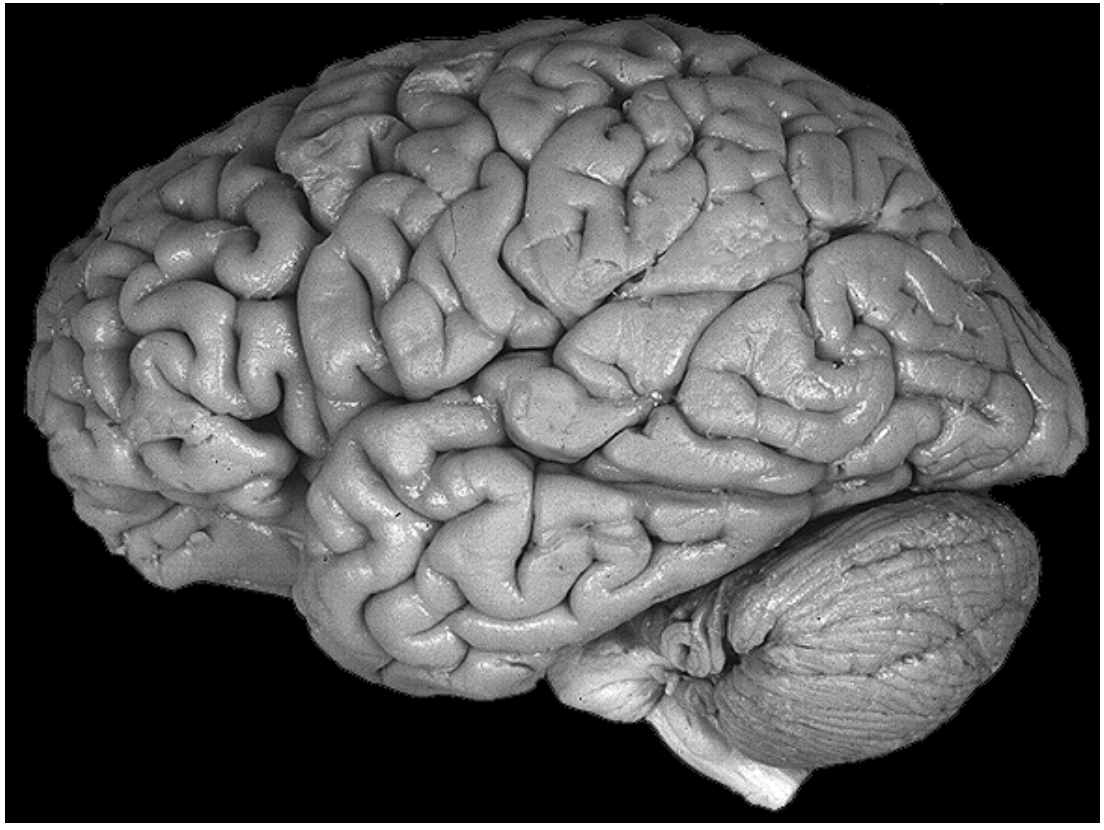
Neuroscience 101

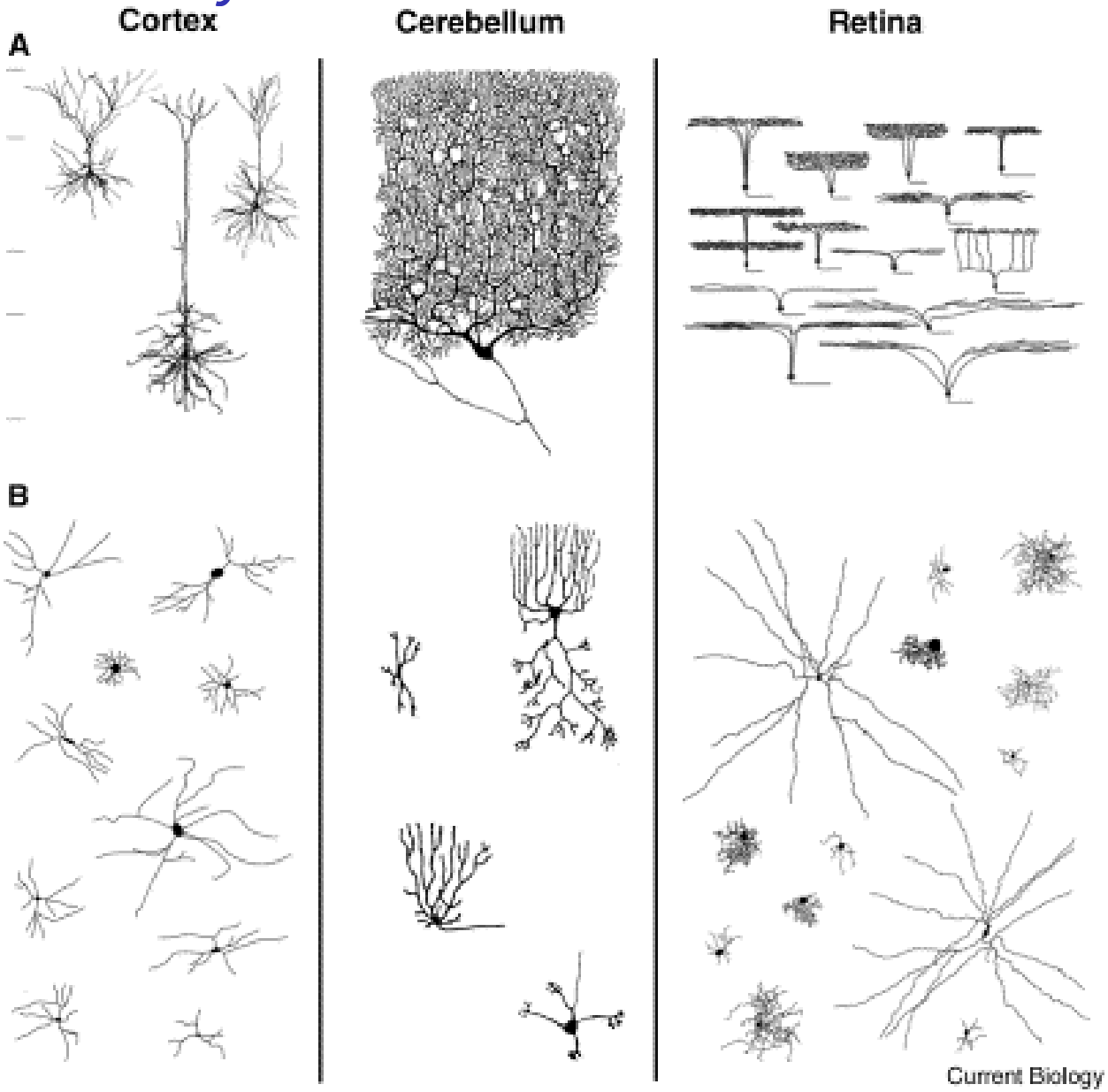
Brain organisation

Structural and functional divisions of mammalian brain.



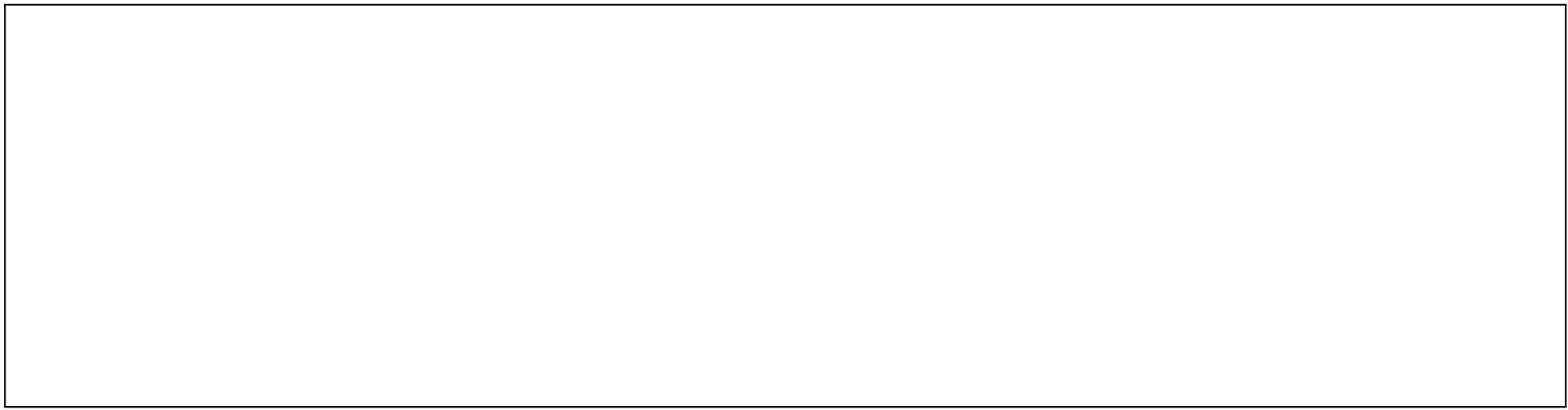
Neurons are the building blocks of the brain. $\sim 10^{11}$ in human brain; each may make $10^0 - 10^3$ connections. Not encoded in the genome!
Vastly distributed architecture exhibiting *parallel processing* and *graceful degradation*.

