil palm, or be a carrier of pathogenic fungal species.	3	The highly lucrative oil palm industry in Malaysia can be drastically affected.	4
4. Animal and human health Pest of stored food products	Weevils are known storage pests of rice and sweetpotato. Data are required to show the absence of such detrimental behaviour on stored food products in the oil palm pollinating weevil.	2	A new stored product pest may be introduced inadvertently.	4

case includes the processes requiring the intervention of Man, e.g. plant and animal breeding procedures, induced mutations, cell fusion (within the taxonomic grouping), and *in vitro* fertilization. The risk assessment of LMOs follows protocols generally accepted internationally, and the results of such assessments are made public through such means as the Malaysian Biosafety Clearing House (website: <http://www.biosafety.nre.gov.my/>). In addition to the technical aspects of risk assessments by GMAC, attention is also given to socio-economic considerations, and public consultations are carried out (in the form of newspaper advertisements and, where necessary, public forums). The latter two procedures serve to take into account the impact of LMOs on livelihood and traditional practices, social, cultural, religious and ethical beliefs of the people who will be impacted by the LMOs.

For these reasons, the general public should rest assured that LMOs which pose any danger or risk of harm to animals, humans and the environment will not be released for private or public use. The sometimes seemingly unreasonable fear of LMOs shown by people, perpetuated and propagated through the internet by half-truths, has no rational basis.

Date of submission: March 2013
Date of acceptance: April 2013

REFERENCES

Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management, 'Guidance on risk assessment of LMOs', viewed 9 April 2013, <http://bch.cbd. int/ onlineconferences/guidance_ra.shtml>.

Anon 2000, 'Asian carp', Upper Midwest Environmental Sciences Center, United States Geological Survey, viewed 11 January 2013, < www.umesc.usgs.gov/invasive_species/ asian_carp.html>.

Anon 2005, *Protecting the pollinators*, FAO of UN, Agriculture and Consumer Protection Department.

Anon 2011, 'Feral European rabbit (*Oryctolagus cuniculus*)', Department of Sustainability, Environment, Water, Population and Communities, Australian Government, viewed 11 January 2013, <www.environment.gov.au/ biodiversity/invasive/.../pubs/rabbit.pdf>.

Biosafety Act 2007 (Act 678), Laws of Malaysia, Government of Malaysia.

European Food Safety Authority (EFSA) 2012, 'Statement of EFSA: review of the Séralini *et al*. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in *Food and Chemical Toxicology*', *EFSA Journal*, vol. 10, no. 10, pp. 2910.

Fatimah, MY & Gopinath, N 1995, 'The status of inland fisheries in Malaysia', in *Regional Symposium on Sustainable Development of Inland Fisheries under Environmental Constraints*, eds. T Petr, & M Morris, FAO Fisheries Report No. 512 Supplement, p. 225–239.

Hall, HG, Zettel-Nalen, C & Ellis, JD 2010, 'African honey bee: what you need to know', University of Florida, IFAS Extension, Entomology and Nemotology Department, Fact Sheet ENY-114 (MG113).

International assessment of agricultural science and technology for development (IAASTD), 2008, 'Bio-technology and modern biotechnology defined', viewed 6 March 2013, <http://www.grida.no/ graphicslib/detail/ biotechnology-and-modern-biotechnology-defined_ b9d8>.

Kua, KS 2001, 'Bakun project revived: Malaysian consumers awake!', *SUARAM*, viewed 11 January 2013, <www. magickriver.net/Bakun.doc>.

Lacroix, R, McKemey, AR, Norzahira, R, Lim, KW, Wong, HM, Teoh, GN, Siti Rahidah, AA, Sawaluddin, S, Selvi, S, Oreenaiza, N, Norhaida Hanum, AT, Chandru, A, Suria Marlina, M, Lees, RS, Naish, N, Scaife, S, Gray, P, Labbe, G, Beech, C, Nimmo, D, Alphey, L, Vasan, SS, Lee, HL, Nazni Wasi, A & Shahnaz, M, 2012, 'Open field release of genetically engineered sterile male *Aedes aegypti* in Malaysia', PLOS ONE, vol. 7, no. 8, <www.plosone.org 9 August 2012>, e42771.

Lim, KB 1992, 'Reservoir choking on silt and sand', *New Straits Times*, Aug. 14, p. 6.

National Park Service (NPS), 2012, 'Burmese pythons', Everglades National Park, viewed 11 January 2013, <www.nps.gov/ever/naturescience/burmesepythonsintro. htm>.

Ronald, P 2011, 'Genetically engineered crops — what, how and why?', Scientific American, August 11, 2011, <http:// blogs.scientificamerican.com/guest-blog/2011/08/11/ genetically-engineered-crops>.

Séralini, G-E, Clair, E, Mesnage, R, Gress, S, Defarge, N, Malatesta, M, Hennequin, D & de Vendômois, JS 2012, 'Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize', *Food and Chemical Toxicology* (in press).

Verbrugge, LNH, Leuven, RSEW & van der Velde, G 2010, *Evaluation of international risk assessment protocols for exotic species: final report, Reports on Environmental Science nr*. **352**, 54 p., Institute for Water and Wetland Research Department of Environmental Sciences and Department of Animal Ecology and Ecophysiology, Radboud University, Nijmegen, The Netherlands.

Appendix 1. Activities involving LMOs as covered by the Biosafety Act 2007

The National Biosafety Board is to be informed of all activities involving LMOs in Malaysia. These cover two broad categories:

1. The export, contained use and import for contained use of LMOs, for which a notification is made to the Board; and
2. The release and import of LMOs, for which approval must be sought and given by the Board.

A contained use activity is defined as an activity which is carried out within the confines of a laboratory, plant house, installation or other physical structure which ensures that the LMO (and all wastes arising from the activity) do not come into direct contact with the outside environment. For example, R&D on LMOs is usually a confined activity.

Release activities, as listed in the Second Schedule of the *Biosafety Act 2007*, are as follows:

1. Research and development purposes in all field experiments
2. Supply or offer to supply for sale or placing on the market
3. Offer as gift, prize or free item
4. Disposal
5. Remediation purposes; and
6. Any other activity which does not amount to contained use

Appendix 2. List of publications by the Department of Biosafety, Ministry of Natural Resources and the Environment.

1. Biosafety Guidelines: Contained Use Activity of Living Modified Organism (2010)
2. Biosafety Guidelines: Confined Field Trial of Living Modified Plants in Malaysia (2012)
3. Biosafety Guidelines: Risk Assessment of Genetically Modified Microorganisms (2012)
4. Biosafety Guidelines: Environment Risk Assessment of Genetically Modified Plants in Malaysia (2012)

ASM Sci. J., **7(2)**, 139–143

Mortality Rate in Association with Foot and Mouth Disease Outbreaks in Cattle and Buffaloes, Pakistan

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This study describes epidemiological characteristics of the foot and mouth disease (FMD) outbreaks in different areas of Pakistan, including the pattern of the outbreak in both time and space, transmission routes among infected areas, and control measures. One of the prominent features of these FMD outbreaks was that the virus infected mostly cattle and buffaloes despite the presence of other susceptible animals (sheep and goats). The other significant feature of each outbreak was the mortality, which was 7.74% and 13.87% in the adult animals and young stock, respectively. Overall, morbidity rate was 64.19% as compared to mortality rate which was 21.61%. The clinical signs that prompted notification of infection included vesicles in and around mouth and hooves. Mouth epithelium and swab samples were collected for the confirmation and sero-typing of FMD virus and sandwich ELISA was used for this purpose. Serotype 'O' was the most consistent serotype in three outbreaks while the Serotype 'A' confirmed from one outbreak. These outbreaks occurred in a period of two months so the same virus circulation could be predicted in various populations. This was due to the main consistent feature of these outbreaks which was the mortality rate, not only in young-ones but also in adults. There was clear evidences of animal movement and introduction of new animals either in the area or in the herd.

Key words: Characteristics; Foot-and-Mouth Disease (FMD); outbreaks; mortality; epidemiology

Foot and mouth disease (FMD), also known as Aphthous fever, is a highly infectious and economically destructive disease of livestock (Rodriguez & Grubman 2009) affecting all cloven-footed domestic and wild animals. It is caused by a picornavirus of the genus aphthovirus (Barnett & Cox 1999).

FMD has a high economic importance because the infected cattle may lose up to 30% of their body weight in a week or two as a result of difficulty to eat, drink and walk for food. It results in high economic impact due to the severe loss in body weight of meat cattle and a significant reduction in milk yield in lactating animals (Mayer & Krudsen 2001). The epidemiology and etiology of FMD have been extensively investigated (Barnett & Cox 1999).

Based on description of FMD by Radostits *et al*. (2007), it was suggested that heat intolerance was a sequel to FMD and was caused by damage to the endocrine system by FMD virus. This was also reported in other studies (Sutmoller *et al.* 2003) that showed the persistence of FMD virus in the pituitary gland and central nervous system of experimentally infected cattle. Moreover, Magoma *et al*. (2003) reported a syndrome of heat intolerance where animals became pyrexic with increased respiratory rates as ambient temperature increased from early morning to afternoon but there was no evidence of mortality in adults due to FMD.

Keeping in view of the diversity of FMD, we investigated recent outbreaks thoroughly and in this article we are describing main epidemiological findings of these outbreaks. The main attribute of these FMD outbreaks was that the virus infected mostly cattle and buffaloes despite the presence of other susceptible animals (sheep and goats) and the occurrence of mortality in adult animals.

MATERIALS AND METHODS

Outbreaks Description and Sample Collection

Samples were collected and submitted by the outbreak attending teams of National Veterinary Laboratories

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[1] National Veterinary Laboratory, Park Road, Islamabad, Pakistan
[2] FAO Regional Project GTFS/INT/907/ITA
[3] FAO National Project, Progressive control of Foot and mouth disease in Pakistan (GCP/PAK/123/USA)
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and FAO regional project from four different locations, following the procedures described by the Office International des Epizooties (2000). Samples were taken aseptically in buffered glycerine and transported to the laboratory under refrigeration temperature.

A total of four outbreaks in cattle and buffaloes, suspected of FMD were attended and investigated in different provinces of Pakistan during 2011. Twenty-two epithelial tissue samples (14 from cattle and 8 from buffaloes) were collected. Serotyping was done at National Veterinary Laboratories, Islamabad.

Laboratory Confirmation

The ELISA kit (IZLAR lab, Brescia, Italy) was used for this purpose. However, test reagents were locally prepared. In this sandwich test different, selected combinations of anti-FMDV monoclonal antibodies (MAbs) were used as coated and conjugated antibodies. The test was applied for detection and typing of FMD viruses (type O, A and Asia-1) in homogenates of vesicular epithelia and in vesicular fluid. Microtitre plates were supplied pre-coated with MAbs.

The test was performed as per directions of the kit's manufacturer. In case of positive samples the conjugated MAb binded to the FMD virus, trapped by the catching MAb forming an Ag-Ab complex. Immediately after incubation the unbound conjugate was removed by washing, and the TMB-chromogen solution was delivered into wells. A colorimetric reaction developed if the conjugate had bound to the sample antigen. The colour development was proportional to the amount of viral antigen present in the test sample. After addition of a stop solution the optical density of the developed colour was read at 450 nm by a microplate photometer (Immunoskan, BDSL, Finland) linked to a computer. Samples with optical density values of >0.2 were consider positive for the respective serotype.

RESULTS

Epidemiological Description of Outbreaks

Outbreak no. 1 in Khushab. The disease outbreak occurred in March 2010 in district Khushab. Topographically the area was partially sandy desert. The disease was reported at three different locations within a kilometer of 10 km from the nidus of the outbreak.

Disease pattern at Farm no. 1. Cattle and buffalo were kept in one compound. Feeding and watering sites were shared by both species. But cases were first seen in cattle. There was no history of purchase of new animals from market and no animal returned unsold from market. It was reported that prior to the first case at this farm FMD cases were seen at another farm about 2.5 km away (being semi desert area these farms are almost isolated and as there were crops in the surroundings so these animals were kept tied within their respective compounds.

Disease pattern at Farm no. 2 (Dera Khan Mohammad). The owner of the farm was a progressive breeder. Cattle and buffalo were kept in one compound in properly constructed sheds. Feeding and watering sites were different for each species. Cases were first seen in cattle. It was reported that prior to these cases vaccination against FMD was done at the farm by NGO (Non-government organization) but farmers had no clue about the brand of the vaccine. There was no history of purchase of new animals from market and no animal returned unsold from market. However Cattle traders frequently visit the Dera. These was no disease in the surrounding area prior to these cases and there was no FMD history on this Dera for the last 15 years.

Disease pattern at Farm no. 3 (Dera Jehanzeb). Animals affected with FMD like symptoms were purchased by the owner of this farm (a butcher by profession) and latter on all the animals kept on the farm were affected.

Outbreak no. 2 in Taxilla. This particular farm is located in Taxilla. It was a commercial dairy unit. The animals were being regularly vaccinated (twice) a year against FMD for the last 5 years.

Outbreak no. 3 in Khairpur district (Province Sindh). There was no history of introduction of new animals; however, people from the surrounding villages did bring their cattle for natural crossing with the breeding bull kept in the farm and reportedly FMD like cases were seen in the 15 km radius. In the surrounding villages it was a routine to take animals to live animal market for sale and unsold animals were brought back. A breeding bull was kept at the farm and people from the surrounding village brought their cattle for natural breeding.

Outbreak no. 4 in Islamabad. This particular farm is located in Sihala (around Islamabad). It was a commercial dairy unit. The animals were being regularly vaccinated (twice) a year against FMD (VRI vaccine) for the last many years. Out of a total of 15 buffaloes kept at the farm, only three animals were affected clinically.

Common signs and symptoms. Mainly the lesions were observed in the mouth (in cattle lesions were mostly on the tongue whereas in Buffalo upper and lower gum regions were involved), also there was high temperature (106ºF – 107ºF) and drooling saliva. A drastic drop (70% to 90 %) in milk production was reported in lactating animals. This drop was more pronounced in cattle.

Figure 1. Location of FMD outbreaks.

FMD Serotyping

FMD diagnosis and virus typing was undertaken at NVL, Islamabad. ELISA test (Type Sandwich) was used to type the virus. A total of 22 samples were analyzed from these recent outbreaks. Based on the data of 4 outbreaks (22 samples), the occurrence of FMDV in large ruminants in Pakistan was confirmed. The most significant feature of each outbreak was the mortalities both in young and adult animals. Overall the mortality rate ranged from 21.61% to 64.19% at seven different farms whereas in young stock mortality rate was around 57%. The clinical signs that prompted notification of infection included vesicles in and around mouth, hooves coupled with high grade fever.

Overall, 15 out of 22 samples were found positive for FMDV. Out of these 15 samples, 11 were confirmed as serotype ‘O’ and 4 as serotype ‘A’. Serotype ‘O’ was predominant strain in the entire out break except one (Islamabad) in which serotype A was detected in epithelial tissue collected from cross bred cattle. Most of the samples collected from buffaloes were positive for serotypes ‘O’.

These outbreaks were reported in a period of two months so the virus circulation could be estimated in various populations. The main consistent feature of these outbreaks was the mortality rate, not only in young-ones but also in adults as well (Table 1). Severe respiratory distress, just before death, was the predominant sign in the animals that sucumbed to disease. Almost all of these out breaks were linked either with introduction of new animals or unrestricted animal or human movement in the farm premises.

Table 1. Area-wise distribution of outbreaks with specie and mortality numbers.

Area	Farm locality	Animal species	Total animal kept	Diseased	Mortality	Mortality rate in adult	Mortality rate in young
Khushab	Farm no. 1 (Dera Shamay Khel)	Buffalo	15	15	Nil	–	–
		Cattle	40	40	Nil	–	–
	Farm no. 2 (Dera Khan Mohammad)	Buffalo	6	6	3 (1 calf)	2/6	1/6
		Cattle	45	45	19 (10 calves)	9/45	10/45
	Farm no. 3 (Dera Jehanzeb)	Buffalo	2	2	Nil	–	–
		Cattle	7	7	Nil	–	–
Taxilla	Farm no. 1	Buffalo	14	Nil	Nil	–	–
		Cattle (Cross breed)	12	6	2 (Both 10–12 months age)	–	2/12
Islamabad	Farm no. 1	Cattle (Cross breed)	10	3	Nil	–	–
Khairpur District (Sindh)	Farm no. 1 (Area Gambat city)	Cattle	85	50	35 (25 calves were 4–6 months old, 10 adults were 3–4 years old)	10/85	25/85
	Farm no. 2	Cattle	74	25	8 (5 calves)	3/74	5/74
Total			310	199 Morbidity rate= 64.19%	67 (43 calves) Mortality rate= 21.61%	24/310 (7.74%)	43/310 (13.87%)

DISCUSSION

Veterinary epidemiology plays a critical role in disease outbreak investigations, both to assist with herd-level decision-making and to contribute relevant information in ongoing national or regional control strategies. Despite the importance of this role, however, very little information has been published on the use of applied (field-based) epidemiological methods during disease outbreaks.

The most significant feature of each outbreak was the mortalities of different levels both in adult and young animals. The mortality rate was 7.74% and 13.87% in the adult animals and young stock, respectively. Overall, morbidity rate was 64.19% as compared to mortality rate which was 21.61%. The clinical signs that prompted notification of infection included vesicles in and around mouth and hooves. Hussain *et al*. (2005) reported similar pattern of FMD occurrence throughout the year. These out-breaks have a positive correlation with the pattern of animal movement and the production systems. For the last many years around Eid-ul-Azha festival due to extensive to and fro animal movement across the country a surge in FMD out breaks was always a regular phenomenon, but in our study we observed outbreaks at the start of the summer season which indicated that the disease could occur at any time of the year.

Prior to the seventies, the FMD was thought to be a seasonal disease, and most of the cases were reported in the hot and dry seasons (April – June) and the second season was September to October. Historically, FMD used to be a mild or sub-clinical disease with a short duration (3–5 days) followed by recovery over the next week. For the last couple of years, disease was reported all round the year. FMD and its sequels, a very recent phenomenon was the mortality in adult animals. A possible explanation for change in disease dynamics and severity could be the change in the pattern of the movement of domestic animals within the country and across the border. Animal movement has increased many folds and as such the disease continues to be present in mild or acute form in one part or the other throughout Pakistan (Zulfiquar 2003).

Another reason for the disease transmission was the unrestricted to and fro movements of animals and personnel between different cattle markets, and cattle markets and villages. At farm level the disease was transmitted either by direct contact or by aerosols from infected to healthy animals. This finding is in congruent with Wee *et al*. (2008) who outlined an investigative template for FMD during the 2002 FMD outbreak in Korea. FMD was probably spread by a contract worker who had participated in the culling operations. Other routes of spread were ruled out during the investigation. The inference to be drawn from this study was that the bio-security was non-existent at our farm level and this issue had its roots in our complex scocio-economic setup. This study further elaborates the complexity involved in devising an appropriate vaccination strategy.

ACKNOWLEDGEMENT

Efforts and support of T. N. Chatta, Department of Livestock and Dairy Development, Punjab, Pakistan and M. N. Markhad, Department of Livestock and Dairy Development Sindh, Pakistan are acknowledged.

Date of submission: February 2013
Date of acceptance: April 2013

REFERENCES

Barnett, PV & Cox, SJ, 1999, 'The role of small ruminants in the epidemiology and transmission of foot-and-mouth disease', *Veterinary Journal*, vol. 158, pp. 6–13.

Hussain, M, Amjad, MM, Fatima, Z & Rizwan, YM 2005, 'Participatory surveillance of livestock diseases in Islamabad Capital Territory', *Int. J. Agri. Biol*., vol. 7, pp. 567–70.

Magoma, G, Samuel, S, Kondela, A, Madege, M & Makungu, S 2003, 'A preliminary clinical investigation of a condition known as luzwiga in the Lake Zone of Tanzania', in *Annual Scientific Conference of the Tanzania, Veterinary Association, Arusha*.

Meyer, RF & Knudsen, RC 2001, 'Foot-and-mouth disease: a review of the virus and the symptoms', *Journal of Environmental Health*, vol. 64, no. 4, pp. 21–23.

Office International des Epizooties 2000, *Manual of standards for diagnostic tests and vaccines*, 4th edn, Paris.

Rodriguez, LL & Grubman, MJ, 2009, 'Foot and mouth disease virus vaccines', *Vaccine*, vol. 27, no. 4, pp. 90–94.

Radostits, OM, Gay, CC, Hinchcliff, KW & Constable, PD 2007, *Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs and goats*, 10th edn, Elsevier Health Sciences, Philadelphia, PA, USA.

Sutmoller, P, Barteling, SS, Olascoaga, RC & Sumption, KJ 2003, 'Control and eradication of foot-and-mouth disease', *Virus Research*, vol. 91, pp. 101–144.

Wee, SH, Nam, HM, Moon, OK, Yoon, H, Park, JY & More, SJ 2008, 'Using field-based epidemiological methods to investigate FMD outbreaks: an example from the 2002 outbreak in Korea', *Transbound Emerg. Dis*., vol. 55, no. 9–10, pp. 404–410.

Zulfiqar, M 2003, *Draft Report for Development of national disease control policy for foot and mouth disease in Pakistan*, FAO Project “Support for Emergency Prevention and Control of Main Trans-boundary Animal Diseases in Pakistan, Rinderpest, FMD, PPR”.

ASM Sci. J., **7(2)**, 144–151

Modeling and Simulation of Artificial Hair Cell Sensor for Underwater Applications

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This article uses finite volume and finite element methods for optimization of the artificial hair cell sensor. The performance of the sensor was investigated for different materials such as sicon and polysilicon and by varying hair cell dimensions including width and length. The silicon material which has low young modulus was proposed based on the simulation performance. The performance of the hair cell sensor was achieved by increasing the hair cell length while increasing the width did not significantly influence the performance. The performance of the sensor was studied for its viscous force, deflection, von mises stress and sensitivity. From the simulation, the hair cell with a length of 1600 μm and 80 μm width was suggested for the subsequent analysis. Another way to improve the performance was by modifying the hair cell geometry and it was proved that the modified hair cell was more sensitive, based on the deflection. The angle of flow that hit the hair cell also affected the deflection of the sensor where the zero angle flow which was parallel to the substrate was the most effective angle. The limitations of the performance of hair cell for various fluid velocity were also discussed in this paper.

Key words: Finite element method; silicon; polysilicon; viscous force; deflection; von mises stress; fluid viscosity; flow sensor

In the recent years, research on the flow sensor for underwater application has been carried out using various designs, materials, and sensing elements. The purpose is to optimize the dimension and to achieve high performance of the sensor. The conventional sensing method such as hot wire anemometry and the Doppler frequency shift have a limitation in terms of size where it is too large and not suitable to form an array especially for measuring the flow distribution (Fan *et al*. 2002). From nature, researchers found the new inspiration in designing the flow sensor based on the hair cells inside the lateral line system in the body of the fish where it is more simpler and can improve the performance. The Micro-electromechanical system (MEMS) fabrication technology also helped the researchers to miniaturize and to achieve high efficiency of the flow sensor. Most of the researchers used piezoresistive, strain gage and capacitor as a sensing element (Tao & Yu 2012). For underwater applications, an array of hair cell sensors helped vehicles to navigate and monitor and that which mimic the function of the lateral line system to form the hydrodynamic images for flow imaging for underwater environments (Coombs 2001).

A lateral line system that span the length in the body of the fish consists of two types of neuromast, that is superficial neuromast and canal neuromast. Superficial neuromast directly expose the flow and canal neuromast exists in subepidermal canals. Generally, fishes that live in distilled water tend to have many superficial neuromasts compared to canal neuromasts which are suitable for the fish to live in turbulent waters. Both neuromasts are composed or hair cells that are embedded in the gelatinous cupula. When the fluid passes the neuromast, it will cause a gelatinous cupula movement and the hair cell will induce neuron signals (Engelmann, Hanke & Bleckmann 2002). The general overview about hair cell is that it consists of a vertical cilium that is attached to a neuron, and this neuron is attached to the cilium stretchers. If the cilium of the hair cell is bent by the fluid flow, the displacement will induce output responses (Fan *et al*. 2002). In this paper, we focus on the modeling and simulation of a single hair cell to study its performance based on the effect of the material, dimension including width and length of the hair cell, geometry and the angle of flow to the sensor performance.

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APPROACH AND METHODS

As mention before, the biomimetic flow sensor was inspired from the hair cell that embedded in the gelatinous cupula as shown in Figure 1a. Generally, the mechanism of the hair cell is evident when the cupula gelatin move, it will deflect the hair cell and induce the neuron signal. By using the same principle, the artificial hair cell sensor was proposed. Figure 1b shows the structure of the artificial hair cell and we considered all the surface had a rectangular cross section. For the sensing principle, when external flow was applied onto the hair cell, it would give some deflection and induce strain at the base of the hair cell. The magnitude of the induced strain could be sensed by many means, for example, by using integrated piezoresistive sensors. The length, thickness and width of hair cell were *L, t,* and *w*, respectively.

Given the relationship between the relative change of resistances (sensitivity) and the flow rate in Equation 1. From the equation, we knew the sensitivity ($\Delta R/R$) of the hair cell was depended on the flow rate (u_o), density fluid (ρ), young's modulus (E), thickness (t), length (L) and the boundary-layer thickness (δ) (Equation 1).

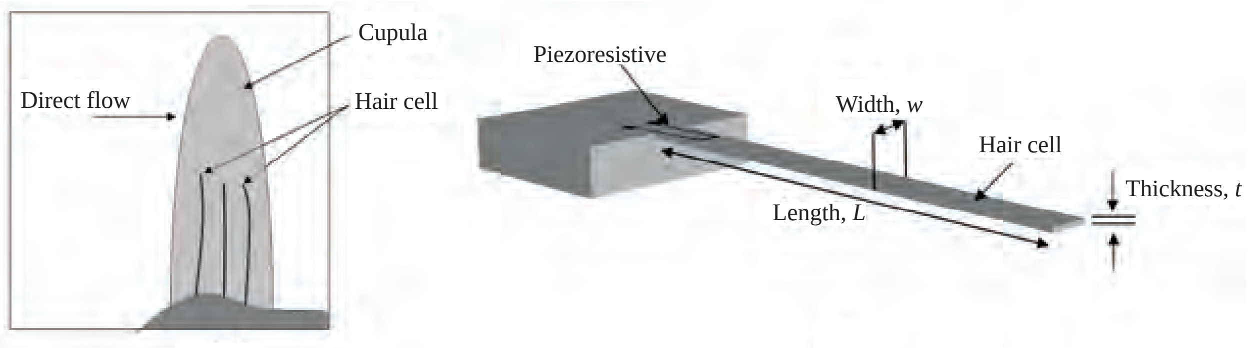
$$\frac{\Delta R}{R} = \frac{3GwC_D \rho u_{o2}\left(\frac{L^4}{\delta^2} + \frac{L^6}{6\delta^4} - \frac{4L^5}{5\delta^3}\right)}{Et^2} \qquad (1)$$

C_D is the drag coefficient and it is depended on the Reynolds number. We assumed the flow was laminar and Reynolds number is given as:

$$Re = \frac{u_o x}{\upsilon} \qquad (2)$$

where, x is the hair cell location from the leading edge and υ is the kinematic viscosity. For the simulation, the biomimetic hair cell was modeled using computer-aided engineering software ANSYS (<http://www.ansys.com>). This software help researchers to analyze the model for the drag force acting on the hair cell, deflection of the hair cell, the distribution of stress and the sensitivity of the sensor. The parameters that were considered in this simulation are the material, width and length of hair cell, and also the angle of flow facing the hair cell. In ANSYS, two tools were used: ANSYS FLUENT and ANSYS Mechanical APDL. Recently, the same method of simulation in the setup was done and compared with the experimental result (Nawi *et al*. 2012). Therefore, the same method was used for this simulation.

When related to the fluid, we need to study the drag force acting on the hair cell. The FLUENT is a finite volume based software that runs a numerical simulation using Navier-Stokes equation. The Gambit software inside the FLUENT was used to model and generated the mesh. In mesh generation, the Tet/Hybrid element was chosen due to design geometry and 1228146 mesh volume was generated. Figure 2 shows the geometry model for hair cell it boundary condition. The hair cell is located *x* mm from the leading edge where in this simulation the leading edge of 3 mm was fixed. The inlet was set to velocity inlet for several of the velocity to apply to the hair cell. Meanwhile the top and outlet was set to the pressure outlet. For the hair cell and the bottom of the hair cell, the boundary was set to the wall. The iteration for simulation was stopped at 250 because it had already met the criterion, and it was limited to 1E-5 for convergence criterion. To study the performance of sensor for deflection and stress to the applied velocity, the result from the ANSYS FLUENT was transferred to the ANSYS Mechanical APDL. Modeling in Mechanical APDL began by choosing an element type, and entering the material properties. The list of property materials such



(a) (b)

Figure 1 (a) Hair cell embedded in gelatinous cupula; (b) Artificial hair cell.

as Young's Modulus and Poisson's ratio are shown in Table 1. The model was then meshed and applied (the load) to the hair cell. The hair cell structure was fixed at one end, and applied load, at the other. The deflection of the hair cell would induce the value to the piezoresistive and sensitivity could be obtained.

RESULTS AND DISCUSSION

In this section, we discuss the effect of hair cell to a certain parameter as mentioned before, that is the material, width and length of the hair cell, geometry and also the angle of flow facing the hair cell. Figure 4 shows a comparison between PolySi and Si hair cell using the same dimension and velocity applied based on deflection. It was clearly shown that Si provided higher displacement over PolySi for the same applied load making Si more suitable to be used as a highly sensitive flow sensor. Therefore, for the next simulation process we used silicon as the material. Then we simulated for different hair cell dimension including the width between 120 µm to 640 µm and length 800 µm to 1600 µm. By assuming that the flow was laminar, the fluid velocity 1m/s which parallel the substrate was applied to the hair cell. From the ANSYS, the three parameters including viscous drag force, deflection and von mises stress could be observed as shown in Figure 5. For the viscous drag force acting on the hair cell, it depended on the surface area of hair cell facing the flow where the drag force increased as a surface area increased. It was proven when we saw the maximum drag force which was 616 µN for the largest surface area of hair cell measuring 640 µm × 1600 µm. It was different for deflection and stress of the sensor where the only highest length gave the maximum value for deflection which was 65.6 µm and for mises stress it was 64.9 MPa. The width of the hair cell did not contribute to the major effort of the performance of the sensor. The same was also true for sensitivity of the sensor where the maximum sensitivity was 0.045E-6 for the hair cell with a length of 1600 µm and a width of 80 µm. However, the effects of hair cell thickness was not investigated. Next, the hair cell with a modification of geometry was simulated to study its effect on the performance of the hair cell sensor.

The modification of the hair cell was by removing a certain area in order to improve the performance of the sensor. The 20 µm deep segment in the left and right was removed at the bottom of the hair cell sensor to reduce the moment inertia at that area as shown in Figure 6. The contour bars represent the stress value where the different colours indicated different values of stress. The red colour for the maximum miss stress value acted on the hair cell. As we can see, the mises stress for original geometry had a uniform stress distributed along the hair cell and

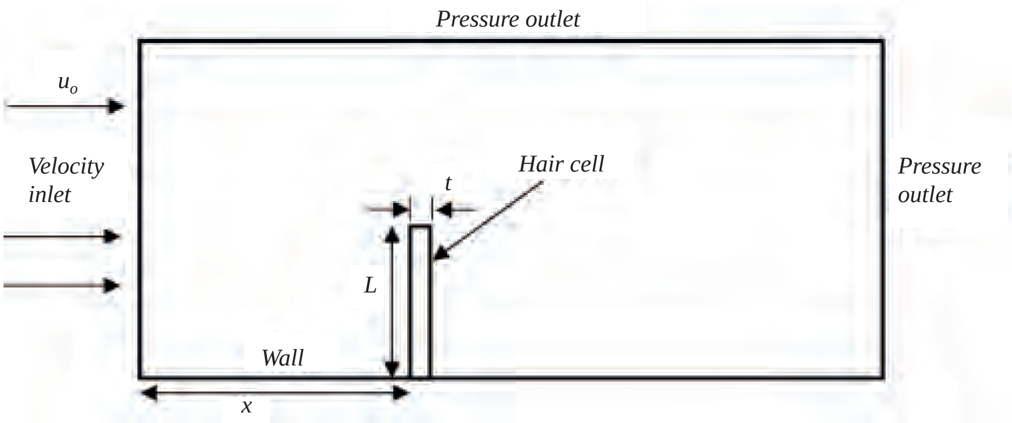


Figure 2. The geometry of the computational domain in FLUENT.

Table 2. Material properties of silicon.

Parameter	Silicon	Polysilicon
Young's Modulus (GPa)	130.1	169
Poisson's Ratio	0.278	0.22
Piezoresistive coefficient (MPa^{-1})	$\Pi_{11} = 6.6 \times 10^{-5}$ $\Pi_{12} = -1.1 \times 10^{-5}$ $\Pi_{44} = 1.381 \times 10^{-3}$	

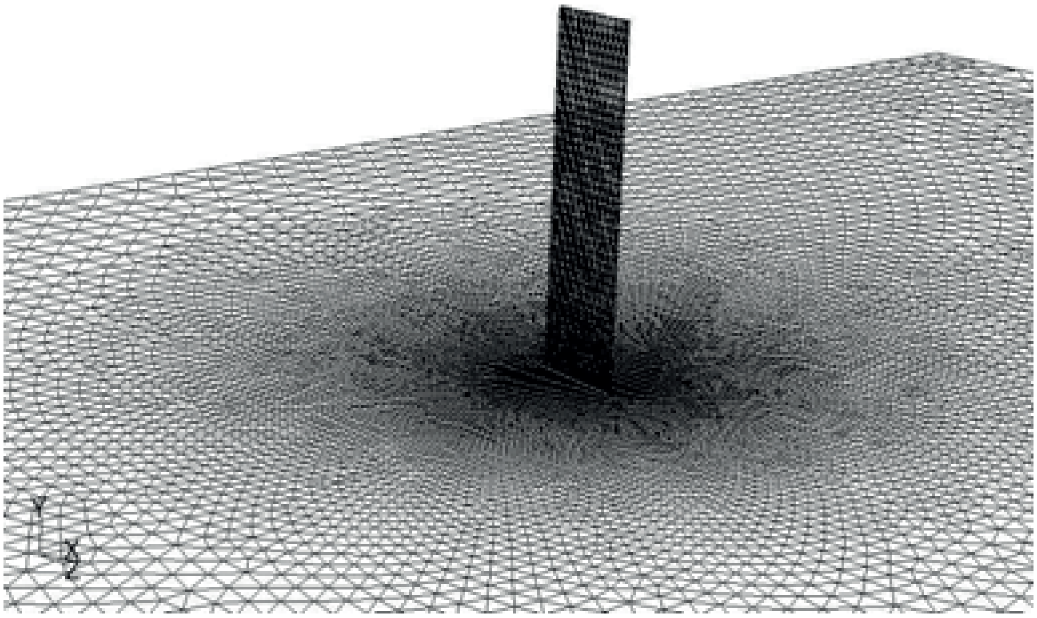


Figure 3. The meshing for the hair cell and the bottom surface.

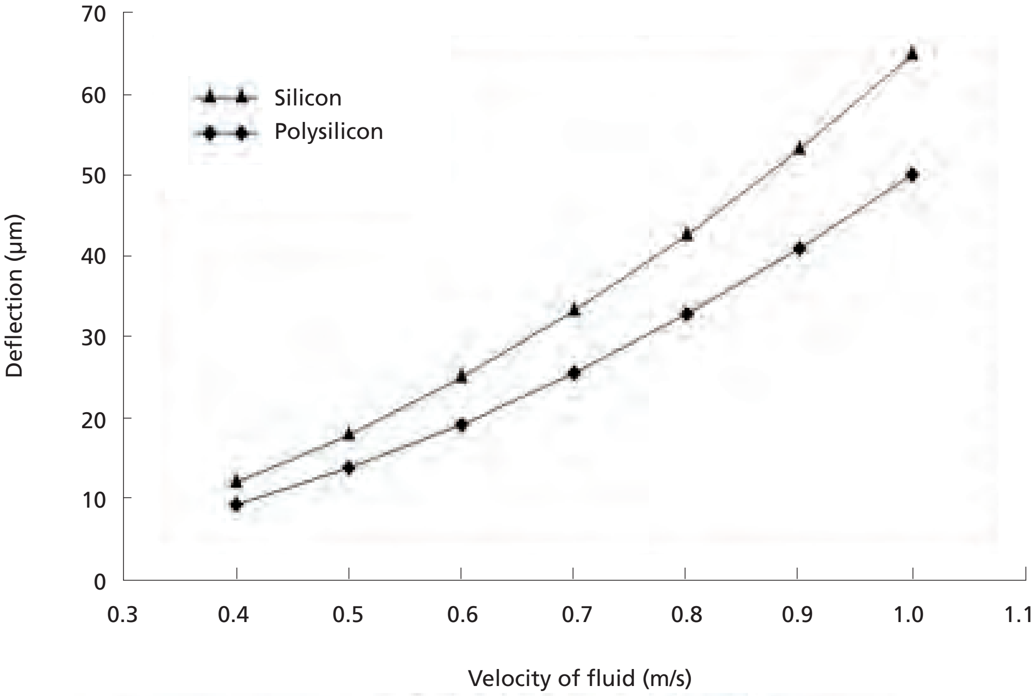


Figure 4. The deflection comparison between PolySi and Si material for the same applied velocity of fluid.

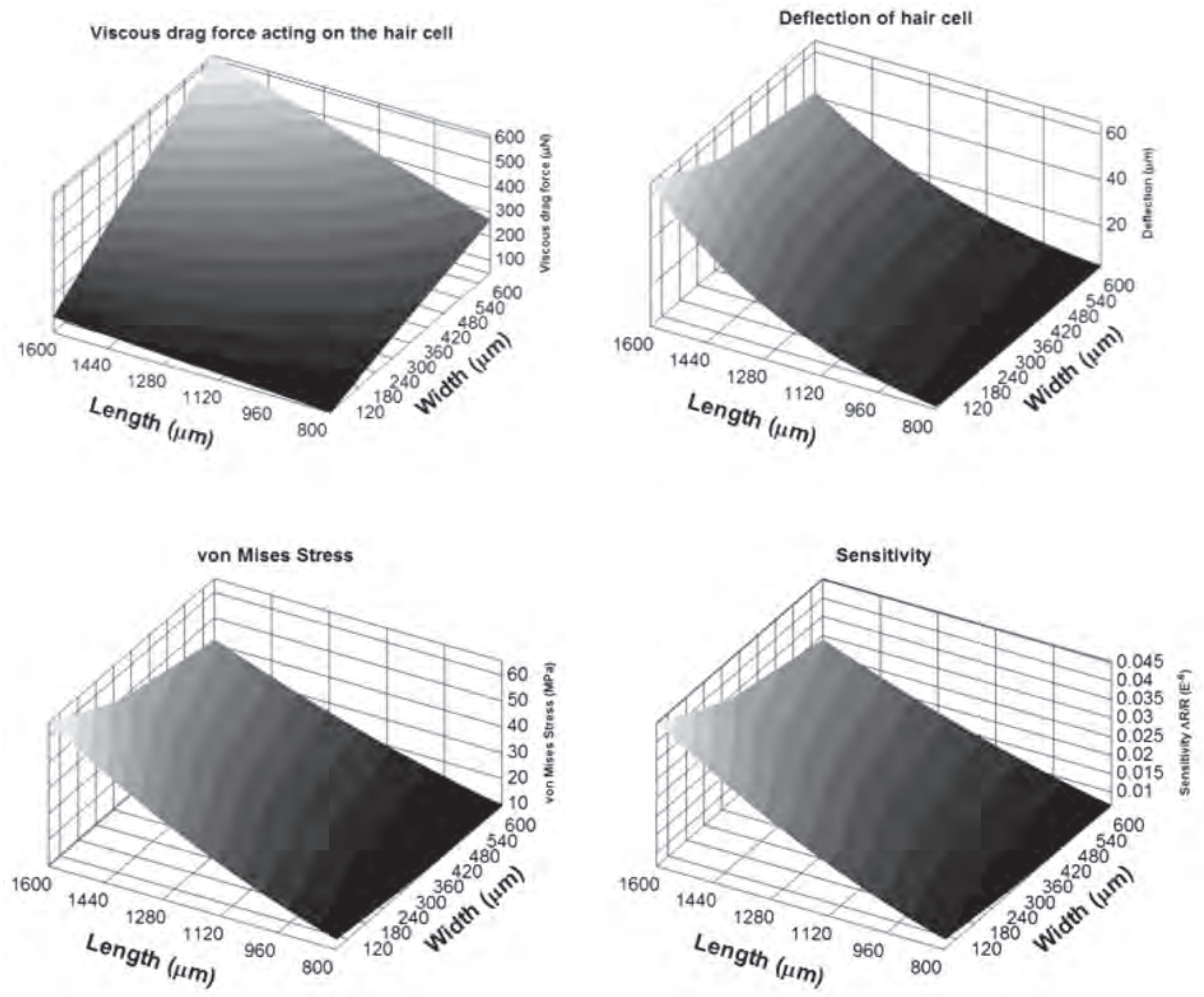


Figure 5. The sensor performance based on the viscous drag force, deflection, von mises stress and sensitivity of hair cell.

the maximum mises stress was 65 MPa. It was different with modified hair cell where the stress was concentrated on the smallest area and the mises stress value was 139 MPa and it was higher than the original geometry. The modified model was simulated for different velocities and we could observe the performance for the deflection and von mises stress as shown in Figure 7. From the figure, we could see the improvement in the modified hair cell where the deflection of the modified hair cell was higher than the original hair cell for the same applied velocity of fluid at 1 m/s. The maximum deflection for the modified original hair cell was 78 µm and 65 µm, respectively. Meanwhile, the maximum mises stress for the modified hair cell was 139 MPa which meant that the hair cell at that condition could not be broken during measurement. Each hair cell geometry had a limitation at certain applied velocity and that limitation would be discussed later.

The other parameter that affected the performance of the hair cell was the angle of the applied velocity of flow. Figure 8 shows the deflection for the original and modified geometry of the hair cell for different angles of flow. The 0º angle which was parallel to the substrate give the maximum deflection to the hair cell. As we could see, the deflection decreased as the angle of flow increased because of the decreasing area that faced the flow. It is recommended to take the measurement in a single direction which flowed parallel to the substrate in order to obtain the maximum performance. Finally, in designing the sensor it was most important to know the limitations of the sensor based on the applied input velocity. The limitation of the hair cell was investigated by applying higher fluid velocity starting at 1 m/s and above. The hair cell could break or fail when the mises stress value exceed the yield strength of the used material. For this sensor, we were using the silicon and its value was 7 GPa. Figure 9 shows the mises stress for hair cell length at 1600 µm and 80 µm width for both original and modified geometry. It showed that the original geometry would break when the velocity of fluid higher than 10 m/s and was different with the modified hair cell

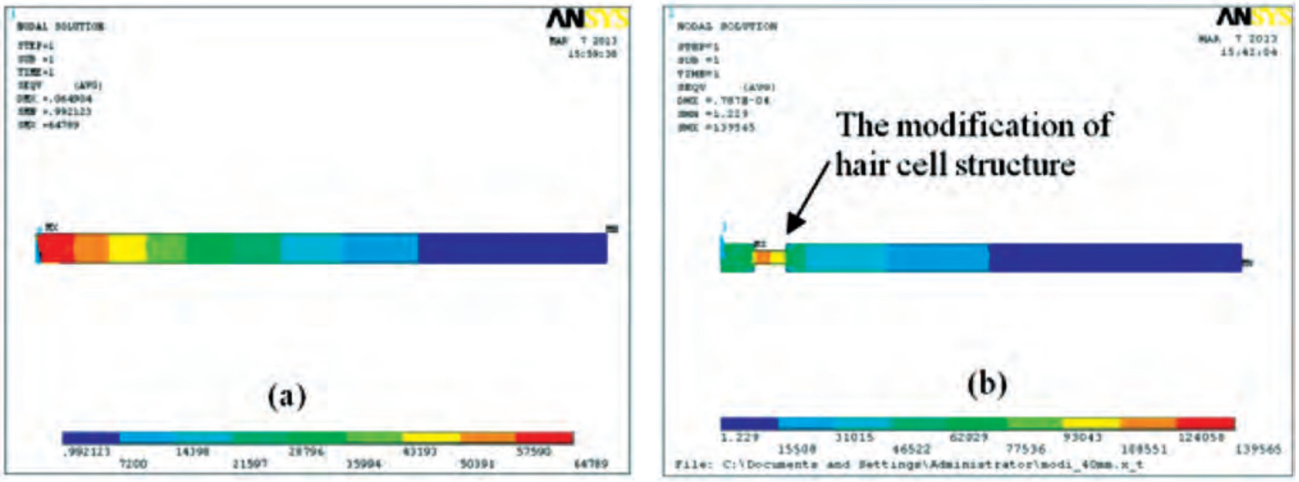


Figure 6. The stress distribution of hair cell in the same applied velocity: (a) The original shape; (b) The modified shape.

