Decoding

How well can we learn what the stimulus is by looking at the neural responses?

Two approaches:

- devise explicit algorithms for extracting a stimulus estimate
- directly quantify the relationship between stimulus and response using information theory
Predicting the firing rate

Starting with a rate response, \( r(t) \) and a stimulus, \( s(t) \),

the optimal linear estimator finds the best kernel \( K \) such that:

\[
    r_{\text{est}}(t) = \bar{r} + \int d\tau \ s(t - \tau)K(\tau)
\]

is close to \( r(t) \), in the least squares sense.

Solving for \( K(t) \),

\[
    K(t) = \frac{1}{2\pi} \int d\omega \ e^{-i\omega t} \frac{\tilde{C}_{rs}(-\omega)}{\tilde{C}_{ss}(\omega)}
\]
Stimulus reconstruction
Stimulus reconstruction
Stimulus reconstruction
Reading minds: the LGN

Yang Dan, UC Berkeley
Computing in carbon

Basic elements of neuroelectronics
  -- membranes
  -- ion channels
  -- wiring

Elementary neuron models
  -- conductance based
  -- modelers’ alternatives

Wiring neurons together
  -- synapses
  -- short term plasticity
Closeup of a patch on the surface of a neuron

- channel
- pore
- lipid bilayer
An electrophysiology experiment

Ion channels create opportunities for charge to flow
Potential difference is maintained by ion pumps
Movement of ions through the ion channels

Energetics: \( qV \sim k_B T \)

\( V \sim 25 \text{mV} \)
The equilibrium potential

Ions move down their concentration gradient until opposed by electrostatic forces

Nernst: \[ E = \frac{k_B T}{z q} \ln \left( \frac{[\text{inside}]}{[\text{outside}]} \right) \]
Different ion channels have associated *conductances*.

A given conductance tends to move the membrane potential toward the equilibrium potential for that ion:

- $E_{\text{Na}} \sim 50\text{mV}$ (depolarizing)
- $E_{\text{Ca}} \sim 150\text{mV}$ (depolarizing)
- $E_{\text{K}} \sim -80\text{mV}$ (hyperpolarizing)
- $E_{\text{Cl}} \sim -60\text{mV}$ (shunting)

When $V > E$, positive current will flow outward.
When $V < E$, positive current will flow inward.

More polarized when $V$ is closer to $E$. 
$E_{\text{Na}}$ is more depolarizing, $E_{\text{K}}$ is more hyperpolarizing.
The neuron is an excitable system
Excitability is due to the properties of ion channels

- Voltage dependent
- Transmitter dependent (synaptic)
- Ca dependent
The ion channel is a complex molecular machine

**K channel**: open probability increases when depolarized

\[ P_K \sim n^4 \]

\( n \) describes a subunit

\[ n \quad \text{is open probability} \]
\[ 1 - n \quad \text{is closed probability} \]

Transitions between states occur at voltage dependent rates

\[ \alpha_n(V) \quad C \rightarrow O \]
\[ \beta_n(V) \quad O \rightarrow C \]

\[
\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n
\]

Persistent conductance
Transient conductances

Gate acts as in previous case

Additional gate can block channel when open

\[ P_{Na} \sim m^3h \]

\( m \) is activation variable
\( h \) is inactivation variable

\( m \) and \( h \) have opposite voltage dependences:
- Depolarization increases \( m \), activation
- Hyperpolarization increases \( h \), deinactivation
First order rate equations

\[
\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n
\]

\[
\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V)m
\]

\[
\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V)h
\]

We can rewrite:

\[
\tau_n(V) \frac{dn}{dt} = n_\infty(V) - n
\]

where

\[
\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}
\]

\[
n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}
\]
A microscopic stochastic model for ion channel function
Different from the continuous model:

interdependence between inactivation and activation transitions to inactivation state 5 can occur only from 2, 3 and 4

$k_1, k_2, k_3$ are *constant*, not voltage dependent
Putting it back together

Ohm’s law: \( V = I R \) and Kirchhoff’s law

\[-C_m \frac{dV}{dt} = \sum_i g_i (V - E_i) + I_e\]

- **Capacitative current**
- **Ionic currents**
- **Externally applied current**
The Hodgkin-Huxley equation

\[ C_m \frac{dV}{dt} = - \sum_i g_i (V - E_i) - I_e \]

\[ -C_m \frac{dV}{dt} = g_L (V - E_L) + \bar{g}_K n^4 (V - E_K) + \bar{g}_{Na} m^3 h (V - E_{Na}) \]
Anatomy of a spike
The integrate-and-fire model

Like a passive membrane:

$$C_m \frac{dV}{dt} = -g_L (V - E_i) - I_e$$

but with the additional rule that

when $V \rightarrow V_T$, a spike is fired
and $V \rightarrow V_{\text{reset}}$.

$E_L$ is the resting potential of the “cell”.

![Graph showing the integrate-and-fire model](image)
The spike response model
Gerstner and Kistler

Kernel $f$ for subthreshold response $\leftarrow$ replaces leaky integrator
Kernel for spikes $\leftarrow$ replaces “line”

• determine $f$ from the linearized HH equations
• fit a threshold
• paste in the spike shape and AHP
An advanced spike response model
Keat, Reinagel and Meister

- AHP assumed to be exponential recovery, $A \exp(-t/\tau)$
- need to fit all parameters
The generalized linear model
Paninski, Pillow, Simoncelli

- general definitions for k and h
- robust maximum likelihood fitting procedure
Signal is carried chemically across the synaptic cleft
Post-synaptic conductances

A

\[ \frac{P_S}{P_{\text{max}}} \]

- **AMPA**
- **GABA_A**

\[ t \text{ (ms)} \]

B

\[ \frac{P_S}{P_{\text{max}}} \]

- **NMDA**

\[ t \text{ (ms)} \]

Requires pre- and post-synaptic depolarization

Coincidence detection, Hebbian
Synaptic plasticity

1. LTP, LTD

2. Spike-timing dependent plasticity

A. 

\[
\begin{align*}
&\text{LTP} \\
&\downarrow \\
&\text{LTD} \\
\end{align*}
\]

\[
t_{\text{post}} - t_{\text{pre}}
\]

B. 

\[
\begin{align*}
&\text{LTP} \\
&\downarrow \\
&\text{LTD} \\
\end{align*}
\]

\[
t_{\text{post}} - t_{\text{pre}}
\]

C. 

\[
\begin{align*}
&\text{LTP} \\
&\downarrow \\
&\text{LTD} \\
\end{align*}
\]

\[
t_{\text{post}} - t_{\text{pre}}
\]

D. 

\[
\begin{align*}
&\text{LTP} \\
&\downarrow \\
&\text{LTD} \\
\end{align*}
\]

\[
t_{\text{post}} - t_{\text{pre}}
\]

E. 

\[
\begin{align*}
&\text{LTP} \\
&\downarrow \\
&\text{LTD} \\
\end{align*}
\]

\[
t_{\text{post}} - t_{\text{pre}}
\]
Short-term synaptic plasticity

A

Depression

B

Facilitation

Depression

Facilitation