Neural circuits for cognition

MIT 9.49/9.490/6.S076

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Class business

- HW 1 up, due Sept 27
- Tutorial -- Gregg announcement
- Math survey
- Psetpartners: https://psetpartners.mit.edu/
- Quick intros
- JC readings: computation in dendrites; computation with multiple cell types (Maas) -- volunteers

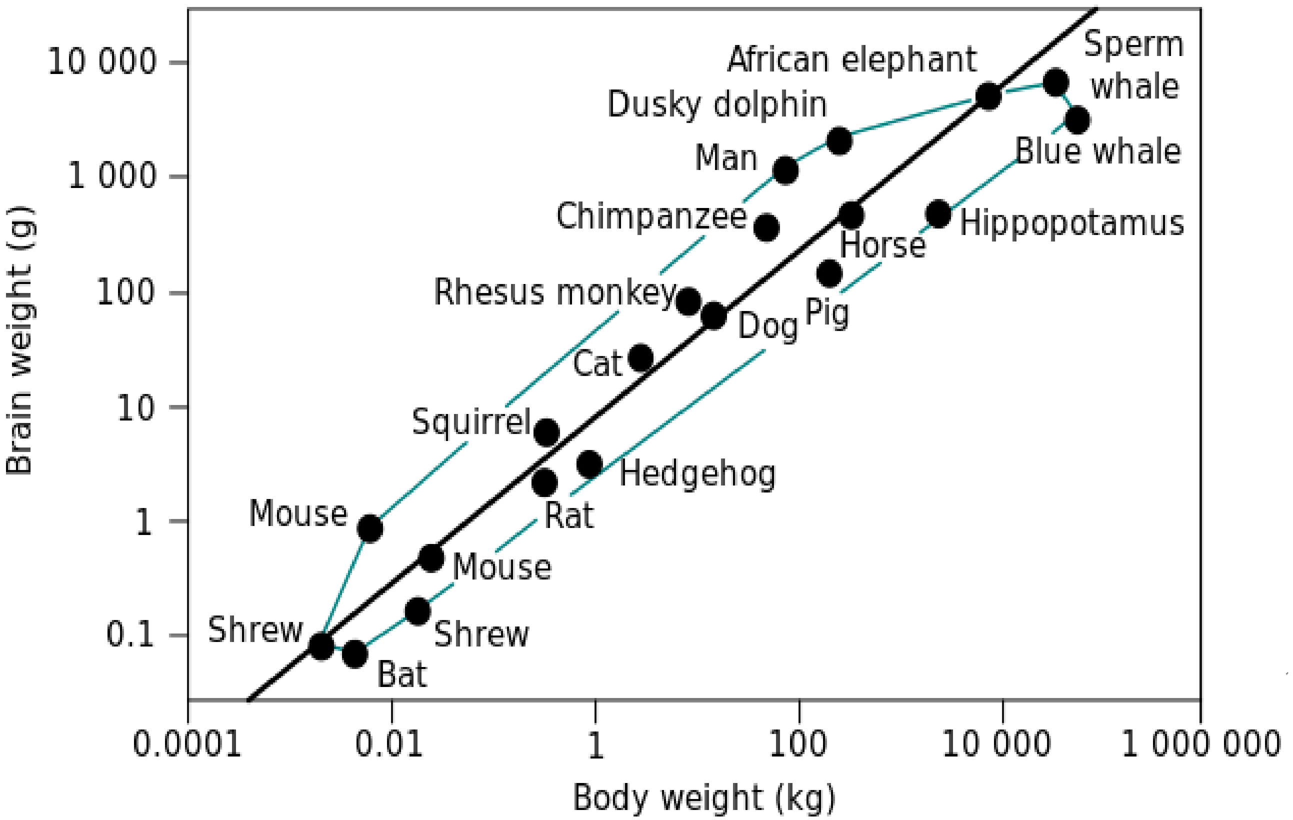
Quick brain facts

Neurons and numbers in the human brain

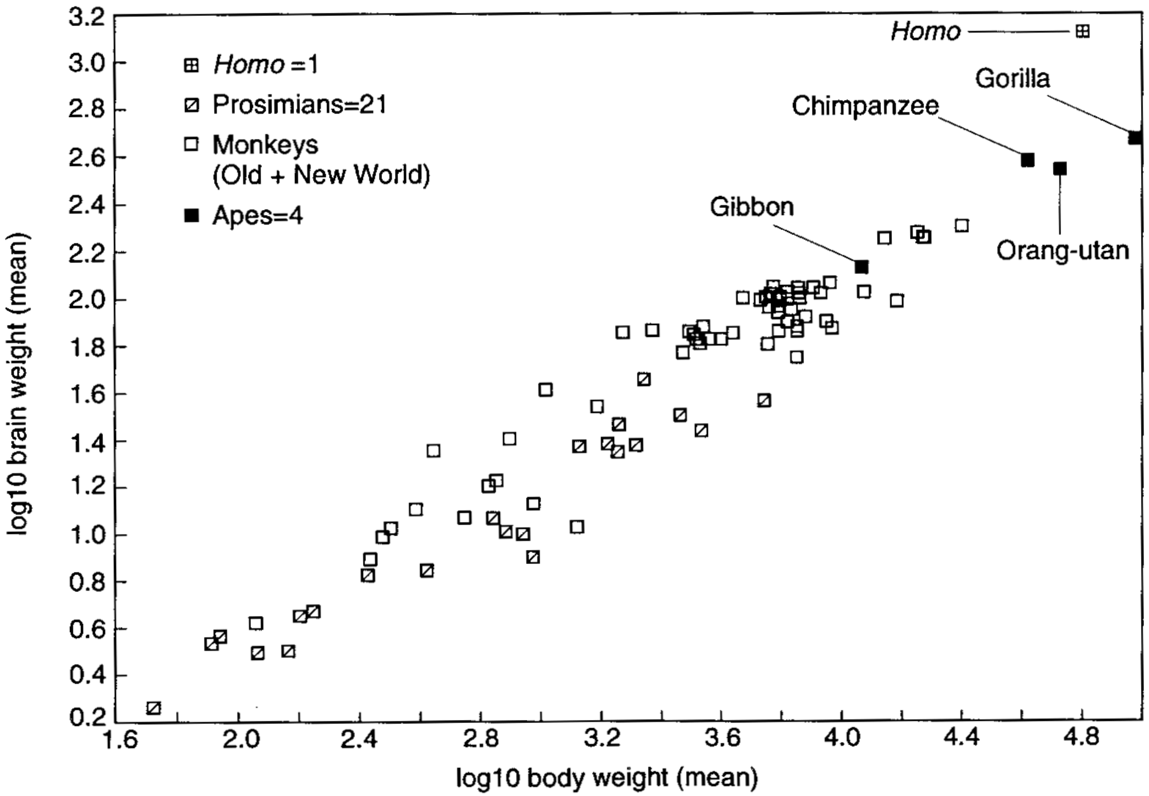
- Brain: 3 lbs
- Brain: 2-3% body weight 20% energy, oxygen use
- ~100 billion neurons (10^{11}) (~10^{10} in cerebral cortex, ~10^{11} in cerebellum); 1 bit/neuron –> 0.1 terabits! (terabit = 10^{12} bits)
- 10-100 trillion synapses (10^{13} - 10^{14}); 1 bit/synapse → 10 terabits – 0.1 petabit (petabit = 10^{15} bits)
- Synapses sparse: only 100-1000/cell (very far from all-to-all connectivity)
- Cell body size: 10 microns (1/10 hair thickness)
- Axon/cell length upto 1 m (see Mouselight, Janelia Farms for highly detailed collateral projections of cells, showing highly specific, extensive across-brain axon projection of single neurons in mice)
- 1 mm^3 of grey matter in cortex contains ~3 km of axons, mainly formed by pyramidal neurons.

Brain weight scaling across species

mammals



primates



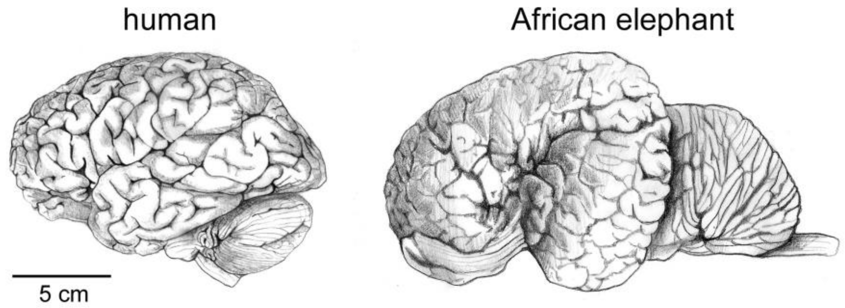
Holloway 1996, *Evolution of the Human Brain*

