Before I start, I want to thank my collaborators, ML and PD.

The human brain contains $10^{15}$ synapses each of which transmit information from one neuron to the next. There are 2 surprising facts about this information transmission that I want to highlight.
Before I start, I want to thank my collaborators, ML and PD.

The human brain contains $10^{15}$ synapses each of which transmit information from one neuron to the next. There are 2 surprising facts about this information transmission that I want to highlight.
Fact 1: Short-Term Synaptic Plasticity

First is that the same input does not give the same output.

horrible. No engineers design like this
Fact 1: Short-Term Synaptic Plasticity

First is that the same input does not give the same output.

horrible. No engineers design like this
First is that the same input does not give the same output.

horrible. No engineers design like this
Fact 1: Short-Term Synaptic Plasticity

First is that the same input does not give the same output. Horrible. No engineers design like this.
Fact 1: Short-Term Synaptic Plasticity

First is that the same input does not give the same output. Horrible. No engineers design like this.
Fact 2: Analog and digital signalling

The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals. Optimal estimation, mean posterior..

- Analog signals are easy to compute with (e.g. sum, non-lin) -> dendritic tree. But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

Optimal estimation, mean posterior..

- Analog signals are easy to compute with (e.g. sum, non-lin) → dendritic tree.
  But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-lin) \( \rightarrow \) dendritic tree.
  But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals

- Analog signals are easy to compute with (e.g. sum, non-lin) -> dendritic tree. But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format
Fact 2: Analog and digital signalling

The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals. Optimal estimation, mean posterior...

- Analog signals are easy to compute with (e.g. sum, non-lin) \(\rightarrow\) dendritic tree. But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-lin) \(\rightarrow\) dendritic tree.
But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-linear) -> dendritic tree.
  But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in a digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-lin) → dendritic tree.
But not very resistant to noise.
On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-lin) → dendritic tree.
  But not very resistant to noise.
- On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in a digital format.
The second surprising fact: Neurons are hybrid computational units: work with both analog and digital signals.

- Analog signals are easy to compute with (e.g. sum, non-lin) \(\rightarrow\) dendritic tree.
  But not very resistant to noise.

  On the other side, digital signals are good for reliable signal transmission since they are more robust to noise. This is what the neuron is doing.

Message is sent in an digital format.
Outline

- Short-term plasticity (STP) and analog-digital signalling

- Model
  - Prior: Neuronal model
  - Optimal membrane potential estimator

- Results:
  - Performance of the optimal estimator
  - Optimal estimator is similar to STP

- Summary
Outline

• Short-term plasticity (STP) and analog-digital signalling

• Model
  ➡ Prior: Neuronal model
  ➡ Optimal membrane potential estimator

• Results:
  ➡ Performance of the optimal estimator
  ➡ Optimal estimator is similar to STP

• Summary
Ornstein-Uhlenbeck process:

\[ u_t = u_{t-1} - \theta (u_{t-1} - u_r) \Delta t + W_t \sqrt{\Delta t} \]
Ornstein Uhlenbeck process:

\[ u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t \sqrt{\Delta t} \]
Neuronal model

Ornstein Uhlenbeck process:

\[ u_t = u_{t-1} - \theta (u_{t-1} - u_r) \Delta t + W_t \sqrt{\Delta t} \]
Ornstein Uhlenbeck process:

\[ u_t = u_{t-1} - \theta (u_{t-1} - u_r) \Delta t + W_t \sqrt{\Delta t} \]
Neuronal model

Ornstein Uhlenbeck process:
\[ u_t = u_{t-1} - \theta(u_{t-1} - u_r) \Delta t + W_t \sqrt{\Delta t} \]

prob. spike: \[ p(s_t = 1 | u_t) = g(u_t) \Delta t \]
Ornstein-Uhlenbeck process:
\[ u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t \sqrt{\Delta t} \]

prob. spike:
\[ p(s_t = 1 | u_t) = g(u_t) \Delta t \]
\[ g(u) = g_0 \exp(\beta u) \]
Neuronal model

Ornstein-Uhlenbeck process:
\[ u_t = u_{t-1} - \theta(u_{t-1} - u_r) \Delta t + W_t \sqrt{\Delta t} \]

prob. spike:
\[ p(s_t = 1 | u_t) = g(u_t) \Delta t \]
\[ g(u) = g_0 \exp(\beta u) \]
Neuronal model

\[ u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t \sqrt{\Delta t} \]

prob. spike:
\[ p(s_t = 1|u_t) = g(u_t)\Delta t \]

