BP 16: Pattern Formation and Developmental Processes

Time: Wednesday 17:30–19:00 Location: C 243

BP 16.1 Wed 17:30 C 243

Coupling vs. Noise: The Rise and Fall of Synchrony in the Segmentation Clock — •Ingmar Riedel-Kruse[1,2], Claudia Mueller[2], and Andrew Oates[2] — [1]California Institute of Technology, Pasadena, USA — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

The "segmentation clock" is thought to coordinate sequential segmentation of the body axis in vertebrate embryos. This clock comprises a multi-cellular genetic network of synchronized oscillators, coupled by intercellular Delta/Notch signaling. How this synchrony is established, and how its loss determines the position of segmentation defects in Delta/Notch mutants is unknown. We analyzed the clock's synchrony dynamics by varying strength and timing of Notch coupling in zebrafish embryos using techniques for quantitative perturbation of gene function. We developed a physical theory based on coupled phase oscillators explaining the observed onset and rescue of segmentation defects, the clock's robustness against developmental noise, and a critical point beyond which synchrony decays. We conclude that synchrony among these genetic oscillators can be established by simultaneous initiation and self-organization, and that the segmentation defect position is determined by the difference between coupling strength and noise.

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BP 16.2 Wed 17:45 C 243

Firewalls in atrial myocytes — •Rüdiger Thul[1], Stephen Coombes[1], and Martin Bootman[2] — [1]School of Mathematical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK — [2]Laboratory of Molecular Signalling, The Babraham Institute, Babraham, Cambridge, CB22 3AT, UK

Atrial myocoytes play a prominent role in the generation of heart beats. Their contraction is controlled by Calcium signals that emerge at the cellular periphery and then proceed centripetally to engage the force-generating myofilaments. Experiments have demonstrated that these initial signals need to overcome a barrier just below the cell membrane before they move inward. Since atrial myoctes lack transverse tubules that transmit external signals to the cell interior as e.g. in ventricular myocytes, such a firewall represents a crucial determinant of atrial dynamics. For instances, it allows atrial myocytes to fine tune their responses to a wide range of vital stimuli. Here, we present a computationally advantageous model to investigate the mechanisms that give rise to these graded centripetal signals. Our framework takes into account the three dimensional organisation of atrial myocytes, especially the spatially restricted release of Calcium from internal storage compartments. We employ a fire-diffuse-fire (FDF) model to examine the spatio-temporal patterns and to probe the dependence of wave propagation on physiologically relevant parameters. Mimicking an excitable medium, the FDF approach reflects the significance of noise in intracellullar Calcium dynamics. The explicit construction of the corresponding Green's function allows for a detailed analysis.

BP 16.3 Wed 18:00 C 243

A stochastic Boolean network model of receptor cross-talk in angiogenesis — •Thimo Rohlf[1,2] and Amy L. Bauer[3] — [1]Santa Fe Institute, 1399 Hyde Park Road, Santa Fe, NM 87501, USA — [2]Max-Planck Institute for Mathematics in the Sciences, Inselstrasse 22, D-04103 Leipzig — [3]Los Alamos National Laboratory (T-14), MS B-262, Los Alamos, NM 87545, USA

How cells interpret and synthesize multiple biochemical signals initiated by key external stimuli during angiogenesis, namely growth factors, matrix molecules, and cell-cell communication via cadherins, is a challenging problem. From available databases, we construct a Boolean network model that highlights the cross-talk between growth factor, integrin, and cadherin receptors, and systematically analyze the dynamical stability of the network under continuous-time Boolean dynamics with a noisy production function.

We find that the signal transduction network exhibits robust and fast response to external signals, independent of the internal cell state. We derive an input-output table that maps external stimuli to cell phenotypes, which is extraordinarily stable against molecular noise, with one important exception: an oscillatory feedback-loop between the key signal molecules RhoA and Rac (as sometimes is postulated in the literature) is unstable under arbitrarily low noise, leading to erratic, dysfunctional cell motion. Finally, we show that the network exhibits an apoptotic response rate that increases with noise, suggesting that the probability of programmed cell death increases in response to conflicting or confusing signals.

BP 16.4 Wed 18:15 C 243

MarkovModelForBoneRemodelling — •Marco Rusconi[1,2], Richard Weinkamer[2], Angelo Valleriani[2], and Juergen Kurths[1] — [1]Non-linear dynamics group,institute of physics,faculty of mathematics and science, Potsdam University,D-14415 Potsdam — [2]Max Planck Institut of Colloids and Interface, Department of Biomaterials,Research Campus Golm, D-14424 Potsdam, Germany

Bone is a continuously regenerated living tissue. During this remodelling process, bone is cyclically resorbed and formed to allow it to achieve the optimal adaptation to the external mechanical environment. The investigation of the connection between external mechanical stimuli and bone remodelling is a not completely understood problem. In this contribution, we introduce a markov model for bone remodelling. We focus our attention on the remodelling of the inner spongy structure of bone, the trabecular structure. Assuming a connection between mechanical stimulus and trabecular cross-sectional area (A), we define phenomenological relations between the probability of formation and resorption and A. This is essentially a *translation* of the Wolff-Roux law in terms of an architectural parameter of the trabecular structure. We evaluate the evolution with time of the trabecular area distribution (TAD) for several different mechanical stimuli proposed in literature. The different assumptions lead to different TAD and we compare them with those obtained from micro tomographic scans of real bone.

BP 16.5 Wed 18:30 C 243

Collective processes set the clock in vertebrate segmentation — •Saul Ares[1], Luis Morelli[1], Leah Herrgen[2], Christian Schroeter[2], Andrew C. Oates[2], and Frank Julicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Somitogenesis, the first stage of the body axis segmentation in vertebrate development, is a complex process driven by the interplay of oscillations in gene expression and the elongation of the body axis. In order to understand it quantitatively at a tissue level, a theoretical framework based on discrete coupled phase oscillators with a time delay in their mutual communication has been proposed. Global properties as the time necessary for the formation of a somite can be calculated, finding a scenario of multiple solutions and multistability. To get analytic expressions from the theory, a continuum limit for arbitrary values of the time delay is formulated. This continuum formulation allows to determine the parameters of the theory from available data on the wavelength of the patterns of gene expression. The fit to the experimental data supports the main conclusion of the theory: the periodicity of somitogenesis arises as a collective process where the intercellular communication plays a key role in the setting of the frequency of the segmentation clock.

BP 16.6 Wed 18:45 C 243

Spatiotemporal patterns in signal transduction: effect of cytoskeleton structure and molecular crowding — •Michael Klann, Alexei Lapin, and Matthias Reuss — Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, Germany

Cellular signaling depends on the efficient translocation of signals from the cell membrane to target proteins. The cytoskeleton network hinders diffusion but also offers express-ways for active transportation along the filaments. Amplification or regulation of the signal strength through a cascade of reactions depends on the local concentration of the molecules, which is strongly affected by molecular crowding. The low number of molecules in signaling pathways leads to a significant level of stochastic noise. Local fluctuations that do not cancel out on the cell level due to nonlinear interactions lead to deviations from continuum ODE-models. To analyze the spatiotemporal signaling patterns affected by the inhomogeneous background of cellular architecture we developed a stochastic simulation method that allows us to track the position of every molecule of interest including reactions, dif-

fusion and active transport through the cell. Simulations show that in presence of the cytoskeleton, diffusion is slowed down but the reaction rate is increased due to the higher effective concentration of reactants. Overall this can reduce the travel time from the plasma membrane to the nucleus. Active transport along the cytoskeleton furthermore increases the efficiency of the signaling cascade.