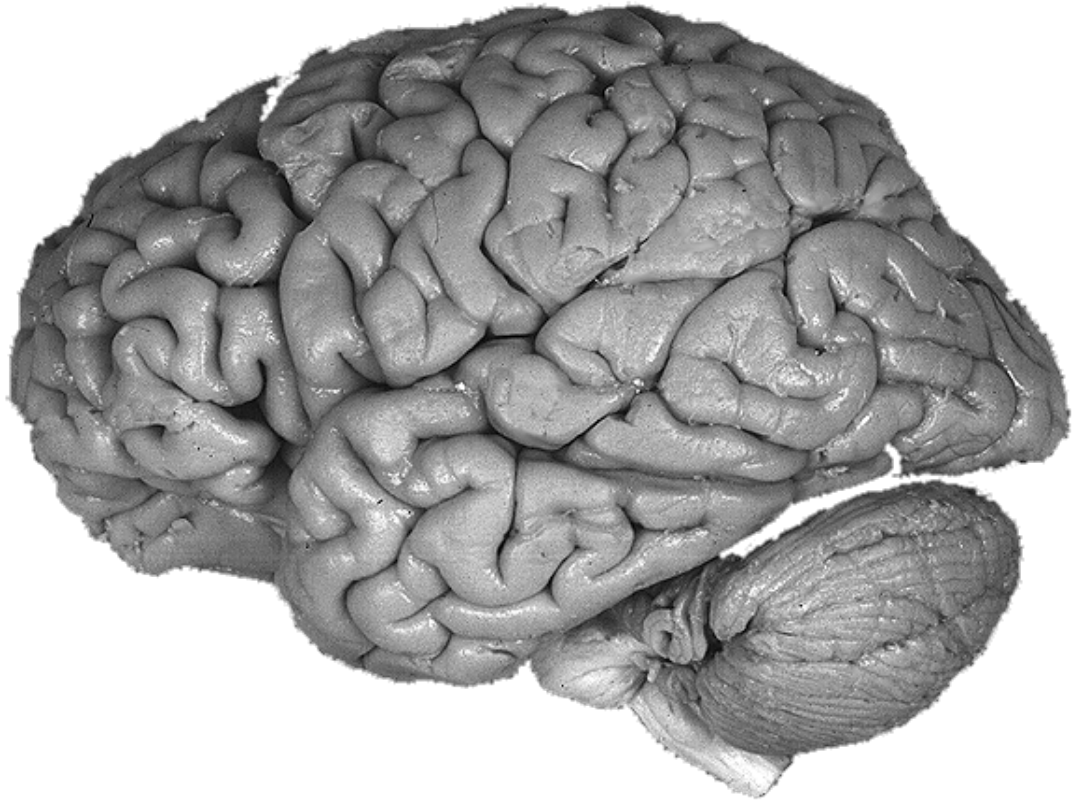
Neuroscience 101

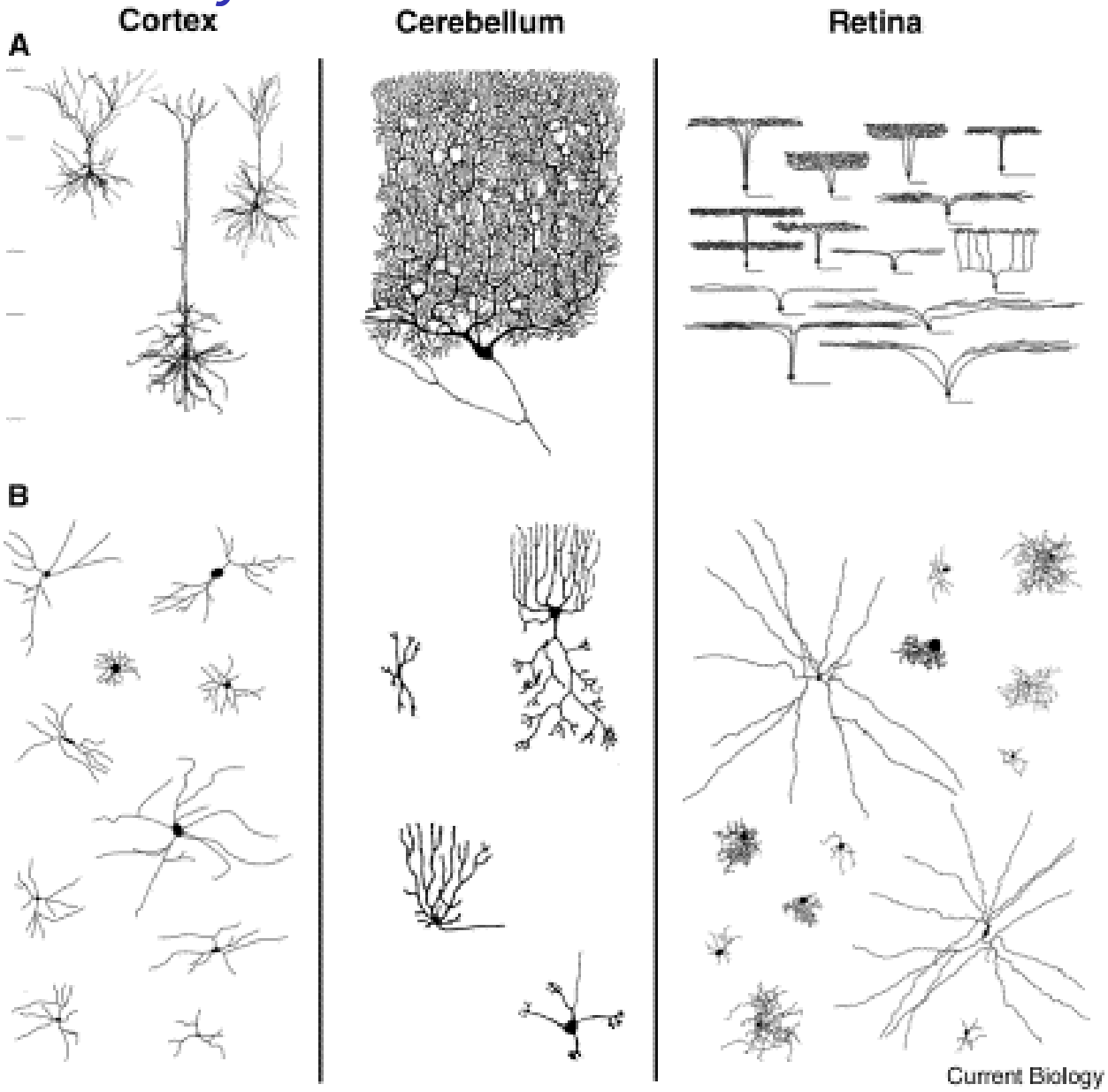
Brain organisation

Structural and functional divisions of mammalian brain.



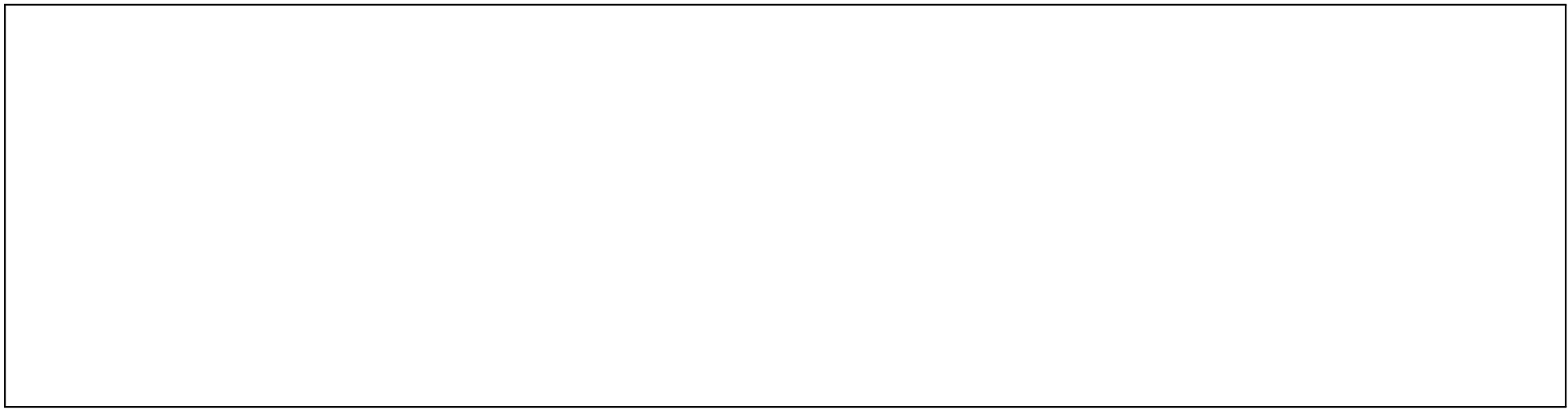
Neurons are the building blocks of the brain. $\sim 10^{11}$ in human brain; each may make $10^0 - 10^3$ connections. Not encoded in the genome!
Vastly distributed architecture exhibiting *parallel processing* and *graceful degradation*.

Neuronal diversity



Masland (2004).

