1. Neuronal Networks

1.1. Introduction

Each human brain is comprised of over 100 billion neurons, each of which receives on average 10 thousand "inputs" from neighboring neurons. To tackle such complexity we naturally restrict ourselves to well defined sub-networks of the brain. Even then however we are far from constructing (for lack of data as well as computational resources) detailed models that capture network architecture, cell morphology and biophysics. Existing strategies fall into 2 large camps, Attractor Neural Networks and Conductance Based Networks.

In the former, network activity of N cells is abstracted to discrete dynamics on the the vertices of the N dimensional cube. For each cell, at a given instant, can take on but two values, e.g., ± 1. One marches from one vertex to the next by applying a threshold to a weighted sum of inputs at each cell. This permits experimentation, and often analytical treatment, with relatively large networks, but suffers in translation to biology.

The modeling of Conductance Based Networks retains biological time, conductance and potential but typically sacrifices ionic machinery and/or cell morphology. The simplest approach adopts the Integrate and Fire (IaF) cell model of Chapter ?? and so sacrifices both but in a way that makes it relatively straightforward to generalize. We therefore follow that course. In particular, in §1.2 we carefully formulate and illustrate the full set of conductance and voltage equations for small networks of excitatory IaF cells. We then recognize, in §1.3, that this approach scales easily to large networks of both excitattory and inhibitory cells. Finally, in §??, we formulate and illustrate a simple rule for evolving the weights between cells.

1.2. Small Integrate and Fire Networks
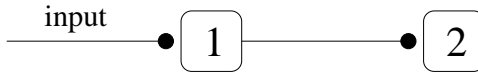
We begin with the simple two cell network below

Figure 1.1. The smallest network

There are 2 cells, with respective membrane potentials V_1 and V_2, and 2 conductances, $g_{E,1}$ and $g_{E,2}$. The circuit is driven by an excitatory input train that spikes at $T_{inp} \equiv \{T_{inp}^n : n = 1, 2, \ldots\}$. Each such spike increments, $g_{E,1}$, the excitatory conductance at cell 1, by a fixed amount, w^{inp}/τ_E. Between such spikes we assume that $g_{E,1}$ returns to zeros at the fixed rate τ_E. In other words, we suppose that $g_{E,1}$ is governed by

$$\tau_E \frac{dg_{E,1}(t)}{dt} = -g_{E,1}(t) + w^{inp}\delta(t - T_{inp}). \tag{1.1}_{\text{ge1}}$$

Similarly, the excitatory conductance at cell 2 is driven by the spikes of cell 1, at times $T_1 \equiv \{T_1^n : n = 1, 2, \ldots\}$. In particular

$$\tau_E \frac{dg_{E,2}(t)}{dt} = -g_{E,2}(t) + w_{21}\delta(t - T_1). \tag{1.2}_{\text{ge2}}$$

These conductances in turn supply synaptic current via the potential equations

$$C_m V_i'(t) = g_L(V_L - V_i(t)) + g_{E,i}(V_E^{syn} - V_i(t)), \quad \text{while } V_i(t) < V_{thr} \tag{1.3}_{\text{Viaf}}$$

and cell i is not refractory. When $V_i(t)$ exceeds V_{thr} we augment the spike time sequence, T_i, and we reset $V_i(t)$ to a fixed reset potential, V_{res} for a set refractory period, t_{ref}. These spike times couple the conductance and potential equations. We decouple this system by specifying an order of operation. In particular, we adopt the marching scheme

(1) check for an input spike
(2) update conductances based on input spikes and networks spike from **previous** time step
(3) update potentials and record spikes
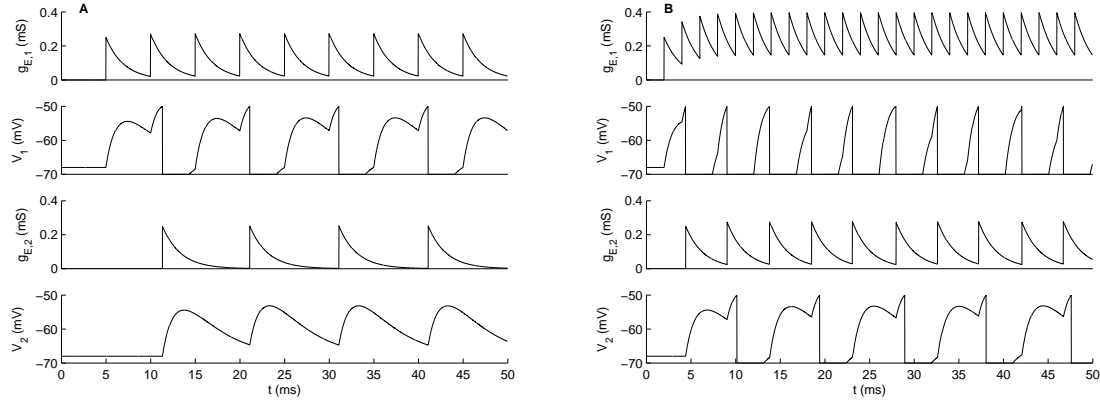
2cellhilo

