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Synaptic Transmission: An Information-Theoretic Perspective

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Abstract

Here we analyze synaptic transmission from an information-theoretic perspective. We derive closed-form expressions for the lower-bounds on the capacity of a simple model of a cortical synapse under two explicit coding paradigms. Under the "signal estimation" paradigm, we assume the signal to be encoded in the mean firing rate of a Poisson neuron. The performance of an optimal linear estimator of the signal then provides a lower bound on the capacity for signal estimation. Under the "signal detection" paradigm, the presence or absence of the signal has to be detected. Performance of the optimal spike detector allows us to compute a lower bound on the capacity for signal detection. We find that single synapses (for empirically measured parameter values) transmit information poorly but significant improvement can be achieved with a small amount of redundancy.

1 Introduction

Tools from estimation and information theory have recently been applied by researchers (Bialek *et. al*, 1991) to quantify how well neurons transmit information about their random inputs in their spike outputs. In these approaches, the neuron is treated like a black-box, characterized empirically by a set of input-output records. This ignores the specific nature of neuronal processing in terms of its known biophysical properties. However, a systematic study of processing at various stages in a biophysically faithful model of a single neuron should be able to identify the role of each stage in information transfer in terms of the parameters relating to the neuron's dendritic structure, its spiking mechanism, *etc*. Employing this reductionist approach, we focus on a important component of neural processing, the synapse, and analyze a simple model of a cortical synapse under two different representational paradigms. Under the "signal estimation" paradigm, we assume that the input signal is linearly encoded in the mean firing rate of a Poisson neuron and the mean-square error in the reconstruction of the signal from the post-synaptic voltage quantifies system performance. From the performance of the optimal linear estimator of the signal, a lower bound on the capacity for signal estimation can be computed. Under the "signal detection" paradigm, we assume that information is encoded in an all-or-none format and the error in deciding whether or not a presynaptic spike occurred by observing the post-synaptic voltage quantifies system performance. This is similar to the conventional absent/present(Yes-No) decision paradigm used in psychophysics. Performance of the optimal spike detector in this case allows us to compute a lower bound on the capacity for signal detection.

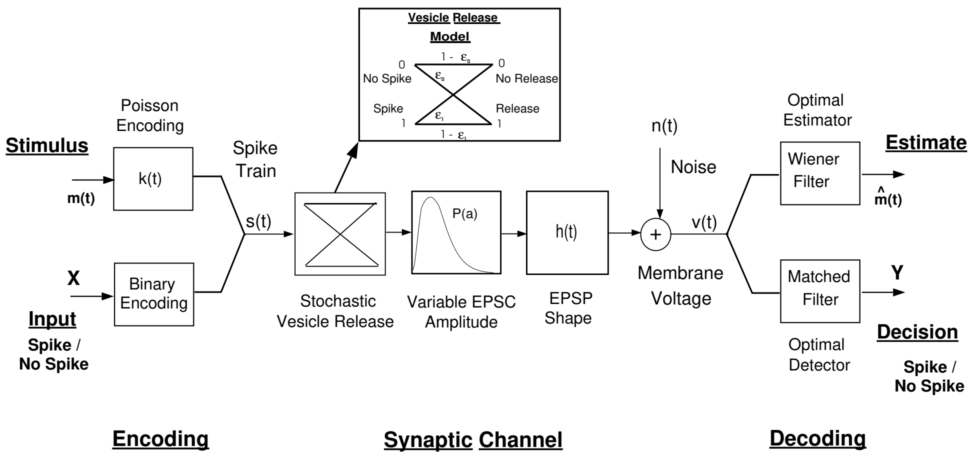


Figure 1: Schematic block diagram for the signal detection and estimation tasks. The synapse is modeled as a binary channel followed by a filter $h(t) = a\ t\ exp(-t/t_s)$. where a is a random variable with probability density, $P(a) = \alpha\ (\alpha a)^{k-1} exp(-\alpha a)/(k-1)!$. The binary channel, (inset, ϵ_0 = Pr[spontaneous release], ϵ_1 = Pr [release failure]) models probabilistic vesicle release and $h(t)$ models the variable epsp size observed for cortical synapses. $n(t)$ denotes additive post-synaptic voltage noise and is assumed to be Gaussian and white over a bandwidth B_n. Performance of the optimal linear estimator (*Wiener Filter*) and the optimal spike detector (*Matched Filter*) quantify synaptic efficacy for signal estimation and detection respectively.

