Ma481 Mathematical Neuroscience

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These notes cover a lot of the 2008-2009 Mathematical Neuroscience course given by Dr. Conor Houghton, with an inclination towards the theoretical aspects of the course (there are no examples involving monkeys, for instance). The material is all taken either from the course lectures or from the book *Theoretical Neuroscience* by Dayan and Abbott.

Contents

1 Membrane electrodynamics

1.1 Introduction to neurons

The brain is composed of neurons - specialised cells which communicate via electrical signals. As the name suggests, mathematical neuroscience is concerned with applying mathematical methods to investigate the workings of the brain.

We begin by analysing the current and voltage of a single neuron. We model the neuron as a simple cell, with an impermeable membrane pierced by specialised channels and pumps that, under certain conditions, allow various types of ions to flow in and out of the cell. The exchange of ions - and the accompanying change in electric current - is what allows the neuron to communicate.

In reality typical neurons are composed of three main parts: a body called the soma which aggregates and responds to signals, a long strand called the axon which carries signals out from the soma, and filament-like structures called dendrites which carry signals into the soma.

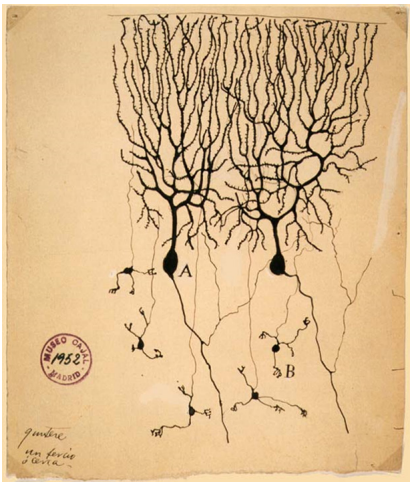

Figure 1: Drawing by Santiago Ramn y Cajal of neurons in the pigeon cerebellum (source: Wikipedia)

The essential idea is that there exist electrical and chemical potential differences between the interior of the neuron and the outside world. The electrical potential difference, or voltage, is a result of excess positive or negative charge accumulating within the neuron. The chemical potential difference, or chemical gradient, is a result of there being different concentrations of particular ions inside and outside the neuron.

For instance, there is an excess of sodium ions (Na^+) outside the neuron, and an excess of potassium ions (K^+) inside. In general the electrical potential is negative, ≈ -70mV (that is to say that we view the electric potential just outside the neuron as being 0mV, while that of the interior as being -70mV).

Positive ions flowing out of the neuron make the membrane potential more negative (as it increases the amount of positive charge on the outside and decreases the amount on the inside), while positive ions flowing in make the membrane less negative. Conversely, negative ions flowing in decrease the membrane potential and negative ions flowing out increase the potential.

We must adopt a convention for current: we say that positive ions leaving the neuron or negative ions entering the neuron is a positive current.

If the voltage rises above a certain threshold value, sodium channels open in the membrane, allowing sodium ions to enter the neuron. By the above this causes the membrane potential to rise, perhaps to positive values. Once it has reached a high enough value, potassium gates in the membrane open, letting potassium ions exit the cell and causing the voltage to decrease rapidly. The overall effect of a sudden rise in voltage is called a spike, and this then propagates down the axon.

1.2 Nernst equation

The ions surrounding and within the neuron are in constant thermal motion. The Maxwell-Boltzman distribution is a model for the energy distribution of a classical gas of non-interacting particles at a constant temperature T:

$$p(E) = \frac{1}{kT} \exp\left(-\frac{E}{kT}\right)$$

where k is Boltzman's constant, $k = 1.38 \times 10^{-23} \mathrm{m}^2\,\mathrm{kg}\,\mathrm{s}^{-2}\,\mathrm{K}^{-1}$ and $p(E)dE$ gives the probability of a particle having energy between E and dE. The average kinetic energy is

$$\langle E \rangle = \frac{1}{kT} \int_0^\infty dE\, E \exp\left(-\frac{E}{kT}\right) = kT$$

We can apply this distribution as a simple model for the sea of ions surrounding and contained within the neuron. We derive the voltage scale of neuron electrodynamics by assuming that the average thermal energy kT is roughly equal to the electrical potential energy qV of an ion of charge q, so that voltage changes can modulate ion flows. This gives the typical voltage V_t as

$$V_t \approx \frac{kT}{q} \approx 27\,\mathrm{mV}$$

taking body temperature $\approx 311.15\mathrm{K}$ as T and the elementary charge $1.6 \times 10^{-19}\mathrm{C}$ as q.

