Lesson 12
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12 Noise, balanced feedback networks, synaptic scaling, and linear response. Part 1

12.1 Variance versus mean driven spiking

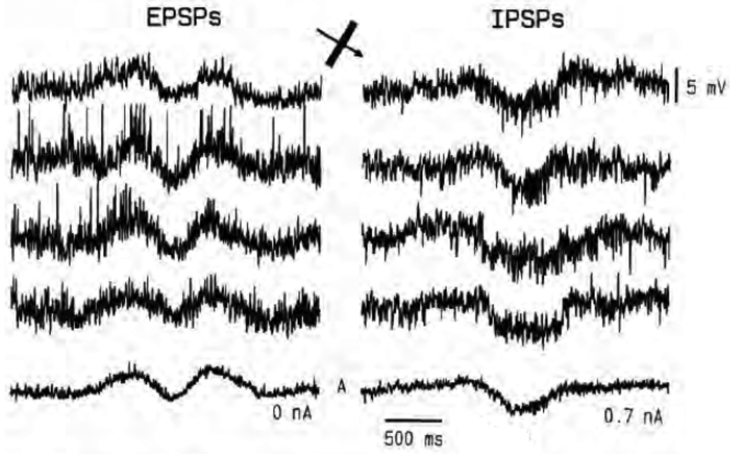
Up to now we have considered driving neuronal by a change in the mean level of the input. We showed that pulse of current will drive a neuron to fire and we even showed back in Lesson One (Figure 8) that a an inhibitory pulse followed by an excitatory pulse is most effective in initiating a spike. We now expand our horizons and, in anticipation of a discussion of neuronal variability, consider how noise, or fluctuations in voltage, can drive a neuron to spike.

Recall that noise has a zero mean value and is specified in terms of its range by the standard deviation or root-mean square value, denoted σ. We are concerned with noise on the scale of synaptic postsynaptic potentials, which sets the scale at 0.2 mV to 2 mV. The later number is similar to what we found in Lesson Eleven for the transition from an inactive Na^+ current to a spike. In fact, intracellular measurements reveal an interesting fact. The postsynaptic potential is rapidly fluctuating with amplitudes of a few millivolts (Figure 1). This is surprising at first glance as neurons are believe to average over many inputs and thus one might imagine that the noise averages away; a Central Limit theorem arguments. But noise prevails, and as expected for a noisy subthreshold potential, the neuronal response to repeated presents of the same stimulus leads to a variable response (Figure 2).

12.1.1 Can noise alone can drive spiking?

Before we consider a mechanism for this noise, it is worth asking asking if noise alone can drive spiking? The answer is yes. When the average input to the neuron is well above threshold, the spiking is primarily driven by changes in the mean rate. But when the average input is held close to threshold, or just below threshold, fluctuations will drive the neuron to spike (Figure 3). In fact, the spike rate of the neurons can be a monotonic function of the standard deviation of the input (Figure 4).

Figure 1: The excitatory and inhibitory postsynapic potentials for a neurons on primary visual cortex of cat. From Ferster 1988



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How do we interpret the mean and variance in terms of spike probability? We use the approximation of neuronal output as a Bernouli, i.e., $V = 1$ if the cell spikes and $V = 0$ if it does not. In the absence of noise the transition for 0 to 1 is sharp at $\mu = \theta$. How does the average probability of spiking smear when the variance is non-zero? The simplest possibility is to assume a Gaussian amplitude distribution, as we did in the study of the capacity of the Hopfield model (Lesson Two), so that

$$\begin{aligned} m(t) &= \frac{1}{\sqrt{2\pi}\sigma} \int_{\theta}^{\infty} dx \; e^{-\frac{(x-\mu)^2}{2\sigma^2}} \\ &= \frac{1}{\sqrt{\pi}} \int_{-\infty}^{\frac{\mu-\theta}{\sqrt{2}\sigma}} dx \; e^{-x^2} \\ &= \frac{1 + \text{erf}\left[\frac{\mu-\theta}{\sqrt{2}\ \sigma}\right]}{2}. \end{aligned} \tag{12.1}$$

