

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

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Abstract

Recent evidence indicate the presence of gap junctions in the olfactory epithelium (OE). This raises the possibility that olfactory receptor neurons (ORNs) might be coupled by electrical synapses. If this scenario is true, propagating self-sustained activity waves might exist in the OE. To investigate this hypothesis a computer model of the olfactory epithelium was constructed consisting of a grid of ORNs connected by electrical synapses receiving simulated odor input. The results challenge the view that odor identity coding in the OE is purely spatial, suggesting that a more complex odor coding scheme involving time might be used by the OE.

Keywords: Olfaction; Olfactory epithelium; Gap junctions; Electrical synapses, Olfactory coding

1. Introduction

Self-sustained waves are typical phenomena of excitable media in physics, chemistry and biology [17]. 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 [20,27] and spreading cortical depression in the nervous system [16]. 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 [26]. This might be due to spiral breakup caused by some modulation of the gap junctions conductances [18].

Several recent evidence indicate that gap junctions are ubiquitous in the central nervous system [2,6,9-11,19,21,28-30]. This has raised the issue of determining possible roles for gap junctions in neural function. The fact that self-sustained waves propagating through excitable media of different nature have common features [17] 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.

Some of the recent gap junction discoveries are related to the olfactory epithelium (OE). In a series of studies, Zhang and Restrepo [28-30] have shown that the OE of adult mice express gap junction protein subunits connexin 43 (Cx43), connexin 45 (Cx45) and connexin 36 (Cx36). Among these, studies in other brain areas indicate that Cx36 seems to be expressed exclusively in neurons (see references in [30]). This suggests that gap junction coupling, and therefore electrical synapses, might exist between ORNs. If this is true the olfactory epithelium would have the necessary conditions for the appearance of self-sustained activity waves propagating across it.

Molecular biology studies have demonstrated that the olfactory system uses a combinatorial receptor coding scheme to encode odor identity [4,15]. In this scheme, different odors activate

different but overlapping combinations of ORNs. The important point to note here is that this combinatorial scheme implies a time-invariant spatial odor representation across ORNs. It is believed that significant temporal aspects in odor coding come into play only downstream of the OE, from the olfactory bulb (OB) onwards, thus altering the initial clustered format of odor coding present in the OE [12,13]. This viewpoint is supported by recent voltage-sensitive dye imaging experiments, which have demonstrated that activity patterns in the OB are not static but evolve over time in an odor specific way [8,24].

Spatio-temporal dynamics in the OB has a component due to the computations carried out in the OE [13]. This implies that, at least in principle, the temporal aspect of odor coding might be initiated in the OE. Evidence in favor of some temporal processing in the OE comes from observed odor-elicited oscillations in field potential recordings from the OE of some vertebrates [1,7], which are generated locally and thus might modulated or trigger OB oscillations [7]. The source of these oscillations is unknown but it has been hypothesized that gap junction coupling among ORNs might account for them [7].

In this work, we use a biologically realistic model of a piece of OE with ORN models connected by gap junctions [23] to investigate the spatio-temporal patterns of activity generated in the OE during odor stimulation. In particular, we investigate the behavior of the spatio-temporal activity pattern as a function of the gap junction coupling strength and, for a given coupling strength, we investigate the spatio-temporal activity patterns evoked by two different odors.

2. The Model

The model consists of a grid of 50x50 identical replicas of an ORN model developed by us [22]. Some cells in the grid were considered as responsive to eight different odors with a spatial pattern of odor distribution over cells based on a work by Ma and Shepherd [14]. Each ORN in the grid was coupled to its eight neighbors via soma-somatic gap junctions modeled by Ohmic elements

with resistance R_{gap} . Soma-somatic coupling can be justified because there is evidence of Cx43, Cx45 and even some Cx36 expression in layers of the OE that contain nuclei of mature ORNs [28-30]. The model was constructed using the GENESIS neural simulator [3] and its details are given elsewhere [23].

3. Results

The simulation results show the emergence of odor-induced spatio-temporal patterns of activity resulting from the propagation and annihilation of voltage waves across the OE (Figs. 1 and 2). For a single input odor with constant concentration, a study of the spatio-temporal patterns of activity as function of the gap junction coupling strength reveals different behaviors (Fig. 1). The first row of Fig. 1 shows the time evolution of OE activity without gap junction coupling. It clearly shows the static representation of the odor given by cell clusters in the OE. The second-to-fourth rows of Fig. 1 show the temporal behavior of OE response for, respectively, ‘weak’ (900 M Ω), ‘intermediate’ (300 M Ω) and ‘strong’ (150 M Ω) gap junction coupling strengths. For ‘weak’ and ‘intermediate’ gap junction coupling strengths there are spatio-temporal activity patterns meandering across the OE grid. These patterns are similar to self-sustained or spiral wave breakup observed in several chemical and biological systems [17-18,26-27]. For ‘strong’ gap junction coupling strength the propagating and annihilating waves do not appear; there are only weak and diffuse activity clouds around the cell clusters seen in the uncoupled case. This may occur due to current leakages from cells through their low resistance gap junction connections (‘strong’ coupling), which prevent them from reaching spike threshold.

