MURPA Seminar Friday 2 September 2011 at 9am: Multi-Scale Modeling of the Heart: from Molecule to Organ

Venue: Seminar Room 135, Building 26, Monash Clayton

Presenter: Dr Andrew McCulloch, Professor and Jacobs Distinguished Scholar, Department of Bioengineering, Adjunct Professor, Department of Medicine, University of California San Diego

Abstract:

Heart diseases like congestive heart failure, coronary heart disease and atrial fibrillation are complex and involve defects at the molecular, cellular, tissue, organ and system scales. We investigate disease mechanisms at multiple scales by developing integrative computational models of cardiac electromechanics that represent and bridge each of these scales. Experimentally, these models can be validated and used to generate and test new hypotheses by making measurements at multi-scales in genetically engineered mouse models of heart disease. Once validated, the models can be applied to clinical problems such as predicting which patients with dyssynchronous heart failure will response best to cardiac resynchronization therapy, or identify optimal sites for ablation in patients with atrial fibrillation.

Bio:

Dr. Andrew McCulloch is Professor of Bioengineering and Medicine and Jacobs School Distinguished Scholar at the University of California San Diego, where he joined the faculty in 1987. He is member of the UCSD Institute for Engineering in Medicine, the California Institute for Telecommunications and Information Technology, a Senior Fellow of the San Diego Supercomputer Center, and a member of the UCSD Center for Research on Biological Systems. Dr. McCulloch is a Principal Investigator of the National Biomedical Computation Resource and Co-Director of the Cardiac Biomedical Science and Engineering Center at UCSD. He served as Vice Chair of the Bioengineering Department from 2002 to 2005 and Chair from 2005 to 2008. Dr. McCulloch is Director of the HHMI-NIBIB Interfaces Graduate Training Program and the accompanying UCSD Interdisciplinary Ph.D. Specialization in Multi-Scale Biology. Dr. McCulloch was educated at the University of Auckland, New Zealand in Engineering Science and Physiology receiving his Ph.D. in 1986. Dr. McCulloch was an NSF Presidential Young Investigator and is a Fellow of the American Institute for Medical and Biological Engineering. He has served on the Board of Directors of the Bio-Medical Engineering Society, and is currently Associate Editor of the Medical and Biological Engineering and Computing and PLoS Computational Biology and co-Editor-in-Chief of Drug Discovery Today: Disease Models. He is on the editorial boards of the American Journal of Physiology: Heart and Circulatory Physiology and Computer Methods in Biomechanics and Biomedical Engineering and Cellular and Molecular Bioengineering. He has given the Konrad Witzig Memorial Lecture and the Donald Wassenberg Memorial Lecture. Recently, he was elected a Fellow of the Cardiovascular Section of the American Physiological Society. He is also chair of the Physiome and Systems Biology Committee of the International Union of Physiological Sciences. Dr. McCulloch's lab uses experimental and computational models to investigate the relationships between the cellular and extracellular structure of cardiac muscle and the electrical and mechanical function of the whole heart during ventricular remodeling, heart failure and arrhythmia. Current interests include developing multi-scale models of myocyte excitation-contraction coupling mechanisms and their regulation by PKA and CaMKII. Dr. McCulloch's group has also scaled cellular level models of these processes up to the tissue and organ scales to investigate mechanisms of arrhythmias and ventricular dysfunction associated with targeted gene defects and congestive heart failure. Genetically engineered mice are an important model system for developing and validating these computational models. Important phenotyping techniques in the mouse include optical electrical mapping, isolated muscle mechanics testing and magnetic resonance imaging. A second major area of research in the lab has been the role of cytoskeletal and membrane proteins in cardiac myocyte mechanotransduction mechanisms and how defects in costameric and z-disk protein complexes can alter mechanotransduction and lead to dilated cardiomyopathy. The effects of stretch on myocyte membrane configuration and electrical conduction are also under investigation. Finally, we have been using Drosophila as a model system to explore hypoxia tolerance and susceptibility mechanisms in conjunction with metabolomics and metabolic network modeling.