

Outline of Traub and Miles: Chapter 5

VIGRE Spring 2006

February 22, 2006

1 Questions

- How do we transfer what we know from experiment \Rightarrow computer simulation?
- How many cells should we use, what types of cells should we use?
- How do we arrange cells in space?
- How do we describe communication both functionally and structurally?
 - How many synapses of each type (i.e. excitatory, GABA_A, GABA_B)?
 - Functional issues: How to handle axon action potentials, axon conduction delays, transformation of pre synaptic impulses to post synaptic conductance changes?
 - Structural issues: How to handle distribution of axonal output?

2 Cells!

- We have 3 types of cells:
 1. Fast Inhibitory (i_1) cells: Inhibitory cells with post synaptic effects resembling GABA_A receptors
 2. Slow Inhibitory (i_2) cells: Inhibitory cells with effects resembling GABA_B receptors
 3. Pyramidal (e) cells: Excitatory cells
- Major simplifications have been made to i_1 cells. The produced unitary conductances and intrinsic properties of different i_1 cells are the same. In practice, however, IPSPs are seen with differing firing patterns, amplitude, latency and time course.
- Ratio of e:i cells is 10:1, number of i_1 and i_2 cells is the same

2.1 How Many Cells?

- Goal: To achieve the same number of cells as with experimental CA3 preparations within a factor of 2 or 3
 - We want to be able to keep parameters physiological (i.e. number of inputs per cell, conductance strength, etc)
 - 20000 cells in longitudinal slice, our model has 9000 e cells and 900 i cells.
 - Significant simulated neuronal populations are critical to population dynamics

2.2 Intrinsic Properties Of The Cells

- In addition to our pyramidal cell model, we have “generic” interneurons formed by omitting g_{Ca} , $g_{K[CA]}$, and the voltage dependence of g_k
- Most i cells are treated as generic
- Excitatory synapses onto all i cells are different than excitatory synapses onto other e cells.

2.3 Arrangement of cells in space

- e Cells are arranged in a $40 \times n$ array, with n varying with the size of the simulation
- $n = 225$ for the full longitudinal slice models in the book
- We use 40 since we have 400μ slices, 20μ soma diameters, and 2 or 3 layers in each slice for excitatory cells
- i cells arranged in a superimposed $4 \times n$ array.

3 Intracellular Communication

3.1 Transduction of soma potentials into axonal output

- We don't explicitly simulate a portion of the axon; saves considerable computation time due to the fast kinetics involved
- Cell sends output if depolarized beyond threshold (20mV relative to rest) and if no output has been sent in the past 3 ms (Experimentally observed refractory period 2-4ms).

3.2 Conduction Delays

- Only on e cell axons.
- None on i cells, which assumes i cells are localized
- Potential travels down axon at 0.5m/s. Note with a 5-10mm long slice, delays can be on the order of 10ms if an axon runs across the entire slice.
- We need to be careful to make sure all potentials depart and arrive when and where correctly.

3.3 Synaptic Actions

- Four Types:
 1. Excitatory synapses onto dendrites of e cells
 2. Excitatory synapses onto somata of i cells
 3. Fast inhibitory onto somata and proximal dendrites of both e and i cells (recall these are from i_1 cells)
 4. Slow inhibitory onto dendrites of both e and i cells (recall these are from i_2 cells)
- Refer back to equations in Chapter 4, see Figure 5.1
- A synaptic action consists of two separate stages:
 1. Activation: the release of neurotransmitter across synaptic cleft, interaction between transmitter and receptors, and all coupling involved from receptor \rightarrow channels. We use 3,1,1,40ms for $e \rightarrow e$, $e \rightarrow i$, i_1 , i_2 respectively
 2. First order Kinetics: Relaxation of activated channels. We use 4,1,7,100ms.
- When a presynaptic signal arrives, it exerts a constant activating effect for 3,1,1,40ms.
- Conductance changes all add linearly (no interaction between inputs from different conductance changes)
- Implementation outlined on p.108

3.4 Arrangement of Synaptic Connections

- First we determine number of e and i inputs per cell
- Full 9900 cell model has 20 inputs per cell
- Can use globally random approach to forming connections, every cell has same probability to connect to every other cell
- Can use locally random:

$$p(\text{Connection from cell } M \text{ to } L) = p(L)e^{-\frac{d(L,M)}{\lambda}}$$

where $p(L)$ scales to ensure a certain average number of connections, λ used to determine localization

- $\lambda_e = 30$, $\lambda_i = 6$, so i cells are much more localized than e cells

3.5 Inhibition onto e cells versus i cells

- The slow IPSP to i cells is the same as to e cells
- Maximum conductance for fast IPSP $\rightarrow i$ cells is kept at 40% of conductance for fast IPSP $\rightarrow e$ cells
- This is primarily done to limit disinhibition

3.6 Electrotonic synapses (gap junctions)

- Not incorporated

3.7 Test Runs

- Look at Figures 5.4, 5.5, 5.6 for network illustrations
- A brief local shock used for the full model
 1. EPSPs in nearby cells to the shock fire
 2. Inhibition terminates depolarization resulting in a long AHP (100s of ms)
 3. 1mm away, stimulus evokes both EPSPs and IPSPs
 4. No significant response 4-5mm away
- The remainder of the chapter discusses technical computational aspects of their code, discussion not necessary for this outline.