Introduction to neuronal modelling (part 1)

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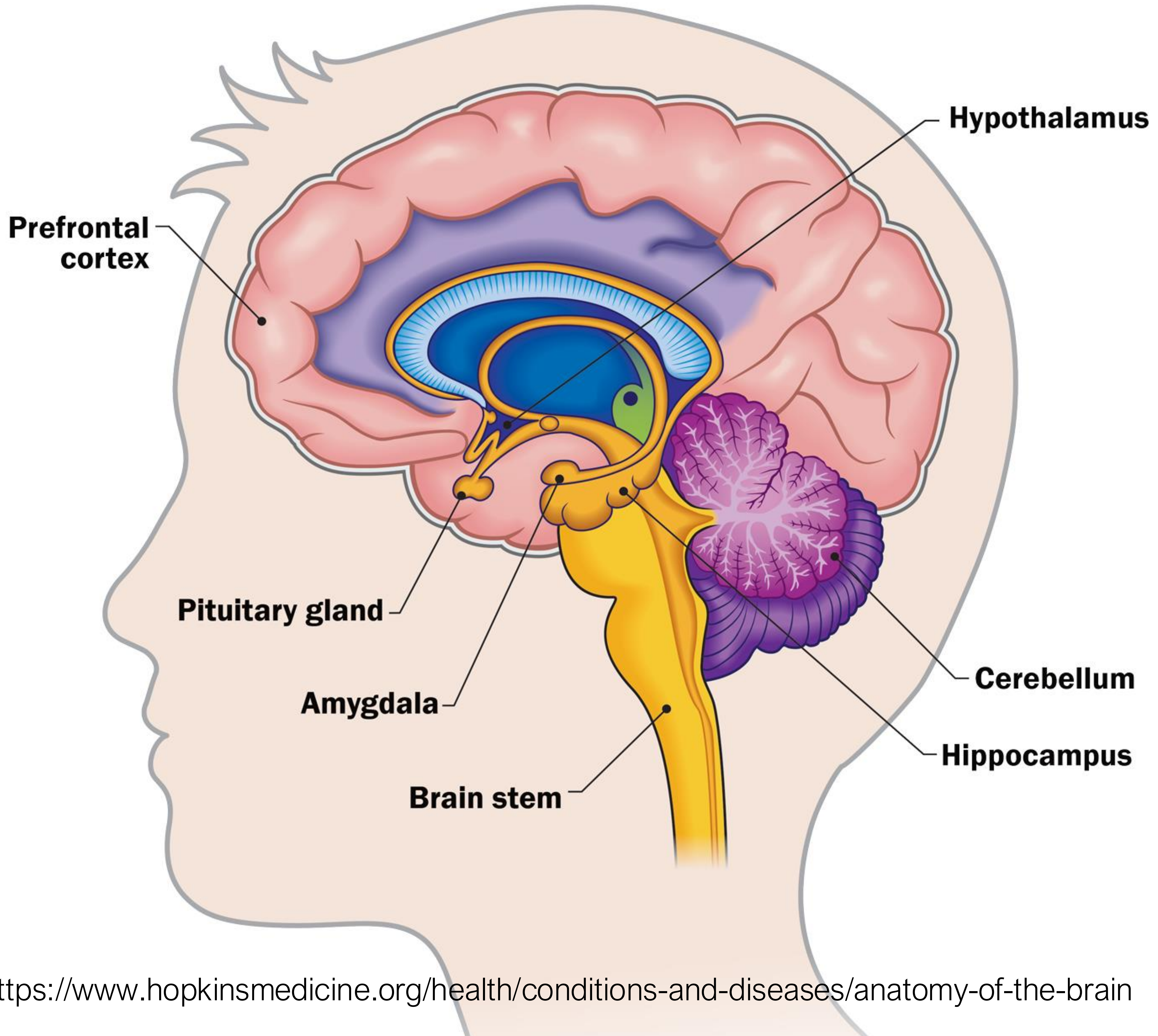
What we will cover in part 1

- How the brain works, in 5 minutes
- Building blocks of neuronal modelling
  - Single neuron models, Hodgkin-Huxley
  - Synapse models
- Neural coding: spikes vs rates
- Feedforward neural network models of the visual system

how the brain works

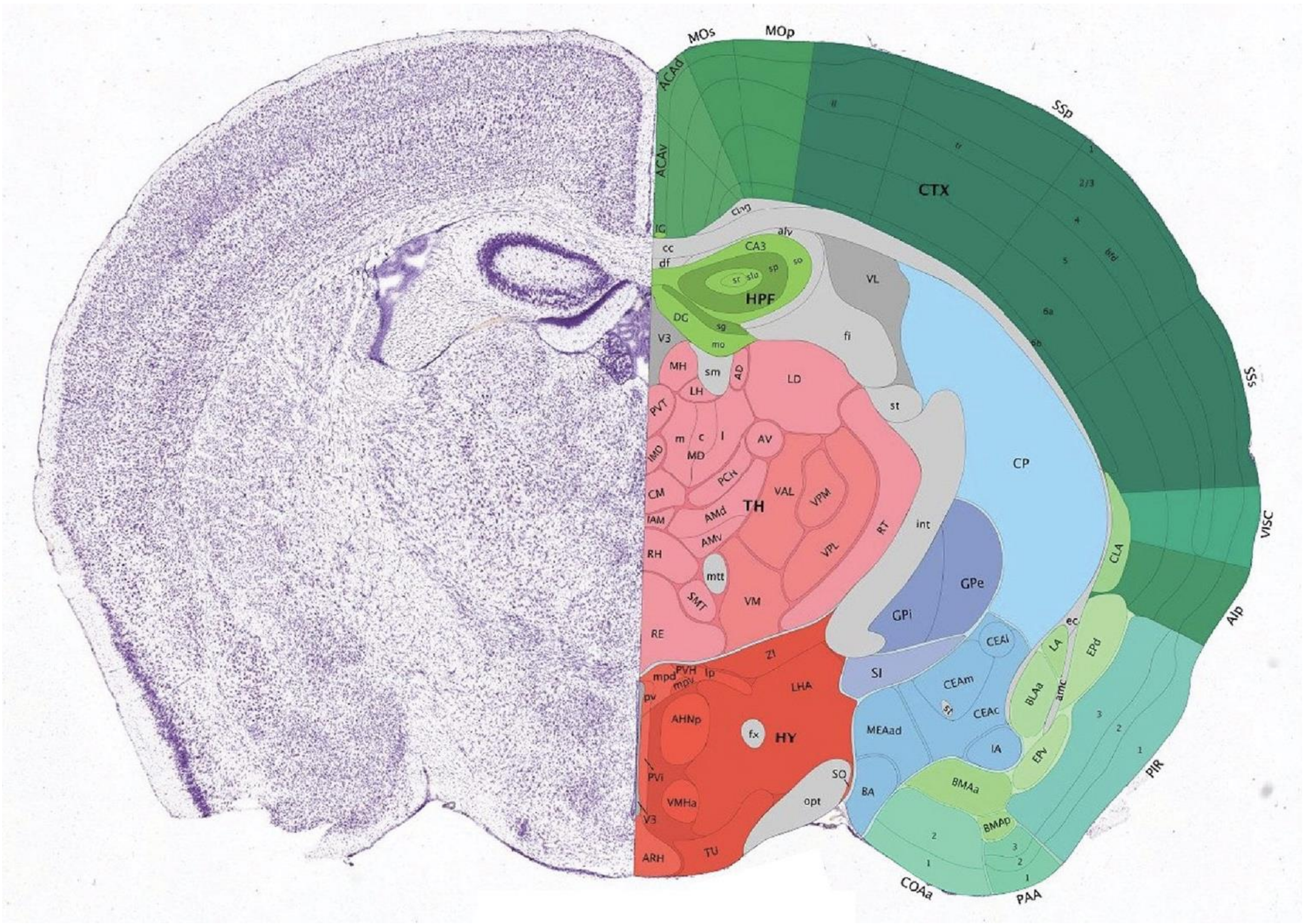
Brain regions

The brain is modular: it has tens of specialised regions that perform different tasks: sensory processing, motor control, learning & memory, decision making, emotional regulation, etc



