Modelling of G protein cascade in olfactory receptor neurons

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ABSTRACT

Moth olfactory receptor neurons (ORNs) sensitive to sexual pheromone molecules present remarkable features. They can fire an action potential in response to activation of a single pheromone receptor and nonetheless respond on a wide dynamic range (6-8 decades in concentration). Moreover certain ORNs can follow frequency of stimulation pulses up to 10 Hz with synchronous action potentials; this is a significant property because in natural odour plumes atmospheric turbulence creates discrete clumps of molecules which are recorded by the flying insect as a temporal signal. Thus, the ORN firing can follow with precision the spatio-temporal variation of the stimulus intensity. and permits the male moths to track the female-released pheromone plumes. We investigated the early reactions in olfactory transduction with the aim of understanding how they can code for the intensitive and temporal structure of the odorant signal with so fast kinetics over such a wide range of intensity.

The early reactions involve the sequential interaction of three types of proteins located in the ORN outer dendritic segment - receptors, G-proteins and enzymes generating second messengers - whose reaction rates are limited by lateral diffusion in the membrane. The network of activating and inactivating reactions involved in the interaction of these proteins was modelled as a system of ordinary differential equations (ODEs). The reaction rate constants were derived from experimental measurements in moth ORNs and, when not available, from other sensory neurons. Without any estimation of parameters based on curve fitting, we found that our dynamical system captured the essential kinetic properties observed experimentally. Moreover, we propose two mechanisms which limit the reactivity and the rapidity of signal transduction. First, we suggest that the ORN can detect small changes around its activated stationary state. Second, we show that it exist a threshold in the stimulation flux above which the intensity of the signal is no longer coded as the height of the response (number of activated enzyme molecules) but as its duration.

We also began to extend this approach in two ways. First, we developed stochastic simulations of the master equations corresponding to the reactive processes in order to study the ORN response to small numbers of activated receptors. In this situation, which cannot be studied with the ODE system, the thresholds (either the physical one, i.e. for a single activated receptor per ORN, or the electrophysiological one) were determined and found to differ from those determined with ODEs. Second, the partial differential equations (PDEs), which describe the reaction and diffusion of the chemical species, were considered. This allowed us to inspect the spatial distribution of the species on the dendritic membrane and to assess its consequence on the kinetics.