Figure 1 about here

In another study, we presented two different combinations of more than one odor (called odors A and B) to the OE grid with gap junction coupling of 300 M Ω . Each odor induced a specific

spatio-temporal pattern in the OE. For some time after odor presentation the activity patterns become stationary spiral waves with cores in different places of the OE grid.

Figure 2 about here

4. Discussion

The simulation results indicate that if there are gap junction-mediated electrical synapses between ORNs there might be spatio-temporal activity patterns in the OE. These spatio-temporal patterns should be odor-specific and depend on the gap junction coupling strength. For some values of the gap junction coupling there may appear spiral waves, which can breakup or reach a stable state. The odor-specific spatio-temporal patterns should be different for different odor concentrations and connectivity degrees in the OE, i.e. number of neighbors with which an ORN make electrical synapses, and these issues will be addressed in a future work.

Recent molecular biological studies have shown the existence of a combinatorial receptor coding scheme for odors in the OE [4,15]. The picture that emerged from these findings is that different odors elicit spatially defined, i.e. static, patterns of activity in the OE [15]. This view is challenged by the results of this work, which imply that a more complex odor coding scheme involving spatio-temporal activity patterns might be used by the OE. If odor-evoked spatio-temporal activity patterns really exist in the OE, they may be related to the oscillations in field potential recordings from the OE of vertebrates [1,7] and might contribute to spatio-temporal aspects of odor processing in the OB [12-13].

Regarding the possible roles of these hypothesized gap junction-modulated spatio-temporal activity patterns in the OE, a recent suggestion is that they may be the underlying mechanism causing the broad dynamic range of the olfactory system [5]. Also, in a similar way with self-sustained waves in cardiac tissue spiral waves in the OE could be related with pathological situations, e.g. sensory hallucinations and schizophrenia [25] and epilepsy [19].

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Figure Captions

Fig. 1. Instantaneous voltage maps of the OE grid model at times 2s (left column), 6s (middle column) and 8s (right column) after simulated presentation of 300 μM of a single input odor. Each row corresponds to a given value of gap junction resistance (R_{gap}). A gray scale code was used to indicate the cell's voltage at the soma (in Volts) with black representing resting voltage and white representing peak voltage.

Fig. 2. Instantaneous voltage maps of the OE grid model with ORNs coupled by gap junctions of 300 $\text{M}\Omega$ at times 2s (first row), 4s (second row), 6s (third row) and 8s (forth row). Each column shows the spatio-temporal patterns induced by presentation of 300 μM of two different odors: odor A (left column) and odor B (right column). The voltage coding scheme is the same as in Fig. 1.

