The Department of Computer Science and Engineering
The Eck Institute for Global Health
The Interdisciplinary Center for the Study of Biocomplexity

Present

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Transitioning Biomedical Modeling and Simulation from Primarily an Engineering (and Mathematical) Exercise into Experimental Science

Our modeling and simulation efforts are intended to advance science on two biomedical research fronts: quantitative pharmacology and epithelial morphogenesis. Advances in biomedical science require more explanatory mechanistic models, and our goal is to develop, instantiate, and challenge such models in silico. Having explanatory mechanistic biological models is a precondition to having predictive biological models. I will argue that (validated) mechanistic models that are more explanatory must employ relational rather than metric and absolute grounding. Grounding: units, dimensions, and/or objects to which a variable or model constituent refers; absolute grounding: variables, parameters, and I/O are in real-world units like seconds and meters; relational grounding: variables, parameters, and I/O are in units defined by other components of the model. I will also argue that models that employ relational grounding and have achieved a degree of validation can become suitable objects of experimentation (analogous to in vitro models used in biomedical research): they enable posing and testing biologically relevant mechanistic questions. Developing such models requires adhering to an Iterative Refinement Protocol, which I will describe. I will draw on examples from our recent research, including exploration of plausible mechanisms involved in drug transport through and metabolism by epithelial monolayers, and in MDCK cell cystogenesis.

Professor C. Anthony (Tony) Hunt is a member of the Department of Bioengineering and Therapeutic Sciences and directs the BioSystems Group at the University of California, San Francisco. He develops and uses advanced modeling and simulation (M&S) methods to achieve deeper insight into the networked micromechanisms designed for linking molecular level events with higher level phenomena and operating principles at cell, tissue, organ, and organism levels under normal and diseased conditions, in the presence and absence of interventions (some of which may have therapeutic potential). The current focus of his BioSystems group includes epithelial cell morphogenesis in vitro, alveolar like cyst wounding and repair in vitro, and the coupled influences of inter-, intracellular, and zonal tissue heterogeneity on transport, metabolism, and response to therapeutic (and potentially therapeutic) molecules in normal and diseased livers and isolated hepatocytes. Professor Hunt is a member of the Editorial Boards of Simulation, Transactions of the SCS, the International Journal of Knowledge Discovery in Bioinformatics, and the Journal of Computational Biology and Bioinformatics Research. He is an AAAS and AAPS Fellow and a Director of The McLeod Modeling and Simulation Network. Since 2000, he has served on three Scientific Advisory Boards. Prior to that he was Director of the University of California, San Francisco, Biotechnology Training Program. Prior to the current M&S adventures, he established a successful track record inventing and developing novel therapeutics, targeted delivery, and siRNA methods. Five of 12 patents resulting from that work earned UC income. Recent publications are posted here: http://biosystems.ucsf.edu/publications.html.

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