

Center for Biocomplexity Colloquium

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“Fluctuation Effects in 2D Models of Gradient Sensing”

Monday, March 22, 2010

4:00pm

127 Hayes-Healy Hall

****Tea at 3:30pm in 257 Hurley****

Chemotaxis, or directed migration of cells guided by chemical gradients, plays an important role in embryogenesis, immune response, wound healing and tumor metastasis. During chemotaxis, a cell detects extracellular chemoattractants and translates these signals into a complex cellular response resulting in morphological reorganization and motility. The accuracy with which a cell can determine an external chemical gradient is limited by fluctuations arising from the discrete nature of second messenger release and diffusion processes within the small volume of a living cell (intrinsic noise) as well as local fluctuations in ligand concentration and receptor occupancy (extrinsic noise). Fluctuation noise has the potential to attenuate or disperse gradient information transduced by the membrane bound receptors. At the same time, models of the intracellular signaling network have been devised that use a combination of local excitation and global inhibition to sharpen the intracellular gradient signal. We approach the effects of fluctuations on gradient sensing in two ways. First, we study the accuracy with which an ideal observer could estimate the gradient direction from receptor occupancies, within a maximum likelihood estimation framework. Second, we implement a stochastic version the "balanced inactivation" model (Levine et. al. 2006) for amplification of directional information in a two dimensional model cell. We develop a fixed timestep approach in which the probabilities of individual molecules making spatial or chemical transitions is treated as a system of multinomial random variables. With this numerical framework we investigate the relationship between the amplification of the gradient signal, the propagation of noise in the signaling pathway, and fundamental limits on the accuracy of the gradient sensing mechanism.