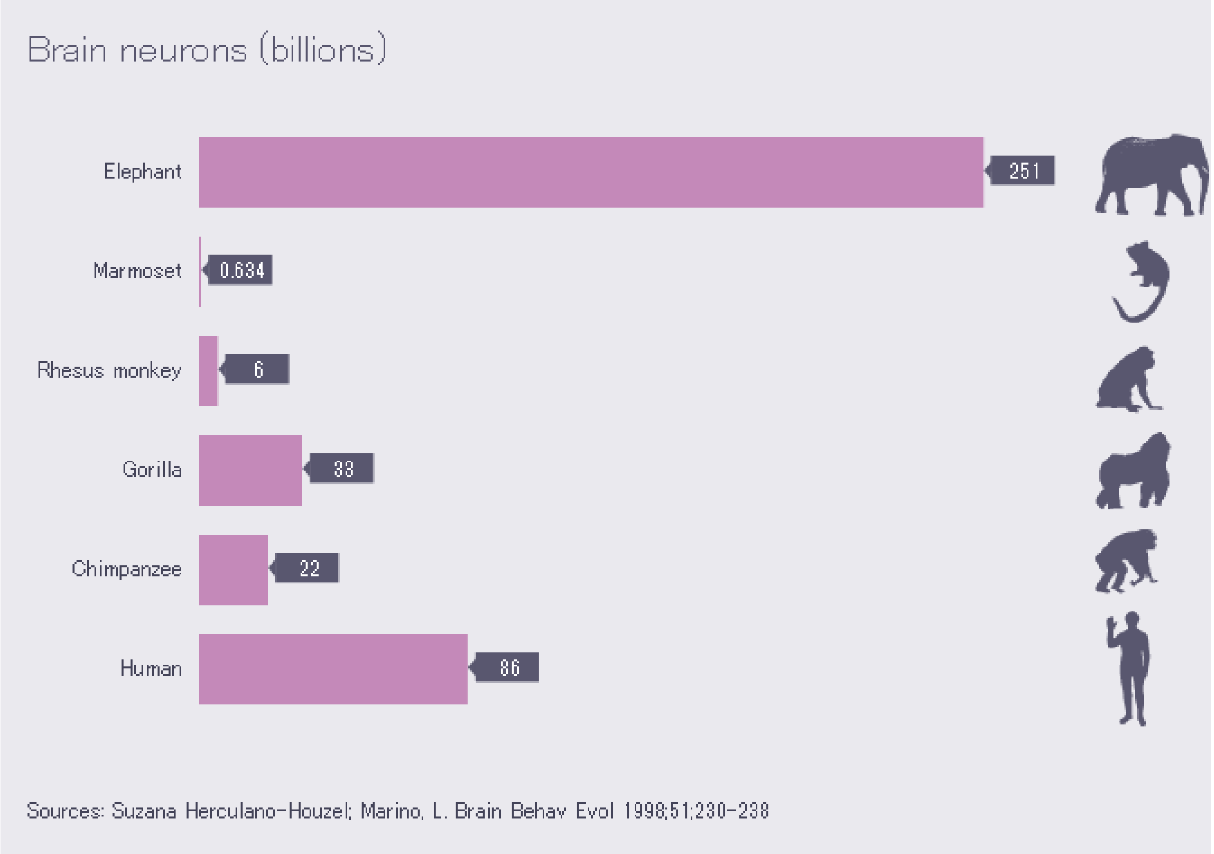
For more info on comparative brain scaling, see:

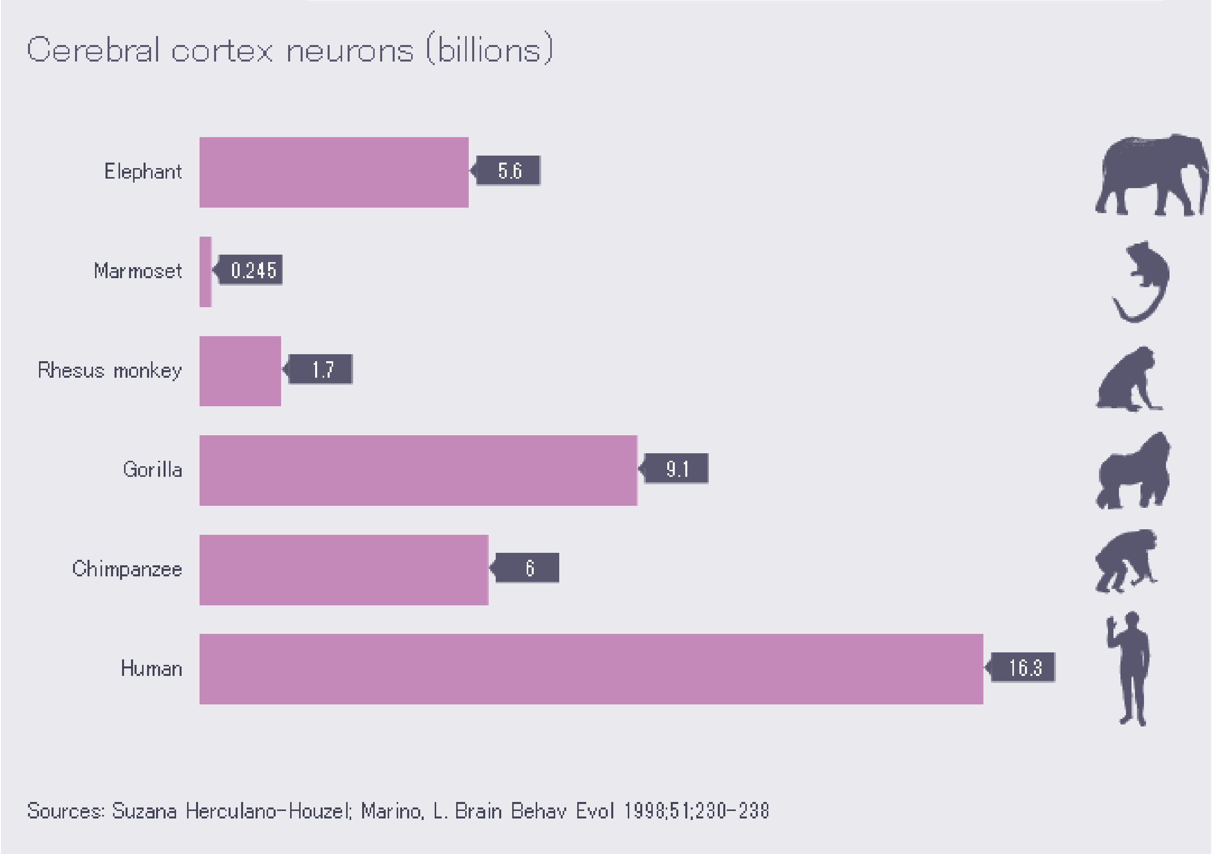
S. Herculano-Houzel. The human brain in numbers: a linearly scaled-up primate brain https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2776484/

S.S. Wang. Functional tradeoffs in brain scaling: implications for brain function https://www.ncbi.nlm.nih.gov/pubmed/18836261

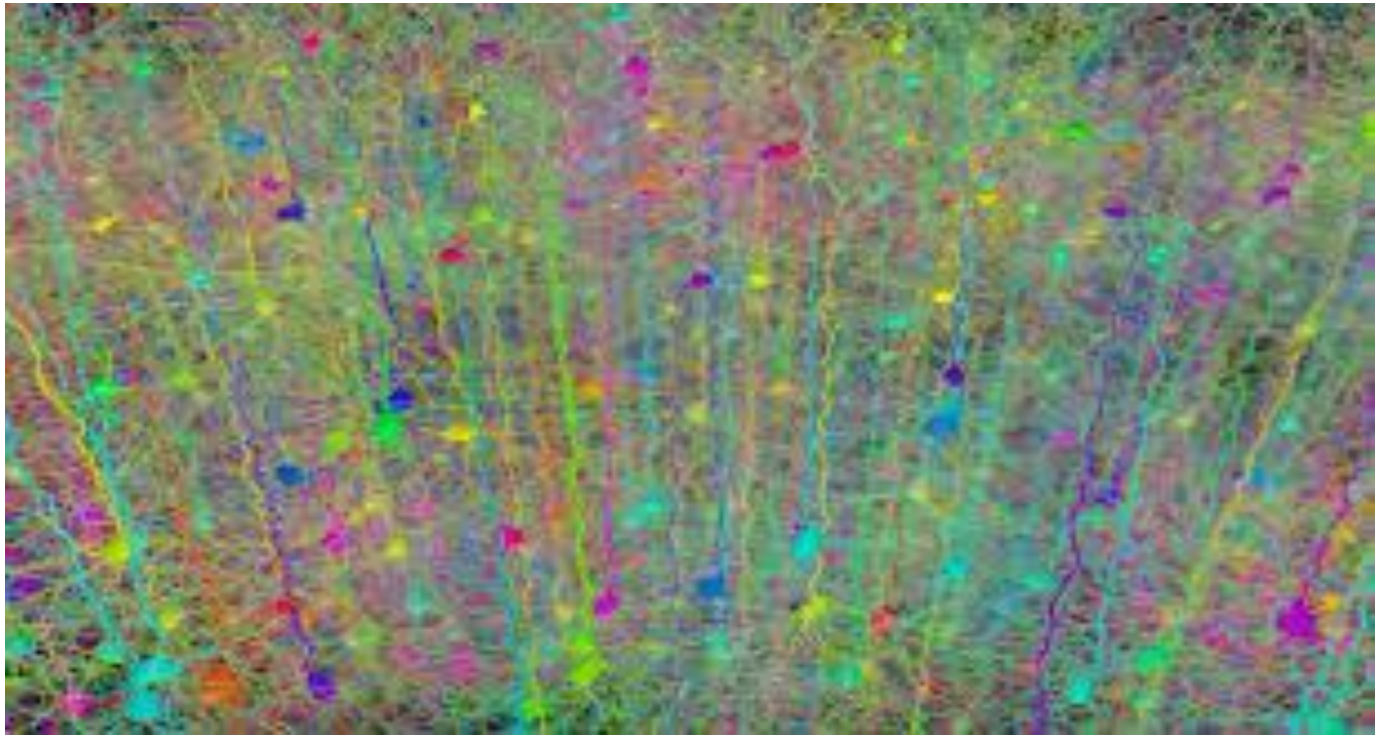
Neurons and cortical neurons across species



