MATH 6397 Homework 3

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November 1, 2020

1. We will derive the Fokker-Planck equation for the membrane potential distribution under excitatory input. Suppose the input rate of pre-synaptic neuron k at time t is $\nu_k(t)$ with weight w_k. We start with the transition probability moving from state u' to u in time t to $t+\Delta t$,

$$P^{trans}\left(u,t+\Delta t\,\middle|\,u',t\right) = \left[1-\Delta t\sum_k \nu_k(t)\right]\delta\left(u-u'e^{-\Delta t/\tau_m}\right)+\Delta t\sum_k \nu_k(t)\delta\left(u-u'e^{-\Delta t/\tau_m}-w_k\right).$$

The Kolmogorov forward equation gives $P(u,t+\Delta t) = \int P^{trans}(u,t+\Delta t\,|u',t)\,P(u',t)\,du'$. Putting this into context, we have

$$\begin{aligned}
P(u,t+\Delta t) &= \int\left\{\left[1-\Delta t\sum_k \nu_k(t)\right]\delta\left(u-u'e^{-\Delta t/\tau_m}\right)+\Delta t\sum_k \nu_k(t)\delta\left(u-u'e^{-\Delta t/\tau_m}-w_k\right)\right\}P(u',t)\,du' \\
&= \left[1-\Delta t\sum_k \nu_k(t)\right]\int\delta\left(u-u'e^{-\Delta t/\tau_m}\right)P(u',t)\,du'+\Delta t\sum_k \nu_k(t)\int\delta\left(u-u'e^{-\Delta t/\tau_m}-w_k\right)P(u',t)\,du'
\end{aligned}$$

We have that

$$\begin{aligned}
\int\delta\left(u-u'e^{-\Delta t/\tau_m}\right)P(u',t)\,du' &= \int\delta\left[-e^{-\Delta t/\tau_m}\left(u'-ue^{\Delta t/\tau_m}\right)\right]P(u',t)\,du' \\
&= \left|-e^{\Delta t/\tau_m}\right|\int\delta\left(u'-ue^{\Delta t/\tau_m}\right)P(u',t)\,du' \\
&= e^{\Delta t/\tau_m}P\left(ue^{\Delta t/\tau_m},t\right)
\end{aligned}$$

and

$$\begin{aligned}
\int\delta\left(u-u'e^{-\Delta t/\tau_m}-w_k\right)P(u',t)\,du' &= \int\delta\left[-e^{-\Delta t/\tau_m}\left(u'-(u-w_k)\,e^{\Delta t/\tau_m}\right)\right]P(u',t)\,du' \\
&= \left|-e^{\Delta t/\tau_m}\right|\int\delta\left(u'-(u-w_k)\,e^{\Delta t/\tau_m}\right)P(u',t)\,du' \\
&= e^{\Delta t/\tau_m}P\left(e^{\Delta t/\tau_m}(u-w_k),t\right)
\end{aligned}$$

Applying these simplifications to $P(u,t+\Delta t)$, we have

$$\begin{aligned}
P(u,t+\Delta t) &= \left[1-\Delta t\sum_k \nu_k(t)\right]e^{\Delta t/\tau_m}P\left(e^{\Delta t/\tau_m}u,t\right)+\Delta t\sum_k \nu_k(t)e^{\Delta t/\tau_m}P\left(e^{\Delta t/\tau_m}(u-w_k),t\right) \\
&= e^{\Delta t/\tau_m}\left\{P\left(e^{\Delta t/\tau_m}u,t\right)+\Delta t\sum_k \nu_k(t)\left[-P\left(e^{\Delta t/\tau_m}u,t\right)+P\left(e^{\Delta t/\tau_m}(u-w_k),t\right)\right]\right\}
\end{aligned}$$

We now expand this expression about $\Delta t=0$ and truncate all terms with powers of Δt higher than 1. We use the following truncated expansions.