Figure 1.2. Response of the two cell net to low frequency, $P = 5$, and high frequency, $P = 2$, stimulus. In each case we see that cell one fires following every second input spike. In the low frequency case the resultant spike rate of cell 1 is not sufficient to bring cell 2 to threshold. `twocell`

Accordingly, if cell 1 receives an input spike in the interval $(jdt, (j+1)dt)$ then the trapezoid rule on (1.1), applied to $\mathbf{g}_{E,1}^j \approx g_{E,1}((j-1)dt)$, requires

$$\tau_E(\mathbf{g}_{E,1}^{j+1} - \mathbf{g}_{E,1}^j) = -(\mathbf{g}_{E,1}^{j+1} + \mathbf{g}_{E,1}^j)dt/2 + w^{inp}$$

which may be rearranged to read

$$\mathbf{g}_{E,1}^{j+1} = a_E \mathbf{g}_{E,1}^j + b_E w^{inp}$$

where

$$a_E = \frac{2\tau_E - dt}{2\tau_E + dt} \quad \text{and} \quad b_E = \frac{2}{2\tau_E + dt}.$$

Similarly, if cell 1 was found to spike in the previous interval, i.e., $((j-1)dt, jdt)$ then

$$\mathbf{g}_{E,2}^{j+1} = a_E \mathbf{g}_{E,2}^j + b_E w_{21}$$

Regarding the potentials, when cell i is nonrefractory, i.e., when

$$(j+1)dt - T_i > t_{ref} \tag{1.4}\text{refcon}$$

the trapezoid rule in (1.3) requires

$$\mathbf{V}_i^{j+1} = \frac{(2C_m/dt - (g_L + \mathbf{g}_{E,i}^j))\mathbf{V}_i^j + 2g_L V_L + (\mathbf{g}_{E,i}^{j+1} + \mathbf{g}_{E,i}^j)V_E^{syn}}{2C_m/dt + g_L + \mathbf{g}_{E,i}^{j+1}}.$$

If (1.4) is not satisfied we enforce $\mathbf{V}_i^{j+1} = V_{res}$. We have coded this update procedure in `twocell` and illustrate our findings for periodic input trains that spike at

$$T_{inp}^n = nP, \quad n = 1, 2, \ldots \tag{1.5}\text{Pstim}$$

where P is the period (ms). Throughout we shall use

$$\tau_E = 2, \ V_E^{syn} = 0, \ g_L = 0.3, \ V_L = -68, \ C_m = 1,$$
$$w_{inp} = 0.5, \ w_{21} = 0.5, \ t_{ref} = 3, \ V_{thr} = -50, \ V_{res} = -70. \tag{1.6}\text{netpar}$$

As most cells receive input from more than one neighbor we move onto the three cell net below. We retain periodic input and to the parameter set above add $w_{32} = w_{31} = 0.5$.

2
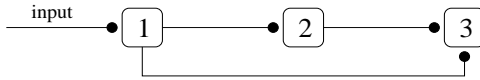
Figure 1.3. A three cell network

We have coded the subsequent model in `threecell.m`. This code is a considerable refinement of the two cell version. In particular, we have laid the weights in a weight matrix, W and we have 'vectorized' the computations of both $\mathbf{g}_E$ and $\mathtt{V}$.
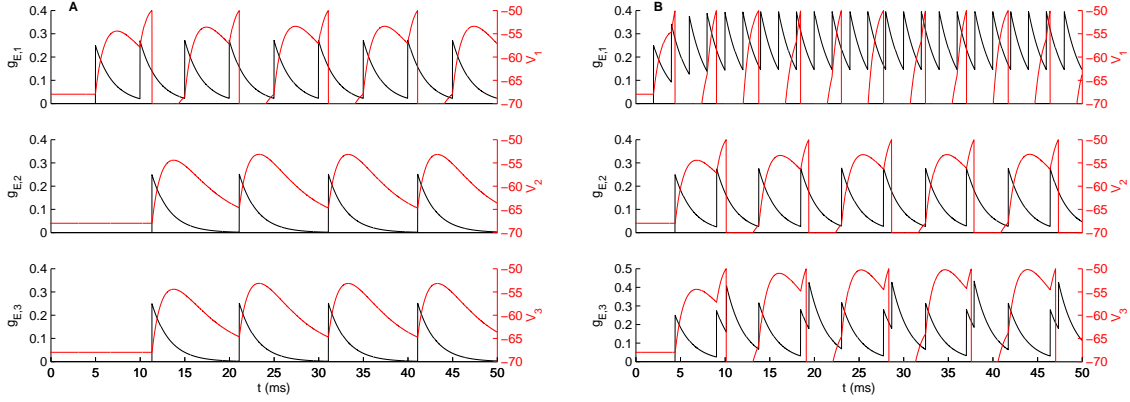
Figure 1.4. Response of the three cell net to low frequency, $P = 5$, and high frequency, $P = 2$, stimulus. Observe in the lower right panel that the third conductance receives a double kick as cell 2 fires just after each second spike of cell 1.`threecell`