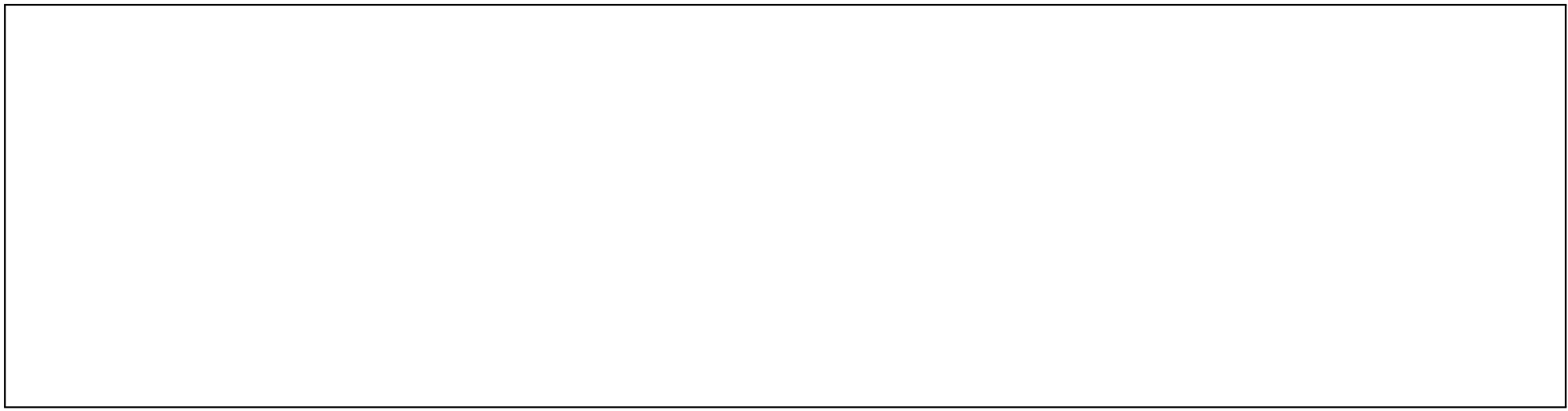
Components of a neuron



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

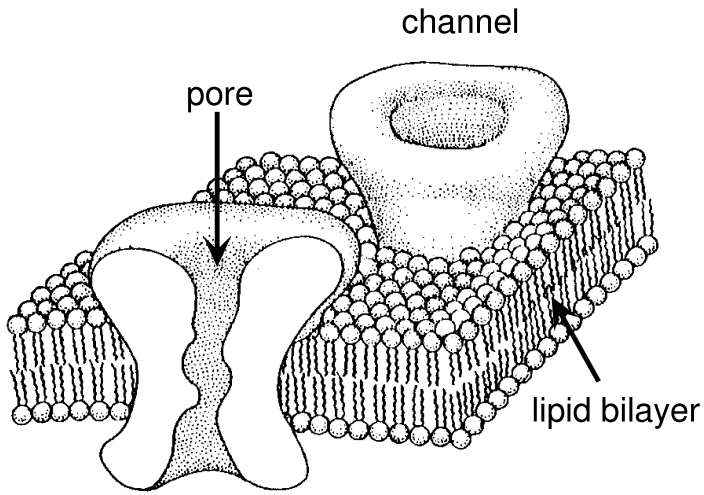
Action potentials (“spikes”) travel along the axon when cell reaches threshold. All-or-none events.

Synapses



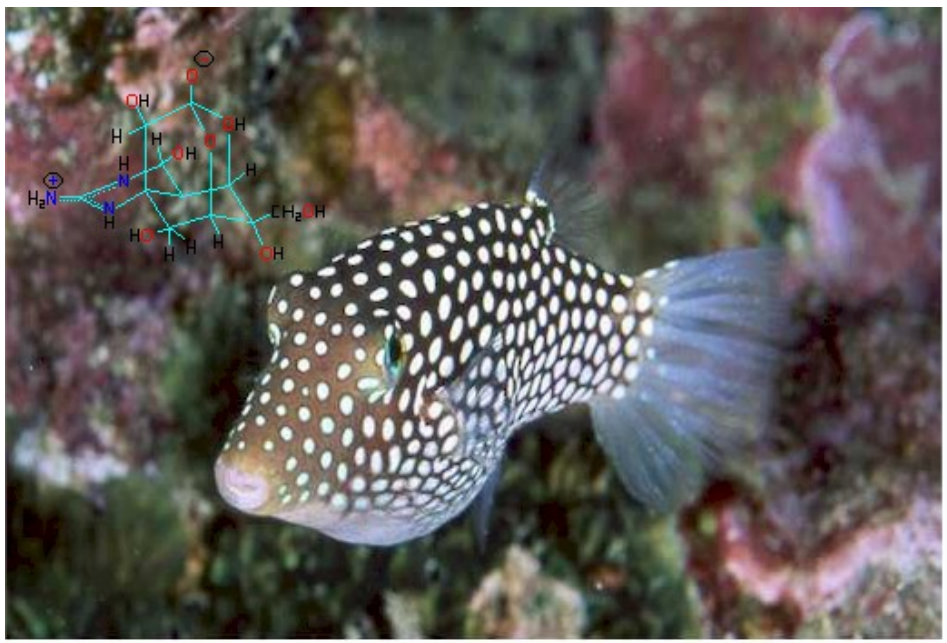
- presynaptic neuron
- postsynaptic neuron
- vesicles
- neurotransmitters (Glutamate, ACh, GABA)
- receptors (type of ion channel; next slide)
- cf. gap junctions for electrical transmission.

