

A new algorithm for segmenting single adult cardiac cells from large-volume serial block-face scanning electron microscopy data

Rajagopal, V.¹, Hussain, A.¹, Ghosh, S.¹, Kalkhoran, S.², Hausenloy, D.² and Hanssen, E.³

¹ University of Melbourne, Australia, ² University College London, United Kingdom, ³ Melbourne Advance Microscopy Facility, Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Australia

Akter Hussaina, Shouryadipta Ghosha,h, Siavash Beikoghli Kalkhoranb,f, Derek J. Hausenloyb,c,d,e,f, Eric Hansseng, Vijay Rajagopala,h,*

a Cell Structure and Mechanobiology Group, Department of Biomedical Engineering, The University of Melbourne, Australia

b Hatter Cardiovascular Institute, University College London, United Kingdom"

c Barts Heart Centre, St. Bartholomew's Hospital, United Kingdom"

d Cardiovascular and Metabolic Disorders Program, Duke-National University of Singapore Medical School, Singapore

e Yong Loo Lin School of Medicine, National University Singapore, Singapore"

f The National Institute of Health Research, University College London Hospitals, Biomedical Research Centre, United Kingdom

g Advanced Microscopy Facility, Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Australia

h Systems Biology Laboratory, Melbourne School of Engineering, University of Melbourne, Australia

We present a new algorithm to automatically segment the myofibrils, mitochondria and nuclei within single adult cardiac cells that are part of a large serial-block-face scanning electron microscopy (SBF-SEM) dataset. The algorithm only requires a set of manually drawn contours that roughly demarcate the cell boundary at routine slice intervals (every 50th, for example). The algorithm correctly classified pixels within the single cell with 97% accuracy when compared to manual segmentations. One entire cell and the partial volumes of two cells were segmented (see Fig. 1). Analysis of segmentations within these cells showed that myofibrils and mitochondria occupied 47.5% and 51.6% on average respectively, while the nuclei occupy 0.7% of the cell for which the entire volume was captured in the SBF-SEM dataset. Mitochondria clustering increased at the periphery of the nucleus region and branching points of the cardiac cell. The segmentations also showed high area fraction of mitochondria (up to 70% of the 2D image slice) in the sub-sarcolemmal region, whilst it was closer to 50% in the intermyofibrillar space. We finally demonstrate that our segmentations can be turned into 3D finite element meshes for cardiac cell computational physiology studies. We offer our large dataset and MATLAB implementation of the algorithm for research use at www.github.com/CellSMB/sbfsem-cardiac-cell-segmenter/. We anticipate that this timely tool will be of use to cardiac computational and experimental physiologists alike who study cardiac ultrastructure and its role in heart function.

Figure 1. (A and B): 3D Rendering of myofibrils, mitochondria and nuclei within the largest cell contained in the SBF-SEM dataset. The inset views provide a closer look at the organization of these components near a branching point. (C and D) are 3D renders of the segmentations of two other cells in the SBF-SEM data.

