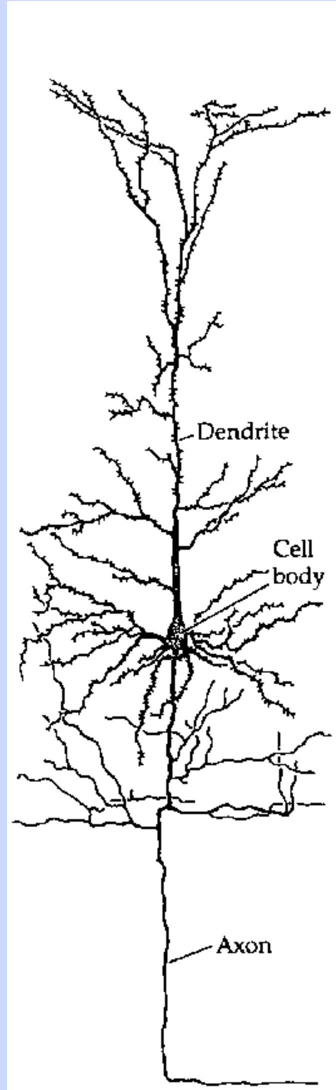
Administrative Stuff

- Labs: Metcalf 107 Tues 5-7pm; Wed 3-5pm
- If you don't finish, download sims (website)
- All assignments (simulation exercises and RR) are due **before** class (1pm) on the date in syllabus. So you will only have this week's lab to work on HW2.
- Reading reactions: Better directly in email & put 1492 in subject title!
- CC Nick on all reactions

Neurons

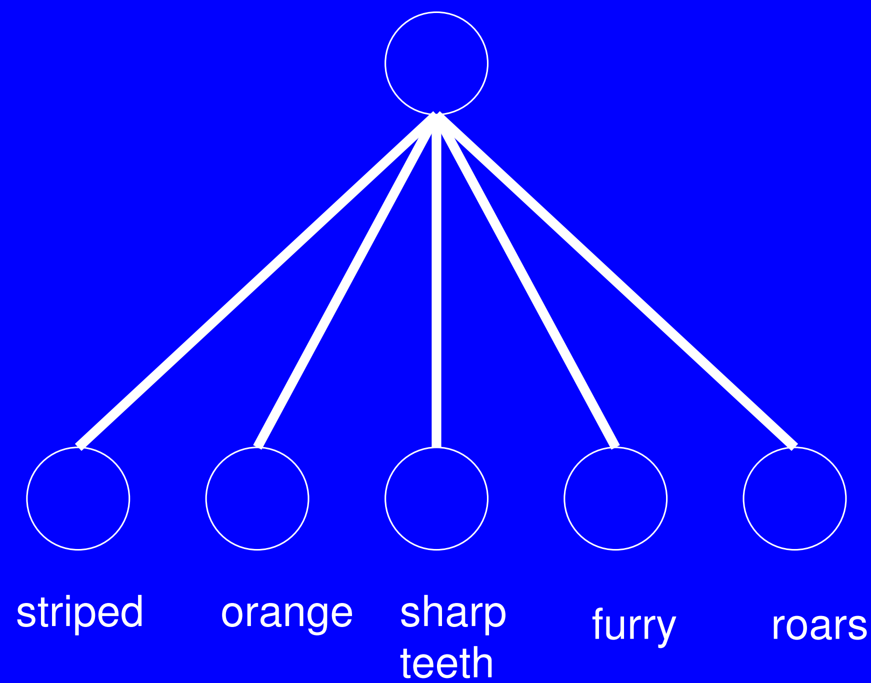


How do they do it?

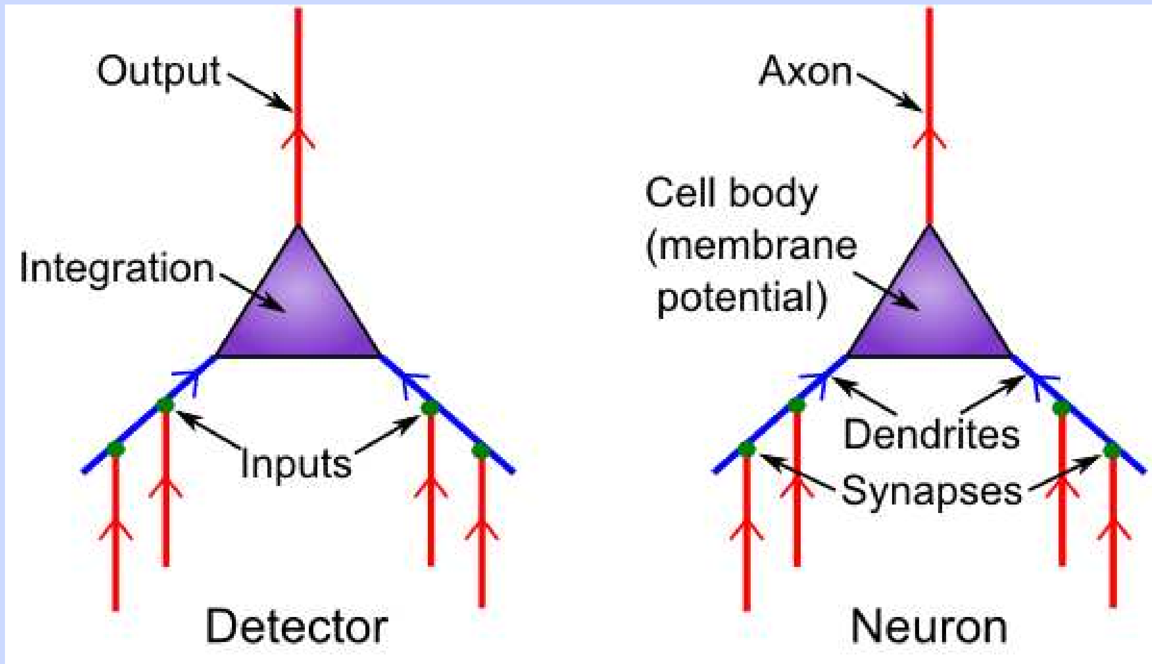
Detector Model

Each neuron detects some set of conditions (e.g., smoke detector).

Neurons are detectors



Understanding Neural Components in Detector Model



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Each neuron detects some set of conditions (e.g., smoke detector).

Neurons feed on each other's outputs — layers of ever more complicated detectors.

(Things can get very complex in terms of *content*, but each neuron is still carrying out basic detector *function*).

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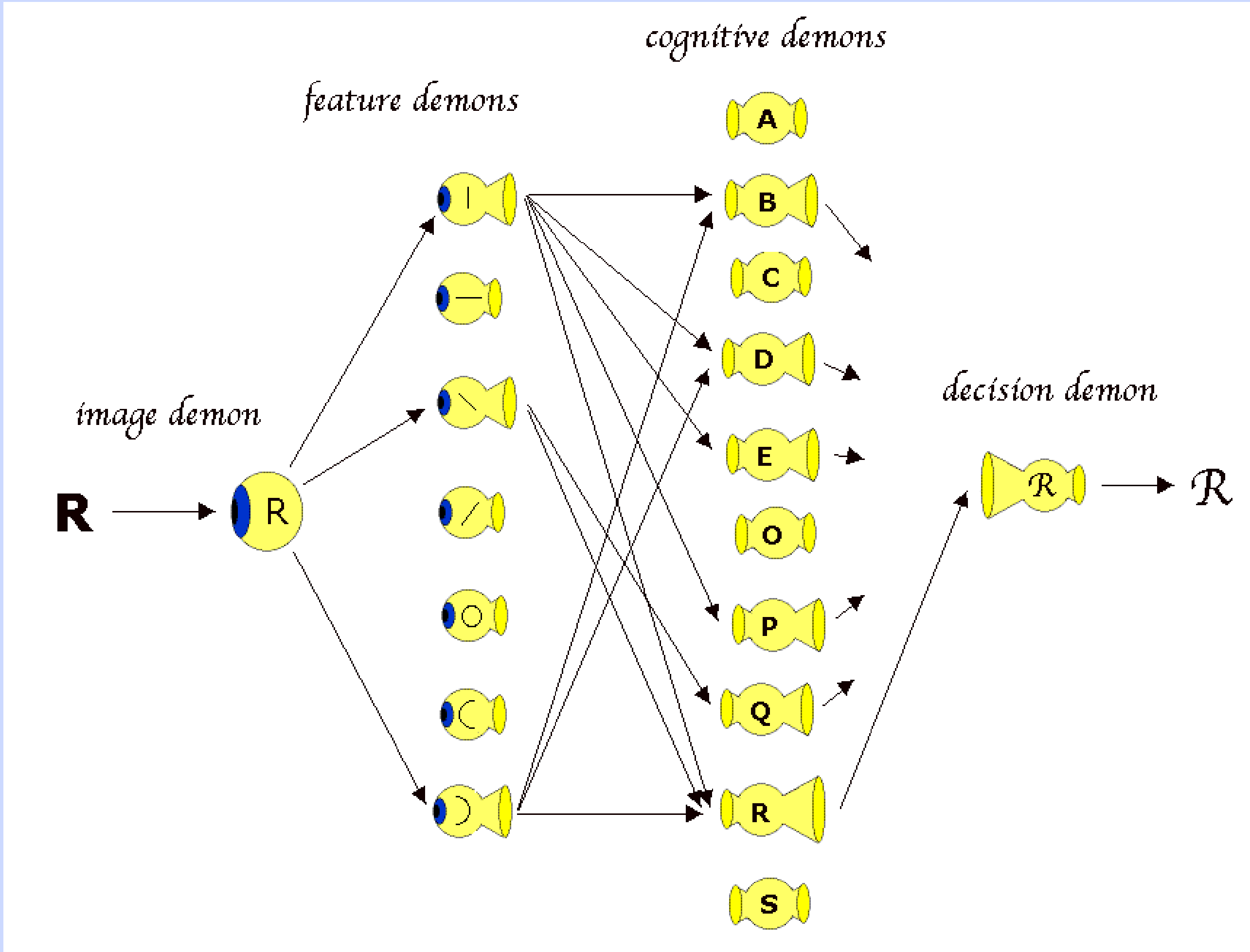
sensory: detect bar of light, edges, tigers
motor: detect appropriate condition to move hand
abstract internal actions: engaging attention
regulation/homeostasis: detect too much overall activity..