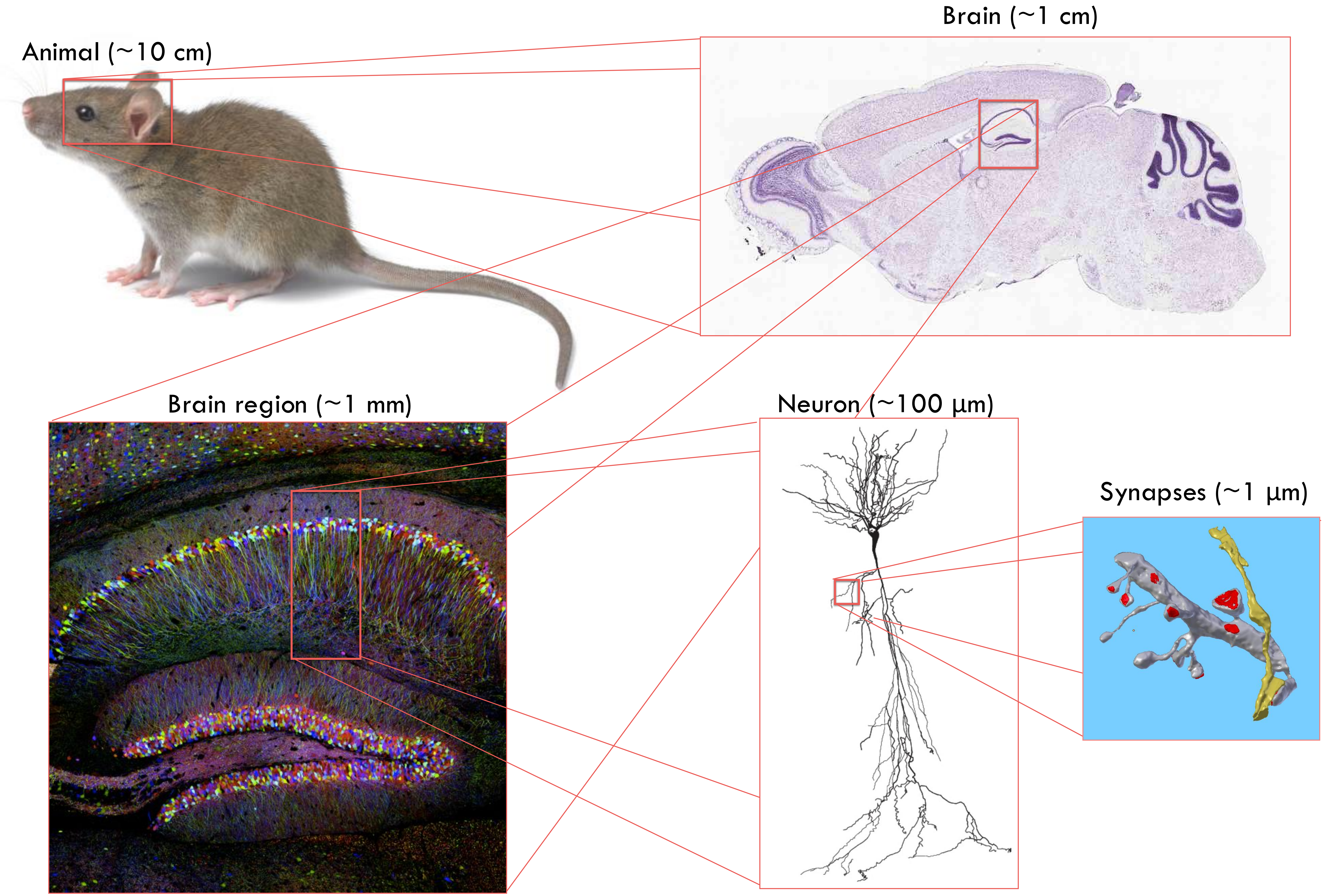
https://www.hopkinsmedicine.org/health/conditions-and-diseases/anatomy-of-the-brain

Mouse brain

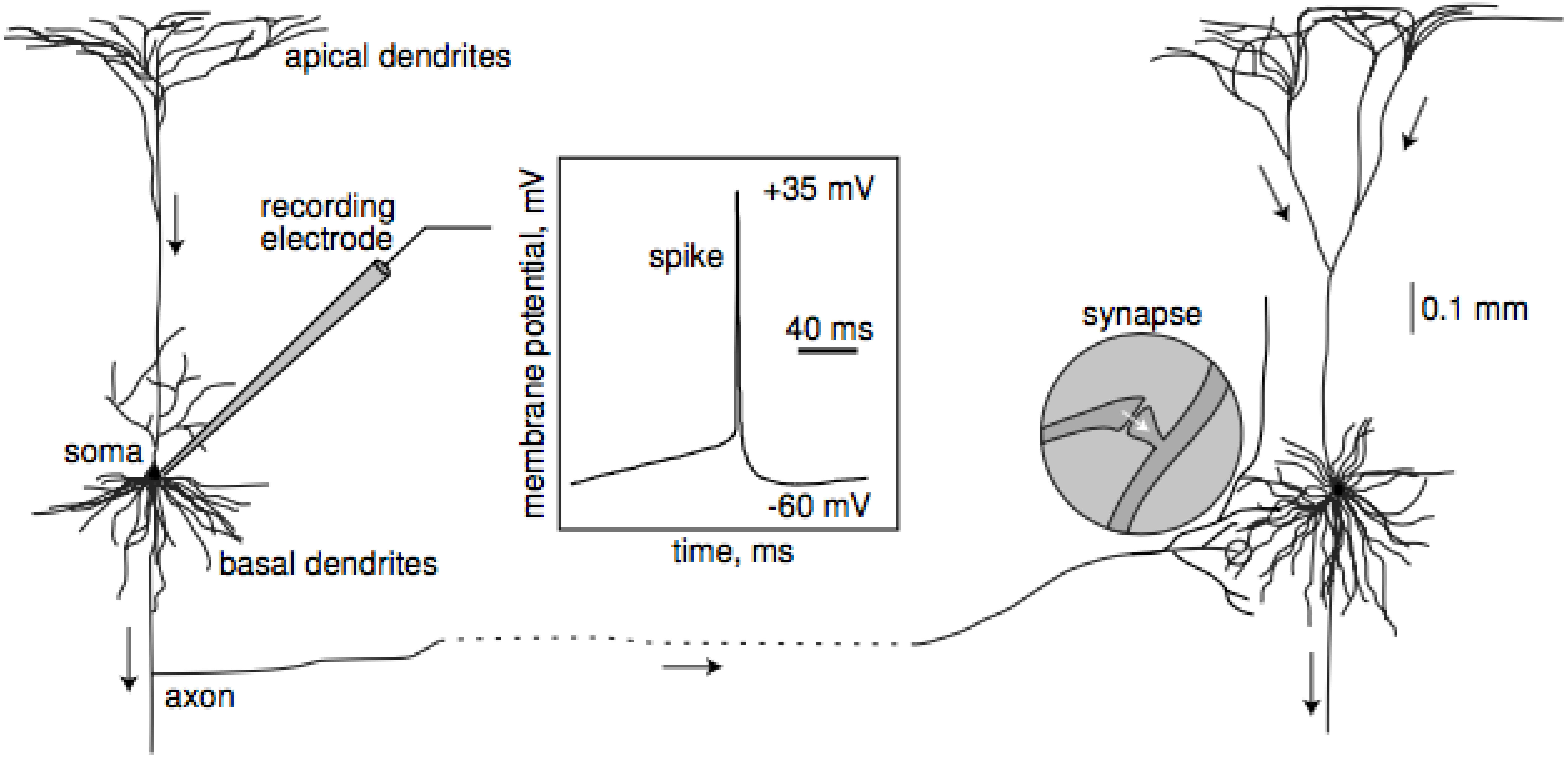


[Allen Institute]