Now let us study the effects of chemical gradients and the membrane potential on an ion of charge zq, where $q = 1.6 \times 10^{-19}$. Let ρ_i denote the concentration of the type of ion inside the neuron, and ρ_o denote the concentration outside the neuron. The chemical gradient can be thought of as the tendency for ions to flow from high concentration to low concentration. From this we see that the flow out due to the gradient will be $\propto \rho_i$ and the flow in will be $\propto \rho_o$.

However whether or not a particular ion is able to move across the membrane depends on its charge and the membrane potential. For instance, a positively charged ion inside a neuron with a negative membrane potential E will only be able to cross the membrane if its kinetic energy exceeds the work needed to overcome the potential barrier. This work is given by the charge on the ion multiplied by the change in potential difference when crossing the boundary, hence $W = zq(0 - E) = -zqE$ (note $E < 0$ and $q > 0$ so this is a positive quantity). The proportion of ions with kinetic energy greater than this is

$$p(E > -zqE) = \frac{1}{kT}\int_{-zqE}^{\infty} \exp\left(-\frac{E}{kT}\right) dE = \exp\left(\frac{zqE}{kT}\right) = \exp\left(\frac{zE}{V_t}\right)$$

where you must excuse the use of E for both the electric potential and the integration variable. We are interested in the membrane potential E at which the flow of ions out equals the flow of ions in. This is known as the equilibrium potential E_x of the ion type x, and is found from

$$\rho_i \exp\left(\frac{zE_x}{V_t}\right) = \rho_o \Rightarrow E_x = \frac{V_t}{z}\log\frac{\rho_o}{\rho_i}$$

For instance, $E_{K^+} \approx -70$mV to -90mV, $E_{Na^+} \approx 50$mV, $E_{Ca^{2+}} \approx 150$mV.

1.3 Hodgkin-Huxley equation

The membrane potential leads to a build-up of negative and positive charge on opposite sides of the membrane. This storage of charge is known as a capacitance and we have the formula

$$Q = C_m V$$

where Q is the charge, V is the voltage (membrane potential) and C_m is the membrane capacitance. We will more often use the specific capacitance c_m, defined as the capacitance per unit area, $c_m = \frac{C_m}{A}$, with A the membrane area.

Now, the current is just the time derivative of the charge, $I = \frac{dQ}{dt}$, so we have

$$I = C_m \frac{dV}{dT}$$

giving us a general equation for the change in voltage. To find I in terms of V, we can use Ohm's law, $V = IR_m$, where R_m is the membrane resistance. Dividing by the membrane area A we get this in terms of specific current and resistance, $i = \frac{V}{r_m} = g_m V$, where $g_m \equiv r_m^{-1}$ is the membrane conductance per unit area. Note that here we have $r_m = RA$.

In analysing the current flow across the membrane we sum the currents i_x flowing as a result of the motion of each ion type x. Notice that the current i_x will obviously vanish at the equilibrium voltage E_x, as then there will be no net movement of ions. We thus apply Ohm's law to the voltage relative to the equilibrium voltage, hence $i_x = g_x(V - E_x)$, and the total membrane current i_m is given by $i_m = \sum_x i_x$.

We also need to take into account the possibility of experimental input - for instance a current I_e induced by an electrode inserted into the cell - and what signs we are to give our

voltage. With our (somewhat confusing) conventions, a positive current (for instance given by positive ions flowing out) decreases V, and so we attach a minus sign to the membrane current. Conversely the electrode current is by convention defined to flow into the neuron, so it has a positive sign. This gives the Hodgkin-Huxley equation

$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A}$$

with $i_m = \overline{g}_l(V - E_l) + g_{K^+}(V - E_{K^+}) + g_{Na^+}(V - E_{Na^+})$ (further currents can obviously be added).

Here $i_l = \overline{g}_l(V - E_l)$ is the leak current. This is the current caused by the constant leakage of ions out of the neuron. The bar over g_l signifies that the leak conductance is constant. The conductances corresponding to the sodium and potassium currents depend on the dynamics of the ion gates involved, and depend on voltage and hence time (see later).