Building on simple detectors: Pandemonium



Pandemonium Example

Each neuron has a simple job, but together...

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Layers of more and more complicated detectors.

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Simple example, but raises question of what kind of detectors needed for language, face recognition, creativity, etc.?

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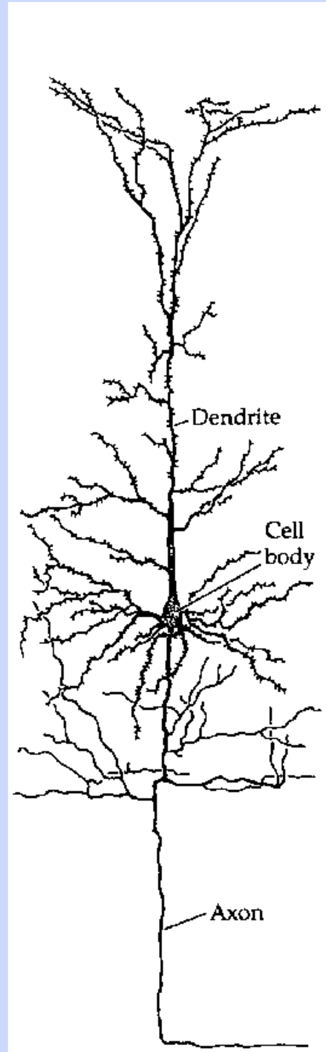
- We use these equations to specify the behavior of artificial neurons.
- The artificial neurons can then be put together to explore behaviors of networks of neurons.

A Real Neuron



Basic Properties of a Neuron

- It's a cell: body, membrane, nucleus, DNA, RNA, proteins, etc.

- **Ions** (charged particles) are present both inside and outside the neuron: Sodium (Na^+), Chloride (Cl^-), Potassium (K^+) and Calcium (Ca^{++}) $\rightarrow$ brain = mini-ocean

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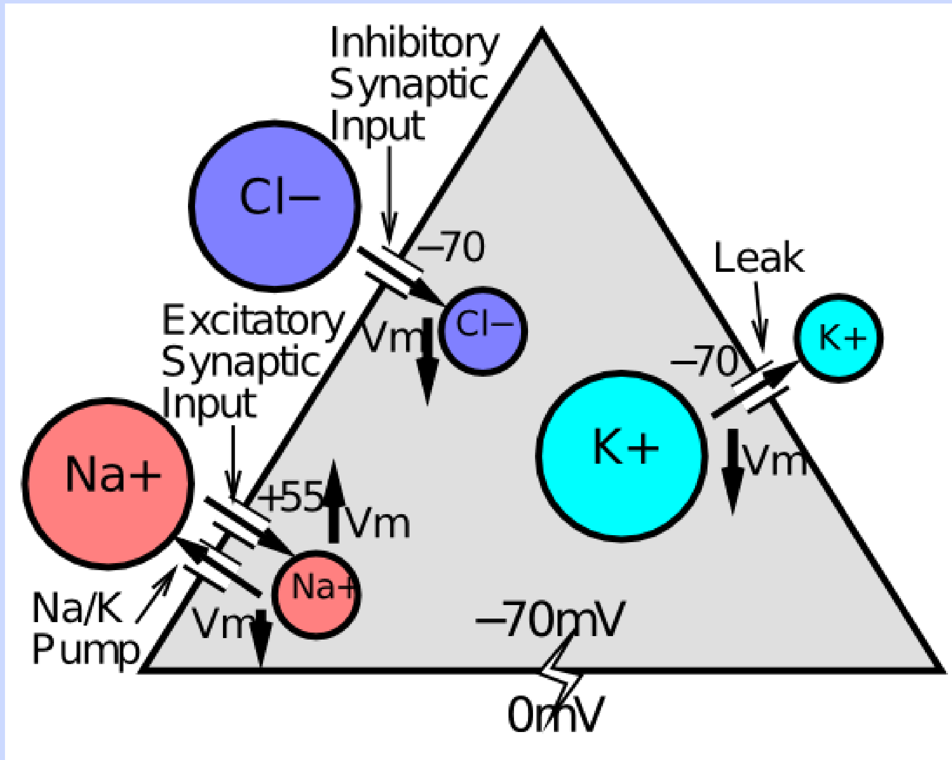
- Cell membrane has **channels** that allow ions (e.g. Na^+) to pass through. Channels can be open or closed (**selective permeability**).

- When a neuron is at rest: greater concentration of negative ions inside the neuron vs. outside; this difference in charge inside vs. outside the neuron is called the **membrane potential** (V_m)