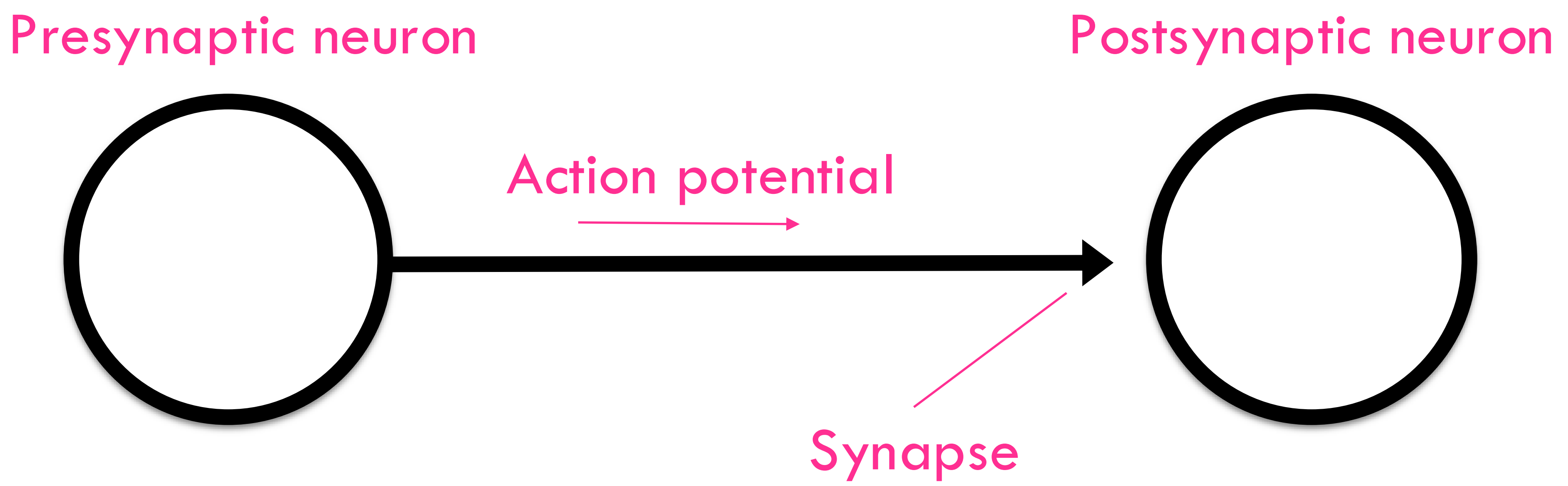
Spatial scales of the brain

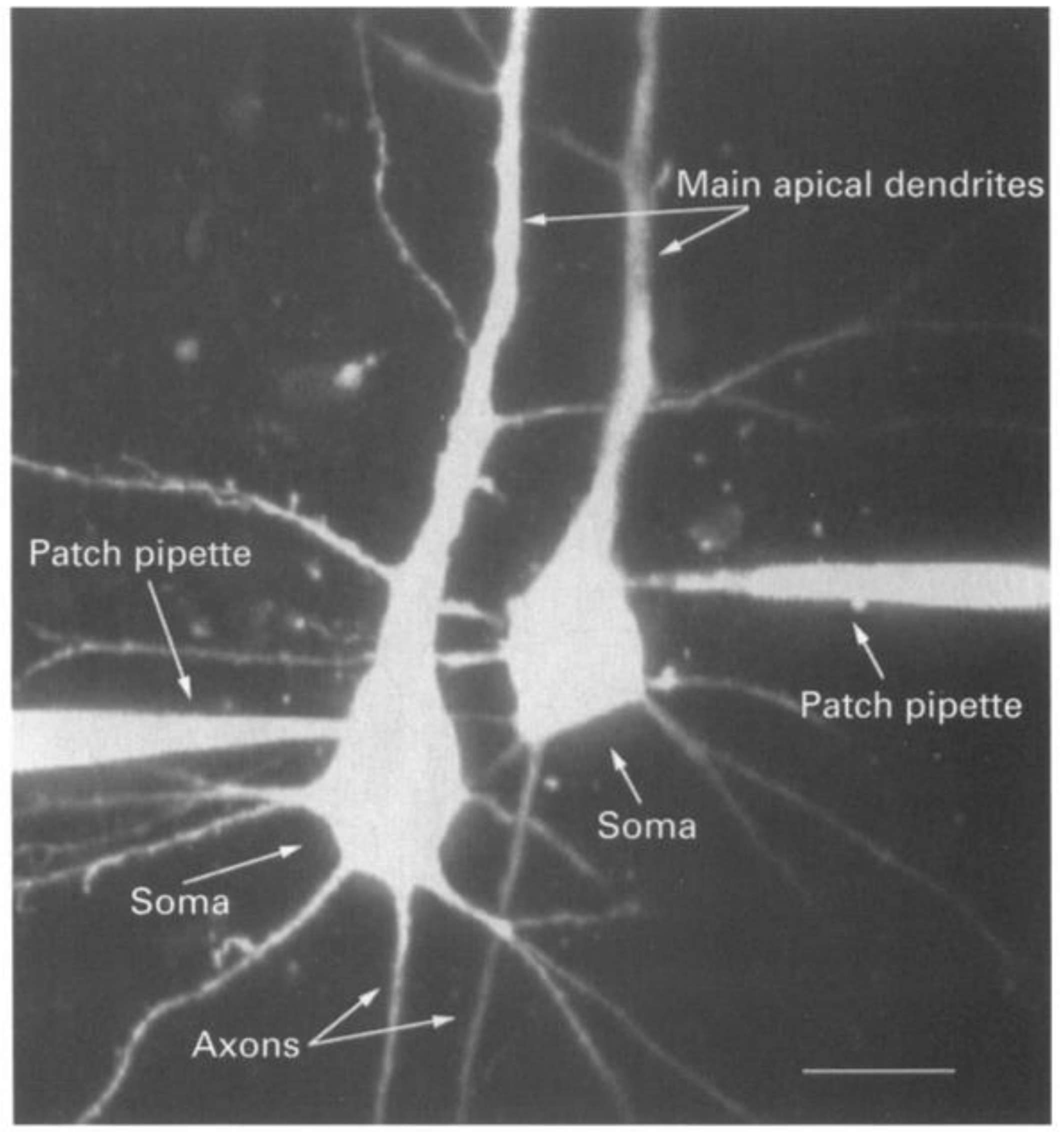


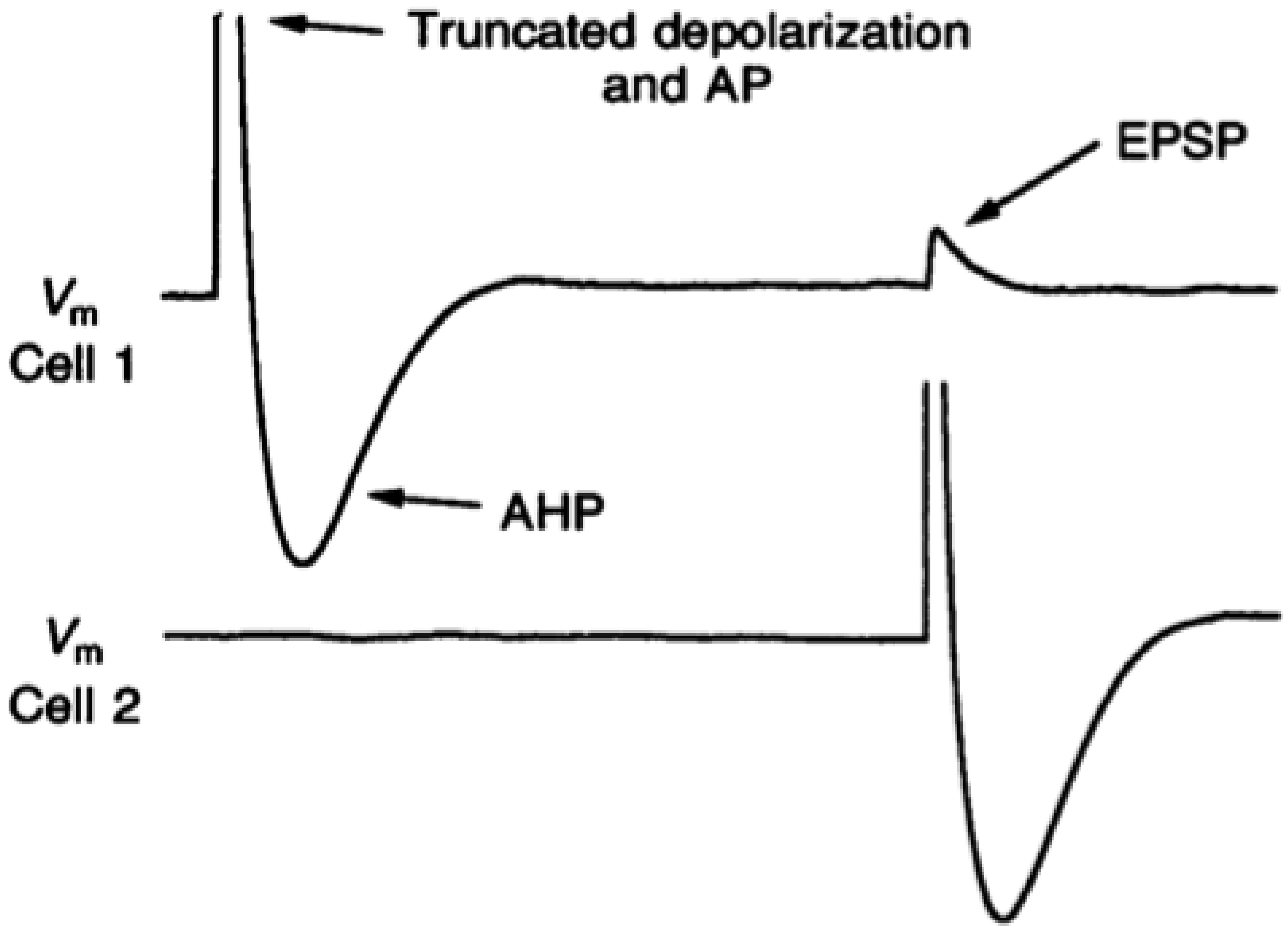
How do brains work?



What is a synapse?







Markram et al, J Physiol (1997)

How do synapses work?

Axon
(presynaptic action potential)

Chemical
signalling

Dendrite
(postsynaptic potential)