Neuronal diversity



Masland (2004).

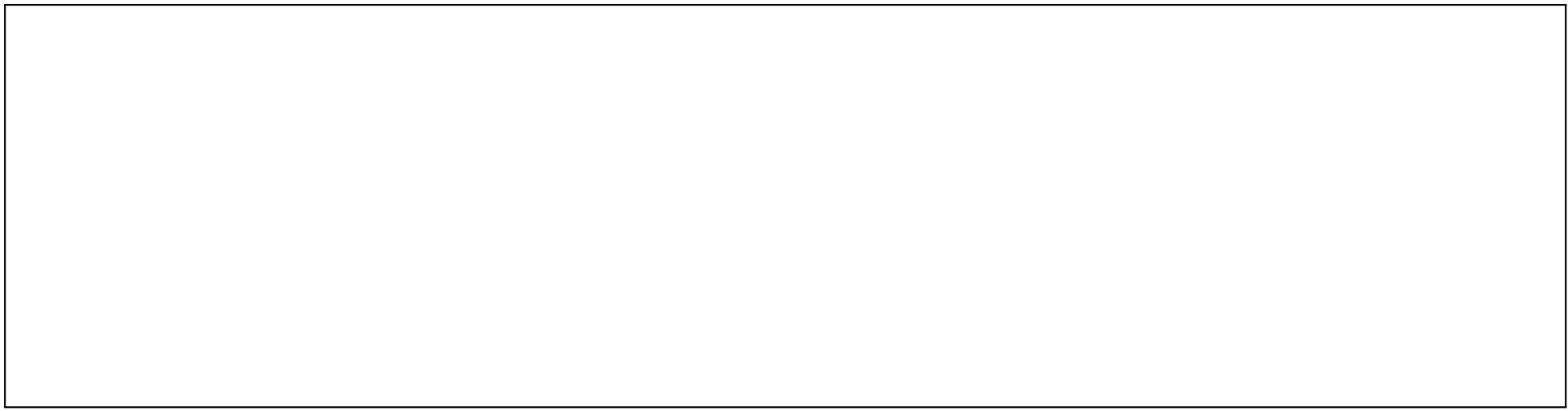
Components of a neuron



- Dendritic tree
- Cell body
- Axon
- Axon terminal
- synapses

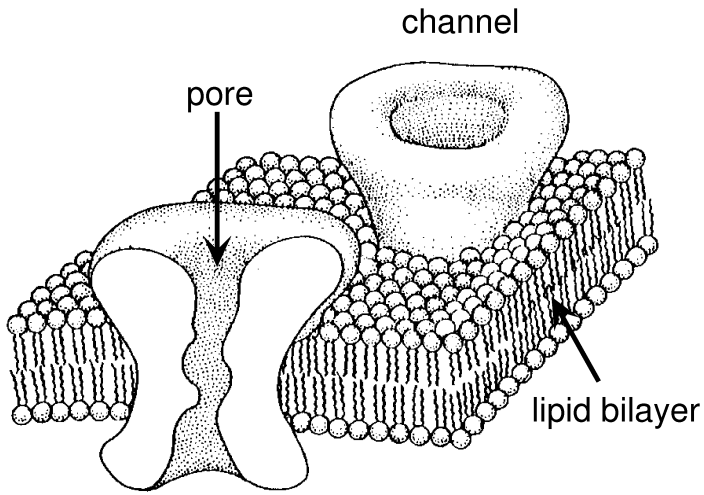
Action potentials (“spikes”) travel along the axon when cell reaches threshold. All-or-none events.