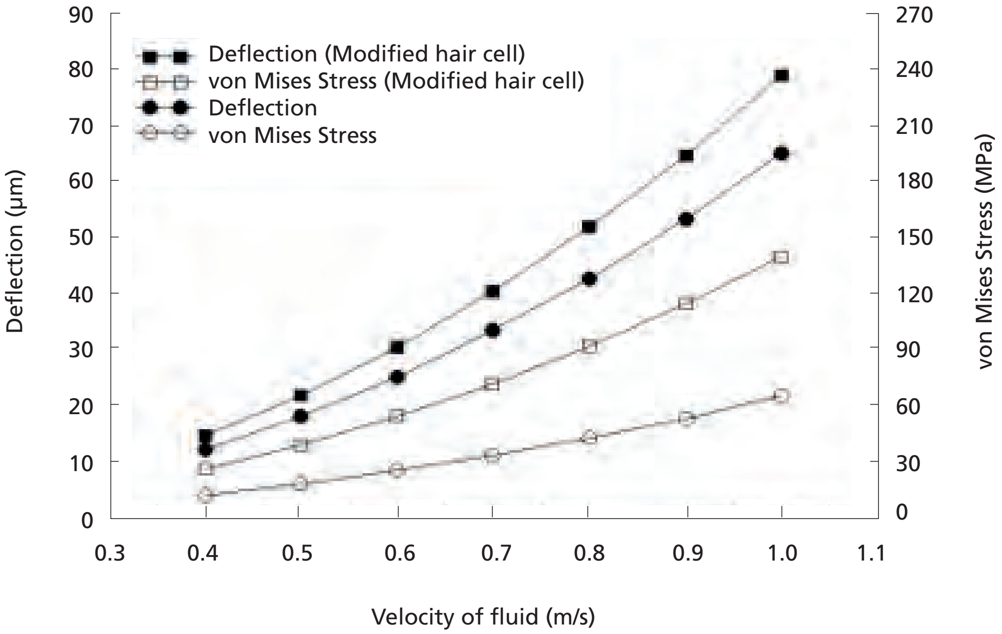


Figure 7. The comparison of deflection and mises stress for original and modified shape for the same applied fluid velocity.

where it only could survive for the 7 m/s velocity. In this paper, we focused on low velocity applications ranging from 0.1 m/s to 1 m/s of velocity. Therefore, the modified hair cell cannot be broken or fail during measurement.

CONCLUSION

The artificial hair cell was successfully simulated using finite volume and finite element methods that solved and analyzed problems that involve fluid flows. Various parameters such as material, width, length, geometry and angle of flow were thoroughly investigated. From the simulation, the silicon-based hair cell with a length and width of 1600 µm and 80 µm respectively, was proposed due to the maximum deflection, mises stress and sensitivity of the hair cell for the same applied fluid velocity. The modification of the hair cell geometry gave the best performance in terms of deflection. The flow that parallel to the substrate means zero angle gave the

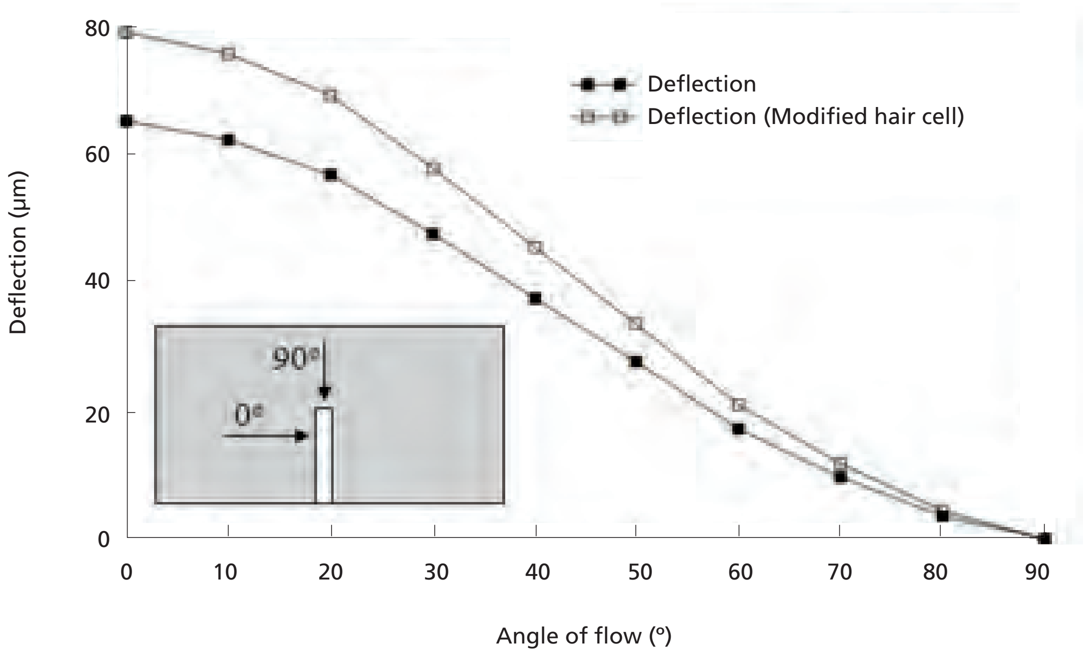


Figure 8. The deflection for different angles of flow applied to the hair cell.

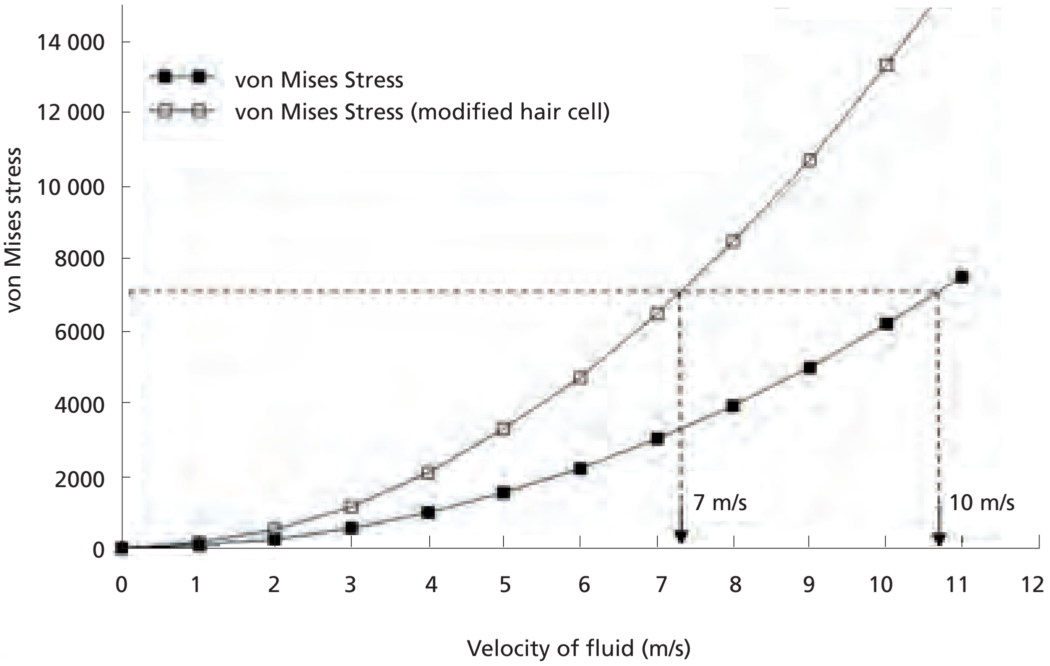


Figure 9. The limitation of the hair cell for the same applied velocity of fluid.

maximum deflection which meant the control of angle was an important parameter for future work. The limitation of the deflection of hair cell was obtained from the mises stress value and the hair cell could not be a failure during measurement when as long as the value of the stress was less than 7 GPa. For future fabrications, the hair cell with modification geometry was proposed to achieve higher sensitivity of the sensor.

ACKNOWLEDGEMENTS

The corresponding author is a USM fellowship holder. This study was supported by a short-term grant (number 304/PELECT/60310023) and also a grant (1001/PELECT/814168). The authors also would like to thank all members of the USM Underwater Robotic Research Group, School of Electrical and Electronics Engineering, for their support and assistance throughout the work.

Date of submission: May 2011
Date of acceptance: March 2013

REFERENCES

Coombs, S 2001 'Smart skins: information processing by lateral line flow sensors', *Autonomous Robots*, vol. 11, pp. 255–261.

Engelmann, J, Hanke, W & Bleckmann, H 2002, 'Lateral line reception in still and running water', *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology*, vol. 188, 2002, pp. 513-526.

Fan, Z, Chen, J, Zou, J, Bullen, D, Liu, C & Delcomyn, F 2002, 'Design and fabrication of artificial lateral line flow sensors', *Journal of Micromechanics and Microengineering*, vol. 12, no. 5, pp. 655–661.

Nawi, MNM, Manaf, AA, Arshad, MR, & Sidek, O 2012, 'Modeling of biomimetic flow sensor based on artificial hair cell using CFD and FEM Approach', in *Proceedings of the International Conference on Simulation of Semiconductor Processes and Devices*, Denver Colorado USA, pp.161–164.

Tao, J & Yu 2012, 'Hair flow sensors: from bio-inspiration to biomimicking— a review', *Smart Materials and Structures*, vol. 21, pp. 1–23.

ASM Sci. J., **7(2)**, 152–165

Systems Perspectives in Agricultural Education, Research and Development: A Vision for Sustaining Food Security in Asia

C. Devendra[1]

Systems perspectives are fundamental in driving technological improvements and yield-enhancing strategies that improve agricultural productivity. These can resolve farmer’s problems and are important pathways for sustaining food and nutritional security for human welfare in Asia. The essential determinants of this objective are the capacity to efficiently manage the natural resource base (land, crops, animals, and water) to resolve constraints to farming systems, and notably the integration of multiple research and development (R&D) issues through all levels of formal and non-formal learning systems. Both formal and informal education systems are important, with the former relating more to universities and colleges, and the latter to the intermediate level. Graduates from this level have the primary responsibility of introducing improved technologies and change to farmers, mainly along production and disciplinary pathways. The traditional research–extension–farmer model for technology delivery is no longer acceptable, due to “top down” extension functions and prescriptions, ineffectiveness to cope with the dynamics of production systems, complex interactions within the natural resources, effects of climate change and globalisation. There are also reservations on the technical capacity and skills of extension agents, constraints identification, methods for technology diffusion and dissemination, and innovative use of beneficial technological improvements that can directly respond to the needs of small farmers, and impact on subsistence agriculture. Agricultural education and systems perspectives are therefore an overriding compelling necessity which transcends prevailing limitations to waning agriculture and rural growth. Their wider recognition and applications provides an important means to maximise efficiency in the potential use; of the natural resources, increase engagement and investments in agriculture, promote ways to become more self-reliant in the development of crucial new technologies and intensification. These together can meet the challenges of the future and overcome the legacy of continuing poverty, food and nutritional insecurity.

Asian farming systems, with their diversity of crops and animals, traditional methods, multiple crop-animal interactions, numerous problems of farmers present increasingly complex issues of natural resource management (NRM) and the environment. Many if not all of these can only be resolved by interdisciplinary R&D, which overcomes a major weakness of many R&D programmes presently and in the past. Improved education and training is a powerful and important driver of community-based participation aimed at enhancing sustainable food security, poverty reduction and social equity in which the empowerment of women in activities that support organising themselves is also an important pathway to enhance self-reliance and their contribution to agriculture. A vision for the future in which improved agricultural education in a systems context can provide the pathway to directly benefit the revitalisation of agriculture and agricultural development is proposed with a three-pronged strategy as follows:

- Define policy for the development of appropriate curricular for formal agricultural education that provides strong multi-disciplinary orientation and improved understanding of the natural resources (land, crops, animals and water) and their interactions
- Organise formal degree education and specialisation at the university level that reflects strong training in understanding of agricultural systems; systems perspectives, methodologies and their application, and
- Define non-formal education and training needs that can be intensified at different levels, including the trainin of trainers as agents of change.

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The agenda and strategies for improving agriculture needs to take a holistic and innovative view of ways to transform the diminishing resource base, potential of rainfed areas to increase food production, improved yield-enhancing technology application including the use of ruminants as the entry point for development, poverty complex, food and nutrition security, and environmental management.

Key words: Agricultural education; training; research–extension–farmer linkages; transfer of technology; systems perspectives and methodologies; farming systems research; transformation; networks; networking; globalisation; Asia

INTRODUCTON

Agricultural education in Asia and the developing world has greatly benefited from the significant technical advances and economic efficiencies that have been achieved in advanced countries. These technological advances have resulted from a combination of several factors, which include *inter alia* concerted R&D adequate funding and investments, improved methodologies, continuing education and extension. Systematic research, innovative interventions, dedicated efforts and enlightened foresight have resulted in five significant achievements:

- Development of improved technologies that continue to drive increased productivity,
- Development of appropriate methodologies that respond to a particular production system or agro-ecological zones
- Education and training that have produced very large numbers of very competent agricultural scientists, technicians and extension agents;
- Engagement and participatory joint endeavours with the private sector, and
- The creation of various advisory services and agencies to facilitate the diffusion of technologies to farmers to instil progress and promote change.

The success story of the Green Revolution in the 1960s and 1980s in Asia serves to reflect the importance of the combined effects. The success involved concerted research to produce new, more adaptable high yielding wheat and rice varieties, coupled with appropriate education and training to sustain production and diffusion of improved technology and knowledge to farmers. The net results were higher yield outputs, increased income and food security, increased efficiency in cereal agronomy, and more enlightened farmers. Similarly, in animal production, major advances have been made in for example, broiler production where hybrid chicks fed with good quality concentrates that promote high efficiencies of feed conversion of between 1.4 –1.6 can be ready for the market in about 35 days at about 2.2 kg per bird live weight; these figures are likely to be improved further.

A historical sweep of the major advances that have been made in agriculture in industrialised countries over the last three decades suggest that together with rapid social and economic development, research, education and extension have made it possible for farmers to greatly benefit from new approaches and technology application. By comparison, the situation is completely different in Asia, where while progress is being made, these are achieved in the face of numerous constraints, various challenging issues, waning agricultural development and progress. These issues are concerned with the following *inter alia*:

- Environment—agro-ecological zones (AEZs), ecoregions, biophysical environment; livestock systems
- Researchers, technicians and extension agents—numbers, scope, focus, level of education, training and skills
- Farmers including landless—numbers, illiteracy, poverty, access to technology and services, willingness to improve, and entrepreneurial skills
- Natural resources—crops, animals, land, water and their interactions, size of farms, land tenure, production inputs, knowledge trends, limitations; environmental services; and
- Services—markets and value chains, access to improved technologies, government services, credits.

These issues emphasise that the process of educating the farmers and the agricultural advisors to improve and promote agricultural production requires their full understanding and empowerment. This is a complex and vast subject and raises several questions. What are the best strategies and improved technological options derived from integrated natural resource management (NRM) for individual AEZs? What kinds of more innovative methodologies are required to ensure adoption and impacts at the farm level? Can the improved technologies be more widely replicated within and outside of individual regions? Is the traditional model of research-extension linkages to diffuse technology outdated, a dilemma and needs revision? What changes are necessary at the formal level to promote understanding of the prevailing issues and their resolution, and at the non-formal ways to ensure social acceptance of improved technologies and innovation? Are prevailing education and training programmes equipped to cope with the threats and effects of climate change on agriculture? Are technologies for the adaptation of crops and animals in place to cope with climate change? These and other issues are directly concerned with agricultural education, training and the changing landscape of agriculture and are considered in this review.

ECONOMIC IMPORTANCE OF AGRICULTURE

The primary function of agriculture is two-pronged. Firstly and most important, it must continue to strive to produce and provide access to reasonably priced food to a rapidly increasing human population. Secondly, agricultural research needs to keep pace with the rapidly rising demand for food through efficiency in sustainable NRM while maintaining or enhancing the integrity of the environment. These functions are associated with the economic importance of agriculture and are reflected in the following:

- Links system components (land, crops, animals and water), small farmers and the landless
- Agricultural growth provides for pro-poor initiatives, development and environmental sustainability
- Enables sectoral links with other sectors such as human health and water
- Links exist to several component industries like food processing and feed milling
- Promotion of nutritional and food security
- Nurtures biodiversity
- Enhances availability of ecosystems services
- Foreign exchange savings from exports e.g. of staples and imports; and
- R&D and innovation link science and society, resolution of problems of farmers, and scale-neutral technology application and adoption

Agriculture is an important sector and contributor to the economies of most ASEAN countries (ADB 2012). Table 1 show that the livelihood of about 45% of the population of ASEAN still depends on agriculture. In terms of the GDP share of agriculture (Gross value added to GDP) in ASEAN, it was shown that agricultural growth in ASEAN is key to equitable economic development for generating employment, increasing exports, enhancing food security and energizing domestic economies. Agricultural growth is particularly effective in reducing hunger and malnutrition, for which reason increased focus given to "*food insecurity*" rather than "*food security*".

About 43%–88% of the total human population depends on agriculture for their livelihoods, of which 12%–93% of the people live in rainfed areas and 26%–84% of the arable land. Some 5%–41% of the agricultural output comes from these areas. Due to low productivity, the shares of total crop and livestock outputs coming from rainfed areas is much lower than the share of the total area under irrigation. Livestock contribute 10% to 45% to the agricultural gross domestic product (GDP) in the developing world, and can be higher if the values of draught power are included in the calculation.

Waning Agriculture

In most countries in Asia, investments and the development of agriculture are on the decline, and the reasons for these are of concern. ESCAP (2008) has reported that the sector involves a large proportion of the region`s surface, provides jobs for 60% of the working population in the Asia-Pacific region, and generates a quarter of the regions' total gross national product (GNP). Associated with these, the reliance on agriculture is especially significant as it provides a number of services to mankind. Agriculture appears neglected, and the share of agriculture in GDP has declined significantly, due to low productivity, resulting in slow growth (ESCAP 2008). In South Asia, growth in agricultural output dropped from 3.6% in the 1980s to 3.0% in 2000–2003. Low product prices and high input prices have also made agriculture less attractive. In East Asia and the Pacific for example, this has dropped from 3.0% in

Table 1. Relevance and importance of agriculture: economic output and its growth in ASEAN (ADB 2012)

ASEAN Countries	Population growth rate (%) (2010)	GDP per capita (m. USD) (2010)	Agriculture GDP per capita (%) (2010)	Agriculture employment (%) (2010)	Poverty ratio (%) (2008)
Cambodia	1.5	797	3.3	80	6.1
Lao PDR	1.7	1048	1.0	70	9.0
Myanmar	1.1	876	–	–	–
Vietnam	1.1	1183	4.0	70	2.3
Brunei Darussalam	2.0	32 648	–	–	–
Indonesia	1.2	2949	3.0	38	3.6
Malaysia	1.3	8373	5.6	14	–
Philippines	1.9	2140	2.6	40	5.5
Singapore	1.8	43 783	3.0	–	–
Thailand	0.6	4613	3.8	42	2.0

the 1980s to a mere 0.1% in 2000–2003. Since then some improvement is apparent, and in South East Asia, during 1990–2010 the share of agriculture gross value-added to the GDP was 21.2% (ADB 2011).

ESCAP (2008) has also reported that while poverty is declining, agriculture alone can lift an estimated 641 million people out of poverty, and that a 1% increase in agricultural productivity would lead to a 0.37% drop in poverty in the Asia-Pacific region. In recent years there has been increasing evidence to underline this important relationship. Increasing attention is being given to revitalize and spur agricultural growth.

SMALL FARMS, SMALL FARMERS, THE LANDLESS AND THEIR KEY DESCRIPTORS

The subject of small farms, their importance and ways to increase their contribution in Asia has been published extensively (Devendra 1983; 2010), including also the World Bank (2003). What is especially important is sensitivity to their descriptors: *deprivation, subsistence, illiteracy, survival*, and due to globalisation additional key word are *vulnerability*. At stake and at the heart of these issues is human dignity (Devendra 2010).

THE GLOBALISATION OF AGRICULTURAL RESEARCH AND DEVELOPMENT

The globalisation of agricultural R&D is an inevitable trend within the broader landscape of economies and sciences. Its key features include international trade liberalisation, opening up of economies, and a free flow of technology, information, labour and capital. It implies moving away from traditional structures, organisational elements and static situations, change is inevitable, but the effects on agriculture are not very clear and need more analyses. Its scope in agriculture extends to animals, crops, markets, owners, producers and consumers. In a globalising world, different countries and their people are likely to become more vulnerable, which implies that the implications and consequences will need careful monitoring.

The potential benefits to agriculture are not very clear, although there is awidespread views that globalisation is beneficial for food security. Agricultural R&D must serve this objective, in which the search for the yield potential is fundamental. Nothing is more important than realising this goal, the focus and foundation for which will continue to be biotechnology and genetic engineering — in this context of meeting the challenge of food availability now and in the future, Swaminathan (1996) has emphasised the importance of science to work in partnership with farmers in new innovative approaches including the following:

- Transforming the most marginalised farmers of the world into agents for poverty alleviation and environmental management
- Production of more food from a diminishing resource base requiring agricultural technologies and management systems; and
- Development of a systems approach marshalling the combined coordinated efforts of several disciplines and empowerment of the poor, especially women.

AGRICULTURAL EDUCATION AND MANPOWER TRAINING

Formal Training

Mahadevan (1984) distinguishes between two levels of training in agriculture: formal degree level training at the university, and an intermediate level training in agricultural colleges.

The first category is mainly from first degree holders who are seldom effective for advisory or other extension work. The training is largely equipped and concerned with the development of technology, when often there is a greater need for them to be involved with the transfer of technology and how to get farmers to employ technology change. The intermediate level training produces persons who have the primary responsibility of introducing change to farmers.

Formal training and the development of technology places much emphasis on disciplines. The type of research was also much the same with reference mainly to commodities such as crops and with animals to their products, such as meat, milk and eggs — with animal science research for example; the following observations are evident (Devendra 1996):

- Disciplinary research was dominant in which animal nutrition and breeding were prominent
- Fundamental and applied research were most common
- Technology development and availability was far in excess than the utilisation of research results. There was also much duplication of research especially in animal nutrition
- Research priorities were often not needs-based and not targeted to resolve constraints on farms
- Technology delivery mechanisms were often not clear
- Systems approaches were rarely used in the research agenda; and
- Research to link and serve development were generally weak and neglected (Devendra 2010).

An important observation concerning these trends is that systems perspectives and systems methodologies that deal with NRM, holistic systems and rural communities and the environment are scarcely considered in the formal curricular in most countries. Indonesia, the Philippines and Thailand may be an exception to this. The looming subject of climate change and its implications remains unconsidered as a subject in most quarters.

Non-formal Training

Non -formal training is very common and is widespread in agriculture. It is conducted at several levels in the colleges and universities, government institutions, as well as in the rural areas at the provincial, district, sub-district and farm levels. The rationale and justification for particular training is determined by prevailing circumstances, constraints or particular needs. Often this is driven by the formulation of new projects or limitations within an ongoing project and can be *ad hoc*. On the other hand it can also be a regular affair to ensure the success of a project.

Examples of common types of training at various levels are as follows:

At the research station and university level

- Prerequisites and rationale for project formulation
- Problem identification and priority setting
- Participatory methodologies and team building
- Systems perspectives
- Development and use of questionnaires
- Field measurements
- Research–extension–farmer linkages
- Coping with constraints.

At the farm level

- Listening to and understanding the farmer
- Developing confidence
- Data collection and storage
- Dealing with feedback
- Resolution of problems
- Promoting wider adoption and spillover effects
- Development of co-operatives and self-help groups.

The list can thus be long and additive, but careful monitoring and establishing priorities will be important to ensure progress and impact. Much of the local training is undertaken through various government and local groups, examples of which are as follows:

China — Provincial and district offices
India — Krishi Vigyankendras (KVKs or farmer knowledge centres, and farmer's training centres)
Indonesia — District and sub-districts (Kechematan)
Philippines — Local government units (LGUs) and focus groups
Korea — Provincial rural development administration (PRDAs)
Malaysia — Farmers organisations
Thailand —Provincial and district offices
Vietnam —Provincial, district and hamlet offices.

Training of Trainers

An important aspect associated with both formal and informal training concerns the training of trainers as agents of change. Training and retraining is essential, to be updated with current knowledge and trends, and participatory ways of dealing with farmers. The essential ingredients for this include the following:

- Understanding the process of technological change
- Maintaining close links with research scientists and subject matter specialists
- Skills in effective communication of new technologies
- Understanding the approaches to work successfully with farmers; and
- Capacity to cope and deal with feedback.

Empowerment and Self-reliance

Central to all education and training is empowerment. Empowerment enables people to have control of their own resources and set their own agenda, access to information and services, and a capacity to determine self-reliance — that is, the ability to make independent decisions and be resourceful with minimum dependence on external inputs.

The intent to manage and use their own resources, and articulation of this is a direct result of empowerment and self-reliance. In this context it is instructive to summarise the significance of empowerment in a case study on the uniquely success story of ‘Operation Flood’ in India. This is as follows:

- The producers of large supplies of buffalo milk from the rural areas of the Kaira district to Bombay (now Mumbai) were disturbed by the unfavourable price and market conditions they were exposed to.
- In January 1946 they met and established resolved to establish Milk Producers' Societies in each village of the Kaira district to collect milk from their members. The Kaira Milk co-operatives consists of a two-tier system with the District Milk Producers Co-operative at the central level, and more than 850 village Milk Producers Co-operative Societies at the village level
- The formation of these provided apposition of strength to argue for higher prices of milk in the strong Bombay market, as well as marginalise the middlemen who exploited the marketing system
- Each Co-operative Society maintains a Milk Collection Centre with trained staff. Milk is received morning and evening, tested for quality, and payment is made for the milk delivered at the previous collection

- Today, the Kaira District Co-operative Milk Producers Union is Confederation supplying milk to the dairy plant owned by the producers, and for the various products: butter, cheese, ghee, milk powder, baby foods and chocolate. AMUL the trade name under which the products are marketed is well known throughout India. AMUL is the acronym for Anand Milk Union Limited, as well as ‘beyond price’ in the local language.
- A comparison of incomes from buffalo milk and cow milk in villages with and without cooperatives indicated that the respective figures were 51% and 62% in the former (Sivastra 1970)
- The AMUL complex continues to demonstrate the benefits of integrated education, research, extension and training activities, and the importance of co-operatives
- The Co-operative Dairy Development in Anand has brought about profound social and economic impacts. The whole fabric of rural life has been enhanced along with increased milk supplies and nutritional well-being, higher income, household stability, village
- Cohesiveness, increased security and. increased employment opportunities. In the words of the genius and mentor Dr V.R. Kurien “dairying is an instrument of social and economic change”.

The Anand model of India's ‘Operation Flood’ integrates many important elements. It involves some 13 million farming families and processing about 90 million kg of milk per year, making farmers shareholders of the whole chain of marketing and processing of milk, with resultant improvements to their livelihoods. It is worthy of note and emulation.

DEVELOPING THE RESEARCH AND DEVELOPMENT FRAMEWORK

A useful prerequisite ahead of the application of FSR methodologies is that of developing a sound research framework. This is achieved initially with a few research questions that are relevant to the situation, as well as provide some indication of having the capacity to provide solutions to such complex interacting issues as AEZs, NRM, environment and people. These questions are as follows:

- Problem definition is the start and this means the following: what is the researchable issue; does it have the potential to generate new information, and is it worth the resources that are needed for this purpose?
- The R&D activities are dynamic, subject to constant critique, and the results are economical beneficial and socially acceptable; and
- Do the resulting improved technologies have the potential for wide replication, scaling up, and impact on increased productivity and improved livelihoods?

RESEARCH—EXTENSION—FARMER LINKAGES: THE ASIAN EXPERIENCE

Research–extension–farmer linkages are synonymous with technology transfer. It is the traditional model that is used for the technology delivery pathway. Public sector extension services and their efficiency vary between countries and programme focus. Presently the subject constitutes a dilemma about its scope and effectiveness.

Of the three words in the chain, the most contentious one is extension. Several issues are involved as follows:

- Concurrently, there is increasing emphasis that public extension services are inadequate to respond to the needs of farmers in many developing countries (Fleischer *et al*. 2004)
- There is lack of clarity in the meaning of the term extension, as well as systems and structures that deal with it
- Implies a partnership and a unified public sector service where technology transfer in which talking and persuasion are key words
- The participatory approach of extension helps to address problems on the farm as well as their resolution
- Variations to the approaches exist. In Indonesia for example, 17 Assessment Institutes for Agricultural Technology (AIAT) have been created since 1995 in decentralised and regional participatory efforts involving researchers, extension agents, farmers and local government officials.
- Currently, extension involves numerous ways: increase production to marketing arrangements. Presently extension orientation is being expanded to include innovative structural, funding and managerial arrangements (Rivera & Sulaiman 2009)
- There is a widespread view that public extension services are no longer adequate to respond to the needs of farmers in many developing countries (Fleischer *et al.* 2004)
- Additionally, there are reservations about the technical capacity, commitment, skills of the extension agent, understanding of constraints and priorities for development, and the methods used for technology diffusion and beneficial improvements.

These issues together suggest that the demands on, and orientation of, extension are many and of particular concern is that extension appears to be detracted from the primary function of technology application to spur development. These concerns raise several questions which include:

- What are the priorities of extension to assist farmers?
- How does extension discern between the needs of different farmers and communities?
- Can extension services cope with farmer's activities and the national development goals?
- Is the traditional technology transfer approach adequate to deal with the more diverse, risk-prone rainfed environments with their considerable biophysical variations?
- Is extension fully familiar with the steps in farming systems research, technology driven inputs and also impacts?
- Is the extension arm effective to deal with new and emerging issues such as mitigation and adaptation options in climate change and the dynamics of agriculture?
- Are the extension services sufficiently trained through formal agricultural research systems, technology transfer processes, and related policy institutions; and
- Are mechanisms in place to retrain extension agents to keep up with changing times?

TRANSFORMING AGRICULTURAL EDUCATION: THE SYSTEMS PERSPECTIVES

In the light of the many foregoing concerns, transforming agricultural education from the traditional methods is necessary. It is now widely acknowledged that systems perspectives and systems approaches are fundamental to enhance NRM, poverty, food insecurity and issues of the environment. While strong disciplinary training is essential, detailed but a more rounded view is necessary that enables the formally trained degree holder to skills and ways of dealing with these issues and their interactions in holistic systems. This is especially the case with Asian farming systems with the diversity of crops and animals, traditional methods of farming, multifunctional contribution of animals, multiple crop-animal interactions, and numerous problems of farmers, all of which present complex issues that cannot be resolved easily. Specific problems cannot be resolved by a single discipline or in a disciplinary context alone, which has been a major weakness of many research programmes involved with NRM in the past.

A vision and agenda for the future of improved agricultural education that can directly benefit agriculture is a proposed three-pronged strategy as follows:

- Define policy for the development of appropriate curricular for formal agricultural education that provides strong multi-disciplinary orientation, systems perspectives and systems methodologies
- Organise formal degree education and specialisation at the university level that reflects strong training in systems perspectives and understanding of agricultural systems; and
- Non-formal education and training needs to be intensified at different levels, including the training of trainers as agents of change.

Community-based participation, interdisciplinary perspectives and deep understanding of farmers' aspirations and development issues in the changing landscape of agriculture is necessary. Improved education and training that is dynamic and futuristic transcend traditional 'top-down' extension functions in shared impact-oriented progress and enhanced agriculture.

Systems perspectives ensure that there is a well organised and sequential R&D process that looks at issues in holistic terms. More importantly, it overcomes the 'top down' approach in which very seldom is the extension agent involved with the R&D agenda and prioritisation of the on-farm activities. Systems perspectives and systems approaches that directly link researchers, extension agents and farmers overcomes these limitations and is much more holistic and impact-oriented. The research–extension–farmer linkages need to be enhanced and strengthened with systems perspectives and methodologies to be of greater assistance to farmers. This is the Asian experience, and the sections below describe how these have been used in several case studies in Asia.

METHODOLOGY FOR FARMER SYSTEMS RESEARCH

Farming systems research (FSR) is central to efficient NRM in that it provides a well defined approach and methodology that is based on careful problem identification and their resolution. FSR owes its origin to cropping systems research and methodologies which were mainly developed in Asia and Latin America. It started with a focus in the early 1970s on agronomic management of one crop — mainly rice, to the management of combinations of crops over space and time (Zandstra *et al*. 1981). In 1984, the animal component was added to cropping systems research, paving the way for FSR. The key features of FSR are that it seeks to provide a good understanding of the farming systems and practices; is needs-based; has systematic methodology; is multidisciplinary; involves the participation of farmers, researchers, community, extension agents, and development agents; and is on-farm.

The methodology for FSR follows several distinct step and these have recently discussed in detail (Devendra 2010). The individual sections have described in detail (Devendra

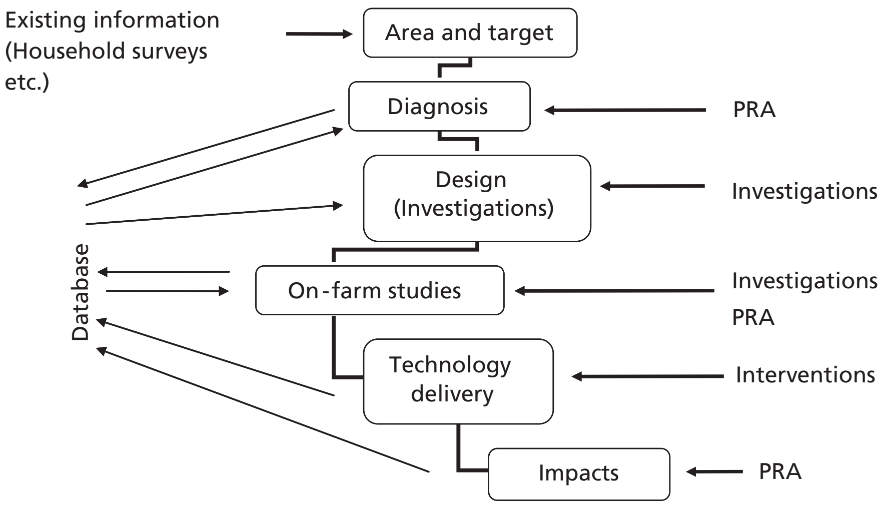

Figure 1. Methodology for farming systems research (FSR).

2011). Farming systems are the practices of agriculture in numerous ways. A myriad of such systems exist, and they are different in different locations and countries, and vary according to the types of agro-ecological zones, biophysical environment, ecoregions, and the extent and quality of the natural resources available. Farming systems are open systems with inputs from, and outputs to, their environment as follows:

- Site selection
- Site description and characterisation (Diagnosis)
- Planning of on-farm research
- On-farm testing, validation of alternatives and lessons learnt
- Diffusion of results; and
- Impact assessment (Plates 1 and 2).

The systems approach needs to be supported by a few other important requirements:

- Recognition of the importance of interdisciplinary participatory approaches
- Formulation of research programmes that have community-based participation to set a common agenda and create ownership. It should involve both production and post-production systems
- Programmes that are needs-led, and have institutional and structural commitment
- Establishment of effective participatory planning, inter-institutional coordination and collaboration, research management, dissemination of information, and resolution of feedback issues
- Long-term commitment to achieving impacts; and
- Education and training in agricultural systems and systems methodologies at various levels.

Figure 1 illustrates the steps involved in farming systems research.

GENDER EQUITY AND EMPOWERMENT IN WOMEN

Associated with FSR is the issue of gender equity and empowerment of women. Women make such an important but underestimated contribution in agriculture, from participating in rice production and cash crops, to raising animals like pigs, poultry and dairy cows. The management of small animals and occasionally large ruminants. They are responsible for food security for their families, the stability of the farm households, and possible participation in national development goals. Women thus play an important role is their contribution to the three pillars of food security (Brown 2001): food production; food access and food utilisation (Plate 3).

Unfortunately, the very poor and the poorest of the poor are women and children. Greater gender equality depends on many factors and includes roles and responsibilities, rights of ownership, control over assets (natural resources and information), food production, and food access and food utilisation. Gender equality is also exacerbated by waning and low priority for agriculture. However, there is increasing evidence that empowerment is central to women's control over productive assets, decision making processes in agriculture, bargaining power, access to livestock services and markets, and decision making increased participation in social and credit programmes and networking. Empowerment of women in activities that support organising themselves promotes greater confidence and self-reliance as follows:

Plate 1. Trainers are the agents of change. The training of trainers is thus an important element in farming systems research and development. Photo shows local project participants engrossed in understanding the project objectives, implementation, monitoring and impacts in Bixi Xiang, Nanjian Couny in China (C. Devendra).

Plate 2. Diiscussion on implementation, monitoring feed back and lessons learnt throughout the project is important. The photo shows a discussion session in progress in Bin Phouc Province municipality in South Vietnam (C. Devendra).

Plate 3. Empowerment enables women to have more control over the use of productive assets, decision making and contributes to the stability of households. It also promotes greater equality between the genders and helps women gender analyses which is an important strategy to revitalize the contribution of women in animal agriculture. Photo shows women owners of goats keenly discussing goat husbandry and potential improvements in Ladavir, Nepal (C. Devendra).

- Unfortunately, these women and children are part of the very poor and the poorest of the poor are women and children. The role of women in agricultural production and in the marketing of the products continue to be underestimated
- A key issue is the consistent tendency by women to reinvest economic gains into their families and the stability of the households more than men
- Small animals (chickens, ducks, goats, sheep, pigs, quails and rabbits) are almost exclusively raised by women and children due very closely to their ownership and management
- Their social status was improved due to their significant contribution to household food and nutritional security
- The contribution to management include, herding, grazing, feeding and watering, housing, addressing animal health problems and also marketing
- During droughts and migrations, women take on the added responsibility of collecting supplementary fodders for the animals and often walk long distances
- In Bangladesh, goats distributed to such women provided more security and more importantly, additional income of between USD35.5 – USD134.0 to distressed women with an initial investment of a doe costing about USD11
- In Nepal, 60% of the total rural credit to women was invested in livestock especially goats and the loan repayment rate was approximately 100%
- Gender equality and the role of women in agricultural production and in the marketing of the products continue to be underestimated
- Factors that impact on gender equality relate to roles and responsibilities, rights of ownership, women`s control over assets (natural resources, information and health), access to livestock services and markets, and decision-making powers.
- There is increasing evidence that empowerment is central to women's control and use of productive assets, bargaining power, increased participation in social and credit programmes, and networking, which in turn leads to improved health, welfare and stability of households.
- Empowering and promoting greater equality between the genders and helps women in ways of organising themselves
- There needs to be much better understanding of the role and contribution of women in farming systems, including women's control and use of productive assets, decision making processes in agriculture and contribution to food security and poverty reduction; and

Table 2. Biological responses (kg/head/day) and profit margins (USD/head/day) due to supplementation in smallholder farms in five countries in South East Asia (Devendra 2005)

Technology Options	China		Indonesia		Philippines		Thailand		Vietnam	
	Biological response[1]	Profit margin (US$)	Biological response[1]	Profit margin (US$)	Biological response[1]	Profit margin (US$)	Biological response[1]	Profit margin (US$)	Biological response[1]	Profit margin (US$)
1. Multi-nutrient block licks (MNBL)[2]	Cattle + 0.187 Goats + 0.030	Cattle + 0.33 Goats + 0.05	Cattle + 0.215	Cattle + 0.43	Cattle + 0.063	Cattle + 0.09	Milking cows + 2.0	Milking cows + 0.42	–	–
2. Concentrate formulated from local feed resources for feeding young animals	Calves + 0.208 Kids + 0.012	Calves + 0.18 Kids + 0.01	–	–	–	–	–	–	–	–
3. Use of cassava hay as a partial substitute for commercial concentrates for dairy cows	–	–	–	–	–	–	Save 3.0 kg concentrates + 1.2 kg milk	+ 0.57	–	–
4. Cassava peelings + mineral mix	–	–	–	–	–	–	–	–	+ 0.227	+ 0.38

[1] Difference due to supplementation

[2] MNBL is a feed supplement formulated from molasses, proteins and minerals from local sources and a binding agent (usually cement), to make nutrients available continuously. It is especially useful in the dry season and is easy to prepare. Farmers are already producing this at low cost in China, Philippines, Indonesia, Thailand and many other developing countries.

Using the above on-farm research results, the implications are:

(i) The use of UMB licks for cattle in China, Indonesia and the Philippines, for a period of 120 days during the critical dry season resulted in additional income per animal of between USD10.80 to USD51.60, after discounting all costs associated to the nutritional intervention. When these were used for milking cows, the additional income per cow per month was USD12.60.

(ii) In China, the use of local resources in the formulation of concentrates for calves, fed for 90 days resulted in an additional income of USD16.20 per animal. In the case of kids, this practice resulted in an additional income of only USD0.90/animal in 90 days.

(iii) In Thailand, the use of cassava hay to partially replace commercial concentrates for dairy cows resulted in savings of USD9.90 per cow per month in feeding costs, and an additional income of USD7.20 per cow per month, due to the increase in milk production.

(iv) In Vietnam, the use of cassava peelings and minerals to supplement grazing cattle for a period of 120-days resulted in an additional income of USD45.60 per animal, after discounting costs of supplementation. Additionally, this is an option to utilize a by-product of starch production that was contributing to pollution.

- Gender analyses are therefore a must in strategies to revitalise the contribution of women in animal agriculture.

IMPROVED TECHNOLOGY APPLICATION TO INCREASE PRODUCTIVITY

There exist dozens of potentially important technology applications that can spur yield-enhancing agricultural development. The overriding need is to apply these large scale on-farm to demonstrate impact using systems methodologies With animal feeds for example, the strategies to ensure that the available feeds can match the animal requirements in developing sustainable all year round feeding systems.

Several examples exist and include *inter alia* the following extensively reviewed subjects. Foremost among these are the reviews on improved feed utilisation (Preston & Leng 1981; Devendra & Sevilla 2001; Devendra 2009; Preston 2009; Devendra & Thomas 2010; Devendra, Sevilla & Pezo 2011; Devendra & Leng 2011). Table 2 serves as an example to reflect of supplementation on animal performance.