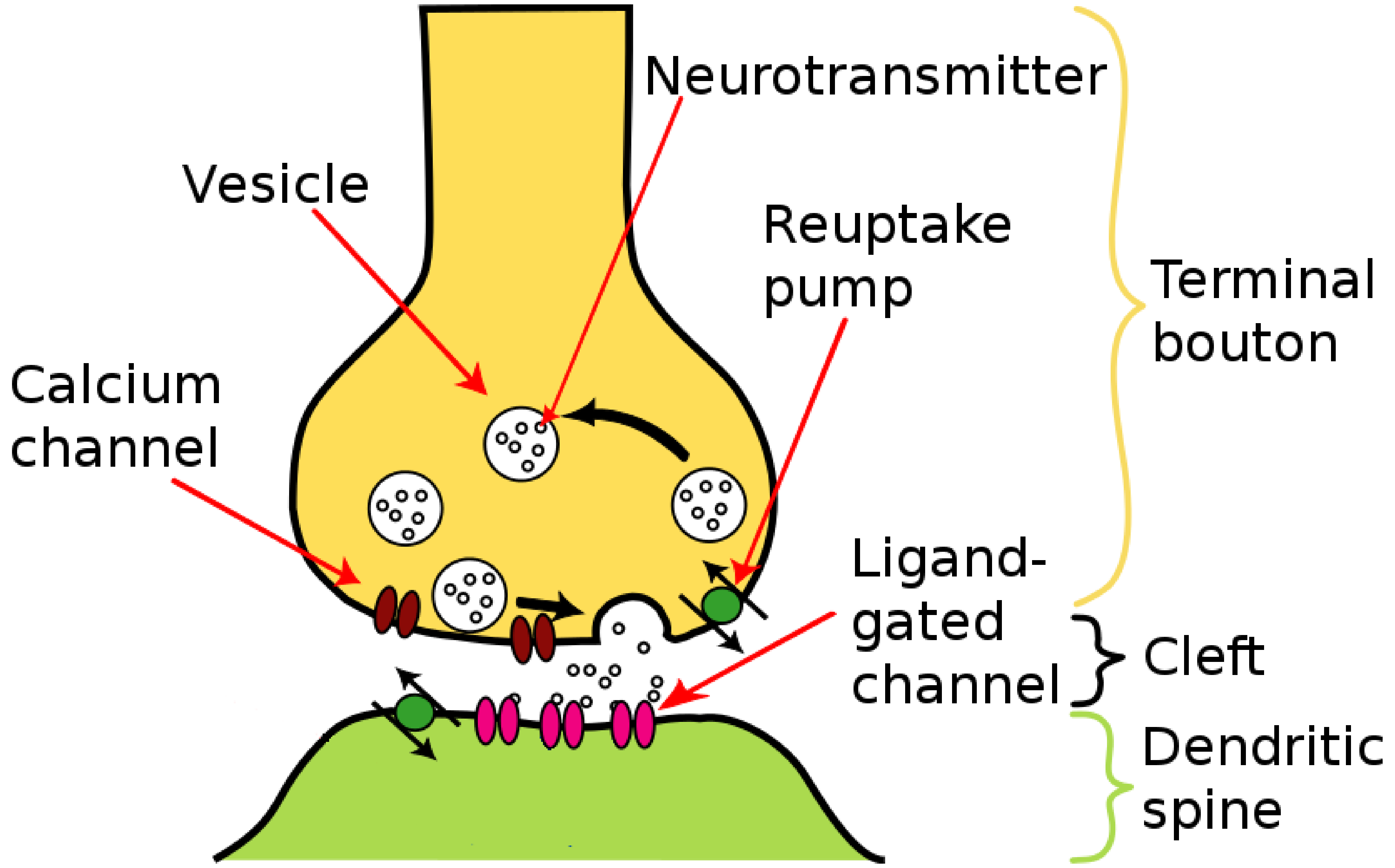


Image from Wikipedia (modified by C Houghton)

Summary on brain basics

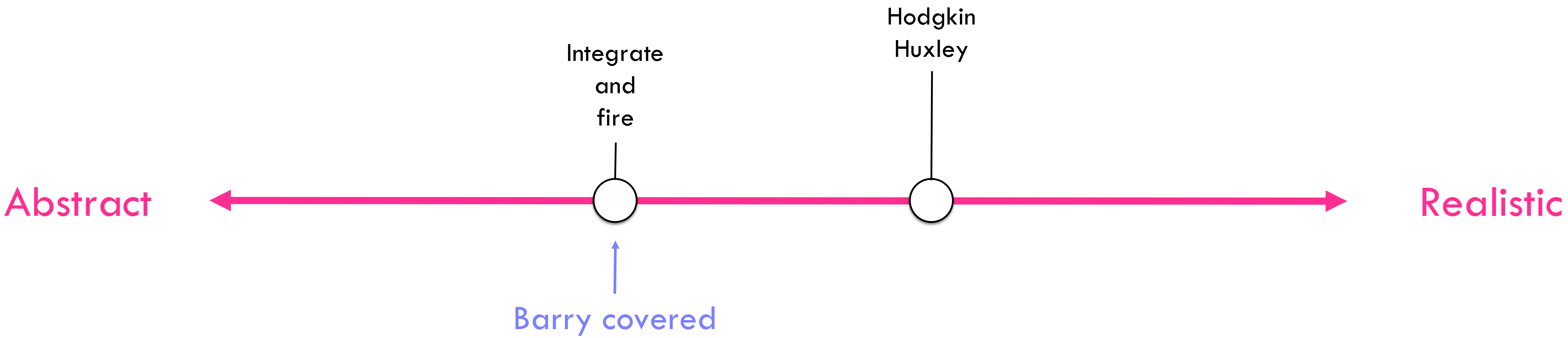
- The brain is a large network of neurons (and glia), with many specialised regions at a macroscale, and lots of cell types and detailed wiring patterns at a microscale.
- It is an electro-chemical computer.
- Each neuron uses it membrane voltage to integrate incoming signals, then sometimes broadcasts a spike output signal (when the voltage crosses a threshold).
- Synapses are the connections between neurons (usually unidirectional).

