SELF-SUSTAINED WAVES IN A COMPUTATIONAL MODEL OF THE OLFACTORY EPITHELIUM WITH GAP JUNCTIONS

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Self-sustained waves are typical phenomena of excitable media in physics, chemistry and biology (Murray 1989). The interest in studying self-sustained wave propagation is stimulated by the fact that interactions of such waves in a medium may result in turbulence and chaos. For example, disturbances of this type may lead to several medical diseases as cardiac arrhythmias (Qu et al. 1999) and spreading cortical depression in the nervous system (Martins-Ferreira et al., 2000). Any excitable media with some kind of coupling between its elements can exhibit self-sustained waves. In cardiac tissue, for example, electrical coupling between cells by means of gap junctions allows the appearance of propagating spiral waves, and modifications of the properties of the gap junctions (remodelling) are hypothesized as having a role in ventricular and atrial fibrillation (van der Velden and Jongsma 2002). This might be due to spiral breakup caused by some modulation of the gap junctions conductances (Panfilov 2002).

There is recent evidence for the presence of gap junction connections between neurons of the central nervous system (Rozental et al. 2000; Zhang et al. 2000; Galarreta and Hestrin 2002; Kosaka and Kosaka 2003). This has raised the issue of the determination of the possible roles of these gap junctions in neural function. The fact that self-sustained waves propagating through excitable media of different nature have common features (Murray 1989) suggests that some properties of the spatiotemporal patterns of excitation in cardiac tissue may also be found in neural systems. In particular, one can predict the emergence of spiral waves of activity in nerve tissue with gap junction coupling between cells. Furthermore, the dynamic behavior of these waves may be affected by modulation of the gap junctions conductances, and phenomena like spiral breakup may be observed in neural tissue as well.

Recent discoveries that mature olfactory sensory neurons (OSNs) of the epithelium of adult mice express connexins 43 and 45 (Zhang et al. 2000; Zhang and Restrepo 2002) raised the possibility that gap junction couplings exist between OSNs. These would give the olfactory epithelium the necessary conditions for the appearance of self-sustained waves of activity propagating across it.

In this work, we use a biologically realistic model of a piece of the olfactory epithelium with OSN models connected by gap junctions (Simões-de-Souza and Roque 2003) to investigate the spatiotemporal patterns of activity generated in the model during odor stimulation. The model consists of a grid of 50x50 identical replicas of an OSN model developed by us ((Simões-de-Souza and Roque 2002). Each cell in the grid is connected to its eight neighbors via gap junctions with constant conductance. Some cells in the grid were considered as responsive to eight different odors with a spatial pattern of odor distribution which was based on the work of Ma and Shepherd (2000). The model was implemented in the GENESIS neural similator and its details are given elsewhere (Simões-de-Souza and Roque 2003).

During simulated presentations of different combinations of the eight odors the model exhibits propagating spiral waves and spiral breakup for several values of the gap junction conductance. A study of the spatiotemporal patterns of activity as a function of the gap junction conductance for a single input odor reveals different behaviors of the self-sustained waves propagating across the grid.

The results' indication that the olfactory epithelium with gap junction coupling may exhibit propagating self-sustained waves of activity is particularly puzzling. Recent molecular biological studies have shown the existence of a combinatorial receptor coding scheme for odors in the olfactory epithelium (Malnic et al. 1999). One odorant receptor in the olfactory epithelium recognizes multiple odorants and different odorants are recognized by different combinations of odorant receptors in the epithelium. The picture that emerged from these findings is that different odorants elicit spatially defined, i.e static, patterns of activity in the olfactory epithelium (Malnic et al. 1999). This view is challenged by the results of this work, which imply that a more complex odor coding scheme might be used by the epithelium.

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