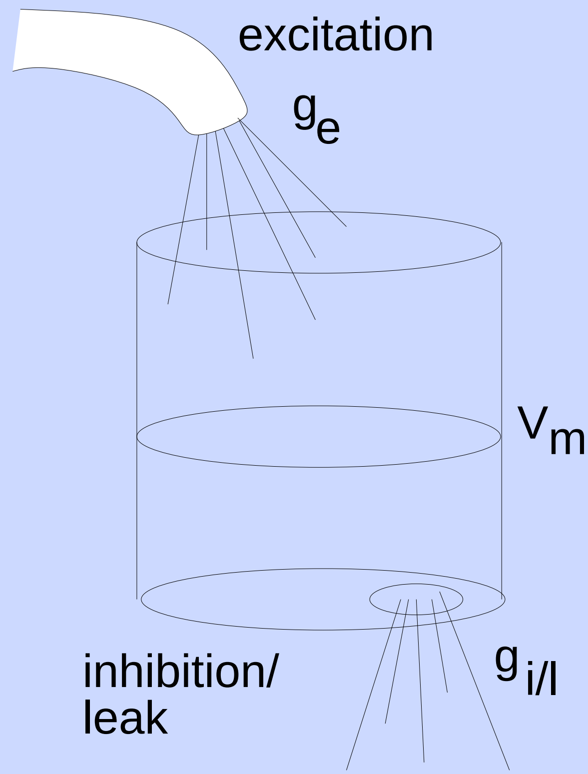
The Neuron and its Ions



- Some ions more or less concentrated inside vs. outside the cell

- Positive and negative ions compete to set the overall ′charge′

It's Just a Leaky Bucket

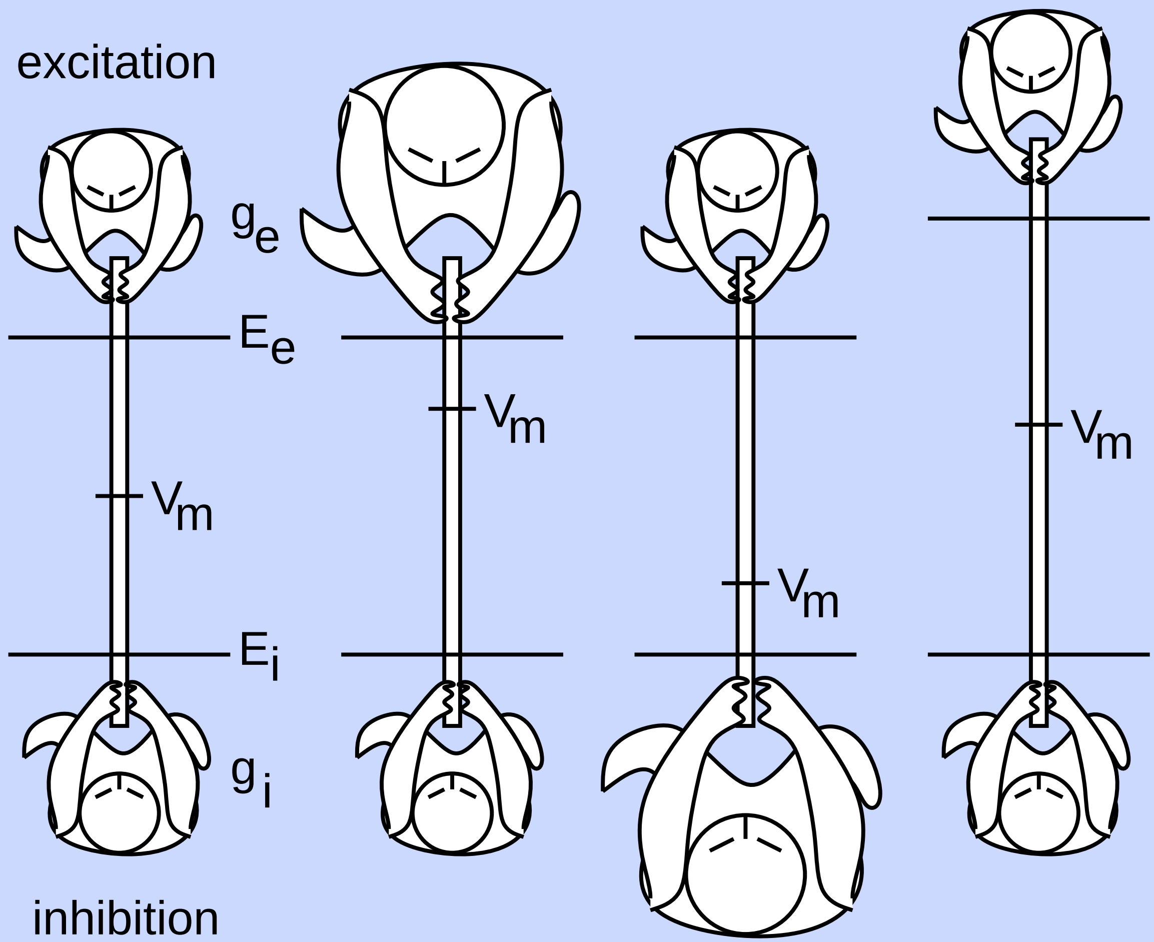


g_e = rate of flow into bucket

$g_{i/l}$ = rate of "leak" out of bucket

V_m = balance between these forces

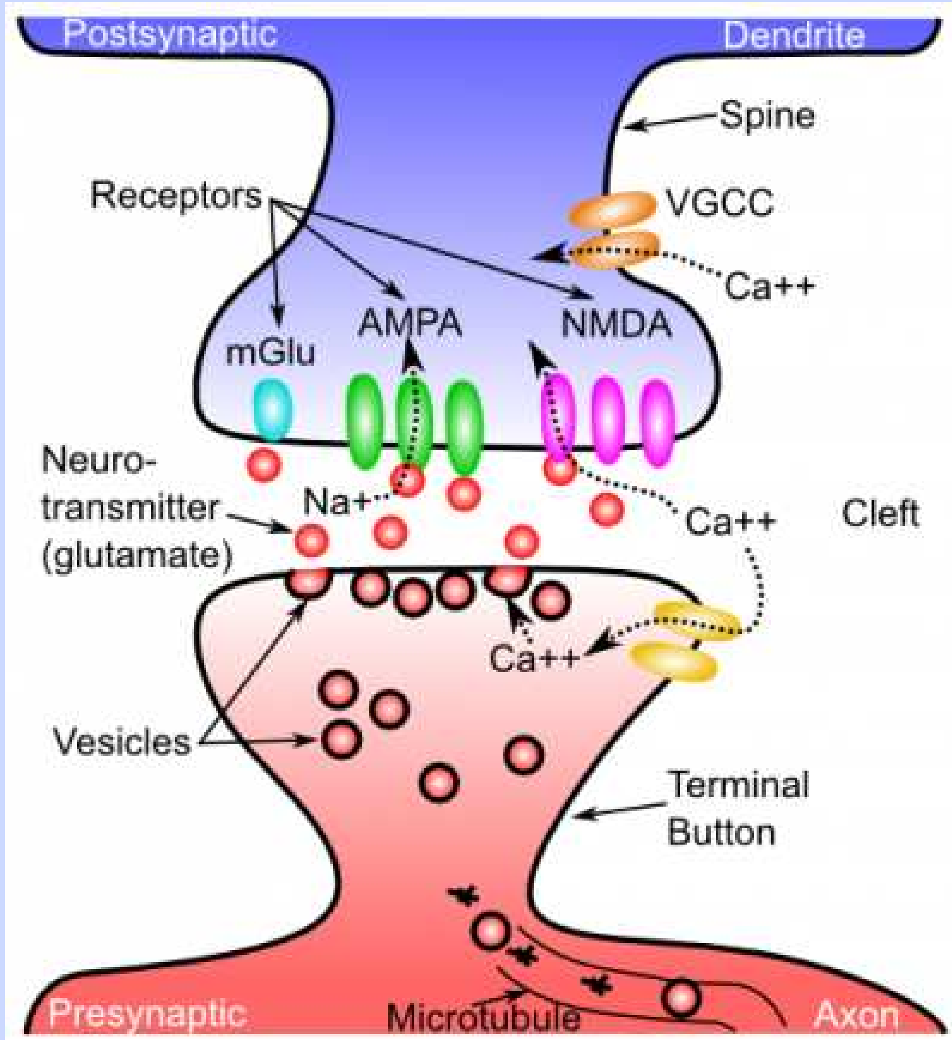
Or a Tug-of-War



How Neurons Communicate

- Neurons communicate by **firing** “spikes” of electricity (**action potentials**) down their axons
- When this current reaches the end of an axon, it triggers release of **neurotransmitter** into the synapse
- Neurotransmitter binds to receptors in the receiving (postsynaptic) neuron, which opens **dendritic synaptic input channels** in the cell membrane
- The flow of ions through these channels changes the membrane potential of the postsynaptic neuron

The Synapse



Postsynaptic
Dendrite
Spine
Receptors
VGCC
Ca++
mGlu
AMPA
NMDA
Neuro-
transmitter
(glutamate)
Na+
Ca++
Cleft
Ca++
Vesicles
Terminal
Button
Presynaptic
Microtubule
Axon

How can biology (e.g., synapse) be reduced to numbers?

Synaptic efficacy = how much is the activity of **presynaptic** (sending) neuron communicated to the **postsynaptic** (receiving) neuron:

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Major Simplification:
Connection weight = synaptic efficacy.

Excitatory vs Inhibitory Synapses

Some synapses are primarily **excitatory**.

- These synapses use glutamate as the primary neurotransmitter.
- Glutamate binds to receptors and allows Na^+ to enter the neuron, which boosts the membrane potential.

Other synapses are primarily **inhibitory**.

- These synapses use GABA
- GABA binds to receptors and allows Cl^- to enter the neuron, which reduces the membrane potential

Bio Neural Nets
(just some static equations for now...)

1. Compute weighted, summed *net input*:

$$\eta_j \approx \sum_i a_i w_{ij} \approx g_e \tag{1}$$

2. Compute V_m (equilibrium):

$$V_m = \frac{g_e \bar{g}_e E_e + g_i \bar{g}_i E_i + g_l \bar{g}_l E_l}{g_e \bar{g}_e + g_i \bar{g}_i + g_l \bar{g}_l} \tag{2}$$

3. Compute *dynamics* of V_m (how it changes in real time)

$$C_m \frac{dV_m}{dt} = g_e(E_e - V_m) + g_l(E_l - V_m) + g_i(E_i - V_m) \tag{3}$$

Summary

- Neuron as detector.
- Can be characterized mathematically.
- Serves as the basis of simulation explorations.

Remaining

- Physiology behind the equations.
- Simple detector network.

Neurophysiology

The neuron is a miniature electro-chemical system:

1. Balance of electric and diffusion forces.
2. Principal ions.
3. Putting it all together.

Balance of Electric and Diffusion Forces

Ions flow into and out of the neuron under forces of electricity and concentration gradients (diffusion).

Net result is electric potential difference between inside and outside of cell — **the membrane potential** V_m.

This value represents an integration of the different forces, and an integration of the inputs impinging on the neuron.

Electricity

Electricity

Ions have net charge: Sodium (Na^{+}), Chloride (Cl^{-}), Potassium (K^{+}), and Calcium (Ca^{++}).

Positive and negative **charge** (opposites attract, like repels).

Current flows to even out distribution of + and - ions.

Disparity in charges produces **potential** (the potential to generate current).

Resistance

Ions encounter **resistance** when they move.

