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Multiscale Computational Modeling of the Heart

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Researchers in the Cardiac Mechanics Research Group at the University of California, San Diego, use multiscale computational models to help interpret their experimental studies of the electromechanical properties of the normal and diseased heart, from molecular to whole-organ scales. In the models, systems of nonlinear ordinary differential and algebraic equations (DAEs) describe the kinetics of biochemical signaling networks, the ion fluxes through voltage-gated channels, and the dynamic interactions of the contractile proteins responsible for cardiac muscle contraction. Because these processes are spatially distributed, compartmentalized, and heterogeneous, the DAE system models must be spatially coupled and solved with numerical methods for the resulting PDEs.

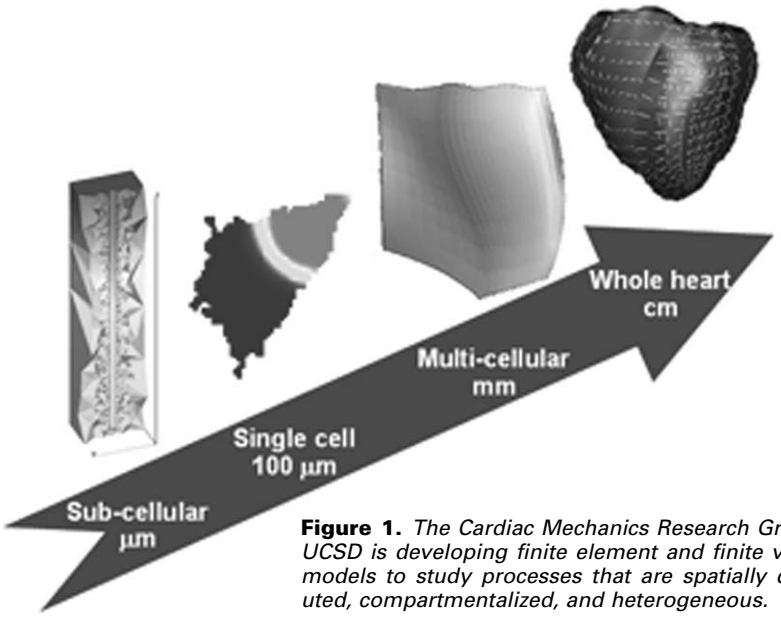

Figure 1. *The Cardiac Mechanics Research Group at UCSD is developing finite element and finite volume models to study processes that are spatially distributed, compartmentalized, and heterogeneous.*

At the subcellular scale, the group is developing finite element models of the diffusion of calcium in the narrow (10-nm) subspace underlying the cell membrane, especially around special invaginations of the membrane into the cell interior known as transverse tubules (shown at far left in Figure 1). At the whole-cell scale (10–100 μm), spatial gradients of the signaling molecules that regulate excitation and contraction are modeled with finite volume methods and the Virtual Cell package developed by Les Loew's National Resource for Cell Analysis and Modeling (http://www.nrcam.uchc.edu/). At the multicellular tissue scale (millimeters), collocation finite element methods are used to model the anisotropic spread of the electrical impulse across a "wedge" of the heart wall; the group is using these results to explore the effects of gene defects on the patterns of impulse propagation and recovery [1]. At the whole-heart scale (centimeters), finite element models of the geometry and fiber architecture of the right and left ventricles are used to study cardiac electromechanical interactions in the normal and diseased heart [2].

The finite element tools developed at UCSD for cardiac electromechanical modeling have been packaged in Continuity 6 (http://www.continuity.ucsd.edu/), a client-server program written in Python, C, and Fortran 95. For commercial applications in medical devices and therapeutics, Continuity has been licensed to the spin-off company Insilicomed (http://www.insilicomed.com).

References

[1] J.J. Saucerman, S.N. Healy, M.E. Belik, J.L. Puglisi, and A.D. McCulloch, *Proarrhythmic consequences of a kcnq1 akap-binding domain mutation: Computational models of whole cells and heterogeneous tissue*, Circ. Res., 95 (2004), 1216–1224.

[2] T.P. Usyk, I.J. LeGrice, and A.D. McCulloch, *Computational model of three-dimensional cardiac electromechanics*, Comput. Visual. Sci., 4:4 (2002), 249–257.

Andrew D. McCulloch, a professor in the Department of Bioengineering at the University of California, San Diego, heads the department's Cardiac Mechanics Research Group. He is a co-founder of Insilicomed. His invited presentation at the conference was titled "Structurally and Functionally Integrated Computational Models for the Heart."