AKB 22 Sensory Biophysics and Signal Transduction

Time: Thursday 14:30–16:15 Room: ZEU 255

Invited Talk AKB 22.1 Thu 14:30 ZEU 255

Signal processing by clusters of membrane receptors — •T.A.J. Duke and I. Graham — Cavendish Laboratory, JJ Thompson Avenue, Cambridge CB3 0HE, UK

One of the main ways that cells receive information about their environment is through the equilibrium binding of ligand molecules to membrane receptors. Typically, ligand binding causes a change in receptor conformation that triggers a signal transduction cascade in the cell. We investigate the logical repertoire of clusters composed of homologous receptors that can bind more than one type of ligand and show that they are capable of quite sophisticated processing. All of the elementary logical functions can be implemented by appropriate tuning of the ligand binding energies and cooperative interactions between receptors can greatly enhance the sharpness of the response. Receptor clusters can therefore act as digital logical elements whose activity can be abruptly switched from fully inactive to fully active, as the concentrations of the regulators pass threshold values. We discuss a particular instance in which this type of protein logic appears to be used in signal transduction - the chemotaxis receptors of E. coli.

AKB 22.2 Thu 15:00 ZEU 255

Precision of Morphogen Gradients — •Tobias Bollenbach[1], Periklis Pantazis[2], Karsten Kruse[1], Marcos González-Gaitán[2], and Frank Jülicher[1] — [1]MPI for the Physics of Complex Systems, Nöthnitzerstr. 38, 01187 Dresden — [2]MPI for Molecular Cell Biology and Genetics, Pfotenhauerstr. 108, 01307 Dresden

A fundamental problem in the field of animal development is to understand how well-defined cellular patterns can emerge in the presence of fluctuations. A well-established means of tissue patterning is given by morphogens. These are signaling molecules that spread from a restricted source into an adjacent target tissue forming a concentration gradient. The fate of cells in the target tissue is determined by the local concentration of such morphogens. In the presence of fluctuations, it is an important question how precise the positional information encoded in a morphogen gradient can be. Here, we investigate the precision of the gradient of the morphogen Dpp in the Drosophila wing disk both experimentally and theoretically. We measure the normalized fluctuations of the Dpp gradient as a function of the distance to the source. We find that these fluctuations grow monotonously for large distances to the source, while close to the source they can decrease. Our theoretical analysis reveals that cell-to-cell variability in the target tissue can generate the observed behavior of the fluctuations. This suggests that the concentration fluctuations in the gradient reflect the random components of intercellular signaling and transport.

AKB 22.3 Thu 15:15 ZEU 255

Polarized dynamics of individual G-protein coupled receptors in Dictyostelium chemotaxis. — •Thomas Schmidt[1], Sandra de Keijzer[1], Freek van Hemert[1], Herman Spaink[2], and Ewa Snaar-Jagalska[2] — [1]Physics of Life Processes, Leiden University — [2]Cell Biology, Leiden Univesity

Single molecule microscopy was used to unravel the role of the G-protein coupled cAMP receptor, cAR1, in establishing polarity during chemotaxis of living Dictyostelium discoideum cells. We analyzed the mobility of individual cAR1-eYFP under different physiological conditions. In all cells an immobile and a mobile receptor fraction was found. The latter increased from 38% to 54% at the anterior of chemotaxing cells. The mobile fraction was characterized by a diffusion constant D = 0.19 um2/s. The anterior/posterior mobility shift was neither caused by a difference in membrane viscosity nor by a conformational change of the receptor due to phosphorylation. Comparison with studies on Ga2-protein deficient cell lines allowed us to conclude that the mobility shift of the receptors at the leading edge resembles the uncoupling/activation of the Ga2-protein. Our data further suggest that the mobility shift is directly related to the primary amplification steps in chemotaxic signalling and leads to a straightforward molecular explanation of the parameters in current models.