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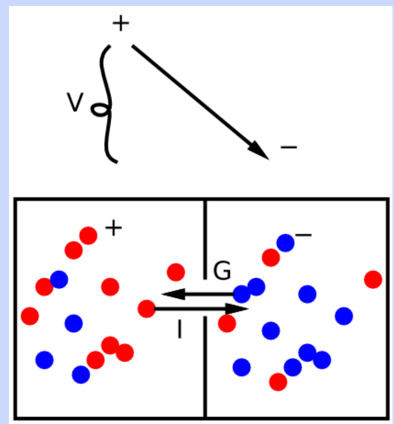

The smaller the channel, the higher the resistance, the greater the potential needed to generate given amount of current (Ohm's law):

$$I = \frac{V}{R} \tag{4}$$

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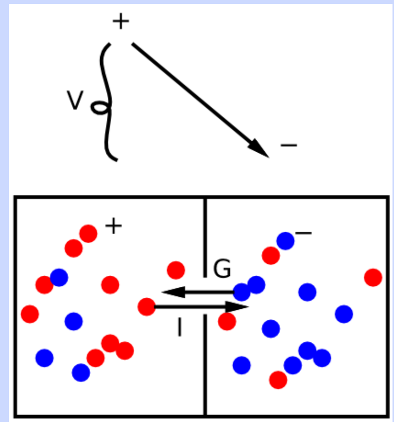

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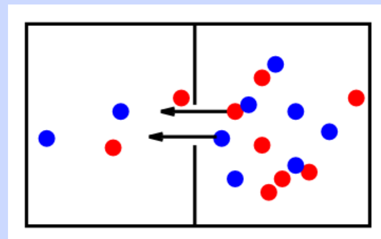
Conductance G = 1/R, so $I = GV$

Diffusion

Constant motion causes mixing – evens out distribution.

Unlike electricity, diffusion acts on each ion *separately* — can't compensate one + ion for another..



(same deal with conductance, potentials, etc)

$$I = -DC \tag{5}$$

(Fick's First law)

D = diffusion coefficient ('diffusivity' $\propto$ viscosity, temp etc),
C = concentration potential difference

Equilibrium: Balance between electricity and diffusion

E = **Equilibrium** potential = amount of electrical potential needed to counteract diffusion:

$$I = G(V - E) \tag{6}$$

E is the electric potential at which the diffusion force would pull current in the opposite direction with equal force.

I flows in proportion to voltage *difference* from equilibrium.

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Other terms for E:

Reversal potential (because current reverses on either side of E)

Driving potential (flow of ions drives potential toward this value)

Each ion has it's own equilibrium

"Eq potential for Na E_{Na}: If sodium had its way, the neuron would settle to into this steady state without any other forces"

For each ion, E is proportional to concentration outside/inside of cell:

$E > 0$ when concentration higher outside, and $E < 0$ when higher inside (Nernst equation).

$$E = \frac{RT}{nF} log \frac{[Xo]}{[Xi]} \tag{7}$$

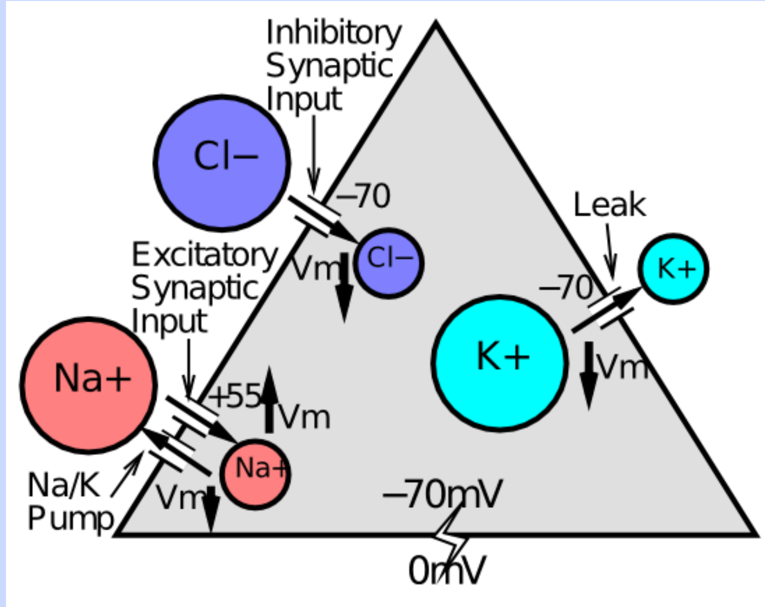
The Na-K Pump: Winding the Spring

- Neurons have a negative resting potential because of the sodium-potassium pump

- This mechanism pumps Na^+ **out** of the neuron and pumps a lesser amount of K^+ **into** the neuron. The result is a net loss in charge.

- This creates a **dynamic tension** in the cell: When the neuron is at rest, Na^+ ***wants*** to come back in (because of both electrical and diffusion forces), but it can't because the Na channels are closed!

The Neuron and its Ions



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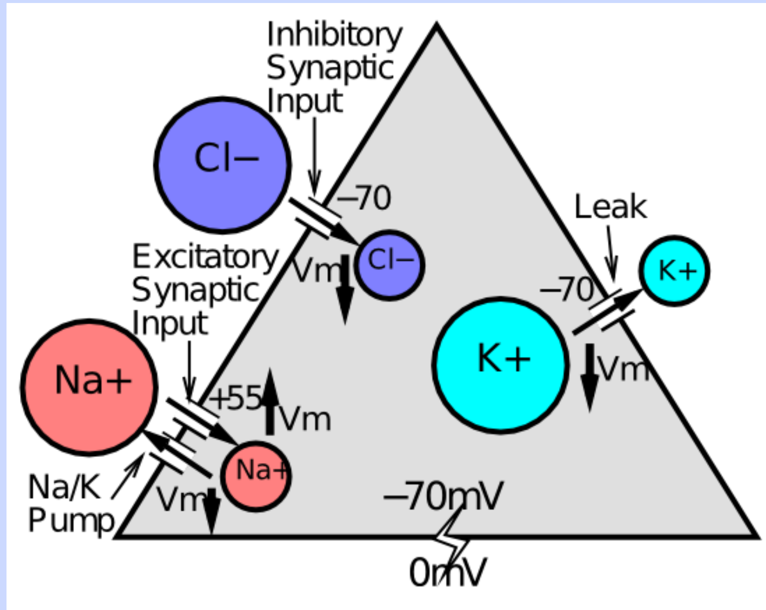
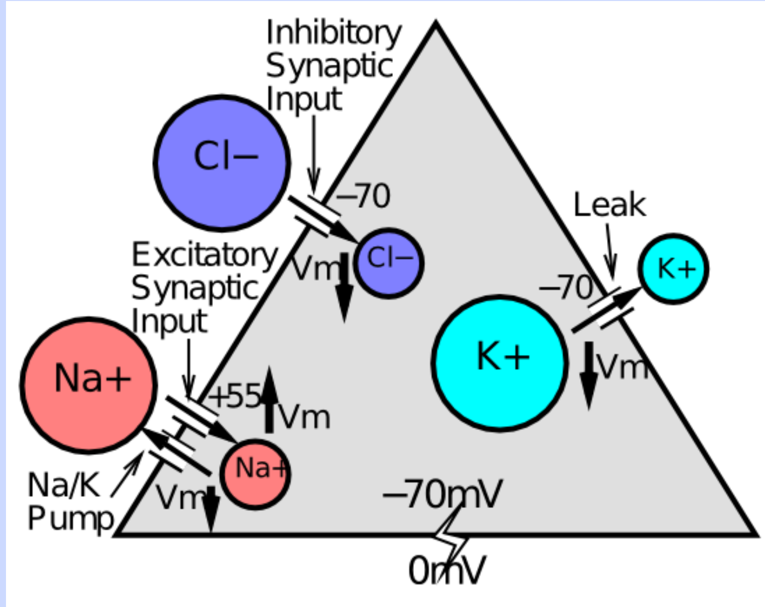


When the neuron is **at rest** (-70mV):

- Na^+ wants in
- Cl^- is in balance (diffusion pushes in, electrical pushes out)
- K^+ is in balance (diffusion pushes out, electrical pushes in)

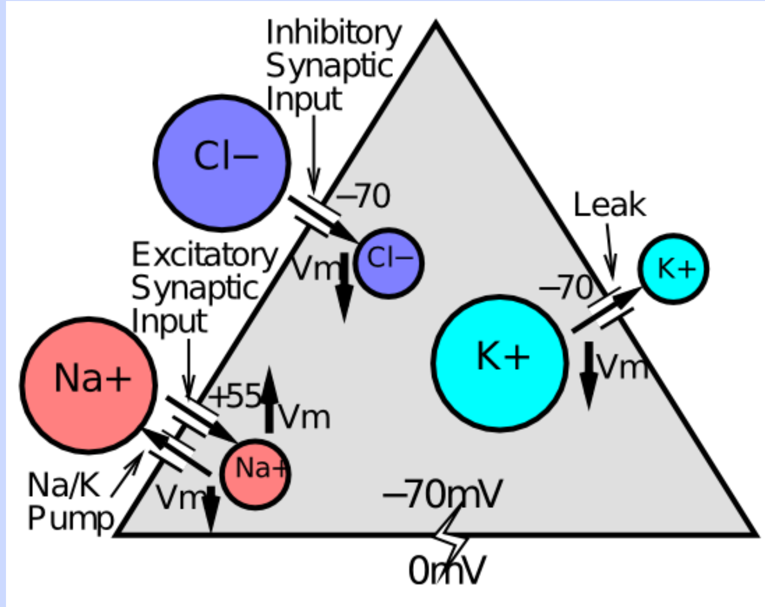
The Neuron and its Ions



When the neuron receives **excitatory synaptic input**:

- Na^+ rushes in, making membrane potential more positive
- If the Na^+ stays open, this influx will continue until membrane potential reaches +55mV
- This is the **reversal potential** for Na^+

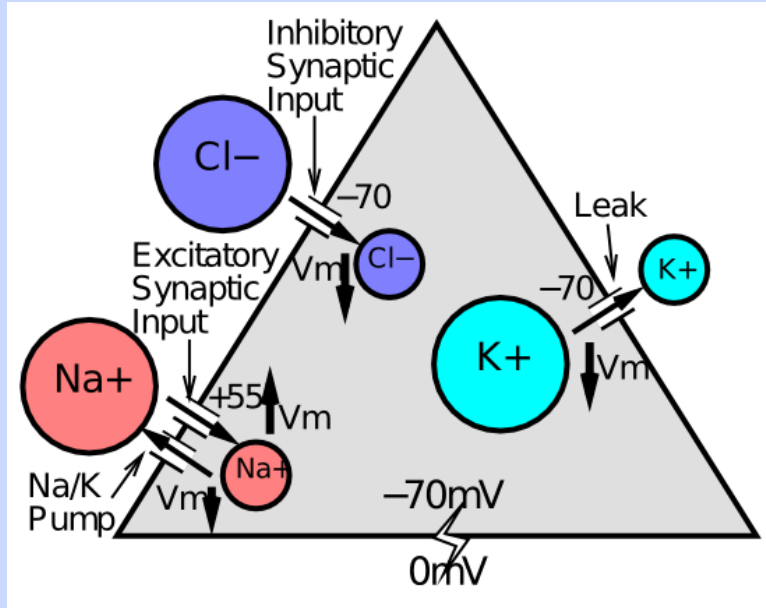
The Neuron and its Ions



Because of the influx of positive charge:

- Cl^- wants to come in, but can't (channels closed)
- K^+ starts to **leak** out of the neuron (through open channels)

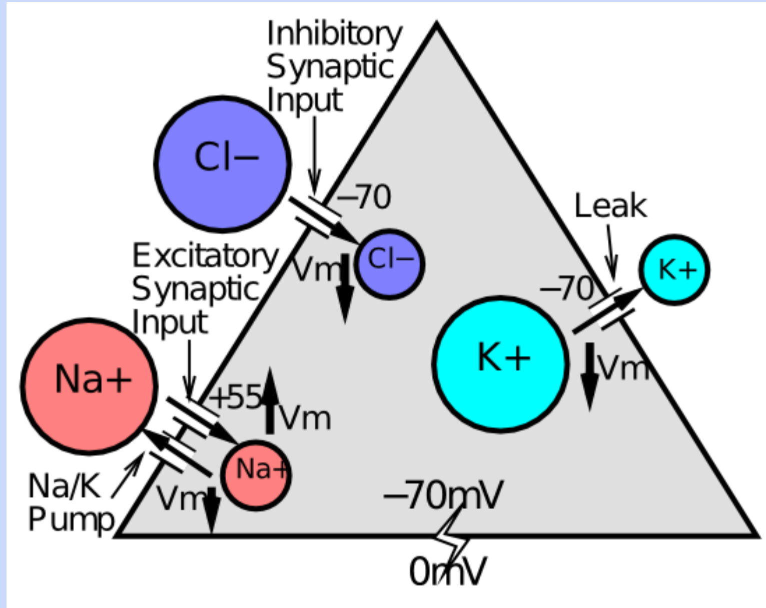
The Neuron and its Ions



When the neuron receives **inhibitory synaptic input**:

- If the membrane potential = - 70 mV?

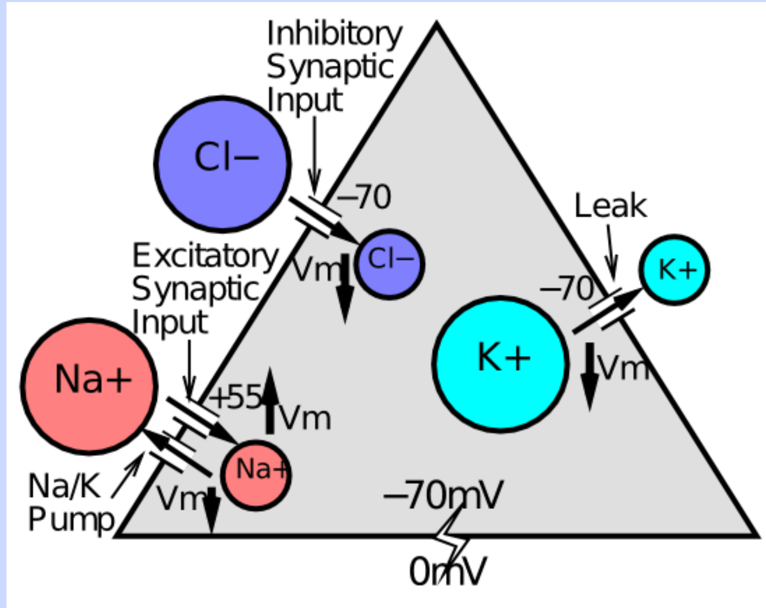
The Neuron and its Ions



When the neuron receives **inhibitory synaptic input**:

- If the membrane potential = - 70 mV, nothing happens

The Neuron and its Ions



When the neuron receives **inhibitory synaptic input**:

- If the membrane potential = - 70 mV, nothing happens
- If the membrane potential > -70mV, Cl- starts to come in; this serves to **counteract** the influx of Na+

Ions: Summary

- Excitatory synaptic input boosts the membrane potential by allowing Na^{+} ions to enter the neuron

- Inhibitory synaptic input serves to counteract this increase in membrane potential by allowing Cl^{-} ions to enter the neuron

- The leak current (K^{+} flowing out of the neuron through open channels) acts as a drag on the membrane potential. Functionally speaking, it makes it harder for excitatory input to increase the membrane potential.

Putting it Together

$$I_c = g_c(E_c - V_m) \tag{8}$$

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$$V_m(t+1) = V_m(t) + dt_{vm} I_{net} \tag{10}$$

Putting it Together: With Time

$$I_c = g_c(t)\bar{g_c}(E_c - V_m(t)) \tag{11}$$

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Differential equation version (common in computation neurosci)

$$
\begin{aligned}
C_m \frac{dV_m}{dt} &= g_e(t)\bar{g}_e(E_e - V_m) + \\
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- C_m = membrane capacitance, determined by surface area of membrane
- holds charge; reduces speed at which voltage can change (dt_{vm})

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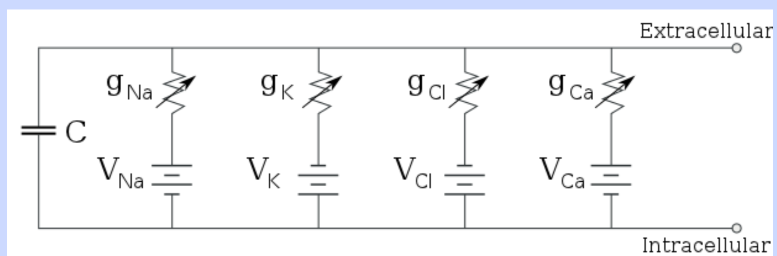
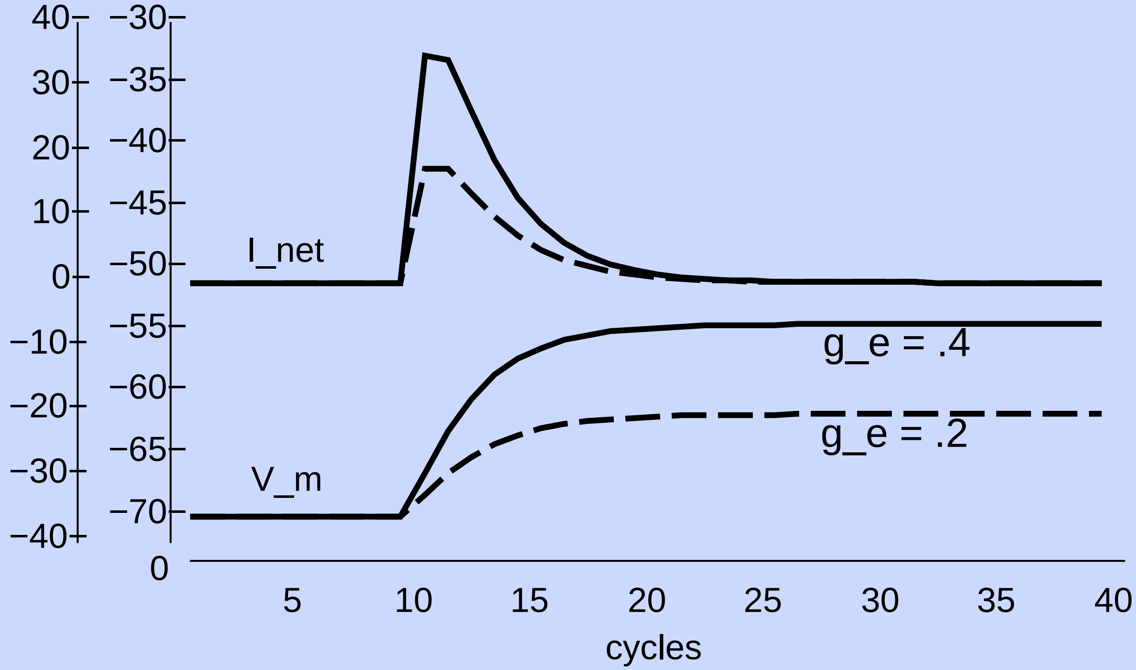


Equivalent circuit.
time constant $\tau = RC = C/g_{net}$

In Action: Neuron.proj



(Two excitatory inputs at time 10, of conductances .4 and .2)

Overall Equilibrium Potential

If you run V_m update equations with steady inputs, neuron settles to new *equilibrium potential*.