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.

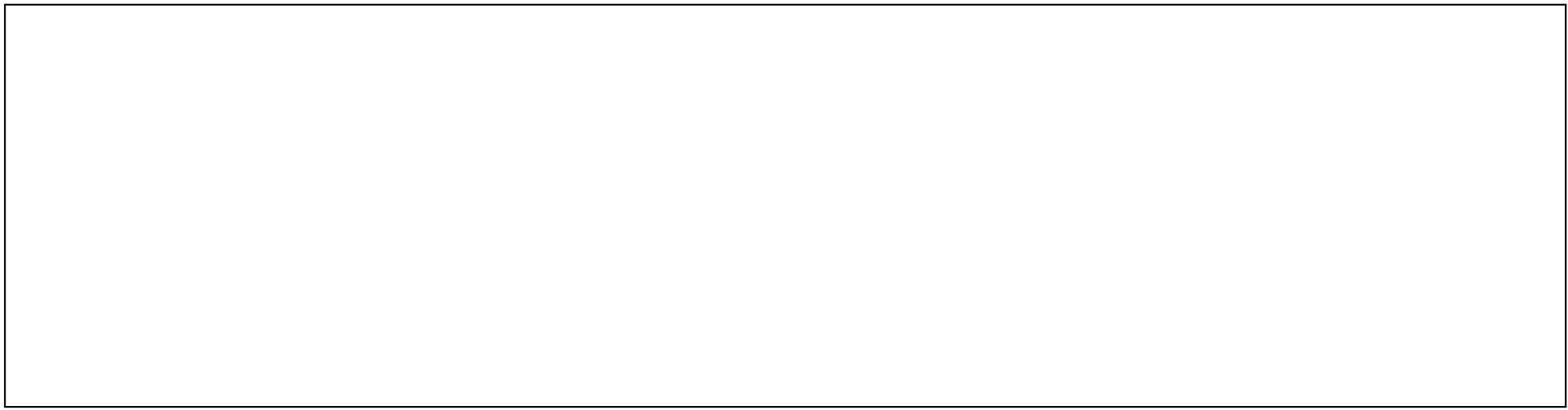
Tetrodotoxin (TTX) will block your sodium channels …



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).

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.

Models of action potentials

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

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

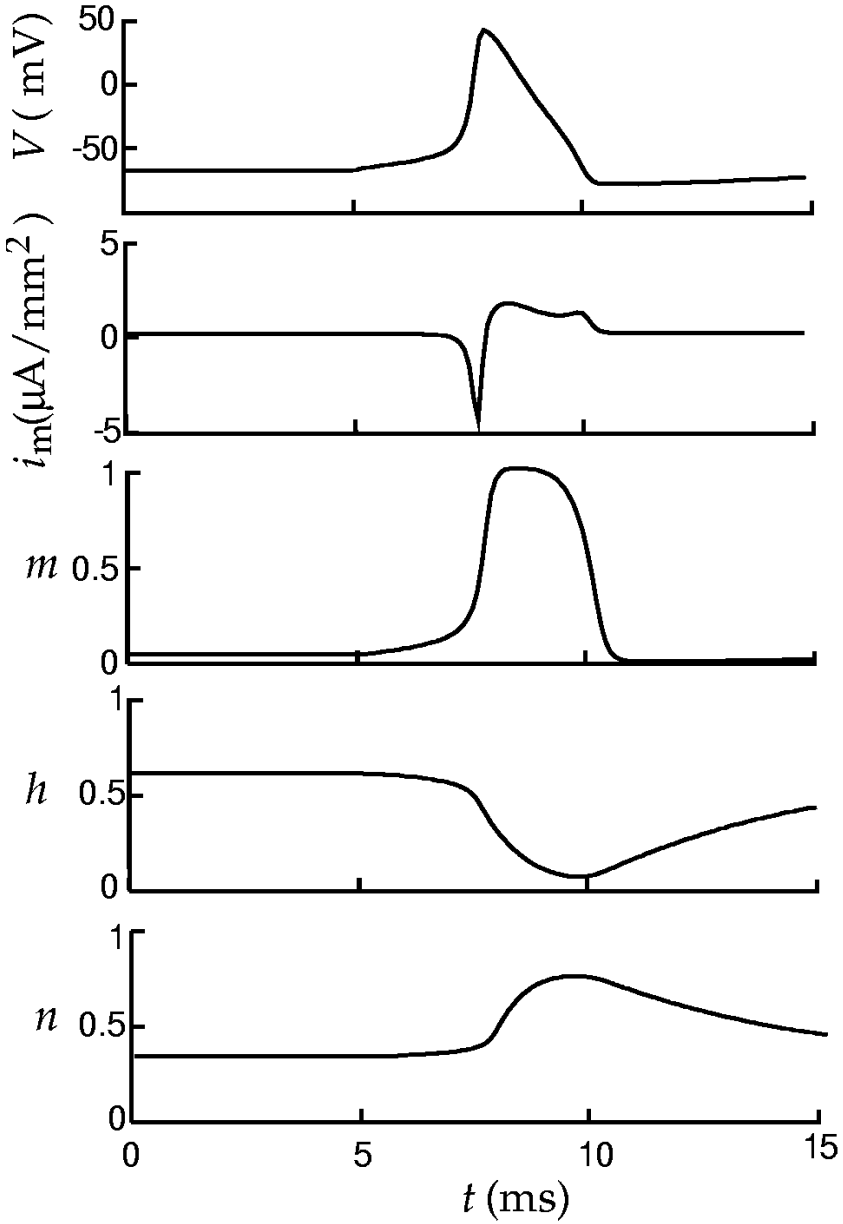
Each ion produces a current which can be summed:

