INFORMATION PROCESSING BY DEPRESSING SYNAPSES

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INTRODUCTION

◊ **Synaptic transmission is dynamic** and it has the ability to control the way in which information in the pre-synaptic spike trains is sent to the post-synaptic neuron.

◊ Depressing synapses **can suppress spikes selectively** by eliminating those which arrive too close in time. This has the potentiality to **eliminate time correlations**.

◊ The capability of the synapse to operate in this way depends not only on the details of the pre-synaptic terminal model but also on the **input spike train statistics**.

◊ We study the conditions that models of synaptic depression based on **vesicle depletion** have to fulfill in order to transmit information efficiently and still reproduce the observed synaptic response.
◊ **Vesicle recovery**: is Poisson with rate $1/\tau_v$

◊ **Neurotransmitter release**:

- Release is *uni-vesicular* and *non linear in $N$*
- Larger synapses have larger release probabilities $p_r(N)$. 
Synapse with $M$ synaptic contacts

Input

Spikes

$P_{\text{trans}}$

EPSPs

$\text{stationary EPSPs}$

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Population of neurons
Input: $[\nu, \tau_c, CV]$
Simple models of release

Dobrunz and Stevens, Neuron 18: 995-1008, June 1998:

\[ p_r = 1 - e^{-aN} \]

\[ p_r = 1 - e^{-aN^{\frac{3}{2}}} \]
Dobrunz and Stevens, Neuron 18: 995-1008, June 1998
The line is a fit with $a = 0.057$

Murthy, Schikorski, Stevens and Zhu, Neuron 32: 673-682, November 2001 (fig 1)
Pre-synaptic spike train statistics

Input spike train: \( S(t) = \sum_j \delta(t - t_j) \)

Rate: \( \nu(t) = \langle S(t) \rangle \)

Time correlations: \( (t > t') \)

\[
C(t - t') \equiv \langle (S(t) - \nu)(S(t') - \nu) \rangle
\]

Exponential correlations:

\[
C(t - t') = \nu \frac{(CV^2 - 1)}{2\tau_c} e^{-(t-t')/\tau_c}
\]

ISI distribution (Renewal Process)

\[
\rho_{isi}(T) = (1 - \epsilon)\beta_1 e^{-T\beta_1} + \epsilon\beta_2 e^{-T\beta_2}
\]
EXAMPLES:

$\nu = 10$ Hz

$\tau_c = 0$

CV = 1.8

CV = 1.8; $\tau_c = 10$ ms

CV = 1.3; $\tau_c = 10$ ms

CV = 1 (Poisson)

CV = 1

CV = 1.3

CV = 1.8
Several possible optimization criteria:

◊ **Estimation:** optimize the accuracy in the estimation of the input rate $\nu$.

◊ **Decorrelation:** minimize the integrated second order correlation of the synaptic response.

◊ **Mutual information:** maximize the information that the output of the “channel” has on the input rate.

And also choose different stages of the information processing pathway:

- The output of a synaptic contact
- The output of the synapse
- A population of synapses
Fisher info, mutual info and correlations

• Fisher information

\[
J(\nu|\Delta) = \int_0^\infty d\Delta \rho_{sr}(\Delta) \left( \frac{\partial \ln(\rho_{sr}(\Delta))}{\partial \nu} \right)^2
\]

• Integrated correlation

\[
K = \int_0^\infty dt \left( \frac{C_{sr}(t|t_{sp} = 0)}{\nu_{sr}} \right)^2
\]

• Mutual information \(I_n\)

\[
I_n = - \int d\nu P_{\nu} \log_2 P_{\nu} - \\
- \frac{1}{2} \int d\nu P_{\nu} \log_2 \left( \frac{2\pi e}{nJ(\nu|\Delta)} \right)
\]
Methods

◊ Find and solve the equations for $\mathcal{N}(t)$, the probability that there are $N$ available vesicles. In particular, find the steady state solution, $\mathcal{N}^{ss}$.