To find, set $I_{net} = 0$, solve for V_m:

$$V_m = \frac{g_e \bar{g}_e E_e + g_i \bar{g}_i E_i + g_l \bar{g}_l E_l}{g_e \bar{g}_e + g_i \bar{g}_i + g_l \bar{g}_l} \quad (14)$$

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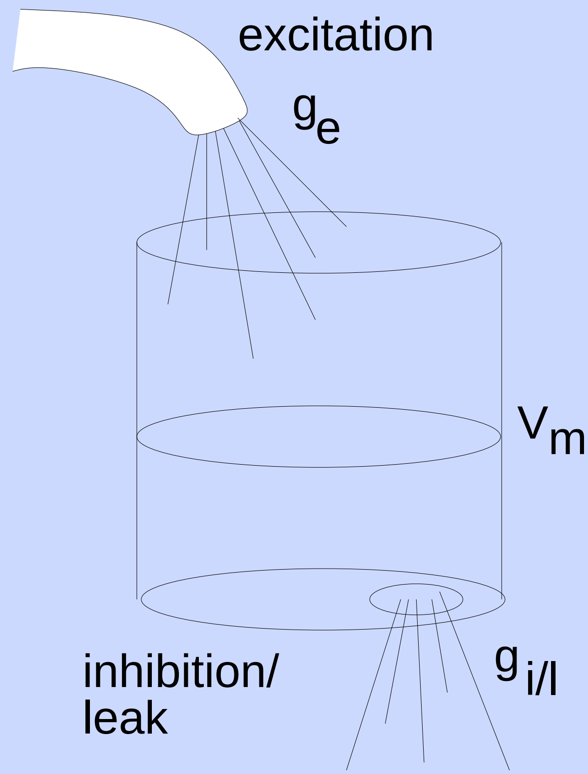
Can now solve for the equilibrium potential as a function of inputs.

Simplify: ignore leak for moment, set $E_e = 1$ and $E_i = 0$:

$$V_m = \frac{g_e \bar{g}_e}{g_e \bar{g}_e + g_i \bar{g}_i} \tag{16}$$

Membrane potential computes a *balance* (weighted average) of excitatory and inhibitory inputs.

It's Just a Leaky Bucket



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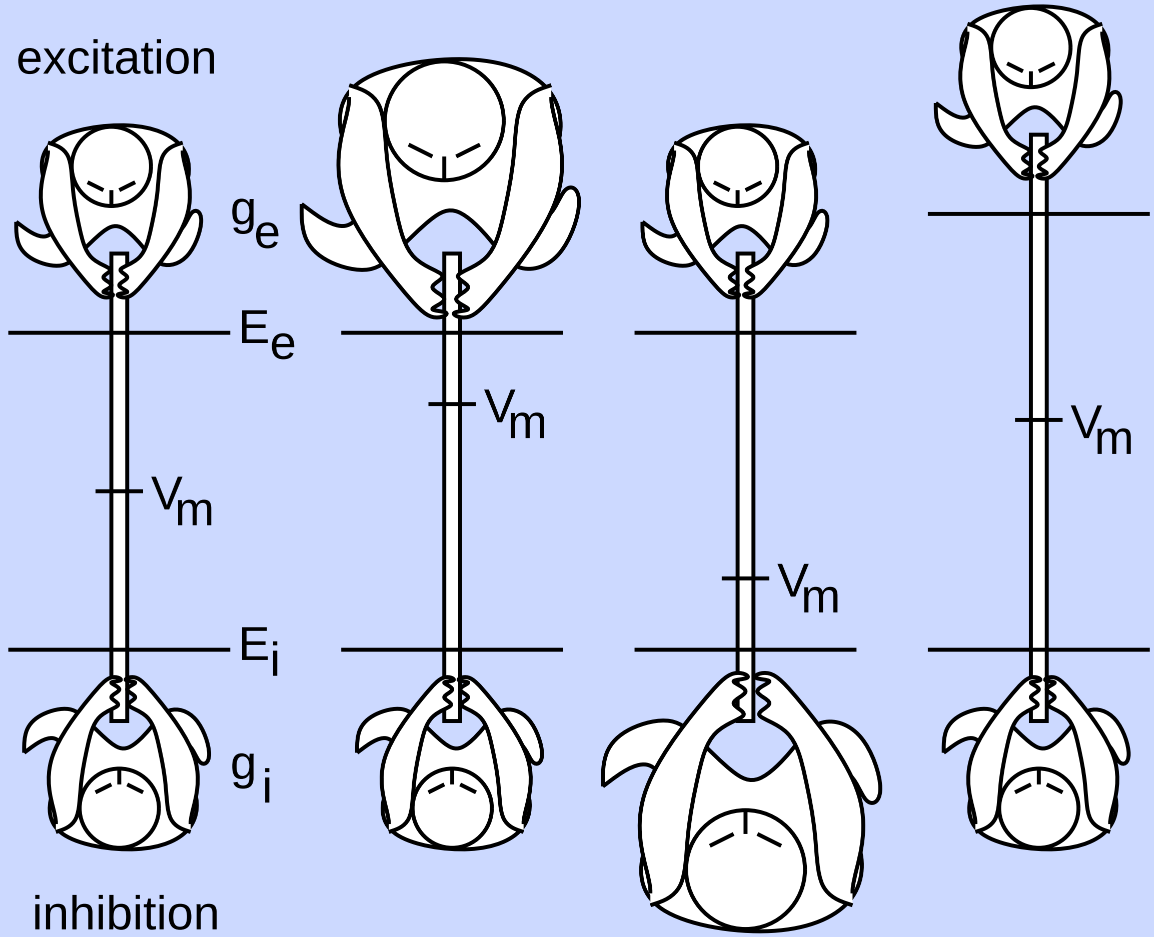
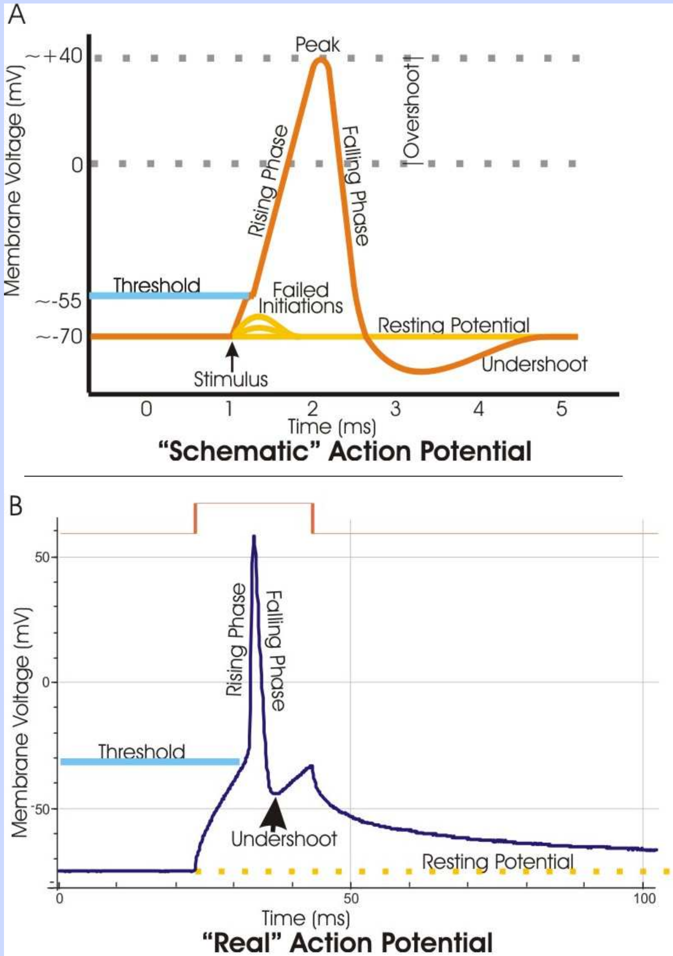


How Does Neuron “Decide” When to Spike?