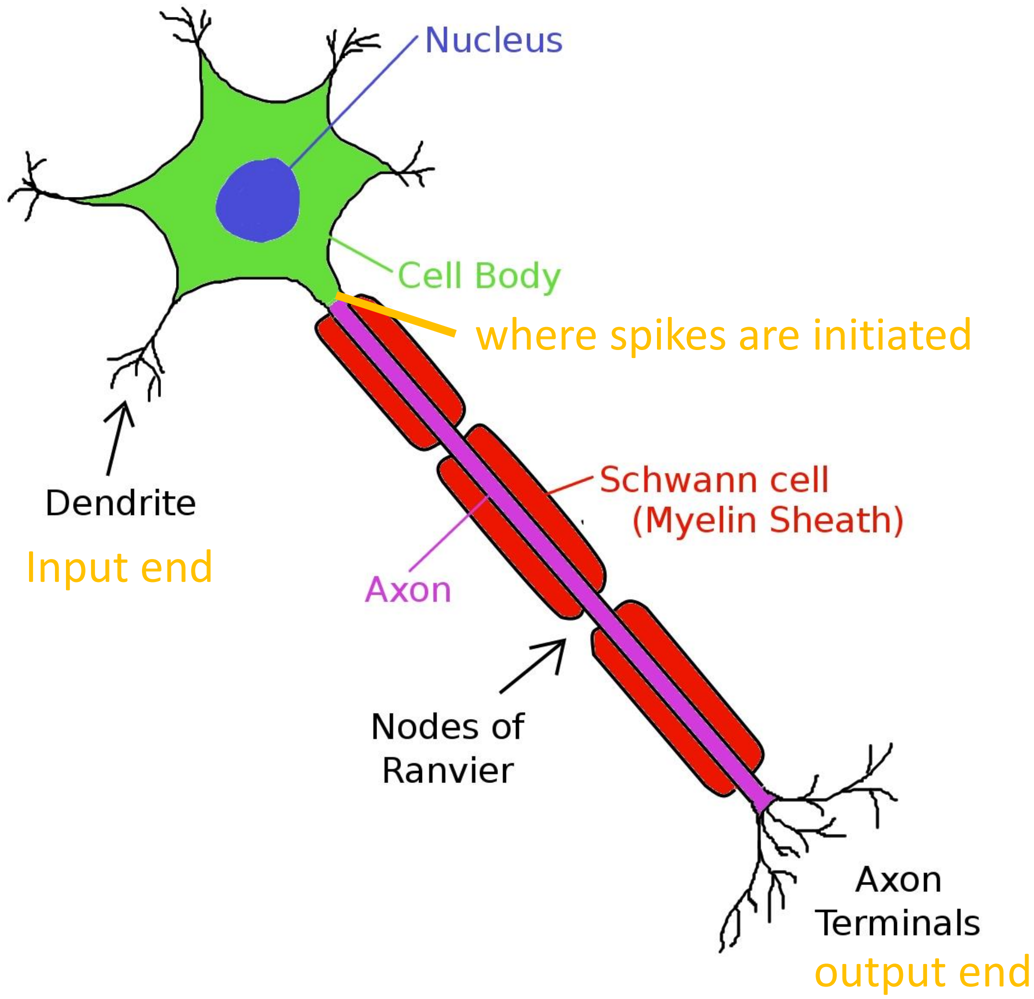




Neurons and single-neuron equations



Parts of a neuron



Resting state: pumps maintain ionic segregation

- Transynaptic membrane pumps use energy (ATP) to actively maintain chemical gradients across the membrane.

- Concentration gradients of various ions:

Ionic species	Pump direction	Outside (mM)	Inside (mM)
Na^+	out	145	12
K^+	in	4	155
Ca^{2+}	out	1.5	10^{-4}

Resting state: Ionic segregation generates voltage drop across membrane

- Chemical gradient of ionic species A sets up voltage difference through Nernst Potential:

$$V_m = \frac{k_B T}{ze} \ln \frac{[A]_{out}}{[A]_{in}}$$

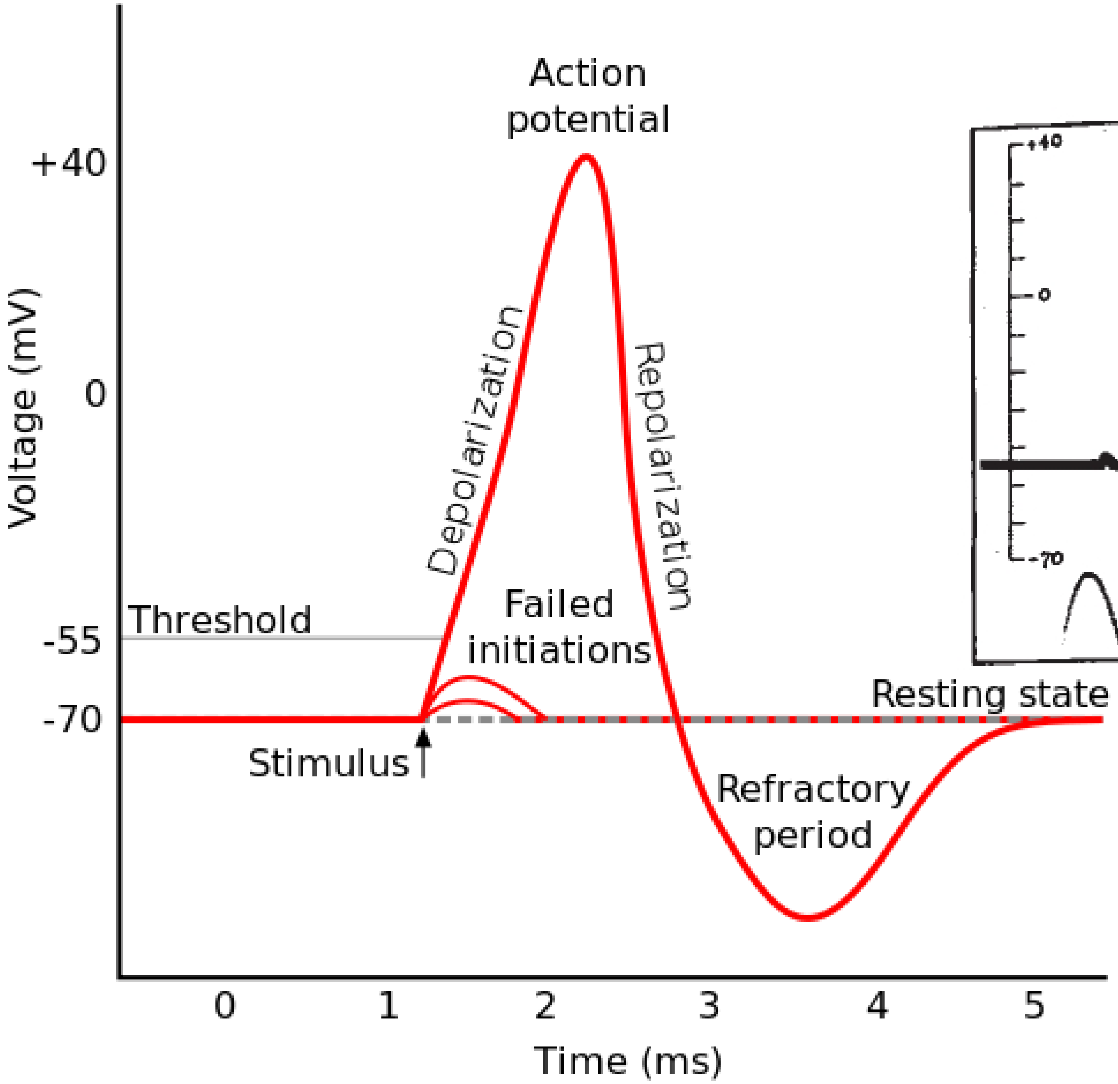
$e =$ electron charge
$z =$ charge of ionic species (Ca^{2+}:2, Na^{+}: 1)
$T =$ temp in Kelvin
$k_B =$ Boltzmann const.

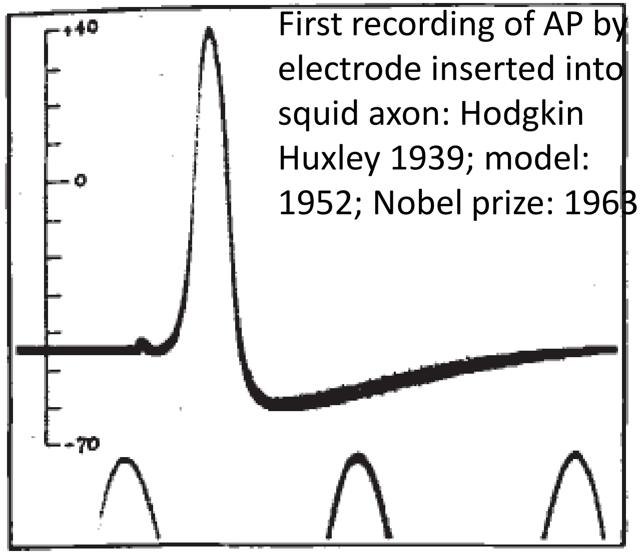
- Generalization to multiple ionic species/non-equilibrium: Goldman-Hodgkin-Katz Potential (see Johnston & Wu textbook): $V_m \approx -55 - 60\ mV$

Activity in a neuron: electrical potential

An action potential is a brief, highly nonlinear, stereotyped and rapid voltage change in the cell's state.

