Tensorflow segmentation of cells in embryonic development

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Background: During vertebrate embryogenesis, body segments (somites) form along the main body axis which differentiate into, among other structures, skeletal muscle. In fish, these highly regular chevron shaped segments are still apparent in adult animals. Zebrafish, investigated in the lab of Timothy Saunders, is an excellent and tractable model system because only a limited number of around 200 cells constitute one somite [1]. These multicellular domains emerge through cell division, shape changes, fusion, migration and rearrangement, all requiring tight integration of biochemical and mechanical signalling. To understand this process in detail, segmenting the positions and boundaries of individual cells from 3D image time series is essential. Currently, 3D contour segmentation of somite boundaries and individual cell contours is performed manually, severely limiting how much data can be processed. Automating this process is difficult, due to rapid cell movements, significant changes in cell morphology, and cell fusion.

Supervised machine learning using convolutional neural networks is very powerful, but hardly applicable to this problem. Obtaining sufficient training data for these complex images is almost impossible. Instead, here, we consider applying the random walker segmentation approach, a well-established graph-based method, which has a number of interesting features. Among those, it naturally allows multi-object segmentation, and secondly, it supports what is coined neutral segmentation. Regions that are known to belong to two different objects, which might be separated by an almost indiscernible boundary, will still be treated as separate objects. The Bretschneider group has recently extended the random walker to obtain highly accurate surface reconstructions of single cells [2].

Mini-project: Because of the large size of the 3D imaging data, highly efficient computational methods are needed. The first part of the project therefore consists of implementing the standard random walker method using Tensorflow on a GPU. Using dual colour channel images where fluorescent cell nuclei serve as seeding points to define individual cells, the random walker method will be adapted to detect cell membranes of somite cells. Long and thin cell shapes with reduced membrane presence during fusion, present a new challenge for membrane segmentation. We will explore extending the standard random walker to a reaction-diffusion PDE model, integrating additional geometric cell features, as we have done in [2] to incorporate curvature, for example.

Deliverable: Tensorflow code, with preliminary segmentations of somite cells.

PhD prospect: Segmentation and cell tracking during embryogenesis is an important problem posing a number of mathematical and computational challenges. Different avenues can be taken, depending on the student's main interest. One important direction could be using advanced graph neural networks to analyse complex spatio-temporal patterns of cell fusion and rearrangement. Importantly, there is an intimate link between cell shape changes and tissue morphogenesis. This project offers the student an exciting opportunity to apply concepts from topology and graph theory to understand how complex organ shape emerges during development.

Student requirements: Programming skills.

References:

[1] Shaping the zebrafish myotome by intertissue friction and active stress. S Tlili, J Yin, J-F Rupprecht, MA Mendieta-Serrano, G Weissbart, N Verma, X Teng, Y Toyama, J Prost, and TE Saunders. PNAS 116 (51) 25430-9; 2019.

[2] A Curvature-Enhanced Random Walker Segmentation Method for Detailed Capture of 3D Cell Surface Membranes. EJ Lutton, S Collier, T Bretschneider. IEEE TMI 40 (2), 514-26, 2020.