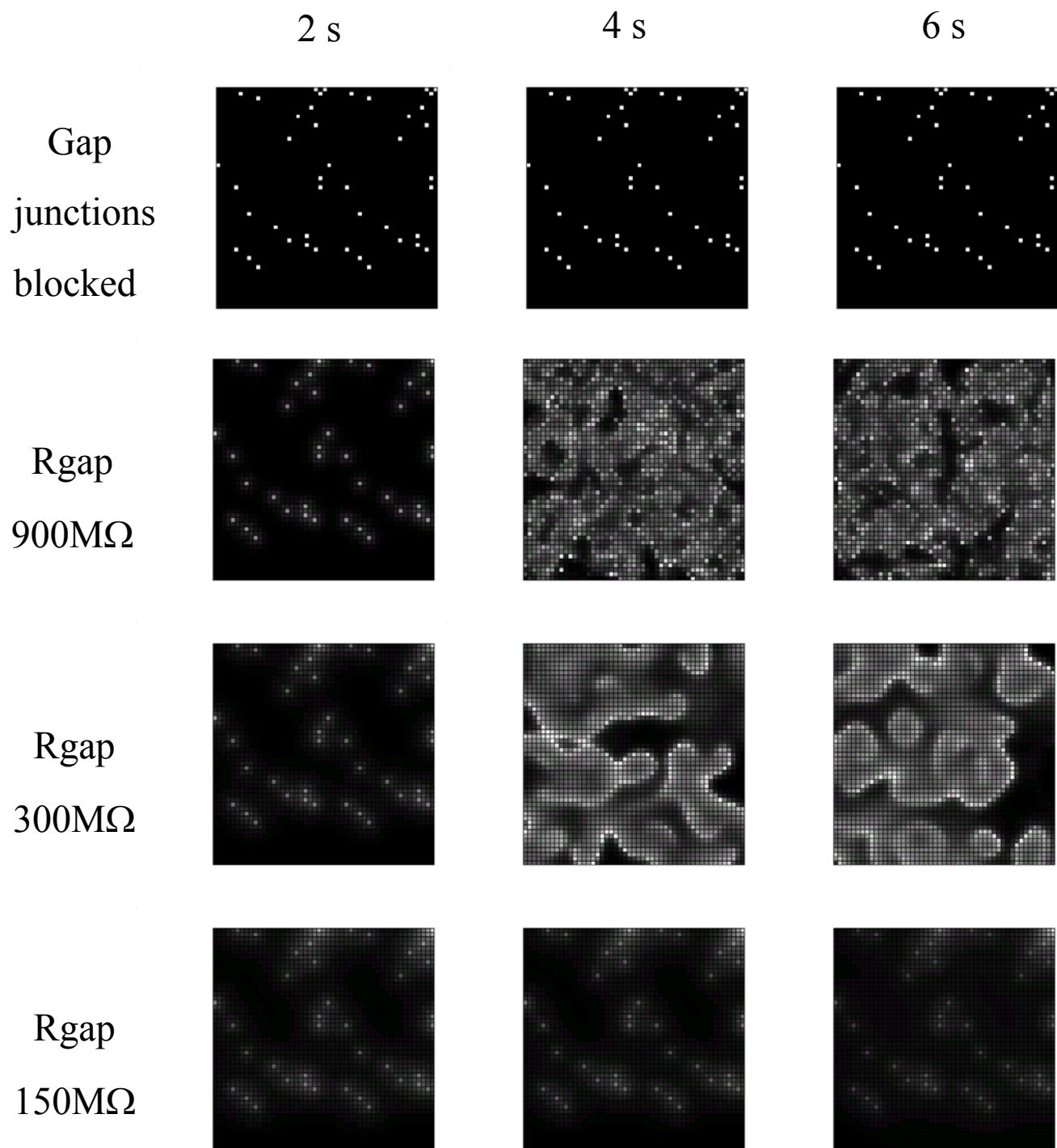
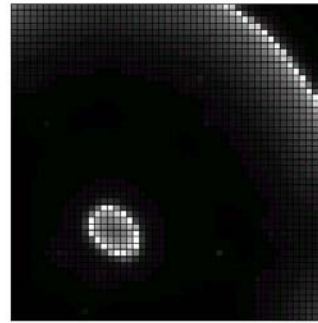
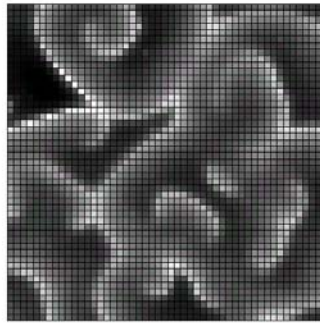


Figure 1

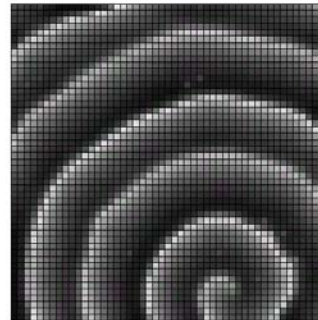
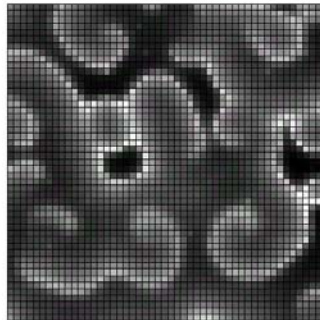
ODOR A

ODOR B

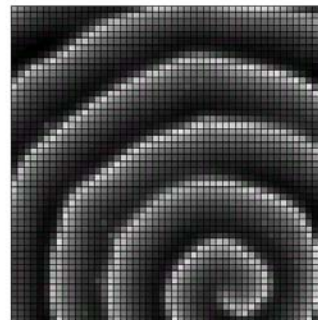
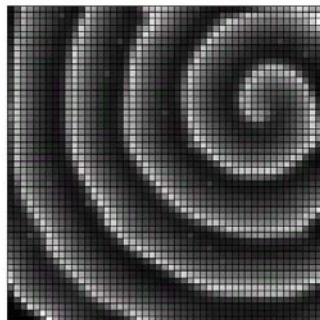
2s



4s



6s



8s

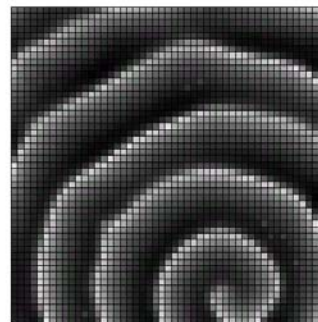
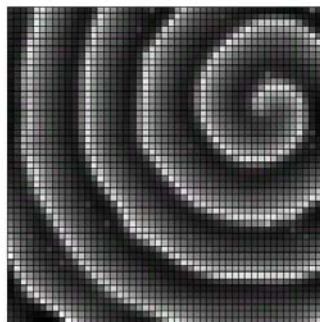


Figure 2