When σ is small compared to $\mu - \theta$, the transition from $m(t) = 0$ to $m(t) = 1$ is weakly smoothed (Figure), with

$$m(t) \quad \overrightarrow{\sigma \ll \mu - \theta} \quad 1 - \frac{\sigma}{\sqrt{2\pi}(\mu - \theta)} e^{-\frac{(\mu-\theta)^2}{2\sigma^2}}. \tag{12.2}$$

When σ is large compared to $\mu - \theta$, the transition from $m(t) = 0$ to $m(t) = 1$ is completely smoothed with

$$m(t) \quad \overrightarrow{\sigma \gg \mu - \theta} \quad \frac{1}{2}. \tag{12.3}$$

The interesting issue for us is to have a fixed input and vary the noise. We see, numerically, that the spike rate increases monotonically with increasing values of σ to a saturation value of $m = 0.5$. Most interestingly, there is a roughly linear region of increase for mean rates between $m = 0.05$ and $m = 0.25$.

Figure 2: Variability in spike rate with repeated presentation of the same visual random dot pattern. Data from monkey. From Shadlen and Newsome 1998

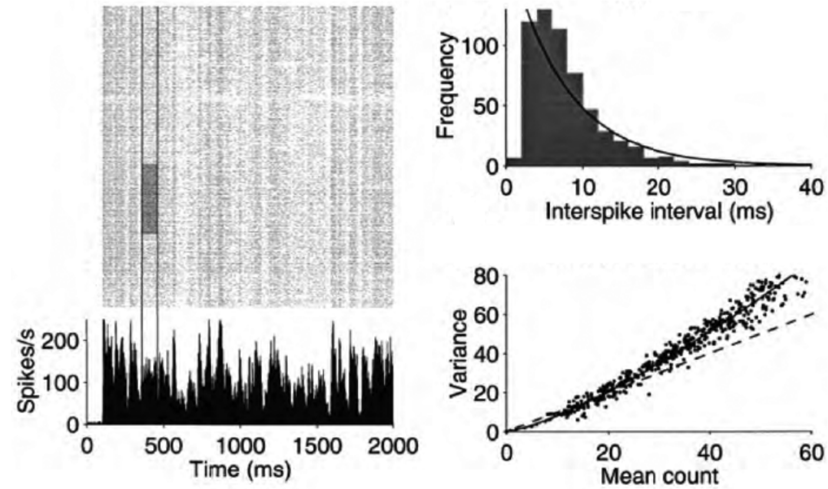

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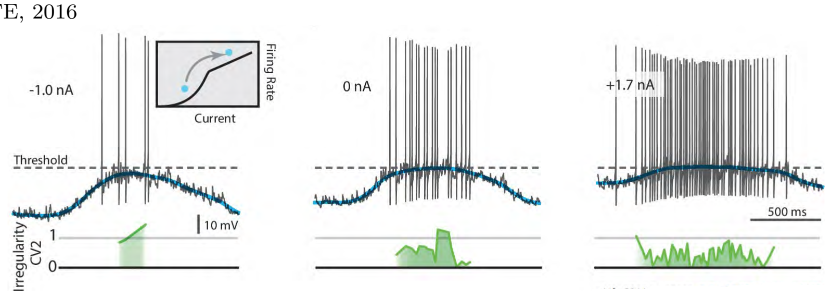
Figure 3: Mean versus noise driven spiking in spinal cord slice. From Petersen and Berg, eLIFE, 2016



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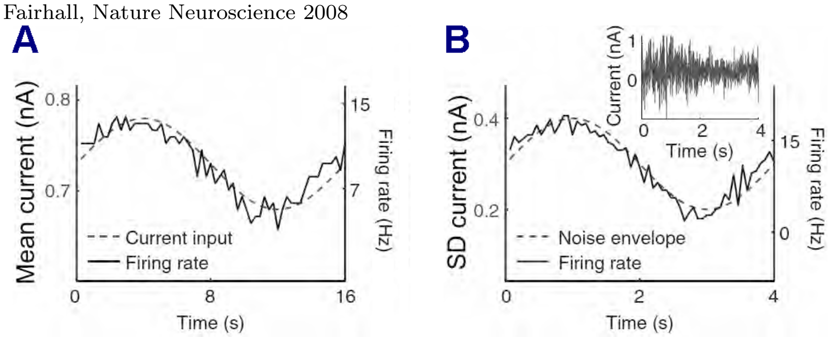
12.2 Variability for a single cell