Building blocks of brain models

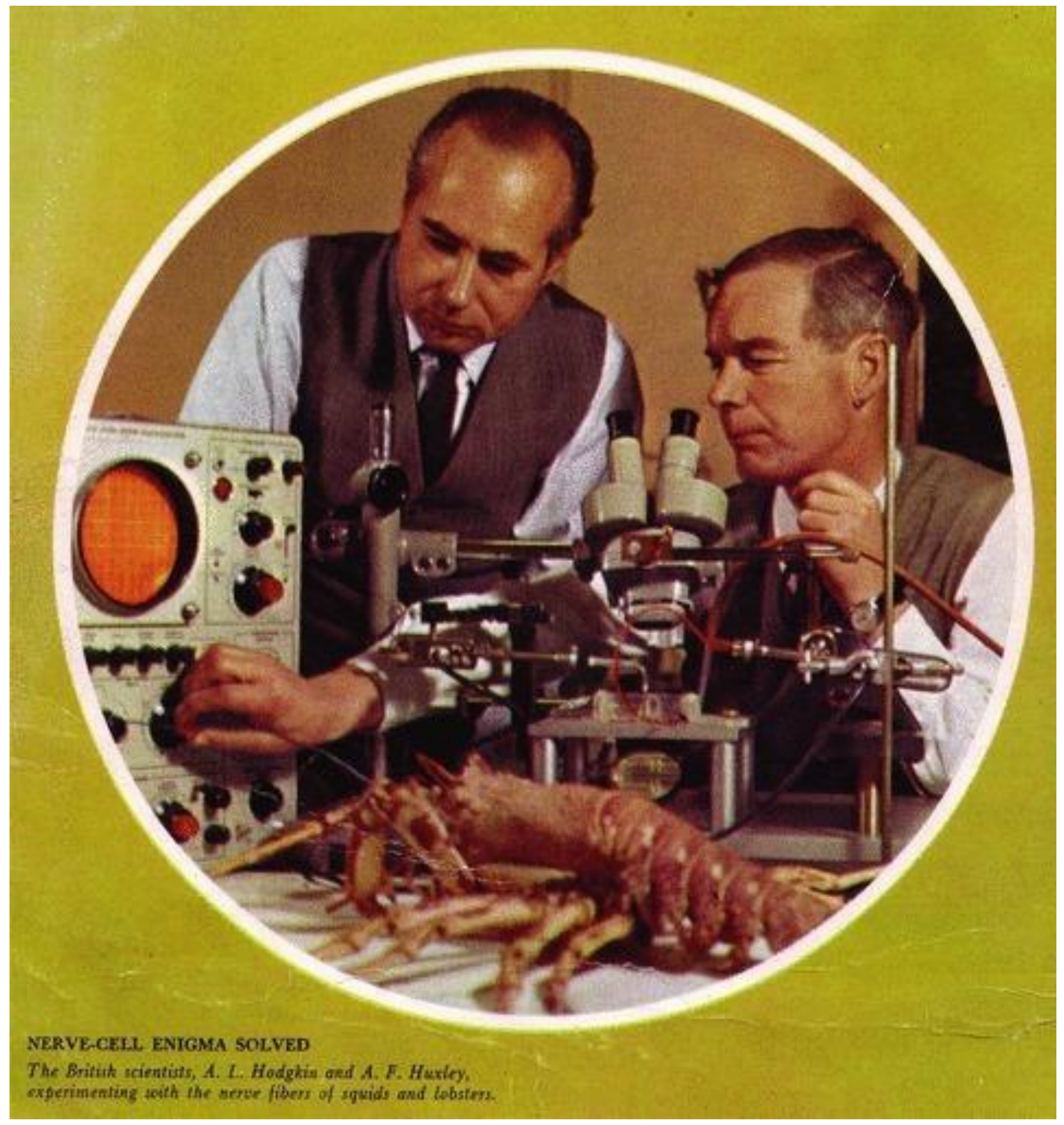
Building blocks of brain models

Neurons

Models of single neurons



The Hodgkin-Huxley model



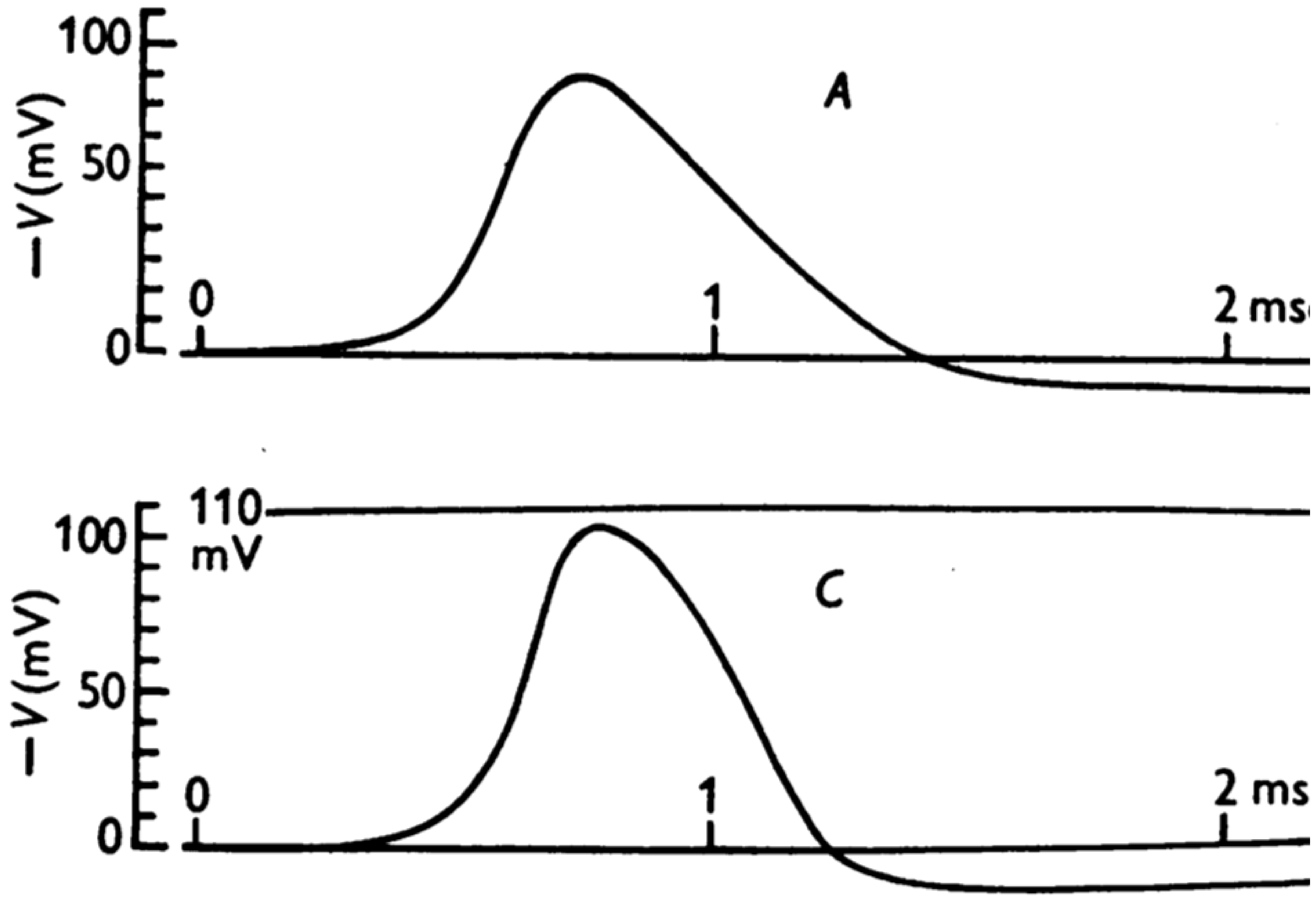
NERVE-CELL ENIGMA SOLVED
The British scientists, A. L. Hodgkin and A. F. Huxley, experimenting with the nerve fibers of squids and lobsters.

- The original Hodgkin-Huxley model is a mathematical model of the electrical dynamics of the 'giant' axon of the squid Loligo forbessi.
- Its key success was to demonstrate that two voltage-gated membrane conductances were sufficient to explain the action potential.
- These days people often use the term "Hodgkin-Huxley style model" more loosely to mean any mathematical model of any neuron that is built using conductance-based dynamics.
- The Hodgkin-Huxley model stands as one of the outstanding successes of computational neuroscience.

Loligo forbessi

Model

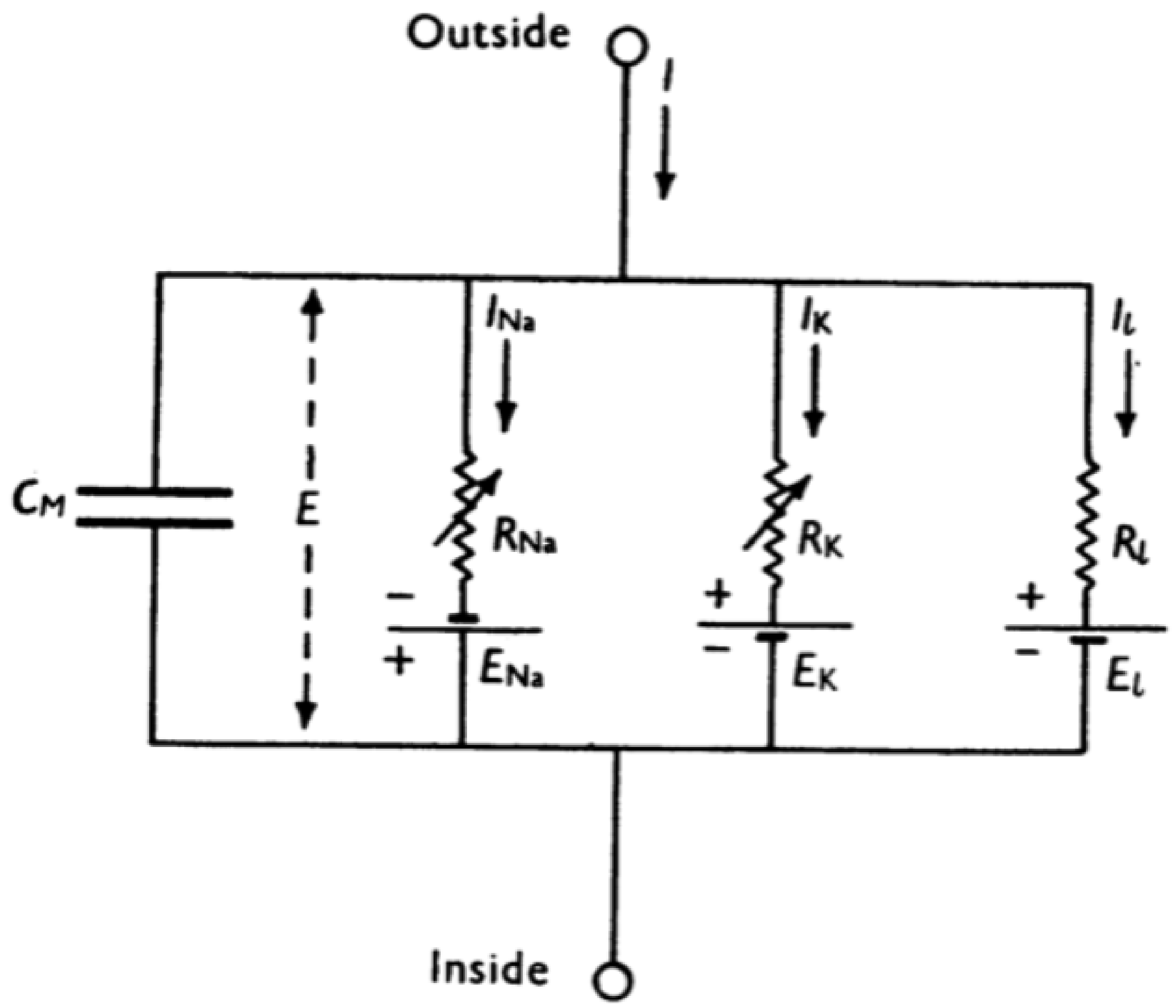
Data



Hodgkin & Huxley, J Physiol (1952e)

What does the model consist of?

The HH model



$$C_M \frac{dV}{dt} = I_{Na} + I_K + I_l$$

$$I_x = g_x(E_x - V)$$ …where x is Na, K or l

$$g_x = ?$$ How do we model the conductances?

How do we model the conductances?

Using time and voltage-dependent gating variables.

$$g_{Na} = \bar{g}_{Na} m^3(V,t) h(V,t)$$

$$g_K = \bar{g}_K n^4(V,t)$$

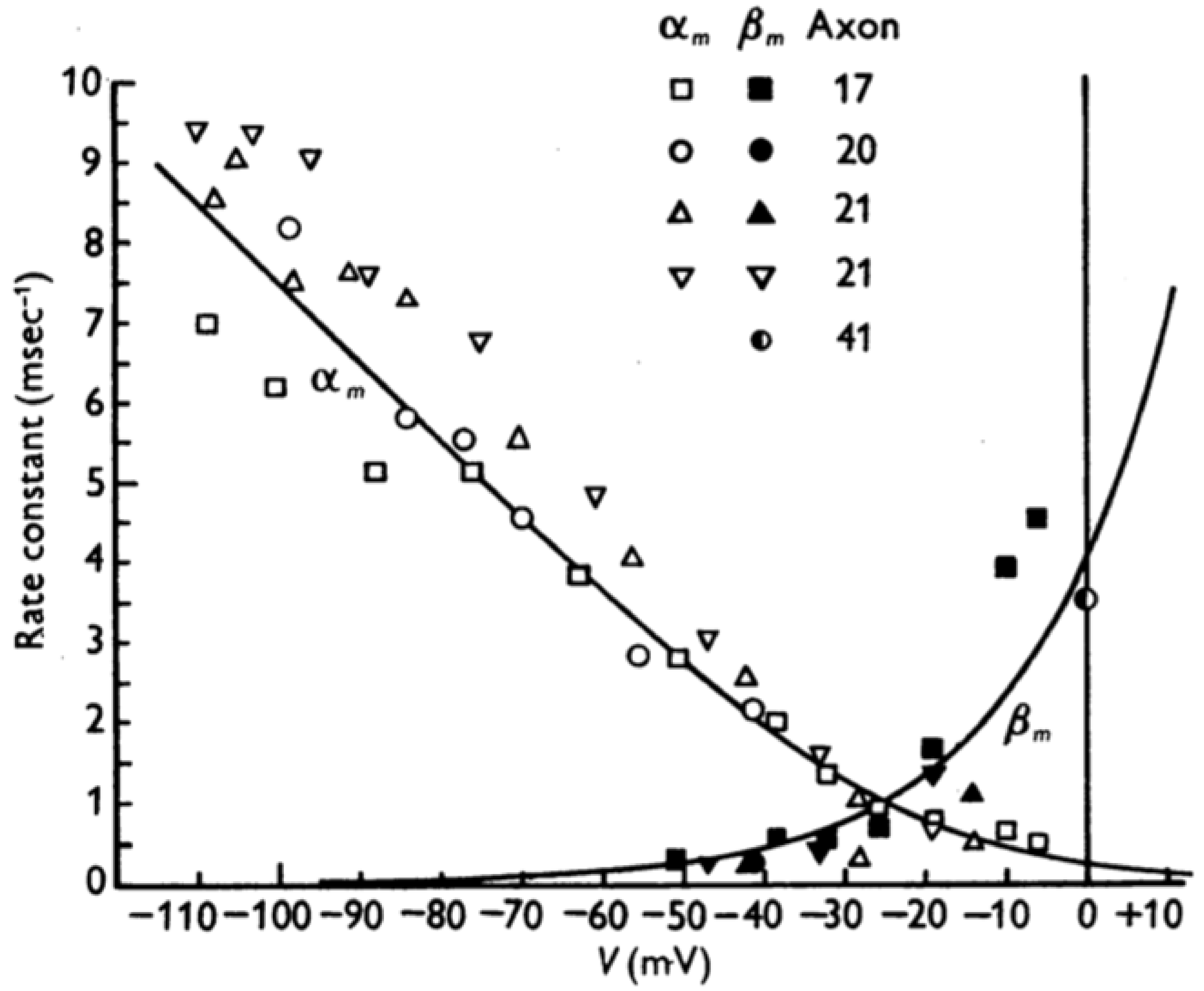
How do the gating variables evolve in time?