◊ Using $\mathcal{N}^{ss}$ compute the (steady state) distribution of times $\Delta$ between consecutive synaptic responses, $\rho_{sr}(\Delta)$

◊ Using $\rho_{sr}(\Delta)$ compute $J(\nu|\Delta)$, $K$ and $I_n$.

◊ Compute the transmission probability $P_{trans}(t)$ and obtain the graded synaptic response through $M$ synaptic contacts. Then find the mutual information at the output of the whole M-contact synapse, $I_M$ (not done).

◊ Dynamics (not done)
Steady State: $\rho_{sr}(\Delta)$ for the general case

\[ \rho_{sr}^{(1)}(\Delta) = \sum_{N=0}^{N_0} \hat{\phi}_N^{ss} \sum_{n_1=1}^{N_0-N+1} P_{rec}(n_1, \Delta|N_0 - N + 1) \times \rho_{isi}(\Delta) p_r(N - 1 + n_1) \]

Stationary prob. of having $N$ vesicles ready for release conditioned to a successful spike: $\hat{\phi}_N^{ss}$

Prob. of recovery of $n$ vesicles out of $N$ in a time-window $\Delta$:

\[ P_{rec}(n, \Delta|N) = \binom{n}{N} (1 - e^{-\Delta/\tau_v})^n (e^{-\Delta/\tau_v})^{(N-n)} \]
Steady State: $\rho_{sr}(\Delta)$ for the general case

$$
\rho_{sr}^{(2)}(\Delta) = \sum_{N=0}^{N_0} \phi_{ss}^{s} \int_0^\Delta dt_1 \rho_{isi}(t_1) \times \\
\times \sum_{n_1=1}^{N_0-N+1} P_{rec}(n_1, t_1|N_0 - N + 1) \times \\
\times (1 - p_r(N-1+n_1)) \rho_{isi}(\Delta - t_1) \times \\
\times \sum_{n_2=1}^{N_0-N+1-n_1} P_{rec}(n_2, \Delta - t_1|N_0 - N + 1 - n_1) \times \\
\times p_r(N-1+n_1+n_2)
$$
Steady State: $\rho_{sr}(\Delta)$ for the general case

$$\rho_{sr}(\Delta) = \sum_{j=1}^{\infty} \rho_{sr}^{(j)}(\Delta)$$

To make the sum, we transform Laplace, and then we choose a release probability model ($p_r(N)$) and assume that the release probability becomes significant only above a minimum size $N_{th}$ of the available pool.
Solution of the Steady State

The model can be solved analytically for any renewal input process $\rho_{isi}(T)$!

$$
\tilde{\rho}_{sr}(s) = \tilde{\rho}_{isi}(s) - Q \frac{\tilde{\rho}_{isi}(s+\frac{N_+}{\tau_v})[s-\tilde{\rho}_{isi}(s)]}{1-\tilde{\rho}_{isi}(s+\frac{N_+}{\tau_v})}
$$

- $Q = \frac{\varphi^{ss}(N_{th})}{\varphi^{ss}(N \geq N_{th})}$
- $\varphi^{ss}(N)$ steady state prob. that the available pool size is $N$.
- $\varphi^{ss}(N \geq N_{th})$ Id., but with $N \geq N_{th}$
- $N_+ = N_0 - N_{th} + 1$ size of the most easily releasable pool.

Besides, the transmission probability is:

$$
P_{trans} = \sum_{N=0}^{N_0} \varphi_N \Pr(N)
$$

We still need to compute $\varphi^{ss}(N)$. 