Synapses



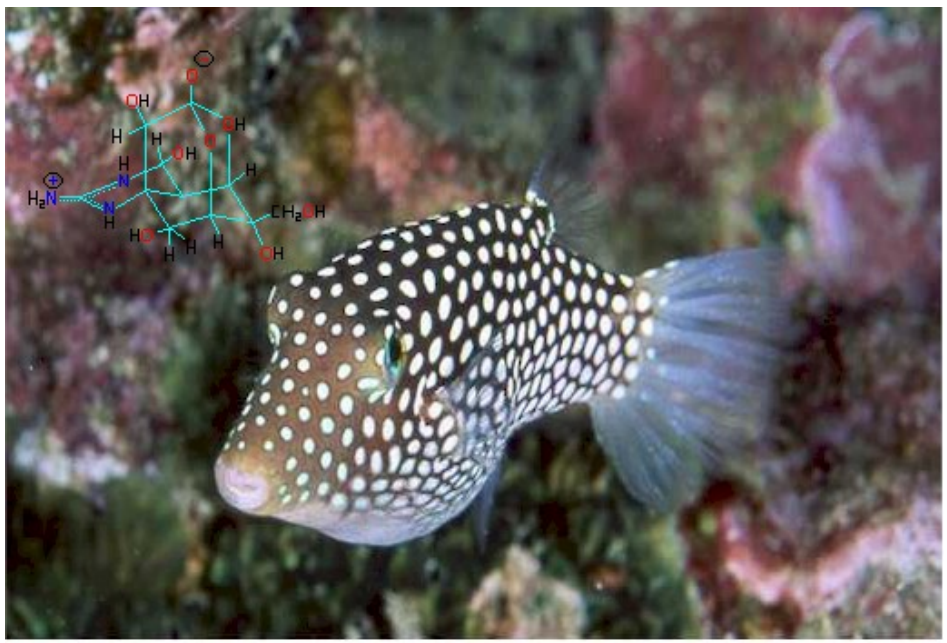
- presynaptic neuron
- postsynaptic neuron
- vesicles
- neurotransmitters (Glutamate, ACh, GABA)
- receptors (type of ion channel; next slide)
- cf. gap junctions for electrical transmission.

Ion channels



- Ion channels (ICs) allow specific ions to selectively diffuse across membrane when channels are “open”.
- State of channel can be modulated by sensing voltage (voltage-gated) or by sensing internal/external concentration of e.g. messengers (Ca) or neurotransmitters (ACh). Ionotropic (fast) vs Metabotropic (slow).
- Typically $10^2 - 10^6$ per μm^2 channels of each type in membrane; each channel about 10 nm high.

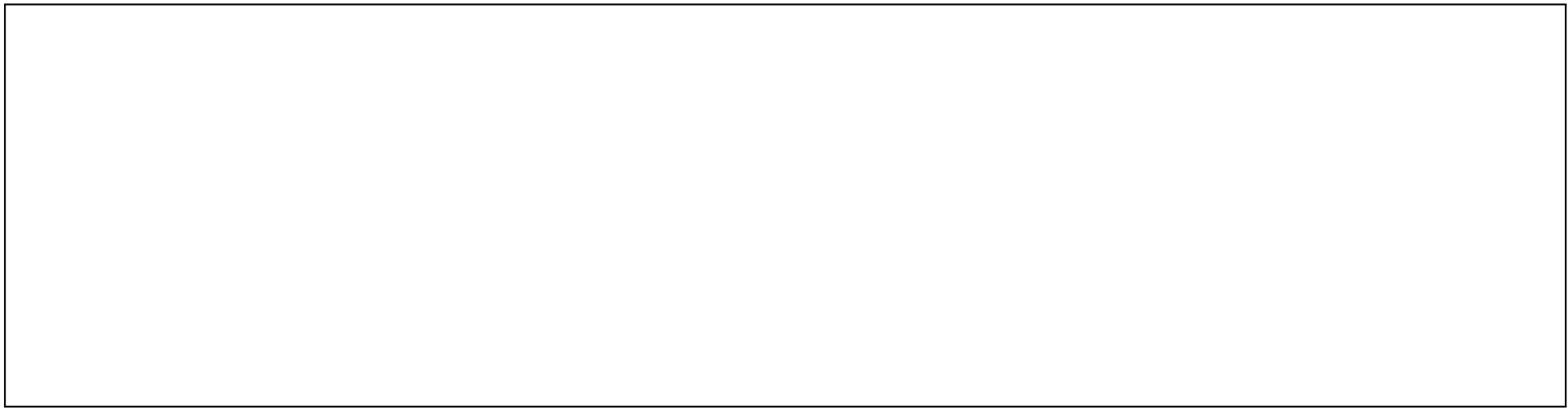
Tetrodotoxin (TTX) will block your sodium channels …



Ionic basis of action potential Hodgkin and Huxley, 1952

- Principal ions Na^+, K^+. Imbalance in numbers across membrane causes electrical gradient and concentration gradient.
- Ion channels *selectively* allow ions to flow down concentration gradient.
- Ion pumps actively move ions against concentration gradient.
- Electrical gradient acts against concentration gradient. Each ion has its own resting potential when two gradients balance.
  ($E_{\mathrm{Na}} = +50mV, E_{\mathrm{K}} = -77mV$).
- This is determined by Nernst potential $E = (RT/Fz) \ln[X_o]/[X_i]$ (RT/F = 25 mV at 25C)
- At rest (-70 mV; inside relative to outside), voltage-gated ion channels are closed.