- Feed resources: non-conventional feeds (Devendra 1992; Devenra & Leng 2011)
- Crop residues: Preston & Leng 1984; Raghavan, Krishna & Reddy 1985; Mudgal & Pradhan 1998; Egan 1989; Cungen *et al*. 1999; Renard 2009; Preston 2009; Devendra & Thomas 2010)
- Oil palm biomass and by-products (Devendra 2005; 2009)
- Intercropping with cereal crops e.g. rice—*Susana rostrata*, alley cropping and relay cropping (Carangal & Sevilla 1993)
- Food-feed cropping systems e.g. cassava-cowpea, rice-mungbean-siratro-rice (Devendra Sevilla & Pezo 2011)
- Forage production on rice bunds e.g. *Sesbania rostrata* (Sturr *et al.* 2011)
- Three-strata forage system (Nitis *et al.* 1990)
- Harvesting aquatic plants (e.g. duckweed) from waste water (Preston 2009);
- Sloping agriculture land technology (Laquihon *et al.* 1997)
- Crop–animal–fish integration (Devendra 1996; Cagayan *et al*. 1997; Nguyen & Nguyen 1997; Devendra & Thomas 2010)
- Reduced methane emission by feeding nitrate salts (Leng 2008; Le 2003, Trinh *et al*. 2008; 2009).
- Listening to farmers (Devendra 2006)
- Negative effects of climate change; reduced animal performance: Parsons *et al*. 2001; King *et al*. 2006; on crops: Pang *et al*. 2001
- Investment on agriculture — Fan, Hazell & Thorat 2000; Fan, Zhang & Zhang 2000; Pardey & Bentema 2001
- Rainfed areas and animal agriculture (Devendra, 2012)

An overriding constraint across ecorgions and AEZs concerns the feed resources without excepton. It is particularly imperative to view feed resources from a farming systems perspective and also consider the following interrelated issues (Devendra and Leng 2011):

- Knowledge of the totality and quantitative availability of feeds (forages, crop residues, AIBP and NCFR)
- Understanding their physical characteristics, nutrient composition and digestibility
- Potential inclusion and efficiency of use in production systems
- Noting that the cost of feeding as percentage of total production costs, which account for about 50%–60% in ruminants (meat and dairy), and 65%–80% in non-ruminants (meat and eggs) in intensive production systems, and
- Self-reliance in the use of feeds.

STRENGTENING TRANS-REGIONAL LINKAGE

Very good opportunities also exist to strengthen trans-regional links, access to various educational institutions in Malaysia, Indonesia and the Philippines across-disciplines. These include the following inter alia:

- Application of appropriate and proven productivity-increasing technologies in similar eco-regions and locations with similar climates. For example, humid South East Asia and West Africa have much in common in crop-animal systems (Defender & Pezo 2004)
- Exchange of information
- Exchange of scientists of, teachers, scientists, extension agents and technicians
- Intensive networking and personal contact
- Promotion of regular joint meetings to share experiences, lessons learnt, and discusses common problems; and
- Promotion of reciprocal visits by farmers.

CONCLUSIONS

Systems perspectives in agricultural education, R&D are key determinants of sustaining productivity and prosperity. Due to the complexity of the issues, this will require the integration at effort and interdisciplinarity, at all levels of formal and non-formal learning systems, from school to college and university as well across systems of research, technology transfer, policy institutions and extension. Educating agriculturists and their advisors calls therefore for an understanding of needs-based priorities, technology development and the process of technology transfer, adoption and impact.

Asian farming systems with the diversity of crops and animals, traditional methods of farming, low input systems, the multifunctionality of animals, multiple crop-animal interactions, have numerous problems, are increasingly complex, multi-scale, and require concerted interdisciplinary R&D efforts. FSR with its well defined approach and methodology provides methodologies to resolve these issues, and is based on careful problem identification, their resolution, productivity and agricultural growth. Technology transfer has its greatest challenge with small farmers and the landless on account of their conservativeness, illiteracy, traditional low input use outlook, and resistance to change. Listening to farmers their environment and low input systems is essential, including the socio-economic consequences of change induced by technology transfer Improved agricultural education and training which is dynamic and futuristic. is necessary to transcend traditional 'top-down' extension functions or specialised disciplines that depend mainly on talking and persuasion. Community-based participation backed by interdisciplinary systems perspectives can promote major improvements in the contribution from agriculture.

Date of submission: February 2013
Date of acceptance: March 2013

REFERENCES

ADB (Asian Development Bank) 2012, *Food security and poverty in Asia and the Pacific: key challenges and policy issues*, Manila.

Brown, LR, Feldstein, H, Haddad, L, Pena, C & Quisemberg A 2011, 'Generating food security in year 2020. Women as producers and gatekeepers and shock absorbers', in *The unfinished agenda*, eds P Pinstrup-Anderson & P Pandya-Lorch), International Food Policy Research Institute, Washington, DC, USA.

Cagauan, AG, Van Hove, C, Orden, EA, Ramilo, NM, & Brankaert, RD 1996, 'Preliminary results of a case study on integrated rice-fish-azolla-ducks system in the Philippines', in, *Proc. Symp. on Integrated Systems of Anim. Prod. in the Asian Region*, eds H Hayakawa, M Sasaki & K Kimura Chiba, Japan, pp. 35–62.

Carangal, VR & Sevilla, CC1993, 'Crop-animal systems research in Asia', in *Proc. V11th Wrld. Conf. Anim. Prod.*, Edmonton, Canada.

Conroy, C 2005, *Participatory livestock research: a guide*, ITDG Publishing, Bourton on Dunsmore, Great Britain.

Cungen, LSZ, Tingshuang, G & Waldron, S 1999, *The "Straw for ruminants" project in China*, Agricultural and Natural Resource Economics Discussion Paper 4/99, School of Natural and Rural Systems Management, University of Queensland, St. Lucia, Australia.

Devendra, C 1992, *Non-conventional feed resources in Asia and the Pacific*, 4th edn, RAPA/APHCA Publication, No. 4, FAO Regional Office, Bangkok, Thailand.

Devendra, C 1996, 'Overview of integrated, animals–crops–fish production systems: achievements and future potential', in *Proc. Symp. on Integrated Systems of Anim. Prod. in the Asian Region,* Chiba, Japan eds H Hayakawa, M Sasaki & K. Kimura.

Devendra, C 1997, 'Crop residues for feeding animals in Asia: technology assessment and adoption', in *Crop Residues in Sustainable Crop Livestock Farming Systems,* ed C Renard, Commonwealth Agricultural Bureau, Wallingford, UK.

Devendra, C 2005, 'Improvement of crop-animal systems in rainfed agriculture in South East Asia', in *Proc. Int. Conf. on Livestock-Crop Systems to Meet the Challenges of Globalisation*, vol. 1, eds P Rawlinson, C Wachirapakorn, P Pakdee, & M Wanapat, Khon Kaen, Thailand, pp 220–231.

Devendra, C 2006, 'Listening to farmers: participatory approaches for developing goat production', in *Proc. 6th Int. Symp. on Agriculture, Biotechnology and Environment*, Daegu, Korea.

Devendra, C 2009, 'Intensification of integrated oil palm — ruminant systems: enhancing productivity and sustainability in South East Asia', *Outlk. Agric.*, vol. 38, pp. 71–81.

Devendra, C 2010, '*Small farms in Asia. Revitalising agricultural production, food security and rural prosperity*, Academy of Sciences Malaysia, Kuala Lumpur, Malaysia.

Devendra, C 2012, 'Rainfed areas and animal agriculture in Asia. The wanting agenda for transforming productivity growth and rural poverty', *Asian-Aust. J. Anim. Sci*. vol., 25, pp. 122–142.

Devendra, C & Leng, RA 2011 Feed Resources for Animals in Asia: Issues, strategies for use, intensification and integration for increased productivity, *Asian-Aust. J. Anim. Sci*., vol. 24, pp. 303–321.

Devendra, C & Pezo, D 2004, 'Crop-animal systems in Asia and Latin America: characteristics, trends and emerging challenges. Comparison with West Africa', in *Proc. Int. Conf. on Sustainable Crop-livestock Production for Improved Livelihoods and Natural Resource Management*, eds TO Williams, S, A Tarawali, P Hiernaux, & S Fernandez-Rivera, International Livestock Research Institute (ILRI), Nairobi, Kenya.

Devendra, C & Thomas D 2001, 'Crop-animal interactions in mixed farming systems in Asia', *Agric. Systems*, vol. 71, pp. 27– 40.

Devendra, C, Sevilla, C & Pezo, D 2001, 'Food-feed systems in Asia', *Asian- Austral. J. Anim. Sci*., vol. 14, pp. 733–745.

Devendra, C, Thomas, D, Jabbar, MA & Kudo, H 1997, *Improvement of livestock production in crop-animal systems in the rainfed agro-ecological zones of South East Asia*, International Livestock Research Institute, Nairobi, Kenya.

Devendra, C, Thomas, D, Jabbar, MA & Zerbini, E 2000, *Improvement of Livestock Production in crop-animal systems in agro-ecological zones of South Asia*, International Livestock Research Institute, Nairobi, Kenya.

Egan, A 1989, 'Living with, and overcoming limits to, feeding value of high-fibre roughages', in *Draught animals in rural development*, eds D Hoffman, J Nari, and RJ Petram, *ACIAR Proc. No 27*, Australian Centre for International Agricultural Research, Canberra, Australia.

Economic and social survey of Asia and the Pacific (ESCAP) 2008, *Sustaining growth and sharing prosperity*, Bangkok, Thailand.

Food and Agriculture Oganisation 2012, *The state of food and agriculture*, eds S, Fan, P, Hazell & S Thorat; 'Targeting public investments by agroecological zone to achieve growth and poverty alleviation goals in rural India', *Food Policy*, vol. 20, pp. 411–428.

Fan S, Zhang L & Zhang X 2000, 'Growth and poverty in rural China: the role of public investments', *Environment and Production Technology Division Discussion Paper No. 66*, International Food Policy Research Institute, Washington DC, USA.

King, JM, Parsons, DJ, Turnpenny, DJ, Nyangaga, JA, Bakari, P & Wathes, CM, 2006, 'Modelling energy requirements Friesians in Kenya smallholdings shows how heat stress and energy stress constrain milk yield and cow replacement rate', *Animal Science*, vol. 82, pp. 705–716.

Laquihon, GA, Suico, G & Laquihon, WA 1997, 'Integration of Salt management of cr livestock in slopeland areas: the case of “super” SALT (sloping agricultural land technology)', in *Proc. Int. Workshop on Sustainable Crop Livestock Integration in Sloping Lands of Asia*, Davao, Philippines.

Leng, RA 1990, 'Factors effecting the utilisation of poor quality forages by ruminants particularly under tropical conditions', *Nutrition Res. Rev.* vol. 3, pp. 277–294.

Leng, RA 2004, 'Requirements for protein meals for ruminant meat production', in *Protein Sources for the Animal Feed Industry*, Expert Consultation and Workshop, Bangkok, FAO, Rome, Italy.

Leng, RA 2005, 'Metabolisable protein requirements of ruminants fed roughage based diets', in *Proc. Int. Conf. on Livestock-Crop Systems to Meet the Challenges of Globalisation*, vol. 1, eds P Rawlinson, C Wachirapakorn, P Pakdee & M Wanapat Khon Kaen, Thailand, pp. 330–347.

Leng, RA 2008, T*he potential of feeding nitrate to reduce enteric methane production in ruminants*, A Report to The Department of Climate Change, Commonwealth Government of Australia, Canberra, ACT. Australia, <http://www.penambulb>.

Le Thi Thuy Hang, Ngo Van Man & Wiktorsson, H 2003, 'Effects of urea and lime treatment of fresh rice straw on storage stability, and hygienic and nutritional quality', <http://www.mekarn.org/msc2003-05/theses05/thuyh_p1.pdf>.

Mahadevan, P 1984, 'Education of livestock producers and agents of change in the use of new technologies', in *World Animal Science, A2; Development of animal production systems*, Elsevier, Amsterdam, Netherlands.

Mudgal, VD & Pradhan, K 1988, 'Animal feed resources and current patterns of utilisation in India', in *Proc. Non-conventional Feed Resources and Fibrous Crop Residues in India*, ed C Devendra, International Development Research Centre, Ottawa, Canada.

Nitis, IM Lana, K, Sukanten, W, Suarna, M & Putra, S 1990, 'The concept and development of the three- strata forage system', in *Shrubs and tree fodders for farm animals*, ed C. Devendra, International Development Research Centre, IDRC-276e, Ottawa, Canada.

Pardey, PG & Beintema, NW 2001, *Slow magic. Agricultural R&D: a century after Mendel*, International Food Policy Research Institute, Washington D.C., U.S.A.

Parsons, DJ, Armstrong, AC, Turnpenny, JR, Matthews, A, Cooper, K & Clark, JA 2001, 'Integrated models of livestock systems for climate change studies 1. Grazing systems', *Global Change Biology*, vol. 7, pp. 93–112.

Peng, SB, Huang, JE, Sheehy, JE, Laza, RC, Vispera, KH, Zhong, XH, Centeno, S, Khush, GS & Cassman, KG 2004, 'Rice yields decline with higher night temperatures from global warming', in *Proceedings of the National Academy of Sciences*, vol. 101, pp. 9971–9975.

Preston, TR 2009, 'Environmentally sustainable production of food, feed and fuel from natural resources in the tropics', *Trop. Anim. Hlth. Prod*., vol. 41, pp. 873–88.

Preston, TR & Leng, RA 1987, *Matching livestock systems to available resources in the Tropics and Sub-Tropics,* Penambul Books, Armidale, Australia.

Raghavan, GV, Krishna, N & Reddy, MR 1995, 'Priorities for feed resources use in the semi-arid Tropics. In Global agenda for livestock research', in *Proc. of the Consultation for South Asia region*, eds C Devendra & P Gardiner, Patancheru, India, International Livestock Research Institute, Nairobi, Kenya.

Sevilla, CC 1994, *Prospects for sustainable cattle production in the Philippines*, University of the Philippines in Los Banos, Philippines.

Rivera, WM & Sulaiman, VR 2009, 'Extension: object of reform, engine for innovation. *Outlk. Agric*., vol. 38, pp. 267–274.

Sturr, WW, Horne, PM, Gabunada, FA & Kerridge, PC 2001, 'Forage options for smallholder crop-animal systems in Southeast Asia: working with farmers to find solutions', *Agric. Systems*, vol. 71, pp. 75–98.

Swaminathan, MS 1996, 'Uncommon objectives for achieving sustainable food and nutrition security; an agenda for science and public policy', in *The globalisaion of agricultural reserach*, eds C Bonte-Friedheim & K Sherdan, The Hague; International Service for National Agricultural Service.

Trinh Phuc Hao, Ho Quang Do, Preston, TR & Leng, RA 2009, 'Nitrate as a fermentable nitrogen supplement for goats fed forage based diets low in true protein', *Livestock Res. for Rural Dev*., vol. 21, no. 10, <http://www.lrrd.org/lrrd21/1/trin21010.htm>.

World Bank 2003, 'Reaching the poor. A renewal strategy for rural development’, Washington, DC., U.S.A.

Zandstra, HG, Price, EC, Litsinger, JA & Morris, RA 1981, *A methodology for on-farm cropping systems research*, IRRI, Los Banos, Philippines.

Acknowledgement of Referees

The Academy of Sciences Malaysia and the Editorial Board of the *ASM Science Journal (ASM Sc. J.)* wish to express sincere appreciation and gratitude to the following respected referees, for their valuable and profound technical evaluation of manuscripts for *ASM Sc. J.*, Vol. 7, No. 2, 2013:

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Taxonomy and Conservation: Overfishing of Sea Cucumber in the Straits of Malacca

S.P. Woo[1]*, I.H. Siti[1], Y. Zulfigar[1] and S.H. Tan[1]

The unsustainable harvesting of sea cucumbers in the Straits of Malacca poses a danger of collapsing population of this marine resource. Recent survey revealed the absence of commercially important sea cucumber species like *Stichopus horrens* was alarming since there were a lot of taxonomical complications in identifying species from this genus. The knowledge of taxonomy and ecology is an integral part in determining resource management strategies and conservation of marine resources like sea cucumber.

Key words: Sustainable harvesting; resource management; *Stichopus*; identification; tradional medicine

Sea cucumber is an important marine commodity enjoyed as a dietary delicacy and medicinal cure especially for Asians throughout many centuries (Conand 2006). They were conventionally traded fresh or more commonly in their dried form called Beche-de-mer. Sea cucumber is believed to reduce joint pain and arthritis, help restore correct intestinal and urinary functions, reinforce the immune system and can treat certain cancers (Chen 2004). In Malaysia, sea cucumber utilization was very much different in the West and East of Malaysia. In East Malaysia and primarily in Sabah, sea cucumbers were important not just for export but rather they provide livelihood, supplement income for the poor coastal communities and also for the indigenous people in coastal areas (Choo 2004). Sea cucumber fisheries in Peninsular Malaysia were smaller in scale and confined to only few locations using artisanal fishing methods compared to East Malaysia (Choo 2004). Generally, sea cucumber fishery saw a marked increase of pressure with decrease of landings, increase landings of lower valued species, soaring prices and increase of effort in collecting these comodities (Choo 2012).

Sea cucumbers were utilized in the traditional medicinal product industry in the coastal area of the Straits of Malacca especially in the island of Langkawi. One example of medicine produced in Malaysia is the *Minyak Gamat*, derived from the sea cucumber belonging to the family of Stichopodidae (Choo 2004). It is traditionally believed to heal cuts, skin rashes, joint pains and helps in post-natal recovery. Recent advancement of research into therapeutic and pharmaceutical values of marine organism has prompted production of modern health products using sea cucumber. Bordbar *et al*. (2011) reviewed extensively the potentials, nutrients and high value bioactive compounds found in various form in sea cucumbers. To date, there are scores of potential medicinal compounds which have been isolated from holothurian species, and these include antitumour, antiviral, anticoagulant and antimicrobial compounds (Kelly 2005).

Traditional Use of Sea Cucumber

The *Minyak gamat* was still predominantly very popular among the local communities in Malaysia as traditional prescription for numerous purposes like cuts, wounds, muscular pain and and so on. This traditional medicine was made only specifically from sea cucumber of the genus Stichopus. Another traditional medicine derived from sea cucumber was the *air gamat* or the coelomic fluid within the body of sea cucumber of the genus *Stichopus* which are consumed especially by fishermen to remain healthy throughout their days in the sea. They believed that consuming them could heal various health complications including hypertension and asthma. The consistent harvesting targeted on only few species has seen marked effect on the population of sea cucumber as demonstrated by Forbes and Ilias (1999) as well as Choo (2004) where in Langkawi Island's sea cucumber fishery dates back to the mid-1900s but markedly disappeared in the early 1940s when the target species *Stichopus hermanni* and *Stichopus horrens* were fished to depletion.

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Taxonomic Status and Knowledge Gaps

The taxonomic status of sea cucumber has been undergoing constant review especially within the commercial species group and a study to revise their taxonomy is identified as a priority (Uthicke & Benzie 2003; Bryne *et al*. 2010). The sea cucumbers from family Stichopodidae and especially genus *Stichopus* (Figure 1) has long been a taxonomic challenge and oftenly misidentified in the field due to its likeness in appearance and outer morphology (Rowe & Gates 1995; Massin *et al*. 2002; Massin 2007). Bryne *et al.* (2010) outlined the complexity and the existence of extensive cryptic species under the genus *Stichopus* especially commercially exploited ones under the name *S. horrens* using molecular taxonomy tools. It was revealed that the species fished under the name *S. horrens* turned out to be of three different species where in South Queensland (East Australia), species thought to be *S. horrens* was *Stichopus naso* and in Samoa was actually *Stichopus monotuberculatus* (Byrne *et al.* 2010). Therefore, managing these resources without having enough knowledge on what was harvested proves to be futile. Malaysia also lacks baseline data and scientific publication in addressing the status of fishery, distribution as well as taxonomy of sea cucumber in the Straits of Malacca resulting in poor knowledge and management strategy towards protecting them. Although there were several studies done on the taxonomy and distribution of sea cucumbers in Malaysia, they were mostly concentrated in the South China Sea and the coast of Sabah (Ridzwan & Che Bashah 1985; George & George 1987; Siti *et al.* 1999; Massin *et al.* 2002; Zulfigar *et al.* 2007; Zulfigar *et al.* 2009; Kamarul *et al.* 2010) if not, were on the biochemistry of sea cucumbers. Most of the cited taxonomic and distribution articles lack revisions on the confusion of taxonomic status within genus *Stichopus* and uses obsolete taxonomic names in identifying the species found.

Fishing Pressure in Straits of Malacca

The depletion of sea cucumber population from the genus *Stichopus* in Langkawi had shifted the fishing pressure towards the nearby islands. To sustain the traditional medicine industry, sea cucumber was imported from the nearby Adang Island in Southern Thailand as well as Pulau Pangkor, further south in the Straits of Malacca. This serial exploitation over spatial

Figure 1. Some examples of sea cucumber from the genus *Stichopus* which look very similar in their outer morphology. A: *S. vastus*; B: *S. horrens*; C: *S. hermanni*.

and temporal was evident here alike in the industry globally suggested by Anderson *et al*. (2011). Recent expedition in accessing the diversity of marine life in the Straits of Malacca showed alarming status of diversity and abundance of sea cucumber there. Woo *et al.* (2012) revealed the missing of highly sought sea cucumber (*S. horrens*) to be absent in most of the islands surveyed including Pulau Pangkor, except in Pulau Payar which was a Marine Protected Area. The threat of overexploitation was not restricted to only sea cucumber from the genus *Stichopus*. Several field observations were made where sea cucumber from the species *Holothuria leucospilota* were seen to be extensively harvested in two locations namely Pulau Langkawi and Pulau Songsong in the Straits of Malacca by the locals. The species *H. leucospilota* was from a low commercial value sea cucumber and not particularly important commercial species locally and globally. Interviews done with the fishermen revealed that sea cucumbers were harvested to be exported to markets in Taiwan (Figure 2). The utilization of low valued sea cucumber was evident of the serial exploitation of decreasing value (Anderson *et al.* 2010) where lower value sea cucumbers become the target in replace of the higher valued ones due to depletion.

CONCLUSION

Management and conservation of marine organisms was not possible without the ability to identify and classify them taxonomically. The over-utilization of commercially important species like sea cucumber had enormous impact not just on the ecology but also on the socio-economic factors of the local communities that were dependent on the subsidiary industries of the marine commodity. More in-depth research and new scientific knowledge in resolving the taxonomy of sea cucumber especially of the genus *Stichopus* was crucial and timely to strategies management and conservation to ensure the sustainability of sea cucumber as a resource.

Figure 2. Sea cucumber collected by local fishermen stored in barrels before processing and sent to Taiwan as export commodity.

ACKNOWELDGEMENTS

The authors would like to sincerely appreciate the Ministry of Natural Resources and Environment, Malaysia and the Department of Marine Park Malaysia for funding and support. The Marine Science Laboratory, Universiti Sains Malaysia and Universiti Teknoloi Mara Kampus Perlis is also acknowledged for their kind assistance throughout this study.

Date of submission: November 2012
Date of acceptance: February 2013

REFERENCES

Anderson, SC, Flemming, JM, Watson, R & Lotze, HK 2011, 'Serial exploitation of global sea cucumber fisheries', *Fish and Fisheries*, vol. 12, no. 3, pp. 317–339.

Bordbar S, Anwar, F & Saari, N 2011, 'High-value components and bioactives from sea cucumbers for functional foods— a review', *Marine Drugs*, vol. 9, no. 10, pp 1761–1805.

Bryne, M, Rowe, FWE & Uthicke, S 2010, 'Molecular taxonomy, phylogeny and evolution in the Family Stichopodidae (Aspidochirotida: Holothuroidea) based on CO1 and 16S mitochondrial DNA', *Molecular Phylogenetics and Evolution*, vol. 56, no. 3, pp. 1068–1081.

Chen, J 2004, 'Present status and prospects of sea cucumber industry in China', Mercier, in *Sea cucumbers: a global review on fisheries and trade*, eds A Lovatelli, C Conand, S Purcell, S Uthicke, JF Hamel & M, *FAO Fisheries and Aquaculture Technical Paper*, no. 516, Rome, FAO, pp 119–142.

Choo, PS 2004, 'Fisheries, trade and utilization of sea cucumbers in Malaysia', in *Advances in sea cucumber aquaculture and management*, eds A Lovatelli, C Conand, S Purcell, S Uthicke, JF Hamel & A, Mercier, *FAO Fisheries Technical Paper*, no. 463, Rome, FAO, pp 57–68.

Choo, PS, 'The sea cucumber fishry in Semporna, Sabah, Malaysia', *SPC Beche-de-mer Information Bulletin*, vol. 32, pp 43–48.

Conand, C 2006, 'Sea cucumber biology, taxonomy, distribution and conservation status', in *Proceedings of the CITES workshop on the conservation of sea cucumbers in the families Holothuriidae and Stichopodidae*, ed Bruckner, AW, NOAA Technical Memorandum NMFSOPR 34, Silver Spring, MD.

Chen, J 2004, 'Present status and prospects of sea cucumber industry in China', in *Sea cucumbers: a global review on fisheries and trade*, eds A Lovatelli, C Conand, S Purcell, S Uthicke, JF Hamel & M, Mercier, *FAO Fisheries and Aquaculture Technical Paper*, No. 516. Rome, FAO, pp 119–142.

Forbes, B & Ilias, M 1999, 'The taxonomy and ecology of sea cucumbers in Malaysia', *SPS Beche-de-mer Information Bulletin,* vol. 12, pp. 5.

George, JD & George, J 1987, 'The coral reefs of the Bodgaya Islands (Sabah: Malaysia) and Pulau Sipadan. 4. Macroinvertabrates', *Malayan Nature Journal*, vol. 40, pp 225–260.

Kamarul, RK, Aisyah, MR, Ridzwan, H & Gires, U 2010, 'An update on diversity of sea cucumber (Echinodrmata: Holothuroidea) in Malaysia', *Malayan Nature Journal*, vol. 62, no. 3, pp 315–334.

Kelly, MS 2005, 'Echinoderms: their culture and bioactive compounds'*, in Echinodermata: progress in molecular and subcellular biology*, ed V, Matranga, *Subseries: Marine Molecular Biotechnology,* Springer-Verlag, Berlin, Heidelberg.

Massin, C, Zulfigar, Y, Aileen Tan, SH & Rizal Boss, SH 2002, 'The genus *Stichopus* (Echinodermata: Holothuroidea) from the Johore Marine Park (Malaysia) with the description of two new species', *Bull. Inst. Roy. Sci. Nat. Bel. (Biol.)*, vol. 72, pp. 73–99.

Massin, C, 2007, 'Redescription of *Stichopus naso* Semper, 1867 (Echinodermata, Holothuroidea, Stichopodidae)', *Bull. Inst. Roy. Sci. Nat. Bel. (Biol.)*, vol. 77, pp. 123–130.

Ridzwan, H & Che Bashah, CC 1985, 'Tinjauan awal taburan dan penilaian holothurians di beberapa kawasan prairan Sabah sebagai sumber pemakanan', *Sumber 1*, pp. 143–155.

Rowe, FWE & Gates, J 1995, 'Echinodermata', in *Zoological catalogue of Australia*, ed A Wells, CSIRO, Melbourne, Australia.

Siti, ZRB, Zulfigar, Y & Tan, SH 1999, Distribution of sea cucumber species at Pulau Besar, Johor with special emphasis on the *Stichopus* genus', *SPC Beche-de-mer Information Bulletin,* vol. 12, pp. 4.

Uthicke, S & Benzie, JAH 2003, 'Gene flow and population history in high dispersal marine invertebrates: mitochondrial DNA analysis of Holothuria nobilis (Echinodermata: Holothuroidea) populations from the Indo-Pacific', *Molecular Ecology*, vol. 12, pp. 2635–2648.

Woo, SP, Siti Hasmah, I, Yaman, IC, Muhammad Shukri, MY, Nithiyaa, N, Norhanis, MR, Siti Balkhis, AB, Teh, CP, Zulfikar, Khalil, M, Zulfigar, Y & Tan, SH 2012, 'The diversity of sea cucumber (Echinodermata: Holothuroidea) in the North Straits of Malacca', in *Bengkel ekspedisi saintifik selat Melaka (Bahagian zon barat utara), 30th October 2012*, School of Biological Sciences, USM, Penang.

Zulfigar, Y, Sim, YK & Tan, SH 2006, 'The distribution of sea cucumbers in Pulau Aur, Johor, Malaysia', in *Selected Paper of NaGISA World Congress*, pp. 73–86.

Zulfigar, Y, Sim, YK, Tan, SH & Shirayama, Y 2008, *Field guide to the Echinoderms (Sea cucumbers and sea stars) of Malaysia*, Kyoto University Press, Japan.

Global Trends in Chemistry Research and the Challenge for Malaysian Scientists: A Perspective Review

V.G. Kumar Das†

Malaysia is currently poised to introduce its Science, Technology and Innovation (STI) Policy and Act to bolster the nation's efforts at economic and social transformation. In championing this initiative, the Academy of Sciences Malaysia, while continuing to advise the Government on STI issues of the day, has made major strides in taking stock of the country's STI strengths in the various sectors of the economy as well as weaknesses that need to be addressed in terms of human capital development. In this article, the author examines the level of research expertise presently in the country in the field of chemistry, and elaborates on the four key areas of energy, catalysis and chemical synthesis, materials science and biological chemistry which will be researched globally in the next few decades that we would also need to be engaged upon to remain competitive. Intended for a wider audience than chemists alone, the descriptive sections in the article by and large belie an interdisciplinary flavour. The article also advocates the need for a more thorough road mapping exercise of the STI efforts in chemistry across the spectrum of academia and industry and makes some recommendations towards forging strong collaborations in research between the universities, public research institutes and the industry which are seen as vital in providing cross-cutting chemical solutions throughout the value chains and to the success of technologies identified as critical to the nation.

INTRODUCTION

Malaysia has a reasonable track record in academic chemical research emanating from universities and public research institutes, but there is little to boast of from private sector companies, although our chemical industry is one of the most developed in the world, especially in the resource-based areas of petrochemicals and oleochemicals[1].

Research engagement by the chemical industry is vital in providing cross-cutting chemical solutions throughout the value chains and to the success of technologies identified as critical to the nation. This point is well underscored in the 2009 Final Report of the High Level Group on the Competitiveness of the European Chemicals Industry[2] (HLG Report). The HLG Report asserts that the challenges being now faced by humanity "*require new solutions, many of which can only be implemented through new materials and substances*". This implies that more innovation is the key to securing the future of the industry where the challenges faced are also inextricably linked to the manufacturing industry across the board.

Many important areas of manufacturing have depended and continue to depend on research by chemists and chemical engineers, for example, the manufacture of petrochemicals and the process technology involved in the manufacture of plastic films and coatings. This is also the case in other fields as in energy and transportation, with such examples as better performing designer gasoline, liquid fuels from natural gas, coal and shale, high energy density batteries, fuel and solar cells; in the technologies that contribute to improved public health as exemplified by biomaterials, biomedical devices, medical diagnostics, drug delivery systems, chemical synthesis of drugs and genetic engineering of recombinant human proteins; and in the ICT field with examples of optical fibres, multilayer electronic packages, electronic displays and single-atom manipulation techniques.

The HLG Report categorically states that "*the chemicals industry is an irreplaceable provider of 'innovations' to 'downstream' industries and is a key component of value chains that end with the great majority of consumer products*".

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The Report also rightly notes that while innovation is more than R&D, the link between research in chemistry (and related sciences) and innovation is particularly strong in the chemicals industry.

Based on the Report's findings, between 1995 and 2005, global chemicals production increased by almost 40%; production now takes place in every region of the world, with an increasing presence in the emerging economies in Asia.

In 2006, China occupied the 3rd, and India the 7th, place among the world's biggest chemical producers. In Malaysia, the resource-based chemical industry contributes almost 55% of the total manufacturing output and includes chemicals and chemical products, food manufacturing, wood and wood-based products, rubber products, non-metallic mineral products and non-ferrous metal industries[3].

Enhancing National Competitiveness in Chemistry

Two recommendations contained in the HLG Report are relevant also to the Malaysian scene:

1. Malaysian companies should strengthen their relationships with universities and public research centres and co-promote public-private partnerships on key medium-long-term research issues.
2. A road mapping exercise and active co-ordination of national efforts in chemistry and chemical engineering research should be undertaken.

Taking a leaf also from the six-Point Plan for R&D strengthening strategized for the Indian Chemical Industry[4] over the period 2012–2017, we could:

3. Establish a Malaysian Chemical Innovation Council (MCIC) that will include representatives from the government, chemical companies, research universities/research institutes and other industry associations (Chemical Industries Council of Malaysia, Federation of Malaysian Manufacturers' Association, Malaysian Petrochemicals Association, Plastic Resins Producers' Group, Tin Industry (R&D) Board, Malaysian Timber Industry Board) to encourage research collaboration, commercialization efforts, facilitate handling of IP issues and provide for stricter enforcement of IP rights
4. Establish an autonomous RM100 Million or more chemical innovation fund by securing a portion of the national five-year R&D budget allocation to encourage commercialization efforts for innovations generating inclusive growth.
5. Develop regional clusters and innovation centres as appropriate in universities dedicated to chemical industry.

Having stated the need for industry engagement in research and strong academia-industry interaction for advancing the country's R&D agenda, we next turn our attention to the prevailing global scenario in chemistry research. The Chemical Sciences Discipline Group of Academy of Sciences Malaysia (ASM) recently undertook a survey of academic chemistry research interest across the various sub-disciplines in a number of Malaysian universities and their findings are summarised in Table 1. A comparison table (Table 2) lists prominent research areas on the global scene as noted by the Group. This paper is intended to elaborate on the above by highlighting several research areas in chemistry of growing importance in the context of emerging technologies which chemists in the country need to take cognizance of.

THE GLOBAL SCENARIO FOR CHEMISTRY-RELATED RESEARCH

The Steering Committee of the US-based group Chemical Industry Vision 2020 Technology Partnership[5a] has identified the following to be the key technologies receiving research attention in the United States: bio-based processes, novel catalysts, sustainable chemistry (includes 'green' chemistry and alternatives to oil-based feed stocks), "smart" materials and advanced composites. Arguably, the buzzwords of the 21st century are ***green chemistry*** and ***technological convergence***.

Green Chemistry covers a variety of topics including catalysis, green solvents, some aspects of environmental chemistry and the impact of modern industry on the environment and the use of renewable feedstocks and renewable energy. The rush is on towards green chemistry, but for any new technology to be accepted as 'green', it has to meet three key criteria, namely, be more environmentally benign than the alternatives, be more economically viable than the alternatives, and functionally outperform the alternatives.

Convergence of different technological systems is the other buzzword that has been gaining momentum both nationally and internationally. It is an evolving reality towards synergistic interactions of technology — one that "*occurs when multiple products come together to form one product with advantages of all of them*"[5b]. Technological convergence will not only spur a drive for creativity but will also be the harbinger of new knowledge, technology and industries.

Prof David MacMillan at Princeton has noted[6] that there are four areas which will represent the bulk of what chemists will be researching over the next 20 years. These are: **Energy, Catalysis and Chemical Synthesis, Materials Science and Biological Chemistry**. This is a view which is also widely shared by most leading researchers. Indeed, these areas are broad enough to address a wide spectrum of important problems of current interest and future challenges, with the research undertaken transcending chemistry's traditional sub-disciplines as much as combining a confluence of biochemical, genetic and engineering methods. ***This paper reviews current research in these key areas, including brief conceptual underpinnings for some of the topics discussed***.

ENERGY

Energy is one of the grand challenges of the present century. Research focus world-wide has perceptibly shifted to **renewable energy** that will see less dependence on fossil fuels which are the cause of greenhouse gas emissions that have adversely impacted climate change globally. ***Solar energy, biomass conversion to bioenergy and hydrogen*** command the lion share of research attention in this respect. Molecular chemistry, materials science (especially with the advent of nanostructured materials: 0D, 1D, 2D and 3D) and protein engineering are at the centre of research methods that are being applied here.

Solar Energy

This is one of the few most promising routes to introduce renewable energy on a large scale. Solar energy can be used directly for spatial heating as well as to heat water. In this process, the energy in the form of solar radiation is converted into thermal or heat energy. Solar energy can also be transformed into electricity through photovoltaic cells or solar power plants. Research on photovoltaic (PV) cells, while addressing the need to make current technology cells cheaper and/or more efficient, has also devoted equal attention to the development of new technologies based on new solar cell architectural designs and (from the chemistry angle) to the development of new materials to serve as light absorbers and charge carriers. Although somewhat still in its infancy, one-dimensional materials with molecular scale properties such as nanowires may spark a revolution in architectural designs, enabling not only easy combination of different materials but also more sophisticated fabrication of tandem cells. In addition, light absorption would be more efficient with conical nanowires in radial geometry as the optical absorption path length can be disentangled from the charge separation distance allowing more design freedom[7].

Cutting-edge research areas on solar cells include dye-sensitized solar cells, flexible organic solar cells, including nano-particle-embedded polymer cells, and quantum dot cells. There is also the concomitant effort to tap the solar energy to produce solar fuels from carbon dioxide reduction (fuel products include carbon monoxide, formic acid, methanol and methane) and water splitting (fuel product is hydrogen). The solar energy is effectively captured in the chemical bonds of these fuels. Three major international consortia of researchers are actively involved in this task at the Joint Centre for Artificial Photosynthesis (USA), Towards Biosolar Cells (The Netherlands) and the Korean Centre for Artificial Photosynthesis. Solar fuels have the advantage that they are easily transported and they can also be combined with fuel cell technologies which convert fuels to electricity, to power a building or small community.

Being blessed with an abundance of sunlight in the country, cross-disciplinary engagement in solar cell research is expected to have special local appeal and, indeed, should be encouraged among both academic and industry researchers.

It is interesting to note that almost half of all the solar energy reaching the Earth is in the infrared, most of it in the near IR region (Figure 1). The mustard coloured wavelengths in the above figure represent the photons that are absorbed by the ubiquitous silicon solar cell (c-Si) to generate electricity. This cell has a bandgap of 1.1 eV. The bandgap specifies the minimum amount of energy that is required to excite an electron from the top of the valence band to the bottom of the conduction band in the semiconductor material.

This creates in the process an electron/hole pair that is drawn away as current before any recombination occurs—holes to anode and electrons to cathode. The red coloured wavelengths which do not have enough energy do not get absorbed by the silicon cell, and the yellow ones which have too much energy only lead to minimal absorption to generate electricity, with much of their energy being lost as heat. If the electron receives enough energy to leave the valence band, and to surpass the conduction band, it becomes a "hot electron". Hot electrons can tunnel out of the semiconductor material and this can lead to heating of the device and increased current leakage.

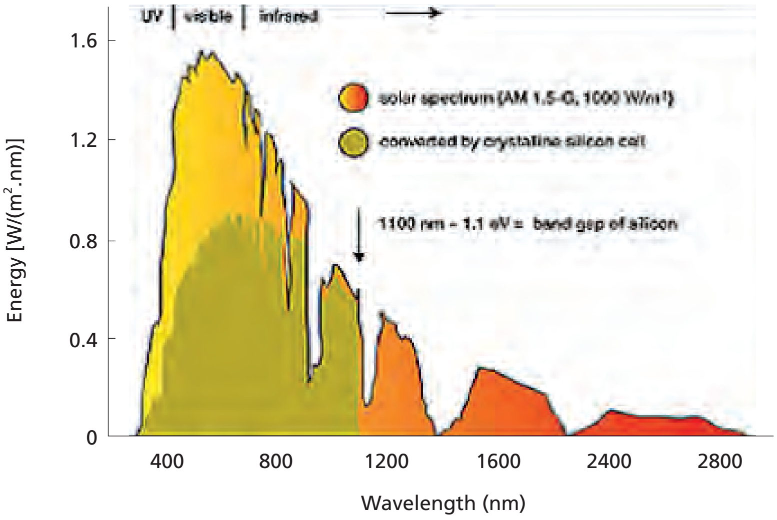

Figure 1. Solar spectrum [Source: Ref. 8].

As with almost all inorganic semiconductors, the e-h pair generated by the photon has only a very small exciton binding energy, and thus as charges are readily drawn away by the electrodes in the device. This, however, may not be true with other semiconductors such as organic semiconductors.

Ever since the advent of the crystal silicon solar cell over half a century ago, scientists have been grappling with a critical limitation of the solar photovoltaic cell — the **Shockley-Queisser (SQ)** limit of 33.7% for a solar cell based on a single material, a single p-n junction and “one sun” source. The strategies[8] that are continuing to be researched to surpass the SQ limit include the use of more than one semiconductor material (multi-junction or tandem solar cells), concentration of the sunlight, combining a PV semiconductor with a heat based technology to harvest the excess photon energy dissipated as heat, and/or the use "quantum dots" to harvest hot electrons/holes that have achieved quasi-equilibrium in the light absorbing material with electronic temperatures higher than the phonon temperature.

Inorganic photovoltaics. Although silicon is an indirect band gap material and, therefore, does not absorb light very well, it is in its stable crystalline wafer form (c-Si) and thin-film versions, (a-Si) and (TF-Si), still among the most common and reliable photovoltaic (PV) cells in use with efficiencies in the range of 15% to 25%. Other inorganic materials in the form of thin films have also been widely researched, among them the CdTe (n-i-p) cell, where the top layer is typically n-type cadmium sulphide (CdS), the middle layer is intrinsic CdTe, and the bottom layer is p-type zinc telluride (ZnTe). The CdTe cell surpasses c-Si in cheapness but with a maximum efficiency[9] of only 16.5%. More elaborate **multi-junction tandem cells** have also been built, most notable among them being the three-junction cell, $Ga_{0.49}In_{0.51}P$/ $Ga_{0.99}In_{0.01}As$/Ge, with band gaps of 1.9, 1.4, and 0.7 eV, respectively[10]. In this multi-junction configuration transmission and thermalization losses of hot carriers were reduced and the cell reached power conversion efficiency of 32.0% under I sun (defined as 1000 W/m^2).

An interesting new development is the discovery by Professor Saki Sonoda and his research group at Kyoto Institute of Technology[11] of a single-junction PV cell that is capable of generating electricity not only from visible light, but from ultraviolet and infrared light as well. This new PV cell was made by 'doping' a wide band gap transparent composite semiconductor — in this case, gallium nitride — with a 3d transition metal such as manganese or cobalt. Notice that this is essentially a “multi-gap” rather than a multi-junction cell.

More recently research focus has shifted away from III-V compound semiconductor cells to inorganic quantum dot (QD) solar cells[12]. These are semi-conducting nanocrystals [CdX and PbX (X = S, Se, and Te)], with diameters in the range 2–10 nm (10–50 atoms), which have relatively small bandgaps and thus are capable of harvesting photons in the visible and infrared region. These materials have been employed as an inorganic dye in four different types of quantum dot solar cells: (i) Metal junction solar cells, (ii) Depleted heterojunction solar cells, (iii) Polymer hybrid solar cells, and (iv) Quantum dot-sensitized solar cells (QDSCs) (see Figure 2).

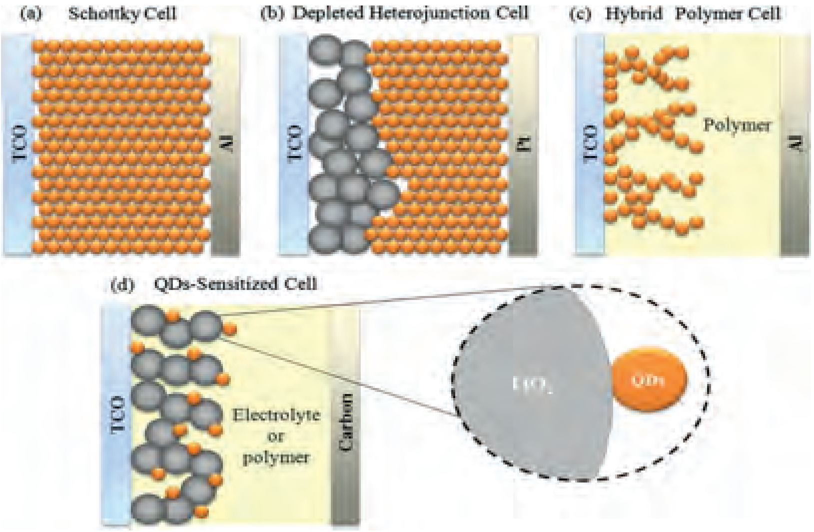

Figure 2. Various QD-based photovoltaic cells [Source: Ref. 12].

QD synthesis is readily achieved using wet chemistry (colloidal quantum dots — CQDs). The long hydrocarbon ligands that are often employed to keep the nanoparticles in solution stable are replaced with short-chain cross-linkers when the solutions are cast into thin films.