Ornstein Uhlenbeck process:

hidden dynamical system. linear gaussian dyn. binary output. (not kalman since)
Inference of the membrane potential

\[ p(u_t \mid s_{1\ldots t}) \propto p(s_t \mid u_t) \int p(u_t \mid u_{t-1}) p(u_{t-1} \mid s_{1\ldots t-1}) \, du_{t-1} \]
Inference of the membrane potential

Posterior distribution:

\[
p(u_t | s_1...t) \propto p(s_t | u_t) \int p(u_t | u_{t-1}) p(u_{t-1} | s_1...t-1) du_{t-1}
\]
Inference of the membrane potential

Posterior distribution:

\[
p(u_t | s_1...t) \propto p(s_t | u_t) \int p(u_t | u_{t-1}) p(u_{t-1} | s_1...t-1) \, du_{t-1}
\]
Inference of the membrane potential

\[ u_1 \rightarrow \ldots \rightarrow u_{t-1} \rightarrow u_t \]

\[ s_1 \rightarrow \ldots \rightarrow s_{t-1} \rightarrow s_t \]

Posterior distribution:

\[
p(u_t | s_1 \ldots t) \propto p(s_t | u_t) \int p(u_t | u_{t-1}) p(u_{t-1} | s_1 \ldots t-1) \, du_{t-1}
\]

\[
\mathcal{N}(u_t | \mu_t, \sigma^2_t)
\]

\[
\mathcal{N}(u_{t-1} | \mu_{t-1}, \sigma^2_{t-1})
\]
Dynamics of the optimal estimator

\[ \dot{\mu} = -\theta (\mu - u_r) + \beta \sigma^2 (S(t) - \gamma(t)) \]

\[ \gamma(t) = \langle g(u) \rangle_{u|\mu(t),\sigma^2(t)} \]
Dynamics of the optimal estimator

\[ \dot{\mu} = -\theta (\mu - u_r) + \beta \sigma^2 (S(t) - \gamma(t)) \]

\[ \gamma(t) = \langle g(u) \rangle_{u \mid \mu(t), \sigma^2(t)} \]

\[ \dot{\sigma}^2 = -2\theta (\sigma^2 - \sigma_{OU}^2) - \gamma(t) \beta^2 \sigma^4 \]
Dynamics of the optimal estimator

\[ \dot{\mu} = -\theta(\mu - u_r) + \beta \sigma^2 (S(t) - \gamma(t)) \]

\[ \gamma(t) = \langle g(u) \rangle_{u | \mu(t), \sigma^2(t)} \]

\[ \dot{\sigma}^2 = -2\theta(\sigma^2 - \sigma^2_{OU}) - \gamma(t) \beta^2 \sigma^4 \]
Outline

• Short-term plasticity (STP) and analog-digital signalling

• Model
  ➞ Prior: Neuronal model
  ➞ Optimal membrane potential estimator

• Results:
  ➞ Performance of the optimal estimator
  ➞ Optimal estimator is similar to STP

• Summary
Optimal estimator vs membrane potential

Membrane potential

Optimal estimator $\mu \pm \sigma$
Steady-state spiking increment

\[
\frac{\text{EPSP}_8}{\text{EPSP}_1} \quad \text{Model}
\]

\[
\frac{\text{EPSP}_8}{\text{EPSP}_1} \quad \text{Data}
\]

\[
\frac{\text{EPSP}_8}{\text{EPSP}_1} = \frac{1}{1 + \text{stimulus rate}}
\]

Figure A. Steady-state spiking increment of the optimal estimator as a function of \( r = \langle S \rangle \).

Figure B. Synaptic depression in the climbing fibre to Purkinje cell synapse average ± s.e.m. normalised "steady-state" magnitude of EPSCs as a function of stimulation frequency. Reproduced from Dittman et al. 2000.