1.4 Integrate and fire

In the leaky integrate and fire model we just take into account the leak and electrode currents:

$$c_m \frac{dV}{dt} = -\overline{g}_l(V - E_l) + \frac{I_e}{A}$$

with the additional rule that if the voltage equals the threshold value, $V = V_{\text{th}}$ we get a spike and the voltage resets, $V = V_{\text{reset}}$. Multiplying across by r_m, the equation becomes

$$\tau_m \frac{dV}{dt} = E_l + R_m I_e - V$$

where $\tau_m = c_m r_m$ has dimension of time. This is an inhomogeneous first order ordinary differential equation and can be solved by multiplying across by the integrating factor e^{t/τ_m}:

$$\frac{dV}{dt}e^{t/\tau_m} + \frac{1}{\tau_m}Ve^{t/\tau_m} = \frac{1}{\tau_m}(E_l + R_m I_e)e^{t/\tau_m} \Rightarrow \frac{d}{dt}(Ve^{t/\tau_m}) = \frac{1}{\tau_m}(E_l + R_m I_e)e^{t/\tau_m}$$

$$\Rightarrow V(t)e^{t/\tau_m} - V(0) = (E_l + R_m I_e)\, e^{t/\tau_m} - (E_l + R_m I_e)$$

and so

$$V(t) = E_l + R_m I_e + (V(0) - E_l - R_m I_e)\, e^{-t/\tau_m}$$

As $t \to \infty$, $V(t) \to E_l + R_m I_e$. If $E_l + R_m I_e > V_{th}$ then at some time t_{isi} we will get a spike, where we let $V(0) = V_{\text{reset}}$ and $V(t_{\text{isi}}) = V_{th}$, with t_{isi} being the interspike interval:

$$V(t_{\text{isi}}) = V_{th} = E_l + R_m I_e + (V_{\text{reset}} - E_l - R_m I_e)\, e^{-t_{\text{isi}}/\tau_m}$$

$$\Rightarrow t_{\text{isi}} = \tau_m \ln\left(\frac{E_l + R_m I_e - V_{\text{reset}}}{E_l + R_m I_e - V_{th}}\right)$$

The firing rate is given by $r_{\text{isi}} = \frac{1}{t_{\text{isi}}}$.

In reality it is found that the firing rate is not constant (for constant I_e) as implied by the above equation, but drops as time progresses. This is due to spike rate adaptation, in which a neuron fires less when subjected to the same input for an extended period of time. We can model this by introducing an extra conductance channel, assumed to allow the passage of K^+ ions:

$$\tau_m \frac{dV}{dt} = E_l + R_m I_e - V - r_m g_{sra}(V - E_K^+)$$

where

$$\tau_{sra} \frac{dg_{sra}}{dt} = -g_{sra}$$

and we set $g_{sra} = g_{sra} + \Delta g_{sra}$ whenever a spike occurs.

1.5 Hodgkin-Huxley equation: gating probabilities

In the Hodgkin-Huxley equation the conductances g_{K^+}, g_{Na^+} are not constant but depend on the number of open ion channels. Letting $\overline{g}_x$ be the conductance for ion type x that would result from all channels being open, we have $g_x = \overline{g}_x P_x$, where P_x is the proportion of open channels.

For K^+ the channel is a persistent channel - it opens as the voltage increases and stays open until the voltage decreases. The channel consists of four subgates, all of which must be open for current to pass through. We write the probability for a gate to be open as n, then $P_{K^+} = n^4$, and we have

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n$$

where α_n gives the rate at which closed subgates open and β_n gives the rate at which open subgates close.

For Na^+ the channel is a transient channel, which opens then closes again as the voltage increases, due to being composed of two subgates with opposite voltage dependences. The first subgate is itself composed of three subgates, and we let m be the probability for one of these subgates to be open. We also let h be the probability for the second subgate to be open, so that $P_{Na^+} = m^3 h$. The probabilities m and h are governed by the equations

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m \qquad \frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

If we divide across by $\alpha_x(V) + \beta_x(V)$ (with $x = n, m, h$) the above equations take the form

$$\tau_x(V) \frac{dx}{dt} = x_\infty(V) - n$$

with $\tau_x(V) = (\alpha_x(V) + \beta_x(V))^{-1}$ and $x_\infty(V) = \alpha_n(V)/\alpha_x(V) + \beta_x(V)$. We see that for fixed V, x relaxes towards $x_\infty(V)$ with timescale $\tau_x(V)$.

These gates contribute towards the spiking dynamics as follows: as V increases m increases and for a brief period both m and h are substantially greater than zero, causing sodium gates to open and sodium ions to enter the neuron. This increases V further (creating a spike),

and makes h decrease to close to zero and n to increase, causing potassium gates to open. Potassium ions enter and this causes V to drop back to its normal level.

2 Synapses

2.1 Introduction to synapses

The point where an axon ends and meets a dendrite or sometimes the soma of a different neuron is called a synapse. The very end of the axon is called the terminal button, and between it and the dendritic spine is a small (approximately 10nm) gap called the synaptic cleft. The terminal button contains vesicles, which can be thought of as a small bubbles of liquid within the axon, containing a special molecule called neurotransmitter. When a spike arrives at the terminal button it causes some vesicles to move to the surface of the axon and release neurotransmitter into the synaptic cleft. The neurotransmitter binds with channels on the other side of the cleft, causing them to open, which allows ions to cross the membrane of the other neuron. This induces a change in the voltage in the other neuron which diffuses towards the soma. The released neurotransmitter is then reabsorbed by the original vesicles.