In QDSCs, the quantum dots are attached to a wide band gap material (e.g. TiO_2 or ZnO) either through an organic linker such as carboxyl or directly without a linker molecule. The excited electrons in the QDs are thus injected into the large bandgap material and the holes are scavenged by a redox couple liquid electrolyte sandwiched between the photoelectrode and a counter electrode. Blends of conducting polymers and QDs are used to facilitate charge separation and charge transport in polymer hybrid solar cells (*vide infra*). The quantum dots are usually surrounded by a ligand capping layer to prevent their coagulation. The nature of the ligand strongly affects the luminescent properties of quantum dots. Thiophenol is commonly used as it is an effective acceptor for photogenerated holes and also exhibits good charge transport.

The outstanding advantages that QDs bring to solar cell technology are their tunable band gap and multiple exciton (electron-hole pair) generation[13]. Decreasing the size of the QD to less than its exciton Bohr radius results in confinement of e-and h-wavefunctions and a significant increase in bandgap (*i.e. bandgap is inversely related to size*). The exciton Bohr radius of PbS, for example, is large (18 nm). By controlling the size of PbS CQDs in synthesis, the absorption onset can be tuned from 3000 nm to ~ 600 nm. Also, QDs of different sizes can be assembled into a gradient multi-layer nanofilm.

One other feature of QDs that warrants mention is their ability to capture ‘hot electrons’ (whose lifetimes are stretched 1000 times in them before they cool). The challenge is to extract the hot electrons from QDs. Success in such extractions has been evidenced[14] with TiO_2. Potentially this strategy can raise solar-to-electric power conversion efficiency to as high as 66%, beyond the Shockley-Queisser limit.

Organic photovoltaics (OPV). In addition to the inorganic technologies, there are also organic solar cells. These are attractive because of their potential low cost manufacture as flexible solar modules, specially facilitating roll-to-roll (R2R) production. However, the main disadvantages in organic photovoltaics (OPV) are low device efficiencies and low stabilities compared to the properties of their inorganic counterparts. Combining the advantage of inorganic materials, namely high conductivity, with the film-forming properties of organic materials is addressed in using so-called hybrid solar cells.

There are three types of organic solar cells, namely, dye sensitized solar cells (DSSC), Small molecule organic solar cells and polymer organic solar cells. In DSSC, the cell’s anode and cathode are separated by TiO_2 nanoparticles coated with light-sensitive ruthenium dye and surrounded by a redox electrolyte solvent/gel containing $3I^-/I_3^-$. The dye molecules have the ability to absorb visible light. They yield electrons upon excitation which are injected into the adjacent titanium dioxide. This leaves “holes” behind on the dye molecule. The injected electrons travel through the titanium dioxide particles and reach the TCO glass of the anode, the negative terminal of the solar cell. When a load is connected, electrons spontaneously move to the positive terminal of the solar cell, the cathode, via the external circuit. The redox couple present in the electrolyte finally serves to transport the electrons from the cathode's surface to the oxidized dye molecules.

Organic photovoltaics (OPVs) are made of organic electron donor and organic electron acceptor materials rather than semiconductor p-n junctions. These are, in fabrication, sandwiched between the anode (typically ITO) and cathode (Al or Ca) electrodes. The molecules comprising the electron donor materials are generally conjugated polymers whose delocalized π electrons can undergo a π-π^* transition from the HOMO to the LUMO orbitals when excited by light. This leaves a hole in the HOMO, thereby forming excitons. The energy bandgap between the HOMO and LUMO orbitals determines which wavelength of light can be absorbed. Fabrication of OPV photovoltaics is often accomplished using a fullerene-based electron acceptor. Illumination of this system by visible light leads to electron transfer from the donor material to the fullerene molecule. Electrostatic forces at the interface between the donor (D) and acceptor (A) layers are strong enough to break up the excitons, but it is more common nowadays to add a buffer layer such as bathocuproine (BCP) , tris-8-hydroxy-quinolinato aluminium, Al(quin)$_3$, poly (3,4- ethylene dioxythiophenene): poly(styrene sulphonate) (PEDOT: PSS) or its PFAS modification on top of the ITO anode surface of the solar cell to improve hole - injection / extraction[15]. Two cell configurations that are often studied are the planar heterojunction cell with its distinct donor and acceptor layers and bulk heterojunction cell (BHJ) where the donor and acceptor are mixed to form a blend, called the active layer.

Small molecule organic cells have as the donor layer low bandgap materials such as pentacene[16] or zinc phthalocyanin or donor–acceptor-type conjugated polymers, such as PDPP-PER[17], comprising 3,9-perylene (PER) and diketopyrrolo[3,4-c] pyrrole (DPP) and the conjugated A-A-D-A-A-type molecules[18] (BCNDTS and BDCDTS), where two terminal electron-withdrawing cyano or dicyanovinylene moieties are connected to a central dithienosilole core through another electron-accepting 2,1,3-benzothiadiazole block.

Polymer organic cells, on the other hand, have as donor molecules highly conjugated conducting polymers such as poly(3-hexylthiophene) or 3PHT; poly[3-potassium-6-hexanoate)thiophene-2,5-diyl] or P3P6T which is water soluble; poly[(2-methoxy5-((2-ethylhexyl)oxy)-1,phenylene)vinylene or MEH-PPV; and poly(3,4-ethylenedioxythiophene)-tetramethacrylate or PEDOT-TMA. The acceptor molecule of choice is the fullerene derivative [6,6]-phenyl-C61-butyric acid methyl ester (PCBM).The highest power conversion efficiencies of OPVs achieved to-date based on small molecular donor/fullerene acceptors or polymeric donor/fullerene acceptors have been 6.7% and 8.3%, respectively[19]. The durability of polymer organic cells remains an issue, but this has been partially addressed by hybrid organic/inorganic tandem cells, such as that shown in Figure 3, which depicts a photovoltaic device structure consisting of a PbSe nanocrystal film and a P3HT/PCBM bulk heterojunction film[20]. The durability of the polymer cell was attributed to the top PbSe film which serves as a photocurrent generator as well as a UV protector. The P3HT/PCBM film (bottom layer) provides the necessary electric field to the top photoconducting layer to extract the photogenerated charge from that layer.

In polymer solar cells, the performance of tandem devices generally lags behind single-layer solar cells on account of the lack of a suitable low-bandgap polymer. Recently, a novel low-bandgap conjugated polymer (PBDTT-DPP: bandgap, ~1.44 eV) has been discovered[21] for application in single-layer BHJ photovoltaic cells based on PBDTT-DPP blended with

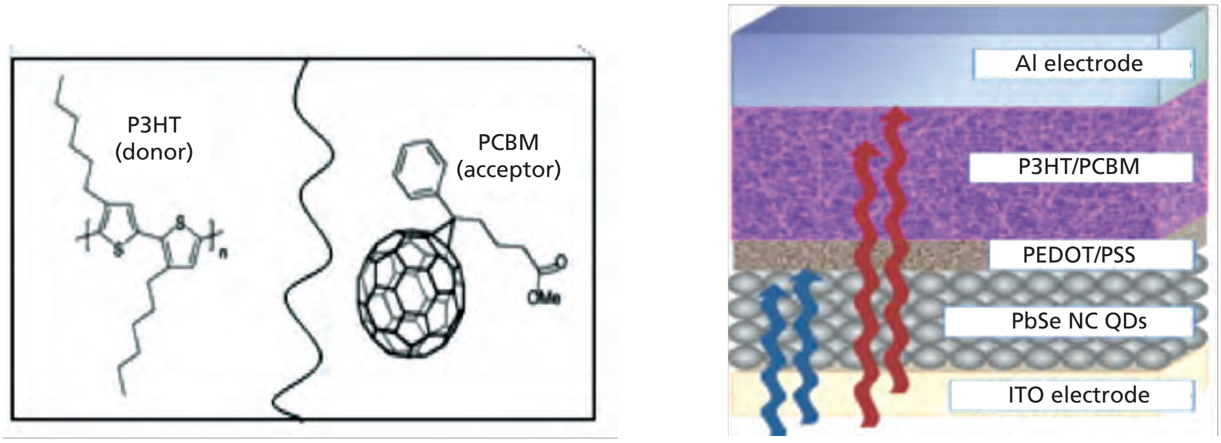

Figure 3. A hybrid organic / inorganic tandem solar cell, consisting of a PbSe nanocrystal film and a P3HT/PCBM bulk heterojunction film [Source: Ref. 20]

PCBM as well as in tandem cells. A tandem cell such as depicted in Figure 4 was fabricated having P3HT (a high-bandgap polymer) and the acceptor indene-C60 bisadduct (IC60BA) as front-cell materials, and PBDTT-DPP together with the acceptor PC71BM as rear-cell materials.

The pentacene / fullerene C_{60} complex relevant to bilayer and bulk heterojunctions elicits special interest on account of the possibility of multi-exciton generation in pentacene, although a prototype OPV cell to achieve this goal remains to be constructed. When a photon of blue or green light falls on pentacene, a high-energy spin-singlet electron-hole pair is initially created. This then undergoes a rapid (80 fs) internal conversion into a dark state of multi-exciton character that efficiently splits into two spin-triplet excitons. The pentacene triplet is non-emissive, but in a pentacene/C_{60} bilayer, slow diffusion of triplet excitons to the heterojunction takes place which leads to charge separation (Figure 5).

Triplet excitons can also be ionized at an organic/inorganic heterointerface such as in pentacene/nanocrystalline PbX (X=S,Se) solar cell[22]. A similar diffusion to heterojunction followed by charge separation pathway has been observed in a pentacene/PbSe/*a*-silicon[23] test cell. In general, to enable multiple exciton generation, the photons have to have energies at least twice the band gap (to obey the law of conservation of energy). Exploiting the dark state can potentially increase solar cell efficiency beyond the Shockley-Queisser (SQ) limit of 31%.

A prime task engaging researchers in the area of organic solar cells is to develop high stability cells that do not degrade rapidly under both environmental and light exposure. Research in the last five years has already made strides in improving stability previously from minutes into many thousands of hours and with power conversion efficiencies being incrementally improved to about 10%. This progress has been gained[24] by several developments, among them, inverted device structures of the bulk heterojunction geometry device, which allows for more stable metal electrodes, the choice of more photostable active materials, and the introduction of interfacial layers. Among new developments, the use of multilayer graphene as top transparent electrodes has been considered; the graphene layers protect the cell from air contamination and conceivably also allows for a package-free OPV product.

Boosting solar cells with nanowires and metamaterials. Research on nano-wired solar cells is still in its infancy and is concerned with design improvements of photovoltaic devices using conical and radial nanowire geometries[7,25] such as derived from silicon and graphene/Pt composite fibres. As conceptualised, a coaxial nanowire such as of silicon becomes essentially the solar cell with a p-doped core, a thin intrinsic (neutrally charged) inner shell and an n-doped outer shell. When a photon strikes the solar cell, it generates an electron and a hole, which readily move away from each other to produce current (Figure 6). *Recombination is thus hugely minimised.*

The rationale for the design is that a single nanowire can concentrate the sunlight up to 15 times of the normal sunlight intensity. An array of nanowires may thus enable a significant enhancement in efficiency over the conventionally designed flat solar panel, although significantly reduced refection losses have recently been demonstrated with six-inch growth of nanostructured antireflection (AR) coatings on glass.

The search for novel antireflective solar cell coatings, however, continues in the hope of getting more light into solar cells. Ideally, the coating material should have a refractive index identical to air to favour enhanced light collection. Better still, if the material had a negative refractive index as this would allow it to bend light into the solar cell and reflect little back. Recent advances in the field of metamaterials suggest that such a metamaterial film may soon be in the offing.

Metamaterials are one of the new discoveries of the last decade. They are a new class of artificial composite materials whose microstructure is engineered to exhibit electromagnetic responses unattainable in their component materials[26a], that is, they gain their properties not from their composition, but from their exactingly-designed structures. In order for the metamaterial to behave as a homogeneous material accurately described by an effective refractive index (effective permittivity and permeability), its structure must have dimension and spacing smaller than the wavelength of operation. Negative-index materials (NIMs) are a special class of metamaterials characterized by an effective negative index that gives rise to such unusual wave behaviour as backward-phase propagation and negative refraction. These extraordinary properties lead to many interesting functions such as superlensing (high-resolution imaging past the diffraction limit) and invisibility cloaking. More recently, researchers working with metamolecule trimers have been able to successfully introduce a unique electromagnetic Möbius symmetry not found in naturally occurring materials, attesting to the extraordinary engineering flexibilities of metamaterials[26b].

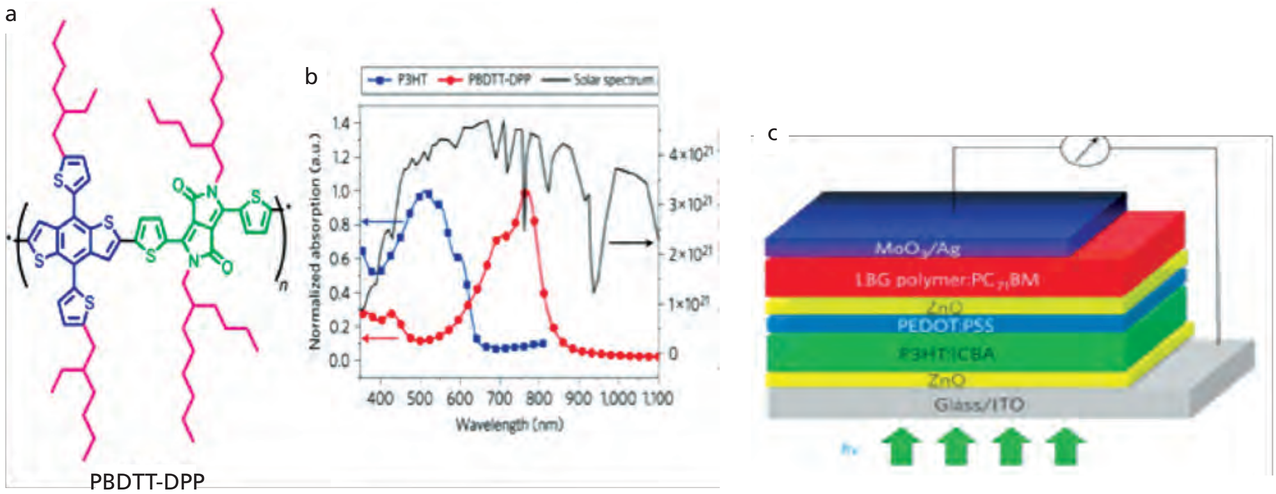

Figure 4. All polymer tandem solar cell [Source: Ref. 21].

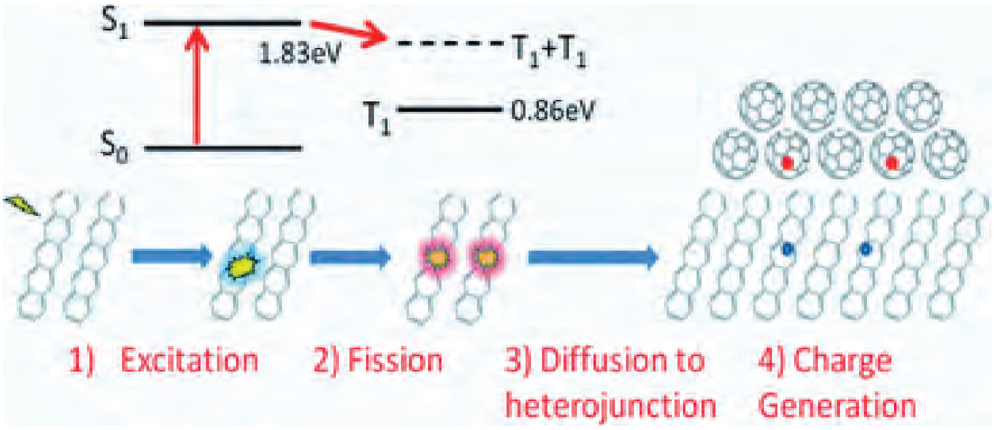

Figure 5. Singlet-triplet fission in pentacene with generation of 2 electrons per photon [Source: Ref. 19].

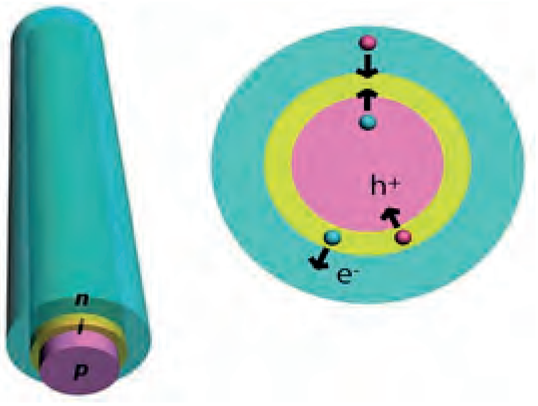

Figure 6. Coaxial silicon solar cell [Source: Ref. 25].

The metamaterial film developed by researchers at Caltech for potential solar cell applications is a single-layer NIM slab consisting of a hexagonal close-packed array of Ag/GaP/Ag coaxial plasmonic waveguides composed of 25 nm GaP annular channels with a 75 nm inner diameter set at a pitch of p= 165 nm in a Ag layer. The film is thus effectively "a single layer of silver permeated with coupled plasmonic waveguide elements[27].

Basically, plasmons can be described in the classical model as oscillations of free electron density against the fixed positive ions in a metal. Plasmon is a quantisation of this kind of oscillations. Light of frequency below the plasma frequency that hits the metal surface gets reflected, because of the screening of the electric field of the light by the electrons in the metal, while light of frequency above the plasma frequency is transmitted, because the electrons cannot respond fast enough to screen it. In most metals, the plasma frequency is in the ultraviolet. Surface plasmons are those plasmons that exist at the interface between any two materials where the real part of the dielectric function changes sign across the interface (e.g. a metal-dielectric interface, such as silver and air in this case). The surface plasmons strongly couple with photons at the interface and the resulting hybridised excitation is called a surface plasmon polariton (SPP).

The waveguide elements in the device guide the SPPs through the material. By simply changing the geometry of the waveguide, the researchers found that the material can be tuned to respond to different wavelengths of light coming from nearly any angle with any polarization.

Energy storage and future progress. It is now being increasingly recognized that the construction of a new generation of highly-efficient photovoltaic devices for solar energy conversion must incorporate the fundamental principles of natural photosynthesis. A bio-inspired chemistry approach may lead us to construct hybrid nano-chemical catalytic structures that would allow for efficient energy conversion.

While solar energy is unquestionably the most abundant energy resource, its widespread use has been hampered by a lack of suitable methods to store energy from sunlight in a cheap and efficient manner. Storing solar energy as hydrogen generated through solar driven water splitting is a promising method, but as elaborated later (in Photocatalytic Water Splitting, see pp. 184) photoelectrochemical water splitting comes with many challenges, especially from the anodic part of the reaction which involves oxygen evolution.

Among current energy storing devices, rechargeable **Li ion batteries (LIBs)** exhibit a large gravimetric and volumetric energy density and are favoured over other rechargeable batteries. However, due to the low specific capacity of the electrode materials, batteries small in size and with a high power supply are presently difficult to fabricate.

Needed improvements include electrode materials with increased capacity, extended voltage range and long lifetime (e.g. cyclability) as well as electrolyte materials with high conductivity and chemical stability.

In an excellent article titled "Reality and Future of Rechargeable Lithium Batteries", Chen and co-workers[28] have detailed the ideal characteristics for materials that can serve as cathode and anode for LIBs. Each electrode in a lithium-ion battery being a host of lithium, the electrode material must be capable of reversibly intercalating/deintercalating Li ions at a large capacity (at high potential for cathode and at low potential for anode), but suffering in the process only minimal structural and redox potential change. These two requirements are important for good cycle performance and a smooth charge/discharge curve. Additionally, the material for both cathode and anode should have high electronic conductivity, high Li ion diffusion rate and conductivity, as required for high charge/discharge rate. Both electrode materials should also be chemically stable with the electrolyte under operating potential; in particular, the anode material should also form a good solid-electrolyte interface with the electrolyte at the first circle, and remain chemically stable with the electrolyte in the subsequent cycles.

The anode in present day LIBs is made up of a graphite mixture while the cathode is a combination of lithium with cobalt oxide or nickel oxide or manganese dioxide or nano-iron phosphate. PVDF is the standard binder material used in the production of such composite electrodes.

The traditional and still dominant liquid electrolytes used in LIBs are composed of ethylene carbonate (EC) and dimethyl carbonate (DMC). The disadvantages associated with them are flammability and a narrow range of operating temperatures. These problems could be solved by novel electrolytes such as ionic liquids, organic solid electrolytes or inorganic solid electrolytes.

To-date ionic liquids and inorganic solid electrolytes have not made much impact. Among solid organic electrolytes, polyethylene oxide mixed with a lithium salt, PEO-LiX, has been the most worked.

In commercially available lithium batteries, microporous polyolefin membranes fabricated from polyethylene and polypropylene are used as separators that also serve a safety purpose.

While graphite has been the standard commercialized anode material for LIBs for several years now, its theoretical gravimetric capacity limits its applications (372 mAh/g, LiC_6). New anode materials with high specific capacity such as Si (4200 mAh/g), Sn (994 mAh/g) and SnO_2 (782 mAh/g) continue to be intensively investigated. However, the enormous volume expansion and structural changes during repeated intercalation/ deintercalation poses a problem with these materials as a significant capacity fading occurs during cycling — a mode of failure often attributed to lithiation-induced fracture. To address this problem, researchers have employed several approaches. One tactic is the fabrication of electrode materials based upon nanostructures that minimize the strain during volume expansion. Another approach is to integrate the electrode material with a carbonaceous matrix such as amorphous carbon, mesoporous carbon, graphene, or carbon nanotubes.

Thus a composite anode made from graphene nanoribbons (GNRs) and tin oxide (SnO_2) nanoparticles (NPs) yielded reversible capacities of over 1520 and 1130 mAh/g for the first discharge and charge, respectively; the reversible capacity retains ~825 mAh/g at a current density of 100 mA/g with a Coulombic efficiency of 98% after 50 cycles[29]. Furthermore, the composite showed good power performance with a reversible capacity of ~580 mAh/g at the current density of 2 A/g. The GNRs act as conductive additives that buffer the volume changes of SnO_2 during lithium insertion and extraction processes.

A high-power-density and high-energy-density LIB has recently been assembled with an electrode (cathode) made from SnO_2/V_2O_5 core/shell-nanowires[30]. This delivers a high power density of about 60 kW/kg while the energy density remains 282 Wh/kg. In addition, the electrode exhibits very-good cycling stability. These features indicate a promising potential for such electrodes in the application of a high-rate lithium battery.

In a recent study[31], electrodes constructed from MoS_2 nanowalls and carboxymethyl cellulose binder have also been demonstrated to exhibit a high specific discharge capacity of 880 mAh/g at a current density of 100 mA/g without any capacity fading for over 50 cycles. The electrode also exhibits outstanding rate capability with a reversible capacity as high as 737 mAh/g and 676 mAh/g at rates of 500 mA/g and 1000 mA/g at 20ºC, respectively.

Lithium ion microbatteries have recently been fabricated by researchers at the University of Illinois with a compact integration of the electrodes on a single substrate that favours microelectronics applications. The electrodes are a thin layer of nickel-tin (anode) and lithiated manganese oxide (LMO) (cathode) conformally coated onto interdigitated highly porous metallic scaffolds[32]. The microarchitecture provides power densities up to 7.4 mW cm^{-2} μm^{-1}, which is 2000 times higher than that of other microbatteries. The microarchitecture of the electrodes is claimed to concurrently optimize ion and electron transport for high-power delivery.

LIBs have not yet reached full maturity and the technology is continually improving, motivated by the automotive industry which has already turned its attention to creating a number of electric vehicle mobility strategies. As electric mobility looms to be the key technology for the replacement of fossil energy sources in the long term, this is strongly impacting research worldwide also on other promising alternatives to LIBs such as lithium air/oxygen and sodium-ion batteries, as well as on fuel cells.

Because of the chemical similarities of sodium with lithium, there is a general expectation that **sodium-ion batteries** (NaIBs) can be successfully developed on similar lines using approaches or methods that work for LIBs. The abundance of sodium relative to lithium offers such batteries an attractive option for low cost grid scale storage. But research on them is still at the infant stage, with many researchers using tin as the preferred high capacity anode material despite its noted limitations such as large volume expansion with cycling, slow kinetics, and unstable solid electrolyte interphase formation. Hu and co-workers[33] appear to have effectively addressed these challenges by fabricating the anode as a thin tin film on a wood fibre substrate. According to these authors, "*the wood fibre acts as a mechanical buffer for the sodiation process and as an electrolyte reservoir that allows for ion transport through the outer and inner surface of the fibre*". A more recent study has focussed on a new ultra-high stability cathode material in $Na_{1.5}VPO_{4.8}F_{0.7}$ that provides an energy density of 600 Wh kg^{-1} for a wide range of charge and discharge rates, which is the highest achieved thus far for NaIBs[34].

Biomass Conversion to Bioenergy

Biomass can be of three broad origins — primary (e.g. starchy crops and lignocellulosic material); secondary, which constitutes processed products from the primary resource (e.g. sawdust, plant oil, manure); and tertiary, which includes post-consumer residue streams such as animal fats and greases, used vegetable oils, and construction and demolition debris. Depending on the type of biomass available, there are four types of biomass to bioenergy conversion technologies that are applicable as may be suited. These are[35]: thermal conversion with or without the presence of oxygen (direct combustion, torrefaction); thermochemical conversion (biogas production); biochemical conversion (liquid fuel production via anaerobic digestion and fermentation); and chemical transformation (biodiesel production via such processes as transesterification, catalysed by KOH, metal-based catalysts or immobilized lipase enzyme). In Malaysia, palm oil mill effluent containing substantial quantities of suspended and dissolved solids and often also registering high BOD and COD values is a serious environmental aqueous pollutant whose negative impact is being addressed through anaerobic digestion in closed tanks to yield biogas.

At present, the primary approach for generating electricity from biomass is combustion direct-firing. Combustion systems for electricity and heat production are similar to most fossil-fuel fired power plants. By converting biomass into a gas, it can be burned directly for heating or cooking, converted to electricity or mechanical work (via a secondary conversion device such as an internal combustion engine), or used as a synthetic gas for producing higher quality fuels such as hydrogen or methanol. Liquid biofuels include pure plant oil, biodiesel, and bioethanol. Ethanol gel is a clean-burning fuel that consists of gelatinized ethanol bound in a cellulose thickening agent and water. Cook-stoves specially designed for use with ethanol gel have been developed in the last few years, as have ethanol gel burners. Global production of biofuels consists primarily of ethanol, followed by biodiesel production. Biodiesel is based on transesterification of plant oils.

The American Society for Testing and Materials International (ASTM) defines biodiesel as “a fuel comprised of monoalkyl esters of long chain fatty acids derived from vegetable oils or animal fats, designated B100”. Current diesel engine designs are optimised for use with petroleum No. 2 diesel fuel. A biodiesel for use as a fuel or fuel additive in blends of 1–20% with No. 2 diesel, No. 1 diesel, kerosene, Jet A or any other distillate fuel must meet ASTM D 6751 specifications[36]. Biodiesel blends are dilutions of the B100 product and are given the B designation followed by the percentage of the B100 in the product. For example, a B20 product comprises of 20% B100 diesel and 80% No. 2 diesel. The main source of biodiesel in the US is soybean oil but in Europe rapeseed oil is primarily used. A typical raw material blend for biodiesel consists of 84% rapeseed oil, 1% palm oil, 1% soybean oil, 13% sunflower oil, and 1% others. In Malaysia, the use of palm oil, in particular palm olein, has been favoured, either as such in 5% additions to diesel oil or following conversion to fatty acid methyl esters.

Biochemical conversion of biomass to biofuels has shown an increasing trend towards the use of genetically-engineered fungal and bacterial microorganisms which hold the promise of substantially lowered processing costs. An example is the use of genetically-engineered fungi[37] (such as *Trichoderma reesei*) to produce large volumes of cellulase, xylanase and hemicellulase enzymes utilised to convert cellulosic biomass into fermentable sugars. As cellulose, in contrast to starchy feedstocks, contains large amounts 5-carbon sugars, fermentation to cellulosic ethanol is best achieved using genetically-engineered *Escherichia coli* bacterium[38]. Such possibilities in the Malaysian context can be similarly researched using our vast agricultural waste. Interestingly, such agricultural waste could also be a potential source of another biofuel — hydrogen. This is based on the recent results reported by researchers at Virginia Tech who used microbial enzymes, which included *T. maritima xylulokinase*[39], in combination with polyphosphate to oxidise xylose (the second most common sugar found in plant tissues) in water to yield hydrogen in high yield and purity. The researchers used a total of 13 enzymes in their bioreactor at 50ºC to achieve the near theoretical yield of 9.5 moles of H_2 per mole of xylose after 20 h.

Interestingly, sugar and sugar polyols in aqueous solution can be hydrogenated to n-alkanes without C-C dissociation over the Ir-ReO_x /SiO_2 catalyst combined with the zeolite H-ZSM-5, using n-dodecane as co-solvent. Thus aqueous xylitol and sorbitol gave n-pentane and n-hexane, respectively, in >95% yields at 140–170ºC in this one-pot conversion[40].

Hydrogen

Notwithstanding the potentiality of enzymatic hydrogen generation based on xylose, being well endowed with large deposits of natural gas, there exist much scope in Malaysia for improved methods for hydrogen gas production from natural gas itself, with concomitant capture and conversion of the released carbon dioxide into useful hydrocarbons. Currently, **steam reforming** is widely used to generate hydrogen from natural gas, but every tonne of hydrogen that is produced gives rise to 11 tonnes of waste carbon dioxide. Amino acids have recently been touted[41] as potential solvents for carbon dioxide capture, but more relevant are efforts aimed at its conversion to useful products.

Carbon dioxide functionalization. Several approaches for conversion of carbon dioxide into gaseous hydrocarbons have been attempted by researchers overseas. Among them is the use of titanium dioxide photocatalyst in the presence of water which yields methane, but the efficiency of the reaction is low; efficiency increase has, however, been observed with the incorporation of nanostructures such as carbon nanotubes and metallic nanoparticles into the TiO_2 matrix[42]. Another approach which is also in the realm of green chemistry is the use of selective catalysts with high turnover frequencies such as developed by Prof Geoffrey Coates at Cornell[43] that economically converts the carbon dioxide into valuable polycarbonates and polyesters by copolymerization with epoxides. In a study at Stanford University[44], oxide-derived nanoparticles (obtained by electrochemically reducing a metal oxide precursor that traps metastable nanoparticle structures) were found to exhibit high efficiency for CO_2 reduction. The pace of research in the area of carbon dioxide reduction (as well as N_2 reduction) is set to grow.

A noteworthy recent example is the use of nickel catalysts such as $Ni(d\mathit{t}bpe)_2$ [d*t*bpe = 1,2-bis(di-*t*-butylphosphino) ethane] in the catalytic synthesis[45] of the industrially highly relevant sodium acrylate from ethylene, CO_2 and a base (e.g sodium *t*-butoxide)]. A nickelalactone intermediate, $Ni\{(CH_2)_2CO_2\}(d\mathit{t}bpe)$, has been postulated in this reaction which is formed from the oxidative coupling of CO_2 to the initially formed Ni-ethylene complex, $[Ni(\eta^2\text{-}C_2H_4)(d\mathit{t}bpe)]$. This intermediate in the presence of the base yields $[Ni(\eta^2\text{-}CH_2\text{-}CH{=}CHCO_2Na)(d\mathit{t}bpe)]$ from which the sodium acrylate is liberated by ligand exchange with ethylene and to deliver $[Ni(\eta^2\text{-}C_2H_4)(d\mathit{t}bpe)]$ to reinitiate the catalytic cycle. Subsequent studies on nickelalactones have shown that these undergo ring cleavage followed by β-H elimination with reagents such as methyl trifluoromethanesulphonate and methyl iodide to yield methyl acrylate and a metal-hydride species[46].

A related study has also reported[47] on the use of the molybdenum tetrahydride species, $[(Triphos)MoH_4PPh_3$;Triphos= $PhP(CH_2CH_2PPh_2)_2]$ to promote CO_2 functionalization in the presence of ethylene; the products are acrylate $(Triphos) Mo(H)(\kappa2\text{-}C_3H_3O_2)(PPh_3)$ and propionate $(Triphos)Mo(H)(\kappa2\text{-}C_3H_5O_2)(PPh_3)$.

The separation and storage of CO_2 in geological form as mineral carbonates such as calcium carbonate has also been seen as a viable method to reduce the concentration of CO_2 from the atmosphere. Reversible hydration of CO_2 to carbonic acid is the rate limiting step in the mineralization process. A recent report[48] indicates that this key step can be effectively catalysed at room temperature and pressure using nickel nanoparticles. The catalytic activity of the nickel nanoparticles is pH independent and as they are water insoluble and magnetic they can be magnetically separated for reuse.

Photocatalytic water splitting. One process envisioned for the creation of a clean and affordable source of hydrogen is the photocatalytic splitting of water, the essential precursor to all globally sustainable fuels, under solar light. With the advent of the hydrogen economy, this area of research ranks among the most worked among material scientists. As opposed to photoelectrochemical water splitting wherein the electricity produced by a photovoltaic system is used to break down water by electrolysis, photocatalytic splitting refers to the one step splitting of water by a photocatalyst suspended directly in it. Water splitting is a highly endothermic process and the photon energy (and hence the bandgap of the photocatalyst) needs to be greater than 1.23 eV, the thermodynamic potential E_o for water splitting under standard conditions. The complexity of transferring 4 electrons and 4 protons for evolution of every molecule of oxygen renders the reaction kinetically sluggish. Thus at any desired current density, for the overall voltage to drive water splitting, the thermodynamic potential needs to be enhanced by an overpotential that is dependent on the catalyst used. The best catalysts IrO_2 and RuO_2 operate between 0.2–0.4V of overpotential when operated at a current density of 10 mA/cm^2.

Another challenge is the long-term stability of catalysts. The anodic electrochemical conditions are extremely oxidizing and consequently catalyst corrosion is a serious issue. MIT researchers under Professor Daniel Nocera have worked on this dual challenge of the oxygen evolution reaction (OER) and catalyst stability culminating in their discovery of cobalt phosphate electrocatalyst which can be deposited as a thin film on FTO-coated glass to serve as the anode[49].

When electricity from a photovoltaic or other source runs through such an electrode immersed in water under neutral conditions at ambient temperature and pressure, and operated at 1000 mA/cm^2 at 35 mV overpotential, oxygen is generated. Furthermore, while the catalyst breaks down during catalysis, it is capable of self-repair. If coupled with another catalyst, such as platinum, that can produce hydrogen gas from water, the system can duplicate the water splitting reaction that occurs during photosynthesis — an artificial photosynthesis. Other scientists have since shown that inexpensive iron carbonyl complexes can replace platinum in a light-driven process to produce hydrogen from protons. More recently, Nocera has reported[50] on another novel electrocatalyst, nickel borate as a promising oxygen evolving catalyst in near-neutral conditions mediating the OER with 100% faradaic efficiency with modest overpotentials of *ca.* 0.4V required for current densities of 1 mA/cm^2. The catalyst exhibits long-term stability in water with no observed corrosion. The mechanism of oxygen evolution reaction on such amorphous electrocatalyst surfaces, however, remains to be much clarified.

What is ideally envisaged by researchers is the development of a solar-driven water-splitting system that can mediate the OER efficiently with proper matching to light harvesting and charge separation manifolds. That is, a triad assembly composed of a photosensitizer linked in tandem between a water oxidation catalyst and a hydrogen evolving catalyst[51]. In such a set-up, the photosensitizer transfers electrons to the hydrogen catalyst when hit by light, becoming oxidized in the process. This drives the water splitting catalyst to donate electrons to the photosensitizer. In a triad assembly, such a catalyst is often referred to as a donor. The oxidized donor is able to perform water oxidation. The charge separation in the triad assembly, with one catalyst oxidized on one end and the second one reduced on the other end of the triad, is the driving force for further electron transfer, and consequently catalysis, to occur.

Coal gasification. As with natural gas, coal has also assumed importance in a number of countries, not merely as a source of fuel for electricity generation based on IGCC but also as a means for producing hydrogen, particularly via coal gasification which yields syngas, a fuel gas mixture consisting primarily of H_2 and CO, and some CO_2. Coal gasification entails four processes[52], namely, steam gasification, carbon dioxide gasification, hydrogasification and partial oxidation reaction. Salts of alkali and alkaline earth metals as well as transition metals (mostly iron, cobalt, nickel and ruthenium) are active catalysts for gasification. In addition to the active metal, the catalysts typically contain a number of promoters, including potassium and copper, as well as high surface area binders/supports such as silica and/or alumina. Although coal gasification is primarily focussed at converting the CO and H_2 in the syngas to hydrocarbon fuels by the judicious choice of catalysts (Fischer-Tropsch synthesis), the technology can be adapted with modifications for hydrogen production that promotes the water-gas-shift reaction. The hydrogen, however, must finally be separated from the CO_2 to be able to use it. This is presently done by pressure swing adsorption (PSA), amine scrubbing, and membrane reactors. However, there is still much scope for research in the areas of product gas cleaning, separation and purification, feedstock flexibility, and integrated or combined process concept as much as in the area of developing suitable and more effective catalysts that will help catalyse steam decomposition and carbon/steam reaction. Coal gasification technology also lends itself with minor modifications to gasification of biomass and solid waste (sewage sludge, municipal wastes, etc.).

Fuel cells. Both natural gas and hydrogen can serve as fuel in polymer electrolyte membrane fuel cells (PEMFCs) which have the ability to generate electricity using electrochemical reactions as opposed to combustion of fossil fuels to generate electricity. The fuel is delivered at the anode side of the cell that contains a carbon-supported electrocatalyst such as platinum. Problems addressing chemical attack of the electrolyte membrane, carbon erosion and platinum instability continue to plague fuel cells[53]. The challenge with fuel cells particularly for automotive applications is in developing new proton exchange membranes that meet the demanding requirement for long-term temperature stability at a desired working temperature of 130ºC. The other is the need to offset the dilution of the electrolytes in the membranes by the water produced during the cell's operation. Among developments to meet such requirements is the use of hybrid membrane materials based on phosphonic acids[30] and alkaline anion exchange membranes[54] for fuel cells operating under basic conditions.

There is tremendous interest in the preparation of carbon supported electrocatalysts using nano-sized materials other than platinum as fuel cell electrodes, especially derived from inexpensive metals, as with the examples of a multiple metal catalyst film recently developed by researchers at Calgary[55], and the advanced electrocatalyst support material, titanium oxycarbide (TiO_xC_y), reported by researchers at the Technical University of Munich[56]. The Munich researchers have also observed that nano-catalysts based on transition metal oxides (e.g. ZrO_2) and carbides (e.g. MC_x, M=Mo, W) offer high potential as new non-noble metal electrocatalysts. Indeed, such nano-catalysts supported on TiO_xC_y are being actively explored as durable anodes for the efficient and selective total conversion of ethanol to carbon dioxide in direct ethanol fuel cells (DEFC) operating in the temperature range 150–200ºC. The liquid EtOH is oxidized at the anode in the presence of water, generating CO_2, hydrogen ions and electrons. Hydrogen ions travel through the polymer electrolyte membrane to the cathode where they react with oxygen from the air and the electrons from the external circuit forming water. The choice for ethanol as an alternative energy source is well founded on the abundance of bioethanol, and on its relatively simpler storage and use with respect to other energy carriers.

Hydrogen storage. Research addressing the challenge of hydrogen gas storage and purification has enjoyed only limited success, with the general approach to-date being based on 'host-guest' chemistry principles. In this context, both organic zeolites [e.g. Tris(o-phenylenedioxy)cyclotriphosphazene (TPP)][57] and metal-organic frameworks (MOF), e.g. $Zn_4O(BDC)_3$ (BDC = 1,4-benzenedicarboxylate)[58] have been explored. Also, two-dimensional polyphenylene, a polymer that resembles graphene structurally but has atom-sized pores, has been shown[59] to exhibit high selectivity for H_2 permeability relative to CO_2, CO and CH_4. 2D polyphenylene is 10^{23} times more selective for hydrogen compared to traditional silica and carbon separation membranes, which suggests a great potential for it for hydrogen purification applications.

On the local scene, research on membrane technology has led to the development of carbon membranes for gas separation and synthesis and production of carbon nanotubes for hydrogen storage for fuel cell application[60]. An ingenious reversible and recyclable hydrogen storage system has recently been reported[61] which involves hydrogenating CO_2 to form formic acid in the presence of a homogeneous iridium catalyst $[\{Ir(Cp^*)(Cl)\}_2(thbpym)]^{2+}$, where thbpym is

4,4',6,6'-tetrahydroxypyrimidine, and an inorganic base in aqueous media at ambient conditions. Reversible H_2 storage is achieved by switching the pH to protonate or deprotonate the catalyst.

CATALYSIS AND CHEMICAL SYNTHESIS

The area of **catalysis** needs no introduction to chemists and has seen numerous advances impacting many areas of chemistry. The search for new catalysts continues unabated driven by the demands of green chemistry, new product synthesis, pharmaceutical process chemistry and product-related technologies of materials science, among others. New market demands of modern petroleum refining and basic petrochemical industries also seek better performing catalyst systems to meet ever changing specifications.

Metal-based Catalysts

Transition metal (TM) catalysed reactions, such as olefin hydrogenation, hydrosilylation, cycloaddition, and polymerization, have long been valuable tools in chemical synthesis. Homogeneous asymmetric hydrogenation of olefinic and ketonic substrates catalyzed by chiral TM complexes has also provided a powerful means for preparing optically active organic compounds. Many transition and main group metals also form organometallic compounds that function as effective catalysts or as stoichiometric reagents for use in C-C bond formation reactions as in carbon monoxide and alkene-derived polymers. Interest in organometallic compounds, as catalysts, intermediates and reagents continues in the field of organic synthesis in the laboratory as much as in the industry in accomplishing several organic transformations in heterogeneous, homogeneous and phase transfer operational modes, and in miscellaneous applications such as stabilizers and biocides. In particular considerable effort in recent years has been directed at understanding the mechanisms and energetics of C-H and C-C bond activation of alkanes by TM ions which proceed via organometallic intermediates[62].

An elusive goal that is being addressed in this regard is C-H bond activation of the abundantly available simple alkanes by TM complexes that could lead to direct conversion into valuable functionalized organic compounds[63]. Pincer-ligated iridium complexes have been well demonstrated to act as catalysts for alkane dehydrogenation and serve as transfer hydrogenation agents. They have recently also been used in a tandem system with Schrock [Mo(IV) - and W(IV) - based alkylidenes] or Grubbs type[Ru(II) carbenoid complexes] olefin **metathesis** catalysts to achieve metathesis of higher alkanes, such as of conversion of n-hexane to n-decane[64].

Researchers at Scripps Energy & Materials Centre (USA) have made remarkable progress in catalytic hydrocarbon functionalization and have demonstrated several working examples of *de novo* C-H activation catalysts[65]. Among the examples are the use of Hg(II) cations and $Pt(bpym)Cl_2$ complex in sulphuric acid at 220ºC to convert methane to methyl bisulphate, the sulphate ester of methanol in high yield and selectivity. The conversion of the product methanol to methyl bisulphate makes it substantially less reactive than methanol towards the catalyst, which is a key factor in securing high yields. The mechanistic pathway involves the formation of organometallic species. They have recently extended this work to demonstrate an aqueous base accelerated C-H activation involving the use of $Ru(II)(IPI)(OH)_n(H_2O)_m$ complex, where IPI = 2,6-diimidizoylpyridine, as the catalyst. The electron-rich catalyst is thought to activate the alkane by net donation of electrons to the anti-bonding orbitals of the C-H bond.

