COMPUTATIONAL SCIENCE AND ENGINEERING RESEARCH GROUP

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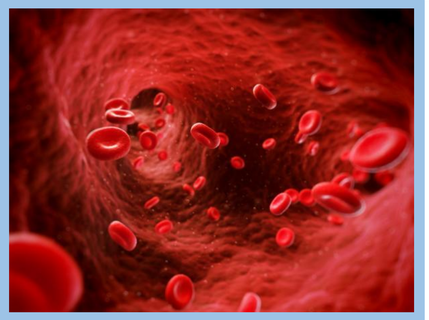
WHAT DO WE DO?

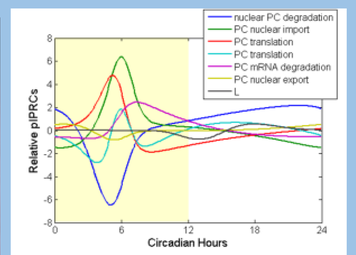
Computational science and engineering (CSE) is a multidisciplinary research area with connections to the sciences, engineering, mathematics and computer science. Our group focuses in particular on multiscale numerical algorithms for simulation and model development. Applications are varied, including modeling and data analytics in systems biology, ecology, medicine, materials science and even social networks. We also work on the development of high-performance computational software for the research community at large to work on important and challenging questions in biology and beyond. This development includes work with cloud computing applications and GPUs.

CURRENT RESEARCH PROJECTS

Modeling Blood Coagulation

When a blood vessel is damaged, the body responds with a long sequence of reactions called the coagulation cascade. Coagulopathy is a term used to describe a problem occurring with the process of coagulation. Coagulopathy is often seen in emergency rooms as a result of trauma. However, the molecular mechanisms are not clearly understood. In this project we look to create a “virtual blood vessel” that can accurately model the dynamics of a blood vessel in the event of an injury. We use this model to predict the outcomes of in vitro experiments.





Comparing the Phase Response Properties of Processes in the Mammalian Circadian Clock

Model from (Geier *et al*, *J Biol Rhythms*, 2005)

Stochastic and Deterministic Analysis of Circadian Clocks

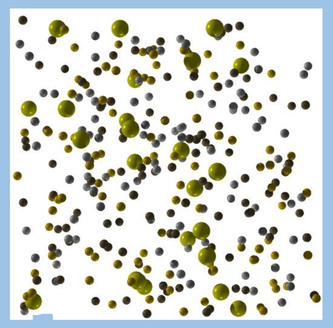
Circadian clocks govern vital daily behaviors in most organisms. Of particular interest is the clock in mammals, which resides in the hypothalamic suprachiasmatic nucleus (SCN). Its behavior is regulated by a hierarchy of mechanisms. The cells of the SCN each contain transcription feedback networks, which induce cell-autonomous oscillations showing a large degree of variability. Via intercellular communication, the population of individual oscillators synchronize to form an SCN-level oscillator with much less variability. The SCN level oscillator is then synchronized to its environment via the process of entrainment with the daily light/dark cycle. To study the circadian clock, we use discrete stochastic methods to capture the variability at the lowest levels, and differential equations to study the clock at the highest levels. At all levels, we are interested in the timing, or phase, behavior of oscillators because it is key to proper synchronization and entrainment behavior.

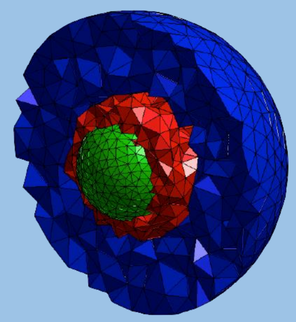
StochSS: Stochastic Simulation Service

StochSS provides an integrated development environment (IDE) for discrete stochastic simulations of biochemical networks and population systems. The powerful and straightforward GUI of StochSS allows the users to easily define their model system (species, initial conditions, species interactions, rates and propensities) and the type of simulation to conduct. StochSS transparently executes simulation workflows using a wide range of underlying platforms such as laptops, workstations and public clouds.

Algorithms for Multiscale Discrete Spatial Stochastic Simulation

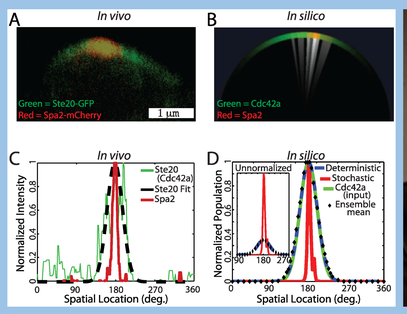
It has been established that traditional deterministic differential equation-based models may fail to capture important dynamics of biochemical systems due to the inherent randomness of the processes. The stochastic simulation algorithm (SSA) derived by Gillespie faithfully captures the behavior of well-mixed systems by tracking the discrete copy number of each species and by simulating every reaction event. In collaboration with Dan Gillespie, we have developed several multiscale stochastic simulation algorithms that take advantage of timescale separation of systems. However, some systems do not satisfy the well-mixed condition, thus requiring a more detailed level of simulation. For such systems, spatial effects can be taken into account by either considering an extension of the SSA to a spatially heterogeneous setting (the next sub volume method (NSM)), or even more fine-grained particle-tracking models. Simulating systems with high spatial resolution is computationally intensive, and to make large computations feasible we are developing multiscale methods, taking advantage of separation of scales. Parts of a simulation can be carried out at a level with less spatial resolution, while other parts are carried out at a more fine-grained level.





Spatial Stochastic Simulation of Cell Polarization in Yeast Mating

Cell polarization is a fundamental process that underlies many aspects of cell and developmental biology. In the polarization process, cellular components that were previously uniformly distributed become asymmetrically localized to create the complexity of form and function that are the hallmark of biological systems. One of the best-studied examples of cell polarization is the growth of the mating projection (shmoo) during yeast mating. Yeast cells localize specific proteins to the front of the cell in response to a spatial gradient of mating pheromone secreted by the partner. The spatial sensing and response exhibit remarkable sensitivity, dynamic range, and robustness. Using a combination of computational modeling and biological experiments we closely examined an important prototype of cell polarity: the pheromone-induced formation of the yeast polarisome. We developed and investigated two mechanistic spatial models of polarisome formation, one deterministic and the other stochastic, and compared the contrasting predictions of these two models against experimental phenotypes of wild-type and mutant cells.



Systems Biology Studies of Post-traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is a severe anxiety disorder that affects a substantial portion of combat veterans and poses serious consequences to long-term health. Left untreated, PTSD can be life-threatening, as it is often linked with substance abuse and severe depression. Consequently, the identification of PTSD indicators (“biomarkers”) that can be detected in the blood or non-invasively is of great interest. Using both a social defeat mouse model of PTSD and minimally invasive data taken from U.S. Army veterans, we aim to identify biomarkers that aid in both the diagnosis and assessment of prognosis of individuals with PTSD. To do this, we use two complementary systems biology strategies: (1) application of statistical and machine learning approaches for building networks of interacting genes related to disease progression, and (2) construction of mechanistic mathematical models of PTSD-relevant neurological circuits. As a result of these strategies, we have constructed both a PTSD “Brain Core Module Network” and a “Fear Conditioning Neuro-Circuit Model” that together suggest many candidate biomarkers relevant to the PTSD disease mechanism.

Other Projects and More Information

Information about all of our projects including a full list of relevant publications can be found online at: http://www.cs.ucsb.edu/~cse

And any other questions can be directed to:

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