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

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

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.)

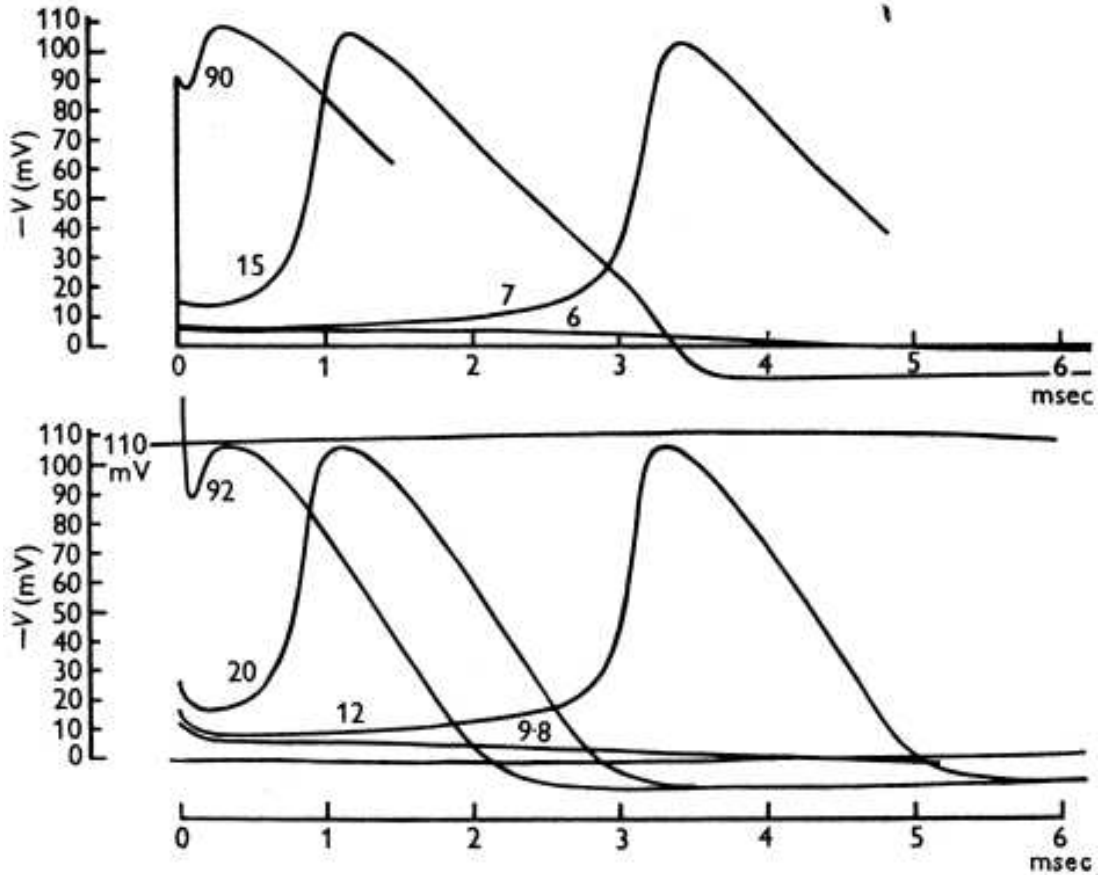
Evolution of a model action potential



Dayan and Abbott (2002) fig 5.11.

