CODING OF PERIODIC STIMULATIONS IN CHEMORECEPTORS

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Chemosensory transduction, especially in olfactory receptor neurons which are at the centre of our interest, is a remarkable biochemical and electrical process in which the presence of a single molecule (ligand) at the cell surface can be detected and amplified into an action potential. This is a multistage process that involves the association of the ligand with a receptor protein on the cell membrane. The production of this signaling complex triggers the activation of G-proteins which in turn activates enzyme units (e.g. anenylate cyclase) that release second messenger molecules (e.g. cyclic AMP) in the cytoplasm. The second messengers open a number of ion channels, resulting in a change of the membrane potential followed by firing of one or more action potentials.

In the present work we are interested in the initial ligand-receptor interaction. It is believed to be the most important event in the cascade, because it is merely amplified by the subsequent events. Two basic models of this interaction have been studied in the context of chemoreception. In the first one, the cell chemosensory membrane is assumed to be directly exposed to the external environment (concentration detectors CD). The second type (flux detectors FD) encompasses a physically distinct perireceptor space and ligand degrading mechanisms. Moreover, in both types, the signaling complex acting on G-proteins can be considered as produced in a single reaction step (binding) or in two steps (binding then activation).

In most of the previous studies on these models only the steady-state responses were analyzed in the presence of a constant concentration of ligand but rarely the transient responses resulting from a step or square stimulation. Moreover, it has been shown in natural conditions that the turbulence of the carrier medium, air or water, physically breaks the initially continuous ligand plume into spatially and temporally discontinuous patches. The importance of this periodic stimulation has been experimentally studied in insects and shown to be a necessary condition of odorant perception. Therefore, the main aim of the present contribution is to investigate the response of the models when they are exposed to a concentration of ligand that varies periodically in time, summarizing and extending our recent research on this topic (Rospars et al., 2000; Lansky et al., 2001).

Two types of time dependency of the concentration of the ligand are studied. In the first type the concentration is the sum of a constant component and a periodic one described by a sinus wave of amplitude . The second type of stimulation is composed of two alternating square pulses of amplitudes off and on. The smallest one is called the "off" pulse (it can be of zero amplitude and its duration is t_{off}), and the other "on". The period of stimulation is defined as the sum $t_{\text{off}} + t_{\text{on}}$. This type of stimulation has several advantages over the sinus wave: it permits to have "on" and "off" pulses of different lengths, and thus it is closer to natural and experimental stimuli. The main variable of interest in the periodic stimulation is its frequency, which may correspond to some external conditions, e.g., segmentation of the air plume in insects or breathing in vertebrates.

The response of the system, i.e. the concentration of the signaling complex, is studied under both types of stimulation in dependency on its parameters. In all cases, after a certain delay, a periodic behaviour is achieved which follows the stimulus with the same frequency. We show that the FD design affords an increase in sensitivity (i.e. a lower response threshold) with respect to the CD design, which is paid for by a lesser ability to follow changes in stimulus intensity. The same conclusion applies for the introduction of the second (activation) step in the formation of the complex.

Three features of the response depend on the stimulation frequency: its amplitude, its time rate of change and its time lag with respect to the stimulus. The relative delay of the response (time lag/stimulation period) is small for a slowly varying stimulation and increases at higher frequencies. For a very fast stimulation the delay itself approaches a quarter of the stimulation period. With increasing frequency of stimulation the amplitude of response gets to zero whereas the time rate of change increases. We show that the product of these two quantities goes through a maximum which yields in some sense the optimal response of the system. Based on this measure of tuning we find, with realistic values of the parameters derived from biochemical and physiological measurements on the sexual pheromone reception system in moths, that the optimum frequency of the stimulus is ca. 2 Hz for sine waves and ca. 3-5 Hz for pulses, in remarkable agreement with behavioural experiments.

References

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