Towards Image-Derived Meshes for Microscale Cardiac Conduction Models at the cm-Scale and Beyond

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Most cardiac diseases, including atrial fibrillation and myocardial infarction, are tightly linked to microstructural remodelling. Cell-by-cell *in silico* models of cardiac conduction hold strong potential to improve our understanding of these diseases. Such simulations are now feasible with thousands of cells, but a major bottleneck remains: building realistic, imaging-informed cardiomyocyte meshes from large microscopic datasets.

To address this need, we identified and sourced three datasets based on confocal microscopy (rabbit, $0.02\,\mathrm{mm}^3$ volume, $0.2\,\mu\mathrm{m}$ voxel size), light-sheet microscopy (mouse, $\gg 5\mathrm{mm}^3$ volume, $0.4\,\mu\mathrm{m}$ voxel size) and synchrotron imaging (human organ atlas; $15\,\mathrm{cm}^3$ volume, $2.2\,\mu\mathrm{m}$ voxel size). We developed two computational pipelines adapted for different imaging regimes: a segmentation workflow for confocal and light-sheet microscopy which resolves individual cardiomyocytes, and a workflow for lower-resolution data. The instance segmentation workflow was built upon our previously developed algorithms for confocal microscopy with image volumes of $\sim 0.002\,\mathrm{mm}^3$. Applying them directly to the light-sheet microscopy datasets increased the computational cost more than 2500-fold. Therefore, we developed a scalable workflow combining semantic segmentation with 3D U-Nets and tile-parallelised supervoxel generation and agglomeration, enabling cardiomyocyte segmentation in light-sheet microscopy datasets. For lower-resolution, but larger-volume synchrotron data, direct identification of intercalated discs and therefore cardiomyocyte segmentation was not feasible. For this modality, we used an imaging-informed approach that predicted a binary cardiomyocyte mask along with a local orientation field. These outputs can guide our previously published synthetic cardiomyocyte mesh generation for much larger volumes, potentially extending to human heart scale.

By combining scalable cardiomyocyte reconstructions with surrogate mesh generation we outline a path from microscopic image data to large-scale, cell-resolved cardiac conduction models, enabling more realistic studies of structurally driven conduction abnormalities and arrhythmia mechanisms.