One might expect that the subthreshold potential would be noisy, if there were relatively few synaptic inputs. This is consistent with the notion of a few strong inputs that one sees in cortical slice experiments. Another possibility is that the subthreshold potential is so noisy because large excitatory inputs are offset by large inhibitory inputs, so that their mean value just about cancels but the variances, of course, add (Figure 6). The notion of large offsetting currents comes from the intracellular recording experiments initially in anesthetized animals (Figure 1) and more recently in awake animals (Figure 7). In general, excitatory and inhibitory inputs are found to be both large and have the same sensory receptive fields or ”tuning curves”, so that their inputs act to balance each other, although this balance is not necessarily exact (Figure 8).

What is gained from this organization of offsetting currents? A transient increase in excitatory input, as may occur with a large

Figure 4: Mean versus noise driven spiking in brain slice. From Lundstrom, Higgs, Spain and Fairhall, Nature Neuroscience 2008



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burst of excitatory input, will rapidly depolarize the cell. So networks with balanced excitatory and inhibitory inputs, which mean large conductances, are believed to trade noise from the balance for the speed gained from a large total leak conductance. We shall see

12.2.1 Weak synaptic inputs

Let's start with a warm up on the scale of noise in the input. We use a rate model. First, some definitions, The input to cell i from cell j is W_{ij} with $j = 1, 2, \ldots, N$, while the output of the neuron is take as taken as V_i with $i = 1, 2, \ldots, N$ where $V = \frac{1}{2}(S+1)$ is a Bernouli variable with $V = 1$ if the cell spikes and $V = 0$ if it does not.

A Bernouli probability distribution of the random variable V can be thought of as a model for the set of possible outcomes of any single measurement whose outcomes is Boolean-valued. The Bernoulli distribution is a special case of the binomial distribution where a single trial is conducted, i.e., $N = 1$ for such a binomial distribution. Let's define the probability that a cell is spiking as m, so that $V = 1$ with probability m and $V = 0$ with probability $1 - m$.

The input to the $i - th$ neuron, denoted as in the past by $\mu_i(t)$, is:

$$\mu_i(t) \equiv \sum_{j=1}^{N} W_{ij} V_j(t). \tag{12.4}$$

The standard thermodynamic scaling, so that total synaptic currents are bounded as the size of the system increases, is that each input has a strength of order $1/N$. For simplicity, let's take all of the inputs to be equal, so

$$W_{ij} \rightarrow \frac{W_o}{N}. \tag{12.5}$$

Figure 5: Gaussian noise threshold model to estimate effect of noise in driving neuronal responses

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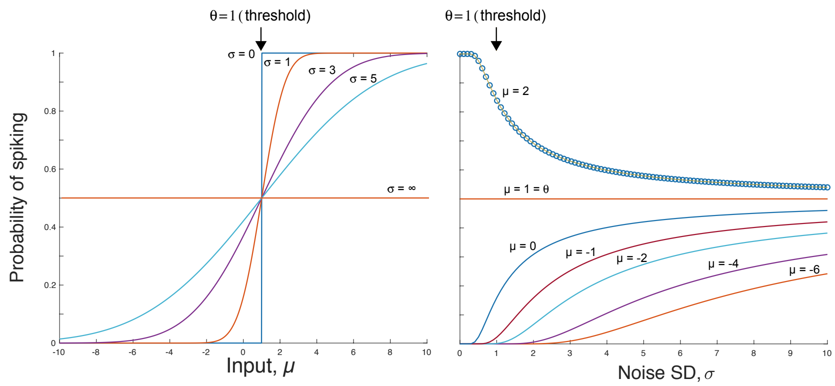


The W_o are of order 1 in magnitude, so the sum over all N inputs is of order 1, with

$$\begin{aligned} \mu_i(t) &= W_o \frac{1}{N} \sum_{j=1}^{N} V_j(t) \\ &= W_o \, m(t) \end{aligned} \tag{12.6}$$

where $m(t)$ is the average across the network, i.e.,

$$m(t) \equiv \frac{1}{N} \sum_{j=1}^{N} V_j(t) \tag{12.7}$$

and is of order 1. Clearly, for constant connection strengths, the input to all neurons is equal so the population average is

$$\begin{aligned} \mu_i(t) &\equiv \frac{1}{N} \sum_{j=1}^{N} \mu_j(t) \\ &\equiv \frac{1}{N} \sum_{j=1}^{N} W_o m(t) \\ &= W_o \, m(t) \; \forall \, i \end{aligned} \tag{12.8}$$

