Special Session 37: Mathematical Models and Computations in Cell and Developmental Biology

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This minisymposium aims to bring researchers to address recent advances of mathematical modeling on cell and developmental biology. In this minisymposium, researchers will discuss a wide range of complex biological systems which include but not limited to cell polarization, cell signaling pathways, cell-cell interaction to developmental biology. The challenges of modeling these complex systems will be discussed, and more beyond, the new modeling and computational techniques to tackle these problems will also be presented.

A stochastic density-dependent switch drives spontaneous cell polarization

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Cell polarization in yeast is a symmetry breaking process, where a cap of polarity regulator Cdc42 forms to mark where a daughter cell will bud off. A simple positive feedback circuit based on dynamics of Cdc42 shows emergent polarity for intermediate ranges of signaling molecule numbers. Below a critical density of Cdc42, positive feedback robustly maintains an off state; exceeding this threshold switches on the recurrent emergence of highly localized signaling clusters. Cluster formation requires only this minimal positive feedback circuit, and does not require additional mechanisms such as diffusion barriers, spatial cues, or biochemical inhibitors. This mechanism is general, and could be applied to a variety of cellular signaling systems to create clusters in the membrane or cytosol.

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PDCD5-regulated cell fate decision after UV-irradiation induced DNA damage

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Programmed cell death 5 (PDCD5) is a human apoptosis-related molecule that is involved in both the cytoplasmic caspase-3 activity pathway by regulating Bax translocation from cytoplasm to mitochondria and the nuclear pathway by interacting with Tip60. In this study, we developed a mathematical model of the PDCD5-regulated switching of the cell response from DNA repair to apoptosis after ultraviolet (UV)-irradiated DNA damage. The model was established by combining several hypotheses with experimental observations. Our simulations indicated that the ultimate cell response to DNA damage is dependent on a signal threshold mechanism, and the PDCD5 promotion of Bax translocation plays an essential role in PDCD5-regulated cell apoptosis. Furthermore, the model simulations revealed that PDCD5 nuclear translocation can attenuate cell apoptosis, and PDCD5 interactions with Tip60 can accelerate DNA damage-induced apoptosis, but the final cell fate decision is insensitive to the PDCD5-Tip60 interaction. These results are consistent with experimental observations. The effect of recombinant human PDCD5 was also investigated and shown to sensitize cells to DNA damage by promoting caspase-3 activity.

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Mathematical models for phototaxis

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Certain organisms undergo phototaxis, that is they migrate toward light. In this talk we will discuss our recent results on modeling phototaxis in order to understand the functionality of the cell and how the motion of individual cells is translated into emerging patterns on macroscopic scales. This is a joint work with Amanda Galante, Susanne Wisen, Tiago Requeijo, and Devaki Bhaya.

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Mathematical modeling and computational studies for cell signaling with scaffolds

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I will present a computational analysis of cell signaling in biology and medicine. Scaffold, a class of proteins, plays many important roles in signal transduction. Through studying various models of scaffold, I will show novel regulations induced by its spatial location and switch-like and bistability responses due to scaffold. To efficiently compute the models, we introduce a new fast numerical algorithm incorporated with adaptive mesh refinement

for solving the stiff systems with spatial dynamics.

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Robust budding site selection and cell polarization in yeast cells

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Cell polarity is induced through the localization of specific molecules to proper location of the cell membrane. In this talk, we propose a generic model including membrane bound molecules undergoing polarization, landmark cue and the effect of inhomogeneous distribution of GAPs to study the mechanisms for different polarized site selection patterns: random polarized site selection in the absence of a pre-localized signal, adjacent positioning of axial polarized pattern and bipolar polarization pattern.

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Quantifying parameters for a mathematical model on the interaction of matrix metalloproteinases and their inhibitors in a wound

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In this work, we present a mathematical model for the interactions of matrix metalloproteinases (MMPs), which degrade the extracellular matrix (ECM), and their inhibitors (TIMPs), and quantify the parameters by fitting the model to data. Measurements of the ratio of MMPs-to-TIMPs may be critical to a successful wound-healing event because an imbalance of these proteins is often found in chronic wounds. Muller et al. measure levels of MMPs and TIMPs in wound fluid. The data were divided into two subgroups – good healers and bad healers – based on healing rate, and averaged for each subgroup. The parameters in the four-equation model, consisting of MMPs, TIMPs, ECM, and fibroblasts, were fit using the commands "GlobalSearch" and "fmincon" in Matlab. Reasonable parameter values were obtained by minimizing a least-squares functional.

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Modeling cell-cell and cell-matrix interactions in single and collective motion in 3D

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Cell migration is a fundamental biological process that regulates a spectrum of events during development, wound healing and tumor metastasis. Until now, our approach to study migration has been focused largely on cells cultured or modeled on artificial two-dimensional substrates that are far from in vivo. Consequently, our understanding of cell migration in vivo has been very limited and often naive and inaccurate. Recent developments in both computational and experimental tools have afforded the possibility to study single and collective cell motion in native like 3D environments, that are quantitative and provide a much more realistic picture of the in vivo environment. Our results using multi-scale modeling, integrating molecular dynamics, coarse grained macro-molecular and continuum cellular level approaches suggest an intricate quantitative balance between matrix mechanics, sterics, signaling and migration speed and directionality. We also study the effect of local cell density and cell-cell contacts in regulating matrix reorganization and cellular speed. Our results have shown very good agreement with single and collective cell migration experiments on cancer cells in 3D scaffolds and matrices and provide a framework for understanding the complexity of cell migration in vitro and in vivo.

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