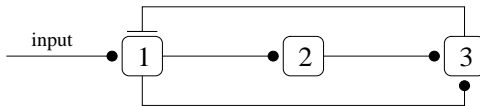We next suppose that cell 3 inhibits cell 1. This new conductance is governed by

$$\mathbf{g}_{I,1}^{j+1} = a_I \mathbf{g}_{EI}^j + b_I w_{inh} \mathbf{s}_3$$

where, as above

$$a_I = \frac{2\tau_I - dt}{2\tau_I + dt} \quad \text{and} \quad b_I = \frac{2}{2\tau_I + dt}.$$

The potential at cell 1 now follows

$$\mathtt{V}_1^{j+1} = \frac{(2C_m/dt - (g_L + \mathbf{g}_{E,1}^j + \mathbf{g}_{I,1}^j))\mathtt{V}_1^j + 2g_L V_L + (\mathbf{g}_{E,1}^{j+1} + \mathbf{g}_{E,1}^j)V_E^{syn} + (\mathbf{g}_{I,1}^{j+1} + \mathbf{g}_{I,1}^j)V_I^{syn}}{2C_m/dt + g_L + \mathbf{g}_{E,1}^{j+1} + \mathbf{g}_{I,1}^{j+1}}$$
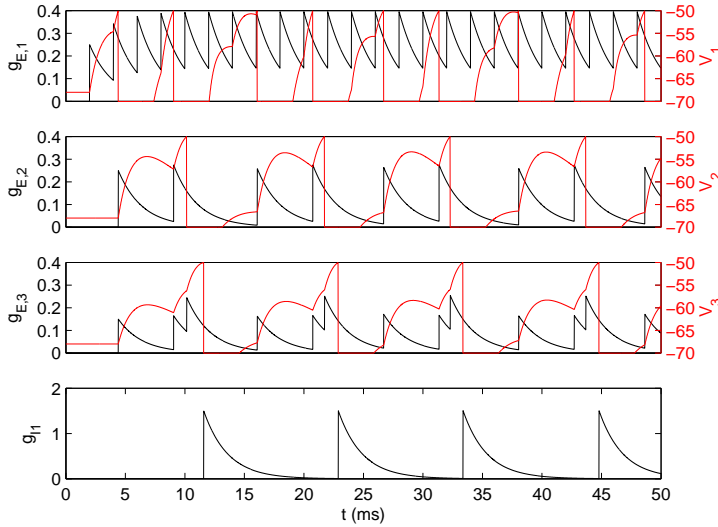
Figure 1.5. A three-cell network with feedback inhibition.

We diminish the drive on cell 3 via $w_{31} = w_{32} = 0.3$ and set the new parameters

$$\tau_I = 2, \ V_I^{syn} = -70 \quad \text{and} \quad w_{inh} = 3,$$

and arrive at

3

Figure 1.6. Response of the network in **Figure** 1.5 to high frequency, $P = 2$, stimulus. We note that cell 3 now staggers the firing of cell 1. `threecellI`