- $e^{\Delta t/\tau_m} \approx 1 + \frac{\Delta t}{\tau_m}$
- $P\left(e^{\Delta t/\tau_m} u, t\right) \approx P(u,t) + \dfrac{u\Delta t}{\tau_m}\dfrac{\partial P(u,t)}{\partial u}$
- $P\left(e^{\Delta t/\tau_m}(u - w_k), t\right) \approx P(u - w_k, t) + \dfrac{(u - w_k)\Delta t}{\tau_m}\dfrac{\partial P(u,t)}{\partial u}$

We put things together, and again truncate powers of Δt higher than 1 to have

$$\begin{aligned}
P(u,t+\Delta t) \approx \left(1 + \frac{\Delta t}{\tau_m}\right)\Bigg\{ & P(u,t) + \frac{u\Delta t}{\tau_m}\frac{\partial P(u,t)}{\partial u} \\
& + \Delta t \sum_k \nu_k(t)\left[-P(u,t) - \frac{u\Delta t}{\tau_m}\frac{\partial P(u,t)}{\partial u} + P(u - w_k, t) + \frac{(u - w_k)\Delta t}{\tau_m}\frac{\partial P(u,t)}{\partial u}\right]\Bigg\} \\
\approx & P(u,t) + \frac{\Delta t}{\tau_m}P(u,t) + \frac{u\Delta t}{\tau_m}\frac{\partial P(u,t)}{\partial u} + \Delta t \sum_k \nu_k(t)\left[P(u - w_k, t) - P(u,t)\right]
\end{aligned}$$

We now have

$$\begin{aligned}
P(u,t+\Delta t) - P(u,t) &= \frac{\Delta t}{\tau_m}P(u,t) + \frac{u\Delta t}{\tau_m}\frac{\partial P(u,t)}{\partial u} + \Delta t \sum_k \nu_k(t)\left[P(u - w_k, t) - P(u,t)\right] \\
\frac{P(u,t+\Delta t) - P(u,t)}{\Delta t} &= \frac{1}{\tau_m}P(u,t) + \frac{u}{\tau_m}\frac{\partial P(u,t)}{\partial u} + \sum_k \nu_k(t)\left[P(u - w_k, t) - P(u,t)\right]
\end{aligned}$$

Again, we do an expansion but this time in w_k. For this we need the truncated expansion

$$P(u - w_k, t) \approx P(u,t) - w_k\frac{\partial P(u,t)}{\partial u} + \frac{w_k{}^2}{2}\frac{\partial^2 P(u,t)}{\partial u^2}.$$

Substitution yields

$$\begin{aligned}
\frac{P(u,t+\Delta t) - P(u,t)}{\Delta t} &= \frac{1}{\tau_m}P(u,t) + \frac{u}{\tau_m}\frac{\partial P(u,t)}{\partial u} + \sum_k \nu_k(t)\left[-w_k\frac{\partial P(u,t)}{\partial u} + \frac{w_k{}^2}{2}\frac{\partial^2 P(u,t)}{\partial u^2}\right] \\
&= \frac{1}{\tau_m}P(u,t) + \frac{\partial P(u,t)}{\partial u}\left(\frac{u}{\tau_m} - \sum_k \nu_k(t)\, w_k\right) + \frac{1}{2}\sum_k \nu_k(t)\, w_k{}^2\frac{\partial^2 P(u,t)}{\partial u^2}.
\end{aligned}$$

Taking $\Delta t \to 0$, we therefore have

$$\begin{aligned}
\tau_m\frac{\partial P(u,t)}{\partial t} &= P(u,t) + \frac{\partial P(u,t)}{\partial u}\left(u - \tau_m\sum_k \nu_k(t)\, w_k\right) + \frac{\tau_m}{2}\sum_k \nu_k(t)\, w_k{}^2\frac{\partial^2 P(u,t)}{\partial u^2} \\
&= -\frac{\partial}{\partial u}\left[\left(-u + \tau_m\sum_k \nu_k(t)\, w_k\right)P(u,t)\right] + \frac{\tau_m}{2}\sum_k \nu_k(t)\, w_k{}^2\frac{\partial^2 P(u,t)}{\partial u^2}
\end{aligned}$$

as desired.

