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# Topological target patterns and population oscillations in a network with random gap junctional coupling

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**Abstract**

Recent evidence suggests that electrical coupling could play a role in generating oscillatory behavior in networks of neurons, however, exact mechanisms have not been identified. Using a cellular automata model, we recently showed that a self-organizing process can generate regular population oscillations in a network with random spontaneous activity and random gap junction-like coupling. The network activity underlying the oscillations is topologically similar to target-pattern activity. Here, we show the process at work in a biophysical model. We demonstrate that population oscillations can also arise from reentrant behavior, but these oscillations look qualitatively different than those generated by the target-pattern-like activity. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Population oscillations; Gap junctions; Random networks

## 1. Introduction

Bursts of high-frequency (~200 Hz) population oscillations have recently been observed in hippocampal slice preparations [1]. The frequency of these oscillations suggest that they could be associated with "ripple" activity recorded in rats during consummatory behavior and awake immobility [4]. Surprisingly, the oscillations in the slice persist when chemical transmission is blocked and they appear to be dependent on gap junctional connections between pyramidal cells. Traub et al. [3] constructed a detailed model of the slice preparation that consisted of pyramidal cells

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coupled by axo-axonal gap junctions. Cells in this network model were randomly and sparsely connected. It was found that the model could replicate the experimentally observed behavior if each cell displayed a low level of spontaneous activity ($\sim 1$ Hz) and if the gap junctional connections was strong enough so that spikes could be transmitted through the gap junction with a short latency. Traub et al. [3] also proposed a cellular automata (CA) model, which has the same network connectivity as the detailed model but has simple rules governing activation, and showed that this simple model can reproduce high-frequency population oscillations. Curiously, despite the fact that both the spontaneous activity and the network connectivity are random, the oscillations are quite regular.

The work of Traub et al. [3] implies that the regular population oscillations arise spontaneously from a self-organizing process. Recently, we identified and characterized the underlying mechanism for this process in the CA model [2]. Here, we briefly describe the mechanism and show that it applies to a biophysical model that consists of only the axonal compartments of the detailed model of Traub et al. [3]. We also show that qualitatively different population oscillations can be generated by reentrant behavior.

## 2. Description of models

The networks in Traub et al. [3] consist of 3072 pyramidal cells. Each cell is described using a multicompartment Hodgkin–Huxley type model in which cells have 64 somato-dendritic compartments and 5 axonal compartments ([3] and references therein). Axo-axonal gap junctions in Traub et al. are placed between randomly selected pairs of cells (between penultimate axonal compartments). The gap junctions are symmetric and nonrectifying and have a conductance of 3.66 nS, which is high enough for rapid transmission of action potentials from one axon to the other in the absence of refractoriness. The network is driven by random spontaneous activity arising in the distal compartment of each axon: independent Poisson processes with rate $\lambda$ determine when current pulses (0.2 nA for 0.3125 ms) are applied. The networks considered here are identical to those in Traub et al. [3] except the "cells" in our network consist only of the axonal compartments (i.e. 5 compartments per 'cell').

Connectivity in our axonal network model is established as in Lewis and Rinzel [2] and in Traub et al. [3]. Cells are set on a uniform $32 \times 96$ grid with lattice spacing at 20 μm. Electrical connections between cells are assigned randomly with the restriction that a cell can only be connected to cells that are no greater than a distance $r_c$ cells away from it, i.e. there is a uniform connectivity footprint. As in Traub et al. [3], we set the average number of connections that a cell makes to be 1.62 and the connectivity radius, $r_c$, to be 200 μm.

The CA model has the same connectivity as above, but time and state are discrete and simple rules govern dynamics. Cells can exist in one of 3 states: activated, resting or refractory. A resting cell becomes activated at time $k$ if at least one of the cells connected to it is activated at time $k-1$. Cells that are activated at time $k$ are absolutely refractory for $r$ time steps and then they return to the rest state. Cells in the