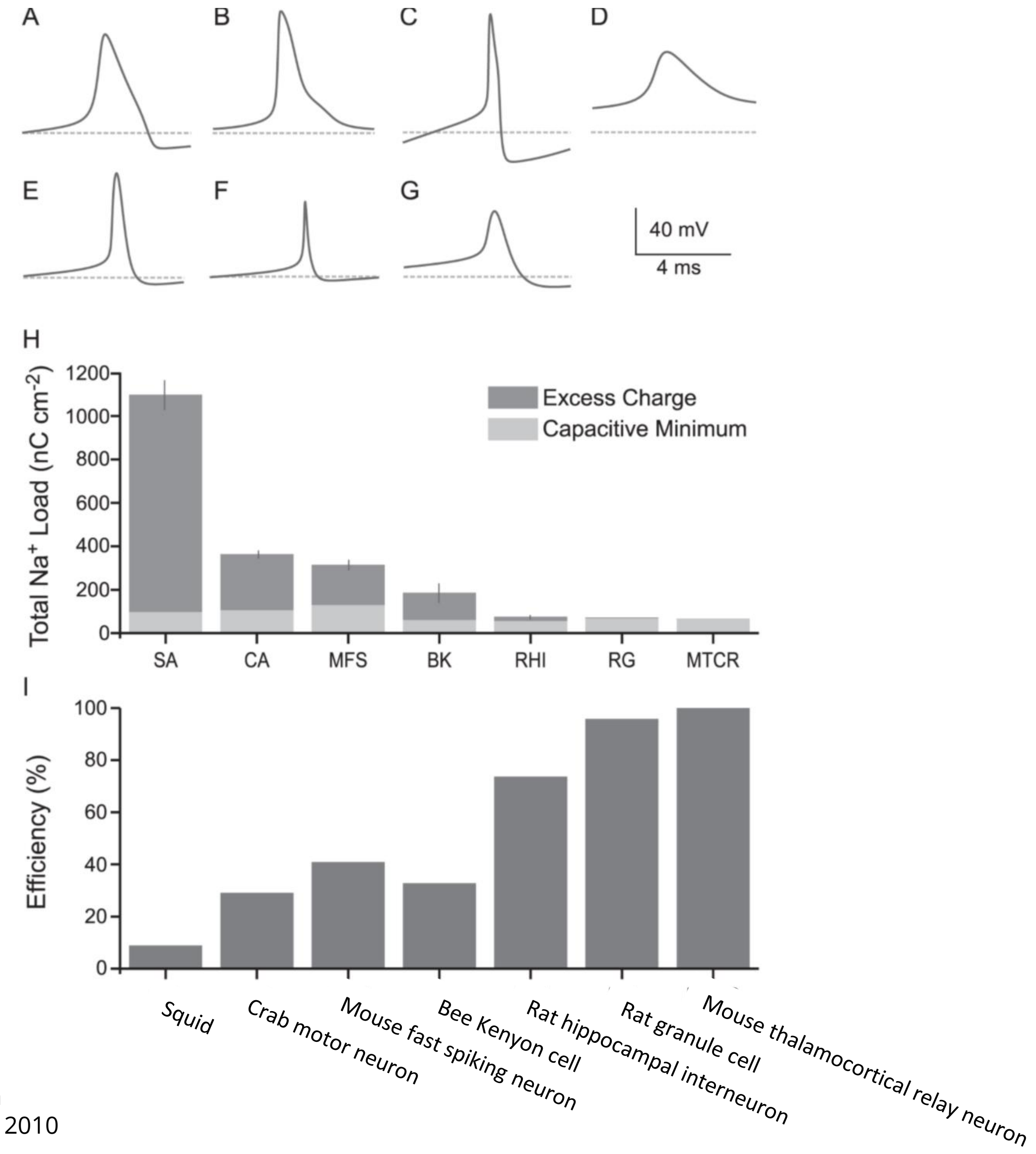
The action potential communicates a binarized version of the somatic state in a way that is regenerative and non-dissipative across short and long distances in the brain.





First recording of AP by electrode inserted into squid axon: Hodgkin Huxley 1939; model: 1952; Nobel prize: 1963

Different AP shapes and energetic costs of AP generation



Energy consumption can increase by more than ten-fold simply by changing the temporal overlap of the inward and outward (Na^+ and $K^{+)}$ currents during the AP, without changing APs shape (more overlap=more energy consumption).

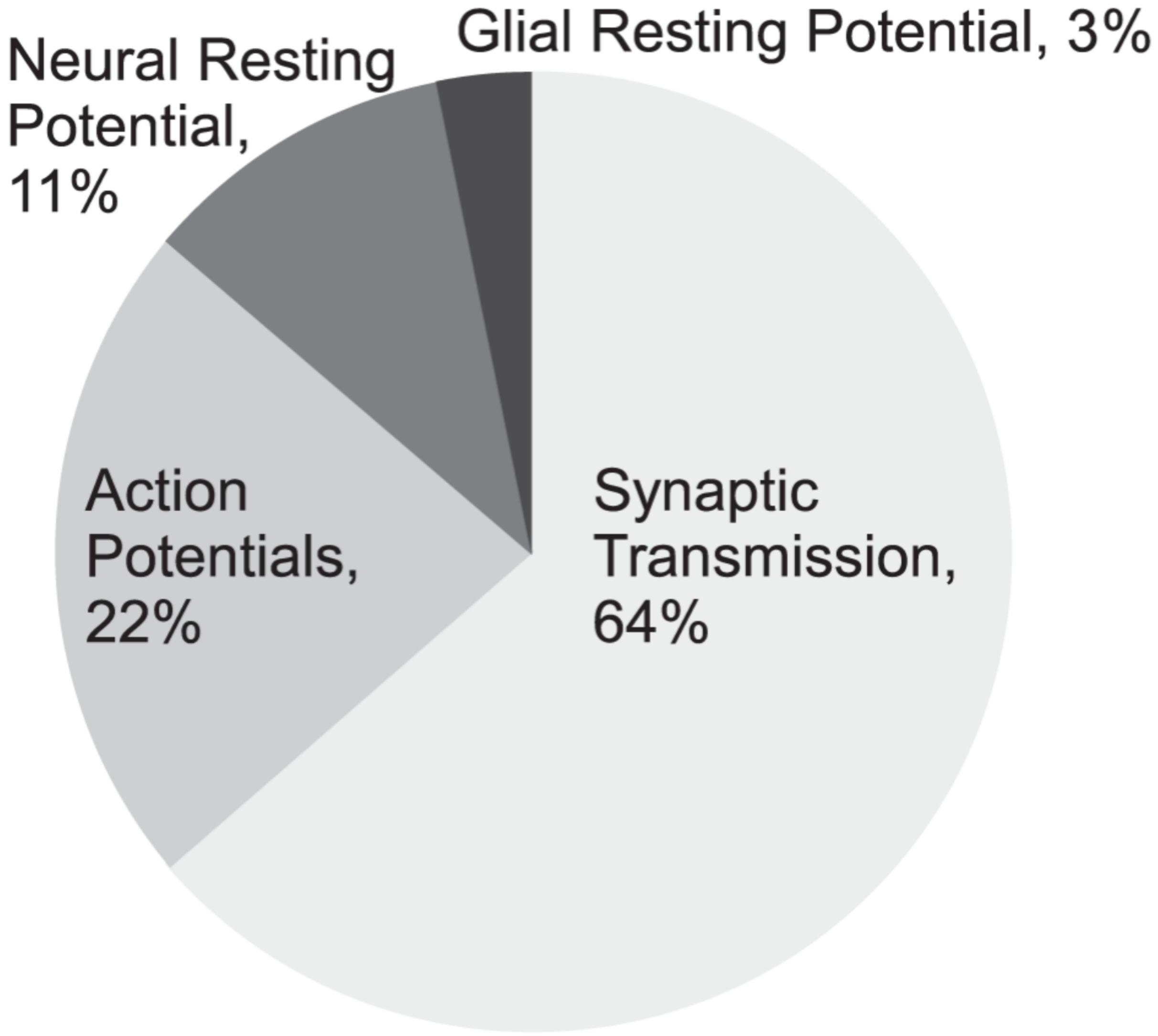
Thus, AP height and width are poor predictors of energy consumption.

In HH model of the squid axon, optimizing the kinetics or number of Na^+ and K^+ channels can whittle down the number of ATP molecules needed for each AP by 4x.

In contrast to the squid AP, the temporal profile of the currents underlying APs of some mammalian neurons are nearly perfectly matched to the optimized properties of ionic conductances so as to minimize the ATP cost.

Action Potential Energy Efficiency Varies Among Neuron Types in Vertebrates and Invertebrates. Sengupta et al., 2010

Energy budget for grey matter in rat brain

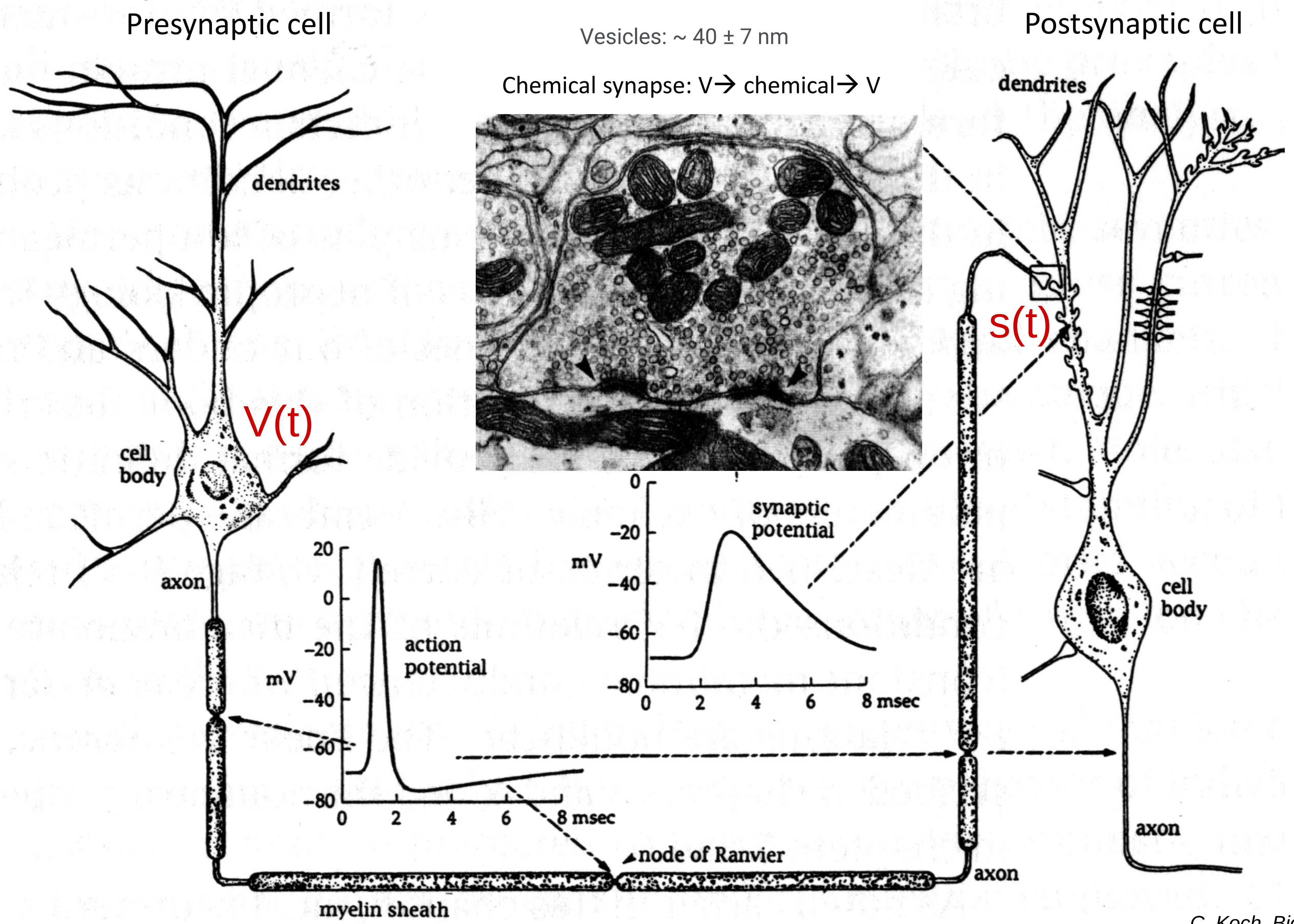


Action Potential Energy Efficiency Varies Among Neuron Types in Vertebrates and Invertebrates. Sengupta et al., 2010