In the simulation of large networks one computes, but does not typically record, the conductances and potentials at each time step. Rather one records and reports the times at which each cell spikes. We have trimmed `threecell` and `threecellI` down to `threecellrast` and `threecellIrast` and illustrated their use below,
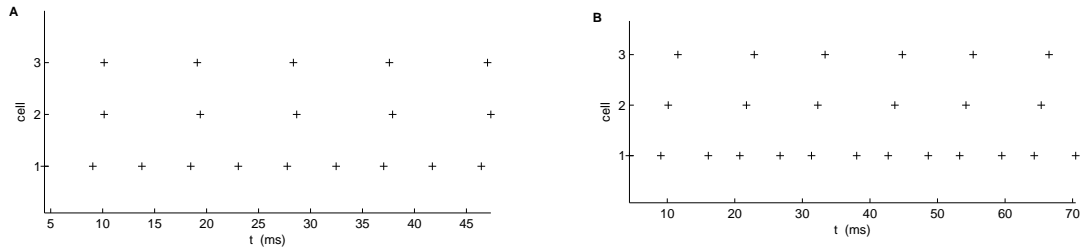
Figure 1.7. Raster plots of spike times of the three cell net without (A), and with (B) inhibition. `threecellrast` and `threecellIrast`

1.3. Large Integrate and Fire Networks

If W denotes the matrix of weights between excitatory cells and W_{inp} denotes the weight of input spikes upon excitatory cells, then, arguing as above, the network equations take the form

$$\mathbf{g}_E^{j+1} = a_E \mathbf{g}_E^j + b_E(W\mathbf{s}^j + W_{inp}\mathbf{s}_{inp}^{j+1})$$

$$\mathbf{V}^{j+1} = \frac{(2C_m/dt - (g_L + \mathbf{g}_E^j))\mathbf{V}^j + 2g_L V_L + (\mathbf{g}_E^{j+1} + \mathbf{g}_E^j)V_E^{syn}}{2C_m/dt + g_L + \mathbf{g}_E^{j+1}}$$

$$\mathbf{s}^{j+1} = (\mathbf{V}^{j+1} > V_{thr})$$

4

where all operations in the voltage update are elementwise. We have coded this in `Enet` with the help of MATLAB's `sprand` function, which generates sparse matrices from the uniform distribution on $[0, 1]$ with a prescribed fraction of nonzeros.
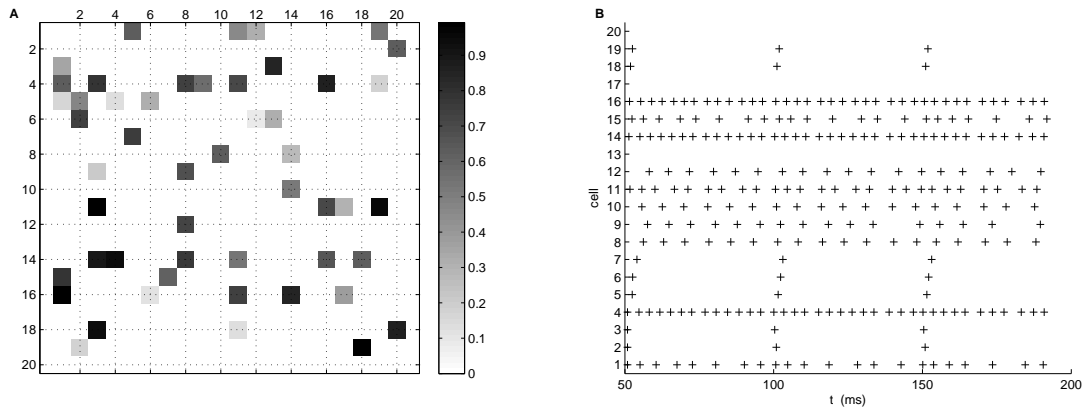
Enet20

Figure 1.8. Weight and spikes in a 20-cell excitatory net with 15% connectivity subject to a periodic train, $P = 30$, with $W_{inp} = 1$, delivered to the first 20% of the cells. `Enet`

To see the meaning of this W matrix note cells 7 and 13 have **no** squares in their columns and hence have no impact on the behavior of the net. Every row has a nonzero and so in fact every cell receives input from at least one neighbor, although cells 13 and 19 each have only one weight and in each case this weight is not enough to fire the cell. We have stripped the diagonal clean and hence no cell excites itself. These nets are capable of generating rich patterns.
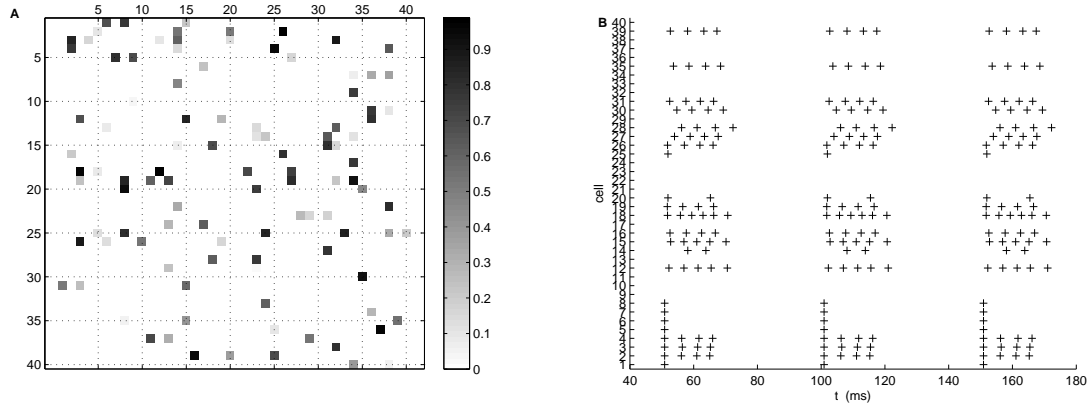
Enet40