Threshold behaviour



- For small depolarizations, ion channels open and Na^+ flow in is balanced by K^+ flow out. Ion channels are voltage-gated.
- For larger depolarizations ($\sim$ 10–15 mV), Na^+ flow faster.
- On fast timescale, more Na^+ channels open, causing more depolarization... action potential. Na^+ inactivates.
- On slower timescale, K^+ channels open, causing hyperpolarization, undershoot (refractory period) and back to resting.
- Action potential ("spikes") travels as a wave down axon; passively diffusing and then regenerating at Nodes of Ranvier (unmyelinated).
- `http://tinyurl.com/matthews-channel`

Propagation of action potential

- Local depolarization causes passive intracellular spread of current, causing local depolarisation. This opens neighbouring channels, causing AP to actively regenerate.
- This is slow. Myelin acts as insulator so that signal (passively) propagates quickly down axon, regenerating at nodes of Ranvier.
- `http://tinyurl.com/matthews-prop`

Models of action potentials

Hodgkin and Huxley model (Chapter 5 of Dayan and Abbott).

$$c_m \frac{\mathrm{d}V}{\mathrm{d}t} = -i_m + I_e/A$$

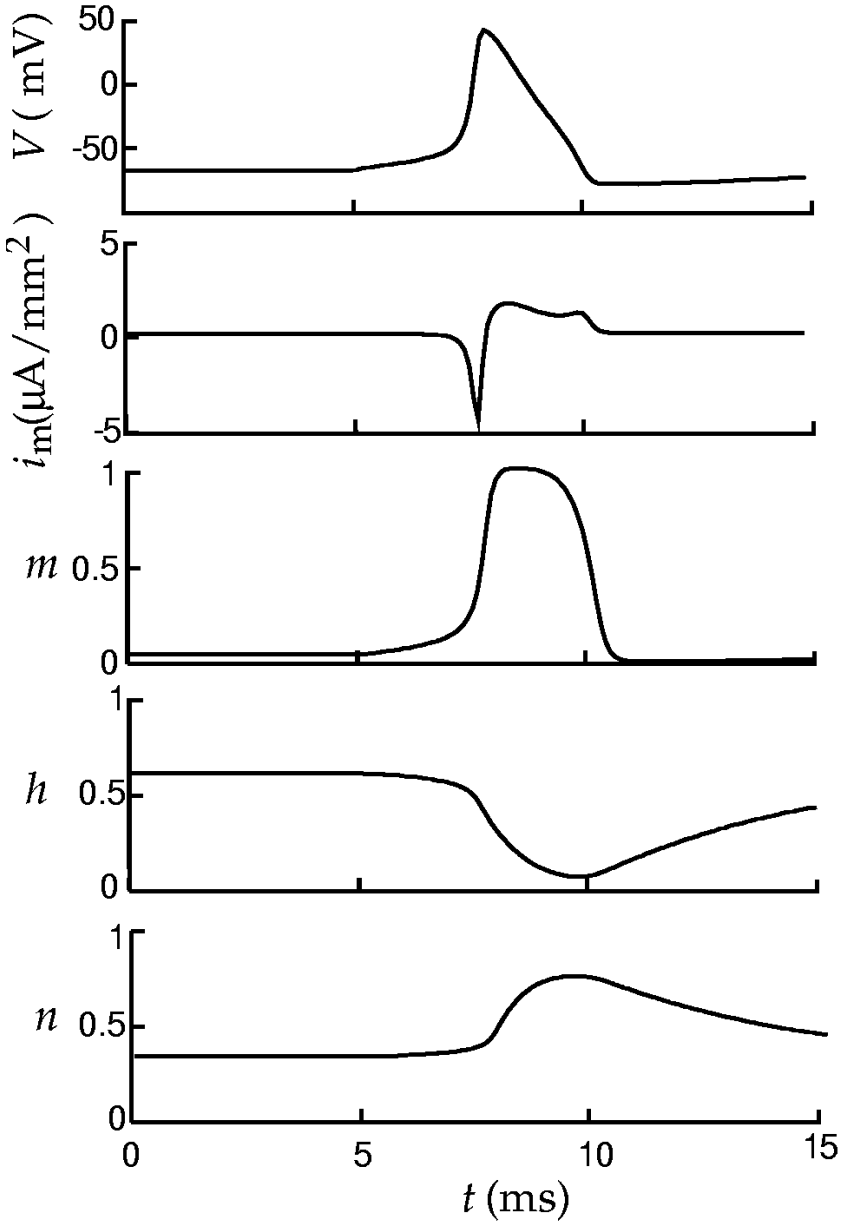
Each ion produces a current which can be summed:

$$i_m = \sum_i g_i[\text{gating}](V - E_i)$$

$$c_{\mathrm{m}} \frac{\mathrm{d}V}{\mathrm{d}t} = g_L(E_{\mathrm{L}} - V) + g_{\mathrm{Na}} m^3 h(E_{\mathrm{Na}} - V)$$
$$+ g_{\mathrm{K}} n^4 (E_{\mathrm{K}} - V) + I_{\mathrm{e}}/A$$