The induced voltage change is called the post-synaptic pulse, and its sign depends on the neuron which released the neurotransmitter. It is positive for excitatory neurons and negative for inhibitory neurons.

2.2 Modelling synapses

We denote the post-synaptic conductance by g_s, then we have $g_s = \overline{g}_s P_{rel} P_s$, where $\overline{g}_s$ is the maximum possible synaptic conductance, P_{rel} is the fraction of maximum possible neurotransmitter released and P_s is the fraction of open channels in the dendritic spine. We set $P_{rel} = 1$ for simplicity. We have

$$\frac{dP_s}{dt} = \alpha_s(1 - P_s) - \beta_s P_s$$

where the closing rate β_s is assumed to be constant, and α_s is proportional to some power k of the transmitter concentration ρ.

When a spike arrives at the terminal button, α_s increases rapidly with the release of neurotransmitter, but then quickly returns to zero due to reabsorption. This gives us a simple model of synapses, where we model α_s as a square pulse: i.e. it jumps from 0 to some large positive value much greater β_s when a spike arrives, stays at this value for a time T and then returns to 0. Thus in the presence of a spike we ignore β_s and have the equation (assuming the spike arrives at time $t = 0$)

$$\frac{dP_s}{dt} = \alpha_s - \alpha_s P_s \Rightarrow \frac{d}{dt}(P_s e^{\alpha_s t}) = \alpha_s e^{\alpha_s t}$$

hence

$$P_s(t) = 1 + (P_s(0) - 1)e^{-\alpha_s t} \qquad 0 \leq t \leq T$$

while after the spike ($t \geq T$)

$$\frac{dP_s}{dt} = -\beta_s P_s \Rightarrow P_s(t) = P_s(T)e^{-\beta_s t}$$

Now suppose $P_s(0) = 0$, i.e. there has been no previous spike in the immediate past. Then we have, for $0 \leq t \leq T$, $P_s(t) = 1 - e^{-\alpha_s t}$, so that P_s rises to a maximum $P_{max} = 1 - e^{-\alpha_s T}$. Now in general using this quantity we have

$$P_s(T) = 1 + (P_s(0) - 1)(1 - P_{max}) \Rightarrow P_s(T) = P_s(0) + P_{max}(1 - P_s(0))$$

so we see that the effect of the spike arriving was to increase P_s by $P_{max}(1 - P_s(0))$.

This leads to the following simple model of synaptic conductivity: we model P_s using the equation

$$\frac{dP_s}{dt} = -\beta_s P_s$$

and when a spike arrives we have

$$P_s(t) \to P_s(t) + P_{max}(1 - P_s(t))$$

3 Decoding

We wish to study the problem where we have a stimulus S, ideally depending on some parameter(s), and a response R, ideally described by some variable(s), related by some mathematical operation.

3.1 Spike trains

Often our response will be in the form a spike train. We can treat this simply as a list of times:

$$\mathbf{t} = \{t_0, t_1, \ldots, t_n\}$$

which we can replace with a function

$$\rho(t) = \sum_{t_i \in \mathbf{t}} \delta(t - t_i)$$

called the neural response function, which in turn allows us to form from some function $h(t)$ a function $\sum_{t_i} h(t - t_i)$ by integrating:

$$\sum_{t_i} h(t - t_i) = \int d\tau\, h(\tau)\rho(t - \tau) = \sum_{t_i} \int d\tau\, h(\tau)\delta(t - t_i - \tau)$$

We define the spike count rate as

$$r = \frac{1}{T}\int_0^T dt\, \rho(t) = \frac{n}{T}$$

where T is the length of the experiment. This number isn't terribly useful as it doesn't take into account the distribution of spikes as a function of time during the course of the experiment, and also relies on just a single experiment. For the latter, we may take average over a number of experiments i.e. add up the results from each experiment and divide by the number of experiments. The trial-averaged neural response function $\langle\rho(t)\rangle$ is then

$$\langle\rho(t)\rangle = \frac{1}{N}\sum_{i,j} \delta(t - t_i^j)$$

where N is the number of trials and t_i^j is the ith spike in the jth trial. We then define the firing rate

$$r(t) = \frac{1}{\Delta t}\int_t^{t+\Delta t} dt\, \langle\rho(t)\rangle$$

where we have $\Delta t \to 0$ and $N \to \infty$. Obviously this is an idealised quantity.