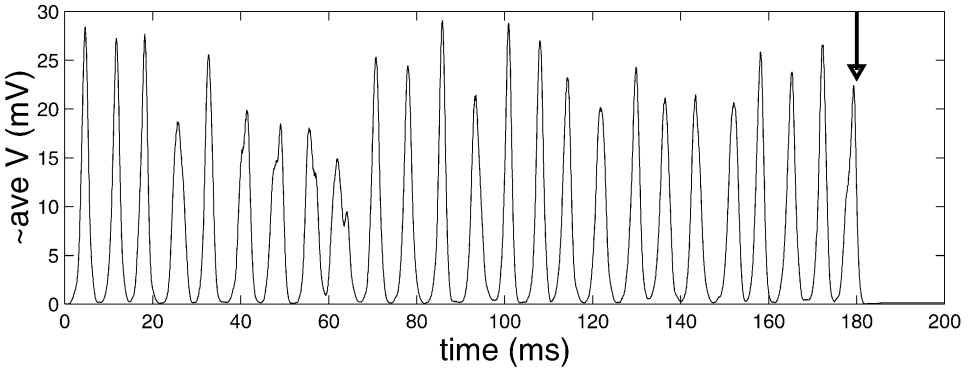


Fig. 1. Population oscillations in the axonal network with the rate of spontaneous activity $\lambda = 0.001$/ms/cell. Network activity is plotted as a function of time. Network activity is taken to be the average instantaneous membrane potential (mV) of all cells (all compartments) with potentials greater than the resting potential. Oscillations stop when spontaneous activity is turned off at 180 ms (arrow).

resting state also can make a transition to the activated state when they undergo random spontaneous activation. Thus, the CA model is consistent with the biophysical network models, which have strong and sparse gap junctional coupling.

## 3. Results

### *3.1. Population oscillations in the axonal network model*

Fig. 1 shows population oscillations in the axonal network model with $\lambda = 0.001$/ms/cell. Despite spontaneous activity being random, the oscillations are quite regular. The mean frequency of the oscillations is about 150 Hz. Note that this frequency is two orders of magnitude larger than the rate of spontaneous activity per cell, $\lambda$, and is an order of magnitude smaller than the total spontaneous activity rate in the network, $3072\lambda$. It is also about half of the maximal firing frequency of the axons. The mechanism that generates the oscillations is not immediately apparent. However, we will show that it is the same as the mechanism underlying the regular population oscillations in the CA model.

### *3.2. Mechanism for population oscillations in the CA model (see [2] for details)*

Because connections in the CA model are infinitely strong, spontaneous activation in a single cell leads to an expanding wave of activation and subsequent recovery. The wave spreads through the network leaving resting cells in its wake and dies out when it reaches boundaries of the network or dead-ends in the network. The spread of the wave can be quite complicated due to the geometrical complexity of network connectivity. Nevertheless, no matter how complicated the network appears, the symmetry

(i.e. bidirectionality) of the strong connections leads to an important topological property: the wave propagates as a closed connected surface in network connection space. This means that there is a true inside and outside of the wave and therefore no paths in the network lead from cells outside the wave to cells interior to the wave (i.e. in the wake of the wave) without passing through the wave.

During repetitive spontaneous activation, multiple waves can be present in the network simultaneously and these waves can interact. However, the above topological property or "symmetry" of the waves is always maintained. If a wave arises interior to another wave, then this new wave expands as a closed connected surface, remaining interior to the original wave for all time. If a wave arises outside of an expanding wave, then the waves expand as closed connected surfaces and eventually collide. Refractoriness behind the wavefronts causes local annihilation of the colliding portions of the waves. The waves then coalesce and form a single larger expanding wave that spreads as a closed connected surface, i.e. the topology of the new wave is the same as that of the individual waves prior to collision.

The above observations imply that the network activity giving rise to the population oscillations in the CA model must be composed entirely of expanding waves. Although very different from a geometrical perspective, the wave activity in the random CA network shares basic topological features with target pattern activity seen in partial differential equation models and integro-differential equation models of excitable media. For this reason, we refer to the network behavior as "topological target pattern activity". By linking the network oscillations to the underlying topological target pattern structure, we were able to describe how dynamical properties of the network can mold random activity into regular rhythmic population oscillations. We were also able to derive semi-analytical expressions for mean frequency and coefficient of variation for the oscillations. These expressions indicated how changes in the rate of spontaneous activity and structure of the random network affect the frequency and the regularity of the oscillations.

### *3.3. Topological target patterns and reentry in the axonal network model*

In the CA model, there are no mechanisms to "break the symmetry" of the expanding waves, therefore topological target pattern activity must underlie the population oscillations regardless of rate of input, network size and size and shape of the connectivity footprint. On the other hand, biophysical models of the physiological system and the physiological system itself have dynamical properties that could potentially break the symmetry of the waves. When the symmetry of an expanding wave is broken, the wave is not a closed connected surface and therefore activity has the potential of effectively "curling" back towards the wake of the initial wave of activation. This could lead to reactivation of cells that have been previously activated by the wave and to the formation of self-sustained activity that circulates around a loop in the network. The circulating activity, known as reentry, can drive the entire network and give rise to population oscillations. The period of the oscillations will be set by the time that it takes for activity to propagate around the reentrant loop. Thus, it is necessary to determine whether the oscillations in