$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)}$$

How do the steady-state values and time constants depend on voltage?

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)} \qquad \tau_m(V) = \frac{1}{\alpha_m(V) + \beta_m(V)}$$

How do the forward and backward rate constants depend on voltage?
Hodgkin and Huxley fit them to match their voltage-clamp data.



$$\alpha_m(V) = \frac{0.1(V+40)}{1-e^{-(V+40)/10}}$$

$$\beta_m(V) = 4e^{-(V+65)/18}$$

$$\alpha_h(V) = 0.07e^{-(V+65)/20}$$

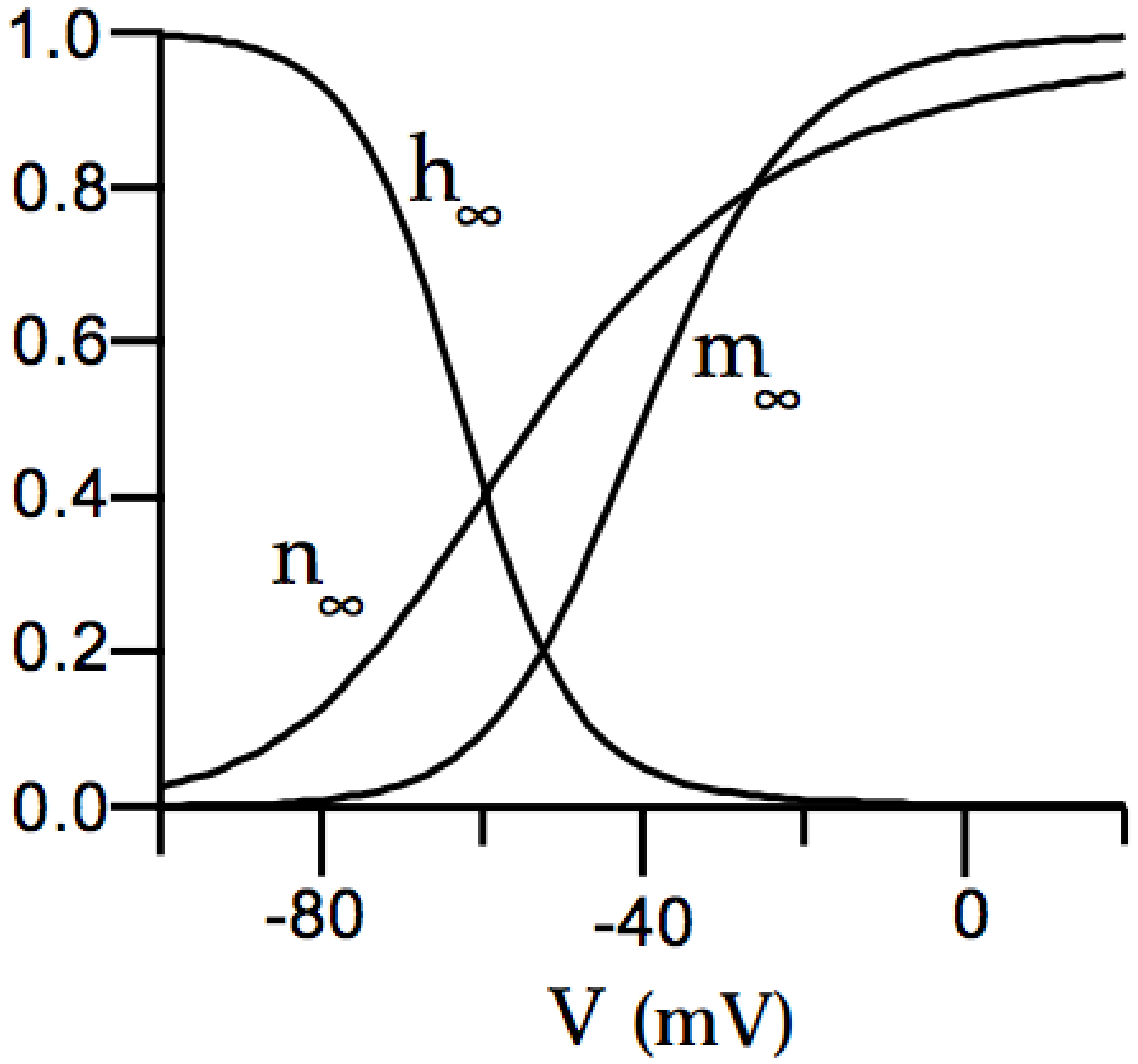
$$\beta_h(V) = \frac{1}{1+e^{-(V+35)/10}}$$

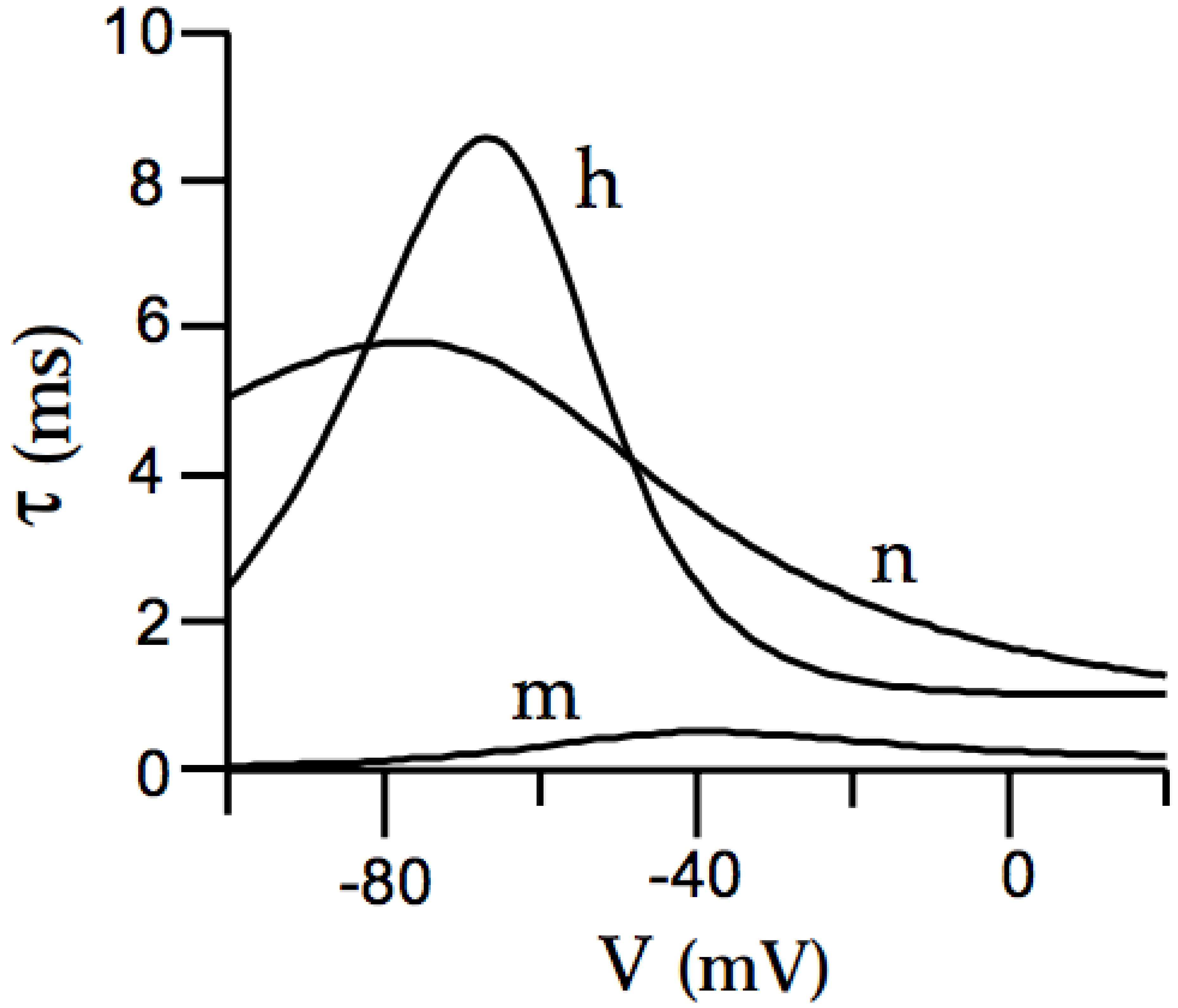
$$\alpha_n(V) = \frac{0.01(V+55)}{1-e^{-(V+55)/10}}$$

$$\beta_n(V) = 0.125e^{-(V+65)/80}$$

Hodgkin & Huxley, J Physiol (1952e)