We can think of $r(t)$ as defined above as giving the average number of spikes occurring between t and $t + \Delta t$, or more formally view $r(t)\Delta t$ as the probability of a spike occurring in

the small interval Δt containing t. The former view gives us a crude method to approximate $r(t)$ from a given spike train: divide the total time interval over which the spike train occurs into intervals of length Δt and count the number of spikes occurring in each interval. The firing rate in a given interval is then given by the number of spikes occurring in that interval, divided by Δt. This gives a graph resembling a histogram. However this is an unsatisfactory method, depending on the position of each interval Δt and only giving discrete values, for instance.

An improvement can be made by sliding an interval or window of width Δt along the spike train, with the spike rate at each point t being given by the number of spikes in the interval $[t, t+\Delta t]$, divided by Δt. If the spikes occur at times t_i, then the rate found in this method is given by

$$r(t) = \sum_i w(t - t_i)$$

where $w(t)$ is the window function

$$w(t) = \begin{cases} \frac{1}{\Delta t} & -\frac{\Delta t}{2} \leq t \leq \frac{\Delta t}{2} \\ 0 & \text{otherwise} \end{cases}$$

i.e. $r(t)$ has no contribution for each i unless $t - t_i$ is within the interval Δt starting at t. Now, we have

$$r(t) = \langle \int_{-\infty}^{\infty} d\tau \, \rho(\tau) w(t - \tau) \rangle$$

where we now consider the firing rate averaged over many trials. This integral is called a linear filter, with w the filter kernel. It also equals the trial-average of the convolution $\rho * w(t)$, where

$$f * g(t) = \int_{-\infty}^{\infty} d\tau \, f(\tau) g(t - \tau)$$

For w we can actually take any function localised near $\tau = 0$ to get an approximate firing rate, for instance a Gaussian $w(\tau) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{\tau^2}{2\sigma^2}\right)$. Note that

$$\int r(t) dt = \langle \int dt \int d\tau \, \rho(\tau) w(t - \tau) \rangle = \langle \int d\tau \, \rho(\tau) \rangle$$

as w is localised and integrates out to one. Hence we see that inside an integral, $r(t)$ and $\langle \rho(t) \rangle$ agree.

3.2 Stimulus and spike-triggered average

We now want to study stimuli $s(t)$. To do so we look at responses - in this case spike times - and see what the stimulus was doing beforehand. This leads to the idea of the spike-triggered average, $C(\tau)$, which gives the average value of the stimulus a time τ before a spike.

It is defined as

$$C(\tau) = \left\langle \frac{1}{n} \sum_{t_i} s(t_i - \tau) \right\rangle \approx \frac{1}{\langle n \rangle} \left\langle \sum_{t_i} s(t_i - \tau) \right\rangle$$

that is, we find the value of the stimulus a time τ before each spike t_i, sum these, and divide by the total number of spikes, as well as averaging over trials (as a consequence of which we assume that $n \approx \langle n \rangle$, i.e. the number of spikes in each trial is roughly equal to the average number of spikes in each trial, over many trials).

We can also write

$$C(\tau) = \frac{1}{\langle n \rangle} \left\langle \sum_{t_i} s(t_i - \tau) \right\rangle = \frac{1}{\langle n \rangle} \int_0^T dt \, \langle \rho(t) \rangle s(t - \tau) = \frac{1}{\langle n \rangle} \int_0^T dt \, r(t) s(t - \tau)$$

as inside an integral $r(t)$ and $\langle \rho(t) \rangle$ coincide. This is similar to the response-stimulus correlation function

$$Q_{rs}(\tau) = \frac{1}{T} \int_0^T dt \, r(t) s(t + \tau)$$

which gives a measure of how much $s(t+\tau)$ depends on $r(t)$. We see that $C(\tau) = \frac{T}{\langle n \rangle} Q_{rs}(-\tau)$.

3.3 Linear filter model

We would also like to develop a method where given some stimulus $s(t)$ we can produce a predicted firing rate $\tilde{r}(t)$ that agrees with the experimentally measured rate $r(t)$ as closely as possible. The starting point is to expand $\tilde{r}(t)$ in powers of the stimulus using a Volterra expansion (the functional equivalent of a Taylor series):

$$\tilde{r}(t) = r_0 + \int_0^\infty d\tau \, s(t - \tau) h(\tau) + \int d\tau_1 d\tau_2 h(\tau_1, \tau_2) s(t - \tau_1) s(t - \tau_2) + \dots$$

where $h(\tau)$ is some weighting function that determines how much the stimulus at $t - \tau$ contributes to $\tilde{r}(t)$. It can be thought of as characterising some property of the neuron that causes spiking.