Attwell & Laughlin 2001

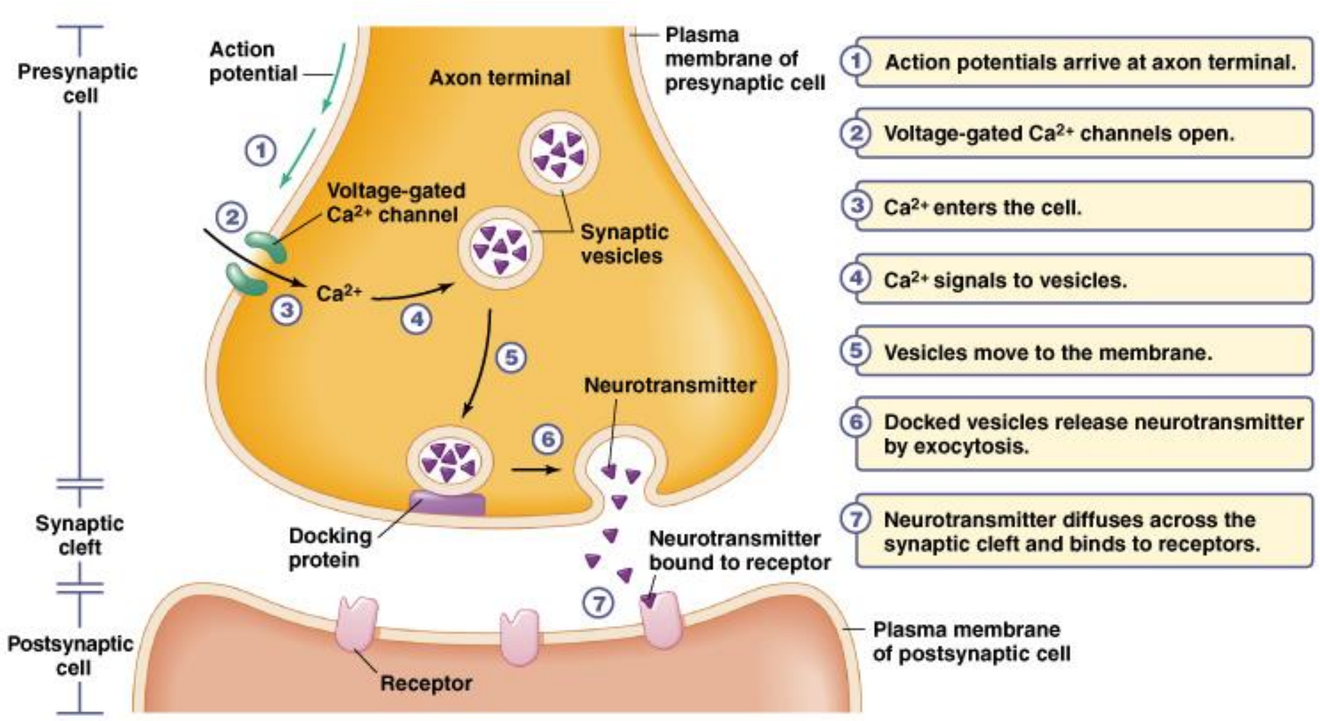
Synaptic communication

The chemical synapse



C. Koch, Biophysics of Computation

The chemical synapse



Chemical synapse:

- Directed
- Flexible/plastic
- Excitation of presynaptic neuron can lead to excitation or inhibition in target, depending on presynaptic neuron type.

Dale's law: A neuron releases the same set of neurotransmitters from all its synapses. (Stated by Eccles in this form.)

CNS neurotransmitters, receptors, and timescales

- Key excitatory neurotransmitters:
  - Glutamate (amino acid);
    - Ionotropic receptors: AMPA (fast; 5 ms), NMDA (slow; 50 ms), Kainate – channels permit Na+, K+, Ca++ passage; other metabotropic receptors…
  - Acetylcholine – motor control, autonomic nervous system, CNS
- Key inhibitory neurotransmitters:
  - Gamma-aminobutyric acid (GABA) (amino acid)
    - Receptors GABA-A, ionotropic (fast; 5 ms); GABA-B, metabotropic (slow; ~100 ms) – channels permit Cl- passage.
  - Glycine (amino acid)
- Various others…

Various timescales

Neural membrane time-constant ~ 10 – 30 ms.
Action potential ~ 1 ms.
Postsynaptic potential/synaptic conductance decay time-constants ~ 5 - 100 ms.
Cross-brain conduction ~ 10-200 ms.
Protein degradation/turnover ~ 1 hour – 1 day.

Cortical cell spiking periods ~10 ms – 1 s (1-100 Hz).
Visual processing latencies ~200 ms.

Short-term memory ~1-100 s.
Long-term memory ~ 1 hour – 100 years.

Simple single-neuron models

Simple RC model for subthreshold voltage

Well below “AP threshold”, cell membrane dynamics well-modeled by a simple RC circuit.

Membrane capacitance

Membrane conductance

Trans-membrane voltage drop

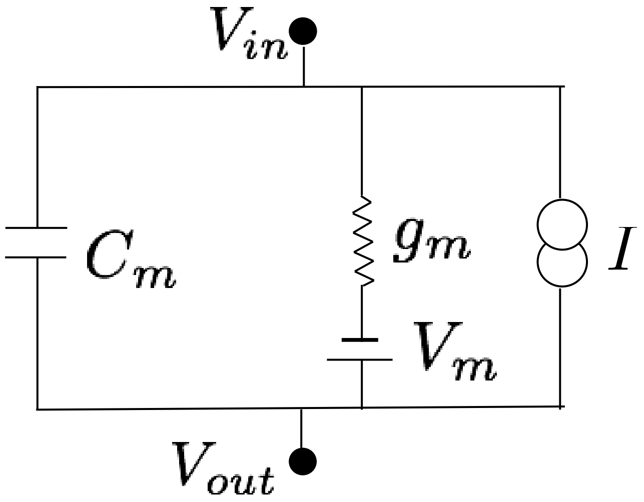
Resting voltage

Other currents (inputs, input-triggered/ voltage-dependent…)

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I$$

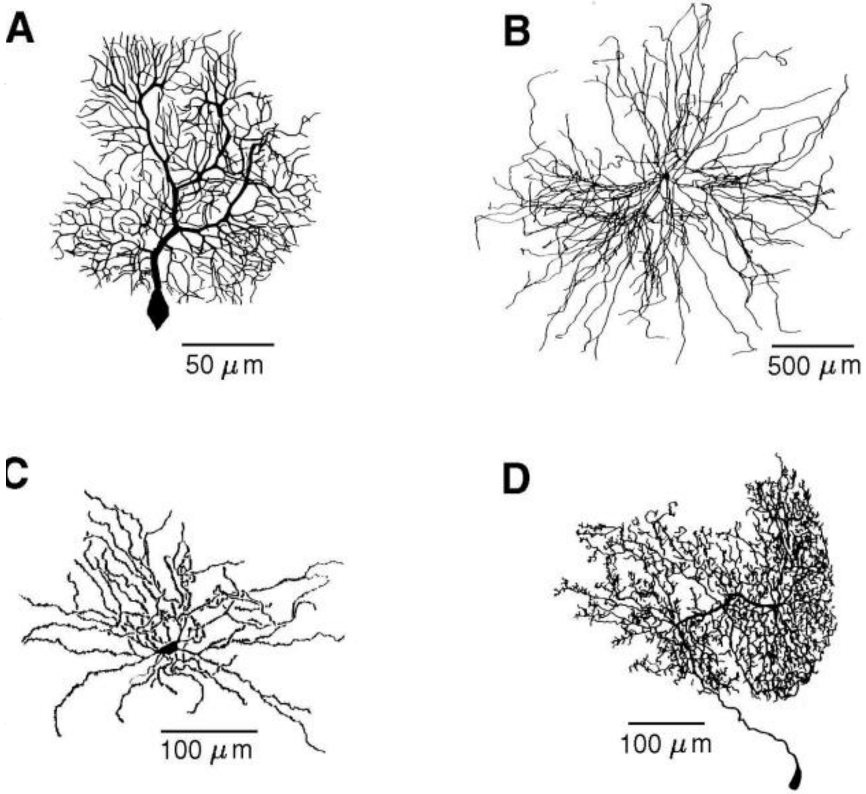
Equivalent RC circuit:

$$V(t) = V_{in}(t) - V_{out}$$

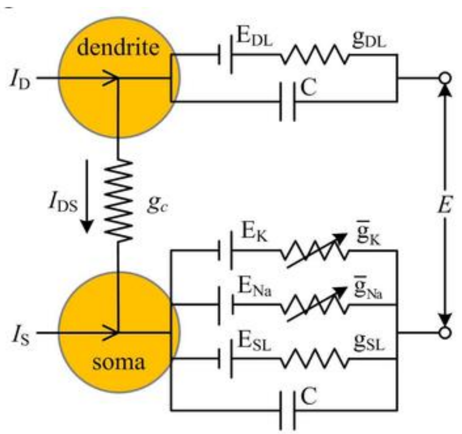


With appropriate choice of I, this includes HH and other models.

Single voltage variable V(t) in model: ignoring spatial dynamics



Simplest spatial models: multiple discrete equi-voltage compartments, resistively coupled.