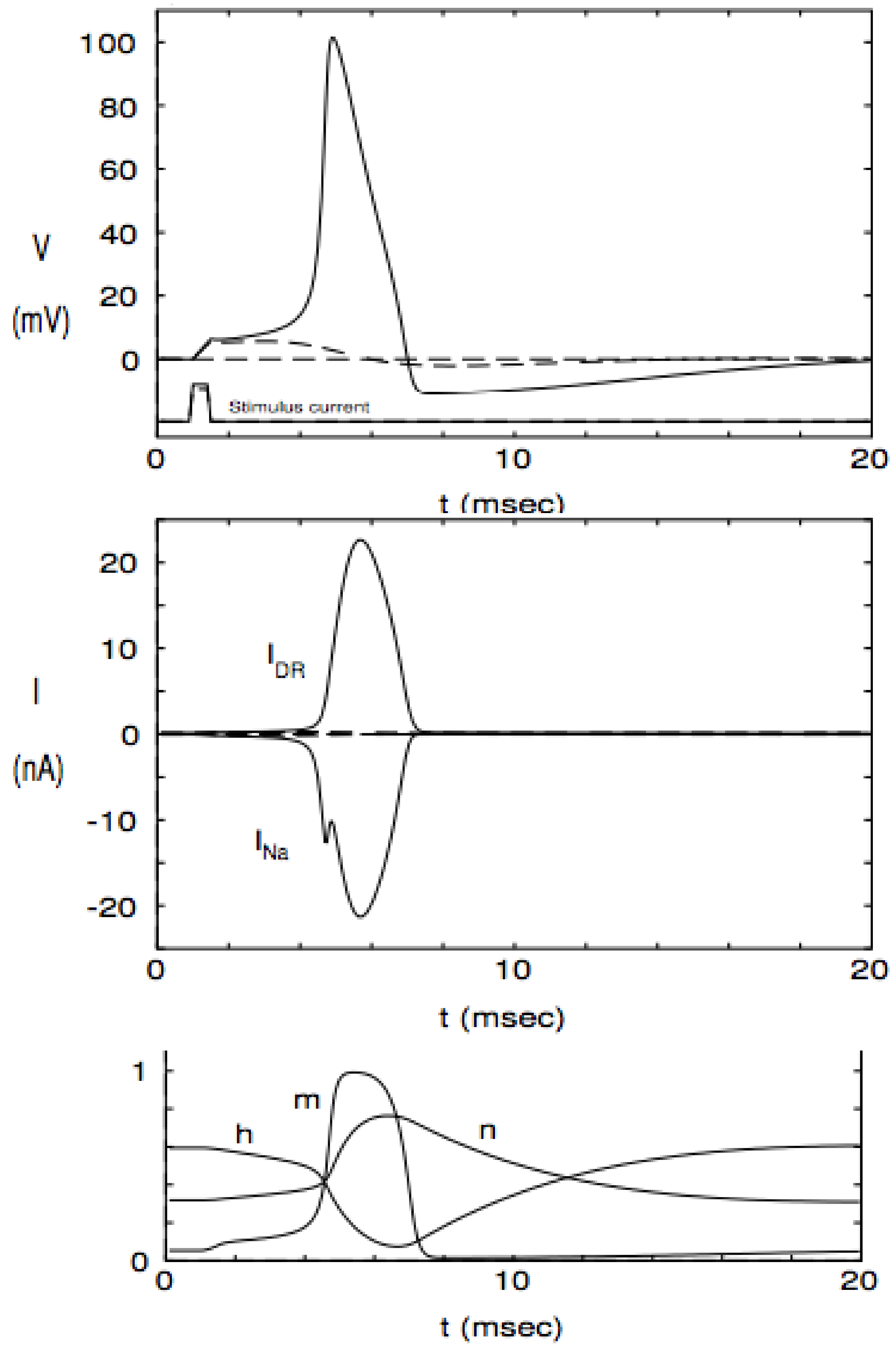
Gating variables steady-state values and time constants as a function of voltage





Dayan and Abbott (2001)

What does the HH model do?

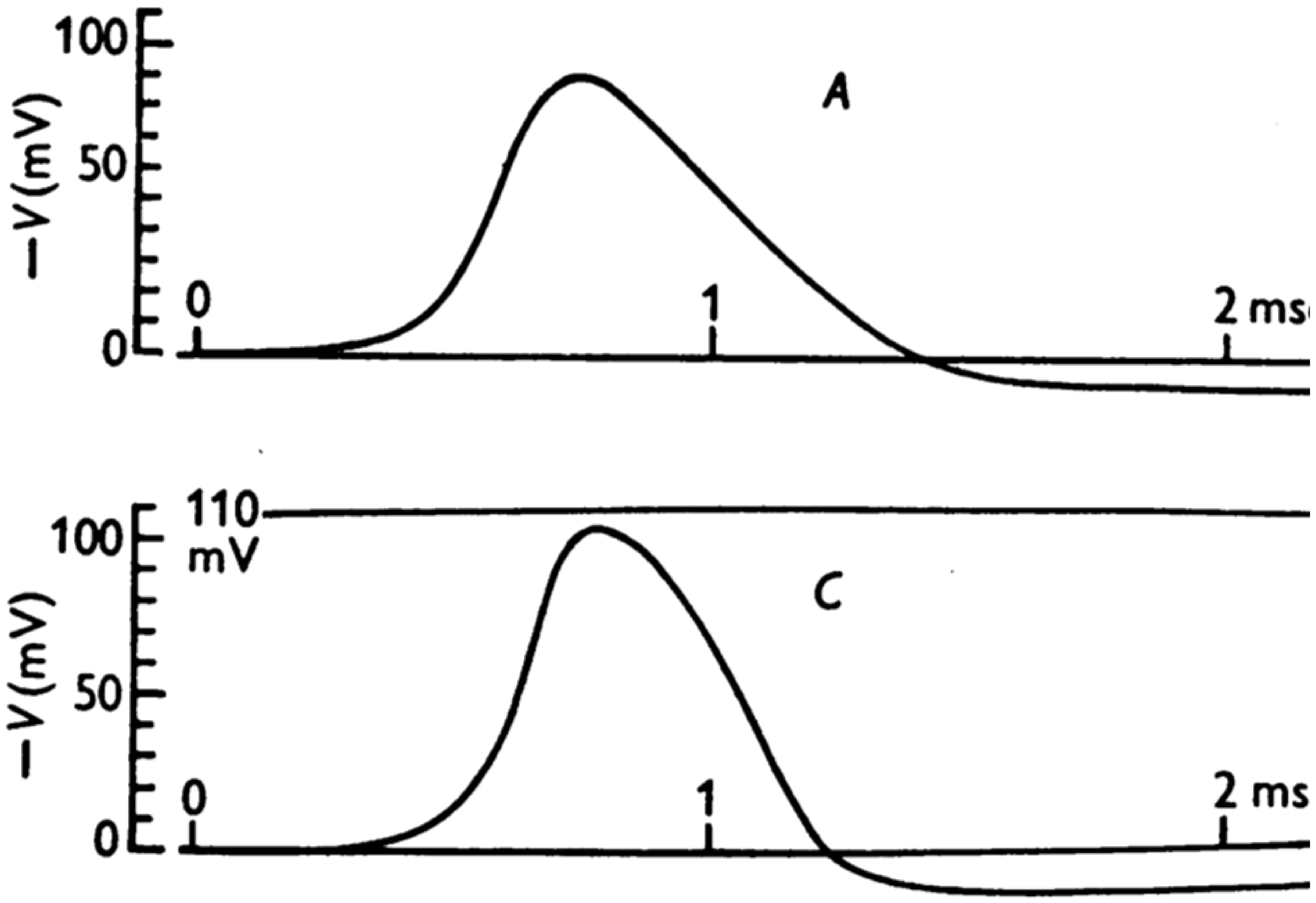


Koch (1999)

What does the HH model do?

Model

Data



Hodgkin & Huxley, J Physiol (1952e)

What does the HH model not do?

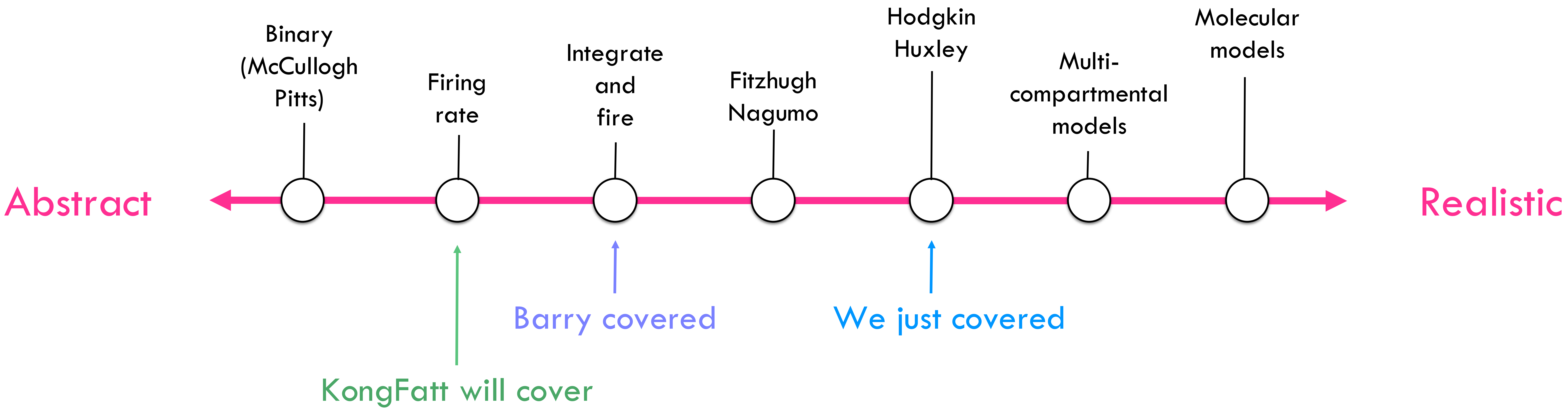
- It is unlike the action potentials in mammalian neurons:
  - different ion channels
  - different waveform
  - energy inefficient

- Not a good model for myelinated axons

- It is deterministic and continuous. We now know that real ion channels are discrete and stochastic.