We will keep only the constant and first order terms of the model, and calculate the function $h(\tau)$ by minimising the error in $\tilde{r}(t)$ i.e. how much it differs from $r(t)$. The error squared is

$$\varepsilon^2 = \int_0^T dt \, (r - \tilde{r})^2$$

and we minimise it with respect to $h(\tau)$ using the functional derivative:

$$\frac{\partial h(\tau')}{\partial h(\tau)} = \delta(\tau' - \tau)$$

As $r(t)$ has no h dependence, we have

$$\frac{\partial \varepsilon^2}{\partial h(\tau)} = - \int dt \, 2(r(t) - \tilde{r}(t)) \frac{\partial \tilde{r}(t)}{\partial h(\tau)}$$

and

$$\frac{\partial \tilde{r}(t)}{\partial h(\tau)} = \frac{\partial}{\partial h(\tau)} \int_0^\infty d\tau'\, s(t-\tau')h(\tau') = \int_0^\infty d\tau'\, s(t-\tau')\frac{\partial h(\tau')}{\partial h(\tau)} = \int_0^\infty d\tau'\, s(t-\tau')\delta(\tau'-\tau) = s(t-\tau)$$

so we get

$$-\frac{1}{2}\frac{\partial \varepsilon^2}{\partial h(\tau)} = \int_0^T dt\, r(t)s(t-\tau) - \int_0^T dt \int_0^\infty d\tau'\, s(t-\tau')h(\tau')s(t-\tau) = 0$$

ignoring the term containing the constant r_0 by assuming $s(t-\tau)$ integrates to zero over the course of the experiment (i.e. the stimulus has zero average). We now let $t-\tau = t'$ in the second integral, obtaining

$$\frac{1}{T}\int_0^T dt\, r(t)s(t-\tau) = \int_0^\infty d\tau' h(\tau')\frac{1}{T}\int dt'\ s(t'+\tau-\tau')s(t') = 0$$

Now on the left-hand side we have a stimulus-response correlation function $Q_{rs}(-\tau)$, while the t' integral on the right-hand side gives a stimulus-stimulus correlation function $Q_{ss}(\tau-\tau')$. So we have the following integral formula for $h(\tau)$:

$$\int d\tau' h(\tau')Q_{ss}(\tau-\tau') = Q_{rs}(-\tau)$$

One way of solving this is to discretise time by letting $\tau = i\Delta t$, then we have

$$Q_{ss}(\tau-\tau') = Q_{ss}([i-j]\Delta t) = Q_{ij}^{ss}$$

which we view as a matrix with entries indexed by i and j. Similarly,

$$h(\tau') = h(j\Delta t) = h_j \qquad Q_{rs}(-\tau) = Q_{rs}(-i\Delta t) = Q_i^{rs}$$

which leads to the following matrix equation

$$Q_{ij}^{ss}h_j = Q_i^{rs}$$

from which we can solve for h_j by inversion. Note that in this discretisation we have $\tilde{r}_k = s_{ki}h_i$ which says that the rate at time $k\Delta t$ is given by a weighted sum over the stimuli at past times $-i\Delta t$.

We can also apply Fourier methods to solve for h, using the fact that the Fourier transform of a convolution $f * g$ equals the product of the Fourier transforms of f and g, as we have $\int d\tau' h(\tau')Q_{ss}(\tau-\tau') = h * Q_{ss}(\tau)$.

A weakness of this linear model is that it gives us no information about the spike times themselves, just the rate. There are also problems related to the matrix inversion - small eigenvalues dominate the inverse, and this increases the amount of noise in the solution. Also the rate $r(t)$ itself depends on the smoothing kernel chosen, so differs from model to model.

4 Poisson processes

One way of obtaining predictions for the spike times is to use Poisson processes. A Poisson process is a statistical model which makes the following assumptions: i) that the occurrences of events are statistically independent, ii) in a sufficiently short length of time δt only one event can occur, and iii) that the probability of exactly one event occurring in the time interval δt is $r\delta t$, i.e. it is proportional to the length of the interval. In the context of spiking, we assume that spikes occur with a rate r and that the timing of one spike has no effect on the timing of any other spike (so we ignore refractory periods and other factors).