AKB 22.4 Thu 15:30 ZEU 255

***Dictyostelium discoideum* Chemotaxis: Threshold for Directed Motion** — •Carsten Beta[1,2], Loling Song[1,3], Sharvari Nadkarni[1], Hendrik Boedeker[1,4], Albert Bae[1,2], Carl Franck[1], Wouter-Jan Rappel[5], William Loomis[6], and Eberhard Bodenschatz[1,2] — [1]LASSP, Department of Physics, Cornell University — [2]Max Planck Institute for Dynamics and Self-Organisation, Göttingen — [3]Harvard Medical School, Department of Cell Biology — [4]Institut für Angewandte Physik, WWU Münster — [5]Department of Physics, University of California at San Diego — [6]Division of Biological Sciences, University of California at San Diego

The chemotactic response of *Dictyostelium discoideum* cells to stationary, linear gradients of cyclic adenosine 3',5'-monophosphate (cAMP) was studied using microfluidic devices. In shallow gradients of less than $10^{-3}\,\mathrm{nM}/\mu\mathrm{m}$, the cells showed no directional response and exhibited a constant basal motility. In steeper gradients, cells moved up the gradient on average. The chemotactic speed and the motility increased with increasing steepness up to a plateau at around $10^{-1}\,\mathrm{nM}/\mu\mathrm{m}$. In very steep gradients, above $10\,\mathrm{nM}/\mu\mathrm{m}$, the cells lost directionality and the motility returned to the sub-threshold level. In the regime of optimal response the difference in receptor occupancy at the front and back of the cell is estimated to be only about 100 molecules.

AKB 22.5 Thu 15:45 ZEU 255

Chemotaxis in Microfluid Channels — •Danica Wyatt[1,2], Carsten Beta[1,2], Wouter-Jan Rappel[3], William Loomis[4], and Eberhard Bodenschatz[1,2] — [1]Max Planck Institute for Dynamics and Self-Organization, Goettingen — [2]LASSP, Department of Physics, Cornell University — [3]Department of Physics, University of California at San Diego — [4]Division of Biological Sciences, University of California at San Diego

Directional sensing in eukaryotic cells has been subject of intensive research over the last decade. Much of this work has been done using the amoeba Dictyostelium discoideum as a model system. Dicty exhibits signaling pathways that appear to be well-conserved in mammalian chemotaxis. To investigate the dynamics of its signaling proteins, experiments must generate stimuli that can be controlled on the same time scale as the intracellular response. Also, it is essential to percisely characterize and manipulate the immediate chemical environment of a cell. Together, these requirements suggest an approach in which the chemoattractant is delivered directly to points of interest on the cell membrane. I will present microfluidic innovations for generating a variety of such stimuli and show how they led to observations of novel cell responses that could not be triggered by traditional experimental methods.

AKB 22.6 Thu 16:00 ZEU 255

PROCEEDINGS IN ODORANT RECEPTOR EXPRESSION: FROM CELLULAR SYSTEMS TOWARDS IN VITRO SYSTEMS — •Eva Sinner[1,2], Rudolf Robelek[1], Eva Lemker[2], Birgit Wiltschi[2], and Dieter Oesterhelt[2] — [1]MPI for Polymer Research , Ackermannweg 10, 55128 Mainz — [2]MPI for Biochemistry, Am Klopferspitz 18a, 82152 Martinsried

An in vitro strategy is now available to generate a platform for investigation of complex membrane proteins, such as odorant receptors. Coding for a complex membrane protein, an odorant receptor OR5 was used as challenging example to be inserted in an artificial planar lipid membrane system. We show the presence and orientation of resulting OR5 protein in the planar lipid membrane by tag-specific immuno- labelling in combination with surface plasmon enhanced fluorescence spectroscopy. Integration of the OR5 proteins are shown by radioactive labelling and a proof of function (specific ligand binding) is shown by surface enhanced infrared spectroscopy.