First, we verify that for a constant input, at $t \to \infty$, the Gaussian density with mean RI_0 and variance $\sigma/\sqrt{2}$ is a solution of the Fokker-Planck equation. Note that at $t \to \infty$, we have $\dfrac{\partial P(u,\infty)}{\partial t} = 0$. Hence, we only have to show that the right-hand side of the equation sums up to zero.

$$-\frac{\partial}{\partial u}\left[\left(-u + \tau_m\sum_k \nu_k w_k\right)P(u,\infty)\right] = P(u,\infty) + \frac{\partial P}{\partial u}(u - RI_0)$$

and

$$\frac{\tau_m}{2}\sum_k \nu_k {w_k}^2 \frac{\partial^2 P}{\partial u^2} = \frac{1}{2}\sigma^2 \frac{\partial}{\partial u}\left[\frac{1}{\sqrt{\pi}\sigma}\exp\left(-\frac{(u-RI_0)^2}{\sigma^2}\right)\left(-\frac{2(u-RI_0)}{\sigma^2}\right)\right]$$
$$= \frac{1}{2}\sigma^2 \frac{\partial}{\partial u}\left[P(u,\infty)\left(-\frac{2(u-RI_0)}{\sigma^2}\right)\right] = -\frac{\partial}{\partial u}\left[P(u,\infty)(u-RI_0)\right]$$
$$= -\frac{\partial P}{\partial u}(u-RI_0) - P(u,\infty)$$

Combining this two make up he right-hand side of the Fokker-Planck equation which is now clearly zero.

Consider a leaky integrate and fire neuron with Poisson input without threshold. Suppose that there is a single pre-synaptic neuron so that the input rate is $\nu = 5$, synaptic weight is $w = 1$, and membrane time constant is $\tau_m = 1$. With this, we have $RI_0 = \tau_m \nu w = 5$ and $\sigma^2 = \tau_m \nu w^2 = 5$. A simulation of such a neuron, up to time $T = 1000$ ms, is found in Figure 1.

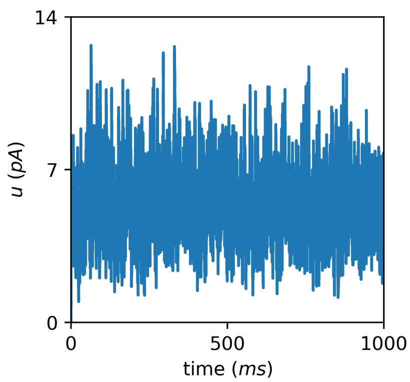

Figure 1: Simulation of a leaky integrate and fire model without threshold.

As given in Eq. 8.46, after a long observation time, the membrane potential follows a Gaussian distribution with mean RI_0 and variance $\sigma\sqrt{2}$. To verify this, we use the simulation above and sample the membrane potential trajectory at 100,000 time points and compare the resulting histogram to the analytic predicton. We see in Figure 2 that indeed this is the case.

2. Consider a leaky integrate and fire neuron with Poisson input with threshold $\theta = 5$. Suppose that there is a single pre-synaptic neuron so that the input rate is $\nu = 5$, synaptic weight is $w = 1$, and membrane time constant is $\tau_m = 1$. With this, we have $RI_0 = \tau_m \nu w = 5$ and $\sigma^2 = \tau_m \nu w^2 = 5$. Given that the resting potential is $u_{rest} = 0$, the analytic prediction for the expected time to firing, $T(x)$ is the solution of the differential equation $A(x)\partial_x T(x) + 0.5B(x)\partial_x T(x) = -1$, with the initial conditions $T(a \to \infty) = 0$ and $T(5) = 0$. If we assume that both $A(x)$ and $B(x)$ are constant, and assign $A(x) = RI_0$ and $B(x) = \sigma^2$, the solution of the ODE is given by

$$T(x,a) == -\frac{e^{-2a}(-a+b)}{5(-e^{-2a}+e^{-2b})} + \frac{a}{5} + \frac{e^{-2x}(-a+b)}{5(-e^{-2a}+e^{-2b})} - \frac{t}{5}.$$