Figure 1.9. Weight and spikes in a 40-cell excitatory net with 7% connectivity subject to a periodic train, $P = 50$, with $W_{inp} = 1$, delivered to the first 20% of the cells. `Enet`

We now introduce a population of inhibitory cells. We note their potentials by V_I and those of the excitatory cells by V_E. Now each cell has two conductances; g_{EE} and g_{IE} will denote the excitatory and inhibitory conductances on an excitatory cell while g_{EI} and g_{II} will denote the excitatory and inhibitory conductances on an inhibitory cell. Coupling occurs through the weight matrices; W_{EE} which connects E cells to E cells, W_{EI} which connects E cells to I cells, W_{IE}, which connects I cells to E cells, and W_{II} which connects I cells to I cells. The subsequent network

5

equations are

$$\mathbf{g}_{EE}^{j+1} = a_E \mathbf{g}_{EE}^j + b_E(W_{EE}\mathbf{s}_E^j + W_{EE}^{inp}\mathbf{s}_{inp,E}^{j+1})$$

$$\mathbf{g}_{EI}^{j+1} = a_E \mathbf{g}_{EI}^j + b_E(W_{EI}\mathbf{s}_E^j + W_{EI}^{inp}\mathbf{s}_{inp,E}^{j+1})$$

$$\mathbf{g}_{II}^{j+1} = a_I \mathbf{g}_{II}^j + b_I(W_{II}\mathbf{s}_I^j + W_{II}^{inp}\mathbf{s}_{inp,I}^{j+1})$$

$$\mathbf{g}_{IE}^{j+1} = a_I \mathbf{g}_{IE}^j + b_I(W_{IE}\mathbf{s}_I^j + W_{IE}^{inp}\mathbf{s}_{inp,I}^{j+1})$$

$$\mathbf{V}_E^{j+1} = \frac{(2C_m/dt - (g_L + \mathbf{g}_{EE}^j + \mathbf{g}_{IE}^j))\mathbf{V}_E^j + 2g_L V_L + (\mathbf{g}_{EE}^{j+1} + \mathbf{g}_{EE}^j)V_E^{syn} + (\mathbf{g}_{IE}^{j+1} + \mathbf{g}_{IE}^j)V_I^{syn}}{2C_m/dt + g_L + \mathbf{g}_{EE}^{j+1} + \mathbf{g}_{IE}^{j+1}}$$

$$\mathbf{V}_I^{j+1} = \frac{(2C_m/dt - (g_L + \mathbf{g}_{II}^j + \mathbf{g}_{EI}^j))\mathbf{V}_I^j + 2g_L V_L + (\mathbf{g}_{II}^{j+1} + \mathbf{g}_{II}^j)V_I^{syn} + (\mathbf{g}_{EI}^{j+1} + \mathbf{g}_{EI}^j)V_E^{syn}}{2C_m/dt + g_L + \mathbf{g}_{II}^{j+1} + \mathbf{g}_{EI}^{j+1}}$$