Various metal halides (e.g. $AlCl_3$, $SnCl_4$, $SbCl_5$, $ZnCl_2$, $TiCl_4$) and their organometallic derivatives (e.g. $RAlCl_2$, R_2AlCl, R_3Al) can be used as Lewis acids for initiating cationic polymerization of styrene and other monomers. Aluminium trichloride is quite widely used in industrial practice, but low selectivity with respect to chain growth reaction as well as a number of side reactions attends its use. This can now be overcome and a ‘living’ polymerization of styrene achieved using the system $H_2O/AlCl_3{\bullet}O(C_6H_5)_2$, a result of considerable relevance to the synthesis of industrially important polymeric resins from the styrene dominated C9 petroleum fraction[66].

The best success story with homogeneous catalysts is probably that of metal carbenes. Continued improvements in selectivity of these catalysts have enormously expanded the scope of their applications in organic synthesis through cross-metathesis, ring-closing metathesis, ring-opening metathesis, ring-opening metathesis polymerization (ROMP) and acyclic diene metathesis polymerization.

Novel chiral Schrock (molybdenum and tungsten imidoalkylidene) catalysts have enabled the stereoregular synthesis of several ROMP polymers[67a]. Thus three of the four possible structures for polymers from an achiral monomer through a single ROMP polymerization step have been prepared, namely, *trans, syndiotactic* structures through chain end control, *cis, isotactic* polymers through enantiomorphic site control, and *cis*, syndiotactic polymers through stereogenic metal control.

Grubb's catalysts, which are easier to handle than Schrock's catalysts, have also proved equally versatile, enabling an exceptionally simpler olefin metathesis-based route for the synthesis of various insect pheromones such as 5-decenylacetate and to active ingredients in the pharmaceutical field such as p-fluorocinnamaldehyde[67b]. A Grubb's catalyst mediated ROMP route to alkaline anion exchange membranes via the copolymerization of a tetraalkylammonium-functionalized norbornene with dicyclopentadiene has been developed for application in lithium-ion batteries[54]. The thin films generated are mechanically strong and exhibit high hydroxide conductivities and exceptional methanol tolerance.

Olefin metathesis, both self-metathesis and cross-metathesis, presents a number of interesting possibilities for modifying seed oil derivatives. Seed oils can be metathesized efficiently at low temperature and pressure using Grubb's ruthenium catalyst without the rigorous exclusion of water and oxygen required with $WCl_6/SnMe_4$. Cross-metathesis of an unsaturated fatty ester with a normal alkene is a versatile way of producing chain-shortened or chain-extended homologues leading to oleochemicals with chain lengths outside the C_{16}–C_{22} range of most commodity oils. Examples of products that could be made more efficiently with olefin metathesis are macrocyclic compounds such as civetone, the ingredient in musk perfumes; 1-triacontanol, a plant growth stimulant; intermediates such as unsaturated diesters or dicarboxylic acids and ω-unsaturated esters; and various polymers[68,69].

Although preferred for large-scale industrial processes, heterogeneous metathesis catalysts show much lower effective turnover numbers for fatty acid methyl esters than most homogeneous catalysts, and particularly in comparison to the newest Grubbs' catalysts. For example, one of the best heterogeneous formulations is Re_2O_7 supported on borated silica-alumina. The addition of a promoter, typically an organotin compound such as tetrabutyltin, is required in order to prevent catalyst deactivation by polar functional groups. The promoted catalyst gave 198 turnovers in methyl oleate self-metathesis[69]. The oleochemical industry in Malaysia should seriously consider the highly atom-efficient olefin metathesis in broadening its product range.

New ROP catalysts differing substantially from Schrock and Grubbs' catalysts have also been devised in recent years, among them, bis(phenolate) amine-supported lanthanide borohydride complexes and alkaline earth tetrahydroborate complexes, $M\{HC(C(Me)NAr')_2\}(BH_4)(THF)_2$ (M = Ca or Sr), which when applied to cyclic esters such as ε-caprolactone and *rac*-lactide yield the commercially important polycaprolactones and polylactides, respectively, with high rates of conversion and excellent molecular weight and tacticity control[70].

Recent research in many University laboratories such as at Princeton[71] seeks to replace the established precious metals used for many organic reactions with more abundant and environmentally compatible base metals such as manganese, iron, cobalt and copper; the last-mentioned has featured prominently in "click chemistry", a chemical philosophy popularised by Nobel Laureate Barry Sharpless. The Princeton researchers have also made extensive headway in the discovery of new reactions for dinitrogen functionalization, including CO induced scission of the N≡N bond yielding two N-C bonds and one C-C bond[71].

In the past five years, visible-light mediated **photoredox catalysis** has been emerging as one of the fastest growing fields in organic chemistry because of its low cost, easy availability and environmentally benign nature. With the advent of the hydrogen economy, photocatalysis has assumed further importance. The catalysts being studied include a number of photosemiconductor catalysts which assist in the conversion of solar energy into hydrogen via a water-splitting process. A prime example involves the catalyst $Ru(bpy)_3]^{2+}$ whose excited state can be described as an Ru^{3+} complex containing a $(bpy)^-$ ligand. The excited state is a triplet relative to the singlet ground state and its longer half-life favours charge separation and endows it both oxidizing and reducing properties[72]. Thus, the photochemical properties of $[Ru(bpy)_3]^{2+}$ are reminiscent of the photosynthetic assembly, which also involves separation of an electron and a hole. $[Ru(bpy)_3]^{2+}$ has been examined as a photosensitiser for both the oxidation and reduction of water. Other applications are being intensively explored.

Another photocatalyst that has attracted wide attention, especially among material scientists, is titanium dioxide. When TiO_2 is exposed to light in the presence of water vapour, two highly reactive oxygen species are formed[73]: hydroxyl radicals [• OH] and a superoxide anion [• O_2^{-1}]. These oxidize airborne volatile organic compounds and toxic organic matter into carbon dioxide and water at room temperature with UV or near-UV light source. This also explains the strong UV light-responsive and visible light-responsive bactericidal activity of TiO_2 as the reactive oxygen species formed cause peroxidation damage to the lipid cell membranes[74].

Besides photooxidation, TiO_2 can also bring about photoreduction. Thus acetylene was converted to a mixture of CH_4, C_2H_4, C_2H_6 and C_3 hydrocarbons when UV-irradiated on incompletely degassed TiO_2 powder[75]. With complete degassing under vacuum, no hydrogenation products were observed save for the photochemical and thermal production of benzene. The result was attributed to loss of chemisorbed water during outgassing which reduces the concentration of surface Ti-OH groups. Indeed, the photolysis of chemisorbed water on incompletely degassed TiO_2 powder was shown[76] to yield hydrogen and oxygen in the molar ratio of 2:1 if conducted under argon. In the presence of molecular nitrogen, oxygen is still obtained but the evolution of hydrogen is inhibited as the chemisorbed nitrogen gets reduced to ammonia and traces of hydrazine.

Organocatalysts

Another area gaining research prominence is the use of organocatalysts[77] where the absence of metal favours contribution to green chemistry. Both chiral and achiral organocatalysts have been successfully applied to organic synthesis, but greater interest in recent research literature appears focused on asymmetric organocatalysis or enantioselective organocatalysis. Mention may be made here of MacMillan organocatalysts[78] (a certain class of imidazolidinone compounds) that have already found use for a myriad of asymmetric transformations (Figure 7). These catalysts exploit the strategy of LUMO-lowering activation of α,β-unsaturated aldehydes via reversible formation of iminium ions with them. This renders the unsaturated aldehydes more susceptible to nucleophilic attack. Central to success of imidazolidinones as **stereoselective iminium activators** is their ability to form, effectively and reversibly, reactive iminium ion intermediates with high levels of both geometry control and π-facial discrimination.

Because organocatalysis utilizes simple organic molecules as catalysts, each individual catalytic system is inherently independent. This hallmark of organocatalysis offers a unique opportunity to build catalytic sequences whereby the product of one catalytic transformation can feed into another catalytic cycle as a substrate. The MacMillan group has advanced this concept ("organocascade catalysis")[78] where multiple catalytic cycles are performed in the same reaction vessel, emulating biosynthetic machinery, and they have advanced mechanisms for such merged catalytic cycles that have resulted in the preparation of novel organic products. Importantly, this concept allows for the straightforward generation of multiple stereocentres in a single operation and thus streamlines synthetic assembly lines.

A simple example involving photoredox catalysis and organocatalysis is the enantioselective α-alkylation, trifluoromethylation, and benzylation of aldehydes using a ruthenium photoredox catalyst with an imidazolidinone organocatalyst[78].

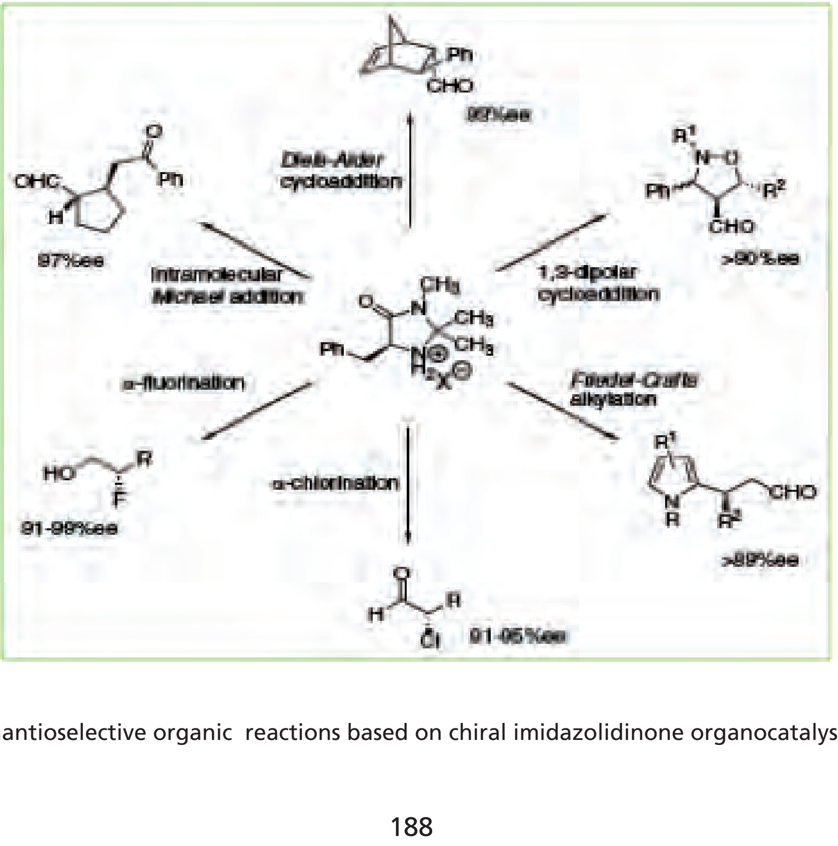

Figure 7. Directed enantioselective organic reactions based on chiral imidazolidinone organocatalysts [Source: Ref: 77].

Metal-free organic catalysts[79] have been developed jointly by researchers from Stanford University and IBM as part of their broad strategy for green polymer chemistry to synthesise biodegradable and biocompatible polyesters, via such techniques as ring-opening, anionic, zwitterionic, group transfer, and condensation polymerization. They also developed organic catalysts to depolymerize poly(ethylene terephthalate)(PET) quantitatively, the strategy for green polymer chemistry to synthesise biodegradable and biocompatible polyesters, via such techniques as ring-opening, anionic, zwitterionic, group transfer, and condensation polymerization. They also developed organic catalysts to depolymerize poly(ethylene terephthalate)(PET) quantitatively, thereby allowing recycling of used PET bottles.

Single-site Heterogeneous Catalysts

Transition metal complexes and organocatalysts are highly active and selective in the homogeneous phase, and their heterogenization by incorporating them into inorganic solid materials potentially allows combination of their excellent catalytic activity with improved separation, recovering and recycling properties. This expectation has recently been borne out in the efficient organocatalysis of an asymmetric Diels-Alder reaction[80] with imidazolidinone catalytic moieties embedded into a chiral organosilica polymer (ChiOSP).

Numerous other examples exist in the literature where the advantages of heterogeneous and homogeneous catalysis have been combined which underpins the strategy of single-site heterogeneous catalysis, among them the Ti/$MgCl_2$-supported Ziegler-Natta catalyst[81]. The principal characteristic of a single-site heterogeneous catalyst (SSHC) is that all of the active sites present in it are identical in their atomic environment making them highly selective. The active sites are also spatially separated, thus ensuring that they are readily accessible to reactants. Single-site heterogeneous catalysts facilitate the determination of the kinetics and mechanism of catalytic turnover-both experimentally and computationally-and make accessible the energetics of various intermediates (including short-lived transition states)[81]. These facts in turn offer a rational strategic principle for the design of new catalysts and the improvement of existing ones.

Catalyst Systems Inspired by Supramolecular Chemistry

To the uninitiated, the field of catalysis might seem to be essentially empirical. Nothing could be further from the truth. The design and understanding of catalysis is of major interest to chemistry and life (if one also includes biocatalysts), and this concern is reflected in the origins of supramolecular chemistry.

The field of supramolecular chemistry[82] has benefitted from landmark contributions by three Nobel Laureates in the persons of Donald Cram (‘host-guest’ complexes), Jean-Marie Lehn (cryptand complexes) and Charles Pedersen (crown-ether complexes). Their work has provided the basis for the insight into the importance of noncovalent interactions (such as hydrogen bonding, metal coordination, hydrophobic forces, van der Waals forces, pi-pi interactions and electrostatic effects) in catalysis, binding reactants into conformations suitable for reaction and lowering the transition state energy of reaction. Important concepts that have been demonstrated by supramolecular chemistry include molecular self-assembly, folding, host-guest chemistry, mechanically-interlocked molecular architectures, dynamic covalent chemistry and molecular recognition[82].

A striking new example of self-assembly is the aggregation of a β-peptide foldamer composed of amino cyclopentane carboxylic into three-dimensional (3D) organic structures such as windmills in water, and other structures such as petals, rectangular rods and molar tooth in the co-presence of a surfactant[83]. These structures could be used to prepare organic materials for nanobioelectronics and molecular machines for biomedical engineering.

Metal-directed self-assembly is now a well-established tool to prepare large and elaborate complexes such as helicates, grids, boxes, rings, and cages from relatively simple components.

Recently, however, it has been shown that ‘innocent’ anions can dictate the course of the assembly process by acting as a template around which a particular combination of metal ions and ligand can assemble in a way which would not occur in the absence of the anion. One example is the ClO_4^- and BF_4^- anion- templated synthesis in solution of the edge-bridged tetrahedral caged complexes, $[(L)Ni(\mu\text{-}L)Ni(L)][X]_4$ and $[Co_4(\mu\text{-}L)_6X]\,[X]_7$,where X= encapsulated anion and L- bis-bidentate ligands containing two *N*,*N*-bidentate pyrazolyl-pyridine units linked to a central aromatic spacer unit (1,2-phenyl or 2,3-naphthyl, respectively)[84].

Another example is the EO_4^{n-} (E=S, Se, Cr, Mo, W) oxoanion-templated self-assembly of M_4L_6 (M=Ni, Zn) tetrahedral cages, where L is a functionalised urea anion ligand[85]. With appropriate functionalization of the organic components L, selective encapsulation of tetrahedral oxoanions could be had from aqueous solutions, based on shape, size, and charge recognition. Upon removal of the templating anion, the tetrahedral M_4L_6 cages rearrange into different co-ordination assemblies. Thus 6 equivalents of urea, 12 equivalents of bipridine and 4 equivalents of $NiSO_4$ undergo subcomponent self-assembly in aqueous solution to form a tetrahedral cage that strongly encapsulates a sulphate anion, which cannot be displaced by addition of Ba^{2+}. The bipyridyl-functionalization holds the six urea molecules in arrangement along the edges of tetrahedron to provide the necessary twelve hydrogen-bonds to the encapsulated SO_4^{2-} (Figure 8). This self-assembly was aided by computer design.

A host-guest system in Nature that is one of the tightest binding molecular systems is the avidin-biotin complex, achieving an extraordinarily high affinity (dissociation constant, $K_d \approx 10^{-15}$ M^{-1}) through non-covalent interactions. Avidin is a protein derived from both avians and amphibians, and biotin is a co-factor that plays a role in multiple eukaryotic biological processes. Avidin and other biotin-binding proteins, including streptavidin have the ability to bind up to four biotin molecules which are normally conjugated to an enzyme, antibody or target protein to form an avidin-biotin complex. The strong avidin-biotin interaction has been exploited for use in many protein and nucleic acid detection and purification methods.

The first example of a fully synthetic, monovalent host–guest system that matches the affinity of avidin and biotin has recently been reported[86] involving the host cucurbit[n]uril (n=7) and the guest molecule, 1,1′-bis(trimethylammoniomethyl) ferrocene (Figure 9).

The equilibrium association constant for this host-guest pair is 3×10^{15} M^{-1}. The cucurbiturils, which can also be functionalised to improve their solubility in common solvents, are macrocyclic molecules made of glycoluril monomers linked by methylene bridges. They have gained much attention in the new millennium for their exceptional molecular recognition ability.

Recently, the potential of streptavidin as a protein scaffold to create artificial metalloenzymes that are able to perform bio-orthogonal reactions, including transfer hydrogenation, allylic alkylation or enantioselective sulphoxidation, has been explored[87]. In this approach an organometallic catalyst is covalently linked to biotin and upon stoichiometric addition of streptavidin, the metal moiety is quantitatively incorporated within the host protein via its biotin binding pocket. This yields a product that potentially combines the features of homogenous catalysis with the beneficial characteristics of enzymes. Additionally to chemical tailoring of the biotinylated catalysts (variation of the biotin-spacer-ligand moiety), an optimization of the protein scaffold can be achieved by applying directed evolution protocols (mutation of streptavidin) such as discussed later (in the section on Industrial Biocatalysis, see pp. 192–195). Such chemogenetic optimization schemes have been successfully applied to generate artificial metallocenes for various enantioselective transformations[87,88].

Template-directed synthesis. Template-directed synthesis is a special case of supramolecular catalysis. It is widely used method to prepare 1D nano-structures, such as wires, rods, tubes, etc. Thus, for example, by using hollow self-assembled metal–organic spheres as templates[89], it is possible to make silica nanoparticles with uniform shapes and sizes in a precisely controlled fashion than would otherwise be possible. Cylindrical polymer brushes[90] have also been exploited as robust unimolecular template for the fabrication of various hybrid nanowires and nanorods, for instance, γ-Fe_2O_3, CdS, CdSe, TiO_2, silica, Au, Te, etc.

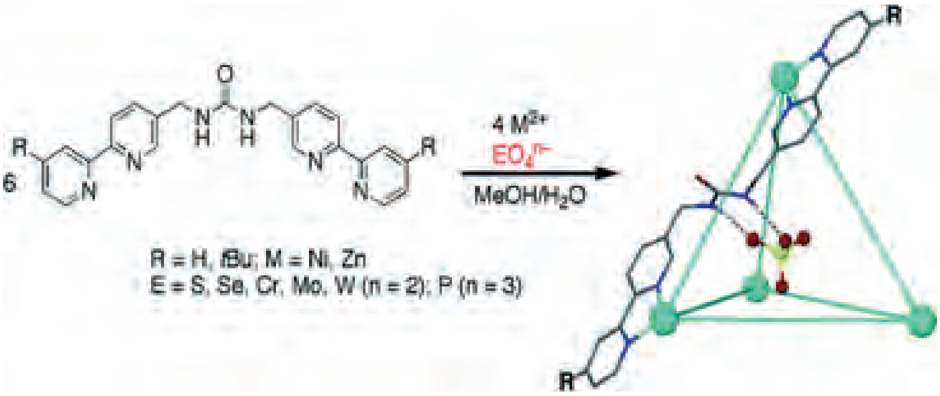

Figure 8. Selective encapsulation of SO_4^{2-} from aqueous solution through self-assembly [Source: Ref. 85].

Yet another example is found in the "active-metal" template synthesis of catenanes, rotaxanes and other interlocked molecular structures[91]. A rotaxane is a molecular arrangement comprising at least one molecule with a linear section threaded through at least one macrocyclic part of another or the same molecule and having end-groups large enough to prevent dethreading[92]. If only a single macrocycle is threaded upon a single linear molecule, the nomenclature applied to the molecule is [2]rotaxane. If two macrocycles are threaded upon the single linear molecule or vice versa, then it is a [3] rotaxane.

Rotaxanes are of interest in molecular electronics as logic molecular switching elements and as molecular shuttles. In their function manipulated by chemical or photochemical inputs, the macrocycle can be made to rotate around the axis like a wheel and axle or slide along the axis from one recognition site to another.

The key feature of the active-metal template strategy is that the metal plays a dual role during the assembly of the interlocked architecture, acting as both a template for entwining or threading the components and as a catalyst for capturing the interlocked final product by covalent bond formation. An example is the copper(I)-catalysed terminal alkyne–azide cycloaddition (CuAAC "click"reaction)[91]. Co-ordination of Cu(I) to an endotopic pyridine-containing macrocycle allows the alkyne and azide to bind to metal atoms in such a way that the metal-mediated bond-forming reaction takes place through the cavity of the macrocycle — or macrocycles — forming a rotaxane (Figure 10).

DNA rotaxanes[93] have recently been created in ring and axle arrangements for potential use as molecular machine.

Encapsulated catalysts. Encapsulation systems such as micelles, dendrimers and clusters are also used in catalysis to create microenvironments suitable for reactions (or steps in reactions) to progress that is not possible to use on a macroscopic scale[84].

A recent report in *Nature Chemistry*[94] has articulated the advantage of encapsulation in a Ga_4L_6 tetrahedral supramolecular cluster of both enzymatic (lipases/esterases) and transition metal (Au^1/Ru^{II}) catalysts to catalyse organic reactions. The absence of diffusion into the bulk solution of the catalysts which would otherwise have compromised their activity through adventitious binding to amino-acid residues on proteins was attributed to the formation of organometallic complexes.

Silica nanocapsules functionalized with thiol or amine groups with sizes between 100 and 400 nm have been synthesised to encapsulate monomers or catalysts (in solution form) that can then be used as additives in coatings to bring about self-healing[95]. The release of the healing agent is triggered by mechanical damage or environmental stimuli.

Zeolites are a class of inclusion compounds in which the occluded guests can be removed without collapse of the host structure[96]. The porous structure that results upon the removal of guests has proved to be technologically important in the area of shape-selective catalysis as in the petrochemical industry. Organic zeolites[97] are a new entrant in the field with potential for the synthesis of chiral organic molecules.

An emerging field of catalysis is based on zeolite-like metal frameworks which consist of metal ions linked together by bridging ligands. These include aluminium phosphates, metal phosphates and hybrid inorganic-organic systems. There

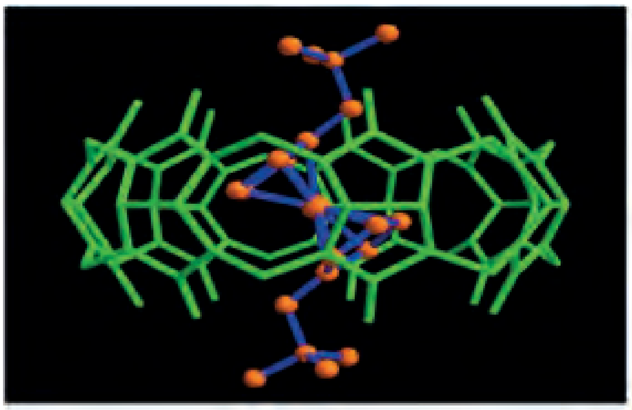

Figure 9. X-ray crystal structure of the CB[7]. Ferrocene complex [Source: Ref. 86].

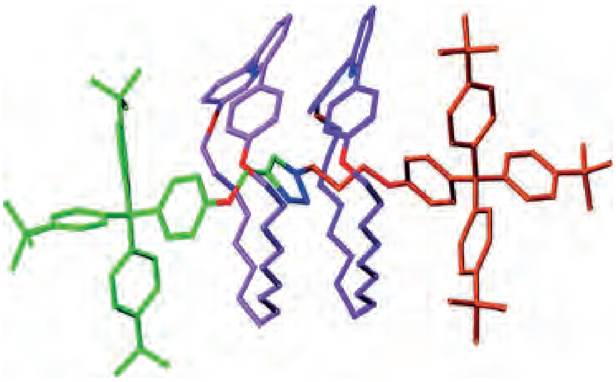

Figure 10. Active-metal template synthesis of a [3]rotaxane molecule [Source: Ref. 91].

is no consensus in the scientific literature about the definitions of the terms coordination polymer and metal-organic framework (MOF)[98]. They constitute an important class of solid-state compounds with potential applications in the field of heterogeneous catalysis that include acid, shape-selective, chiral, ship-in-a-bottle and shape-recognition-driven reactions. Thus, a palladium-containing metal–organic framework (Pd-MOF) was found to be an active catalyst for alcohol oxidation, Suzuki C-C coupling, and olefin hydrogenation. The MOF structure is preserved throughout catalysis, and the material is reusable. The Pd-MOF demonstrates remarkable shape-selectivity for olefin conversion. The literature also contains numerous references to catalysis by homogeneous catalysts incorporated as framework struts, catalysis by MOF-encapsulated molecular species, catalysis by metal-free organic struts or cavity modifiers, and catalysis by MOF-encapsulated clusters.

Nanomaterial-based Catalysts

Nanomaterials enjoy a broad scope of applications, including in medicine, catalysis, molecular imprinting, coatings and imaging. In their catalytic application, they are usually heterogeneous catalysts comprising of metal nanoparticles. The high surface-to-volume ratio of the nanoparticles contributes to their enhanced catalytic activity over bulk materials. They can be readily separated following reaction and are often reused with little impairment of activity. In their catalytic role, they may serve as actual catalytic sites or as support for catalytic processes. Functionalizing the nanoparticles presents the advantage of retarding aggregation through van der Waal's attractions; such functionalising groups can include ligands that can coordinate to the metal and oligomers which give steric stabilization.

The oxidation of cyclohexane to adipic acid which is used as a monomer for nylon production uses cobalt nanoparticles as catalysts. Nanostructured $Cu/ZnO/Al_2O_3$ catalysts are employed in industrial methanol synthesis. An example taken from the recent literature where nanoparticles serve as support is that of ferrite nanoparticles peripherally functionalized with phosphine groups[99]. One, two, and up to three noble metals can be loaded onto the surface. Palladium loading is shown to occur with participation of both the phosphine function and the surface hydroxyl groups. Hybrid nanoparticles containing simultaneously Pd and Au (or Rh) are obtained by successive loading of metals. Similarly, ferrite nanoparticles decorated with Pd, Au, and Rh have also been formed by using the same strategy. The catalytic properties of the new nanoparticles have been demonstrated in processes such as reduction of 4-nitrophenol and hydrogenation of styrene as well as in Suzuki C-C cross-coupling reactions. The catalysts are magnetically recoverable and reusable.

Catalysis in Ionic Solvents

During the past few years, room temperature ionic liquids which are salts of organic cations, for example, tetraalkylammonium, alkylpyridinium, 1,3-dialkylimidazolium, tetraalkylphosphonium, have been increasingly considered as replacements for volatile organic solvents. Although all are not environmentally benign, the majority possess "green" credentials. They possess other potential advantageous properties such as reasonable thermal stability, ability to dissolve a wide range of organic, inorganic and organometallic compounds, controlled miscibility with organic solvents, ease of separation from products, and potential for recycling. They have already found use in chemical synthesis, catalysis, fuel cells, and other applications[100].

Examples[100] of organic transformations that have been carried out using ionic liquids as solvents include hydrogenation, oxidation, Heck cross-coupling reaction, Suzuki reaction, Diels-Alder reaction, aldol condensation, alkylation, Michael addition, Schmidt reaction, ring-closing metathesis, esterification reaction, and enzyme-catalyzed organic reactions. However, since the application of the first ionic liquid sample as solvent for organic transformations, the synthetic focus has been essentially on homogeneous catalysis in ionic liquids.

Recently, the combination of chitosan as a renewable heterogeneous catalyst and 1-Butyl-3-methylimidazolium bromide as ionic liquid has been applied for the Knoevenagel condensation between benzaldehyde and malononitrile (an activated methylene compound) to yield benzylidene malononitrile[101]. The chitosan could be recovered for re-use after the reaction. Conventionally, this reaction is catalyzed by alkali metal hydroxides or by organic bases under homogeneous conditions with the attendant difficulties in catalyst recovery and recycling.

Industrial Biocatalysis

This field has received much attention in recent years, especially in regard to industrial-scale synthesis of specialty chemicals and pharmaceuticals where biocatalysis is applied to the synthesis of their key intermediates and/or key building blocks or synthons. A number of recent texts and review articles[102–106] give a comprehensive coverage of the field where literature citations to various important enzyme based processes applicable in kilogram or ton scale synthesis can be found.

Biocatalysis is fast emerging as a vital part of organic and green chemistry, and its growth has been spurred by biotechnology which has progressed in the present decade with clear strategic alignments to sustainability[106].

Most biocatalytic processes still operate in aqueous environments and in a batch mode; continuous processes are still the exception. A persistent concern is the low product concentration, and the requirement of special methods for product extraction. Biotransformations in organic media are often incompatible with enzymes (exceptions include such enzymes as lipases), leading to enzyme degradation or inactivation. Advantages to be gained with enzymatic catalysis in nonaqueous media include enhanced enzyme thermostability and altered specificity, and thermodynamic equilibria which are shifted to favour synthesis over hydrolysis, e.g. esterification and peptide formation. A further advantage is that the risk of microbial contamination is lower than is the case in aqueous systems. However, enzyme activity in organic solvents is intimately related to water content, size and morphology of the catalyst particles and the enzyme micro-environment[107]. These parameters have been adjusted by preparing lyophilized complexes of enzymes with carbohydrates, organic buffers or salts, an example being subtilisin Carlsberg. Suspensions of this protease enzyme, prepared by lyophilizing an aqueous preparation in the presence of non-buffer salts, yielded rate enhancements of more than 20 000-fold[103]. Another example[103] is the use of KCl-activated bacterial protease thermolysin to acylate selectively and in 100% yield the 2'-hydroxyl group of paclitaxe (taxol) in *t*-amyl alcohol medium. Thermolysin has also featured in the enzymatic synthesis of the peptide compound aspartame (L-[alpha]-aspartyl-L-phenylalanine methyl ester] on an industrial scale from N-protected L-aspartic acid and D/L-phenylalanine methyl ester in mixed organic media[103,105].

Other approaches[103,108,109] to the problem of low enzyme activity in biotransformations carried out in organic solvents have included the use of surfactants, microencapsulation of the biocatalyst within reverse micelles, cross-linked enzyme crystal technology, enzyme immobilization and use of supercritical fluids and ionic liquids.

Whole cell catalysis has also been successfully employed in a number of instances, among them in the industrial production (notably by the Schering Group, Germany) of steroids such as androstendione and androsta-dien-dione from natural phytosterols using mutants of *Mycobacterium* sp. devoid of steroid-ring degradation activities[103]. These steroids are used as basic substrates for subsequent chemical and biotechnological syntheses of drugs.

Similarly, whole cells of *Agrobacterium* DSM6336 have been developed by Lonza (Switzerland) for the preparation of 5-hydroxypyrazinecarboxylic acid from the starting material 2-cyanopyrazine[103]. This involves a two-step biotransformation- the hydrolysis of the nitrile group to pyrazinecarboxylic acid and the subsequent regioselective hydroxylation to 5-hydroxypyrazinecarboxylic acid. The 5-substituted pyrazine-2-carboxylic acid was then used for the preparation of novel antituberculosis drugs. The same company has also successfully used wild-type *Pseudomonas putida* ATCC 33015 for the enzymatic oxidation of methyl groups on aromatic heterocycles.

Proprietary genetically engineered strains of microorganisms for improved enzyme variants have also been developed for many applications, as in the case of the production of cellulosic ethanol discussed earlier (in Biomass Conversion to Bioenergy, see pp. 182–183). Other genetically modified microrganisms include the fungus *Penicillium chrysogenum* whose fermentation yields benzylpenicillin (Penicillin G) and phenoxymethylpenicillin (Penicillin V)[103], and the anaerobic bacterium *Clostridium diolis* DSM 15410 for improved fermentation of glycerol to 1,3-propanediol[110] (1,3-PD).The 1,3-PD is the precursor for the production of the polyester polytrimethylene terephthalate.

A new magnetic biocatalyst, namely penicillin G acylase (PGA), immobilized in sol-gel matrices with magnetic properties, ultimately aimed for catalysing the synthesis of cephalexin (CEX) from D-α phenylglycine methyl ester and 7-aminodeacetoxycephalosporanic acid, has been reported[111]. The immobilized PGA retained high specific activity throughout ten consecutive runs for PG hydrolysis, suggesting adequate biocatalyst stability.

Baeyer-Villiger monooxygenases represent a specific class of flavin-containing monooxygenases that are capable of catalyzing a variety of oxidation reactions, including Baeyer-Villiger oxidations of a wide range of carbonylic compounds, epoxidations, and enantioselective sulphoxidations. A broad range of biocatalytic conversions of cyclic ketones to lactones, linear ketones to esters, sulphoxidations and other oxidations have been achieved, for example, with encapsulated recombinant cells *Escherichia coli* overexpressing cyclohexanone mono-oxygenase[112]. The encapsulated cells were tested in a continuous packed-bed minireactor connected with flow calorimeter and integrated with bubble-free oxygenation. The minireactor exhibited high operational stability; the cells also showed high enzyme stability and yielded higher than 80% substrate conversions following storage up to 60 days.

Throughout all phases of drug discovery and development, for structural elucidation, biological testing or as analytical references, having qualified metabolite standards is advantageous. Chemical synthesis of metabolite standards is often difficult and expensive. As an alternative, biological generation and isolation of metabolites in the nanomole range are readily feasible. A broad toolbox is applied for the synthesis of both Phase 1 (Functionalization) as well as Phase 2 (Conjugation) metabolites at Novartis[103]. This toolbox comprises of, among others, recombinant *Escherichia coli* overexpressing human cytochrome P450 mono-oxygenases and a collection of wild-type micro-organisms pre-selected for their oxidative biotransformation capacity.

Lipases are a long established class of industrial biocatalysts used (notably by BASF, Germany) in the synthesis of enantiomerically pure alcohols and chiral amines[102]. The synthesis is essentially a transesterification reaction using acyl donors; only enantiomer may be acylated. For the alcohols the acyl donors are typically vinyl esters, anhydrides or diketene, while for amines ethylmethoxyacetate is an efficient acylating agent for resolution of the racemic amines[102–104].

Use of a racemic chiral acyl donor group such as vinyl 3-phenylbutanoate has been shown to improve the enantioselectivity of the kinetic resolution for lipase catalysed transesterification of a primary alcohol which has a chiral centre at the β-position of the hydroxyl group as in 2-phenyl-1-propanol[113] (E = 98; solvent: hexane).

The source of the lipase can be a factor in the efficiency of the biocatalytic reaction. This is shown by the superior activity of lipases of *Pseduomonas aeruginosa* MTCC 5113 relative to commercially available lipases of *Candida antarctica* and porcine pancreas in the transesterification of benzyl alcohol and vinyl acetate in heptane to produce the flavoring agent benzyl acetate[114].

There are extensive reports on lipase-catalysed transesterification for biodiesel production. A mycelial lipase from *Rhizopus rhizopodiformis* showed exceptionally high thermal stability in transesterification studies (alcoholysis) conducted on palm oil mid-fraction (PMF) in organic solvents such as hexane. Of the two prevalent fatty acids in PMF, palmitic acid was preferred over oleic acid in the formation of methyl and propyl esters[115].

The palm oil effluent compost is itself a veritable source of lipase producing fungal strains belonging to *Aspergillus, Penicillium, Trichoderma* and *Mucor* genera[116]. The lipase producing profile showed that *Trichoderma* (8.07–8.24 u/ml) and *Aspergillus* (6.25 –7.54 u/ml) spp. were the highest lipase producers, while *Mucor* (5.72 u/ml) was the least.

In a review on the subject of lipase-catalysed transesterification, Parawira[117] notes that there is much scope for optimisation research, especially in the development of new reactor systems with immobilised biocatalysts, the use of lipases tolerant to organic solvents, intracellular lipases (whole microbial cells) and genetically modified micro-organisms (intelligent yeasts).

Different enzymatic routes can sometimes be brought to bear on a drug synthesis, such as of halohydrin dehalogenase, a nitrilase or an aldolase in the biocatalytic synthesis of the key side chain of atorvastatin (Lipitor)[118].

In new developments, the potential of using tailored single species biofilms for protecting and immobilising enzymes for biotransformation is being actively investigated[119]. There are also endeavours to convert fungal laccases into valuable biomolecular platforms on which new functions can be tailored by directed evolution. Fungal laccases are generalist biocatalysts with potential applications that range from bioremediation to novel green processes.

Directed evolution has led the search for new biocatalysts with more efficacious properties such as activity, selectivity (enantio- and regio-), substrate specificity, stability, and solubility. The molar concentrations typically used in industrial chemical processes to reduce costs, speed up reactions, and to improve product purification would frequently have deleterious toxic effects on the biocatalyst, or result in the accumulation of unwanted by-products. Directed evolution, with its repertoire of tools embracing error- prone PCR, site-directed mutagenesis, Gene Shuffling and Computational Modelling, has the potential to reduce the effects of product inhibition or by-product formation[120,121].

Two illustrative examples underscore the growing importance of structure based rational design followed by directed evolution in the biocatalytic synthesis of pharmaceuticals.

The first of these concerns the P450 cytochrome family of hemoproteins which catalyze the monooxygenation of a diversity of hydrophobic substrates. Labrou *et al.*[122] have reported their study on the catalytically active cytoplasmic P450 enzyme CYP102A2 obtained from *Bacillus subtilis*. This was subjected to error-prone PCR to generate mutants with enhanced activity towards fatty acids and other aromatic substrates. The library of CYP102A2 mutants was then expressed in BL21(DE3) *Escherichia coli* cells and screened for their ability to oxidize different substrates by means of an activity assay. After a single round of error-prone PCR, the variant Pro15Ser exhibiting modified substrate specificity was generated. This variant was efficiently immobilized on epoxy-activated Sepharose CL6B and its efficacy was demonstrated in the hydroxylation reaction of sodium dodecyl sulphate (SDS). The immobilization method offers the possibility for scaled up applications.

The second example concerns the biocatalytic synthesis of the antidiabetic compound, Januvia® (Sitagliptin Phosphate Monohydrate, a Merck product)[123] to replace the current chemical synthesis which involves the key step of asymmetric hydrogenation of the enamine derived from prositagliptin ketone at high pressure using a rhodium-based chiral catalyst (Figure 11). Undesirable process conditions and problems with product quality led Savile et al[124] to explore a transaminase biocatalyst as substitute. Transaminases are enzymes that catalyze the enantioselective transfer of an amino group from a donor substrate via a pyridoxamine intermediate onto the carbonyl group of an acceptor substrate. Transaminases, however, have a limited substrate range, most accepting only substrates with a substituent no larger than a methyl group at the position adjacent to the ketone. Noting that commercial transaminases showed no activity for amination of the prositagliptin ketone (the immediate precursor to the final chiral amine product), Savile *et al.*[124] chose a homolog of ATA-117, a broad R-selective transaminase from *Arthrobacter* sp., also without activity towards the substrate, to create a transaminase with marginal activity by applying a substrate walking, modelling, and mutation approach; this variant was then further engineered via directed evolution for practical application in a manufacturing setting.

Computational modelling enabled the enzyme's binding pocket for the substrate's triazolo piperazine moiety to be optimized by site-saturation mutagenesis of a single position while substitutions in three positions expanded the binding pocket for the substrate's trifluorophenyl group. Once detectable transaminase activity was established for the target substrate, they next applied 10 rounds of directed evolution which included such protocols as site-saturation, random mutagenesis and DNA shuffling to obtain a mutant library from which the most catalytically active variant was identified that could withstand the operating conditions of 50% organic solvent fraction, reaction temperature to 40ºC, and the prositagliptin ketone concentrations to 200 g/l. The enzyme variant that best met these selection criteria harboured 25 mutations and catalysed the transamination with >99.9% enantiomeric excess.

It is important for Malaysian scientists to engage in all these representative areas of catalysis to gain expertise in the design and use of catalytic materials that can gainfully impact their future research.

New Horizons in Organic Synthesis and Catalysis Science

Synthetic organic chemistry has been enriched in recent decades by the aforesaid advances in the field of catalysis that have made seemingly difficult syntheses possible and allowed several new techniques to emerge, among them molecular self-assembly, click chemistry and cascade or tandem syntheses to construct complex carbocycles and heterocycles. It is also relevant to point out that the philosophy of sustainable or green chemistry has also pervaded current research across the spectrum of chemistry.

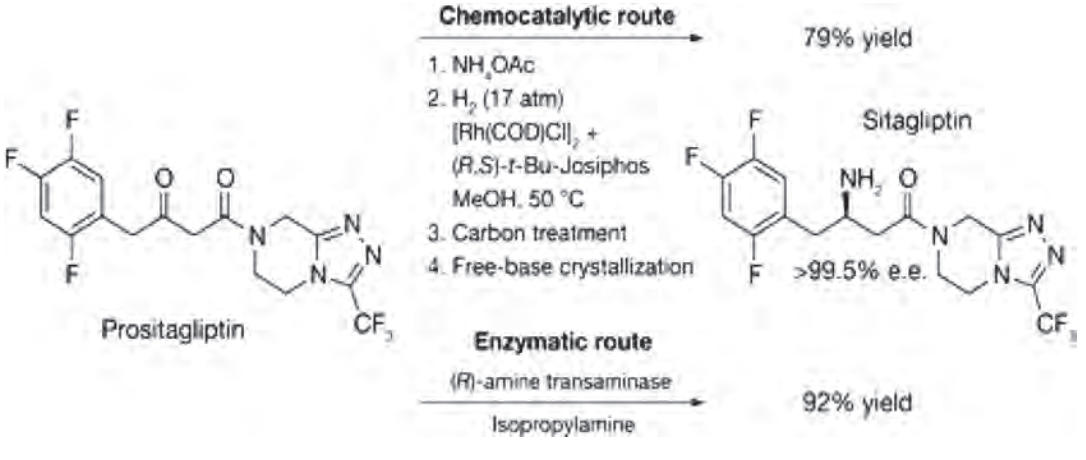

Figure 11. Biocatalysis advances synthetic chemistry [Source: Ref. 124].

Newer innovations in organic synthesis which are still in various stages of development or refinement include combinatorial chemistry[125] — a technology for creating molecules *en masse* and testing them rapidly for desirable properties — and solvent-free microwave-assisted[126] and ultrasound-assisted[127] syntheses. The above cited references provide excellent reviews on these, including insights on applications. Although less well studied, some good examples of solvent-free mechanochemical synthesis of compounds are found scattered in the literature, among them that of the organic LED material, *tris* (8-hydroxy-quinolinato) aluminium, by the ball-milling of $Al(OAc)_2OH$ and 8-hydroxyquinoline with subsequent heating[128].

In organic synthesis, the handling of free-radicals in a controlled way still remains a challenge, but new results involving manganese (III) acetate suggest that this difficulty could be overcome by deploying a wide range of protocols for its use under mild and efficient reaction conditions. Thus $Mn(OAc)_3$ mediated oxidative radical cyclizations have been used to synthesize a range of densely functionalized and sterically congested cyclopentane-lactones with vicinal all-carbon quaternary stereocentres[129], as well as in the synthesis of a host of complex biologically active compounds[129].

In general, the $Mn(OAc)_3$ induced radical reaction requires an acceptor and a donor in order to form a carbon–carbon bond[130]. The acceptor is usually a carbonyl partner having an α-hydrogen which is used to produce the corresponding Mn(III)-enolate complex; the donor is usually an electron-rich carbon–carbon double bond partner which oxidatively transfers one electron to the enolate complex.

The grand challenge for catalysis science in the 21st century is to understand how to design catalyst structures to control catalytic activity and selectivity. Towards this goal there is wide consensus that 'in situ *measurements of chemical, spatial, and temporal properties of working catalysts be undertaken using state-of-the-art characterization methodologies, including existing and future synchrotron and neutron facilities*" so that deeper insights on catalyst structure and function could be had[131]. There is also a need to couple experimental studies with theoretical studies, including such predictive methods as density functional theory (DFT), to understand and predict how catalysts work at the nano scale and atomic scale. Such studies are to be extended to high temperatures and pressures used in current industrial processes as well as to newer efforts at catalytic production of new fuels and chemicals by selective oxidation of alkanes such as methane. New insights into protein structure and activity are also serving as inspiration for the design of catalytic structures.