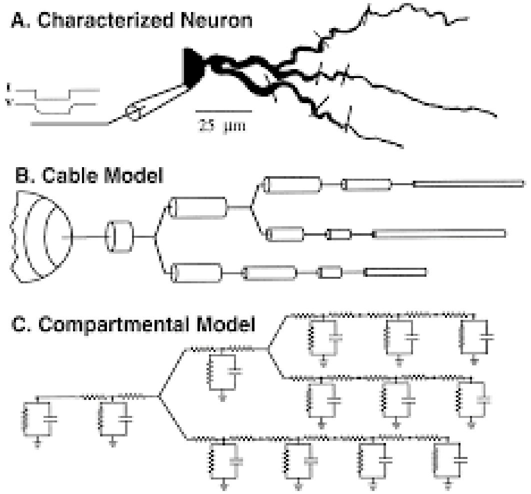


Image: from Genesis project

Modeling software for biophysically detailed and spatially extended neurons: NEURON, BRIAN.

Simple RC model for subthreshold voltage

Well below “AP threshold”, neuron dynamics very well-modeled by a simple RC circuit

Membrane capacitance

Membrane conductance

Trans-membrane voltage drop

Resting voltage battery

Input currents

$$C_m \frac{dV}{dt} = -g_m (V(t) - V_m) + I$$

At rest, the inside of neuron is maintained (with energy expenditure: setting up Nernst potential through chemical gradients) at a negative potential relative to the outside:

$$V_m \approx -55 - 60\ mV$$

(Assuming *I* is small enough that cell is maintained below “AP threshold”; next slides.)

Simple RC model for subthreshold voltage

Membrane capacitance

Membrane conductance

Trans-membrane voltage drop

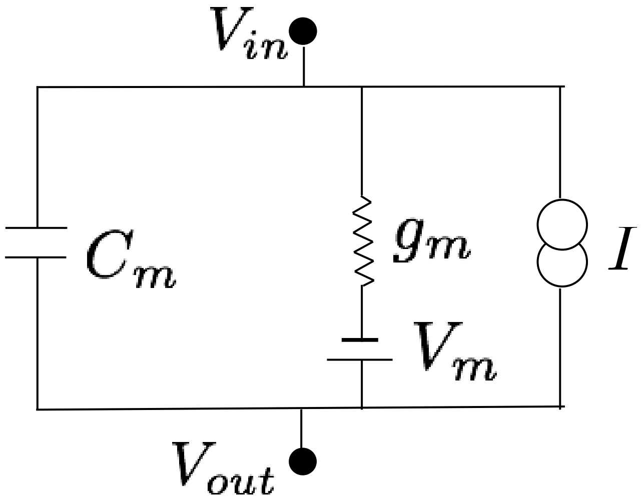
Resting voltage

other currents

$$C_m \frac{dV}{dt} = -g_m (V(t) - V_m) + I$$

Equivalent RC circuit:

$V(t) = V_{in}(t) - V_{out}$



$$C_m = 1\ \mu F/cm^2$$
$$1/g_m \sim 10000\ \Omega\ cm^2$$
$$\Rightarrow \tau_m = C_m/g_m \sim 10\ ms$$

Take note of the short single-neuron time-constant (memory of single cells).

Simple RC model for subthreshold voltage

Membrane capacitance

Membrane conductance

Trans-membrane voltage drop

Resting voltage

Input currents

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I$$

Steady-state with $I = I_{app} \ll g_m(V_{th} - V_m)$

$$\bar{V} = V_m + \frac{I_{app}}{g_m}$$

Numerical integration

$$\frac{dx}{dt} = f(x,t)$$

1st order (nonlinear) differential equation

$$x(t+\Delta t) \approx x(t) + \Delta t * f(x,t)$$

for sufficiently small Δt

Here, $x(t)$ takes single value across one time-bin, replacing the continuously varying $x(t)$ in the original.

The discrete-time $x(t)$ can be viewed as a time-average of the continuous $x(t)$ over the bin.

Numerical integration

- For first order differential equation with no delay, given x(0), can obtain all subsequent x(t).

- Euler method is very simple, but slow (have to choose Δt small to get reasonable accuracy; “small” depends on dynamics).

- Other, more efficient methods for matched accuracy: Runge-Kutta; adaptive step-size; etc.

Numerical integration of subthreshold voltage

Membrane capacitance

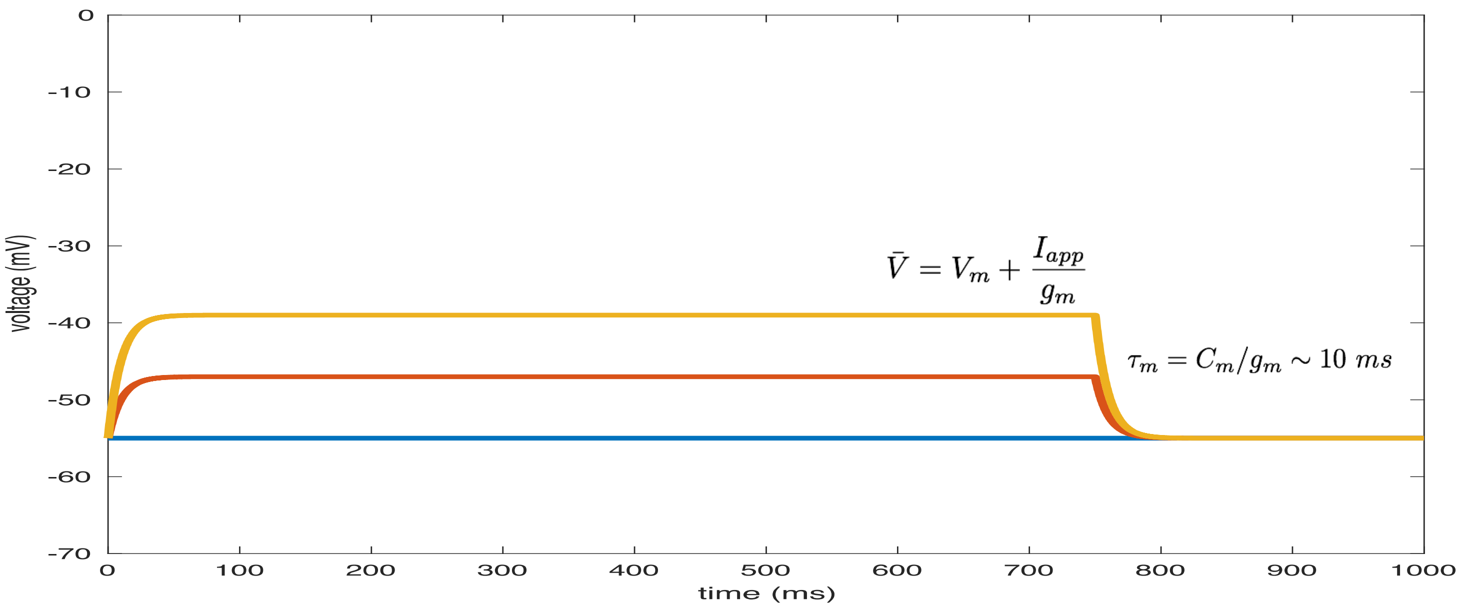
Membrane conductance

Trans-membrane voltage drop

Resting voltage

Input currents

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app}$$



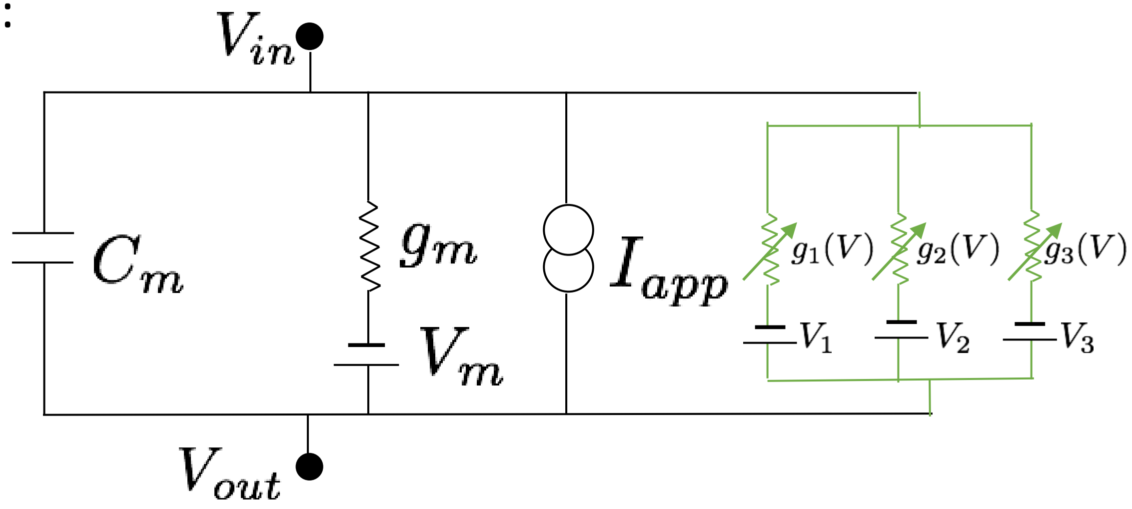
Add spike mechanism

Hodgkin-Huxley model for both subthreshold voltage and AP generation

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}(V(t), t)$$

Complex, nonlinear voltage-dependent currents for AP generation (see Hodgkin-Huxley model for details)

Equivalent RC circuit:



Leaky integrate-and-fire (LIF) model

Replace complex, detailed AP currents with a simple reset condition

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app}$$

+ spike-and-reset condition

When $V \nearrow V_{th}$
then reset $V \rightarrow V_{reset}$
and consider that the cell has spiked