The probability distribution for n spikes at times $(t_1, \ldots, t_n)$ in the time interval $[0, T]$ is given by

$$P[(t_1, \ldots, t_n)] = \frac{n!}{T^n} P_T[n]$$

where $P_T[n]$ is the probability that n spikes occur in the time interval $[0, T]$, the $n!$ factor takes into account that there are $n!$ orderings of the spike times and the $1/T^n$ factor arises as given that there is one spike in $[0, T]$ then the probability density for spike time is $p(T) = 1/T$. We calculate $P_T[n]$ using the assumption that spiking follows a Poisson process.

4.1 Homogeneous Poisson process

In the homogeneous Poisson process we assume that the rate r is time-independent. Subdivide $[0, T]$ into M non-overlapping subintervals of length $\delta t = T/M$. The probability of a spike in an interval of length δt is $r\delta t$ and the probability of no spike is $1 - r\delta t$. Hence the probability of n spikes in n intervals is $(r\delta t)^n$ and the probability of no spikes in the remainder is $(1 - r\delta t)^{M-n}$. The number of ways of choosing n intervals from M is given by $\binom{M}{n} = \frac{M!}{n!(M-n)!}$, so

$$P_T[n] = \lim_{M\to\infty} \binom{M}{n} (\delta r)^n (1 - r\delta t)^{M-n} = \lim_{M\to\infty} \frac{M!}{n!(M-n)!} \left(\frac{rT}{M}\right)^n \left(1 - \frac{rT}{M}\right)^{M-n}$$

Now for large M,

$$\frac{M!}{(M-n)!} \frac{1}{M^n} = \frac{(M)(M-1)\ldots(M-n+1)}{M^n} = 1 \cdot \left(1 - \frac{1}{M^n}\right) \ldots \left(1 - \frac{n+1}{M^n}\right) \approx 1$$

and

$$\lim_{M\to\infty} \left(1 - \frac{rT}{M}\right)^{M-n} \approx \lim_{M\to\infty} \left(1 - \frac{rT}{M}\right)^{M} = e^{-rT}$$

so we obtain

$$P_T[n] = \frac{(rT)^n e^{-rT}}{n!}$$

and

$$P[(t_1, \ldots, t_n)] = r^n e^{-rT}$$

We now compute some statistical properties of $P_T[n]$. First, we note that

$$\sum_{n=0}^{\infty} P_T[n] = e^{-rT} \sum_{n=0}^{\infty} \frac{(rT)^n}{n!} = 1$$

as expected. The average number of spikes (in statistics, the first moment) is

$$\begin{aligned}
\langle n \rangle = \sum_{n=0}^{\infty} n P_T[n] &= e^{-rT} \sum_{n=0}^{\infty} n \frac{(rT)^n}{n!} \\
&= e^{-rT} rT \frac{d}{d(rT)} \sum_{n=0}^{\infty} \frac{(rT)^n}{n!} \\
&= e^{-rT} rT \frac{d}{d(rT)} e^{rT} \\
&= rT
\end{aligned}$$

The second moment is

$$\begin{aligned}
\langle n^2 \rangle = \sum_{n=0}^{\infty} n^2 P_T[n] &= e^{-rT} \sum_{n=0}^{\infty} n^2 \frac{(rT)^n}{n!} \\
&= e^{-rT} rT \frac{d}{d(rT)} \sum_{n=0}^{\infty} n \frac{(rT)^n}{n!} \\
&= e^{-rT} rT \frac{d}{d(rT)} (rT e^r T) \\
&= e^{-rT} rT (e^{rT} + rT e^{rT}) \\
&= rT + (rT)^2
\end{aligned}$$

so the standard deviation is

$$\sigma^2 = \langle n^2 \rangle - \langle n \rangle^2 = rT$$

The Fano factor is the ratio of the standard deviation to the mean:

$$\frac{\sigma^2}{\langle n \rangle} = 1$$

Experimentally we fit data to $\sigma^2 = \alpha \langle n \rangle^\beta$, and find $\alpha \simeq 1 - 1.5$, $\beta \simeq 1 - 1.5$.

4.2 Inhomogeneous Poisson process

The inhomogeneous Poisson process allows for the spike rate to have time dependence. The probability of a spike between t and $t+\delta t$ is given by $\int_t^{t+\delta t} r(t) dt$, and we assume that the probability of a spike at time t only depends on $r(t)$. To derive the probability distribution

in this case, consider two consecutive spikes at t_i, t_{i+1} and divide the time interval $[t_i, t_{i+1}]$ into M subintervals. The probability of a spike in the mth subinterval is

$$\int_{t_i+m\delta t}^{t_i+(m+1)\delta t} r(t)dt$$

and the probability of no spike is

$$1 - \int_{t_i+m\delta t}^{t_i+(m+1)\delta t} r(t)dt$$

Thus the probability of no spike in $[t_i, t_{i+1}]$ is

$$\prod_{m=0}^{M-1} \left(1 - \int_{t_i+m\delta t}^{t_i+(m+1)\delta t} r(t)dt\right)$$