2 The Synaptic Channel

Synaptic transmission in cortical neurons is known to be highly random though the role of this variability in neural computation and coding is still unclear. In central synapses, each synaptic bouton contains only a single active release zone, as opposed to the hundreds or thousands found at the much more reliable neuromuscular junction. Thus, in response to an action potential in the presynaptic terminal at most one vesicle is released (Korn and Faber, 1991). Moreover, the probability of vesicle release p is known to be generally low (0.1 to 0.4) from *in vitro* studies in some vertebrate and invertebrate systems (Stevens, 1994). This unreliability is further compounded by the trial-to-trial variability in the amplitude of the post-synaptic response to a vesicular release (Bekkers *et. al*, 1990). In some cases, the variance in the size of EPSP is as large as the mean. The empirically measured distribution of amplitudes is usually skewed to the right (possibly biased due the inability of measuring very small events) and can be modeled by a Gamma distribution.

In light of the above, we model the synapse as a binary channel cascaded by a random amplitude filter (Fig. 1). The binary channel accounts for the probabilistic vesicle release. ϵ_0

and ϵ_1 denote the probabilities of spontaneous vesicle release and failure respectively. We follow the binary channel convention used in digital communications ($\epsilon_1 = 1 - p$), whereas, p is more commonly used in neurobiology. The filter $h(t)$ is chosen to correspond to the epsp profile of a fast AMPA-like synapse. The amplitude of the filter a is modeled as random variable with density $P(a)$, mean μ_a and standard deviation σ_a. The CV (standard deviation/mean) of the distribution is denoted by CV_a. We also assume that additive Gaussian voltage noise $n(t)$ at the post-synaptic site further corrupts the epsp response. $n(t)$ is assumed to white with variance σ_n^2 and a bandwidth B_n corresponding to the membrane time constant τ. One can define an effective signal-to-noise ratio, $SNR = E_a/N_o$, given by the ratio of the energy in the epsp pulse, $E_h = \int_0^\infty h^2(t)\,dt$ to the noise power spectral density, $N_o = \sigma_n^2/B_n$. The performance of the synapse depends on the SNR and not on the absolute values of E_h or σ_n. In the above model, by regarding synaptic parameters as constants, we have tacitly ignored history dependent effects like paired-pulse facilitation, vesicle depletion, calcium buffering, etc, which endow the synapse with the nature of a sophisticated nonlinear filter (Markram and Tsodyks, 1997).

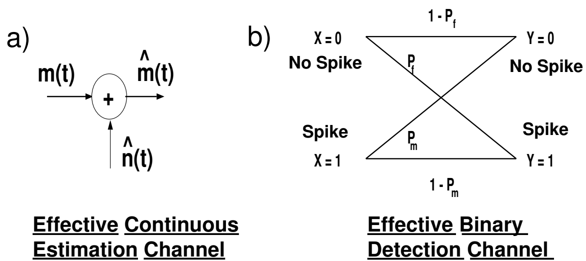


Figure 2: (a) Effective channel model for signal estimation. $m(t)$, $\hat{m}(t)$, $\hat{n}(t)$ denote the stimulus, the best linear estimate, and the reconstruction noise respectively. (b) Effective channel model for signal detection. X and Y denote the binary variables corresponding to the input and the decision respectively. P_f and P_m are the effective error probabilities.

3 Signal Estimation

Let us assume that the spike train of the presynaptic neuron can be modeled as a doubly stochastic Poisson process with a rate $\lambda(t) = k(t) * m(t)$ given as a convolution between the stimulus $m(t)$ and a filter $k(t)$. The stimulus is drawn from a probability distribution which we assume to be Gaussian. $k(t) = exp(-t/\tau)$ is a low-pass filter which models the phenomenological relationship between a neuron's firing rate and its input current. τ is chosen to correspond to the membrane time constant. The exact form of $k(t)$ is not crucial and the above form is assumed primarily for analytical tractability. The objective is to find the optimal estimator of $m(t)$ from the post-synaptic voltage $v(t)$, where optimality is in a least-mean square sense. The optimal mean-square estimator is, in general, nonlinear and reduces to a linear filter only when all the signals and noises are Gaussian. However, instead of making this assumption, we restrict ourselves to the analysis of the optimal linear estimator, $\hat{m}(t) = g(t) * v(t)$, *i.e.* the filter $g(t)$ which minimizes the mean-square error $E = \langle (m(t) - \hat{m}(t))^2 \rangle$ where $\langle . \rangle$ denotes an ensemble average. The overall estimation system shown in Fig. 1 can be characterized by an effective continuous channel (Fig. 2a) where $\hat{n}(t) = \hat{m}(t) - m(t)$ denotes the effective reconstruction noise. System performance can be quantified by E, the lower E, the better the synapse at signal transmission. The expression for the optimal filter (*Wiener filter*) in the frequency domain is $g(\omega) = S_{mv}(-\omega)/S_{vv}(\omega)$ where $S_{mv}(\omega)$ is the cross-spectral density (Fourier transform of the cross-correlation R_{mv}) of $m(t)$ and $s(t)$ and $S_{vv}(\omega)$ is the power spectral density of $v(t)$. The minimum mean-square error is given by , $E = \sigma_m^2 - \int_{\mathcal{S}} \mid S_{mv}(\omega) \mid^2 / S_{vv}(\omega)\,d\omega$. The set $\mathcal{S} = \{\omega \mid S_{vv}(\omega) \neq 0\}$ is called the *support* of $S_{vv}(\omega)$.