Leaky integrate-and-fire (LIF) model

Replace complex, detailed AP currents with a simple reset condition

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app}$$

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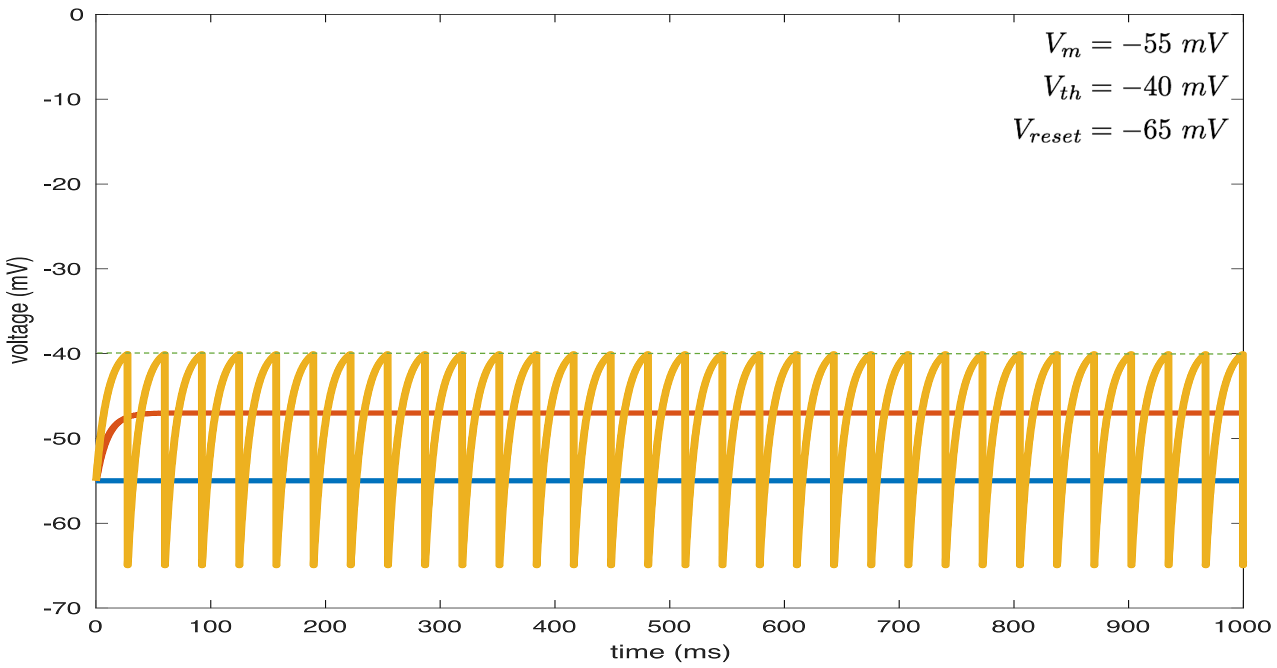
then reset $V \to V_{reset}$
and consider that the cell has spiked

→ Simulation



As I_{app} increases,
firing rate will increase
(HW: derive this).

Synaptic activation model

Each synapse is a linear, low-pass filter of the presynaptic neuron's spikes; activation is a dimensionless variable than can be thought of as "fractional activity"

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

Simple exponential decay

Upward increment whenever there is a spike (when $t = t_{spk,\,\alpha}$)

Aside: Dirac delta function

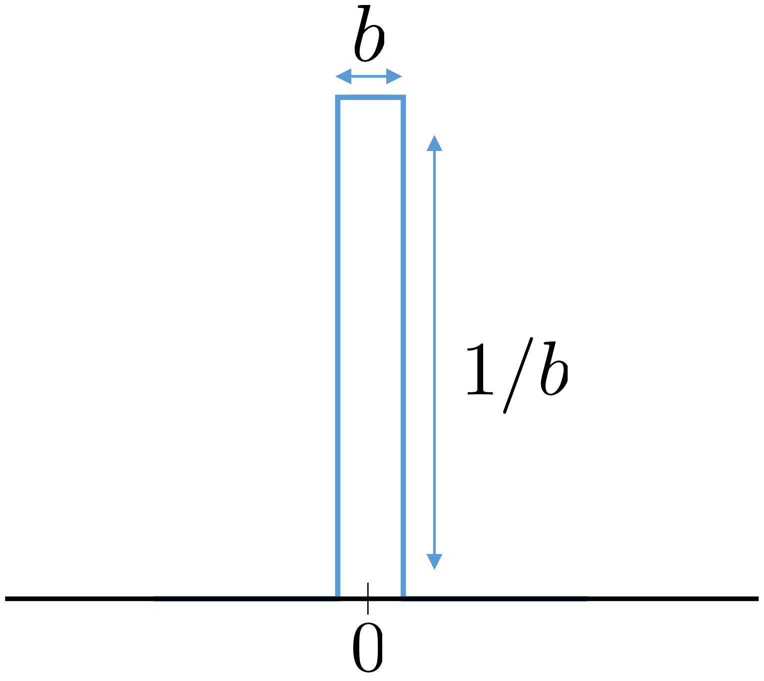
$$\int_{-\epsilon}^{\epsilon} \delta(x)dx = 1$$

→ has units of the inverse of its argument

$$\int^{I} f(x)\delta(x-a)dx = f(a) \quad \text{if } a \in I$$

$$\int^{I} f(x)\delta(x-a)dx = 0 \quad \text{if } a \notin I$$

$S(-b/2, b/2)$



$$\delta(x) = \lim_{b\to\infty} S(-b/2, b/2)$$

Aside: Kronecker delta

$$\delta_{ij} = \begin{cases} 1 & \text{if } i = j \\ 0 & \text{if } i \neq j \end{cases}$$

Synaptic activation model numerical integration

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

Discretize equation in time

$$\frac{s(t+\Delta t) - s(t)}{\Delta t} = -\frac{s(t)}{\tau_{syn}} + \frac{\beta}{\Delta t} \int_{t}^{t+\Delta t} dt' \sum_{\alpha} \delta(t' - t_{spk,\alpha})$$

$$= -\frac{s(t)}{\tau_{syn}} + \frac{\beta}{\Delta t} \sum_{\alpha} \delta_{t,t^b_{spk,\alpha}}$$

where the b superscript in $t^b_{spk,\alpha}$ indicates the spike time bin in place of the precise spike time

$$s(t+\Delta t) = (1 - \frac{\Delta t}{\tau_{syn}}) s(t) + \beta \sum_{\alpha} \delta_{t,t^b_{spk,\alpha}}$$

Synaptic activation model

Each synapse is a linear, low-pass filter of the presynaptic neuron's spikes; activation is a dimensionless variable than can be thought of as "fractional activity"

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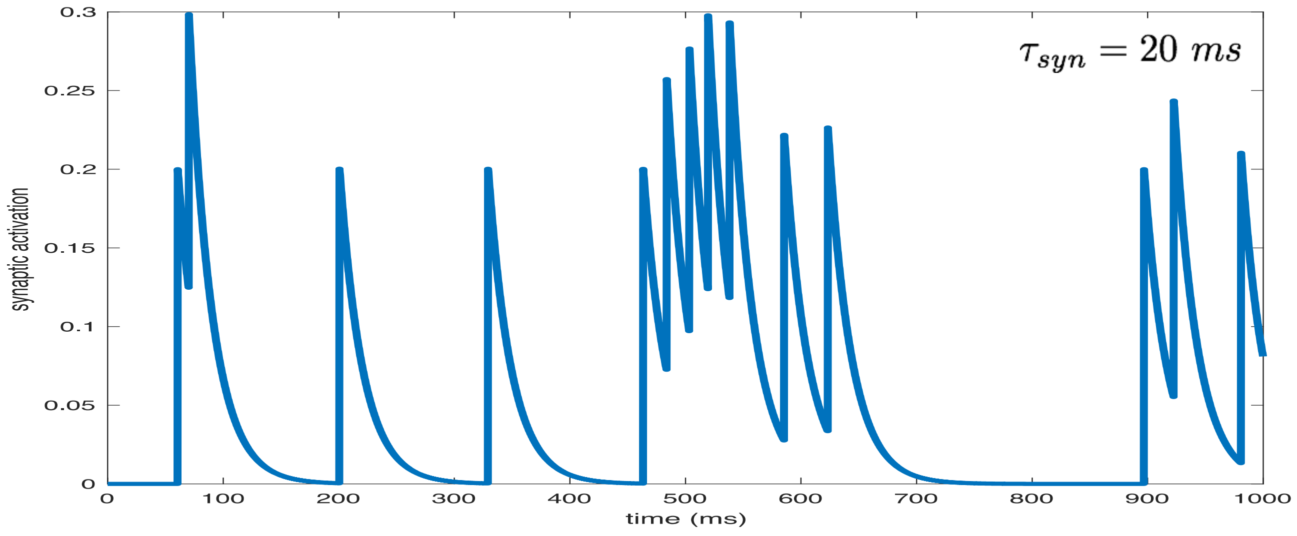

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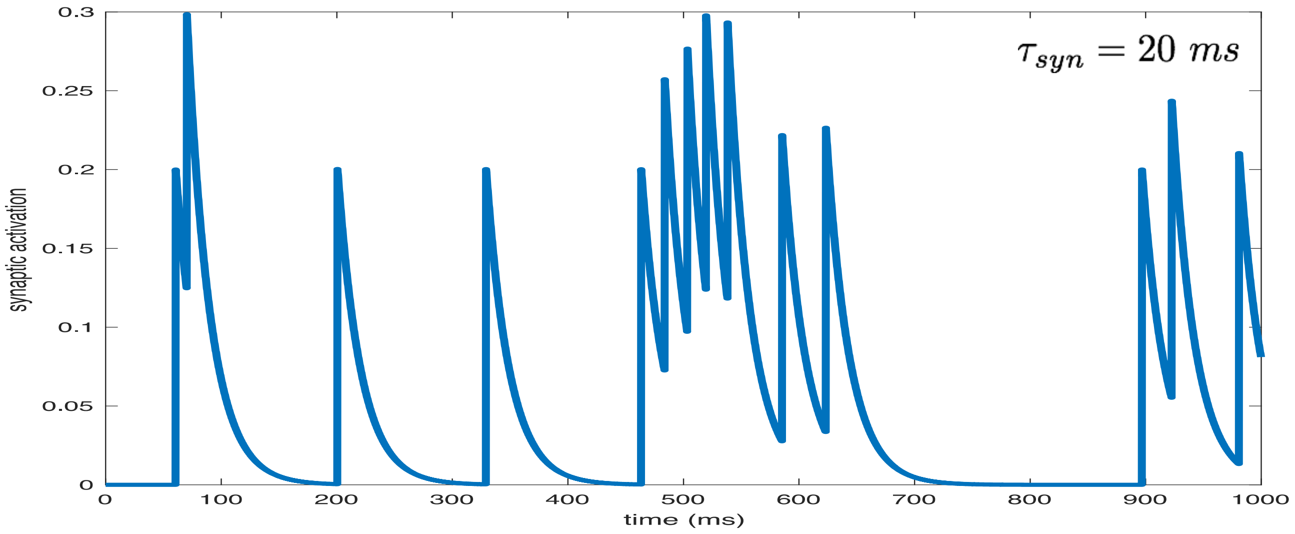
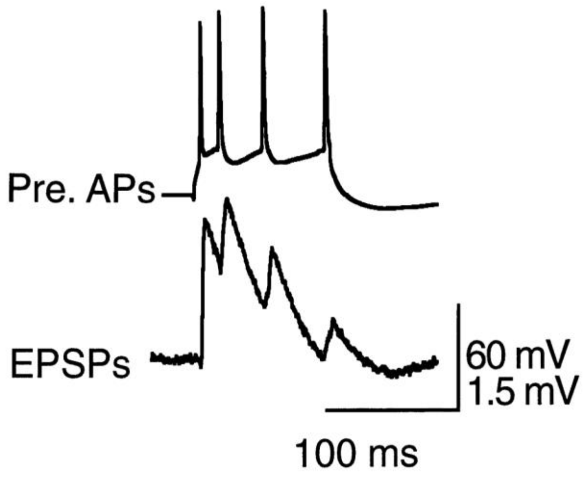