The reader is referred to two excellent literature sources for additional information on the progress and challenges in the field, namely, the 2002 Report of the Basic Energy Sciences Advisory Committee to the US Department of Energy[131] and the Handbook of Heterogeneous Catalysis[132], 2nd edition, 8 volumes (2008).

Femptosecond spectroscopic techniques[133] have recently added a new dimension to methodologies aimed at probing the transition states and intermediates of catalysed chemical reactions on ultrafast time scales, in conjunction with theoretical/ computational studies. Such approaches may well hold the key to the design of more efficient catalyst systems in the future.

Industrial biocatalysis is on the verge of significant growth with directed evolution becoming the method of choice for developing enzyme- and microorganism-based biocatalysts[134]. The recent development of new efficient diversity-generation methods such as random insertion/deletion (RID) to randomly introduce codon-based mutations in a gene, along with high-throughput screening methods is poised to bolster this field and further advance the contribution of biocatalysis to the chemical and the pharmaceutical industries.

A new area of catalysis has also dawned with the advent of artificial metalloenzymes created by incorporating an organometallic catalyst within a host protein. The resulting hybrid can thus provide access to the best features of two distinct, and often complementary, systems: homogeneous and enzymatic catalysts. Such catalysts can be subjected to chemogenetic optimization schemes as demonstrated by Ward *et al.*[87,88,135] for biotinylated organometallic catalysts anchored to the streptavidin protein scaffold. They have applied these catalysts to the following enantioselective conversions:

> (i) The rhodium-diphosphine catalyzed hydrogenation of N-protected dehydroaminoacids (ee up to 95%); (ii) The palladium-diphosphine catalyzed allylic alkylation of 1,3-diphenylallylacetate (ee up to 95%); (iii) The ruthenium pianostool-catalyzed transfer hydrogenation of prochiral ketones (ee up to 97% for aryl-alkyl ketones and ee up to 90% for dialkyl ketones); and (iv) The vanadyl-catalyzed oxidation of prochiral sulphides (ee up to 93%).

Such studies pave the way for chemical biology applications of artificial metalloenzymes.

MATERIALS SCIENCE

Materials Science is said to hold great potential for 21st century manufacturing and innovation, according to Global Research Report[136] (2011). This view point is also shared by such chemical industry giants as DuPont. The global research landscape reveals that Asia now produces half the world's papers in materials science, with China being the largest single country producer. The Report also notes the enormous research output in the areas of graphene, metal organic frameworks and electrospun polymeric nanofibre scaffolds.

After the discovery of **fullerene and carbon nanotubes**, graphene has emerged as the most exciting of the new nanomaterials that has captured the imagination of the scientific community world-wide as a replacement for silicon in electronics as well as for new applications. Semiconductors grown on graphene could become the basis for new types of device systems. A step in this direction is the recent effort of researchers at the Norwegian Institute of S&T in successfully growing GaAs nanowires[137] on graphene, a hybrid material with competitive properties. Meanwhile, the field of carbon nanotubes continues to elicit wide interest in experimental and theoretical research aimed at developing new technologies based on the material's excellent electronic and mechanical properties which have already stimulated application in fabrication of flat panel displays, gas storage devices, toxic gas sensors, Li ion batteries, robust and lightweight composites, conducting paints, electronic nanodevices, etc.

Graphene and Graphene Oxide

Graphene is a flat monolayer of sp^2 carbon atoms tightly packed into a two-dimensional (2D) honeycomb lattice (Figure 12). Just one atom thick, graphene exhibits excellent mechanical, electronic, optical, thermal and chemical properties. With its eminent manifested properties such as the quantum Hall effect, ambipolar electric field effect and transport via relativistic Dirac fermions, graphene is now at the forefront of nearly every rapidly developing field of science and engineering, including biochemistry, biomedicine and other cutting-edge interdisciplinary fields. Application areas cited in the literature[138] that leverage specific graphene properties include THz detectors and lasers, liquid crystal devices, single-electron transistors, superconducting FETs, room temperature spintronics and in chemical sensors and MEMSA-based applications.

The electronic properties of graphene, which has zero band gap, are rather unusual. The interaction between the electrons and graphene's honeycomb atomic structure causes the electrons to behave as if they have absolutely no mass, and because of this the electrons are governed by the Dirac equation — the quantum mechanical description of electrons moving relativistically — and are therefore called Dirac fermions. A non-zero band gap (which is needed to create transistors) can be achieved with a graphene bilayer by having electrical gates on both the top and bottom layers; the average effect of the displacement fields in each layer breaks the bilayer's inversion symmetry and hence gives rise to a non-zero band gap which is tunable from 0 to 0.25 eV by varying the voltage applied to the gate electrodes.

Graphene sheets can be obtained by Hummer's method by oxidising graphite in sulphuric acid to graphitic oxide and then exfoliating the graphitic oxide sheets by sonication. Reduction of a colloidal suspension of the exfoliated graphene oxide sheets in water with hydrazine hydrate results in their aggregation and subsequent formation of a high-surface-area carbon material which consists of thin graphene-based sheets.

A low-temperature reduction method to graphene sheet synthesis has been proposed by Russian scientists[139] using sodium in liquid ammonia at –30ºC to treat the graphite and then subjecting the graphite, intercalated with the sodium ammoniate and solvated electron, to careful hydrolysis in a chamber which explosively releases ammonia and hydrogen. The gaseous products give rise to pressure that cleaves the graphite structure into separate sheets, ultimately into graphene sheets. Scalable levels of graphene at high yields, high purity and controlled structure are achievable by this method. Other sources of graphene investigated include polyphenylene and polycyclic aromatic hydrocarbon precursors.

A bottom-up process to make gram scale quantities of graphene was recently reported by Australian scientists[140] starting from completely non-graphitic precursors — ethanol and sodium. The approach simply involves mixing the two components together under pressure to produce a white powder than turns black when heated. This material is made up of fused carbon sheets that can be broken down into single sheets of carbon using mild sonication.

Intercalation of graphene sheets has been investigated with such metals as lithium and calcium. The lithium-intercalated material has found use as an electrode material in lithium batteries, thus serving as a method for electrochemical energy storage[141]. The calcium-intercalated graphene bilayer, fabricated on silicon carbide, has enabled researchers to construct an unconventional organic superconductor, C_6CaC_6, at its two-dimensional limit[142].

The graphene derivative, graphene oxide, can be prepared[143] from graphite flakes by treating it with a mixture of potassium permanganate, sulphuric acid and phosphoric acid. This strictly yields graphite oxide (GO) which possesses chemically reactive oxygen groups such as carboxylic acid, epoxy and hydroxyl groups[144] which can be functionalised[145] with compounds such as $HO(SO_2)(CH_2)_nNH_2$ (n: 3–24) to make it dispersable in high concentrations in appropriate solvents. Graphite oxide has attracted much interest recently as a possible route for the large-scale production and manipulation of graphene. GO disperses in basic solutions, which weaken the platelet–platelet interactions, to yield monomolecular sheets, known as graphene oxide by analogy to graphene, the single-layer form of graphite. A variety of thermal and mechanical methods can also be used to exfoliate GO to graphene oxide, though sonicating and/or stirring GO in water are the most common[138].

Graphene oxide has evinced excellent properties as a carbocatalyst in bringing about organic transformations[146]. To cite a few: the oxidation of hydrocarbons, oxidation of alkenes to diones, oxidation of methyl benzenes to their respective aldehydes, oxidation of disubstituted methylenes, such as diarylmethanes, to their respective ketones, hydration of alkynes to ketones, and dehydrogenation reactions, such as the aromatization of tetralin to form naphthalene.

An interesting new use for graphene oxide has been reported for the efficient and rapid removal of highly toxic radionuclides from contaminated water, even under acidic solutions ($pH < 2$)[147].

Other Stable 2D and Lower Dimensional Material Systems

The discovery of graphene can be considered as a defining point in the research and development of other stable 2D material systems[148]. This breakthrough has opened up the possibility of isolating and exploring the fascinating properties of atomic layers of several other layered materials, which upon reduction to single/few atomic layers, will offer functional flexibility, new properties, and novel applications. Counted among them are nitrides (e.g. hexagonal boron nitride), dichalcogenides (e.g. molybdenum disulphide[149]: Figure 12) and oxides (e.g. vanadium pentoxide).

There is enormous interest in building devices and functional materials based on such isolated atomic layers of different compositions to complement those from graphene. Nano-electronic devices built on 2D materials is seen by many in the electronics field to offer benefits for further miniaturization beyond Moore's Law and as a high-mobility option in the emerging field of large-area and low-cost electronics that is currently dominated by low-mobility amorphous silicon and organic semiconductors. However, challenges in isolating such materials into free-standing 2D atomic layers have to be overcome in order to obtain such structures in controllable ways.

Interest in low dimensional compounds stems from the observation that some properties such as high-temperature superconductivity is phenomenologically coupled to two-dimensional layered arrangements, while antiferromagnetic frustration requires specific transition metal arrangements such as one dimensional chains or columns. Magnetic frustration is a hypothetical stress in the alignments of spin directions between neighbouring electrons. When frustration arises due to the geometry or topology of a lattice, it is called geometric frustration.

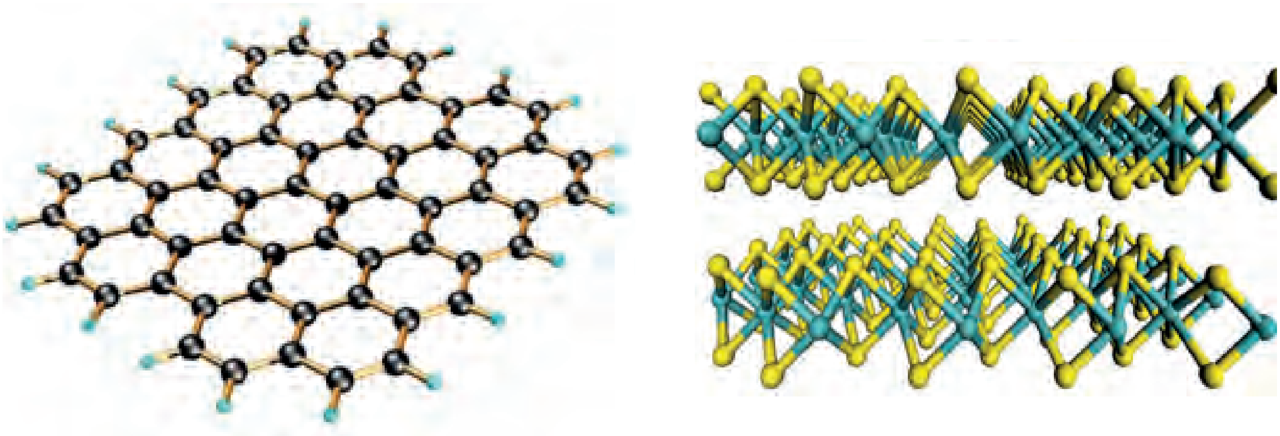

Figure 12. Structures of 2D materials: Graphene (left) and molybdenum disulphide* (right) [*Source: Ref. 149; Mo atoms in teal, S atoms in yellow].

Transition metal oxohalides are among several classes of compounds that have been investigated for access to low dimensional structures. Takagi[150], for example, has synthesised several two-dimensional compounds of the variety AE-Te^{IV}-TM-O-X (AE = alkaline earth element, TM = Co^{II}, Ni^{II} and Cu^{II}, X = Cl and Br). When the AE forms irregular co-ordination polyhedra e.g. [AEO$_v$], [AEX$_w$] or [AEO$_y$X$_z$], their polyhedra tend to link together to form larger units, such as chains or layers. The stereochemically active lone pair of electrons on Te along with the presence of alkaline earth element polyhedra serves to block or reduce the dimensionality of the transition metal oxide/halide network. They thus influence the structural arrangement at the transition metal by functioning effectively as spacers. The structure[151] of [$CaCo_2Te_3O_8Cl_2$], for example, reveals helical chains of [CoO_5Cl] octahedra along the [010] direction, connected by [CaO_8] polyhedra, [TeO_3E] tetrahedra and [TeO_4E] trigonal bipyramids (the lone pair of electrons on Te^{IV} is designated as E) to form a layer. The layers are held together only by weak van der Waals forces.

Recently, the literature of low-dimensional Cu^{II} molecular magnetic systems in which superexchange pathways involve halide ions and/or cyclic 1,4-diazines has been reviewed[152]. Compounds are organized by lattice type between 1D systems (including uniform and alternating chains, and ladders) and 2D systems (including square and rectangular layers).

Nanoscale one-dimensional (1D) structures, like nanowires, nanoribbons and nanotubes, have gained much attention in the past decade as attractive building blocks for fabricating electronic and optoelectronic devices. Carbon nanotubes have turned out to be useful precursors for quasi-1D graphene nanoribbons (GNRs). The nanotubes are readily unzipped in sodium/potassium solutions. The GNRs exhibit tunable electrical properties through dimension confinement as well as edge morphology or functionalization. Their application as electrode materials in lithium-ion batteries[30] has been discussed in earlier (in the section, Energy Storage and Future Progress, see pp. 181–182).

A prime example among other 1D nanostructures is tin oxide (SnO_2), a n-type direct wide-band semiconductor (E_g= 3.6 eV at 300K), which possesses both good conductivity and transparency in the visible region. The nanowires may be obtained by carbothermal synthesis or laser ablation of pure tin in oxidising Ar/O_2 atmosphere. Important electronic and optoelectronic devices built on 1D SnO_2 nanostructures include gas sensors, lithium-ion batteries, and nanophotonics (LEDs, lasers, and detectors)[153]. The bulk material itself has a long history of applications ranging from catalyst supports, transparent conducting electrodes, antireflective coatings and a proto-type material for metal oxide sensors.

Metal Oxides

Metal oxides, in particular transition metal oxides, are some of the most important inorganic solids. Three common structures adopted by these compounds are the rutile (TiO_2), rhenium trioxide (ReO_3) and the perovskite ($CaTiO_3$), and many complex structures have been found to be variants of these, for example, yttrium barium copper oxide (YBCO), $YBa_2Cu_3O_{7-x}$, the first material to superconduct ($0 \leq \times \leq 0.65$) above liquid nitrogen temperatures, which can be viewed as an oxygen-deficient perovskite. In this sense, it may be termed a doped insulator. The term doping is understood in the materials science world as the creation of carriers in a system that would otherwise be insulating, and results from the formation of defects. The range of defects formed includes metal-site substitution, metal anti-site defects, metal-site vacancies, oxygen vacancies, interstitial oxygen, and the incorporation of excess oxygen made possible by the modulation of local atom displacements. In some systems, the defect itself is the doping mechanism; in others, defect formation plays a key role during synthesis and, in fact, permits the synthesis of compounds that would otherwise not be attainable.

Complex oxide materials, whether doped or otherwise, possess a wide range of electrical, optical, and magnetic properties. For instance, insulators, dielectrics, ferroelectrics, piezoelectrics, semiconductors, ferromagnetics, transparent conductors, colossal magnetoresistance materials, superconductors, and nonlinear optic materials have all been produced using oxide materials. Thin films and heterostructures of oxide materials have thus great potential for novel device applications. A major challenge is to prepare these materials with epitaxial thin film form with atomic layer control and integrate them so that these properties can be fully utilized in electronic devices.

As elegantly summarised by Rao[154a], the phenomenal range of electronic and magnetic properties exhibited by transition metal oxides is truly astounding. "Thus we find oxides with metallic properties (e.g. RuO_2, ReO_3, $LaNiO_3$) at one end of the range and oxides with highly insulating behaviour (e.g. $BaTiO_3$) at the other. There are also oxides that traverse both these regimes with change of temperature, pressure or composition (e.g. V_2O_3, $La_{1-X}S_{rx}VO_3$). Interesting electronic properties also arise from charge density waves (e.g. $K_{0.3}MoO_3$), charge ordering (e.g. Fe_3O_4), and defect ordering (e.g. $Ca_2Mn_2O_5$, $Ca_2Fe_2O_5$). Oxides with diverse magnetic properties anywhere from ferromagnetism (e.g. CrO_2, $La_{0.5}Sr_{0.5}MnO_3$) to antiferromagnetism (e.g. NiO, $LaCrO_3$) are known. Many oxides possess switchable orientation states as in ferroelectric (e.g. $BaTiO_3$, $KNbO_3$) and ferroelastic [e.g. $Gd_2(MoO_4)_3$] materials. In respect of high-temperature superconductivity, we now have oxides with transition temperatures in the region of 130K."

It has recently been shown[154b] that barium titanate, which normally forms a perovskite cubic structure, precipitates as a 2D quasicrystal at high temperatures on a Pt(111) substrate. The unexpected interface-driven structure with the triangular and square atomic structures forming a non-repeating quasicrystalline tile pattern is the first such documented case for a metal oxide. The work demonstrates that frustration at the interface between two periodic materials can drive a thin film into an aperiodic quasicrystalline phase. The newly discovered oxide-based quasicrystalline surface which is chemically stable has sparked interest in potential new technological applications.

Perovskite rare earth manganites, [$M_y R_{1-y} MnO_3$] (M=Ca, Sr, Ba; R= La, Nd, Eu, etc., $0.1 < y < 0.3$), also popularly known as "**colossal magnetoresistive**" (CMR) oxides, have recently been a focus of materials research. CMR is magnetoresistance associated with a paramagnetic-to-ferromagnetic phase transition that occurs when the parent compound, $LaMnO_3$, is hole–doped by the alkaline-earth cation (20–40% holes/Mn ion). Near the phase transition temperature, which can exceed room temperature in some compositions, these materials record a large magnetoresistance; their electrical resistance drops significantly by 10–20% in the presence of a magnetic field. From a theoretical standpoint, CMR is only partially explicable in terms of either the double exchange model which relies on the presence of mixed valency Mn(III)/ Mn(IV) states or the half-metallic ferromagnetic model which posits a metallic majority spin band and a non-metallic minority spin band in the ferromagnetic phase; a fuller explanation of the phenomenon is still awaited which might necessitate the inclusion of electron-lattice coupling effects.

From the applications perspective, however, these materials command much interest as CMR is 200 times stronger than ordinary magnetoresistance. IBM was the first to realise that read heads incorporating CMR materials would be able to sense much smaller magnetic fields, allowing the storage capacity of a hard disk to increase from 1 to 20 gigabits. This has now spawned the field of **magnetoelectronics (spintronics)** where two fundamental properties of the electron, namely its charge and its spin, are manipulated simultaneously, with such developments as magnetic random access memory devices, hybrid devices incorporating semiconductors such as silicon, and motion sensors.

In addition to CMR, several of the manganites (e.g. $Ba_{0.3}La_{0.7}MnO_3$) also exhibit giant volume magnetorestriction (GVM) in the vicinity of the magnetic-ordering phase transition temperature (i.e. the Curie temperature)[155]. Magnetorestriction is a property of ferromagnetic materials that causes them to change their shape or dimensions during the process of magnetization. Both CMR and GVM have negative values. Both phenomena are attributed to the presence of magnetic (ferromagnetic-antiferromagnetic) two-phase states in these systems, which is associated with a strong s-d exchange. Local disorder in the M_yR_{1-y} sub-lattice (the so-called perovskite A-site), which is occasioned by the presence of cations of different radii, leads to a displacement of oxygen atoms and to crystal lattice softening.

A new series of manganese oxides, $ALaMn_2O_{6-y}$, for A = K, Rb, and Cs, with an ordered superstructure of the perovskite, has also been synthesised and studied[156] wherein the tetragonal K and Rb phases were found to be ferromagnetic (Curie temperatures ≈ 327K and 300K, respectively) metals, exhibiting a negative giant magnetoresistance behaviour similar to alkaline earth metal substituted lanthanide manganites. The results revealed that it is possible to induce Mn(III)/ Mn(IV) mixed valency and the related electronic properties through anion deficiency in ordered perovskites of the kind $ALaMn_2O_6$.

Besides their obvious application in the spintronics field, CMR manganites have promising potential for bolometric infrared detection in a wide range of temperatures from room temperature down to liquid nitrogen temperatures[157].

An unexpected research result that has recently been announced by researchers at the National Institute of Materials Research (Japan) is that $NaCr_2O_4$, which is not a ferromagnetic metal, but rather, is an antiferromagnetic semiconductor, exhibits CMR behaviour over a wide temperature range[158], i.e., the entire temperature range below the magnetic transition temperature. This appears to involve a new CMR mechanism which has the novel feature of not displaying history effects with respect to temperature or the magnetic field. The result has important implications for the search for CMR materials.

The recent literature contains reports on the successful growth of high quality thin films of vanadium dioxide[159] and samarium nickelate[160]. The VO_2 thin film undergoes a phase transition upon application of an electric field — proof that the material could be used as an electronic switch. A phase transition frees electrons from their localized state near each atom, without moving them through the bulk material. By contrast, silicon switches work by pulling electrons through the material to a channel where they conduct current, a process which consumes more power. The successful deposition of the $SmNiO_3$ thin film on top of a silicon substrate which leaves the underlying silicon layers intact has raised the possibility of manufacturing metal oxides on top of silicon wafers to form three-dimensional chips.

At the University of Wisconsin, a multi-university team of researchers have developed a promising new high temperature **superconducting material** composed of 24 layers that alternate between an iron-based pnictide superconductor and a layer of the oxide strontium titanate[161]. In its structure, the material seamlessly alternates between metal and oxide layers to achieve extraordinary superconducting properties.

In conventional superconductors, transition temperatures (temperatures below which they superconduct, Tcs) are below 30K as with Nb-Ti alloy (Tc 11K). The superconductivity here is explained by the Bardeen-Cooper-Schrieffer (BCS) theory which posits that the electrons are held together in Cooper pairs (as bosonic bound states; S=O, rarely 1) by an attraction mediated by lattice phonons. In unconventional, that is, high-temperature superconductors [Tcs considerably above the previous limit of about 30K; up to about 130K), it has been theorised that Cooper pairing is mediated by short-range spin-density waves known as paramagnons.

It is clear from the foregoing that metal oxides, especially involving transition metal oxides, whose properties depend on such external parameters as temperature, mechanical pressure, chemical composition, oxygen concentration, applied magnetic field or electric field, represent a wide variety of exotic and imperfectly understood structures, properties and phenomena that will continue to engage the interest of material scientists.

A facile synthetic route to high temperature superconducting and CMR oxides that does away with the normal high furnace synthesis has been advanced by Nobel Laureate Alex Muller[162]. This involves photoirradiation of the reagent mixture with halogen light (1200ºC) for less than half a minute. If a combination of halogen and UV light is used, the level of superconductivity can be maximized.

The metal oxide, TiO_2, is worthy of special mention. It is perhaps one of the most studied of the metal oxide materials owing to the facile chemical reduction of Ti^{IV} to Ti^{III}, which can act as catalytic redox centres. It has potential as a photovoltaic material and also shows promise as a useful photocatalyst, which may be used for water splitting applications. The electronic properties of TiO_2 can be modified by chemical doping or alloying or through the absorption of organic moieties on the surface, as in dye-sensitized solar cells. Defects in TiO_2 primarily arise from oxygen vacancies, typically with a +2 charge, and also on account of titanium defects which exist mainly as interstitials with charge states of +3 and +4.

Recently, a hybrid inorganic–organic material derived from TiO_2 has been synthesised which can be classified as a photoactive metal-organic framework (MOF)[98,163]. This material, titanium(IV) diterephthalate, was obtained as a highly porous and crystalline compound whose crystal structure reveals it is composed of octameric rings of Ti-O polyhedra connected by aromatic dicarboxylate linkers which gives rise to a three-dimensional periodic array of two types of hybrid cages with accessible pore diameters of 6.13 and 12.55 Å. Under nitrogen and alcohol adsorption, this material uniquely showed reversible photochromic transition from white to dark blue upon irradiation with UV light which has been assigned to the occurrence of new absorption bands at 2.10 and 2.47 eV. Walsh and Catlow[164] have explained this behaviour in terms of the material's remarkable defect chemistry: optical excitations larger than the band gap have sufficient energy to reduce titanium (Ti^{IV} to Ti^{III}) which introduces new states in the electronic gap; charge compensation was achieved either through loss of oxygen ($O^{2-} \rightarrow \frac{1}{2} O_2$) or hydroxyl formation. This photoactive porous MOF holds the potential for applications in smart photonic devices, sensors, and catalysis.

Single-molecule Magnets

Single-molecule magnets or SMMs are a class of catenated metal compounds that show superparamagnetic behaviour below a certain 'blocking' temperature[165]. The archetype is the "Mn_{12}", $[Mn_{12}O_{12}(OAc)_{16}(H_2O)_4]\cdot 4H_2O\cdot 2AcOH$. Others based on "$Mn_4$" and iron clusters are also known. The first example, however, of an **organometallic single-metal-ion magnet** has recently been discovered in the compound Erbium cyclooctatriene pentamethyl-cyclopentadiene[166]. This molecule displays a butterfly-shaped hysteresis loop at 1.8K up to even 5K and has two thermally activated magnetic relaxation processes. The molecule has elicited interest as a prototype for further development of single-molecule magnets (SMMs), which are being sought for applications such as high-density information storage and quantum computing.

Organometallics

Organometallic compounds of transition metals[167] and of the Main Group metals[168] continue to engage the interest of researchers world-wide, both from a synthetic and structural perspective as well as with regard to their applications in stoichiometric and catalytic processes, especially involving carbon monoxide and alkene-derived polymers.

Many Main Group organometallics, especially organo-magnesium, -lithium, -aluminium, -thallium, -mercury and - tin compounds have become the cornerstone of organic synthesis in their use as stoichiometric reagents or in-situ intermediates, but among these organotin compounds, which have a wide range of chemical and biological applications, boast of an extensive coordination and structural chemistry which has engaged the attention of Malaysian academics as tin is a natural resource in the country[169].

Metal-organic chemical vapour deposition (MOCVD), a highly complex process for growing crystalline layers to create complex semiconductor multilayer structures, is a major process in the manufacture of optoelectronics. Several Group III-V, IV and IV-V-VI semiconductors are grown by this method.

Since 1997 six organometallic chemists have been honoured as Nobel Laureates because their work has had such an enormous impact not only on the field but also to related areas of the chemical sciences, especially organic synthesis. The mechanistic pathways unravelled from such works have since become standard textbook material for chemists. In the meanwhile advances in the organometallic field continue to contribute to the discovery of new technologies and materials, from novel polymers and nanomaterials to more efficient syntheses of pharmaceuticals and industrial feed stocks.

The illustrative example of how advances in metathesis catalysts have further impacted organic synthesis (has already been discussed in Metal-based Catalysts, see pp. 186–188). Another is the improvement on the palladium catalysed Suzuki cross-coupling reaction of aryl halides using boronic acids which goes by the name of Suzuki–Miyaura coupling reaction. This is one of the most versatile methodologies for the selective formation of the C–C bond, in particular for the production of biaryls. Biaryl moieties are found in a variety of pharmaceuticals, liquid crystals, conductive polymers and natural products. A further improvement has come in the wake of palladium replacement with nickel which has appeal on both economic and environmental grounds. The coupling reaction can also be performed under phosphine-free conditions as in the reported[170] aryl coupling with polyethyleneimine ligand, $NiCl_2{\bullet}6H_2O$ and K_2CO_3 in ethylene glycol at 80–100ºC. Excellent yields were obtained of the biaryl derivatives, with the catalyst also being recyclable. As with palladium, an organonickel intermediate has been postulated in the catalytic cycle.

In a recent review[171] a broader application for the nickel-based Suzuki–Miyaura coupling reaction has been envisaged using other aryl electrophiles such as phenols, aryl ethers, esters, carbonates, carbamates, sulphamates, phosphates, phosphoramides, phosphonium salts and fluorides, as well as various alkyl electrophiles.

Current research in organometallic chemistry includes such areas as cluster synthesis, main-group derivatives in unusual oxidation states, organometallic polymers, new olefin polymerization and oligomerization catalysts, unstable organometallic compounds and intermediates in matrices, structure determination of organometallic compounds in the solid state [X-ray diffraction] and gaseous states [electron diffraction], and mechanisms of reactions of transient silylenes and related species.

Cluster research spans both mixed transition metal clusters and mixed main group-transition metal clusters; the latter aims to assess how the competition between the fundamental bonding properties of p-block and d-block elements is expressed in geometric and electronic structure as well as reactivity[172]. Transition metal hydrazides, $(L)M{=}NNR_2$, because of their relevance to the biological conversion of N_2 to ammonia, is another area of compelling research interest. Several research laboratories have their focus on the synthesis, structure, bonding and reactivity of unusual organometallic complexes, as may be exemplified by the recently reported studies of Professor Mountford at Oxford University on a stable two-coordinate silylene[173], the first Group 4 metal bis(imido) and tris(imido) complexes[174], and the first calcium-transition metal bonded compound[175] in the heterobimetallic $[Ca\{CpFe(CO)_2\}_2(THF)_3]_2$.

Unlike magnesium which readily forms organomagnesium compounds, there are few known organometallic compounds of Ca, Sr or Ba. Rieke *et al.*[176] have shown that the difficulty in the synthesis of organocalcium compounds can be overcome by using reactive calcium prepared by lithium biphenylide reduction of calcium halides in THF. When reacted with organic halides such as 1-adamantyl chloride, the reactive calcium yields the corresponding organocalcium compounds which undergo facile Grignard-type reactions.

Researchers at the RIKEN Advanced Science Institute in Japan have recently succeeded in the isolation and structural characterization of a new series of rare earth dialkyl complexes of scandium and yttrium, which were previously thought difficult to isolate[177]. Treatment of the dialkyl complexes with the borate compound $[Ph_3C][B(C_6F_5)_4]$ generated the corresponding cationic monoalkyl species which were shown to be catalytically active in the polymerization and copolymerization of a variety of olefins, including ethylene, styrene, 1,3-conjugated dienes, and cyclic olefins. Cationic half-sandwich scandium alkyls were also shown by these researchers to be excellent catalysts for the methylalumination of internal alkynes and alkenes, showing unprecedented regio- and stereoselectivity[178]. On the other hand, the rare-earth-catalyzed regio- and stereoselective dimerization of terminal alkynes led to the discovery of π-conjugated aromatic enynes as a novel single-emitting component for white electroluminescence. The RIKEN investigations are poised to open up research interest in organometallic derivatives of other rare earth metals.

Researchers at RIKEN have also extended their electroluminescent studies to main group organometallics and have reported on the use of diphenyl bis(8-hydroxyquinolinato)tin(1V), $Ph_2Sn(quin)_2$, as an emitting and electron injection layer in bilayer devices[179]. The 8-hydroxyquinoline ligand (Hquin) bound to aluminium as in $Al(quin)_3$ is widely used as an organic emission material layer (EML) in commercial fabrication of organic light-emitting diodes, such as in the Samsung patented high performance electroluminescence 2×2 mm^2 device, ITO/$Al(quin)_3$/NaF/Al, wherein the novelty lies in the improved electron mobility caused by the interposing NaF interlayer between the EML and the cathode. The device does not include a separate electron transporting layer. The interlayer works as an interface-dipole-control layer and transports electrons and blocks holes so as to provide a high light-emitting efficiency[180]. More recently, inorganic tin(11) compounds such as $SnCl_2$.(Hquin-R) (R=H, Cl, Me) have been added to the list of electroluminescent materials[181].

Polymers

In the search for new materials in bringing a new technical concept to fruition, **polymers** are often the materials of choice. Natural and synthetic polymer chemistry is thus very much a dynamic and growing field. National research expertise is strong in rubber and other elastomer plastic materials and adhesives as well as in a range of polymer composites, but there is a need to take cognizance of the progress in a number of areas where polymers portend advanced technological applications. Polymer chemistry is a vast field and embraces a wide array of materials that continue to be actively researched. Not so long ago, however, the search for new polymers was regarded as no longer appealing since most of the important goals of polymer research were supposed to be achievable using the then available classes of compounds. Revival of interest in polymer synthesis can be traced to the following developments: increase in the efficiency and scope of polymer synthesis as a result of new synthetic methods developed in organic and organometallic chemistry, the introduction of novel polymer topologies made from biopolymers and synthetic polymers or equally important synthetic polymers and inorganic materials, and the discovery that macromolecules have the potential to form supramolecular assemblies with unique properties.

The range of **industrially relevant synthetic polymer materials** (organic and inorganic) and composites derived from them is very wide[182]. They include: conducting polymers (such as polypyrroles, polythiophenes and polyanilines) for applications in molecular electronic devices, batteries and biosensors; photo-electro conductive polymers (in new generation solar cells); conjugated and hyperbranched polymers for electroluminescence applications; liquid-crystalline and high-performance polymers and fibres; polymeric gels and networks; self-reinforced polymer composites; stimuli-responsive ‘smart' polymers, including corrosion-sensing and self-healing coatings; reactive non-ionic and anionic surfactants that can be employed as emulsifiers or as pigment dispersants for improvement of latex stability, foam reduction and water resistance; self-assembling polymers and nanostructured polymer thin films for use as advanced coatings for marine and biomedical applications; metal nanoparticles and hydrogels investigated as novel solution-phase support systems for the immobilization of transition metal complexes and for their use in combinatorial solution-phase chemistry; nanoporous membranes based on peptide residues; proton exchange membranes for fuel cells; heat resistant composites comprising glass-ceramic matrix systems reinforced with silicon carbide or carbon fibers; flame retardant and flame resistant polymers; self-oscillating polymers and gels based on the Belousov-Zhabotinsky (BZ) reaction; polymer brushes for applications in areas such as prevention of bacterial adherence, cell attachment, electrochemistry, and formation of colloidal crystals; and biocompatible/ bioabsorbable /biodegradable polycarboxylic- and polyphosphoesters. Other macrocyclic materials such as cyclodextrins, calixarenes and functionalized cucurbiturils, which offer much scope in pharmaceutical and industrial applications, may also be broadly placed under this category.

Research on **metal-containing polymers** has advanced substantially in recent years. These macromolecular materials possess unique chemical and physical properties that lead to their potential application in an assortment of areas such as organometallic, coordination, and medicinal chemistry, as well as biotechnology. On account of the metal centre, these polymers can adopt various co-ordination numbers, oxidation states, geometries, types of bonding, and degrees of polymerization, all of which can impact the properties of this class of polymers. Furthermore, these macromolecules may have catalytic, electrochemical, optical, and/or magnetic properties that contribute to the applications of metal-containing macromolecules. The π-conjugated class among these polymers has aroused special interest as they could be used in energy harvesting devices such as solar cells or LEDs, where high charge carrier mobilities of the conjugated material could be combined with either light-absorbing or emitting metal groups. Additionally, metal complexes may be used to geometrically orient π-conjugated materials in specific three-dimensional arrangements in the solid state and thus influence emission properties and charge mobility of these materials[183].

The metal-containing polymers can be of three types: polymers with tethered metal complexes (type 1), polymers with pendant metal complexes (type II), and polymers with metals in the backbone (type III). Among key methods used for their synthesis is electropolymerization. A fuller understanding of the effects of coupling metal and polymer redox moieties on the conductivity and optical properties of these materials remains to be achieved. Potential uses of these materials include sensory and catalytic applications.

Developing scaffolds that mimic the architecture of tissue at the nanoscale is one of the major challenges in the field of tissue engineering. The development of nanofibers (by electrospinning or self-assembly) has greatly enhanced the scope for fabricating scaffolds that can potentially meet this challenge. Tissue-engineered medical implants, such as **polymeric nanofiber scaffolds**, are potential alternatives to autografts and allografts, which are short in supply and carry risks of disease transmission[184]. These scaffolds have been used to engineer various soft connective tissues such as skin, ligament, muscle, and tendon, as well as vascular and neural tissue. Bioactive versions of these materials have been produced by encapsulating molecules such as drugs and growth factors during fabrication.

While most engineered tissue is layered in scaffolds that take the shape of circular or square holes, a research team at the University of California (San Diego) in 2011 has bioengineered two new shapes using polyethylene glycol scaffolds (Figure 13) called "re-entrant honeycomb" and "cut missing rib". Both shapes exhibit the property of negative Poisson's ratio (i.e. not wrinkling when stretched) and maintain this property whether the tissue patch has one or multiple layers[185]. This new biomaterial closely mimics human tissue.

Compared with synthetic polymers, naturally occurring polymers normally exhibit better biocompatibility and low immunogenicity, when used in biomedical applications. All four major classes of biopolymers: proteins, polysaccharides, DNAs and lipids, have been fabricated into electrospun scaffolds[186]. Mats of electrospun chitosan nanofibers were found effective in immobilizing microalgal cells. Their application for wastewater treatment has been demonstrated by the removal of around 87% nitrate from liquid effluents[186].

A major advance in **fluorescent biopolymers** has been made by Texas University researchers Jian Yang and co-workers[187] who have developed aliphatic biodegradable photoluminescent polymers (BPLPs) and their associated cross-linked variants (CBPLPs) for biomedical applications. BPLPs are synthesized from biocompatible monomers including citric acid, aliphatic diols, and various amino acids via a convenient and cost-effective polycondensation reaction. BPLPs can be further cross-linked into elastomeric cross-linked polymers, CBPLPs. The researchers have shown representatively that BPLP-cysteine and BPLP-serine offer advantages over the traditional fluorescent organic dyes and quantum dots because of their preliminarily demonstrated cytocompatibility *in vitro*, minimal chronic inflammatory responses *in vivo*, controlled degradability and high quantum yields (up to 62.33%), tunable fluorescence emission (up to 725 nm), and photo-stability. The researchers have further examined the in vitro cellular uptake of fluorescent BPLP nanoparticles and

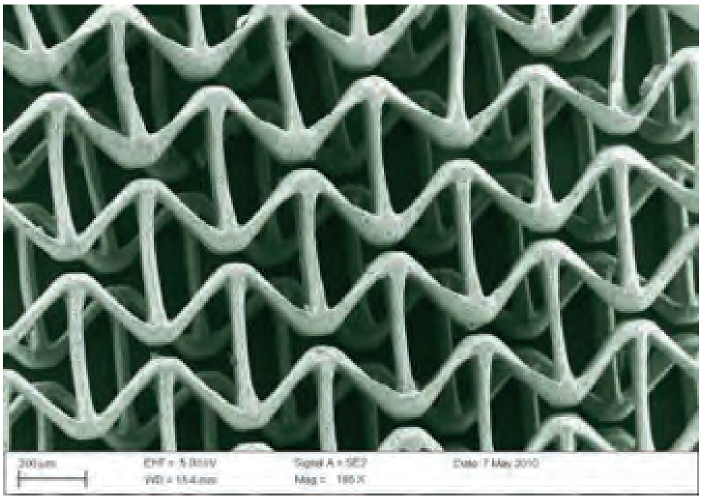

Figure 13. Optical images of polyethylene glycol scaffolds expanding in response to stretching [Source: Ref. 185].

conducted in vivo fluorescence bioimaging of CBPLP scaffolds to demonstrate their potential use in cellular fluorescence labelling, drug delivery and tissue engineering.

Biocompatible **hydrogels** are of special interest as a class of biomaterials for tissue engineering, regenerative medicine and controlled drug delivery. These materials offer three-dimensional scaffolds to support the growth of cells and development of hierarchical tissue structures. Very recently a synthetic zwitterionic hydrogel [polyethleneglycol-cross-linked polyhydroxyethylmethacrylate hydrogel] has been discovered which when applied as a coating on a medical implant has been found to thwart formation of a collagen capsule around the medical implant and thus prevent immune rejections[188]. The collagen capsule blocks mass transport and/or electric communication between the implant and the body and this is what prompts foreign-body reaction.

A polyisocyanopeptide hydrogel[189] that mimics the stress response of cytoskeletal proteins that form a cell's internal, shape-controlling scaffold, has also been added to the growing list of new discoveries. Eventually, the gel might be able to help heal wounds, build artificial cells, and deliver drugs to targeted areas.

Inspired by the amino acid 2-chloro-4,5-dihydroxyphenylalanine (Cl-DOPA) present in the composition of the proteinaceous glue of the sandcastle worm *Phragmatopoma californica*, a marine polychaete, researchers at the Max Planck Institute for Polymer Chemistry at Mainz have recently developed a simple strategy to confer antifouling properties to polymer surfaces using (but not releasing) (Cl-DOPA) which is easily incorporated into hydrogels or co-deposited as a thin coating[190]. Polymer-bound Cl-catechol groups effectively prevent attachment of bacteria and show no toxicity to attached cells. The antifouling performance of Cl-dopamine depends on the flexibility of the polymer chain to which it is attached (i.e. the accessibility of the Cl-catechol groups to interact with the bacterial membrane) and it is concentration dependent. The simplicity, low cost, and flexibility of the Cl-DOPA functionalization strategy promises wide application for antibacterial coatings for any kind of biomedical device.

"Smart" Materials

These are materials which possess one or two properties that can dramatically be altered by environmental stimuli. Mostly, "smart" materials are embedded in systems whose inherent properties can be favourably changed to meet performance needs. A wide variety of smart materials have been prepared. These include[191] piezoelectric materials, magneto-rheostatic materials, electro-rheostatic materials, stimuli-responsive polymer brushes, smart gels and shape memory alloys.

The mechanism of structural phase transition in ferromagnetic shape memory alloys such as $Ni_2Mn_{1-x}Sn_{1-x}$ has recently been elucidated[192]. This alloy has a cubic structure (cubic crystal) with high symmetry in the high-temperature phase, and a low-symmetry structure (orthorhombic crystal) in the low-temperature phase after the martensitic transformation (Figure 14).

The low-symmetry structure is composed of several regions with different crystallographic orientations called variants. The boundaries between variants form twin interfaces that move relatively easily. Thus when a stress is applied to the interfaces in the low-temperature phase, they move and cause a large distortion. The alloy returns to its original shape upon restoration of the high temperature.

Some everyday items are already incorporating smart materials (coffeepots, cars, the International Space Station, eyeglasses) and the number of applications for them is growing steadily.

An interesting new application is the development of a smart biodegradable polymer that breaks apart when exposed to low power near infrared (NIR) light[193]. Introduced via hydrogel implant, the new polymer could potentially be used to release medications or imaging agents when hit with NIR.

Metamaterials

A final area of research that elicits mention here is that relating to "metamaterials" which have been discussed in an earlier section (pp. 179–180). Metamaterials have become a new subdiscipline within physics and electromagnetism, especially optics and photonics. The overarching goal of the field is to design and realize artificial composite material structures built with subwavelength components that can exhibit unconventional electromagnetic, acoustic, thermal or mechanical properties that are not readily available in natural materials. Metamaterials have made possible implantable antennas for application in health sector, detectors in the security sector for biological- and chemical-agents, structural materials for

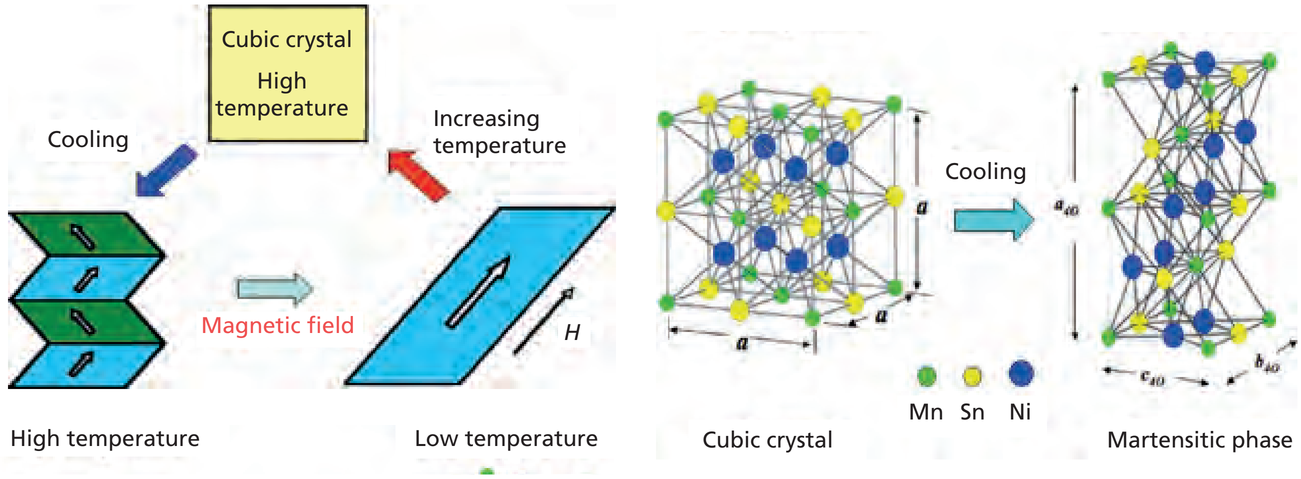

Figure 14. Left: Variant conversion in shape-memory alloys; Right: Crystal structures of $Ni_2Mn_{1-x}Sn_{1-x}$ in high-temperature and low-temperature phases [Source: Ref. 192].

soundproofing applications with perfect acoustics including for stealth submarines, photonic computer chips (combination of a metamaterial with a semiconductor) and they also herald the next generation research in microwave engineering, The current and future status of metamaterials research have been critically reviewed[26a].