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Recurrence equations for $\varphi_N$

- For a fixed stimulus $\Delta$ we set a recurrent relation:

$$\varphi_n(t_j) = \varphi_n(t_{j-1}^+) P_{\text{rec}}(0, \Delta | N_0 - n)$$

$$+ \varphi_{n-1}(t_{j-1}^+) P_{\text{rec}}(1, \Delta | N_0 - n + 1)$$

$$+ \ldots + \varphi_0(t_{j-1}^+) P_{\text{rec}}(n, \Delta | N_0)$$

- Probabilities before and after the spike are related by $p_r(n)$:

$$\varphi_n(t_j^+) = \varphi_n(t_j)(1 - p_r(n)) + \varphi_{n+1}(t_j)p_r(n)$$

---

Prob. of recovery of $n$ vesicles out of $N$ in a time-window $\Delta$:

$$P_{\text{rec}}(n, \Delta | N) = \binom{n}{N} (1 - e^{-\Delta/\tau_v})^n (e^{-\Delta/\tau_v})^{(N-n)}$$
Recurrent equations for $\varphi_N$

- We average over the stimulus $\langle \cdot \rangle_\Delta$:

$$\varphi_n(t_j) = \varphi_n(t_{j-1}^+) \langle P_{\text{rec}}(0,\Delta|N_0 - n) \rangle$$

$$+ \varphi_{n-1}(t_{j-1}^+) \langle P_{\text{rec}}(1,\Delta|N_0 - n + 1) \rangle$$

$$+ \ldots + \varphi_0(t_{j-1}^+) \langle P_{\text{rec}}(n,\Delta|N_0) \rangle$$

- In the steady state: $\varphi_n(t_{j-1}) = \varphi_n(t_j) = \varphi_n^{ss}$.

- We reach a linear system of $N_0$ eqs. (plus $\sum_N \varphi_N^{ss} = 1$) for the $\varphi_n^{ss}$ ($n = 0 \ldots N_0$)

$$\langle P_{\text{rec}}(n,\Delta|N) \rangle = \int_0^\infty d\Delta \rho_{isi}(\Delta) P_{\text{rec}}(n,\Delta|N)$$
One vesicle per synaptic contact

◊ **POISSON INPUT:** $\rho_{isi}(T) = \nu e^{-\nu T}$

- **Synaptic response (SR) distribution:**
  $$\rho_{sr}(\Delta) = \frac{\nu U}{1 - \nu U \tau_v} \left( e^{-\nu U \Delta} - e^{-\Delta / \tau_v} \right)$$

- **SR correlation:**
  $$C_{sr}(t - t') = - \left( \frac{\nu U}{1 + \nu U \tau_v} \right)^2 e^{-\frac{(t - t')}{\tau_{sr}}}$$

- **SR correlation time:**
  $$\tau_{sr} = \frac{\tau_v}{1 + \tau_v \nu U}$$

- **SR rate:**
  $$\nu_{sr} = \nu U \frac{1}{1 + \nu U \tau_v}$$

- **SR CV:**
  $$CV_{sr}^2 = 1 - 2 \tau_{sr} \nu_{sr}$$

- **Stationary transmission probability:**
  $$\mathcal{P}_{trans}^{ss} = U \mathcal{P}_{trans}^{ss} = \frac{U}{1 + \nu U \tau_v}$$
One vesicle per synaptic contact

◊ EXPONENTIALLY CORRELATED INPUTS:

\[ \rho_{isi}(T) = (1 - \epsilon) \beta_1 e^{-T\beta_1} + \epsilon \beta_2 e^{-T\beta_2} \]

- **SR distribution:**
  \[ \rho_{sr}(\Delta) = U \sum_{i=1}^{4} I_i e^{-\Delta/\tau_v^i} \]

- **SR correlation:**
  \[ C_{sr}(t - t') = \sum_{i=1}^{3} C_i e^{-(t-t')/\tau_c^i} \]
  \[ (I_i, C_i, \tau_v^i, \tau_c^i \text{ functions of } \nu, CV, \tau_c, \tau_v, \text{ and } U) \]

- **Stationary transmission probability:**
  \[ \mathcal{P}_{trans}^{ss} = U \left[ 1 + \tau_v \nu U + U \frac{\tau_v}{\tau_v + \tau_c} \left( \frac{CV^2 - 1}{2} \right) \right]^{-1} \]

- **SR rate:**
  \[ \nu_{sr} = \nu \mathcal{P}_{trans} \]
\( v = 10 \text{Hz}, \ U = 0.5, \ \tau_c = 0.1s \)

\[
\begin{align*}
V_{SR} (s^{-1}) & \\
\nu (s^{-1})
\end{align*}
\]