Another measure of system performance is the mutual information rate $I(m;v)$ between $m(t)$ and $v(t)$, defined as the rate of information transmitted by $v(t)$ about $s(t)$. By the Data Processing inequality (Cover 1991), $I(m,v) \geq I(m,\hat{m})$. A lower bound of $I(m,\hat{m})$ and thus of $I(m;v)$ is given by the simple expression $I_{lb} = \frac{1}{2}\int_{\mathcal{S}} \log_2[\frac{S_{mm}(\omega)}{S_{\hat{n}\hat{n}}(\omega)}]\, d\omega$ (units of bits/sec). The lower bound is achieved when $\hat{n}(t)$ is Gaussian and is independent of $m(t)$. Since the spike train $s(t) = \sum \delta(t-t_i)$ is a Poisson process with rate $k(t) * m(t)$, its power spectrum is given by the expression, $S_{ss}(\omega) = \bar{\lambda} + \mid K(\omega) \mid^2 S_{mm}(\omega)$ where $\bar{\lambda}$ is the mean firing rate. We assume that the mean (μ_m) and variance (σ_m^2) of $m(t)$ are chosen such that the probability that $\lambda(t) < 0$ is negligible[1] The vesicle release process is the spike train gated by the binary channel and so it is also a Poisson process with rate $(1-\epsilon_1)\lambda(t)$. Since $v(t) = \sum a_i h(t-t_i) + n(t)$ is a filtered Poisson process, its power spectral density is given by $S_{vv}(\omega) = \mid H(\omega) \mid^2 \{(\mu_a^2+\sigma_a^2)(1-\epsilon_1)\bar{\lambda} + \mu_a^2(1-\epsilon_1)^2 \mid K(\omega) \mid^2 S_{mm}(\omega)\} + S_{nn}(\omega)$. The cross-spectral density is given by the expression $S_{vm}(\omega) = (1-\epsilon_1)\mu_a S_{mm}(\omega) H(\omega) K(\omega)$. This allows us to write the mean-square error as,

$$E = \sigma_m^2 - \int_{\mathcal{S}} \frac{S_{mm}^2(\omega)}{\lambda_{eff}(\omega) + S_{mm}(\omega) + S_{eff}(\omega)}\, d\omega$$

$$\lambda_{eff}(\omega) = \frac{\bar{\lambda}(1+CV_a^2)}{(1-\epsilon_1) \mid K(\omega) \mid^2}\ ,\ S_{eff}(\omega) = \frac{S_{nn}(\omega)}{(1-\epsilon_1)^2 \mu_a^2 \mid H(\omega) \mid^2 \mid K(\omega) \mid^2}$$

Thus, the power spectral density of $\hat{n}(t)$ is given by $S_{\hat{n}\hat{n}} = \lambda_{eff}(\omega) + S_{eff}(\omega)$. Notice that if $K(\omega) \rightarrow \infty, E \rightarrow 0$ *i.e.* perfect reconstruction takes place in the limit of high firing rates. For the parameter values chosen, $S_{eff}(\omega) \ll \lambda_{eff}(\omega)$, and can be ignored. Consequently, signal estimation is *shot noise* limited and synaptic variability increases shot noise by a factor $N_{syn} = (1+CV_a^2)/(1-\epsilon_1)$. For $CV_a = 0.6$ and $\epsilon_1 = 0.6, N_{syn} = 3.4$, and for $CV_a = 1$ and $\epsilon_1 = 0.6, N_{syn} = 5$. If $m(t)$ is chosen to be white, band-limited to B_m Hz, closed-form expressions for E and I_{lb} can be obtained. The expression for I_{lb} is tedious and provides little insight and so we present only the expression for E below.