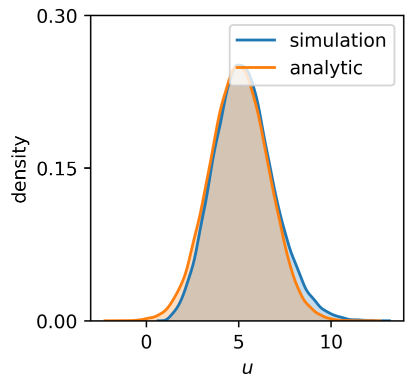

Figure 2: A comparison of the analytic prediction of the distribution of membrane potential and simulated values.

It we start at u_{rest}, then $\langle T(u_{rest})\rangle = \lim_{a\to-\infty} T(u_{rest}) = \lim_{a\to-\infty} T(0) = 1$ ms. All these computations were done in MATLAB. Empirical results show that the mean passage time is around 2 ms, as seen in Figure 3.

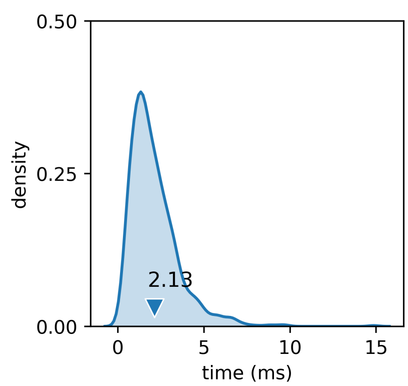

Figure 3: Distribution of passage time at threshold.

3. Suppose inter-arrival times X of spikes follow a gamma distribution $\Gamma(\alpha,\beta)$, α being the shape parameter, and β the rate. Then $E[X] = \dfrac{\alpha}{\beta}$ and $Var[X] = \dfrac{\alpha}{\beta^2}$. It follows that the coefficient of variation is $CV = \dfrac{\sqrt{Var[X]}}{E[X]} = \dfrac{1}{\sqrt{\alpha}}$.

   A special case of the gamma distribution is the Erlang distribution where the shape parameter α is a positive integer. We parametrize the Erlang distribution with the shape parameter k and rate parameter λ. Given X following the Erlang distribution, we have that $E[X] = \dfrac{k}{\lambda}$ and $Var[X] = \dfrac{k}{\lambda^2}$. It follows that the coefficient of variation is $CV = \dfrac{\sqrt{Var[X]}}{E[X]} = \dfrac{1}{\sqrt{k}}$.

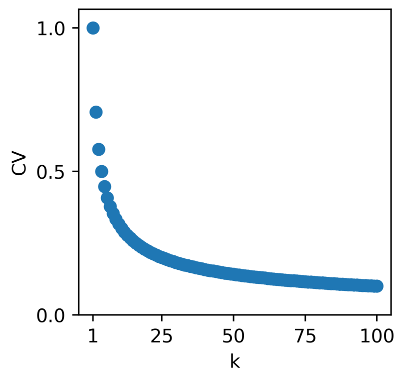

Figure 4: Coefficient of variation of an Erlang distributed random variable given increasing values of the shape parameter k.

As seem in Figure 4, increasing the parameter k decreases the CV. This means that as the number of exponential random variable summands increase, the variation around the resulting mean decreases.

4. We will derive the Fokker-Planck equation corresponding to the haploid Moran model with mutation. The are are two alleles, a and A, with a single locus. The rate of mutation from a to A is given by u, and from A to a is ν. Suppose that the total population is N and that $u, \nu \in O\left(\frac{1}{N}\right)$. Given the population n of allele a, we do the substution $x = \frac{n}{N}$. First, we setup the following transition probabilities.