\( U = 0.5, \ \tau_c = 0.1s \)
Fisher information and $\tau_{opt}$ for $N_0 = 1$

Solid=Count, Dashed=Time, $U=0.5$, $\tau_e=0.1s$, $\nu=10Hz$

$\tau(s)$

$J(s)^2$

$U=0.5$, $\tau_e=0.1s$

$\nu$
Shannon information, Correlation and $CV_{sr}$

$U=0.5; \tau_c=100$ ms; $\nu=10$ Hz

$I(\Delta \nu)$

$K$

$CV_e$

$\tau_v$ (s)

$I(\Delta \nu)$ vs $\tau_v$ with different $CV$ values:
- $CV=1$ (Poisson)
- $CV=1.8$
- $CV=2.1$

$K$ vs $\tau_v$ with different $CV$ values:
- $CV=1$ (Poisson)
- $CV=1.8$
- $CV=2.1$

$CV_e$ vs $\tau_v$ with different $CV$ values:
- $CV=1$ (Poisson)
- $CV=1.8$
- $CV=2.1$
$N_0$ vesicles per synaptic contact

1. **Linear release probability**: $p_r(N) = UN$

   ◇ For Poisson inputs:

   $$P_{trans}^{ss} = \sum_{N=0}^{N_0} \phi_N^{ss} p_r(N)$$

   $$= \frac{UN_0}{1 + \nu \tau_v U}$$

   ◇ Agreement with phenomenological models of synaptic depression.

   ◇ But this system **cannot optimize** because it can't switch between $P_{trans}(t) \sim 1 \iff P_{trans}(t) \sim 0$ rapidly enough.
\( N_0 \) vesicles per synaptic contact

2. **Non-linear release prob:** \( p_r(N) \sim U\Theta(N - N_{th}) \)

\( \diamond \) With this step-wise model, rapid transitions between \( P_{\text{trans}}(t) \sim 1 \iff P(t)_{\text{trans}} \sim 0 \) can be achieved if in the steady state the system *lives near the threshold* \( N_{th} \) where \( p_r(N) \) changes abruptly.

\( \diamond \) Thus, \( \tau_v \) *can be optimized* if in the steady state the pool of available vesicles has a size of about \( N_{th} \) vesicles.
◊ For Poisson inputs:

\[ P_{trans}^{ss} = \sum_{N=0}^{N_0} \Phi_N^s \Pr(N) \]

\[ \approx U \sum_{N=N_{th}}^{N_0} \Phi_N^s \]

◊ Comparison with phenomenological models:

\[ P_{trans}^{ss} = U P_{trans}^{ss} \] obeys

\[ \frac{dP_{trans}}{dt} = \frac{1-P_{trans}}{\tau_v/N_0} - U \Phi_{N_{th}} \sum_j \delta(t - t_j) \]

to be compared with:

\[ \frac{dP_{trans}}{dt} = \frac{1-P_{trans}}{\tau} - U P_{trans} \sum_j \delta(t - t_j) \]

• \( N_0 = 1 \): \( N_{th} = 1 \) \( \Rightarrow \) \( \Phi_{N_{th}} = P_{trans} \)
and the release model averages exactly to the phenomenological model.
\begin{itemize}
  \item $N_0 > 1$:
    \[
    \tilde{\rho}_{sr}(s; N_0, \tau_v) = \tilde{\rho}_{sr}(s; 1; \tau_v / N_+ ) + (1 - Q) \frac{\tilde{\rho}_{isi}(s + \frac{N_+}{\tau_v})(1 - \tilde{\rho}_{isi}(s))}{1 - \tilde{\rho}_{isi}(s + N_+ / \tau_v)}
    \]
    
    If the probabilities
    \[
    \varnothing_{N_{th}+1}^{ss}, \varnothing_{N_{th}+2}^{ss}, \ldots, \varnothing_{N_0}^{ss} \ll \varnothing_{N_{th}}^{ss}
    \]

    ★ Agreement with phenomenological models:
    \[
    Q \sim 1 \Rightarrow \tilde{\rho}_{sr}(s; N_0, \tau_v) \sim \tilde{\rho}_{sr}(s; 1; \tau_v / N_+ )
    \]

    The $N_0$ vesicle system behave like a one-vesicle synaptic contact with recovery time $\tau_v / N_+$.