$$E(\gamma, B_T) = \sigma_m^2[1 - \frac{\gamma}{\sqrt{1+\gamma}} \frac{1}{B_T} tan^{-1}(\frac{B_T}{\sqrt{1+\gamma}})]$$

$$\gamma = \frac{\sigma_m^2 \bar{\lambda}}{2\mu_m^2 N_{syn} B_m}\ ,\ B_T = 2\pi B_m \tau$$

E is a monotonic function of γ (decreasing) and B_T (increasing). γ can be considered as the effective number of spikes available per unit signal bandwidth and B_T is the ratio of the signal bandwidth and the neuron bandwidth. Plots of normalized reconstruction error $E_r = E/\sigma_m^2$ and I_{lb} versus mean firing rate ($\bar{\lambda}$) for different values of signal bandwidth B_m are shown in Fig. 3a and Fig. 3b respectively. Observe that I_{lb} (bits/sec) is insensitive to B_m for firing rates upto 200Hz because the decrease in quality of estimation (E increases with B_m) is compensated by an increase in the number of independent samples ($2B_m$) available per second. This phenomenon is characteristic of systems operating in the low SNR regime. I_{lb} has the generic form, $I_{lb} = B\ \log(1 + S/(NB))$, where B, S and N denote signal bandwidth, signal power and noise power respectively. For low SNR, $I \approx B\ S/(NB) = S/N$, is independent of B. So one can argue that, for our choice of parameters, a single synapse is a low SNR system. The analysis generalizes very easily to the case of multiple synapses where all are driven by the same signal $s(t)$. (Manwani and Koch, in preparation). However, instead of presenting the rigorous analysis, we appeal to the intuition gained from the single synapse case. Since a single synapse can be regarded as a shot noise source, n parallel synapses can be treated as n parallel noise sources. Let us make the plausible

[1] We choose μ_m and σ_m so that $\bar{\lambda} = 3\sigma_\lambda$ (std of λ) so that Prob$[\lambda(t) \leq 0] < 0.01$.

assumption that these noises are uncorrelated. If optimal estimation is carried out separately for each synapse and the estimates are combined optimally, the effective noise variance is given by the harmonic mean of the individual variances *i.e.* $1/\sigma^2_{neff} = \sum_i 1/\sigma^2_{ni}$. However, if the noises are added first and optimal estimation is carried out with respect to the sum, the effective noise variance is given by the arithmetic mean of the individual variances, *i.e.* $\sigma^2_{neff} = \sum_i \sigma^2_{ni}/n^2$. If we assume that all synapses are similar so that $\sigma^2_{ni} = \sigma^2$, $\sigma^2_{neff} = \sigma^2/n$. Plots of E_r and I_{lb} for the case of 5 identical synapses are shown in Fig. 3c and Fig. 3d respectively. Notice that I_{lb} increases with B_m suggesting that the system is no longer in the low SNR regime. Thus, though a single synapse has very low capacity, a small amount of redundancy causes a considerable increase in performance. This is consistent with the fact the in the low SNR regime, I increases linearly with SNR, consequently, linearly with n, the number of synapses.