Compare: neural recording



$$\tau_{syn} \sim 5 - 100\ ms$$

From single neurons to networks

Spiking networks

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}(V(t), t)$$

Input to neuron i

Output of neuron j

$$I_{i,app} = \sum_j W_{ij} s_j(t)$$

Current-based model

OR:

$$I_{i,app} = \sum_{j \in E} W_{ij} s_j(t)(V_i(t) - V_E) + \sum_{j \in I} W_{ij} s_j(t)(V_i(t) - V_I)$$

Conductance-based model:
Efficacy of synaptic input depends on postsynaptic neuron voltage

Deriving rate-based neuron equations

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

input (I_{app}) → voltage → voltage spikes

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

voltage spikes → output (s)

Can we model input (I_{app}) → output (s) and bypass V?

Deriving rate-based neuron equations

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

input (I_{app}) → voltage

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

voltage (spikes) → output (s)

- Replace sum of fast-varying delta function input in (ii) by an average over one one inter-spike-interval, T_{isi}
- Reasonable if $T_{isi} << \tau_{syn}$

Deriving rate-based neuron equations

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

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- Replace sum of fast-varying delta function input in (ii) by an average over one one inter-spike-interval, T_{isi}
- Reasonable if $T_{isi} << \tau_{syn}$
- Now: $$\frac{1}{T_{isi}} \int_t^{t+T_{isi}} dt \sum_{\alpha} \delta(t - t_{spk,\alpha}) = \frac{1}{T_{isi}} \equiv r$$

Instantaneous firing rate of cell

Deriving rate-based neuron equations

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

input (I_{app}) → voltage

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

voltage (spikes) → output (s)

- Replace sum of fast-varying delta function input in (ii) by an average over one one inter-spike-interval, T_{isi}
- Reasonable if $T_{isi} << \tau_{syn}$
- Since: $$\frac{1}{T_{isi}} \int_t^{t+T_{isi}} dt \sum_{\alpha} \delta(t - t_{spk,\alpha}) = \frac{1}{T_{isi}} \equiv r$$ Instantaneous firing rate of cell
- Thus: $$\frac{ds}{dt} \approx -\frac{s}{\tau_{syn}} + \beta r$$

Deriving rate-based neuron equations

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

input (I_{app}) → voltage

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_\alpha \delta(t - t_{spk,\alpha})$$

voltage (spikes) → output (s)

- Replace sum of fast-varying delta function input in (ii) by an average over one one inter-spike-interval, T_{isi}
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- Thus: $$\frac{ds}{dt} \approx -\frac{s}{\tau_{syn}} + \beta r$$
- Finally, note that: $r = f(I_{app})$ (*f* depends on neuron model; IF model for homework)

From spike-based to rate-based neural models

$$C_m \frac{dV}{dt} = -g_m(V(t) - V_m) + I_{app} + I_{spk}$$

input (I_{app}) → voltage

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta \sum_{\alpha} \delta(t - t_{spk,\alpha})$$

voltage (spikes) → output (s)

- Replace sum of fast-varying delta function input in (ii) by an average over one one inter-spike-interval, T_{isi}
- Reasonable if $T_{isi} << \tau_{syn}$
- Since: $$\frac{1}{T_{isi}} \int_t^{t+T_{isi}} dt \sum_{\alpha} \delta(t - t_{spk,\alpha}) = \frac{1}{T_{isi}} \equiv r$$ Instantaneous firing rate of cell
- Thus: $\frac{ds}{dt} \approx -\frac{s}{\tau_{syn}} + \beta r$
- Finally, note that: $r = f(I_{app})$ (*f* depends on neuron model; IF model for homework)
- Thus:

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta f(I_{app})$$

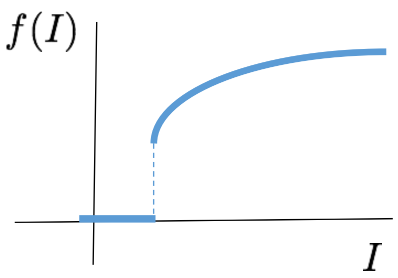
This equation relates neural **input** (I_{app}) to **output** (s) without intervening voltage: **rate-based equation**.

The rate-based equation

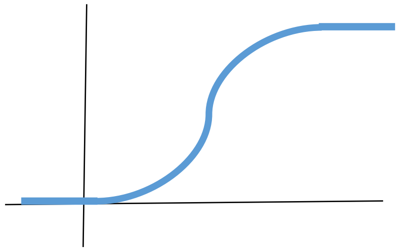
$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta f(I_{app})$$

F-I curve
Neural transfer function
Neural nonlinearity

Common transfer functions (approximations to forms observed in neurons):



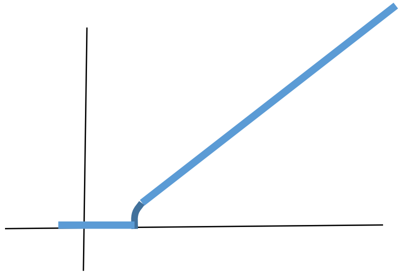
Hodgkin-Huxley neuron



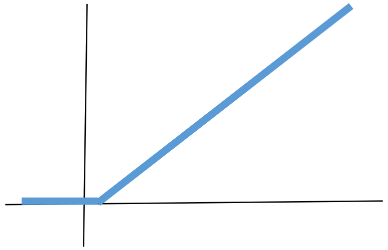
sigmoid

$1 + \tanh(I)$

$\frac{e^I}{(1 + e^I)}$



LIF neuron
Similar to cortical neuron (homework)



threshold-linear or ReLu (rectified linear unit)

$\max(0, I - b)$

The rate-based network equation: McCullough-Pitts, Wilson-Cowan

$$\frac{ds}{dt} = -\frac{s}{\tau_{syn}} + \beta f(I_{app})$$

F-I curve
Neural transfer function
Neural nonlinearity

In network, each neuron, *i*, has a synaptic output: $s_i(t)$
The input to the neuron *i* is the sum of the outputs of all its connections: $I_{app,i}(t) = \sum_j W_{ij} s_j(t)$

It might also receive some input from outside the network: $b_i(t)$

$$\frac{ds_i}{dt} + \frac{s_i}{\tau} = f(\sum_j W_{ij} s_i + b_i(t)) \equiv r_i$$

Interpretation of terms

synaptic activation: output

Firing rate

$$\frac{ds_i}{dt} + \frac{s_i}{\tau} = f(\overbrace{\underbrace{\sum_j W_{ij} s_i}_{\text{Network input}} + b_i(t))}^{\text{Total input } (g_i) \text{ or input conductance}} \equiv r_i$$

External input

Biophysical
time-constant
(cell or synapse,
depending on
which is slow
for method of
averaging)

Discrete-time dynamics (for numerical integration)

$$\frac{ds_i}{dt} + \frac{s_i}{\tau} = f(\sum_j W_{ij} s_i + b_i(t)) \equiv r_i$$

Replace derivative by discrete time-difference:

$$\frac{s_i(t + \Delta t) - s_i(t)}{\Delta t} = -\frac{1}{\tau} s_i(t) + f(g_i(t))$$

Iteration equation for numerical integration:

$$s_i(t + \Delta t) = \left(1 - \frac{\Delta t}{\tau}\right) s_i(t) + \Delta t f(g_i(t))$$

Neural dynamics in ANNs

Discrete-time approximation for leaky rate-based neuron dynamics

$$s_i(t + \Delta t) = \big(1 - \frac{\Delta t}{\tau}\big) s_i(t) + \Delta t f(g_i(t))$$

Discrete-time equation for RNN unit activity

$$s_i(t + \Delta t) = f(g_i(t))$$

Does not correspond to taking any simple limit on τ in the leaky neuron dynamics.
(It can be obtained by setting $\Delta t/\tau=1$, an unclear process since Δt should be small for accurate numerical integration.)

Many simplifications in our model

“Point” neuron: space-clamped cell held at equipotential so it can be described by single voltage variable (vs actual branched structure; spatial coincidence detection)

That there is a “threshold” for activation (LIF models, not in HH); actually depends on timecourse of deporalizing response (HH models capture this).

All synapses emanating from a neuron have the same dynamics (vs stochastic transmission and separate history dependence at each synapse).

Neuron input-output can be described by firing rates not spikes. This ignores possible non-linear effects of coincident spiking/temporal coincidence detection, etc.

There is immense structure in synaptic organization and projections

http://ml-neuronbrowser.janelia.org/

Summary

- Biophysics of cells
- Electrical properties of a point neuron
- Simple model for spiking point neurons: Leaky IF neuron
- Derived simple model for rate-based point neurons
- Contrasted with unit dynamics in ANN
- Many simplifications of our models compared to the spatiotemporal richness real neurons