Malaysian chemists and chemical engineers have engaged in a broad spectrum of research on materials both in academia and public research institutes, and there is much expertise in the country in the areas of natural rubber products, plastic-rubber blends and composites, rubber recycling, biodegradable gloves, oleochemicals derived from palm oil for applications such as biodiesel, detergents and bioplastics, pressure sensitive adhesives from palm oil resins, palm products that include butter oil, carotenoids and Vitamin E, wood composites, value-added tin-based chemicals, photonic and optoelectronic materials, metamaterial antennas and filters, and ceramic supports for catalysts, to name just a few areas.

BIOLOGICAL CHEMISTRY

The interface between chemistry and biology is an exciting research frontier and has adherents in many countries. It brings the synthetic, mechanistic and analytical powers of chemistry to bear on new and exciting areas of biology. Some examples of such research that might be broadly categorised as **Biological Chemistry** have already been mentioned in the preceding sections on industrial biocatalysts and polymers.

Interest in biological chemistry has received much impetus in recent times from in-depth studies on biocatalysis based on rational design and directed evolution and concomitant advances in biotechnology. The semipermeable lipid bilayer of cell membranes, which plays a pivotal role in energy conversion, material translocation, signal transduction and information processing, is still a frontier area of research in cellular biology. One of its most important properties is that it can exist in a liquid crystalline state. Research on cell membranes has witnessed with each passing decade the use of increasingly sophisticated probing techniques that now include freeze-fracture electron microscopy, atomic force microscopy (AFM) and high resolution X-ray diffraction. Two recent Nobel award winning discoveries in chemistry fall into this category, namely, the structure and mode of action of transmembrane **aquaporins (AQP) and G-protein coupled receptors (GPCRs)**.

The advent of high technology instrumentation such as LC-Q ion-trap, hybrid quadrapole time-of-flight mass spectrometers, ID PFG equipped NMR spectrometers, MALDI-TOF/TOF and Qq-FTMS, backed by informatics resources (e.g. CCSD, KEGG, SymGlycan) and structure predicting tools (e.g. GlycoMod, GlycoFragment), has similarly provided a huge impetus to the growing multidisciplinary research interest in **glycobiology**[194a]. Glycoconjugates (i.e., glycoproteins, glycolipids, etc.) are widely distributed in nature, and play diverse and important functions. Once considered merely supporting structures, the sugars (glycans) in the glycoconjugates are now considered essential for life, both under normal and pathological conditions. Glycans are at the centre of many disorders and diseases and the possible therapeutic use of this class of compounds has been reviewed[194b].

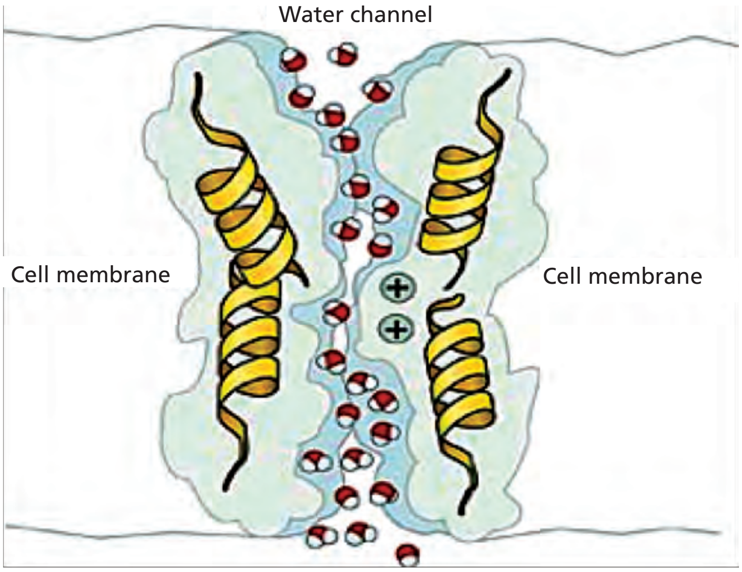

Figure 15. Passage of water molecules through the aquaporin AQP1 channel [Source: Ref. 196a].

Aquaporins

Found throughout nature, aquaporin water channels confer high water permeability to cell membranes. They are involved in a wide range of physiological functions (including water/salt homeostasis, exocrine fluid secretion, and epidermal hydration) and human diseases (including glaucoma, cancer, epilepsy, and obesity)[195].

More than ten different aquaporins have been found in human body, and genetic diseases caused by loss-of-function mutations in aquaporins include nephrogenic diabetes insipidus and congenital cataracts. Among the best studied aquaporin proteins is AQP1, widely found in the kidney as well as in red blood cells, vascular endothelium, gastrointestinal tract, sweat glands, and lungs. AQP1 is a homotetramer. It is highly selective and completely impermeable to charged species, such as protons, a remarkable property that is critical for the conservation of membrane's electrochemical potential. Recently, high resolution 3D structures have been obtained for AQP molecules which shed light on their mode of action. The AQP1 membrane channel, for example, consists of four AQP1 monomers arranged so that water molecules can pass through the narrow channel in single-file, but positively-charged amino acid residues lining the channel repel H_3O^+ (see Figure 15)[196a]. This prevents proton leakage through the channel.

Nobel Laureate Peter Agre has likened the AQP1 membrane channel to an hourglass; the 3 Å diameter at the narrowest part of the pore is only slightly larger than the 2.8 Å diameter of a water molecule. Furthermore, using molecular dynamics simulation, it has been shown that the local electrostatic field within the channel switches polarity in the middle, forcing the water molecules to rotate as they pass through. This hinders hydrogen-bonding interactions and thereby prevents leakage by proton-hopping. Although the span of this constriction is only one amino-acid residue, this would block passage of large solutes and ions as well.

Similar structural investigations on AQPs in plasma membranes of animal, insect and plant cells are underway in many laboratories, included among them the recent identification of AgAQP1 from the genome of the malaria-carrying mosquito *Anopheles gambiae*. This aquaporin is actively involved in water homeostasis during blood feeding and humidity adaptation of the mosquito. Similar to mammalian AQPs, water permeation of AgAQP1 is inhibited by $HgCl_2$ and tetraethylammonium salts[196b].

G-protein Coupled Receptors

The G-protein coupled receptors (GPCR), found only in eukaryotes, are the largest and most diverse group of seven-transmembrane receptors that sense molecules outside the cell and activate inside signal transduction pathways and, ultimately, cellular responses. G protein-coupled receptors are involved in many diseases, and are also the target of approximately 40% of all modern medicinal drugs. The 2012 Nobel Prize in Chemistry was awarded to Brian Kobilka and

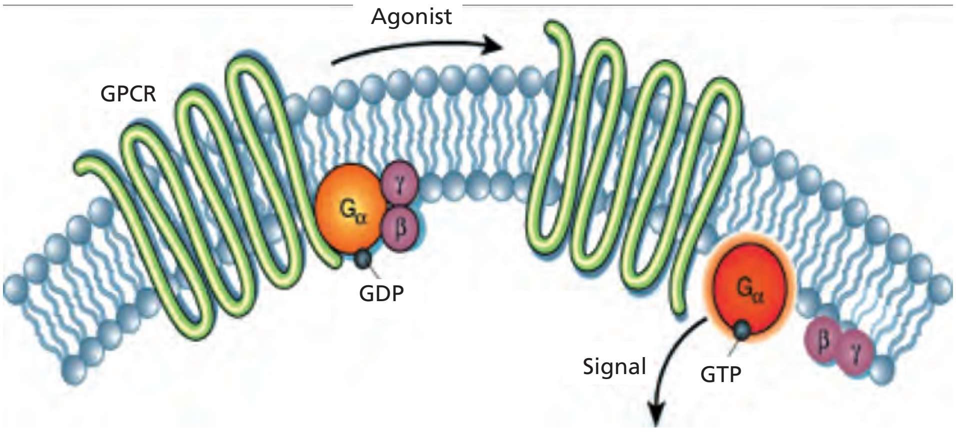

Figure 16. Activation of the G alpha subunit of a G-protein-coupled receptor [Source: Ref. 198].

Robert Lefkowitz for their work with β2-adrenergic receptors that was ‘crucial for understanding how G-protein–coupled receptors function’. The crystal structure[197] of the human β2-adrenergic receptor was undertaken by Kobilka using two different approaches to stabilize receptor protein and increase polar surface area. The molecular structure determination of several other G-protein coupled receptors has since followed his lead.

The G proteins are specialized proteins with the ability to bind the nucleotides guanosine triphosphate (GTP) and guanosine diphosphate (GDP). However, the G proteins that associate with GPCRs are heterotrimeric, comprising of an alpha subunit, a beta subunit, and a gamma subunit. Two of these subunits — alpha and gamma — are attached to the plasma membrane by lipid anchors[198] (Figure 16).

In un-stimulated cells, the state of G_α (orange circles) is defined by its interaction with GDP, G_β (purple circles), and GPCR (light green hoops). Upon receptor stimulation by a ligand called an agonist, a conformational change is induced in the GPCR, which allows it to act as a guanine nucleotide exchange factor (GEF). The GPCR can then activate an associated G-protein by exchanging its bound GDP for a GTP. The G-protein's α subunit, together with the bound GTP, can then dissociate from the β and subunits to further affect intracellular signalling proteins or target functional proteins directly depending on the α subunit type.

GPCRs have recently emerged as crucial players in tumour growth and metastasis. Malignant cells often hijack the normal physiological functions of GPCRs to survive, proliferate autonomously, evade the immune system, increase their blood supply, invade their surrounding tissues and disseminate to other organs[199].

There is much pharmacological interest in identification of genes for GPCRs and AQPs so that therapeutic agents could be developed. Both the AQPs and GPCRs are illustrative of the impact of structural biology and other scientific advances on future drug discovery efforts.

Phytochemistry of Medicinal Plants

Medicinal plants remain still the main source for drug discovery and for providing new and important leads against various pharmacological targets including cancer, HIV/AIDS, Alzheimer’s, malaria, and pain. All 119 plant-derived drugs used worldwide in 1991 came from fewer than 90 of the 250 000 plant species that have been identified. Of the 252 drugs considered as basic and essential by the WHO, 11% are exclusively of plant origin[200] e.g. digoxin from *Digitalis* spp., quinine and quinidine from *Cinchona* spp., vincristine and vinblastine from *Catharanthus roseus*, morphine and codeine from *Papaver somniferum*, pilocarpine from *Jaborandi* and taxol from *Pacific Yew*. Furthermore, a significant number are synthetic drugs obtained from natural precursors. It is further estimated that 60% of anti-cancer and anti-infectious drugs already on the market or under clinical trials are of natural origin. Among such plant-based new drugs which have recently been introduced to the United States market are arteether, galantamine, nitisinone, and tiotropium[201].

The discovery of new pharmaceuticals, however, does not necessarily have to be in the habitat of the primary tropical forest; rather even weeds[202] which are believed to contain relatively high levels of bioactive secondary compounds can harbour potentially useful medicinal compounds, an example being wild tomatillo (*Physalis longifolia* Nutt)[203]. An ethnobotanical approach is thus favoured by most researchers.

Phytochemical research has often been seen as a painstakingly slow effort, but researchers in the field in recent years have been able to quicken their pace of work and gain a better understanding of the mechanisms underlying the production and function of an enormous variety of plant metabolites, and of their regulation and evolution. As pointed out by Muranaka and Saito[204], this boost to secondary metabolism has come from two new technologies that are now becoming increasingly available to researchers, namely **metabolomics** and **ultra-high throughput DNA sequencing**. According to these authors, metabolomics now makes possible comprehensive profiling of nearly all the metabolites that accumulate in plant cells. Mass DNA sequencing similarly has allowed genomics-based studies to be applied with greater frequency to medicinal and other exotic plants.

Metabolomics[205] allows a systematic study of a complex mixture such as phytochemical preparation, without the need of isolating active principles. It combines strategies to identify and quantify large arrays of cellular metabolites using sophisticated analytical technologies such as NMR and/or MS with the application of statistical and multi-variant methods for information extraction and data interpretation. Metabolite annotation and identification is often made by reference to spectral libraries and other electronic databases such as the MassBank and Madison Metabolomics Consortium Database.

Genomics, transcriptomics, and proteomics merely indicate the potential cause for a phenotypic response, but cannot predict what will happen at the next level. This is where metabolomics has the edge — it provides a functional readout of the physiological state of an organism as the sum of its genetic blueprint, regulation, protein abundance, and environmental influences[206]. The biochemical information that is extracted from large arrays of metabolites reflects the true functional endpoints of biological events. Metabolomics thus plays a key role in the field of molecular biotechnology where plant cells are modified by the expression of engineered genes.

A major limitation of plant genetics previously has been the tedious isolation of DNA from many plant samples in parallel. This has now been effectively overcome by *high-throughput purification* of the genomic DNA using commercially available sequencing kits. For plants, rather than sequencing the entire genome of the various species, the approach usually taken is to focus on targeted amplicon sequencing and transcriptome sequencing. This is justified by the focus on biochemical pathways where only the genes producing the involved proteins are required to understand the synthetic mechanism. The numbers of coding genes in plant species can vary considerably, but are numerous enough to make the transcriptome a large collection of information.

The advent of second-generation sequencing technologies[207] has provided unprecedented opportunities for ultra-high throughput screening of plant amplicons and transcriptomes. The key advance in all second generation technologies has been the avoidance of the bottleneck that resulted from the individual preparation of DNA templates that first generation approaches required. When coupled with powerful new bioinformatic tools and computational capabilities optimized for these new technologies, a prodigious output of data could be had.

An application of second-generation, high-throughput sequencing of DNA has recently been reported to be an effective means for genetically auditing organic ingredients (especially plant and animal DNA arising from the presence of undisclosed constituents that could be potentially toxic) within complex traditional Chinese medicines (TCM)[208]. Targeting both the p-loop region of the plastid trnL gene and the mitochondrial 16S ribosomal RNA gene, over 49 000 amplicon sequence reads were generated from 15 TCM samples presented in the form of powders, tablets, capsules, bile flakes, and herbal teas.

Yet another inflection point in terms of technology has now come with the development of **single-molecule sequencing** in which individual DNA or RNA molecules, derived directly from biological samples, are sequenced not only in a massively parallel manner, but also without any type of amplification before or during the sequencing reaction[207]. It offers the potential for lower costs, higher throughput, improved quantitative accuracy and increased read lengths.

As sequencing technologies push the limits towards single cell and single molecule resolution, it is also relevant to reduce the scale of upstream DNA fragmentation step. A recent effort in this direction has been reported by Merten et al[209] who describe a miniaturized DNA shearing device capable of processing sub-microliter samples based on acoustic shearing within a microfluidic chip. DNA fragment sizes ranging from ~180 bp to 4 kb were obtained.

Application of the techniques of metabolomics and ultra-high throughput sequencing thus appears to be the way forward for serious research on our indigenous flora and fauna.

With Traditional Medicine (TM) slowly gaining acceptance into main stream medicine, there is also considerable scope for research in the country for determining the active ingredients in many herbal medicines as well as the their mode of action at the cellular level to complement the widespread work on medicinal plants.

A general challenge facing efforts to take traditional medicine mainstream is '**biopiracy**'. This problem has now been addressed in some countries such as India which in 2001 launched a traditional knowledge digital library (TKDL), a 24 million page, multilingual database on traditional remedies and medicinal plants. Malaysia may do well to take a similar path while enunciating national policy, laws and regulations for traditional medicine.

Current Research Focus in Biological Chemistry

Research in biological chemistry in Malaysia has a strong following among chemists and biologists/biotechnologists working in collaborative projects at the institutional level. Among the research areas worked are the following: biological properties (including anti-diabetic, anti-inflammatory, anti-hypertensive and anti-tumour) of phytochemicals derived from Malaysian medicinal plants; biological (anti-fungal/anti-bacterial/ insecticidal/ molluscicidal/ wood preservative/ antifouling/anti-tumour) properties of organotin and other synthetic metal products; bioactivity of natural products in cell lines which includes gene and protein expression; decoding of the rubber tree genome (*Hevea brasiliensis*); antioxidants and nutraceuticals; microbial synthesis of antibiotics; mining of enzymes and secondary metabolites from microbial sources and of compounds regulating biomineralization; biofuels from algae and seaweeds; production of bromelain enzyme powder as *halal* meat tenderiser from pineapple peel and crown, halal gelatine from fish and *halal* functional foods from natural products; the discovery and studies of interactions for non-coding RNA; molecular mechanisms of bacterial pathogenicity; semi-solid lipid matrices for the controlled release of therapeutic drugs and self-emulsifying drug delivery systems; calixarene derivatives for use as chemoreceptors, including in environmental and biomedical monitoring; biocompatible polymers and biomedical diagnostic kits.

An indication of the research focus in biological chemistry elsewhere is provided by the current research agenda at MIT[210], viz:

- Development of new technologies and synthesis of molecules to measure metal ion concentrations and protein movement, protein interactions and enzyme activities inside cells.
- Efforts to understand the structure and function of metallo-proteins with novel cofactors and macromolecular protein complexes involved in glycosylation, DNA replication and repair, and controlled protein degradation and signalling pathways.
- Use of single molecule methods to study ion transport and protein movement within membranes and solid state NMR methods to examine membrane protein structure and function.
- Development of new mechanism-based chemotherapeutic agents and monitoring the distribution of these agents in cells and tissues by novel mass spectrometric methods; and
- Synthesis of molecules to study protein folding and catalyst design and use of proteins in organic solvent to make new materials.

At other overseas institutions[211–219], the biological questions/topics being addressed by chemists together with biologists, in addition to spectroscopic and X-ray studies on the structure, dynamics and interactions of biological macromolecules, include the following:

- Hydrogen tunnelling in enzymes — spearheading a major paradigm shift
- Mechanisms of biological electron transfer
- Behaviour of enzymes at the single molecule level
- Discovery of novel enzymes for biocatalysis by metagenomics
- De novo design of enzyme catalysts for the stereocontrolled preparation of important target structures
- Mechanisms of the cytochrome P450 enzymes
- Mechanism and function in haem (non-P450)-dependent enzymes
- Mechanisms of flavin-dependent and quinone-dependent enzymes
- Chitosan derivatives for gene delivery
- DNA replication and repair
- Structure and function of metallo-proteins with novel cofactors
- Controlled protein degradation and signalling pathways
- Studies on mutation of P53 and other tumour suppressor proteins

- Functionalized magnetic nanoparticles for tissue engineering
- Studies on peptide surfactants
- Studies on virus-like particles: new process routes based on chemical processing by self-assembly
- Polyaminoacids (such as polyleucine) as synthetic enzymes
- Artificial, non-antibody binding proteins for pharmaceutical and industrial applications
- Thermally responsive polymer–metal nanoparticle composites for biomedical applications
- Organic and inorganic nanostructured biomaterial thin layers for applications in drug delivery, biosensing and biomimetic coatings
- Molecular and cellular biology of plant responses and tolerance to environmental stresses
- Chemistry, molecular biology, and neuroscience of chemosensory signals and receptors in mammal, insect, plant, and microorganism
- Protein based biosensors for metal ions and small molecules
- Studies on the mechanisms and kinetics of ligands binding to receptors using surface plasmon resonance
- Electrochemical magneto-immunosensors for fast and ultrasensitive detection of virus particles such as H9N2 avian influenza virus
- Photo-affinity probes for studying protein-protein interactions in living cells
- Bioorthogonal Chemistry in living cells
- Bioactive luminiscent transition metal complexes for biomedical applications
- Strained ruthenium complexes as novel agents for photodynamic therapy
- Development of drugs based on 5-aminolevulinic acid (a biological precursor of porphyrins in humans) for fluorescence diagnosis of bladder and other intracavitary tumours.
- Studies on protein folding and misfolding using peptidic foldamers
- Anticalins(R) — a new class of engineered proteins based on the lipocalin scaffold which offer an alternative to antibodies
- Design of molecules for interaction with cell surface receptors of tumour and healthy cells for imaging and chemotherapeutic applications
- Design of novel bio-hybrid materials for the visualization and initiation of directed drug delivery
- Ionic Liquids as non-aqueous solvents for biocatalysis
- Polymer films with embedded silver nanoparticles combining antifouling and antibacterial properties
- Role of specific membrane proteins such as ATP-Binding Casette transporters in bacterial pathogenesis
- Study of chemically modified and artificial proteins to gain better insight into the mechanisms involved in gene transfection
- Development of graphene-based enzymatic analysis methodology
- Synthesis of chiral cyclic ethers, amines and RNA analogues from carbohydrate derivatives
- Synthesis of oligosaccharides and neo-glycoproteins as vaccine candidates
- Glycoscience, embracing research across organic chemistry, molecular and cellular biology, enzymology and allied domains.
- Studies on mimicking the natural microenvironment of cells through integration of microfluidics, microfabrication technologies and biomaterials.

At the University of Dundee, the Biological Chemistry and Drug Discovery Division proclaims[220]: "*The overarching theme of the Division is 'the discovery of chemical solutions to biological problems' through excellence in basic and applied multidisciplinary research. Discovery, characterization and validation of drug targets in neglected diseases such as* Leishmaniasis, Trypanosomiasis, *malaria and other bacterial pathogens is a major research focus. Knowledge gained from these fundamental studies forms the foundation for translation into novel drug-like leads through a combination of high throughput screening, structure based design and medicinal chemistry. We also have an interest in discovering small molecules that influence stem cell fate in order to develop specific cell types for drug discovery. To meet these challenges in basic and translational research, members of the Division include specialists in glycobiology, molecular biology, bioinformatics* in vitro *and* in vivo *pharmacology and synthetic organic and medicinal chemistry.*"

Clearly, the engagement of multidisciplinary research teams is implicit in driving forward new research agenda in all areas of biological chemistry.

Table 1. Main Research Areas of Chemistry in Malaysia[a]

University	Research Groups
University of Malaya	Analytical Chemistry Catalysis Colloid Chemistry Computational Chemistry Electrochemistry Environmental Chemistry Glycolipids Materials Chemistry/Advanced Materials (Photonics/optical materials/lasers) Natural Product Chemistry Organometallic Chemistry Organotin Chemistry Physical Organic Chemistry Polymers and Composites Quantum structures Structural Characterization Studies, including Crystallography Synthetic Chemistry
Universiti Kebangsaan Malaysia	Analytical and Environmental Sciences Catalysis Chemical Sensors & Biosensors Confectionary Technology Food Ingredients Food Quality and Safety Fuel Cells Natural Products Nutritional Chemistry Oleochemistry Polymers and Composites Synthesis of Inorganic and Organometallic Compounds
Universiti Teknologi Malaysia	Advanced Materials Analytical Methods Biotechnology Computational Chemistry Environmental Chemistry Forensic Science Natural Products Chemistry Solid State Chemistry
Universiti Putra Malaysia	Catalysis Environmental Chemistry Fats and Oil Chemistry Materials Science, including metamaterials Multimedia in Chemistry Teaching Natural Products Chemistry Polymer Chemistry Surfactant Chemistry Synthesis and Characterization of Organometallic Compounds

[a] Source: Extracted from ASM Chemical Sciences Discipline Group Report 2012

Table 1 (cont.). Main Research Areas of Chemistry in Malaysia[a]

University	Research Groups
Universiti Sains Malaysia	Analytical Methods Antioxidants Corrosion Electrochemistry Electro-Biosensors Environmental Chemistry Heterogeneous Catalysis Liquid Crystals Materials Chemistry/ Advanced Materials Microscale Experiments Nanohybrid Materials Natural Products Polymers — Organic and Inorganic Separation Science Synthesis and Structural Characterization
ADDENDUM (Research clusters with chemistry/chemical engineering inputs)	
Universiti Teknologi Petronas/ Universiti Tenaga Nasional/ Multimedia University/ Universiti Teknologi Mara	Advanced Materials Catalysis Composites Clean Water and Clean Energy Enhanced Oil Recovery Gas Technology Lipids Engineering Nanotechnology Process System Engineering Renewable Energy Systems Separation Processes and Thermodynamics Steel Technology Sustainable Technology and Environment

[a] Source: Extracted from ASM Chemical Sciences Discipline Group Report 2012

Table 2. Global R&D Trends in Areas and Sub-areas of Chemistry[b]

Basic Areas	Topics
Analytical Chemistry	Molecular and Surface Imaging, Microfluidics and Miniaturization, Sensors and Detectors, Single-Cell Analysis, Proteomics, Atmospheric Chemistry
Biological Chemistry	Chemical and Structural Biology, Biocatalysis, Nucleic Acids and Functional Genomics, Signalling Pathways, *in vivo* Molecular Imaging
Inorganic Chemistry	Main Group Chemistry, Organometallic Chemistry and Homogeneous Catalysis, Bioinorganic Chemistry, Solid State Chemistry
Macromolecular Chemistry	Macromolecular Synthesis, Physical Characterization of Macromolecular Systems, Supramolecular Chemistry, Rheology
Materials Science and Nanoscience	Self-Assembly Science, Nanocrystals and Cluster Science, Nanomaterials: Energy and Applications, 'Smart' Materials, Biomaterials/Bioinspired Materials Synthesis, Bionanomaterials, Tissue Engineering/ Biocompatibility
Organic Chemistry	Synthetic Organic Chemistry, Physical Organic Chemistry, Organocatalysts, Natural Products Chemistry, Medicinal Chemistry, Drug Discovery
Physical Chemistry	Reaction Dynamics, High-Resolution Spectroscopy, Ultrafast Spectroscopy, Biophysical Chemistry, Heterogeneous Catalysis, Single-Molecule Imaging and Electronics, Surfaces and Interfaces Chemistry
Other	Chemical Education, Nuclear and Radiochemistry, Theoretical and Computational Chemistry

[b] Source: Extracted from ASM Chemical Sciences Discipline Group Report 2012

REFERENCES

1. 1. Chemical Industry in Malaysia, *Economy Watch*: 29 June 2010. www.economywatch.com/world-industries/chemical/Malaysia.html/

2. *http://www.cefic.org/Documents/.../2009-07-HLG-Chemical-Final-report.pdf.*

3. Choo Yuen May, Federation of Asian Chemical Societies (FACS) Newsletter, 1, 2000.

4. Indian Chemical Industry – XIIth Five Year Plan: *http://planningcommission.nic.in/aboutus/committee/.../wg_chem0203.pdf.*

5. *a) http://www.icis.com/Articles/2008/10/13/.../global-chemical-industry-r.html*
   b) J.O.Olawuyi and M.Friday, Science Journal of Physics, 2012 (2012), 5 Pages, doi: 10.7237/ sjp/221

6. *http://www.princeton.edu/research/news/features/a/?id=4814*

7. *http://www.tue.nl/en/university/...and.../nanowires/nanowire-solar-cells/*

8. *http://solarcellcentral.com/limits_page.html)*

9. *http://en.wikipedia.org/wiki/Cadmium_telluride_photovoltaics*

10. F. Dimroth, *Phys. Stat. Sol*., 3 (2006), 373–379.

11. Saki Sonoda *et al.*, 57th Meeting of Japan Society of Applied Physics, March 19,2010; *http://techon.nikkeibp.co.jp/english/NEWS_EN/20100323/181272/*

12. S. Emin et al, *Solar Energy*, 85 (2011), 1264–1282.

13. Arthur J Nozik *et al*., *Science*, 334 (2011), 1530–1533.

14. P.V. Kamat, *Nature Chem*., 2 (2010), 809-810; X. Zhu *et al.*, *Am. Chem. Soc. Nano*, 7 (2013), 1388–1394.

15. L.-C. Chen *et al.*, *J. Mater. Chem*., 22(2012), 22899-22905; Q.L. Song *et al.*, *Chemical Physics Letters*, 416(2005), 42-46; Idem, *Thin Solid Films*, 515 (2007), 8050–8053.

16. P.J. Sullivan and T.S. Jones, *Organic Electronics*, 9 (2008), 656–660.

17. D.-H. Hwang *et al.*, *Chem. Commun*., 49 (2013), 3248–3250.

18. L.Y. Lin *et al.*, *Org. Letters*, 13 (2011), 4962–496.

19. Y. Lin, Y. Li and X. Zhan, *Chem. Soc. Rev*., 41 (2012), 4245-4272; *http://www.sigmaaldrich.com/materials-science/organic-electronics/opv-tutorial.html*

20. A.N. Cartwright *et al.*, *Solar Energy Materials & Solar Cells*, 93 (2009), 657–661.

21. G. Li, R. Zhu and Y. Yang, *Nature Photonics*, 6 (2012), 153–161.

22. N.C. Greenham *et al.*, *Nature Commun*, 3 (2012), Article number 1019.

23. R.H. Friend *et al.*, *Appl. Phys. Letters*, 101 (2012), 153507–153509; R.H. Friend *et al.*, *Acc. Chem. Res*. (2013), Article ASAPDOI: 10.1021/ar300345h

24. F.C. Krebs *et al.*, *Adv. Mater.*, 24 (2012), 580-612; see also: F. Yan *et al.*, Adv. Mater., 25(2013) 4296–4301.

25. *http://spectrum.ieee.org/semiconductors/design/nanowire-silicon-solar-cell-for-powering-small-circuit*; see also: H. Peng, *et al.,* (2013): *Angew. Chem. Int. Ed*., doi: 10.1002/anie.201301776

26. a) N.I. Zheludev, "The road ahead for metamaterials", Science, 328(2010), 582-583; Y. Liu and X. Zhang, "Metamaterials: a new frontier of science and technology", *Chem. Soc. Rev*., 40 (2011), 2494–2507.
    b) X.Zhang, *et al.*, *Phys. Rev. Lett*. 105 (2010), 235501.

27. H.A. Atwater *et al.*, *Nature Materials Letters*, 2010; http*://www.nature.com/naturematerials; DOI: 10.1038/NMAT 2747*

28. P. Chen *et al.*, *The Open Materials Science Journal*, 5 (2011), 204–214.

29. J.M. Tour *et al.*, *ACS Nano*, 7 (2013), 6001–6006; *http://dx.doi.org/10.1021/am4013165*; See also Max-Planck Institute for Polymer Research: Polymer Research 2009, p. 61.

30. P.S. Lee *et al.*, *Adv Materials*, 23 (2011), 746–750.

31. U.K. Sen and S. Mitra, *ACS Appl. Mater. Interfaces*, 5 (2013), 1240–1247; doi: 10.1021/am3022015

32. James H. Pikul *et al.*, *Nature Communications* (2013) [4:1732] DOI:10.1038/ncomms2747

33. L. Hu *et al.*, *Nano Lett.*, 13 (2013), 3093–3100.

34. Young-Uk Park *et al.*, *J. Am. Chem. Soc.*, 135 (2013), 13870–13878.

35. P. McKendry, *Bioresource Technology*, 83 (2002), 47–54.

36. Campbell, *New markets for Bio-based Energy and Industrial Feedstocks*". In: Agricultural Outlook Forum 2000; "2004 Biodiesel Handling and Use Guidelines", US Department of Energy, 2004.

37. A. Cavaco-Paulo, L. Almeida and D. Bishop, *Textile Research Journal*, 68 (1998), 273–280.

38. US Patent 5,000,000, (March 1991).

39. *http://www.greencarcongress.com/2013/04/vt-20130403.html*; Y.-H. Percival Zhang *et al.*, *Angewandte Chemie*, 52 (2013), doi: 10.1002/anie.201300766

40. K. Chen *et al.*, *ChemSusChem*,6 (2013), 613–621.

41. Gabriel da Silva *et al.*, *Energy Fuels*, 27(2013), 3898-3904; doi:10.1021/ef400413r

42. Kimberly A. Gray *et al.*, *Environ. Sci. Technol*, 42(2008), 4952–4957; http://en.wikipedia.org/wiki/Photocatalysis

43. *http://www.epa.gov/greenchemistry/pubs/pgcc/winners/aa12b.html*

44. *http://kananlab.stanford.edu/research.html*

45. P. Hoffman *et al.*, *Chem. Eur. J.*, 18 (2012), 14017–14025.

46. P. Hoffman *et al.*, *Organometallics*, 32 (2013), 3327–3338.

47. W.H. Bernskoetter *et al.*, *Organometallics*, 32 (2013), 3969–3979.

48. G.A. Badhuri and L. Siller, *Catal. Sci. Technol.*, 3 (2013), 1234–1239.

49. D.G. Nocera *et al.*, *J. Am. Chem. Soc*, 131 (2009), 3838–3839.

50. D.G. Nocera *et al.*, *Proc. Nat. Acad. Sci.*,USA, 107 (2010), 10337–10341.

51. *http://en.wikipedia.org/wiki/Artificial_photosynthesis.*

52. Sunggyu Lee, *Gasification of Coal*, in: S. Lee, J.G. Speight & S.K. Loyalka, *Handbook of Alternative Fuel Technology*, CRC Press, Taylor& Francis Group, 2011, Chapter 2, pp 25–79.

53. *http://en.wikipedia.org/wiki/Fuel_cell*

54. G. Coates *et al.*, *J.Am. Chem. Soc.*, 131 (2009), 12888–12889.

55. *www.cbc.ca/news/.../technology-water-electrolysis-calalyst-calgary.html*

56. "*Research towards innovative energy systems and materials*", 3rd Colloquium of the Munich School of Engineering (MSE), Tech Univ of Munich, 4 July 2013; colloquium booklet, pages 17 & 43; J. Kunze *et al.*, Electrochim Acta, 71(2012), 1–9.

57. W. Li , G. Gahungu, J. Zhang and L. Hao, *J. Phys. Chem. B*, 113(2009),16472–16478.

58. A.C. Tella and I.Y. Aaron, *Acta Chim. Pharm. Indica*, 2 (2012), 75–81.

59. Z.Zhou *et al.*, *Chem. Commun.*, 46 (2010), 3672–3674.

60. *http://www.utm.my/amtec/research-area/;* see also: http://www.sjsu.edu/faculty/selvaduray/page/papers/mate115/chiaoku.pdf

61. J.F. Hull *et al.*, *Nature Chemistry*, 4 (2012), 383–388.

62. P.B. Armentrout *et al.*, *J. Am. Chem. Soc.*, 113 (1991), 2359–2369.

63. J.A. Labinger and J. E. Bercaw, *Nature*, 417 (2002), 507–514.

64. D. Morales-Morales, *Rev. Soc. Quím. Méx*., 48 (2004), 338–346; A. S. Goldman et al, *Science*, 312 (2006), 257–261.

65. R.A. Periana, *Acc. Chem. Res*., 45 (2012), 885–898.

66. F.N. Kaputsky *et al*., *Russian J. Appl. Chem*., 75 (2002),1006-1008.

67a. R.R. Schrock, *Dalton Trans*., 40 (2011), 7484–7495.

67b. R.H. Grubbs (ed), *Handbook of Metathesis, Three Volume Set*, 2003, Wiley–VCH (ISBN: 978-3-527-30616-9).

68. J.C. Mol, *Green Chem*., 4 (2002), 5–13.

69. S.L. Scott, HELIA, 30 (2007) 133–142.

70. P. Mountford *et al*., *Organometallics*, 29 (2010), 3602-3621; *Dalton Trans*., 42 (2013), 759–769.

71. *http://www.princeton.edu/chemistry/faculty/profiles/chirik/ and references therein.*

72. A.J. Bard and M.A. Fox, *Acc. Chem. Res*. 28 (1995), 141–145.

73. *http://en.wikipedia.org/wiki/Photocatalysis*

74. Pin-Ching Maness *et al*., *Appl. and Environ. Microbiol*., 65 (1999), 4094–4098.

75. G.N. Schrauzer and T.D. Guth, *J. Am. Chem. Soc*. 99 (1977), 7189–7193.

76. *en.wikipedia.org/wiki/Organocatalysis; http://www.scs.illinois.edu/burke/files/group.../Organocatalysis%2011.19.11.pdf.*

77. *http://www.sigmaaldrich.com › ... › Chemical Synthesis › Technology Spotlights.*

78. *http://www.princeton.edu/chemistry/macmillan*

79. *http://www.epa.gov/greenchemistry/pubs/pgcc/winners/aa12a.html*

80. W. Wang *et al*., *Chemistry-An Asian J*, 8 (2013), 1110–1114.

81. J.M. Thomas, R. Raja and D.W. Lewis, *Angew Chem. Int. Ed. Engl*., 44(2005), 6456-6482; see also: A. Zecchina , S. Bordiga and E. Groppo, "*The Structure and Reactivity of Single and Multiple Sites on Heterogeneous and Homogeneous Catalysts: Analogies, Differences, and Challenges for Characterization Method*", in: A. Zecchina , S. Bordiga and E.Groppo (eds), Selective Nanocatalysts and Nanoscience, First Edition, Wiley-VCH Verlag GmbH & Co. KGaA, 2011, Chapter 1, pp 1–27.

82. *https://en.wikipedia.org/wiki/Supramolecular_chemistry* and references therein.

83. H.-S. Lee *et al*., *Angew. Chem. Int. Ed*. 49(2010), 8232–8236.

84. M.D. Ward *et al*., *Proc. Natl. Acad. Sci.* U S A., 99 (2002), 4883–4888 and references therein.

85. R. Custelcean *et al*., *J. Am. Chem. Soc*.,134 (2012), 8525–8534; A.E. Kaifer *et al*., *Chem. Commun*., 48 (2012), 10295–10297.

86. L. Isaacs *et al*., *Proc. Natl. Acad. Sci. U S A*., 104 (2007), 20737–20742; see also: K. Kim *et al*., *Chem Soc Rev*., 36 (2007), 267–279.

87. T.R. Ward, *Acc. Chem. Res*., 2011, 44, 47–57.

88. M. Dürrenberger *et al*., *Angew Chem Int Ed Engl*. 50 (2011), 3026–3029.

89. B.Breiner and J.R. Nitschke, *Nature Chemistry*, 2 (2010), 6–7.

90. A.H.E. Muller (2010), *Phys. Status Solidi B*, 247: 2436–2450, doi: 10.1002/pssb.201046176.

91. D.A. Leigh *et al*., *Chem. Soc. Rev*., 38 (2009), 1530-1541; *J. Am. Chem. Soc*., 129 (2007), 11950–11963; see also: K.E. Griffiths and J.F. Stoddart, *Pure Appl. Chem*., 80 (2008), 485–506.

92. A. Yerin *et al*., *Pure Appl. Chem*., 80 (2008), 2041–2068.

93. D. Ackermann *et al*., *Nature Nanotech*., 5 (2010), 436–442.

94. Z. J. Wang, K.N. Clary, R.G. Bergman and K.N. Raymond, *Nature Chemistry*, 5 (2013), 100–103.

95. D. Crespy *et al.*, *J. Mater. Chem*., 22 (2012), 2286–2291.

96. *Zeolites and Catalysis*, J. Cejka, A. Corma and S. Zones (eds), Wiley-Weinheim, 2010, (ISBN: 978-3-527-32514-6).

97. S.Lee and D. Venkataraman, *Organic Zeolites*, in: H. Son, S.I. Wu and S.-E. Park *(eds.), Recent Advances and New Horizons in Zeolite Science & Technology*, Elsevier Science BV; 1996, Chapter 3, pp. 75–95.

98. J.J. Perry IV, J.A. Perman and M.J. Zaworotko, *Chem. Soc. Rev*., 38 (2009), 1400–1417.

99. O. Rossell *et al.*, *Chem. Eur. J.* (2013) doi: 10.1002/chem.201301769

100. R.D. Rogers and K.R. Seddon; *Science*, 302 (2003), 792-793; M. J. Earle and K.R. Seddon, *Pure Appl. Chem*., 72 (2000),1391–1398.

101. Nam T.S. Phan *et al.*, ISRN Organic Chemistry, vol. 2012 (2012), Article ID 928484, 9 pages; doi:10.5402/2012/92848

102. *Industrial Biotransformations*. 2nd edn., 2006. (eds) A. Liese, K. Seelbach and C. Wandrey. Wiley-VCH Verlag GmbH & Co. KGaA,. Weinheim.

103. A. Schmid *et al.*, *Nature*, 409 (2001), 258–268.

104. H. Groger, *Industrial Synthesis of Pharma Intermediates via Biocatalysis, http://www. medchem. uni-erlangen.de/msc/msm1/11-45-Groeger.pdf*

105. K. Faber and M.C.R. Franssen, *Trends in Biochem. Tech*., 11 (1993), 461–470.

106. P.W. Sutton et al. "*Biocatalysis in the Fine Chemical and Pharmaceutical Industries*", in: J.Whittal and P.W. Sutton (eds.), *Practical Methods for Biocatalysis and Biotransformations* 2, 2012. John-Wiley & Sons Ltd.

107. A.M. Klibanov, *Trends in Biochem. Sci*., 14 (1989), 141–144.

108. N.L. St. Clair and M.A. Navia, *J. Am. Chem. Soc*., 114 (1992), 7314–7316; See also: US Patent 6042824 A (March 2000).

