

Computational Modeling of the Heart

Objective: To give a presentation of about 60 minutes at the end of the week covering the key aspects of understanding the heart by computational means.

The biosciences are clearly experiencing a long and major growth in the ability to gather data at multiple levels, to design dynamic models and to perform computational experiments. One stellar example of a multiscale, multilevel project is the so called physiome project (www.physiome.org), where the human heart is being modeled in as much detail as possible. This activity has lasted decades and is only going to accelerate and will also be done in other organs as well. This project has been going on for about 4 decades with Auckland (NZ) and Oxford as major collaborators. The integration of many models and data types have lead to the need to focus on standards for models and data allowing exchange and durability of these. Integration of models from different levels have lead to many interesting problems and the application of new methods.

The Big Questions Are:

- What are the key levels that models and data are defined at?
- How are models at different levels integrated and coordinated/
- At a given level, which kind of information can be safely ignored (otherwise no reduction)?
- How hard are the physiome project in the sense that will the ability to simulated eventually be perfect?
- How much does heart models augment interpretation of the genotype→phenotype map for heart diseases?
- What are the future challenges in better heart models?

Maximal Contents of Presentation

The history of physiological heart research
The Heart and its phylogenetic evolution
The Physiome Project
Key Classes of Data
Key Classes of Models
Data and Model Standards necessary for the project
Empirical Predictions from the physiome project
Sisterprojects to the physiome project.

Recommended literature

Caldwell, BJ, Trew, ML, Sands, GB, Hooks, DA, LeGrice, IJ and Smaill, BH 2009.. Three Distinct Directions of Intramural Activation Reveal Nonuniform Side-to-Side Electrical Coupling of Ventricular Myocytes. *Circ Arrhythm Electrophysiol* 2:433-440

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Hunter PJ, McCulloch AD and ter Keurs HEDJ 1998. Modelling the mechanical properties of cardiac muscle. *Prog. Biophys. Molec. Biol.* 69:289-331

Hunter PJ, McNaughton PA and Noble D. 1975. Analytical models of propagation in excitable cells. *Prog Biophys Mol Biol.* 30: 99-144

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Hunter, PJ and Borg, TK. 2003. Integration from proteins to organs: The Physiome Project. *Nature Reviews Molec & Cell Biol.* 4:237-243

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Le Grice IJ, Young A, Hunter PJ and Smaill BH 2000. New views of cardiac structure. *J Mol Cell Cardiol* 32(3) A1

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Nickerson, DP, Smith NP and Hunter PJ. 2005. New developments in a strongly coupled cardiac electromechanical model. *Europace*, 7, S118-S127

Nielsen PMF, LeGrice IJ, Smaill BH & Hunter PJ. 1991. Mathematical model of geometry and fibrous structure of the heart. *Am. J. Physiol.* 260 (4), H1365-H1378

Sands G, Gerneke DA, Hooks DA, Green CG, Smaill BH and LeGrice IJ. 2005. Automated imaging of extended tissue volumes using confocal microscopy. *Microscopy Research and Technique* 67:227-239

Young AA. 1999. Model Tags: Direct 3D tracking of heart wall motion from tagged magnetic resonance images. *Medical Image Analysis* 3:361-372

Young AA, LeGrice IJ, Young MA and Smaill BH 1998. Extended confocal microscopy of myocardial laminae and collagen network. *J Microscopy* 192, 139-150