The smallest known functional neural circuit in cerebral cortex, the cortical minicolumn, is composed of approximately 80 to150 neurons (up to twice that in striate cortex) grouped together in a vertically oriented bundle ~30μm in diameter (Mountcastle, 1997). These bundles occur with a center-to-center spacing of ~80μm in the brains of primates and are remarkably similar to the radially oriented clusters of neurons observed during the ontogenesis of the neocortex. The neural circuit and its elements were modeled using the NEURON simulation environment. NEURON is a biophysical neural modeling program that accurately simulates the electrophysical response and spiking behavior of individual neurons and the interactions between coupled networks of neurons over time.

The modeled circuit is made up of four groupings of cells representing the six layers of cortex; layers I, II & III are treated as one layer in the model. Each layer contains up to three different types of cells. Electrophysiologically, each of the modeled cells corresponds to one of the three classes of neocortical neurons described by Connors & Gutnick (1990): Regular-spiking excitatory cells, fast-spiking interneurons, and intrinsically bursting excitatory cells. Each cell is modeled as a two-compartment structure (one axosomatic and one dendritic compartment) and includes models of several ionic currents. The structure of the intra- and inter-laminar and inter-minicolumnar connectivity is a result of a specific structured connection scheme based upon empirical data from the literature (e.g. Hellwig, 2000; Melchitzky, Gonzalez-Burgos, Barrionuevo, Lewis, 2001; Yuste, Tank & Kleinfeld, 1997). Within the bounds of this structured connectivity, variability is introduced through a probabilistic variation in the exact mapping of cell-to-cell connectivity. The spatial properties of the neural circuit are based upon signal delays. Delay values are used to simulate the time needed for an action potential to travel down a fiber of passage and reach its target and are a function of conductance rate and fiber length. Each simulation is run with time-steps of 0.05 ms and simulates on the order of magnitude of 10 seconds of network activity. Both individual minicolumns and 2-dimensional arrays of up to 20 interconnected minicolumns are simulated.

EEG and *in vivo* recordings of sleeping and anesthetized subjects reveal recurring oscillations within the 0.1-0.5 Hz frequency band. The slow oscillation is characterized by the recurrence of a period of depolarization (‘up’ state), followed by a period of hyperpolarization (‘down’ state). Steriade, Nunez & Amzica (1993) suggest that NMDA-mediated EPSPs may be at least one mechanism by which the network sustains or prolongs the ‘up’ state. These oscillations survive thalectomy and brain-stem transections, leading some to believe that the slow oscillation is a cortically generated rhythm resulting from the high density of cortico-cortical connectivity (Steriade et al. 1993).

In support of the theory that the slow oscillation is cortically generated, *in vitro* intracellular and multi-unit recordings from deafferented cortical slices reveal the existence of the slow oscillation. However, these results suggest that the slow rhythm is not necessarily a result of the interactions of large (whole cortex) networks of neurons, but is an intrinsic property of cortical circuits at least as small as a cortical column (Sanchez-Vives, McCormick, 2000). Sanchez-Vives & McCormick (2000) observed that the ‘up’ state begins in layer V and propagates vertically, arrives first in layer VI and then in layer IV and the supragranular layers. They suggest that the ‘up’ state is sustained through an excitatory recurrent network; eventually the excitatory activity fails due to the buildup of outward conductances (e.g. Ca^{2+}, and Na+ activated K+ currents). However,

they don't give a mechanistic account of how the 'up' state itself is initially generated.

One clue toward answering the question of how the cortical microcircuit is able to generate activity reveals itself in Mao et al.'s (2001) study of spontaneous activity in neocortical slices. Mao et al. (2001) observed that spontaneous activity in layer V pyramidal cells persists even in the presence of APV/CNQX (NMDA & non-NMDA glutamate receptor blockers), but is abolished by hyperpolarization-activated cationic (I_h) and persistent, noninactivating Na current (INaP) antagonists. Thus, the initial excitatory activity needed to produce the synaptic barrage characterizing the beginning of the 'up' state of the slow oscillation may be a result of intrinsic cellular properties of the primary elements that populate cortical layer V.

The network model is able to reproduce many aspects, at both the cellular and network levels, of the slow oscillation, supporting the theory that cortical oscillations can be generated by the unstimulated cortical microcircuit as discussed above. With only non-NMDA glutamate receptors, the network model exhibits population oscillations at ~0.5 Hz, but the duration of the 'up' state is drastically shorter (~0.1 sec) than is seen in biological preparations (with fully functional NMDA receptors). This supports Steriade et al.'s suggestion that NMDA-mediated EPSPs prolong the 'up' state. Activity in the model propagates vertically in the manner described by Sanchez-Vives & McCormick (2000); beginning first in layer V, then layer VI and finally in the supragranular layers. Furthermore, the modeled neural circuit generates 'up' state activity as a result of intrinsically generated action-potentials of infragranular pyramidal cells. Removing or reducing Ih or INaP from the infragranular pyramidal cells abolishes or drastically reduces oscillatory activity in the modeled neural circuit suggesting that intrinsic cellular events, then, underlie the generation of the slow oscillation.

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