$$
\begin{aligned}
T\left(x \middle| x+\frac{1}{N}\right) &= (1-v)\left(x+\frac{1}{N}\right)\left(1-x-\frac{1}{N}\right)+u\left(x+\frac{1}{N}\right)^2 \\
T\left(x \middle| x-\frac{1}{N}\right) &= (1-u)\left(1-x+\frac{1}{N}\right)\left(x-\frac{1}{N}\right)+\nu\left(1-x+\frac{1}{N}\right)^2 \\
T\left(x+\frac{1}{N}|x\right) &= (1-u)(1-x)x+\nu(1-x)^2 \\
T\left(x-\frac{1}{N}|x\right) &= (1-v)x(1-x)+ux^2
\end{aligned}
$$

We also need the following Taylor expansions of P.

$$
\begin{aligned}
P\left(x+\frac{1}{N},t\right) &= P(x,t)+\frac{1}{N}\frac{\partial P}{\partial x}+\frac{1}{2N^2}\frac{\partial^2 P}{\partial x^2}+O\left(\frac{1}{N^3}\right) \\
P\left(x-\frac{1}{N},t\right) &= P(x,t)-\frac{1}{N}\frac{\partial P}{\partial x}+\frac{1}{2N^2}\frac{\partial^2 P}{\partial x^2}+O\left(\frac{1}{N^3}\right)
\end{aligned}
$$

Putting things together, we have

$$\begin{aligned}
\frac{\partial P(x,t)}{\partial t} =& T\left(x\middle|x+\frac{1}{N}\right)P\left(x+\frac{1}{N},t\right)+T\left(x\middle|x-\frac{1}{N}\right)P\left(x-\frac{1}{N},t\right)-P(x,t)\left[T\left(x+\frac{1}{N}|x\right)+T\left(x-\frac{1}{N}|x\right)\right]\\
=&\left\{(1-v)\left(x+\frac{1}{N}\right)\left(1-x-\frac{1}{N}\right)+u\left(x+\frac{1}{N}\right)^2\right\}\left[P(x,t)+\frac{1}{N}\frac{\partial P}{\partial x}+\frac{1}{2N^2}\frac{\partial^2 P}{\partial x^2}\right]\\
&+\left\{(1-u)\left(1-x+\frac{1}{N}\right)\left(x-\frac{1}{N}\right)+v\left(1-x+\frac{1}{N}\right)^2\right\}\left[P(x,t)-\frac{1}{N}\frac{\partial P}{\partial x}+\frac{1}{2N^2}\frac{\partial^2 P}{\partial x^2}\right]\\
&-\left[(1-u)(1-x)x+v(1-x)^2+(1-v)x(1-x)+ux^2\right]P(x,t)+O\left(\frac{1}{N^3}\right)\\
=&\frac{1}{N^2}\left\{\frac{\partial P}{\partial x}(2-u-3v-4x+4ux-4vx)+2P(u+v-1)+\frac{\partial^2 P}{\partial x^2}\left(\frac{u}{2}+x-x^2-\frac{ux}{2}-\frac{3vx}{2}+ux^2+vx^2\right)\right\}\\
&+\frac{1}{N}\left\{\frac{\partial P}{\partial x}(ux+vx-v)+P(u+v)\right\}+O\left(\frac{1}{N^3}\right)
\end{aligned}$$

Since $u,v\in O\left(\frac{1}{N}\right)$, we have $\frac{u}{N^2},\frac{v}{N^2}\in O\left(\frac{1}{N^3}\right)$. The above equation now simplifies to

$$\frac{\partial P}{\partial t}=\frac{1}{N^2}\left\{\frac{\partial^2 P}{\partial x^2}\left(x-x^2\right)+\frac{\partial P}{\partial x}(2-4x)-2P\right\}+\frac{1}{N}\left\{\frac{\partial P}{\partial x}(ux+vx-v)+P(u+v)\right\}+O\left(\frac{1}{N^3}\right)$$

After removing the $O\left(\frac{1}{N^3}\right)$ term, a simple expansion will verify that the above is equivalent to

$$\frac{\partial P}{\partial t}=\frac{1}{N}\frac{\partial}{\partial x}\left[(ux-v(1-x))P\right]+\frac{1}{N^2}\frac{\partial^2}{\partial x^2}\left[x(1-x)P\right]$$

as required.