Figure 6: Balanced excitatory and inhibitory currents can lead to noisy input currents; calculated consequences of tight versus loose balance of excitatory and inhibitory currents. From Denuve and Machens 2016.

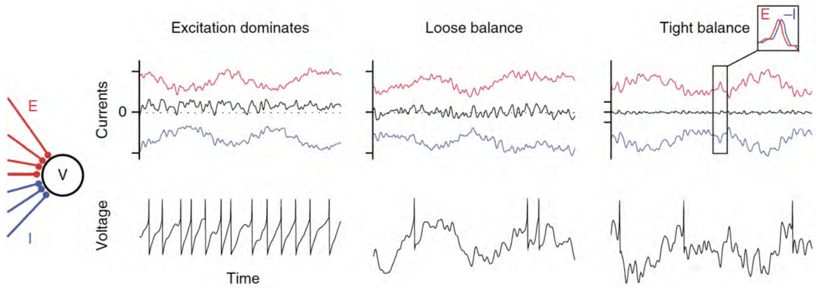
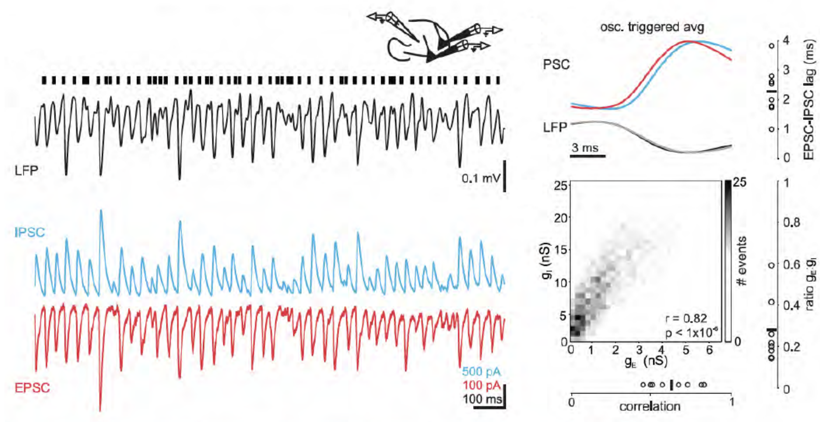


Figure 7: Balanced currents are observed in vivo in terms of balance of the gamma rhythm. From Atallah and Scanziani 2009.



and the time average is

$$\begin{aligned} \langle \mu \rangle &\equiv \frac{1}{T} \int_{-T/2}^{T/2} dt\ \mu_i(t) \\ &\equiv W_o \frac{1}{T} \int_{-T/2}^{T/2} dt\ m(t) \\ &= W_o\ m \end{aligned} \tag{12.9}$$

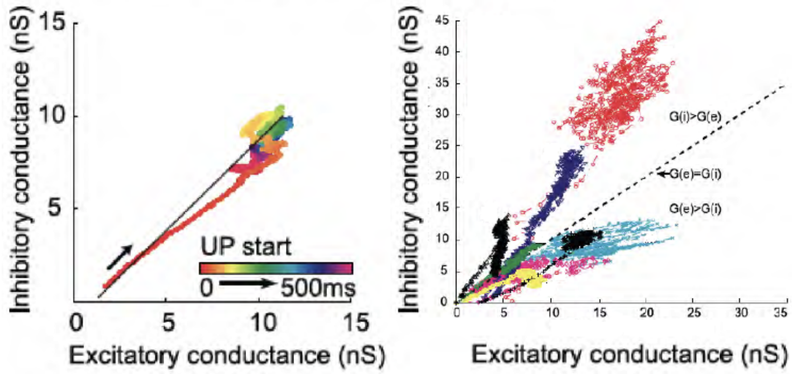
The variance across time is

$$\begin{aligned} \sigma_i^2 &= \left\langle (\mu_i(t) - \langle \mu \rangle)^2 \right\rangle \\ &= \left[\left\langle \mu_i^2 \right\rangle - \langle \mu \rangle^2 \right] \\ &= \left\langle \mu_i^2 \right\rangle \ - \ W_o^2\ m^2. \end{aligned} \tag{12.10}$$

