

Interdisciplinary Center for the Study of Biocomplexity Colloquium

Scott Diamond

Director of the Penn Center for Molecular Discovery
University of Pennsylvania

will give a lecture entitled:

High Throughput and Multiscale Patient-Specific Systems Biology

Abstract

Predicting tissue function based upon an individual's unique cells requires a multiscale Systems Biology approach to understand the coupling of intracellular signaling with spatiotemporal gradients of extracellular biochemicals controlled by convective-diffusive transport. During thrombotic or hemostatic episodes, platelets bind collagen and release ADP and thromboxane A₂ (TXA₂) to facilitate the recruitment of additional platelets to a growing deposit that distorts the flow field. Using high throughput experimentation, we obtained a large set of platelet calcium responses to combinatorial activators in order to train a neural network (NN) model of platelet activation for several individuals. Each NN model was then imbedded into a kinetic Monte Carlo/finite element/lattice Boltzmann simulation of stochastic platelet deposition under flow. Simulations predicted the unique clot buildup dynamics for each donor and responses to various pharmacological inhibitors (measured in microfluidic assays). Consistent with measurement and simulation, one donor displayed a gain of function phenotype, while another donor was distinguished by combined aspirin-resistance and U46619-insensitivity, consistent with a thromboxane receptor mutation. In silico representations of an individual's platelet phenotype allows prediction of blood function, essential to prioritizing patient-specific cardiovascular risk and drug response or to identify unsuspected gene mutations.



**Monday, September 19th, 2011
4:00 p.m. to 5:00 p.m.
127 Hayes-Healy Center**