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Key words:

Introduction

A spiral wave in the broadest sense is a rotating wave traveling outward from a center. Such spiral waves have been observed in many systems (Winfree, 2001; Murray, 2003), including biological systems, such as heart ventricular fibrillation (Davidenko et al., 1992), retinal spreading depression (Gorelova and Bures, 1983), fertilizing [illegible]

tion in cortex that we are aware of is the finding of phase [illegible] larities in optical imaging of turtle visual cortex, which de[illegible] strated circular waves persisting for up to four rotations (P[illegible] et al., 1997).

Although circular waves were predicted from early mod[illegible] cortical activity (Beurle, 1956), true spiral wave formatio[illegible] not observed until the more sophisticated Wilson–Cowa[illegible] mulation (Wilson and Cowan, 1972, 1973) and modern co[illegible] ing simulation strategies (Milton et al., 1993). Our experim[illegible] work was inspired by such theoretical considerations. Nev[illegible] less, a close link between computational models of spira[illegible] formation in cortex and experiment has not been atte[illegible] previously.

In this report, we present evidence for stable spiral wav[illegible] to 30 cycles) in rat neocortical slices with robust phase sing[illegible] ties. We also introduce a computational model of a cortica[illegible] that predicts and replicates many of the features of our e[illegible] mental findings. Our results suggest the possibility that [illegible] dynamics participate in the spatial organization of prolonge[illegible] periodical activities such as seizures and oscillations in neo[illegible] related to sensory and motor events.

Materials and Methods

. Neocortical slices were obtained from Sprague Dawley rats (postnatal days 21–35). Tangential slices were cut with a vibratome on the rostrocaudal and mediolateral coordinates of bregma □2 to □8 mm and lateral 1–6 mm, respectively (see Fig. 1, left). The first cut was made 300 m deep from the pial surface, and the tissue was discarded. The second cut was made 500 m deeper to obtain a 500- m-thick slice of middle cortical layers. The slice was perfused with artificial CSF (ACSF) containing the following (in mM): 132 NaCl, 3 KCl, 2 $CaCl_2$, 2 $MgSO_4$, 1.25 NaH_2PO_4, 26 $NaHCO_3$, and 10 dextrose (saturated with 95% O_2 and 5% CO_2 at 28°C for 1 hr before experiments). When the

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slices were perfused with 100 M carbachol and 10 M bicuculline, oscillations (4–15 Hz) occurred spontaneously, and the activity appeared as spiral and other waves in the voltage-sensitive dye imaging. These activities lasted as long as the preparation was perfused with carbachol and bicuculline, similar to coronal slices (Lukatch and MacIver, 1997; Bao and Wu, 2003).

. An oxonol dye, NK3630 (Nippon Kankoh-Shikiso Kenkyusho, Okayama, Japan) was used as an indicator of transmembrane potential. Slices were stained with 5–10 g/ml of dye dissolved in ACSF for 60–120 min (26°C) and perfused in a submersion chamber during the experiment (28°C). Imaging was performed with a photodiode array on an upright microscope with transillumination (absorption) arrangement (Wu et al., 1999; Jin et al., 2002). Data were

Phase singularity

To distinguish the spirals from other types of rotating waves, we analyzed the spatial phase distribution of the spirals (Fig. 2*C*). During the entire period of the spiral, the phase distribution within the field of view was mapped between □ and (Fig. 2*C*). The highest spatial phase gradient was observed at the pivot of the spiral (Fig. 2*C*, white dots). The presence within such a phase gradient of a phase singularity would be the hallmark of a true spiral wave (Ermentrout and Kleinfeld, 2001; Winfree, 2001; Jalife, 2003).

We hypothesized that a phase singularity in the slice would be observed as a small region containing oscillating neurons with nearly all phases represented between □ and . Such phase mixing would result in amplitude reduction in the optical signal.

In the experiment in Figure 3, we used higher spatial resolution to search for the singularity. Using a 25 □ 25 hexagonal array with 464 elements, each detector covered a circular area 128 m in diameter (total field of view, 3.2 mm in diameter). All of the detectors showed high-amplitude oscillations before the formation of spirals (Fig. 3*A*, traces a–e, before the first broken vertical line). During spiral waves, the phase singularity drifted slowly across the tissue (□1 mm/10 turns).

fourfrom7.234t3()twavegetwer.9634t3(3)]TJ/F834t3 most widely used models for such medium are based on the Wilson–Cowan equations (Wilson and Cowan, 1972, 1973). Later, modifications by Pinto and Ermentrout (2001) described one-dimensional wave propagation in excitatory disinhibited neural networks. We extended this approach into two dimensions.

We seek the simplest model possible, reducing the neurons to points in a continuum that has excitation and recovery but, as in our experiments, no inhibition. Such a model represents the qualities of a disinhibited network dominated by fast excitation (perfused by carbachol and bicuculline) and with an intact recovture of the wave front, because, within a given set of anatomical connections, different wave patterns occur (Fig. 2) (movies 1–4, available at www.jneurosci.org as supplemental material). Interestingly, all of the patterns were associated with the oscillation in the same manner: one-cycle–one-wave for nonrotating waves and one-cycle–one-rotation for spirals. This is consistent with previous characterizations of one-dimensional waves in coronal slices (Wu et al., 1999; Bao and Wu, 2003).

Although oscillations are commonly observed in sensory (Gray and Singer, 1989; Franowicz and Barth, 1995) and associational (Pesaran et al., 2002) cortices, little is known about the spatial organization that accompanies such oscillatory activity. It has been shown in visual cortex that sensory-evoked oscillations can demonstrate intercolumnar coherency (Eckhorn et al., 1988; Gray et al., 1989). We speculate that rotation waves of spirals may provide a spatial framework to organize cortical oscillations. Dynamic stability of spirals might extend the duration of evoked activity and interact with incoming input streams, and, in pathological conditions, might contribute to seizure generation. Spiral waves might serve as emergent population pacemakers to generate periodic activity in a nonoscillatory network without individual cellular pacemakers. Spirals might be used for coordinating oscillation phases over a population of neurons, serving functions such as binding sensory information or dynamical temporal storage in working memory.

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