We evaluate the first term under the assumption that the correlations in the neuronal outputs are zero, i.e.,

$$\left\langle \mu_i^2 \right\rangle = \langle \mu_i \mu_i \rangle \tag{12.11}$$

Figure 8: Balanced currents are proportional but do not necessarily exactly balance each other. Data from anesthetized mouse cortex. From Haider, Duque, Hasenstaub and McCormick 2006.



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\begin{aligned}
&= \left\langle \frac{W_o^2}{N^2} \sum_{j=1}^{N} \sum_{k=1}^{N} V_j(t) V_k(t) \right\rangle \\
&= W_o^2 \left\langle \frac{1}{N^2} \sum_{j=1}^{N} V_j^2(t) + \frac{1}{N^2} \sum_{j=1}^{N} \sum_{k \neq j}^{N} V_j(t) V_k(t) \right\rangle \\
&= \frac{W_o^2}{N} \left\langle \frac{1}{N} \sum_{j=1}^{N} V_j(t) \right\rangle + W_o^2 \left(\frac{N^2 - N}{N^2} \right) \left\langle \left(\frac{1}{N} \sum_{j=1}^{N} V_j(t) \right)^2 \right\rangle \\
&= \frac{W_o^2}{N} \langle m(t) \rangle + W_o^2 \left(1 - \frac{1}{N} \right) \left\langle m^2(t) \right\rangle \\
&= \frac{W_o^2}{N} (m - m^2) \ + \ W_o^2 m^2 \qquad (12.12)
\end{aligned}
$$

and thus

$$\sigma_i^2 = \frac{W_o^2}{N} m(1 - m). \qquad (12.13)$$

The variance for the population is the same, i.e.,

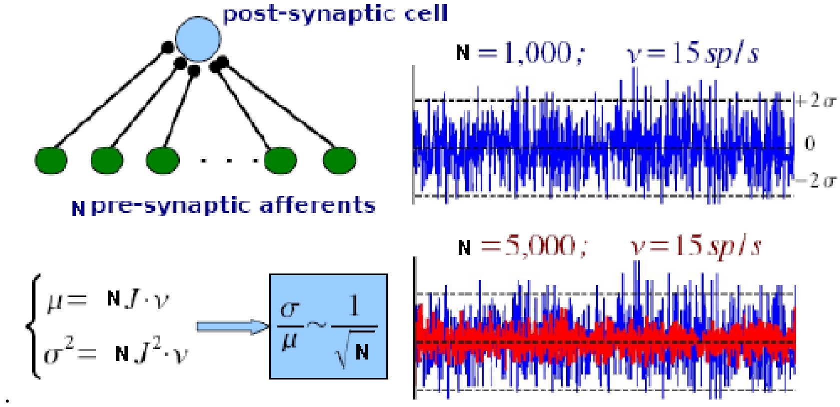
$$\sigma^2 = \frac{W_o^2}{N} m(1 - m). \qquad (12.14)$$

We see that for large networks the mean level drives the spiking and the variability goes to zero as $1/N$, or equivalently the standard deviation goes to zero as $1/\sqrt{N}$ (Figure 9). As expected for a binomial variable, the variance is also zero when all neurons are active, i.e., $m = 1$, or quiescent, i.e., $m = 0$. Lastly, for a Poisson process, we get the slightly different answer of $\sigma^2 = (W_o^2/N)m$ where $m =$ rate $\times$ time interval.

12.2.2 Strong synaptic inputs

How can we have a network with high noise? Let's recall the issue of networks with a small fraction of strong connections. The challenge

Figure 9: Averaging over synapses decreases the RMS noise



is to recast the input so that the variance does *not* diminish to zero as a function of the number of input neurons. This is where the idea of balanced inhibition and excitation comes into play.