Plus we have equations for $\frac{\mathrm{d}n}{\mathrm{d}t}, \frac{\mathrm{d}m}{\mathrm{d}t}, \frac{\mathrm{d}h}{\mathrm{d}t}$.
(Notes: this is space-clamped; note I_e defined as positive inward, whereas i_m are defined as positive-outward.)

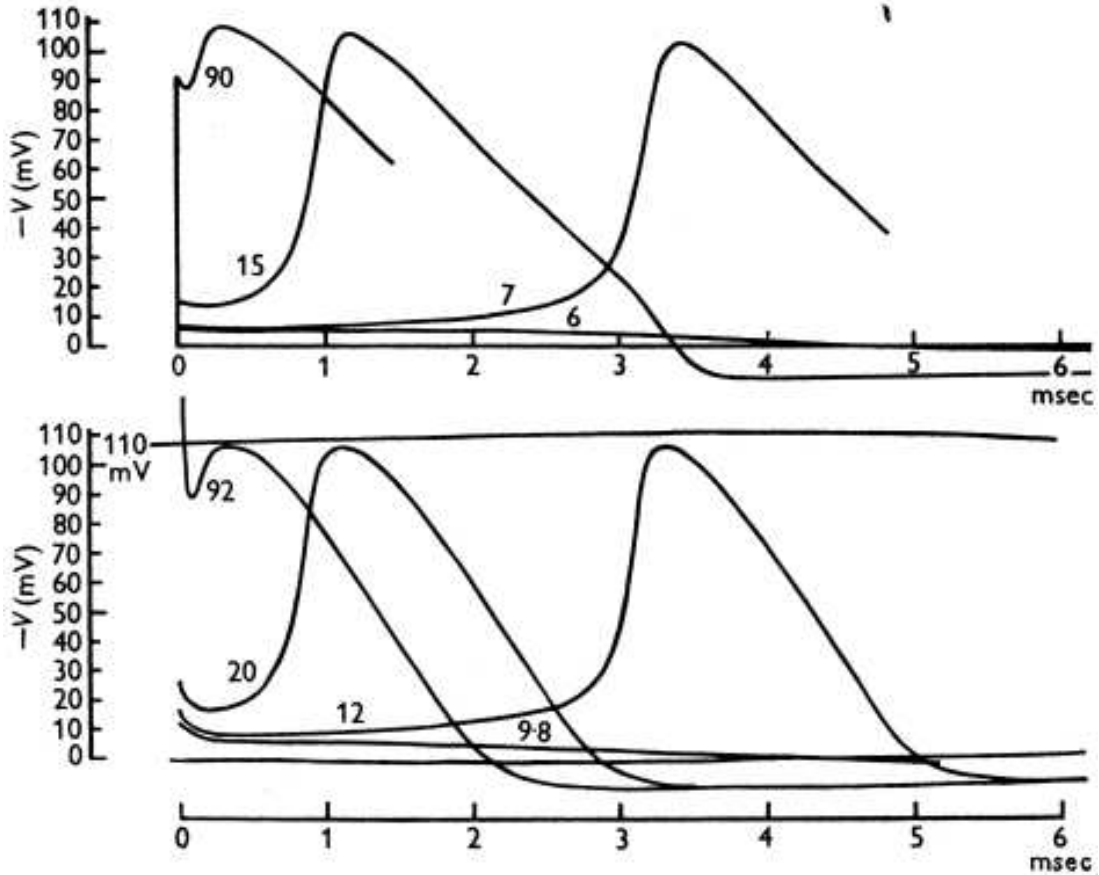
Evolution of a model action potential



Dayan and Abbott (2002) fig 5.11.

Hodgkin-Huxley: model vs experiment

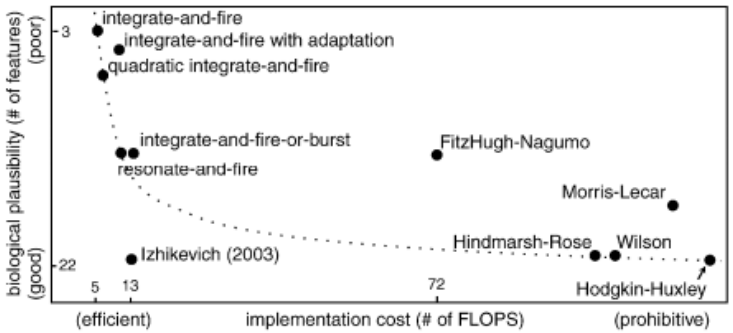
Data taken from squid giant axon; much wider axonal diameter (800 μm) than normal (2 μm) for rapid signal propagation [escape behaviour].