- When membrane potential exceeds a **threshold** value, voltage-gated Na^+ channels open up
- This leads to an influx of Na^+ and (consequently) a very large and rapid increase in membrane potential
- Shortly afterward, voltage gated K^+ channels open up
- This leads to a rapid flow of K^+ out of the neuron and thus a very large and rapid decrease in membrane potential
- The result is a discrete “spike” in membrane potential

Spike = Action Potential



This travels down the axon in a wave of activity...

Bio Neural Nets

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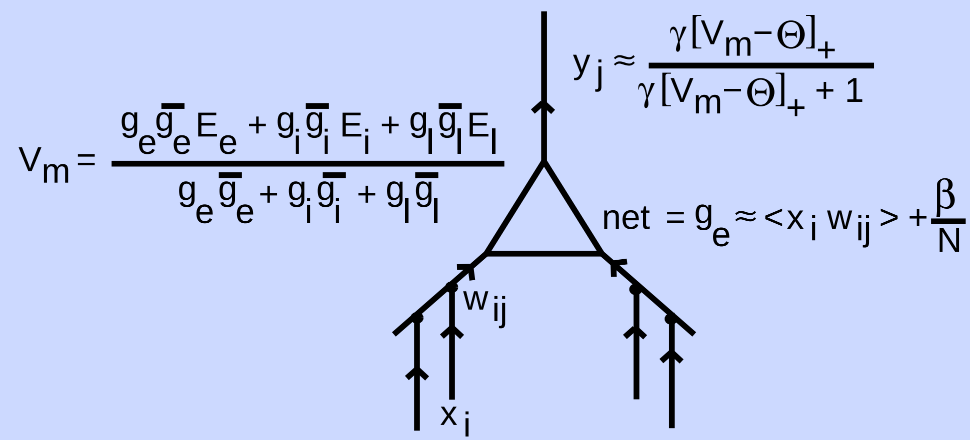
3. Compute output as: Spikes, or rate code equivalent via *sigmoidal* function:

$$a_j = \frac{\gamma[g_e(t) - g_e^{\Theta}]_+}{\gamma[g_e(t) - g_e^{\Theta}]_+ + 1} \tag{19}$$

$g_e^{\Theta} = \frac{g_i(E_i - \Theta) + g_l(E_l - \Theta)}{\Theta - E_e} =$ g_e value that puts V_m at threshold Θ given all forces

Computational Neurons (Units) Overview



1. Weights = synaptic efficacy; weighted input = $x_i w_{ij}$.

2. Net conductances (average across all inputs) excitatory ($net = g_e(t)$), inhibitory $g_i(t)$.

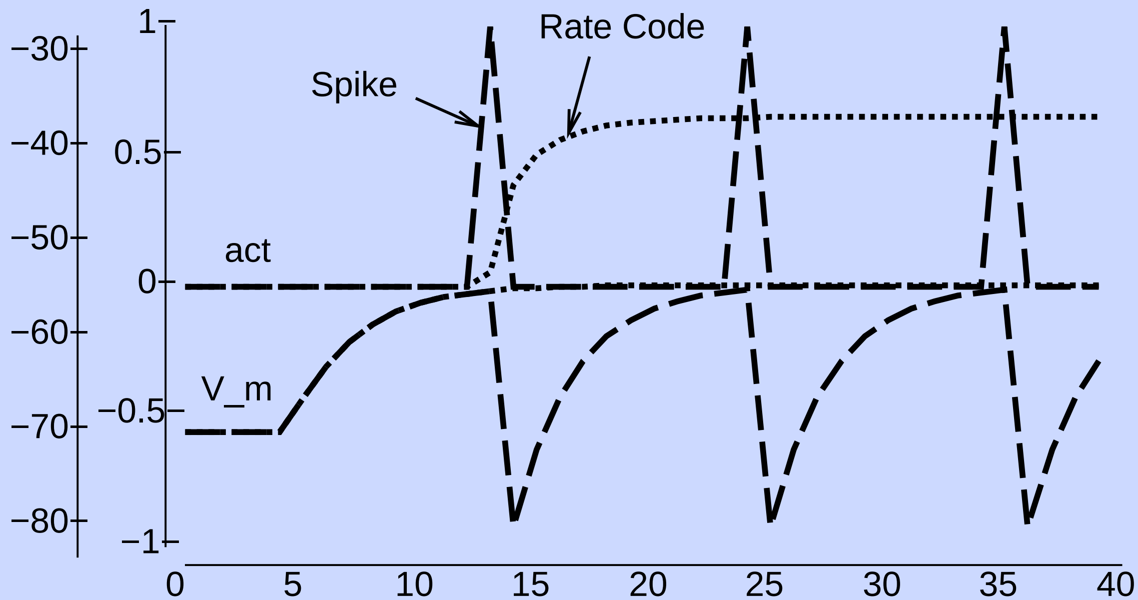
3. Integrate conductances using V_m update equation.

4. Compute output y_j as spikes or *rate code*.

Thresholded Spike Outputs

Voltage gated Na^+ channels open if $V_m > \Theta$, sharp rise in V_m.

Voltage Gated K^+ channels open to reset spike.



In model: $y_j = 1$ if $V_m > \Theta$, then reset (also keep track of rate).

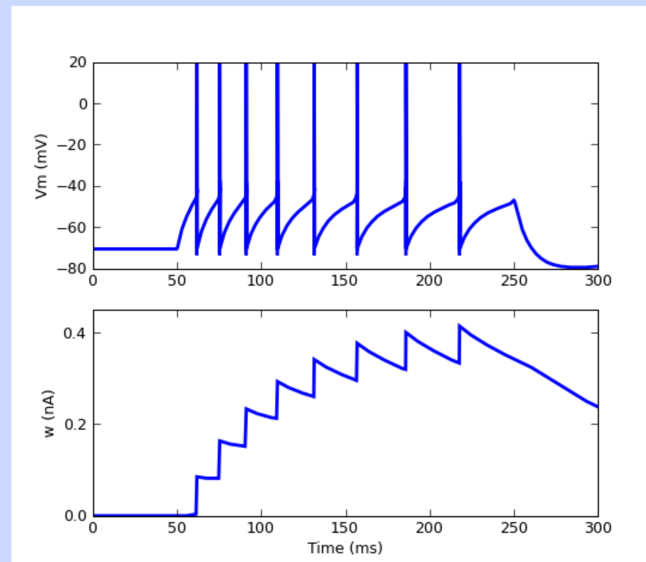
Optional: Adaptive Exponential (AdEx) spiking model

$$C_m \frac{dV_m}{dt} = g_e(E_e - V_m) + g_l(E_l - V_m) + g_l \beta e^{\left(\frac{V-\theta}{\beta}\right)} - w$$

$$\tau_w \frac{dw}{dt} = a(V_m - E_l) - w$$

$$w \rightarrow w + b; \quad t = t_{spike}$$

β = slope, sharpness of spike
θ = threshold
w = adaptation variable
τ_w = time constant of adaptation
a = gain on adaptation as V_m rises



Brette & Gerstner, 2005

Rate Coded Output

Output *is* average firing rate value.
One unit = % spikes in population of neurons?

Rate approximated by X-over-X-plus-1 ($\frac{x}{x+1}$):

$$y_j = \frac{\gamma[g_e(t) - g_e^{\ominus}]_+}{\gamma[g_e(t) - g_e^{\ominus}]_+ + 1} \tag{20}$$

which is like a sigmoidal function:

$$y_j = \frac{1}{1 + (\gamma[g_e(t) - g_e^{\ominus}]_+)^{-1}} \tag{21}$$

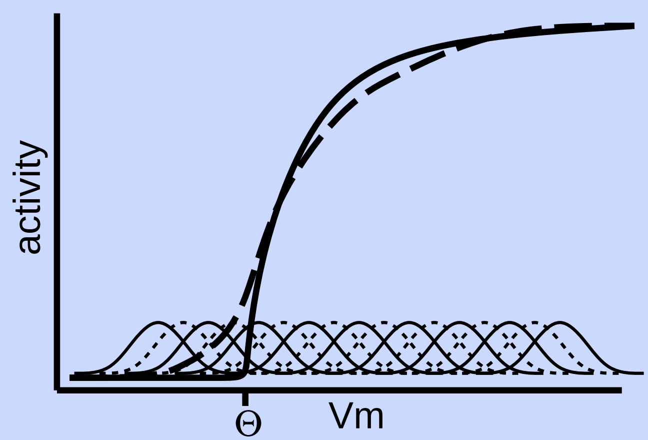
compare to sigmoid: $y_j = \frac{1}{1+e^{-\eta_j}}$

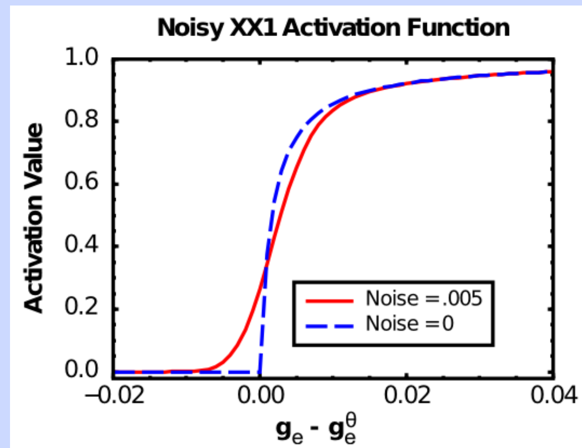
γ is the *gain*: makes things sharper or duller.