1. We need the input to be the sums of two terms, one excitatory and one inhibitory.

2. We need the total current from these two term to cancel, i.e., be equal and opposite in sign, to first order. The time dependent variation in the firing rate of a neuron will reflect variations in the balance of the inputs.

3. We need a small fraction of active inputs, defined as K, where $1 \ll K \ll N$.

4. With a small number of inputs, the total variance, which is the sum of variances of the excitatory and inhibitory terms, can be high.

The input to the i-th neuron is now the sum of outputs from excitatory cells, i.e., the $V_i^E(t)$, and inhibitory cells, i.e., the $V_i^I(t)$. Thus

$$\begin{aligned} \mu_i(t) &= \mu^E(t) + \mu^I(t) \qquad (12.15) \\ &= \sum_{j=1}^{K} W_{ij}^E V_j^E(t) + \sum_{j=1}^{K} W_{ij}^I V_j^I \end{aligned}$$

Let W_{ij}^E be an excitatory input and W_{ij}^I be an inhibitory input, simplified as above but now scaled to be large, where large is defined as order $\frac{1}{\sqrt{K}}$ rather than order $\frac{1}{K}$. Thus

$$W_{ij}^E \rightarrow \frac{W_o^E}{\sqrt{K}} \quad \text{and} \quad W_{ij}^I \rightarrow -\frac{W_o^I}{\sqrt{K}} \qquad (12.16)$$

where we implicitly fix the sign of the inhibition. The mean input under the assumed scaling is

$$\begin{aligned}
\mu_i(t) &= W_o^E \frac{1}{\sqrt{K}} \sum_{j=1}^{K} V_j^E(t) \; - \; W_o^I \frac{1}{\sqrt{K}} \sum_{j=1}^{K} V_j^I(t) \qquad (12.17) \\
&= \sqrt{K} \left[W_o^E \frac{1}{K} \sum_{j=1}^{K} V_j^E(t) \; - \; W_o^I \frac{1}{K} \sum_{j=1}^{K} V_j^I(t) \right] \\
&= \sqrt{K} \left[W_o^E m^E(t) \; - \; W_o^I m^I(t) \right]
\end{aligned}$$

where the order parameters for excitation and inhibition are defined by are defined by

$$m^E(t) \equiv \frac{1}{K} \sum_{j=1}^{K} V_j^E(t) \quad \text{and} \quad m^I(t) \equiv \frac{1}{K} \sum_{j=1}^{K} V_j^I(t) \qquad (12.18)$$

and we have assumed without loss of generality that the same number of excitatory and inhibitory inputs.The input is large if the excitatory and inhibitory terms do not cancel balance to within a factor of $1/\sqrt{K}$. The variance, following the derivation for the single input case, is

$$\begin{aligned}
\sigma^2 &= \frac{1}{K} \sum_{i=1}^{K} \left\langle \left(\mu_i^E(t) - < \mu^E > \right)^2 \right\rangle + \frac{1}{K} \sum_{i=1}^{K} \left\langle \left(\mu_i^I(t) - < \mu^I > \right)^2 \right\rangle \qquad (12.19) \\
&= \frac{(\sqrt{K} W_o^E)^2}{K} \, m^E(1 - m^E) + \frac{(\sqrt{K} W_o^I)^2}{K} \, m^I(1 - m^I) \\
&= (W_o^E)^2 \, m^E(1 - m^E) + (W_o^I)^2 \, m^I(1 - m^I).
\end{aligned}$$

The important point is that there is no decrement in the variance as $K \to \infty$. Further, the variance remains nonzero for the special case of $W_o^E m^E = W_o^I m^I$, where the network is in "perfect" balance.

12.2.3 Experimental evidence for $\sqrt{k}$ scaling

It is fair to ask if there is evidence to support this scaling, which would depend on a homeostatic mechanism for maintenance. The data comes from networks in cell culture of different size. The data supports scaling of the synaptic inputs, *i.e.*, the post synaptic potentials, as $1/K^{0.6}$ (Figure 10). This is close to the predicted value of $1/\sqrt{K}$ for strong inputs, as opposed to $1/K$ for weak input. Not bad!

Figure 10: In vitro synaptic scaling preserves excitatory-inhibitory balance. From Barres and Reyes, Nature Neuroscience, 2016