$$\mathbf{s}_E^{j+1} = (\mathbf{V}_E^{j+1} > V_{thr})$$

$$\mathbf{s}_I^{j+1} = (\mathbf{V}_I^{j+1} > V_{thr})$$

We have coded this system in `EInet` with

$$\tau_I = 1 \quad \text{and} \quad V_I^{syn} = -70$$

and illustrate its findings below.
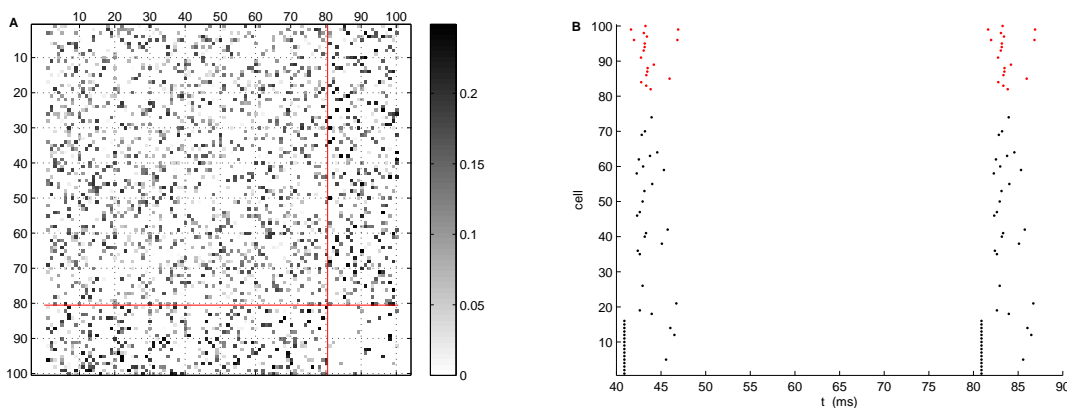
EInet

Figure 1.10. Weight and spikes in an EI-net with 80 E-cells and 20 I-cells subject to a periodic train, $P = 40$, with $W_{inp} = 1$, delivered to the first 20% of the E-cells. W_{EE}, W_{EI} and W_{IE} each have 25% connectivity while W_{II} has 5%. `EInet`

1.4. Integrate and Fire Networks with Plastic Synapses

Spikes not only increment synaptic conductances they also increment the associated elements of the synaptic weights. If $W_{i,j}$ is the weight of cell j upon cell i we will implement a Hebbian rule that provides a positive increment when j spikes before i and a negative increment when i spikes before j. The size of the weight change is a function of the time between spikes and the current weights. Let us begin with the simple four-cell net below.
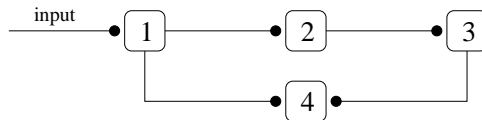
4cell

Figure 1.11. A four-cell net.

We excite cell 1 every 40 ms. This activity propagates quickly to fire cells 2 and 4 and eventually cell 3. As 1 fires 4 we expect this weight, $W_{4,1}$, to increase and as 3 does not fire 4 we expect $W_{4,3}$ to decrease. To do this, when a cell

fires we potentiate the weights from presynaptic cells that have recently fired and depress the weights to postsynaptic cells that have recently fired. We quantify "recent" by adopting a scheme that is in line with the observations of Bi and Poo that the degree of both potentiation and depression decays exponentially with the interval between the pre- and post-synaptic spikes.
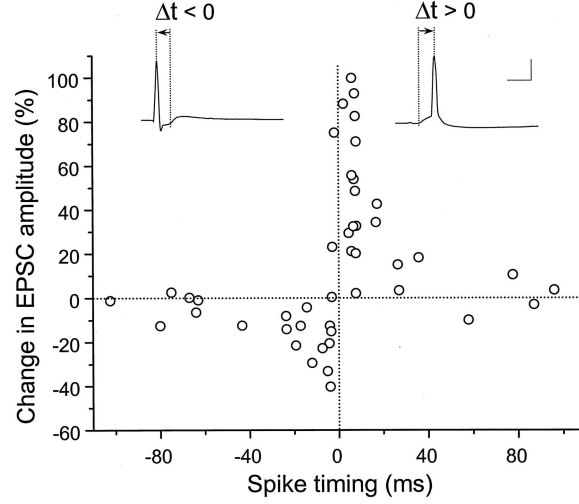
Figure 1.12. Bi and Poo, Synaptic Modifications in Cultured Hippocampal Neurons: Dependence on Spike Timing, Synaptic Strength, and Postsynaptic Cell Type J. Neurosci. 1998 18: 10464-10472, Figure 7. Here $\Delta t = T_{post} - T_{pre}$ and EPSC denotes Excitatory Post-Synaptic Potential. This data suggests potentiation when $\Delta t > 0$ and depression when $\Delta t < 0$.

