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Analysis of Spatial Organisation of Tissues: Application to the Study of the Islets of Langerhans of Mice and Monkeys

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Thanks to the development of new 3D Imaging techniques, the volumetric data of thick samples, especially tissues, are commonly available. Quite a number of algorithms were proposed to analyse cells or nuclei in tissues, but only a few of the analysed tissues were seen as a whole, and not as a set of individual cells. Within a tissue, cells are not randomly organised, as they interact with each other, forming a complex network of interactions. In this paper, we proposed a new approach to segment and analyse tissues in 3D. We applied our methodology to the study of Langerhans islets. These islets are composed of three main different types of cells, whose organisation differs between species.

In this work, we proposed a new automated framework to analyse the multi-cellular structure of tissues, which allowed us to investigate the cytoarchitecture of the islets of Langerhans. This framework included i) the automated identification of nuclei, ii) cytoplasmic markers, iii) the predicted position of the cell's membrane, and finally iv) the reconstruction of the cells' network. Our toolbox could be applied to not only thin slices of islets tissues but also achieved good results on a whole 3D islet.

We applied our tool to the study of the islets of Langerhans in two different species having different organisations, namely mice and monkeys. Our nuclei segmentation algorithm had > 98% accuracy. This framework also enabled us to detect and identify all three major cell types in the islets of mice and monkeys with 97% accuracy. Moreover, we could compute the cellular interactions and reconstruct the cell network. Cell-cell interactions play an important role for islet function. Our results favoured the hypothesis that interactions between the cells in the islets did not occur at random, supporting the idea that specific signalling pathways were important in order to support proper islet function and glucose homeostasis.

We developed this framework in a widely used software platform (i.e. ImageJ) with unbiased analytical capabilities. We believe that our technology has much potential in the study of spatial organization of tissues in general.

COLLABORATION

IPAL is a French-Singaporean lab, we can then easily benefit from international collaborations especially with South-East Asia. This work was done in collaboration with the NTU medical school in Singapore.

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