109. N. Krieger *et al.*, *Food Technol. Biotechnol.,* 42 (2004), 279–286.

110. S. Jennewein *et al., Appl. and Environ. Microbiology*, 75 (2009), 7610–7616.

111. S.M. Bernardino *et al.*, *Biotechnol J*., 4 (2009), 695–702. doi: 10.1002/biot.200800287

112. Marek Bučko *et al.*, *Enzyme and Microbial Technology*, 49 (2011), 284–288.

113. K. Hirose *et al.*, *Tetrahedron: Asymmetry* 11 (2000), 1199–1210.

114. M. Singh *et al.*, *Bioresource Technology*, 99 (2008), 2116–2120.

115. M. Basri *et al.*, *Journal American Oil Chemists' Soc*., 74 (1997), 113–116.

116. C.O. Nwuche and J.C. Ogbonna, *Brazilian Archives of Biology and Technology*, 54 (2011), 113–116;www.sciencepub.net/newyork/ ny0603/ 011_16860ny0603_77_85.pdf

117. W. Parawira, *Crit. Rev. Biotechnol*, 29 (2009), 82–93.

118. U.T. Bornscheuer *et al.*, " Engineering the third wave of biocatalysis", *Nature*, 485 (2012),185–194.

119. R.J.M. Goss *et al.*, C*atal. Sci. Technol*., 2 (2012), 1544–1547.

120. E.G. Hibbert *et al.*, *Biomol Eng*., 22 (2005), 11–19.

121. Stefan Lutz, "Reengineering Enzymes", *Science*, 329 (2010), 285–287.

122. N.E.Labrou *et al.*, *Biomol Eng*., 22 (2005), 81–88.

123. J. Janey, "*A Biocatalytic Manufacturing Route for Januvia®*". Paper presented at 'Challenges in Catalysis for Pharmaceuticals & Fine Chemicals III', The Royal Society of Chemistry, Nov 2, 2011; www.soci.org/News/Fine-chems/~/.../Jake_Janey_Presentation.ashx

124. C.K. Savile *et al.*, *Science*, 329 (2010), 305–309.

125. *http://www.udel.edu/chem/C465/senior/fall00/DrugDiscovery/WhatisCombinatorialChemistry.htm*

126. J. Jacob, *International Journal of Chemistry*, 4 (2012), 29–43.

127. D.H. Bremner, *Ultrasonics Sonochemistry*, 1 (1994), S119–S124.

128. S.L. James *et al*., *Cryst. Growth Design*., 12 (2012), 5869–5872; DOI: 10.1021/cg301291w

129. J.W. Burton et al, *Org. Lett*., 14 (2012), 2940–2943.

130. A.S. Demir and M. Emrullahoglu, *Current Organic Synthesis*, 4 (2007), 223-237; See also: M. Mondal and U.Bora, RSC Adv., 2013, Advance Article; DOI: 10.1039/C3RA42480D

131. "Opportunities for Catalysis in the 21st Century" –Report from the Basic Energy Sciences Advisory Committee to US Department of Energy, May 14–16, 2002; http://science.energy.gov/~/media/bes/besac/pdf/Catalysis_report.pdf

132. *Handbook of Heterogeneous Catalysis*, 8 Volumes, 2nd edn. 2008. (Eds.) G. Ertl , H. Knözinger , F.Schüth , J. Weitkamp. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

133. A.H. Zewail, *Pure Appl. Chem*., 72 (2000), 2219–2231.

134. H. Zhao *et al*., *Current Opinion in Biotechnology,* 13 (2002), 104–110.

135. M.R. Ringenberg and T.R. Ward, *Chem. Commun*., 47 (2011), 8470–8476.

136. Global Research Report: *Materials Science and Technology (2009)* — report from Thomson Reuters: http://researchanalytics.thomsonreuters.com/m/pdfs/grr-china-nov09.pdf

137. *www.ntnu.edu/news/2012-news/semiconductors-on-graphene*

138. Y. Obeng and P. Srinivasa: *www.electrochem.org/dl/interface/spr/spr11/spr11_p047-052.pdf*; Dal Hee-Min, *et al.* Acc. Chem. Res, 2013: pubs.acs.org/doi/ abs/ 10.1021/ar300159f

139. V.P. Novikov and S.A.Kirik, *Tech. Phys. Lett*., 37 (2011), 565–567.

140. M. Choucair, P. Thordarson and J.A. Stride, *Nature Nanotechnology*, 4 (2009), 30–33.

141. A.L.M. Reddy *et al*., *ACS Nano*, 5 (2011), 4345–4349.

142. K. Sugawara *et al*., *Proc Natl. Acad Sci USA*, 109 (2012), 19610–19613.

143. James M. Tour, *et al*., *Adv. Materials*, 24 (2012), 4924–4955.

144. R.S. Ruoff, *et al*., *Chem. Soc. Rev*., 39 (2010), 228–240.

145. Patent US 20110052813 A1, (March 2011).

146. R. Dreyer, H.-P. Jia and C. W. Bielawski, *Angew. Chem*.,122 (2010), 6965–696.

147. J.M. Tour *et al*., *Phys. Chem. Chem. Phys*., 15 (2013), 2321–2327.

148. "*Beyond Graphene—2D Atomic Layers from Layered Materials*": Materials Research Society Symposium, April 2013; www.mrs.org/s13-cfp-o/

149. Han Wang *et al*., *Nano Lett*. 2012, doi:10.1021/nl302015v

150. R.F. Takagi, "New synthetic strategy for low-dimensional compounds", Doctoral dissertation, Stockholm University,2008; www.divaportal.org/smash/get/diva2:197982/FULLTEXT01.pdf

151. R.F. Takagi *et al*., *Solid State Sciences*, 11 (2009), 13–17.

152. C.P. Landee and M.M. Turnbull, *Eur. J. Inorg, Chem*, 2013 (13), 2266–2285.

153. Jun Pan *et al*., *J. Nanotechnology*, 2012 (2012), Article ID 917320, 12 pages; h*ttp://dx.doi.org/10.1155/2012/917320*

154. (a) C.N.R. Rao, *Annu. Rev. Phys Chem*., 40 (1989), 291–326.
(b) W. Widdra *et al*., *Nature*, 502 (2013), 215–218.

155. L.I. Koroleva *et al*., *J Exp & Theor Phys*, 104 (2007), 76–86; *link.springer.com/ article/10.1134%2FS1063776107010098*

156. R.L. Greene *et al*., *Chem. Mater*., 10 (1998), 1436–1439.

157. M. Rajeswari, *ssed.gsfc.nasa.gov/tdw03/proceedings/docs/session_3/Rajeswari.pdf*

158. H. Sakurai *et al*., *Angew. Chem. Intl. Edn*., 51 (2012), 6653–6656.

159. Nakano, M. *et al., Nature*, 487 (2012), 459–462.

160. S. Ramanathan *et al., J. Mater. Chem. C*, 1(2013), 2455–2462.

161. C.B. Eom *et al.*, *Nature Materials*, 12 (2013), 392–396.

162. K.A. Muller, Plenary lecture entitled "*Novel Synthesis for Ceramics: Superconductors, Magnets and Others*", 63rd Lindau Nobel Laureate Meeting, 30 June–5 July 2013, Germany.

163. M. Dan-Hardi *et al.*, *J. Am. Chem. Soc*., 131 (2009), 10857–10859.

164. A. Walsh and C. Richard A. Catlow: *Chem. Phys. Chem*., 11 (2010), 2341–2344.

165. *http://en.wikipedia.org/wiki/Single-molecule_magnet*

166. Song Gao *et al.*, *J. Am. Chem. Soc*., 133 (2011), 4730–4733.

167. Robert H. Crabtree. "*The Organometallic Chemistry of the Transition Metals*", 5th edition, 2009, Wiley.

168. V.G. Kumar Das. "*Main Group Elements and their Compounds: Perspectives in Materials Science, Chemistry and Biology*", 1997, Springer.

169. V.G. Kumar Das. "*Tin: An Under-exploited Resource in National Wealth Creation*", 2011, Academy of Sciences Malaysia Publication.

170. N. Goudarzian *et al.*, *J. Chem. Sci*., 123 (2011), 485–489.

171. F.S. Han, *Chem Soc Rev*., 42 (2013), 5270–98.

172. P. Fehlner, 2011. *Cluster Compounds: Inorganometallic Compounds Containing Transition Metal & Main Group Elements*. Encyclopaedia of Inorganic and Bioinorganic Chemistry.

173. P. Mountford *et al.*, *J. Am. Chem. Soc*., 134 (2012), 6500–6503; N*ature Chem*., 4 (2012), 525–526.

174. P. Mountford *et al.*, *Chemical Science*, 3 (2012), 819–824.

175. P. Mountford *et al.*, *J. Am. Chem. Soc*., 133 (2011), 15359–15361.

176. R.D. Rieke *et al.*, *Organic Syntheses, Coll*. Vol. 9, p. 9 (1998); Vol. 72, p.147 (1995).

177. M. Nishiura and Z. Hou, *Nature Chem*., 2(2010), 257–268. See also: *http://www.asi.riken.jp/en/laboratories/chieflabs/organometallic*.

178. Z. Hou *et al.*, *J. Am. Chem. Soc*., 131 (2009), 18266–18268.

179. X.T. Tao *et al.*, *Appl. Phys. Lett.* 76 (2000), 3522–3524; *http://dx.doi.org/10.1063/1.126694*

180. US Patent US20040217698 A1 (April 2004); *http://www.google.com/patents/US 20040217698*

181. M. Janghouri *et al.*, *J. Electronic Materials*, 42 (2013), 2915–2925.

182. M.O. Wolf *et al.*, *J. Inorg. & Organomet Polymers and Materials*,16 (2006), 189-199 ; M.O. Wolf, A*dv. Mater*., 13 (2001), 545–553.

183. D. Kumar and R.C. Sharma, *Eur. Polym. J*., 34 (1998), 1053–1060.

184. *http://www.ncbi.nlm.nih.gov/pubmed/21424454*

185. *http://www.jacobsschool.ucsd.edu/news/news_releases/release.sfe?id=1075*

186. C.L. Raston *et al.*, *Green Chem*., 14 (2012), 2682–2685.

187. Jian Yang *et al.*, *Proc Natl. Acad Sci*, *USA*, 2009; *http://www.pnas.org_cgi_doi_10.1073_pnas.0900004106*

188. B.D. Ratner, *et al.*, *Nature Biotechnology*, 2013 / doi:10.1038/nbt.2580; *http://www.nature.com/nbt/journal/vaop/ncurrent/full/nbt.2580.html?elq.*

189. P.H.J. Kouwer and M. Koepf, *Nature*, 493 (2013), 651–655.

190. A. del Campo *et al.*, *Adv. Mater*., 25 (2013), 529–533.

191. *http://www.cs.ualberta.ca/~database/MEMS/sma_mems/smrt.html*

192. A. Kimura *et al.*, *Physical Review Letters*,104 (2010), 176401; *http://www.spring8.or.jp/en/news_publications/press_release/2010/100427*

193. *http://www.sciencecentric.com/News/Chemistry; see also: http://www.mesg.nl/wiki/images/c/ca/Paper_UPT_01.pdf*

194. (a) *www.premierbiosoft.com/glycan/index. html*
(b) Mauro S.G. Pavão (Ed.). *Glycans in Diseases and Therapeutics*, 2011, Springer, ISBN: 978-3-642-16832-1.

195. A.S. Verkman, *Annual review of medicine*, 63 (2012), 303–316.

196. (a) P. Agre *et al.*, *http://www.haverford.edu/ biology/ Courses/Bio303.../membrane11.pdf; http://aquaporins.org/peter.htm*
(b) P. Agre *et al.*, *http://www.pnas.org/ content/ early/2011/03/21/ 1102629108. abstract*

197. B.K. Kobilka *et al.*, *Nature*, 450(2007), 383–387; *Trends Pharmacol Sci*., 29 (2008), 79–83.

198. J. Li, *et al.*, *Nature*, 420(2002), 716–717.

199. R.T. Dorsam and J. S. Gutkind, *Nature Reviews Cancer*, 7 (2007), 79–94.

200. S.M.K. Rates, 'Review: Plants as source of drugs', *Toxicon*, 39 (2001), 603–613.

201. M.J. Balunas and A.D. Kinghorn, *Life Sciences*, 78 (2005), 431–441.

202. J.R. Stepp, *J. Ethnopharmacology*, 92 (2004) 163–166.

203. K. Kindscher *et al.*, *Economic Botany*, 20 (2012), 1–13.

204. T. Muranaka and K. Saito, *Plant Cell Physiology*, 54 (2013), 645-646 and references therein.

205. Y. Okazaki and K. Saito, *Plant Biotechnol Rep*., 6 (2012), 1–15.

206. *http://www.biocrates.com/technology/about-metabolomics*

207. J.F. Thompson and P.M. Milos, *Genome Biology*, 2011, 12:217; *http:// genomebiology.com/2011/12/2/217*

208. M.L. Coghlan *et al.,* (2012), *PLoS Genet* 8(4): *e1002657. doi:10.1371/journal.pgen.1002657*

209. C.A. Merten *et al.*, *Lab Chip*, 12 (2012), 4677–4682.

210. *http://www.mit.edu/~chemistry/faculty/biological.html*

211. *http://www2.le.ac.uk/Academic Departments/Chemistry/Research*

212. *http://www.a.u-tokyo.ac.jp › Home › Departments › Departments (GSALS)*

213. *http://www.chem.pku.edu.cn/index.php?id=274&styleid=2*

214. *http://en.wikipedia.org/wiki/Korea_Institute_of_Science_and_Technology*

215. *http://iicb.res.in/chemistry.html*

216. *http://URN.fi/URN:NBN:fi:tty-201006081149*

217. *http://www.uq.edu.au/cbe/research*

218. *http://www.liv.ac.uk/research*

219. *http://www.biolchem.bs.jhmi.edu*

220. *http://www.lifesci.dundee.ac.uk/research/bcdd*

Date of submission: September 2013

Patenting of Genes

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The US Supreme Court issued a ruling on Thursday, 13 June 2013 that banned the patenting of naturally-occurring genes in a case brought against the Utah-based Myriad Genetics on patents they held for the BRCA1 and BRCA2 genes. These are genes associated with an increased risk of breast and ovarian cancer.

In a survey, taken in May and June 2013, of the Fellows from both the Medical and Biological Sciences Disciplines from the Academy of Sciences Malaysia (ASM), there was a unanimous consensus that human genes, because they are in a natural state and the discoverer only found them, should not be patented and neither are they patentable.

Further, as mutation is a natural process, discovery of mutations should also not be patented nor be patentable.

The exception to the above is that if a scientist discovers a cure for the disease caused by the mutation, then this scientist deserves to have the cure patented as ’cures’, for they are processes designed to mend the mutation. These processes can be patented with due respect to the discoverer.

Even for cures, the patents would necessarily be limited by time so that other scientists can still be allowed to research further on the original cure, if the original cure had been found to have merit in its approach. Nonetheless, an arrangement has to be worked out satisfactorily to all parties whereby exceptions can be made for research or verification by third parties. The exclusivity in licensing the patent as well as the scope of protection accorded are points of concern.

The occurrence of too many blocking patents, particularly in the United States, that covering either the gene sequence or the basic method of genetic testing, is remarkable. Together with a highly restrictive licensing protocol, these patents appear to exclude all laboratories, except the patent holder, from offering the genetic testing in the US and other parts of the developed world until the expiry of the patent.

ASM is aware that the total disallowing of patents on genes will certainly discourage research. As an example, currently, already many companies are not working on antibiotics because they do not bring as much rewards as cures for chronic diseases. This is further compounded by the fact that many of these diseases are in third-world developing countries (the so-called ‘bottom billion’).

What could, however, be patented, the Fellows felt, are protocols designed to test for these cancer-causing mutations in genes.

What do the Malaysian patent laws say about this matter? We raised the issues with P. Kandiah, a local expert from KASS International, an organisation dealing in Malaysian intellectual property rights as well as the patent laws. The following are his replies with a caveat that the views expressed below were his own, and that they need not reflect the views of KASS International, nor of its clients, past or present:

(i) Should human (let us limit this conversation to human genes) genes be allowed to be patented?
Human genes (or for that matter any genes merely of any other living organism occur in nature) the mere discovery of genes (or its nucleotide sequence) does not make the genes patentable, unless there is some human intervention in the gene making the gene man- made. Similarly, the isolation of a gene from its natural state in a cell no matter how much effort was put into the isolation does not make the gene patentable though the method of isolation is novel and non-obvious (inventive) may qualify for a patent. The Malaysian Patent Act does allow the grant for a patent for microbiological process.

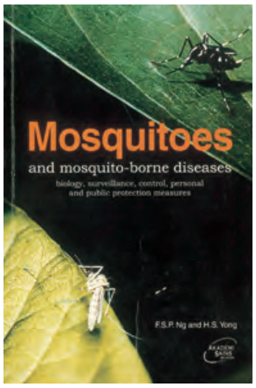
(ii) What about mutated human genes? Can mutated human genes be also patented?
Naturally occurring mutated human genes (mutation occurring in nature) are product of nature and the discovery of novel mutated genes, no matter how much effort was expended in the discovery or isolation, does not make that gene patent eligible. But mutation induced by man producing a previously non-existent mutated gene would be patent eligible. To qualify for a patent, there must be some industrial application of the mutated gene.

(iii) Should only cures for mutated genes allowed to be patented?
There is a moral and legal discussion to this question. Legally, under the Patent Act in Malaysia and of many other countries, the method of diagnosis or treatment of the human or animal body is not patent eligible but products used in such diagnosis or treatment (such as drugs) are patentable. It follows that cures for disease or sickness caused by mutated gene are not patentable.

(iv) If cures are allowed to be patented, how do you allow for second opinions as a third party using the patented cure will need to pay fees to the company holding the patent?
If cures are patentable, then it would be necessary for a third party to obtain a license before using the same patented cure, which invariably would involve payment of license or royalty fees.

(v) Will disallowing patents on genes (mutated or otherwise) discourage research companies from spending huge amounts on such research?
The fundamental basis of the patent regime is to incentivize research and bring about solution (technical, medical, etc.) to a problem with a guarantee of fixed term of exclusivity to the solution. However, this grant of near monopoly has to be balanced against the public intent of using new knowledge and technical solution. This is a delicate balance. There is empirical evidence to show that unless there is going to be substantial revenue (profit by utilizing the result of research) no private institution would take the risk in funding expensive research. This partly explains why private companies are not expending fund in research on diseases where there is no market or very small market (one of the reasons for lack of cures for orphan diseases) but if the government or the public fund such research, then institutions would undertake research or otherwise 'non- profitable' research.

Date of submission: October 2013



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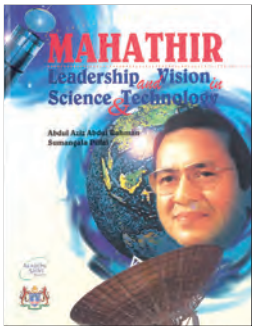

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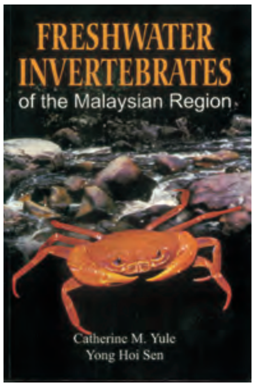

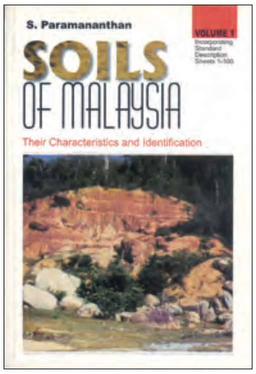

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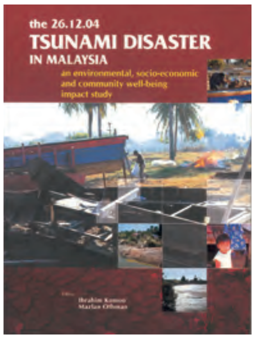

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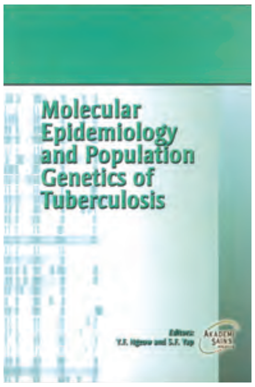

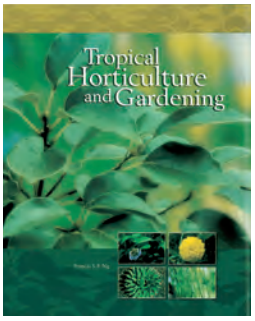

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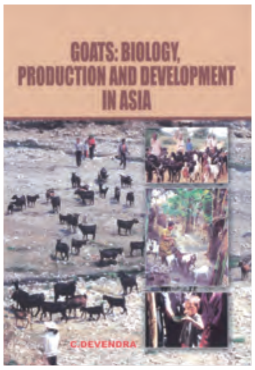

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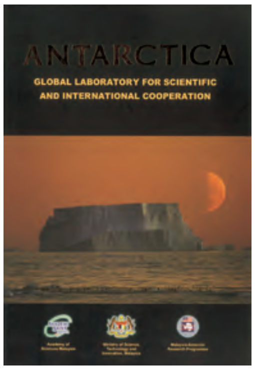

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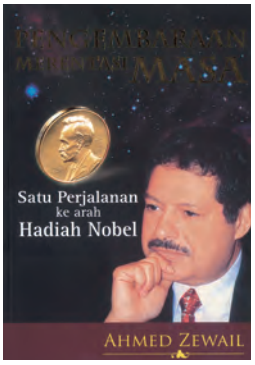

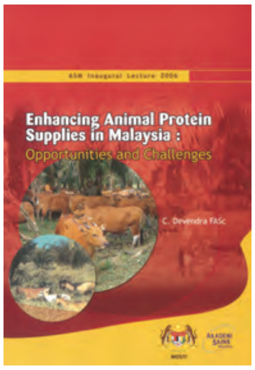

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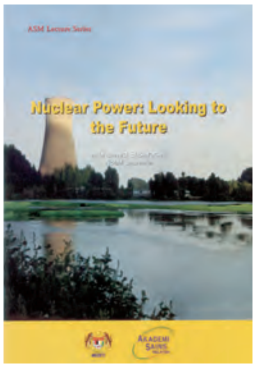

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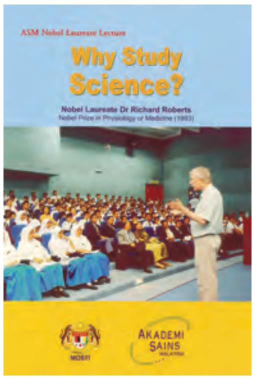

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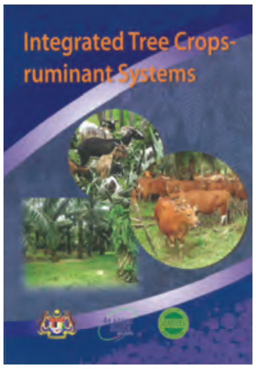

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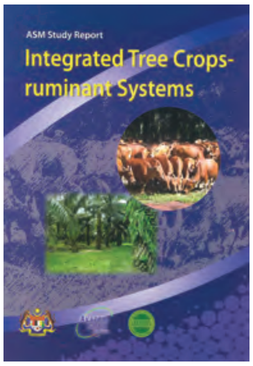

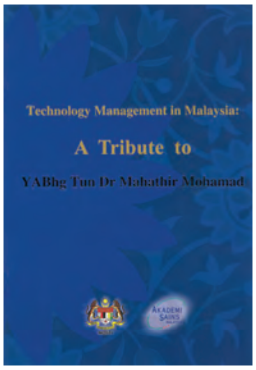

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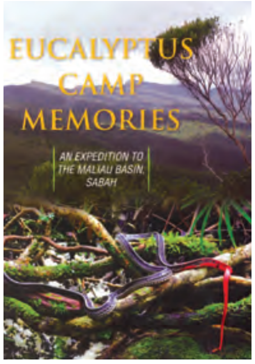

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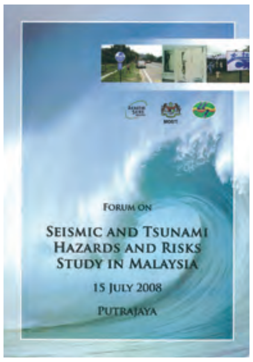

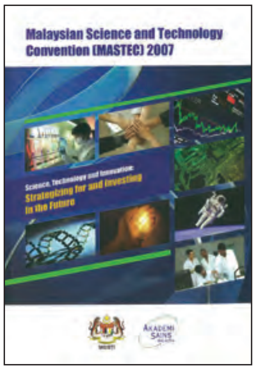

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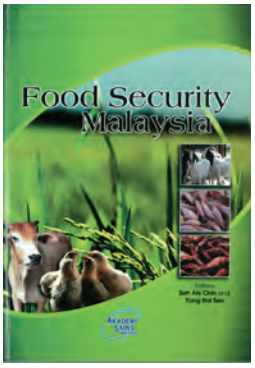

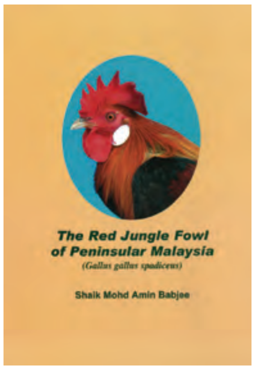

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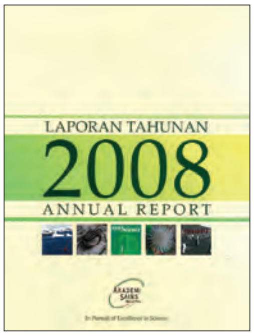

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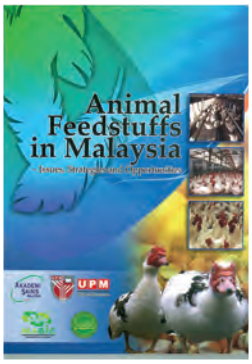

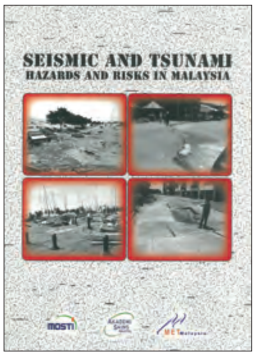

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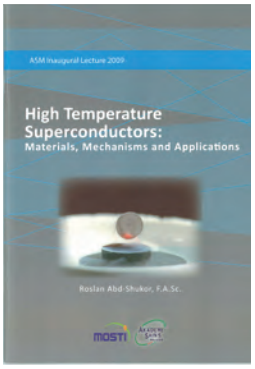

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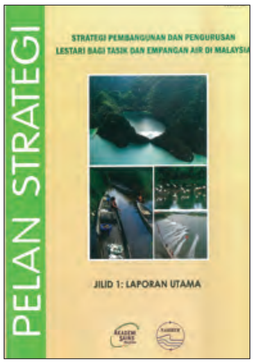

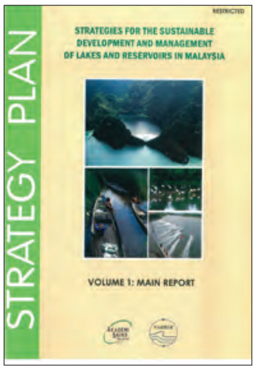

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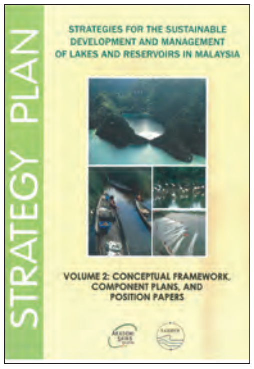

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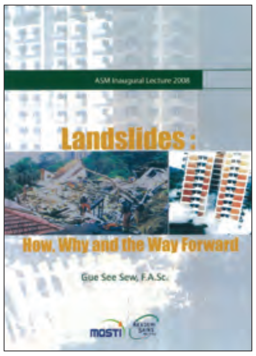

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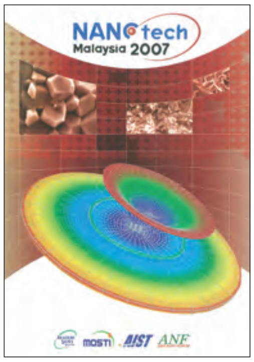

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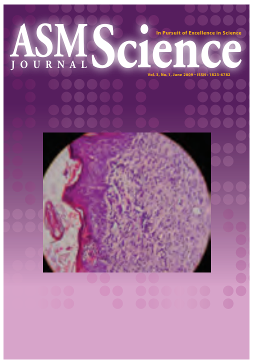

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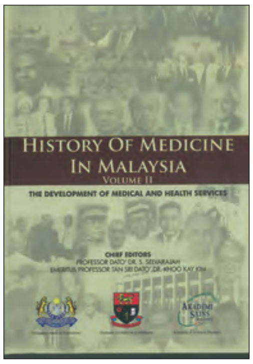

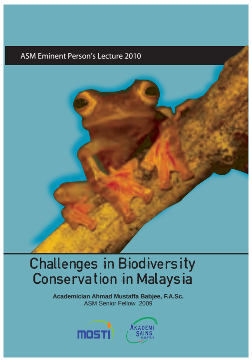

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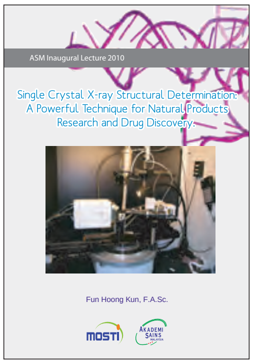

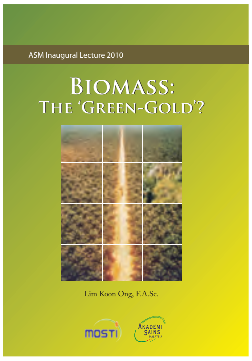

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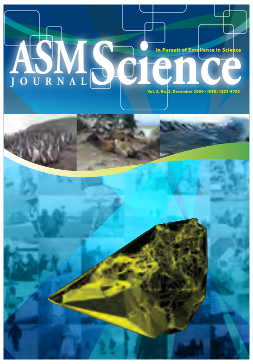

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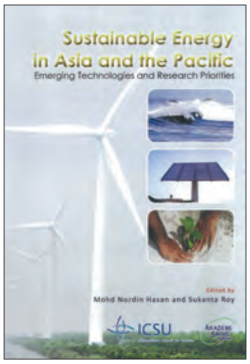

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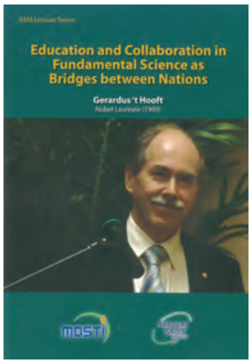

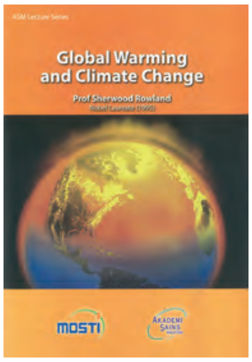

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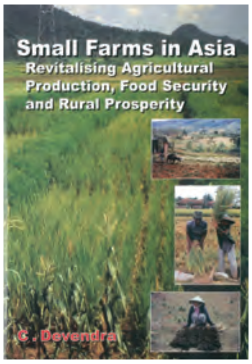

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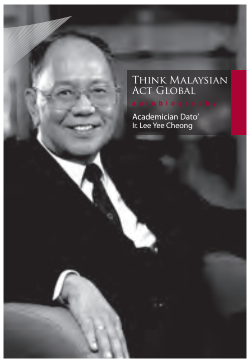

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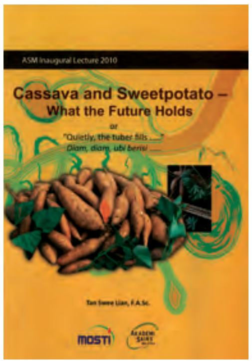

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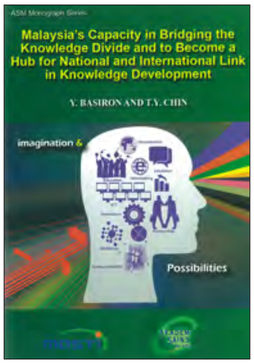

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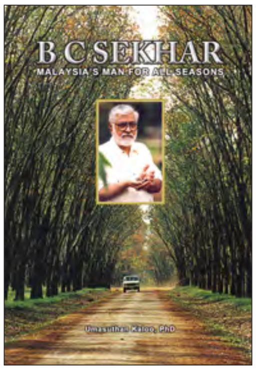

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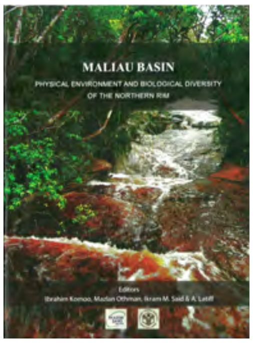

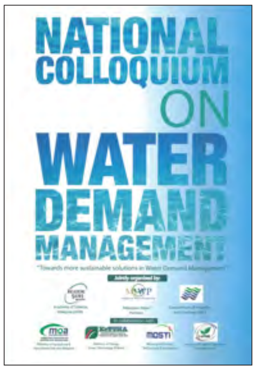

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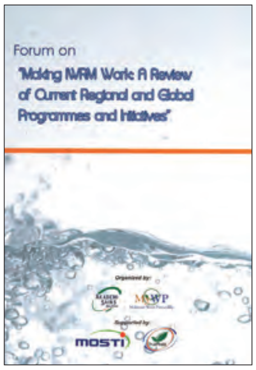

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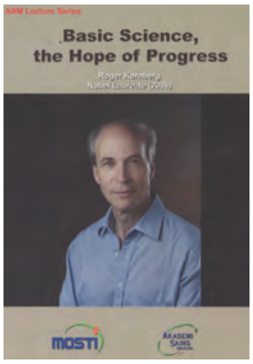

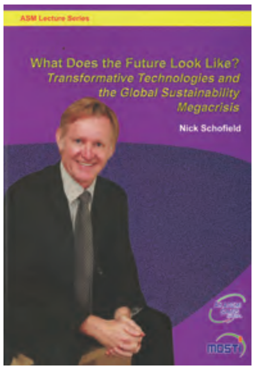

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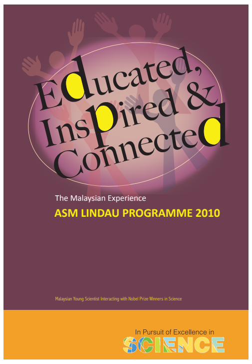

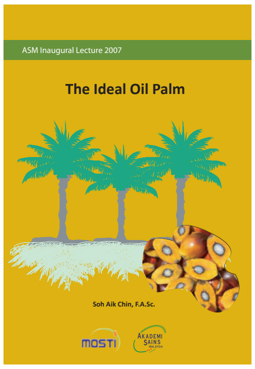

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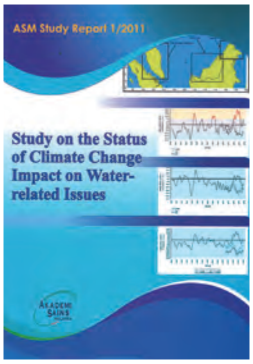

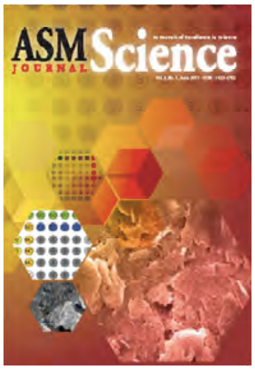

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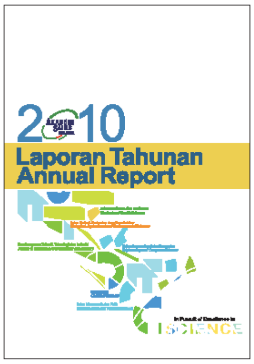

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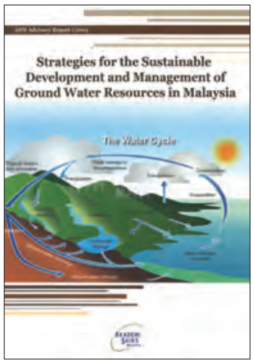

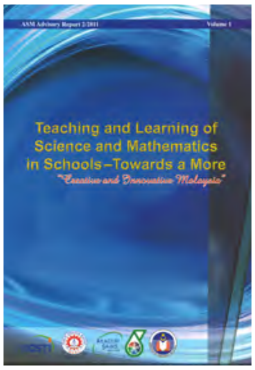

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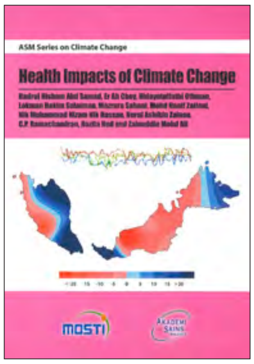

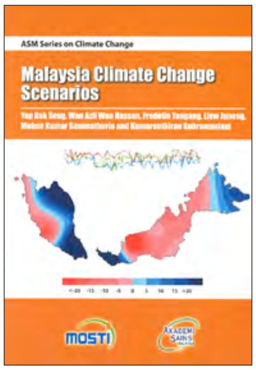

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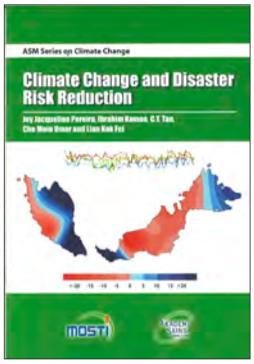

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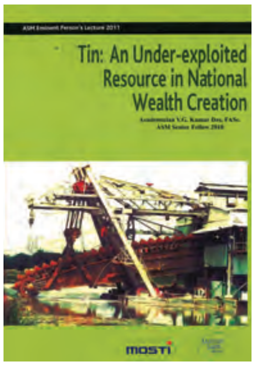

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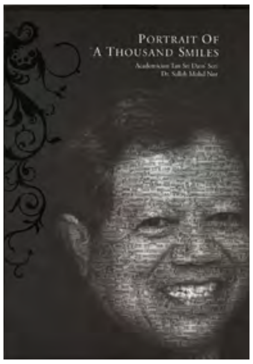

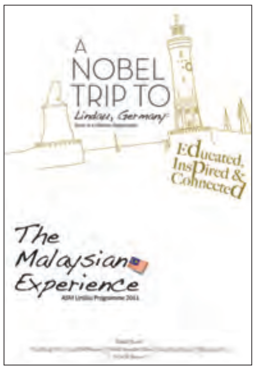

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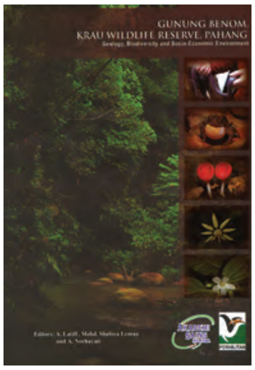

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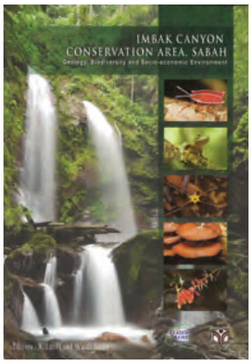

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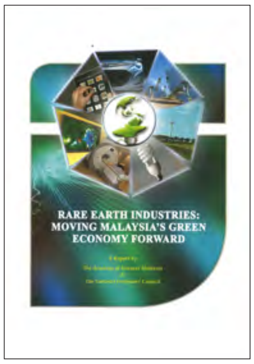

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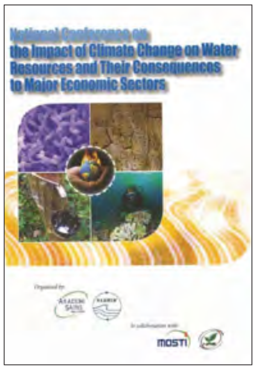

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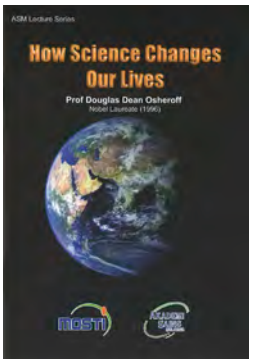

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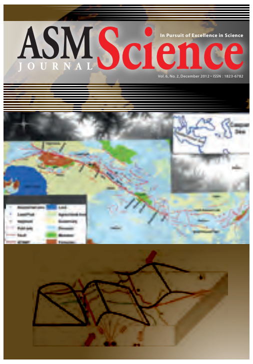

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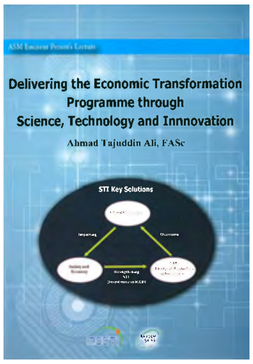

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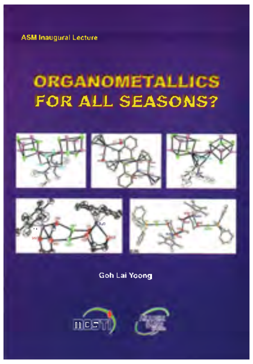

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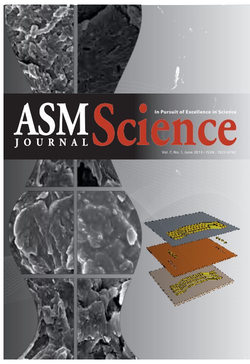

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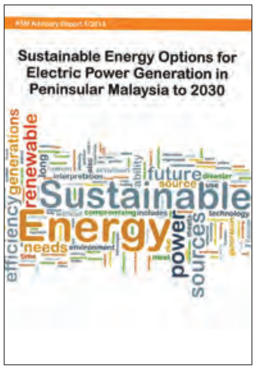

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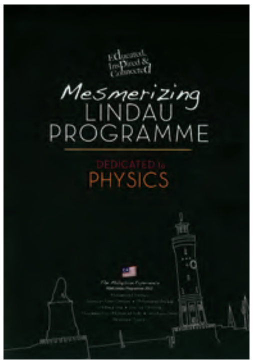

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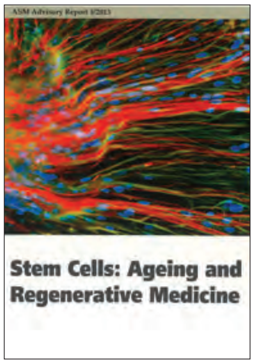


The Essentials of
SCIENCE, TECHNOLOGY AND INNOVATION POLICY
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To serve as the forum for the dissemination of significant research, S&T and R&D policy analyses, and research perspectives.

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The *ASM Science Journal* publishes advancements in the broad fields of medical, engineering, earth, mathematical, physical, chemical and agricultural sciences as well as ICT. Scientific articles published will be on the basis of originality, importance and significant contribution to science, scientific research and the public.

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Each issue of the journal will contain no more than 10 research articles. These are papers reporting the results of original research in the broad fields of medical, engineering, earth, mathematical, physical, chemical and life sciences as well as ICT. The articles should be limited to 6000 words in length, with not more than 100 cited references.

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These are papers that analyse recent research in a particular field, giving views on achievements, research potential, strategic direction etc. A Research Perspective should not exceed 2000 words in length with not more than 40 cited references.

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Individuals who make the news with breakthrough research or those involved in outstanding scientific endeavours or those conferred with internationally recognised awards will be featured in this section. Policy promulgations, funding, science education developments, patents from research, commercial products from research, and significant scientific events will be disseminated through this section of the journal. The following will be the categories of news:

- Newsmakers
- Significant Science Events
- Patents from Research
- Commercial Products from Research
- Scientific Conferences/Workshops/Symposia
- Technology Upgrades
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- The whole citation finishes with a full stop.

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Journal

Kumar, P & Garde, RJ 1989, 'Potentials of water hyacinth for sewage treatment', *Research Journal of Water Pollution Control Federation*, vol. 30, no. 10, pp. 291–294.

Monograph

Hyem, T & Kvale, O (eds) 1977, *Physical, chemical and biological changes in food caused by thermal processing*, 2nd edn, Applied Science Publishers, London, UK.

Chapter in a monograph

Biale, JB 1975, 'Synthetic and degradative processes in fruit ripening', in *Post-harvest biology and handling of fruits and vegetables*, eds NF Hard & DK Salunkhe, AVI, Westport, CT, pp. 5–18.

Conference proceedings

Devendra, C 2005, 'Improvement of crop-animal systems in rainfed agriculture in South East Asia', in *Proc. Int. Conf. on Livestock-Crop Systems to Meet the Challenges of Globalisation*, vol. 1, eds P Rawlinson, C Wachirapakorn, P Pakdee, & M Wanapat, Khon Kaen, Thailand, pp 220–231.

Website reference

Thomas, S 1997, *Guide to personal efficiency*, Adelaide University, viewed 6 January 2004, <http://library.adelaide.edu.au/~sthomas/papers/perseff.html>.

Report

McColloch, LP, Cook, HT & Wright, WR 1968, *Market diseases of tomatoes, peppers and egg-plants*, Agriculture Handbook no. 28, United States Department of Agriculture, Washington, DC.

Thesis

Cairns, RB 1965, 'Infrared spectroscopic studies of solid oxygen', PhD thesis, University of California, Berkeley, CA.

Footnotes, spelling and measurement units

If footnotes are used, they should be numbered in the text, indicated by superscript numbers and kept as brief as possible. The journal follows the spelling and hyphenation of standard British English. SI units of measurement are to be used at all times.

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General. Soft copy of the manuscripts should be submitted in *MS Word* format. The paper should conform to the style and format of the *ASM Science Journal*. Intending contributors will be given, on request, a copy of the journal specifications for submission of papers.

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Results. Data of significant interest should be included.

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Tables. These should have short descriptive titles, be self explanatory and typed on separate sheets. They should be as concise as possible and not larger than a Journal page. Values in tables should include as few digits as possible. In most cases, more than two digits after the decimal point are unnecessary. Units of measurements should be SI units. Unnecessary abbreviations should be avoided. Information given in tables should not be repeated in graphs and vice versa.

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Acknowledgements. Appropriate acknowledgements may be included.

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