We implement this scheme, with respect to the weight $W_{4,3}$, via the simple difference

$$\frac{dW_{4,3}(t)}{dt} = \delta(t - T_4)A_P \exp((T_3 - T_4)/\tau_P) - \delta(t - T_3)A_D \exp((T_4 - T_3)/\tau_D) \tag{1.7}_{\text{heb431}}$$

where we emphasize that this expression is indeed causal, for T_3 and T_4 denote the latest respective spike times **prior to** t. To best appreciate this we integrate Eq. (1.7) over each such spike and uncover the increment rules

$$W_{4,3}(T_4^+) = W_{4,3}(T_4^-) + A_P \exp((T_3 - T_4)/\tau_P)$$
$$W_{4,3}(T_3^+) = W_{4,3}(T_3^-) - A_D \exp((T_4 - T_3)/\tau_D).$$

When called repeatedly these increments may lead to runaway weight loss and gain. There are a number of remedies for this. The most simple is to return to zero any weights that tend negative and to return to W_{max} all weights that exceed this specified maximum. A smoother way of enforcing these bounds is to replace Eq. (1.7) with

$$\frac{dW_{4,3}(t)}{dt} = \delta(t - T_4)A_P \exp((T_3 - T_4)/\tau_P)(W_{max} - W_{4,3}(t))$$
$$- \delta(t - T_3)A_D \exp((T_4 - T_3)/\tau_D)W_{4,3}(t)$$

for this leads to self-limiting update rules

$$W_{4,3}(T_4^+) = W_{4,3}(T_4^-) + A_P \exp((T_3 - T_4)/\tau_P)(W_{max} - W_{4,3}(T_4^-))$$
$$W_{4,3}(T_3^+) = W_{4,3}(T_3^-) - A_D \exp((T_4 - T_3)/\tau_D)W_{4,3}(T_3^-).$$

Another advantage of this procedure is that now the maximum adjustments, A_P and A_D, are dimensionless. Regarding the implementation of these rules, if our marching scheme determines that cell k fires in the interval $(jdt, (j+1)dt)$ we potentiate its presynaptic weights via

$$\mathbb{W}_{k,k_{pre}}^{j+1} = \mathbb{W}_{k,k_{pre}}^{j} + A_P \exp((T_{k_{pre}} - (j+1)dt)/\tau_P)(W_{max} - \mathbb{W}_{k,k_{pre}}^{j}),$$
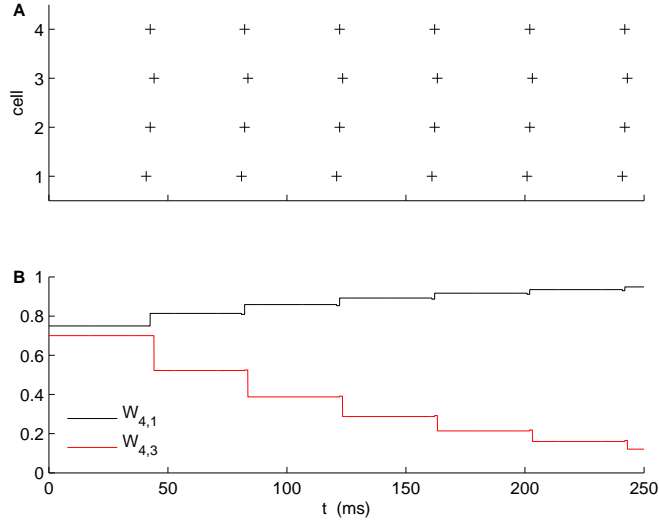
and depress its postsynaptic weights via

$$W_{k_{post},k}^{j+1} = W_{k_{post},k}^{j} - A_D \exp((T_{k_{post}} - (j+1)dt)/\tau_D)W_{k_{post},k}^{j},$$

We have coded these rules for the four-cell net, with

$$A_P = A_D = 0.3 \quad \text{and} \quad \tau_P = \tau_D = 10 \qquad\qquad (1.8)_{\text{hebb4p1}}$$

and initial weights

$$W_{2,1} = W_{3,2} = W_{4,1} = 0.75 \quad \text{and} \quad W_{4,3} = 0.7. \qquad\qquad (1.9)_{\text{hebb4p2}}$$


fourcell

Figure 1.13. Spike and weight evolution in the 4-cell net parametrized by (1.8)–(1.9). We see indeed that the direct connection, w_{41} is strengthened while the indirect connection, $w_{4,3}$ is dminished. `fourcell`