Hodgkin-Huxley: model vs experiment

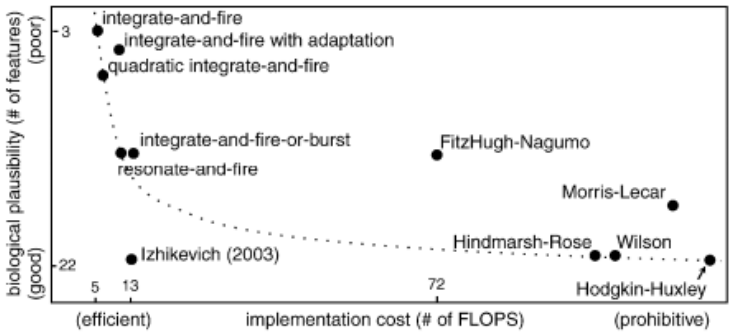
Data taken from squid giant axon; much wider axonal diameter (800 μm) than normal (2 μm) for rapid signal propagation [escape behaviour].



(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):



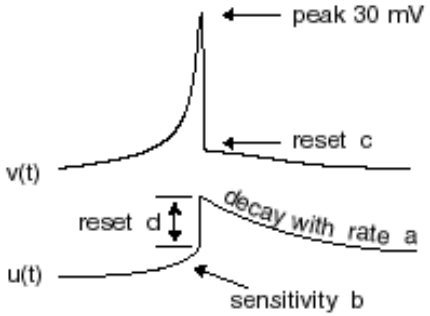
Models	biophysically meaningful	tonic spiking	phasic spiking	tonic bursting	phasic bursting	mixed mode	spike frequency adaptation	class 1 excitable	class 2 excitable	spike latency	subthreshold oscillations	resonator	integrator	rebound spike	rebound burst	threshold variability	bistability	DAP	accommodation	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

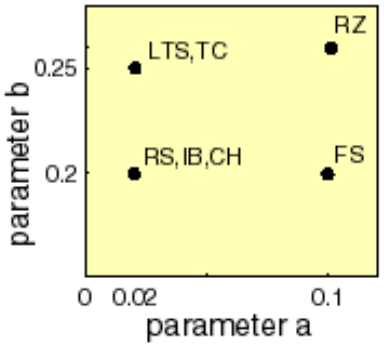
Fig. 2. Comparison of the neuro-computational properties of spiking and bursting models; see Fig. 1. "# of FLOPS" is an approximate number of floating point operations (addition, multiplication, etc.) needed to simulate the model during a 1 ms time span. Each empty square indicates the property that 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.

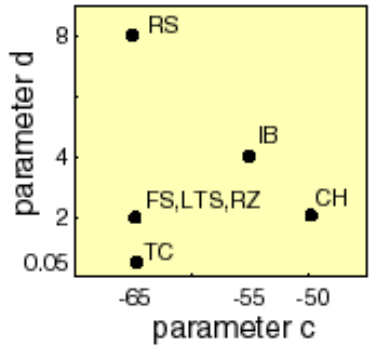
The Izhikevich model

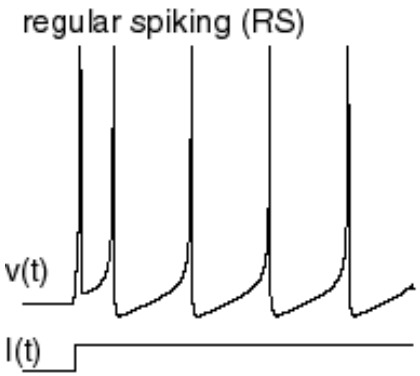
$$v' = 0.04v^2 + 5v + 140 - u + I$$
$$u' = a(bv - u)$$

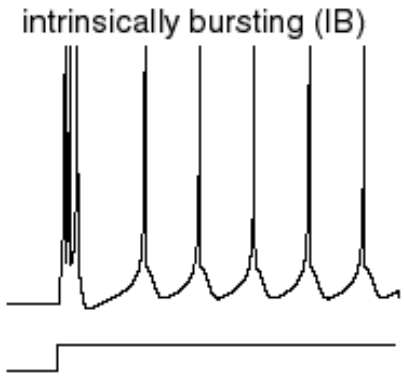
if $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$

