

Penn Symposium on Mathematical & Computational Biology



May 23-24, 2016

Steve Altschuler – UCSF

Reverse engineering wiring principles of the fly eye: how flies avoid double, double, double vision

Abstract: How do complex neural circuits assemble during development? The wiring of compound eyes to the brain of flies provides a fascinating model system for studying this question: each point in visual space is captured by multiple photoreceptors, each in a different ommatidium, which wire to the same synaptic unit in the brain. We will describe recent studies that combine intravital imaging and data-driven computational modeling to identify three simple self-organizing principles that underlie this wiring process.

Carina Curto – Pennsylvania State University

Emergent dynamics from network connectivity: a minimal model

Abstract: Many networks in the brain display internally-generated patterns of activity – that is, they exhibit emergent dynamics that are shaped by intrinsic properties of the network rather than inherited from an external input. While a common feature of these networks is an abundance of inhibition, the role of network connectivity in pattern generation remains unclear. In this talk I will introduce Combinatorial Threshold-Linear Networks (CTLNs), which are simple “toy models” of recurrent networks consisting of threshold-linear neurons with binary inhibitory interactions. The dynamics of CTLNs are controlled solely by the structure of an underlying directed graph. By varying the graph, we observe a rich variety of emergent patterns including: multistability, neuronal sequences, and complex rhythms. These patterns are reminiscent of population activity in cortex, hippocampus, and central pattern generators for locomotion. I will present some theorems about CTLNs, and explain how they allow us to predict features of the dynamics by examining properties of the underlying graph. Finally, I’ll show examples illustrating how these mathematical results guide us to engineer complex networks with prescribed dynamic patterns.

Leah Edelstein-Keshet – UBC

Rho GTPases in cell polarization, shape, and motility

Abstract: The family of small GTPases are known to coordinate actomyosin dynamics in eukaryotic cells, regulating both cell polarization, shape changes, and cell motility. Over the past years, we have studied the dynamics of these proteins, their crosstalk, and their participation in regulating cell motion and cell behavior. Here I will survey some of these efforts, with particular emphasis on recent Rac-Rho mutual inhibition. I will describe models that we have been studying, and several mathematical simplifications (sharp switch limit and local perturbation analysis) that allowed us to understand the models and their dependence on parameters. I will provide examples of the link between theory and experiment, and how mathematical models provided insights into the mechanisms underlying observed behaviour. Finally, I will briefly describe recent work on collective cell migration in a developmental context.

Lior Pachter – UC Berkeley

Distance models for phylogenetics

Abstract: Distance based phylogenetics involves estimating distances between biological sequences as a prelude to phylogenetic tree estimation. This approach to phylogenetics is popular due to the simplicity of the methods involved, an example being the widely used neighbor-joining algorithm. I will review some mathematical results that shed light both on the appropriate distance measures to use, as well as on the performance and interpretation of distance-based phylogenetic algorithms.

Charles S. Peskin – NYU

Optimization of Stochastic Docking and Release of Vesicles in Synaptic Transmission

Abstract: Neurotransmitter is released in discrete packets known as quanta, each of which is the content of one synaptic vesicle. We consider a mathematical model in which synaptic vesicles dock on the membrane of the presynaptic terminal between action potentials according to a Poisson process, and then, when an action potential arrives, each docked vesicle has a probability p_θ of releasing its content of neurotransmitter into the synaptic cleft. For this simple model, we study the effect of the parameter p_θ on the ability of the synapse to transmit signals. Surprisingly, performance improves as p_θ decreases. This is because of a compensating increase in the number of docked vesicles as p_θ decreases. When the possibility of undocking is considered, we find instead that there is an optimal (nonzero but small, if the undocking rate is small) p_θ , and we determine its asymptotic behavior as a function of the undocking rate.

*joint work with Calvin Zhang.

Arjun Raj – University of Pennsylvania

Probability and determinism in cancer biology

Abstract: Cancer is a disease of single cells behaving badly, with mutations to certain proteins causing uncontrolled cellular proliferation. This has led to the development of therapies targeting those proteins, such as vemurafenib for melanoma. Yet while most cells will respond to drug, some do not, ultimately repopulating the tumors and causing relapse. This process is often thought to be Darwinian, with genetic underpinnings. Here, we show that the acquisition of resistance may have in fact have non-genetic origins, and we decompose the resistance process into an early, transient priming phase before the addition of drug, following by a later reprogramming phase consisting of a stepwise epigenetic progression. We discuss some implications of this probabilistic and deterministic behavior for cancer treatment as well as cell fate plasticity.

Sebastian Schreiber – UC Davis

Species Coexistence in Stochastic Environments: A Mathematical Perspective

Abstract: Stochastic fluctuations in temperature, precipitation and a host of other environmental factors occur at multiple spatial and temporal scales. As the survival and reproduction of organisms, whether they be plants, animals, or viruses, depend on these environmental factors, these stochastic fluctuations often drive fluctuations in population abundances. This simple observation leads to a fundamental question in population biology. Namely, under what conditions do stochastic environmental fluctuations hinder or facilitate the maintenance of biodiversity? This question is particularly pressing in light of global climate models predicting increasing temporal variation in

many climatic variables over the next century.

One fruitful approach to tackling this question from population biology is the development and analysis of models accounting for nonlinear feedbacks among species, population structure, and environmental stochasticity. In this talk, I will discuss progress in the development of a mathematical theory for stochastic coexistence where the dynamics of the interacting species are encoded by random difference equations and coexistence corresponds to the limit points of empirical measures being bounded away from an extinction set. I will illustrate the theory with empirical based examples involving checkerspot butterflies, Kansas prairies, and coastal dunes.

Caroline Uhler – MIT

Packing Models of Chromosomes and their Expression

Abstract: Although the genetic information in each cell within an organism is identical, gene expression varies widely between different cell types. I will analyze the hypothesis that cell shape and the spatial organization of chromosomes controls gene expression. I will describe a bi-level optimization formulation to find minimal overlap configurations of ellipsoids to model chromosome arrangements. Analyzing the resulting ellipsoid configurations is central to understanding geometric control of genetic programs and has important implications for cell differentiation and the reprogramming of cells during development.

John Wakeley – Harvard University

The effects of population pedigrees on gene genealogies

Abstract: The models of coalescent theory for diploid organisms are wrongly based on averaging over reproductive, or family, relationships. In fact, the entire set of relationships, which may be called the population pedigree, is fixed by past events. Because of this, the standard equations of population genetics for probabilities of common ancestry are incorrect. However, the predictions of coalescent models appear surprisingly accurate for many purposes. A number of different scenarios will be investigated using simulations to illustrate the effects of pedigrees on gene genealogies both within and among loci. These scenarios include selective sweeps, the occurrence of very large families, and population subdivision with migration.

Lani Wu – UCSF

Reverse engineering the neutrophil polarity network

Abstract. A central question in biology is how complex, spatial-temporal cellular behaviors arise from biochemical networks. Much work has led to the identification and cataloguing of various network architectures, and the explication of how static network motifs can give rise to dynamic response characteristics, including ultrasensitive, switch-like, and oscillatory behaviors. However, the wiring diagrams of signaling networks are often inferred by combining results from diverse assays. Such diagrams may not represent accurately the operating state of the network in any cell, condition or time point. In this talk, we will discuss recent progress in using perturbation analysis and cellular heterogeneity to constrain network crosstalk from cellular behaviors.