We proceed to illustrate this learning rule on E-to-E connections within a large random net. We consider 80 E-cells and 20 I-cells with random connectivity and with EE-, IE-, and EI densities of 25% and an II-density of 5%. In addition, we use

$$\tau_E = 2, \ \tau_I = 1, \ \tau_P = 5, \ \tau_D = 5, \ A_P = 0.1, \ A_D = 0.3, W_{max} = 0.4,$$

and as aobove drive the first 20% of the E-cells with the same spike pattern with period of $P = 50$.
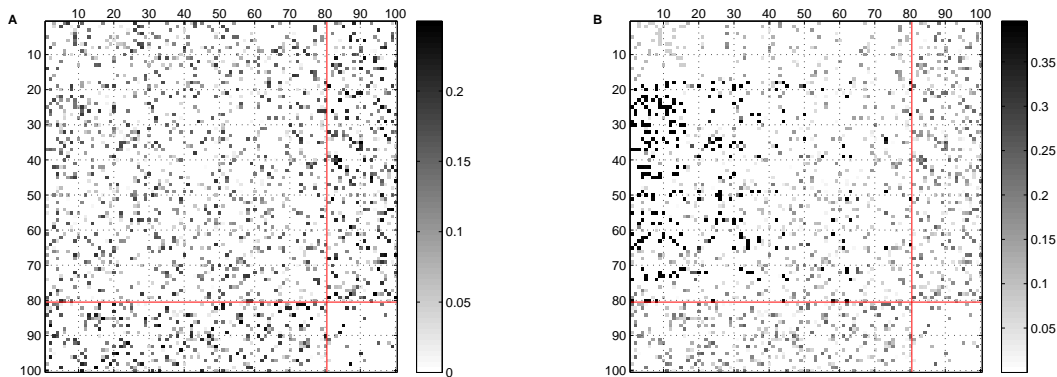
EInetHa

Figure 1.14. Weights before and after learning. The red lines partition the E- and I-cell weights. Note the distinct weight increase from the cells receiving input (columns 1–16) to the "output cells" (rows 25–75). `EInetH`

8

These gray-scale weight plots are not the best means of tracking weight shifts over time. Rather we compute a histogram at regular intervals.
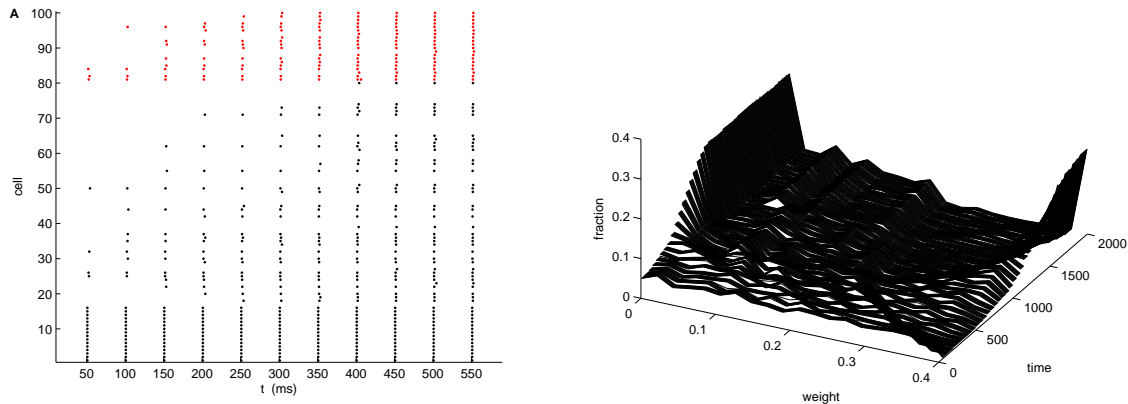
EInetHb

Figure 1.15. Spike and Weight evolution. $P = 30$. `EInetH`

1.5. Exercises

1. In the case of periodic input, Eq. (1.5), for the two-cell network we may solve Eq. (1.1) for $g_{E,1}$ by hand. In particular, please show that

$$g_{E,1}(t) = \frac{w_{inp}}{\tau_E} \exp((P-t)/\tau_E) \frac{1 - \exp(P\lfloor t/P \rfloor /\tau_E)}{1 - \exp(P/\tau_E)} \qquad (1.10)_{\text{ge1ex}}$$

where $\lfloor x \rfloor$ denotes the largest integer less than x. First show that $g_{E,1}(P^+) = w_{inp}/\tau_E$, then $g_{E,1}(t) = \exp((P-t)/\tau_E)w_{inp}/\tau_E$ for $P \le t < 2P$, then $g_{E,1}(2P^+) = (1 + exp(-P/\tau_E)w_{inp}/\tau_E$ and so

$$g_{E,1}(t) = \exp((P-t)/\tau_E)(1 + \exp(P/\tau_E))w_{inp}/\tau_E, \quad 2P \le t < 3P.$$

Continuing in this fashion you will find a (summable) finite geometric series.

2. Experiment with `threecell.m` to further delay the spiking of cell 3. In particular, retain $P = 2$ but set $W_{3,1} = W_{3,2} = w$ and find the smallest w (to two decimal places) such that cell 3 fires once for every two spike of cell 2. Submit your code and associated figure.

9