Outline of Traub and Miles: Chapter 6

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1 Questions and Comments

- Under what conditions does population firing become synchronized?
- What factors regulate synchronization?
- What is the influence of a small number of cells on the entire population?
- If there is any partial synchronization, what determines which selected cells participate?

1.1 Why do we care about synchronization?

- It is observed in vivo (i.e. with theta rhythms) and in vitro (epileptiform population bursts) that these aggregate into waves, supporting synchronization as a representation of some signaling mechanism
- Synchronized behavior is very characteristic of many parts of the brain, thus it may have neurobiological significance.

1.2 General Comments on Synchronization

- Population firing can occur from at least two things:
  1. Synchronized afferent input
  2. Coupling forces between neurons. These are most likely the most significant (read p.120)

2 2 and 3 cell circuits

2.1 Burst Transmission Depends on Strength of Excitatory Connections and the Strength and Timing of Inhibition

- Observe Figures 6.1-6.4

2.2 Synchronized Population Bursts (Epileptiform Bursts)

- All pyramidal and interneurons fire
- Even lasts 50-100ms, with period 2-12 ms. There may be after-discharges
- Generated by blocking $GABA_A$ (i_1) with various toxins
- We ask: How are these initiated?
- This question is difficult, as we speculate triggering involves a small number of cells, which may even have different properties
- We can, however, elicit these population bursts via extracellular current pulses

2.3 What Forces Synchronize Hippocampal Neurons?

- We know of at least 4 possibilities:
  1. The chemicals used (such as high $[K]_o$) can excite cells, but it is hard to explain how this would couple particular neurons to particular other neurons
  2. Electrotonic coupling, but these interactions occur between very few cells
  3. Field Effects, but these effects should be very small (at the very least they are not large contributors)
  4. Synaptic Interactions with one pyramidal cell begin able to evoke a burst in another cell, this should be the major force behind synchronization

2.4 What About the 50-100ms Interval Between Stimulus and Population Burst?

- Studied in Traub and Wong, 1982. They do a nice job with 100 randomly connected cells with 5 other e cells
- Latent period corresponds to activity buildup where most cells receive either no or only subthreshold inputs
- In the 9000 cell simulations, they did not observe more than three bursts under similar conditions
- They are not a result of a simple layering build-up (p.129)
- See Figure 6.5

2.5 Network Implications of Epileptiform Bursting

- Every cell must lie on cycle(s) in the network
- Estimate that at least 1000 cells required
- In general the network is sparsely connected by strong excitatory connections
- p.130-131 for more detail

2.6 Other Related Observations

- These principles underlying synchronization do not change when we scale the model up in size
- Principles don't change either when i_2 cells are added
- Growth of synchrony critically depends on the strength of excitatory synapses
- See Figures 6.6, 6.7

2.7 Propagating Synchronous Firing and the Local Structure of Synaptic Connectivity

- We are now back to working with full 9900 cell model
- Experimental responses to extracellular stimulus has two separable components, R_1 and R_2
  1. R_1: Travels at about 0.5m/s, falls off with distance as it traverses a few synapses (Figure 3.7)
  2. R_2: .1-.15 m/s, similar to a propagating action potential with no inhibition, with inhibition, things slow down considerably
- All of these responses are observed in the model
- Also observed that synchronization with 1400 (globally randomly connected) cells and larger with fast inhibition removed (Figure 6.10)
- Also seen that reducing cellular excitability may allow synchronization to occur only after stimulation of a threshold number of cells (Figure 6.11)

3 Partial Synchronization in Presence of Inhibition

- We still observe partial synchronization with some inhibition

3.1 Why Study Synchronization When Inhibition is not Completely Blocked?

- Some experiments show epilepsy without completely blocked inhibition
- Functional Importance since inhibition regulates a single cell's influence on the population
- Inhibition itself may vary with different factors (i.e. - with repetitive stimulation, with high extracellular concentrations of $[K]_o$, etc.)

3.2 Experimental Example of Inhibition Controlling the Effect of One Cell on Another

- Varying levels of inhibition have expected effects on EPSPs and spiking

3.3 What About Inhibitory "Holes" in the Network?

- These are observed both experimentally and in simulation
- Also observed that with inhibition (resulting in slowed spread of excitatory activity), prolonged groups of excitatory synaptic events precede synchronized bursts
- No experimental observations related to this yet

3.4 Critical Behavior of the Network as Inhibition is Blocked

- Large inhibition results in small (but positive) number of cells firing. This number is strictly positive due to inhibitory holes
- As inhibition is decreased from 2.5 to 1.5nS, there is a huge jump in the number of firing cells
- Recall from 3 cell network that a conductance of 3nS is enough to transmit firing of one cell to another. This shows that both slow propagation of bursting and the action of delayed/slow IPSPs suppresses excitation, as it should
- Not yet demonstrated experimentally
- Note that these simulations have been done to a population starting at rest, and by choosing arbitrary number of cells to stimulate. Chapter 7 examines spontaneous activation.
- See Figure 6.16

3.5 Can Strengthening Excitation Cause Synchrony in the Presence of Inhibition?

- Partially yes. With $c_i = 10nS$, we increase c_e all the way to 20nS and we get 2/3 of the population firing
- Curve increases roughly linearly (no sudden jump, see Figure 6.17)

3.6 The Inhibitory Surround

- This is when in vivo inhibition is blocked in a bounded region still large enough for synchrony.
- Experiment shows near focus we get a hyperpolarized– depolarized (with maybe some firing) – hyperpolarized sequence
- Experiment also shows farther away we get prolonged hyperpolarization
- Using the model, they hypothesize this is probably from $e \to i \to e$ pathway being stronger and faster than $e \to e \to e$ pathway

4 Afterdischarges in the Presence of Picrotoxin

- These are also observed in the simulations
- Consists of a prolonged primary burst with secondary synchronized bursts
- Needs 1000-2000 cells to happen