ANDERSON LABORATORY RESEARCH

The Anderson laboratory focuses on the computational modeling of epilepsy as a method to understand the time and spatial evolutionary properties of seizures. Modeling methods include large array single compartment models and multicompartment simulations for the extraction of electrophysiological observables. Using these modeling tools, we explore how fast seizures spread, the spatial extent of spread, the spread of interictal spikes, and the introduction of therapies such as drug diffusion and electrical stimulation. Other ongoing projects include real time detection of mesial temporal theta production and phase-locked stimulation effects, and motor imagery activity of subcortical structures.

COMPUTATIONAL MODELING

Previously, we have developed an architecturally realistic computational model of neocortex to investigate the spatial and temporal properties of evolving epileptic activity in a single compartment format. On a layer by layer basis, several classes of excitatory and inhibitory single-compartment neurons, including pyramidal and stellate cells as well as three inhibitory types (basket, chandelier, and double bouquet) are represented. This model has a horizontal and vertical spatial size scale, and has proven useful in investigating the effects of external electrical stimulation on the emergent bursting activity (1,2). These modeling efforts have made specific predictions about frequency and orientation dependent effects of applied electrical pulses on ongoing cortical epileptic activity (1). Furthermore, they have allowed us a means to extract parameters from the system (the time-frequency behavior and an approximate mean field potential) which can be compared to experimental studies. For instance, Lesser et al. studied the ability of cortical stimulation pulses to stop afterdischarges during cortical mapping sessions (3,4). Aspects of the phase dependence of the applied stopping pulses have been reproduced by our modeling efforts on a 1.6 mm X 1.6 mm region of simulated neocortex (2). These simulations, with their laminar based structure and imposed horizontal geometry, can provide a basis for investigating the rate of seizure spread as a function of cortical layer. Our goal is to make these modeling efforts more accurate in a multicompartment format to calculate precise local field potentials and current source density distributions.

A. Modeling of Stimulation Effects

The architecturally realistic models we have used in previous neocortical stimulation studies consist of an array of one-compartment neurons, with four different classes of cells representing excitatory pyramidal cells in cortical layers II and III (treated as one layer), layer V, and layer VI, as well as excitatory stellate cells in layer IV (1,2). There are also three classes of inhibitory interneurons represented as basket cells, double-bouquet cells, and chandelier cells. Each cell type has a defined location within the vertical layers and has distinct electrophysiologic properties. The cells are organized around a square minicolumn array of 25 µm center-to-center spacing in both cortical tangential directions (the x- and y- axes in our coordinate system). This dimension is similar (23 µm) to the spacing between vertically oriented bundles of myelinated axons in monkey visual cortex. The minicolumn hypothesis of Buxhoeveden et al. (5), or a size-scaled version of that concept has been used to come up with a spatially repeating local circuit, which is then used as a skeleton to fashion together longer range connections guided by neuroanatomic data.

The total number of neurons per minicolumn as well as the size scale used was similar to that found by Buldyrev et al. (6) and Buxhoeveden and Casanova (7). We have chosen specific paradigms to pattern the intrinsic connections of the excitatory cells utilizing elements of both the neocortical model of Douglas and Martin (8), as well as the more general cortical connectivity provided by Nieuwenhuys (9). As outlined in detail in (1), electrophysiologic properties were derived from modified Hodgkin-Huxley excitable cells in a one-compartment format. The total size of the simulated array has ranged from 800 µm X 800 µm to 1600 µm X 1600 µm. Each minicolumn consists of 12 pyramidal cells, 1 stellate cell, and 1 each of the inhibitory subtypes, making a total of 16 neurons per minicolumn. Versions of the model have been run with up to 65,536 simulated neurons. There are internal axonal connections involving the members of a given minicolumn, as well as external connections to neurons in other minicolumns at a range of distances away. A schematic of the different connection types is shown in Figure 1.