    ★ The system lives around $N = N_{th}$ and it can be optimized.
\end{itemize}
Fisher information and $\tau_{opt}$ for $N_0 > 1$

$v = 10 \text{ Hz}; \; cv = 1.8; \; U = 1; \; \tau = 10 \text{ ms}$

![Graph showing Fisher information and $\tau_{opt}$ for different $N_0$ values.](image)
Poisson Input

\( \tau = 100 \text{ ms}; \ \tau_v(N_0) = N_0 \tau; \ \ U = 0.8 \)

\[ P_{\text{trans}} = N_0 \left( \frac{<R>^{ss}}{M} \right) \]

- \( N_0 = 1 \)
- \( N_0 = 2 \)
- \( N_0 = 3 \)
- \( N_0 = 4 \)
- \( N_0 = 5 \)
- \( N_0 = 10 \)
When are depressing synapses advantageous?

◊ First, it has to be below saturation: $\nu < \nu_{sat}$

◊ But this is not enough:
  
  - Spikes in absence of correlations: $\nu \tau_c$
  - Excess of correlated spikes: $\sim (CV^2 - 1)$

Since while the vesicle is recovering all spikes are lost, one needs:

$$\nu \tau_c < \text{const} \ (CV^2 - 1)$$

U=0.5, \(\nu=10Hz\)
When are depressing synapses advantageous?

◊ Suppression of correlations is advantageous *only* over a restricted range of $\tau_c$, beyond which it is not longer beneficial to eliminate correlations because of the lost of informative spikes.

◊ Optimal synapses are **tuned** to $\tau_c$.

![Graph](image-url)

$U=0.5$, $\nu=10\text{Hz}$

- CV=1.0
- CV=1.3
- CV=2.0

$I(\tau_{opt})/I(\tau=0)$

$\tau_c (s)$
When are depressing synapses advantageous?

◊ This range of values of \( \tau_c \) shrinks as the number of vesicles \( N_0 \) increases.
When are depressing synapses advantageous?

◊ The magnitude of the correlations \((CV^2 - 1)\) needed to obtain \(\tau_{opt} > 0\) increases with \(N_0\).
CONCLUSIONS

• *Only* when the input spike train has temporal auto-correlations, depressing synapses transmit information more efficiently than static ones.

• In order to find $\tau_{opt} > 0$, a condition like

$$\nu \tau_c N_0 < const \, (CV^2 - 1)$$

(1)

must hold.

• Vesicle depletion models of synaptic depression predict large ($\sim 1$ sec) values of $\tau_{opt}$ only for low input rates ($\sim 1 - 2$Hz).

• The graded synaptic response (EPSPs) of the model reproduces well phenomenological models of synaptic depression, although the effect of a large vesicle pool can be observed at moderate rates.
Appendix A

The parameters $\beta_1$, $\beta_1$ and $\epsilon$ depend on $\nu$, $CV$ and correlation time $\tau_c$

$$\nu = \beta_1 \beta_2 / A$$
$$\tau_c = 1 / A$$
$$CV^2 - 1 = 2 \epsilon (1 - \epsilon) (\beta_1 - \beta_2)^2 / A^2$$
$$A = (1 - \epsilon) \beta_2 + \epsilon \beta_1$$

Appendix B

For $\tau_c \to 0$:

$$\rho_{isi}(T) = (1 - \epsilon) \beta e^{-T^\beta} + \epsilon \delta(T)$$
$$\nu = \beta / (1 - \epsilon)$$
$$CV^2 = 1 + \frac{2\epsilon}{1 - \epsilon}$$