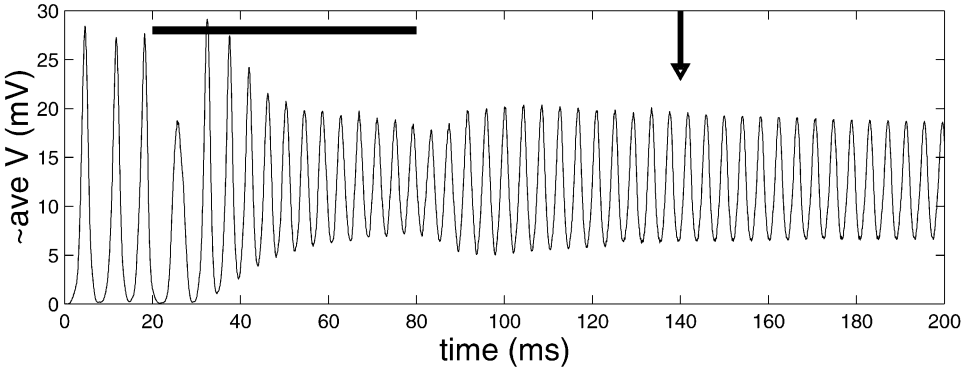


Fig. 2. Population oscillations in the axonal network due to reentry. The network is identical to that used in Fig. 1. The rate of spontaneous activity $\lambda$ is 0.001/ms/cell before being turned off at 140 ms (arrow). From 20 ms to 80 ms, a cell in the center of the network is stimulated with a frequency of 250 Hz (bar).

the axonal network model are associated with reentrant activity or topological target pattern activity.

Various lines of evidence indicate that topological target patterns, and not reentrant activity, underlie population oscillations in the axonal network shown in Fig. 1. Firstly, the population oscillations of the axonal network model look qualitatively similar to those observed in the CA model [2]. Secondly, oscillations due to reentrant activity are self-sustained, whereas the oscillations here stop immediately following the termination of spontaneous activity. Finally, we have verified the closed connected topology of a few representative waves in the network activity.

The topological target pattern behavior appears to be quite robust; it persists for as long as we have carried out simulations (some up to 3 s) and for many (tens of) realizations. However, reentry can be induced in the network without changes in system parameters. When cells have low excitability as a result of refractoriness, the propagation of activity can fail locally in regions of high connectivity due to the dilution of current spreading from an active cell to several resting cells. Thus, an expanding wave could propagate in certain directions but not others and the symmetry of the wave would be broken. This can lead to reentry. Indeed, this phenomenon can be unmasked in our axonal network by rapid stimulation at a fixed point in the network (250 Hz for 60 ms). Fig. 2 shows the resulting population oscillations. The oscillations due to reentrant behavior are very regular. Both the period and peak-to-peak amplitude of the oscillations are almost half that of the oscillations due to target pattern activity. This is consistent with the population oscillations observed in the CA model when reentry is "artificially" induced, e.g. choosing appropriate initial conditions. As expected, these oscillations continue following termination of random spontaneous activity. We have also verified that a few representative waves in the reentrant network activity do not form closed connected surfaces.

## 4. Discussion

Our axonal network model, which is a reduction of the detailed network model of Traub et al. [3], appears to include the essential elements needed to reproduce much of the oscillatory behavior observed in the detailed model and the hippocampal slice preparation of Draguhn et al. [1]. Simulations with the axonal network model suggest that multiple expanding waves underlie the population oscillations. Indeed, the topological target pattern activity in the axonal model appears to be quite robust. The fact that reentry can be induced by local high frequency stimulation implies that it can be induced by the random spontaneous activity but this is highly improbable. Also, preliminary simulations without the high-frequency stimulation suggest that gap junctions need to be substantially weakened or there must be substantial heterogeneity in cellular properties for the topological target pattern activity to be destroyed and reentry to arise.

It must be noted however that intrinsic bursting dynamics in soma-dendrite portions of the pyramidal cells are not included in our axonal network model. These bursting dynamics are likely to underlie some aspects of the oscillations in the detailed model and the corresponding experimental preparation. It is possible that topological target pattern activity in the "axonal plexus" underlies the high frequency activity during the interburst dynamics that leads to the bursts (i.e. there are no somatic action potentials during this activity only somatic spikelets due to axonal activity) but not during the bursting phase. More work is needed before definitive conclusions can be made.

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