(Hodgkin and Huxley, 1952). Reproduced from David Sterratt. Upper trace: model; numbers give initial depolarisations (in mV); recordings at 6 C.

Do we need all that machinery?

Various simplifications to Hodgkin-Huxley (Izhikevich, 2004; Figure 2):



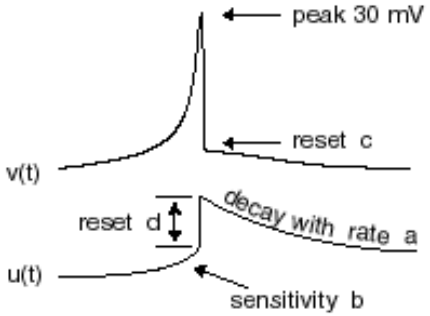
Models	biophysically meaningful	tonic spiking	phasic spiking	tonic bursting	phasic bursting	mixed mode	spike frequency adaptation	class 1 excitable	class 2 excitable	spike latency	subthreshold oscillations	resonator	integrator	rebound spike	rebound burst	threshold variability	bistability	DAP	accommodation	inhibition-induced spiking	inhibition-induced bursting	chaos	# of FLOPS
integrate-and-fire	-	+	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	5
integrate-and-fire with adapt.	-	+	-	-	-	-	+	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	10
integrate-and-fire-or-burst	-	+	+		+	-	+	+	-	-	-	-	+	+	+	-	+	+	-	-	-		13
resonate-and-fire	-	+	+	-	-	-	-	+	+	-	+	+	+	+	-	-	+	+	+	-	-	+	10
quadratic integrate-and-fire	-	+	-	-	-	-	-	+	-	+	-	-	+	-	-	+	+	-	-	-	-	-	7
Izhikevich (2003)	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	13
FitzHugh-Nagumo	-	+	+	-		-	-	+	-	+	+	+	-	+	-	+	+	-	+	+	-	-	72
Hindmarsh-Rose	-	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	120
Morris-Lecar	+	+	+	-		-	-	+	+	+	+	+	+	+		+	+	-	+	+	-	-	600
Wilson	-	+	+	+			+	+	+	+	+	+	+	+	+	+		+	+				180
Hodgkin-Huxley	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	1200

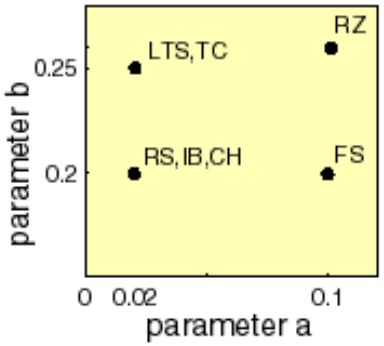
Fig. 2. Comparison of the neuro-computational properties of spiking and bursting models; see Fig. 1. "# of FLOPS" is an approximate number of floating point operations (addition, multiplication, etc.) needed to simulate the model during a 1 ms time span. Each empty square indicates the property that the model should exhibit in principle (in theory) if the parameters are chosen appropriately, but the author failed to find the parameters within a reasonable period of time.

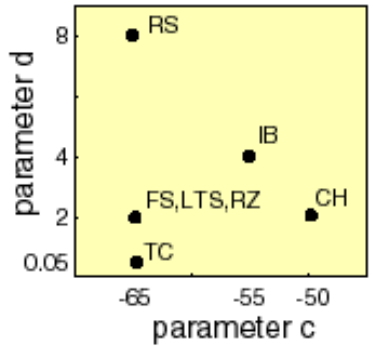
The Izhikevich model

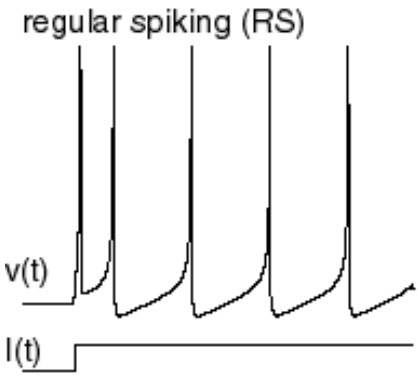
$$v' = 0.04v^2 + 5v + 140 - u + I$$
$$u' = a(bv - u)$$