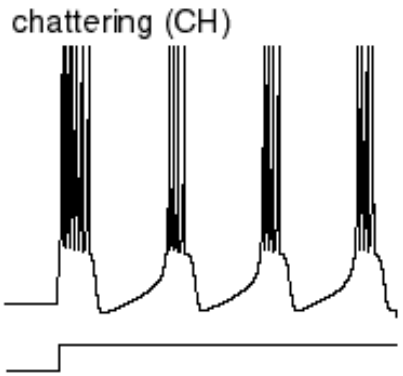


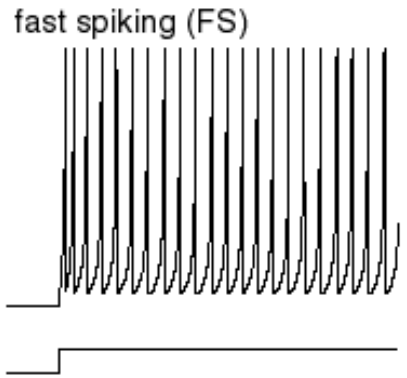


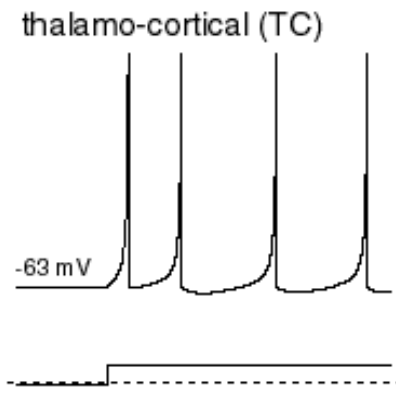


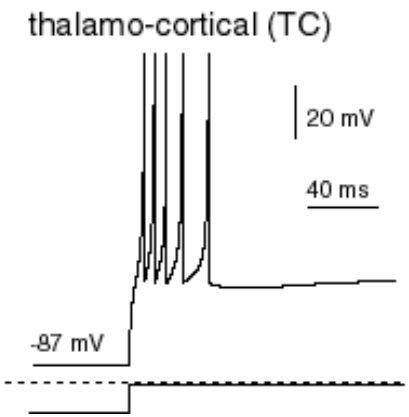


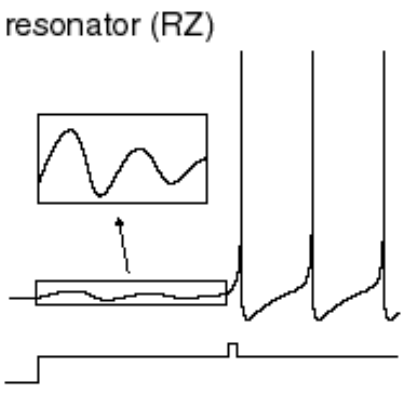


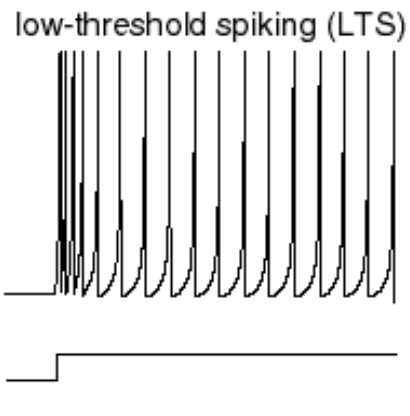












To explore this model interactively see `https://github.com/sje30/cnw`

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:

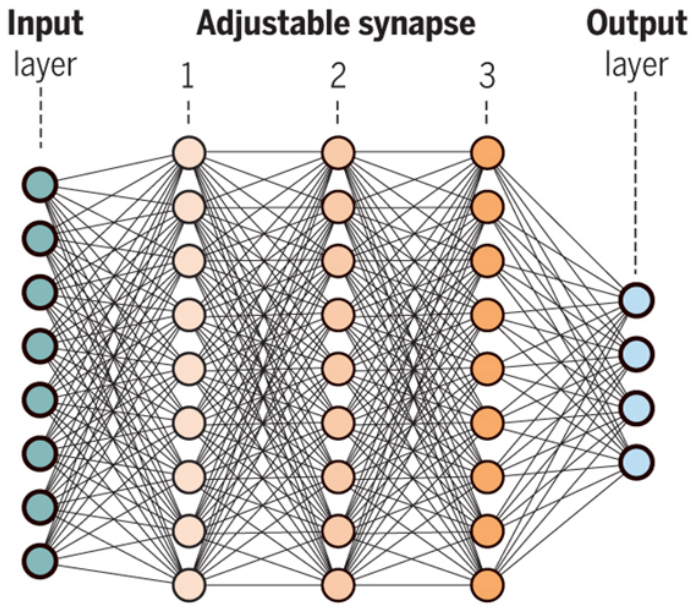
1. More analytical work can be done with firing rates.
2. Computationally more tractable models. ("Simple models provide dynamical insight")
3. Spiking models often have more free parameters than firing rate models.
4. If modelling individual neurons, prob. of connections between any two neurons is low.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

What is a neural network? (Ullman, 2019)

Brain circuitry and learning

A major open question is whether the highly simplified structures of current network models compared with cortical circuits are sufficient to capture the full range of human-like learning and cognition.

Complex neural network
Connectivity in cortical networks includes rich sets of connections, including local and long-range lateral connectivity, and top-down connections from high to low levels of the hierarchy.