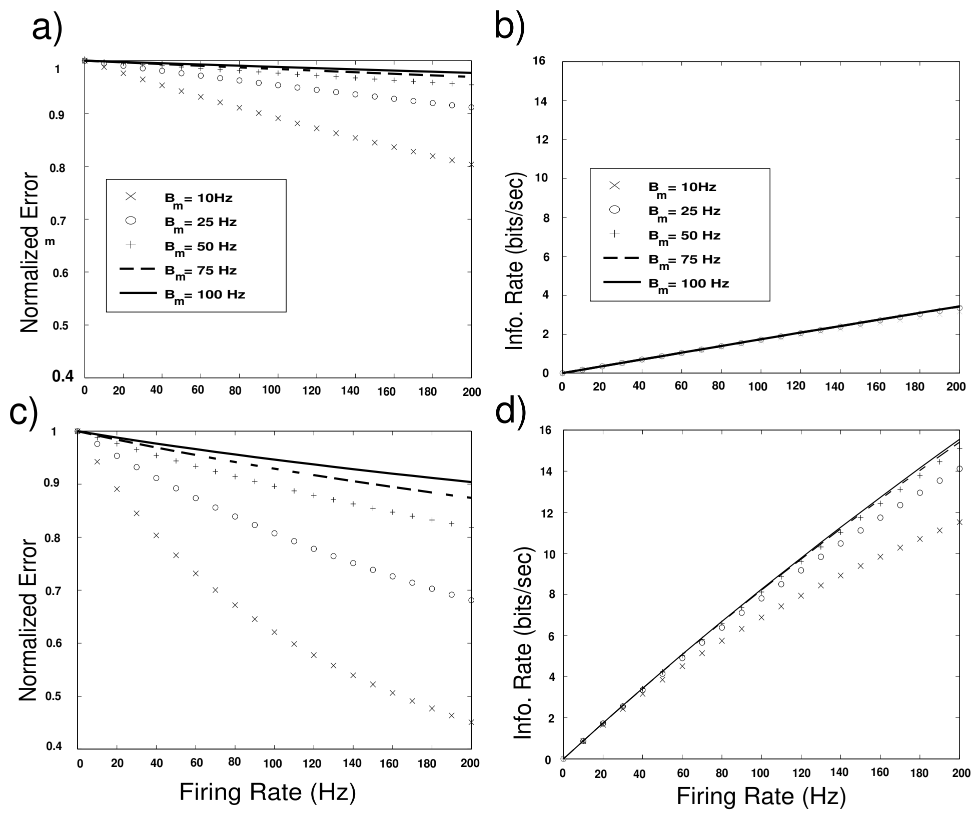


Figure 3: E_r and I_{lb} vs. mean firing rate ($\bar{\lambda}$) for n = 1 [(a) and (b)] and n = 5 [(c) and (d)] identical synapses respectively (different values of B_m) for signal estimation. Parameter values are $\epsilon_1 = 0.6$, $\epsilon_0 = 0$, CV_a = 0.6, t_s = 0.5 msec, τ = 10msec, σ_n = 0.1 mV, B_n = 100 Hz.

4 Signal Detection

The goal in signal detection is to decide which member from a finite set of signals was generated by a source, on the basis of measurements related to the output only in a statistical sense. Our example corresponds to its simplest case, that of *binary detection*. The objective is to derive an optimal spike detector based on the post-synaptic voltage in a given time interval. The criterion of optimality is minimum probability of error (P_e). A false alarm

(FA) error occurs when a spike is falsely detected even when no presynaptic spike occurs and a miss error (M) occurs when a spike fails to be detected. The probabilities of the errors are denoted by P_f and P_m respectively. Thus, $P_e = (1-p_o)\,P_f + p_o\,P_m$ where p_o denotes the a priori probability of a spike occurrence. Let X and Y be binary variables denoting spike occurrence and the decision respectively. Thus, $X = 1$ if a spike occurred else $X = 0$. Similarly, $Y = 1$ expresses the decision that a spike occurred. The *posterior likelihood* ratio is defined as $\mathcal{L}(v) = Pr(v \mid X = 1)/Pr(v \mid X = 0)$ and the prior likelihood as $\mathcal{L}_o = (1 - p_o)/p_o$. The optimal spike detector employs the well-known *likelihood ratio* test, "If $\mathcal{L}(v) \geq \mathcal{L}_o$ **Y = 1** else **Y = 0**". When $X = 1$, $v(t) = a\,h(t) + n(t)$ else $v(t) = n(t)$. Since a is a random variable, $\mathcal{L}(v) = (\int Pr(v \mid X = 1; a)\; P(a)\; da)/Pr(v \mid X = 0)$. If the noise $n(t)$ is Gaussian and white, it can be shown that the optimal decision rule reduces to a *matched filter*[2], *i.e.* if the correlation, r between $v(t)$ and $h(t)$ exceeds a particular threshold (denoted by η), $Y = 1$ else $Y = 0$. The overall decision system shown in Fig. 1 can be treated as effective binary channel (Fig. 2b). The system performance can be quantified either by P_e or $I(X;Y)$, the mutual information between the binary random variables, X and Y. Note that even when $n(t) = 0$ ($SNR = \infty$), $P_e \neq 0$ due to the unreliability of vesicular release. Let P_e^* denote the probability of error when $SNR = \infty$. If $\epsilon_0 = 0$, $P_e^* = p_o\,\epsilon_1$ is the minimum possible detection error. Let P_f^o and P_m^o denote FA and M errors when the release is ideal ($\epsilon_1 = 0,\ \epsilon_0 = 0$). It can be shown that

$$P_e = P_e^* + P_m^o[p_o(1-\epsilon_1) - (1-p_o)\epsilon_0] + P_f^o[(1-p_o)(1-\epsilon_0) - p_o\epsilon_1]$$