Convolution with Noise

X-over-X-plus-1 has a very sharp threshold

Smooth by *convolve* with noise (like “blurring” or “smoothing”):





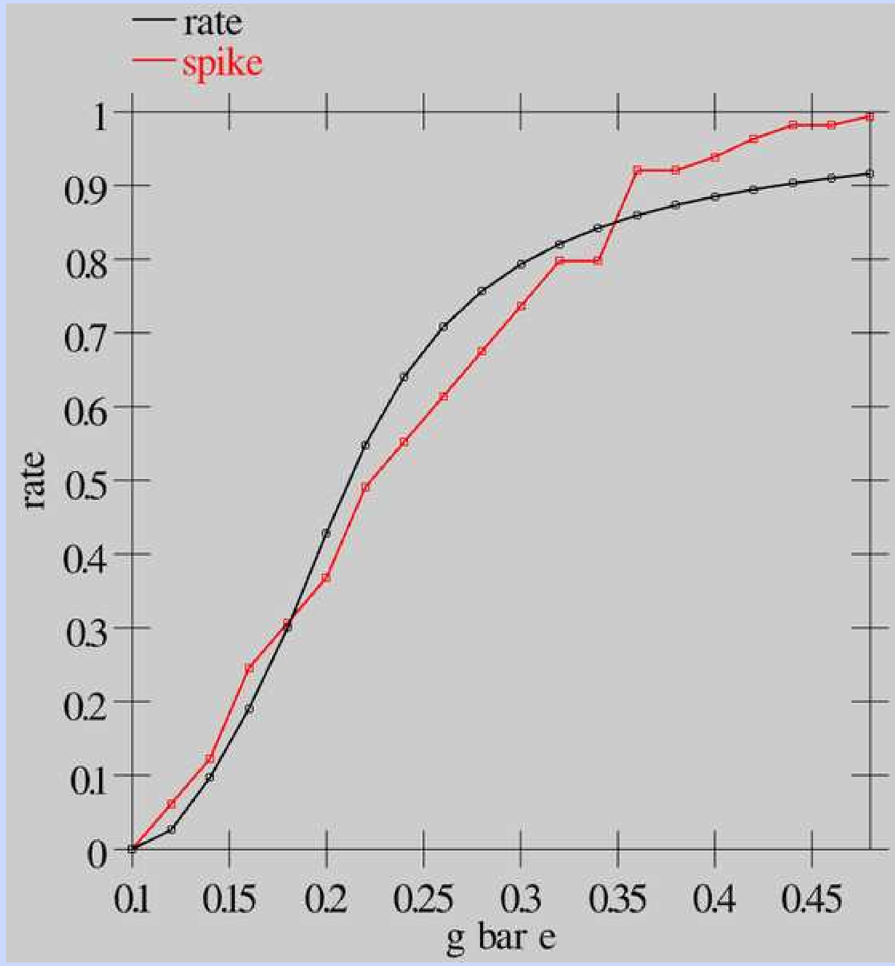
Restoring iterative dynamics

- Rate code approximation uses $g_e(t)$ (relative to g_e^{Θ}) to determine firing rate

- But as we saw earlier, V_m takes time to adapt to changes in conductance, and spiking is based on V_m

- $\rightarrow$ restore V_m sluggishness into rate code:
  $a_j(t) = a_j(t-1) + dt_{vm}(a_j^* - a_j(t-1))$

Fit of Rate Code to Spikes



Dynamics: Hysteresis and Accommodation

- So far considered 3 channels, but in reality there are several more.

- Some channels are *voltage-gated*, which means they open and close as a function of current activity. Rapid influx of Ca^{2+} can allow cell to stay active even after input fades away: *Hysteresis*.

- Other channels are *calcium-gated*: where Ca^{2+} reflects averaged prior activity. Inhibitory channels based on prev activity lead to *accommodation* (fatigue).

Dynamics: Hysteresis and Accommodation

$$I_a = g_a(E_a - V_m) \tag{22}$$

$$I_h = g_h(E_h - V_m) \tag{23}$$

g_a and g_h are time-varying functions that depend on previous activity, integrated over different time periods. E_h is excitatory; E_a inhibitory.

Dynamics: Hysteresis and Accommodation

$$I_a = g_a(E_a - V_m) \tag{22}$$

$$I_h = g_h(E_h - V_m) \tag{23}$$

g_a and g_h are time-varying functions that depend on previous activity, integrated over different time periods. E_h is excitatory; E_a inhibitory.

$$g_a(t) = \begin{cases} g_a(t-1) + dt_{g_a}(1 - g_a(t-1)); & \text{if}(b_a(t) > \Theta_a) \\ g_a(t-1) + dt_{g_a}(0 - g_a(t-1)); & \text{if}(b_a(t) < \Theta_d) \end{cases} \tag{24}$$

basis variable b_a is time average of activation state:

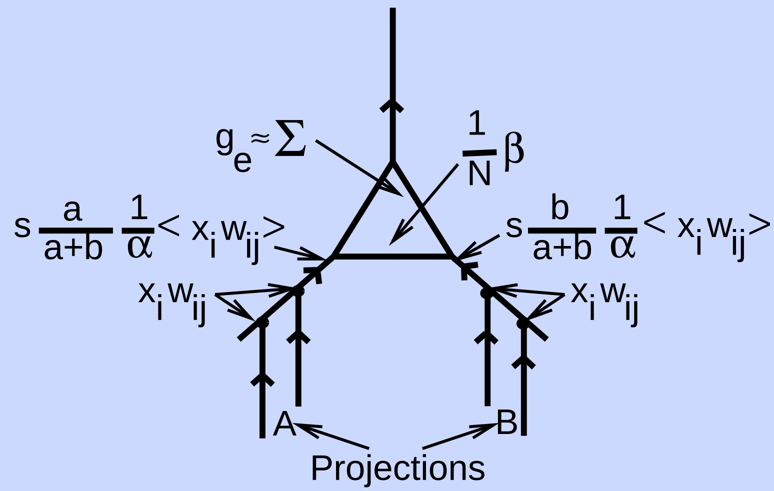
$$b_a(t) = b_a(t-1) + dt_{b_a}(y_j(t) - b_a(t-1)) \tag{25}$$

with dt_{b_a} fast for hysteresis, slow for accommodation

[detector.proj]

Extra

Computing Excitatory Input Conductances



One projection per group (layer) of sending units.

Average weighted inputs $\langle x_i w_{ij} \rangle = \frac{1}{n} \sum_i x_i w_{ij}$.

Bias weight β: constant input.

Factor out expected activation level α.

Other scaling factors a, s (assume set to 1).

Computing V_m

Use $V_m(t+1) = V_m(t) + dt_{vm} I_{net-}$ with biological or normalized (0-1) parameters:

Normalized Neuron Parameters

Parameter	Bio Val	Norm Val		Parameter	Bio Val	Norm Val
Time	0.001 sec	1 ms		**Voltage**	0.1 V or 100mV	-100..100 mV = 0..2 dV
Current	1×10^{-8} A	10 nA		**Conductance**	1×10^{-9} S	1 nS
Capacitance	1×10^{-12} F	1 pF		**C (memb capacitance)**	281 pF	1/C = .355 = dt.vm
g_bar_l (leak)	10 nS	0.1		**g_bar_i (inhibition)**	100 nS	1
g_bar_e (excitation)	100 nS	1		**e_rev_l (leak) and Vm_r**	-70mV	0.3
e_rev_i (inhibition)	-75mV	0.25		**e_rev_e (excitation)**	0mV	1
θ (act.thr, V_T in AdEx)	-50mV	0.5		**spike.spk_thr (exp cutoff in AdEx)**	20mV	1.2
spike.exp_slope (Δ_T in AdEx)	2mV	0.02		**adapt.dt_time (τ_w in AdEx)**	144ms	dt = 0.007
adapt.vm_gain (a in AdEx)	4 nS	0.04		**adapt.spk_gain (b in AdEx)**	0.0805nA	0.00805

Normalized used by default.

Detector vs. Computer

	Computer	Detector
Memory & Processing	Separate, general-purpose	Integrated, specialized
Operations	Logic, arithmetic	Detection (weighing & accumulating evidence, evaluating, communicating)
Complex Processing	Arbitrary sequences of operations chained together in a program	Highly tuned sequences of detectors stacked upon each other in layers