Importantly, the similarity between the optimal membrane potential estimator and short-term plasticity is not limited to stationary properties. Indeed, the actual dynamics of the optimal estimator can be well approximated by the dynamics of synaptic depression. In a canonical model of short-term depression, the postsynaptic membrane potential, \( v \), changes as:

\[
\dot{v} = -v - v_0 \tau + J Y x(S) (t),
\]

with

\[
\dot{x} = \frac{1}{\tau_D} - x \tau - Y x(S) (t),
\]

where \( J \) and \( Y \) are constants (synaptic weight and utilisation fraction), and \( x \) is a time varying 'resource' variable (e.g., the fraction of presynaptic vesicles ready to fuse to the membrane). Thus, \( v \) is increased by each presynaptic spike, and in the absence of spikes it decays to its resting value, \( v_0 \), with membrane time constant \( \tau \). However, the effect of each spike on \( v \) is scaled by \( x \) which itself is decreased after each spike and increases between spikes back towards one with time constant \( \tau_D \).

Thus, the postsynaptic potential, \( v \), behaves much like the posterior mean of the optimal estimator, while the dynamics of the synaptic resource variable, \( x \), closely resemble that of the posterior variance of the optimal estimator. This qualitative similarity can be made more formal under appropriate assumptions, for details see section " of supplementary information. Indeed, the capacity of a depressing synapse (with appropriate parameters) to estimate the presynaptic membrane potential can be nearly as good as that of the optimal estimator (Fig. A, top). Interestingly, although the scaled variance \( \sigma^2 / \sigma^2_\infty \) does not follow the resource variable dynamics perfectly just after a spike, these two quantities are virtually identical at the time of the next spike, i.e., when they are used by the membrane potential estimators (Fig. A, bottom).

Performance analysis

In order to quantify how well synaptic dynamics with depression perform in estimating presynaptic membrane potentials, we measure performance by the mean-squared error (MSE) between the true membrane potential, \( u \), and the estimated membrane potential, and compare the MSE of three alternatives estimators.

The simplest model we consider is a static (non-depressing) synapse, in which \( v \) is given by Eq. , with constant \( x = 1 \). This estimator has only one tuneable parameter, \( \tau \).

The second estimator we consider includes synaptic depression, i.e., \( x \) is also allowed to vary (Eq. ,). This estimator contains three tuneable parameters, \( v_0, \tau, Y, J \).

Finally, we consider the optimal estimator (Eqs. ). This estimator has no tunable parameters. Once the parameters of presynaptic membrane potential dynamics (\( \sigma_W, \theta, u, r, \beta, g_0 \)) and spiking (\( \beta, g_0 \)) are fixed, the optimal estimator is entirely determined. The comparison of the performance of these three estimators is displayed on Fig. -.

The optimal estimator (black circles) is obviously a lower bound on any type of estimator. For a wide range of parameter values, the depressing synapse performs almost as well as the optimal estimator, and both perform better than the static synapse (Fig. -).
Postsynaptic Membrane potential
\[ \mu \leftrightarrow \nu \]

Resource variable
\[ \sigma^2 \leftrightarrow x \]

\[ \dot{v} = -\tau^{-1}(v - v_0) + JxS(t) \]

\[ \dot{x} = \tau_D^{-1}(1 - x) - YxS(t) \]

Tsodyks et al. 1998
Depressing synapses as near-optimal estimators

Membrane potential
Optimal estimator
Depressing synapse

\[ x, \sigma^2/\sigma_0^2 \]

\[ \text{time [ms]} \]

0 200 400 600 800 1000
Depressing synapses vs static synapses

\[ \beta \text{ [mV}^{-1}\text{]} \]
Depressing synapses vs static synapses

\[ \beta \text{ [mV}^{-1}] \]

stochastic limit

-2 \hspace{1cm} 0 \hspace{1cm} 2
Depressing synapses vs static synapses

\[ \beta \text{ [mV}^{-1}\text{]} \]

stochastic limit

\[ u \text{ [mV]} \]

Deterministic limit

\[ u \text{ [mV]} \]
Summary

• Synapses have a rich dynamics which can be useful for computation.
• We derived analytically the exact on-line optimal estimator of the presynaptic membrane potential.
• Synapses with short-term depression closely match the behaviour of the optimal estimator.
• Testable predictions: dynamics of short-term plasticity should be matched to the membrane potential dynamics of the presynaptic neuron.
Normative electrophysiology: Explaining cellular properties of neurons from first principles

Friday, December 11th, 2009
Alpine Room A
Whistler