5. Here we simulate a two-step adaptation process and track the number of individuals with genotypes 1, 2, and 3, which we will denote by n_1, n_2, and n_3. Suppose that at any given time $n_1+n_2+n_3=N$. Also, assume that genotype 1 mutates to genotype 2 with rate μ_{12} and genotype 2 mutates to genotype 3 with rate μ_{23}. Given these mutation rates, the transition probabilities are given by

$$\begin{aligned}
P(n_1+1,n_2-1,n_3|n_1,n_2,n_3) &= (1-\mu_{12})\left(\frac{n_1}{N}\right)\left(\frac{n_2}{N}\right)\\
P(n_1+1,n_2,n_3-1|n_1,n_2,n_3) &= (1-\mu_{12})\left(\frac{n_1}{N}\right)\left(\frac{n_3}{N}\right)\\
P(n_1-1,n_2+1,n_3|n_1,n_2,n_3) &= (1-\mu_{23})\left(\frac{n_2}{N}\right)\left(\frac{n_1}{N}\right)+\mu_{12}\left(\frac{n_1}{N}\right)\left(\frac{n_1}{N}\right)\\
P(n_1-1,n_2,n_3+1|n_1,n_2,n_3) &= \left(\frac{n_3}{N}\right)\left(\frac{n_1}{N}\right)\\
P(n_1,n_2+1,n_3-1|n_1,n_2,n_3) &= (1-\mu_{23})\left(\frac{n_2}{N}\right)\left(\frac{n_3}{N}\right)\\
P(n_1,n_2-1,n_3+1|n_1,n_2,n_3) &= \left(\frac{n_3}{N}\right)\left(\frac{n_2}{N}\right)+\mu_{23}\left(\frac{n_2}{N}\right)\left(\frac{n_2}{N}\right)
\end{aligned}$$

Taking $N=1000$ and $\mu_{12}=\mu_{23}=\mu$, with different mutation rates, we perform 3000 simulations of this process, and record the time when the first individual with genotype 3 arrives. The distribution of the arrival times is presented in Figure 5 and a comparison of the mean arrival time and expected arrival time when $\mu \ll \frac{1}{N^2}$ is seen in Table 1. A quick look shows that the actual mean arrival times are far larger than expectation. This may in fact be due to the fact that for all the considered cases, μ is not significantly less than $\frac{1}{N^2} = 0.000001$.

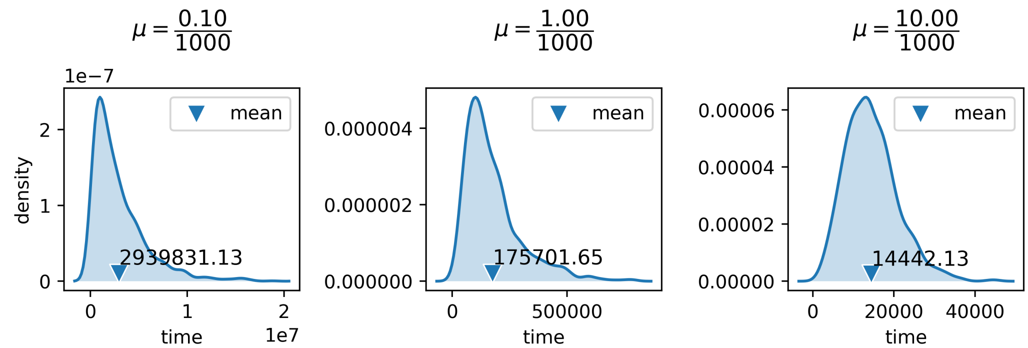

Figure 5: Distribution of time to first arrival of an individual with genotype 3 given different rates μ.

	empirical mean	$\frac{1}{\mu}$
$\mu = 0.1/N$	2,939,831	10,000
$\mu = 1/N$	175,701	1,000
$\mu = 10/N$	14,442	100

Table 1: Comparison of the mean time of arrival of the first individual with genotype 3 and the expected time $\frac{1}{\mu}$.