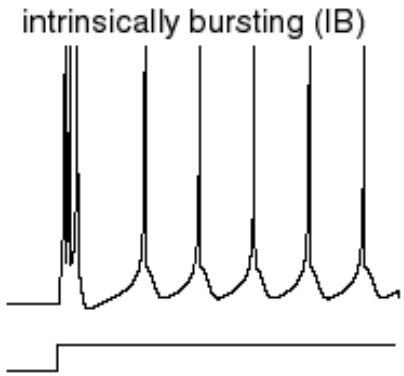
if $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$

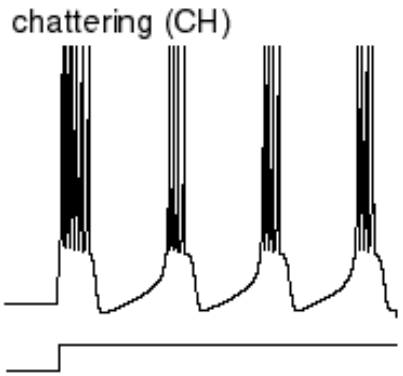


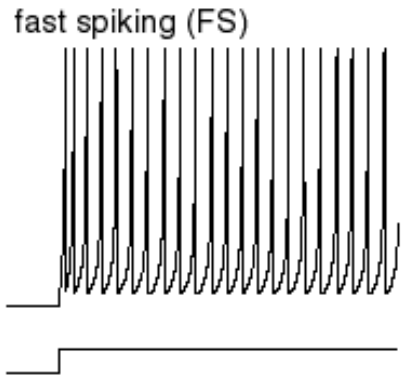


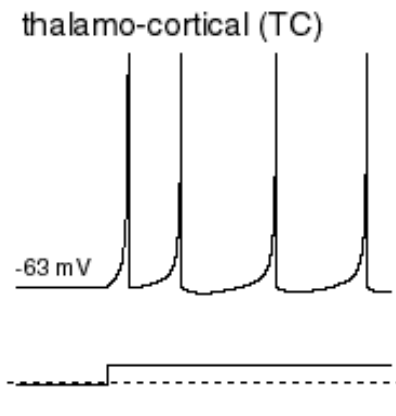


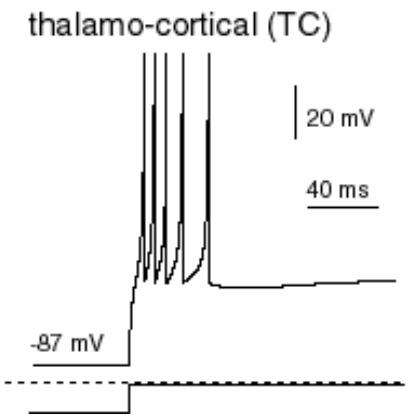


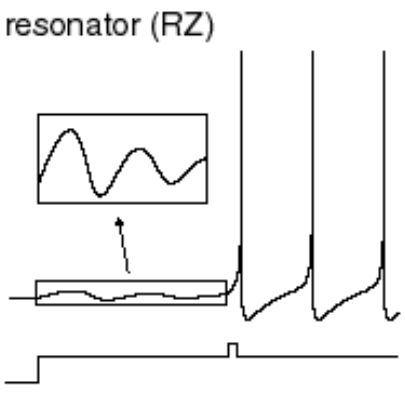


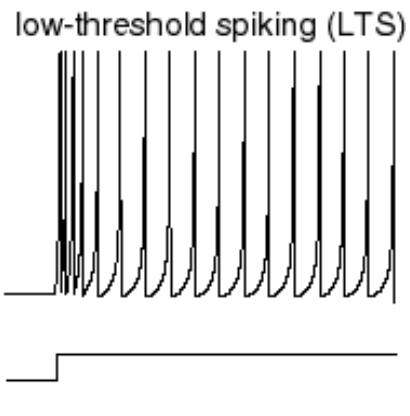












To explore this model interactively see `https://github.com/sje30/cnw`

From spike trains to firing rates

Instead of working with spike times t_i, perhaps model as:

$$\tau \frac{\mathrm{d}r_i}{\mathrm{d}t} = -r_i(t) + F\left(I_e(t) + \sum_{j=1}^{N} w_{ij} r_j(t)\right)$$

Advantages of working with firing rates:

1. More analytical work can be done with firing rates.
2. Computationally more tractable models. ("Simple models provide dynamical insight")
3. Spiking models often have more free parameters than firing rate models.
4. If modelling individual neurons, prob. of connections between any two neurons is low. Firing rate neurons can represent "average" of group of neurons; how do you make an "average" spike train to represent N neurons?