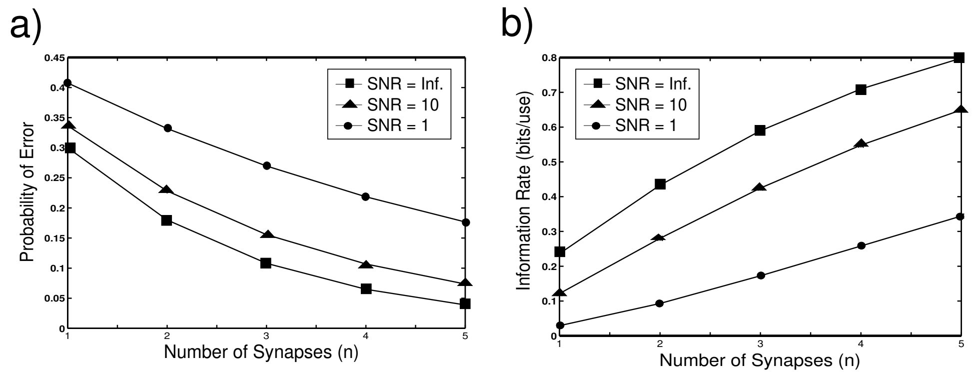
$$P_f = P_f^o\ ,\ P_m = P_m^o + \epsilon_1(1 - P_m^o + P_f^o)$$

Both P_f^o and P_m^o depend on η. The optimal value of η is chosen such that P_e is minimized. In general, P_f^o and P_m^o can not be expressed in closed-form and the optimal η is found using the graphical *ROC analysis* procedure. If we normalize a such that $\mu_a = 1$, P_f^o and P_m^o can be parametrically expressed in terms of a normalized threshold η^*, $P_f^o = 0.5[1 - Erf(\eta^*)]$, $P_m^o = 0.5[1 + \int_0^\infty Erf(\eta^* - \sqrt{SNR}\,a)\; P(a)\; da]$. $I(X;Y)$ can be computed using the formula for the mutual information for a binary channel, $I = \mathcal{H}(p_o\,(1 - P_m) + (1 - p_o)\,P_f) - p_o\mathcal{H}(P_m) - (1-p_o)\mathcal{H}(P_f)$ where $\mathcal{H}(x) = -x\log_2(x) - (1-x)\log_2(1-x)$ is the binary entropy function. The analysis can be generalized to the case of n synapses but the expressions involve n-dimensional integrals which need to be evaluated numerically. The Central Limit Theorem can be used to simplify the case of very large n. Plots of P_e and $I(X;Y)$ versus n for different values of SNR (1,10,∞) for the case of identical synapses are shown in Fig. 4a and Fig. 4b respectively. Yet again, we observe the poor performance of a single synapse and the substantial improvement due to redundancy. The linear increase of I with n is similar to the result obtained for signal estimation.

5 Conclusions

We find that a single synapse is rather ineffective as a communication device but with a little redundancy neuronal communication can be made much more robust. Infact, a single synapse can be considered as a low SNR device, while 5 independent synapses in parallel approach a high SNR system. This is consistently echoed in the results for signal estimation and signal detection. The values of information rates we obtain are very small compared to numbers obtained from some peripheral sensory neurons (Rieke *et. al*, 1996). This could be due to an over-conservative choice of parameter values on our part or could argue for the preponderance of redundancy in neural systems. What we have presented above are preliminary results of work in progress and so the path ahead is much

[2]For deterministic a, the result is well-known, but even if a is a one-sided random variable, the matched filter can be shown to be optimal.



P_e (a) and I_{lb} (b) vs. the number of synapses, n, (different values of SNR) for signal detection. SNR = Inf. corresponds to no post-synaptic voltage noise. All the synapses are assumed to be identical. Parameter values are p_o = 0.5, $\epsilon_1 = 0.6$, $\epsilon_0 = 0$, CV_a = 0.6, t_s = 0.5 msec, τ = 10 msec, σ_n = 0.1 mV, B_n = 100 Hz.

longer than the distance we have covered so far. To the best of our knowledge, analysis of distinct individual components of a neuron from an communications standpoint has not been carried out before.

Acknowledgements

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