The log of the probability is

$$\sum \log\left(1 - \int_{t_i+m\delta t}^{t_i+(m+1)\delta t} r(t)dt\right) \approx -\sum \int_{t_i+m\delta t}^{t_i+(m+1)\delta t} r(t)dt = -\int_{t_i}^{t_{i+1}} r(t)dt$$

Taking into account the intervals before and after the last spike, the total probability distribution is then given by

$$\exp\left(-\int_0^{t_1} r(t)dt\right) \prod_{i=1}^{n-1} r(t_i) \exp\left(-\int_{t_i}^{t_{i+1}} r(t)dt\right) r(t_n) \exp\left(-\int_{t_n}^{T} r(t)dt\right)$$

i.e. by the product of the probabilities of a spike $r(t_i)$ where there are spikes with the product of the probabilities of no spikes when there aren't. It's easy to see we then find

$$P[(t_1, \ldots, t_n)] = \prod_{i=1}^{n} r(t_i) \exp\left(-\int_0^T r(t)dt\right)$$

5 Plasticity

Plasticity refers to long-term changes to synapses, usually to strength (i.e. amplitude of post-synaptic potential) or efficiency. It is important as it is believed to be the mechanism supporting long-term memory and learning. An increase in synaptic strength is called long-term potentiation (LTP) while a decrease is called long-term depression (LTD).

Hebb's law states that if input from neuron A often contributes to the firing of neuron B then the synapse from A to B should be strengthened. A similar statement is that neurons that fire together wire together. Note that Hebb's law is not stable, as it naturally leads to positive feedback. A possible solution to this is to use the idea of synaptic competition: the summed strength of all synapses in some area is fixed.

A simple model of plasticity involves a neuron with firing rate v and N inputs u_i with weights w_i so that the total input is $\sum_{i=1}^{N} w_i u_i = \vec{w} \cdot \vec{u}$. The weights w_i can be either positive (representing excitatory synapses) or negative (representing inhibitory synapses). As v and the u_i are firing rates they should be positive, but we ignore this in the model. The equation governing v is

$$\tau_r \frac{dv}{dt} = -v + \vec{w} \cdot \vec{u}$$

and we model plasticity using

$$\tau_w \frac{d\vec{w}}{dt} = v\vec{u}$$

which tells us that if v and u_i are both large, w_i grows. If we average over timescales in between $\tau_r \simeq 10 - 100$ms and $\tau_w \simeq 1$ day we can put $\langle v \rangle = \vec{w} \cdot \vec{u}$ as this represents the steady state solution to the equation for v, and our equation is

$$\tau_w \frac{dw_i}{dt} = \langle \vec{w} \cdot \vec{u} u_i \rangle \approx \sum_j \langle u_j u_i \rangle w_j$$

as $\vec{w}$ changes on a larger timescale. We define the correlation matrix $Q_{ij} = \langle u_i u_j \rangle$ and this becomes

$$\tau_w \frac{d\vec{w}}{dt} = Q\vec{w}$$

Note that this model leads only to LTP. To make it more realistic we add a threshold either as

$$\tau_w \frac{d\vec{w}}{dt} = (v - \theta_v)\vec{u}$$

or

$$\tau_w \frac{d\vec{w}}{dt} = v(\vec{u} - \vec{\theta}_u)$$

so that in the first case we need $v > \theta_v$ for LTP and in the second we need $u_i > (\theta_u)_i$. Upon averaging and setting $v = \vec{w} \cdot \vec{u}$ again we find

$$\tau_w \frac{d\vec{w}}{dt} = \langle \vec{u} \cdot \vec{w} \, (\vec{u} - \vec{\theta}_u) \rangle$$

It is convenient to take $\vec{\theta_v} = \langle \vec{u} \rangle$, i.e. the average value of input over the averaging period. Then

$$\tau_w \frac{d\vec{w}}{dt} = \langle \vec{u} \cdot \vec{w} \, (\vec{u} - \langle \vec{u} \rangle) \rangle$$

or

$$\tau_w \frac{dw_i}{dt} = (\langle u_i u_j \rangle - \langle u_i \rangle \langle u_j \rangle) w_j$$

with the covariance matrix (a multivariable standard derivative)

$$C_{ij} = \langle u_i u_j \rangle - \langle u_i \rangle \langle u_j \rangle$$

or

$$C = \langle (\vec{u} - \langle \vec{u} \rangle) \vec{u} \rangle$$