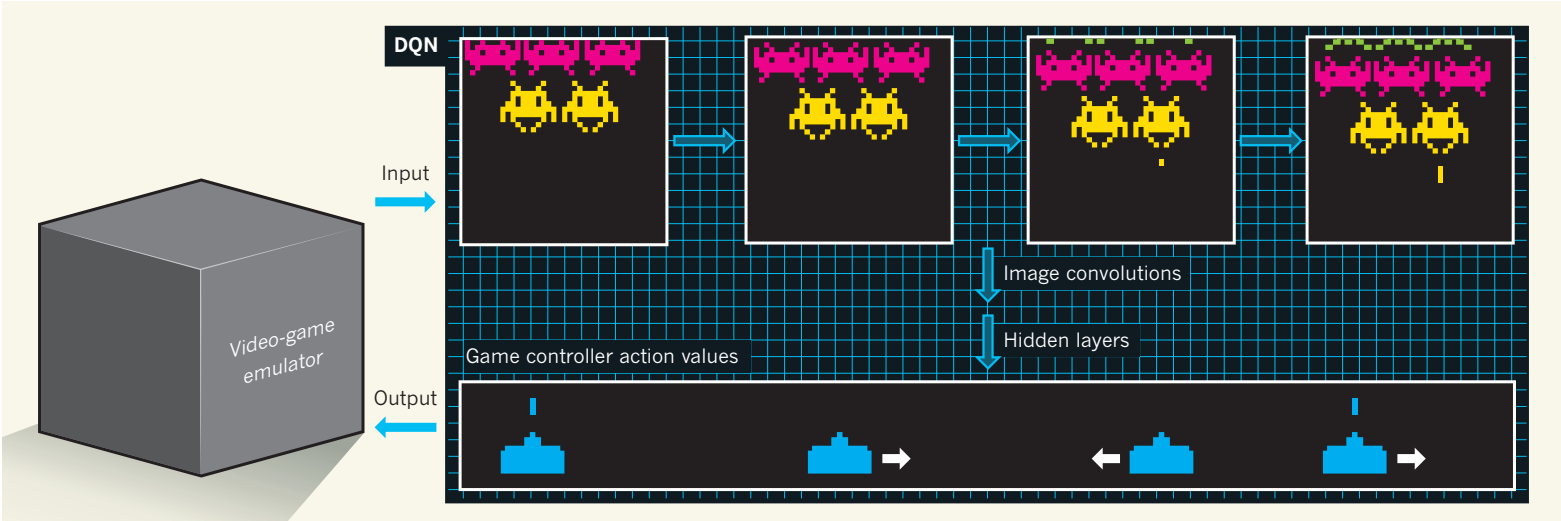
Informed AI network
Biological innate connectivity patterns provide mechanisms that guide human cognitive learning. Discovering similar mechanisms, by machine learning or by mimicking the human brain, may prove crucial for future artificial systems with human-like cognitive abilities.

Why are they useful?

1. Speech recognition (Android) since 2012 (LeCun et al 2015).
2. Image recognition since 2012.
3. Atari video games (2015)
4. Go and Chess (Silver et al 2016; 2018).

Deep reinforcement learning: breakout

Mnih et al (2015) Human-level control through deep reinforcement learning. Nature 518:529–533.



System played better than professional human on 49 Atari 2600 games.

`https://www.youtube.com/watch?v=V1eYniJ0Rnk`

A brief history of Neural networks

1. McCulloch and Pitts (1943): all-or-nothing model of neurons.
2. Rosenblatt (1957): perceptron – mechanism for learning based on Hebb (1949).
3. Limitations of perceptrons: Minksy and Papert (1969)
4. 1973: Lighthill report led to first AI winter.
5. Backpropagation (Werbos; 1974). Popularised by Hinton et al in 1980s.
6. Limitations in hardware led to 2nd AI winter late 1990s.
7. 2012: resurgence due to hardware and some new “tricks”.
8. Computational biology now a big user (Angermueller et al 2016), e.g. protein folding (ALphaFold) and biomedicine (Ching et al 2018).

See Schmidhuber (2015) for further history.

Why now?

1. Advances in computational hardware (GPU, CPU, TPU)
2. Some algorithmic developments, help in training
3. Advent of big data: many more samples now than ever before

Practical matters

- Like computational biology, 80% of the work is mundane but critical (data collection, cleaning, hyper-parameter selection).
- Good news: many frameworks. We will use Keras (with Tensor Flow backend) or pytorch/Flux.jl.
- GPU vs CPU
- Desktop vs Cloud

Summary

1. Function and anatomy of neurons
2. Complexity arises from interactions
3. Hodgkin and Huxley model (1952)
4. Izhikevich model (2003)
5. History of neural networks, and reasons