- Assumption of multiple independent gates per channel type is biophysically unrealistic.

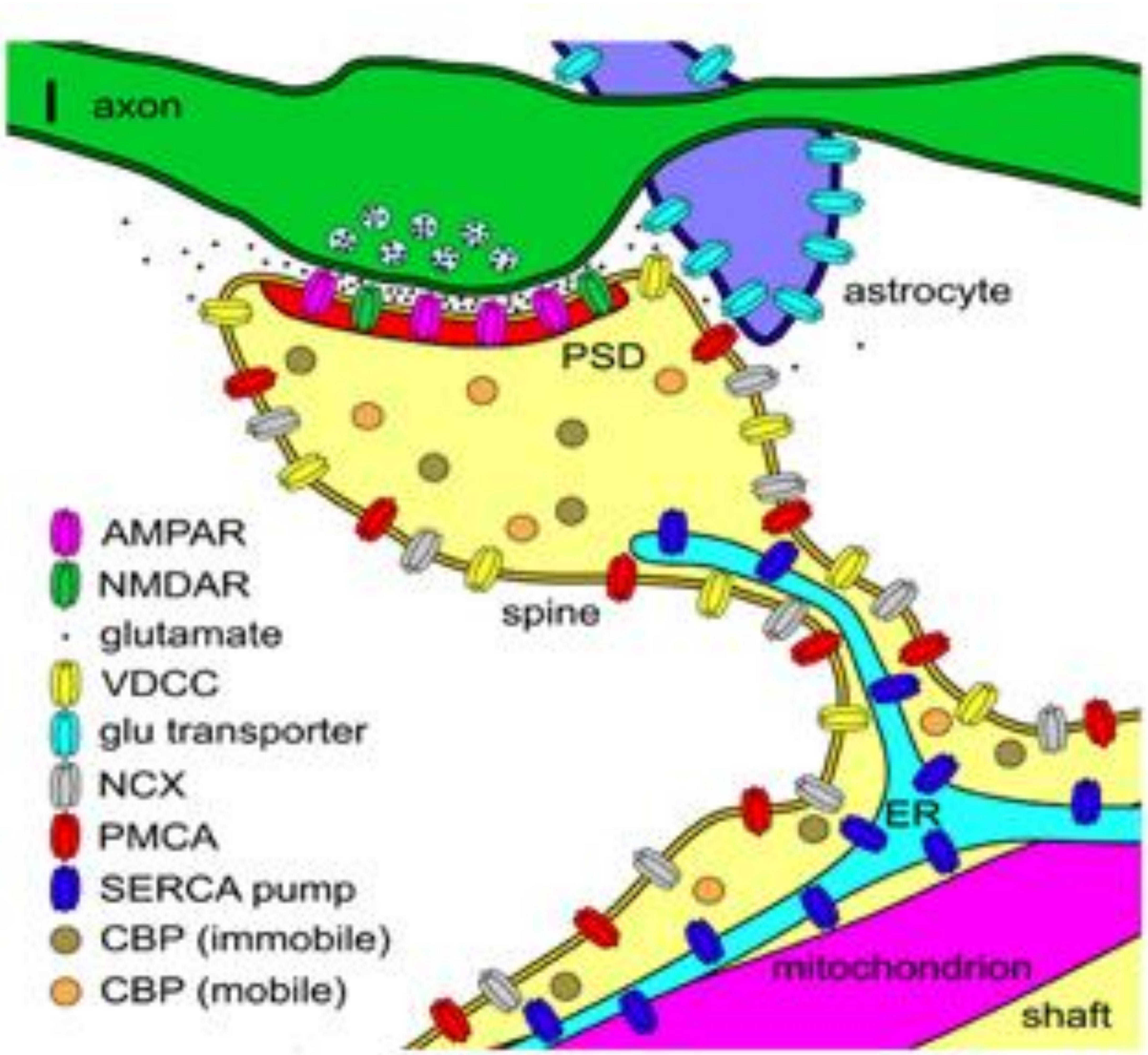
Models of single neurons

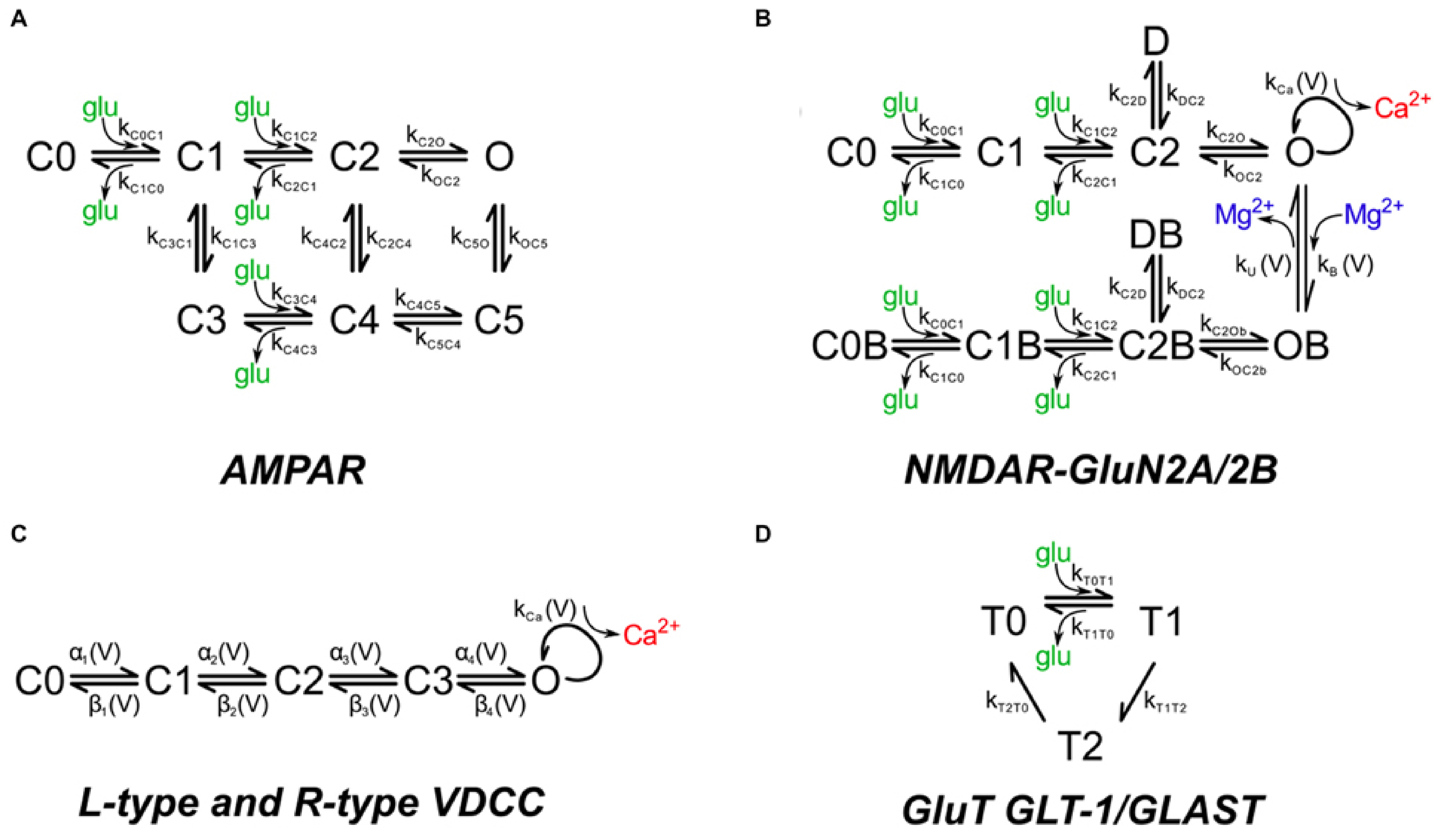


Building blocks of brain models

Synapses

MCell simulation of synaptic release





Bartol et al, Frontiers Syn Neuro (2015)

from Tom Bartol (Salk Institute)

How can we computationally model a synapse?

- We could simulate the dynamics of each molecule involved in the signalling process (like the MCell simulation).
- But since that is very computationally expensive, we might instead go for a reduced mass-action chemical-kinetics model.
- However a lot of people still find even that too expensive and parameter-heavy, so instead use even simpler phenomenological models that black-box the synapse as a simple input-output system.

Simple synapse models

The most common way to phenomenologically model a synapse is as a time-dependent conductor in series with a battery.

$$I_s(t) = \bar{g}_s s(t)(E_s - V)$$

The value of E_s determines whether the synapse is excitatory or inhibitory:

for excitatory synapses E_s usually = 0 mV

for inhibitory synapses E_s usually = V_{rest}

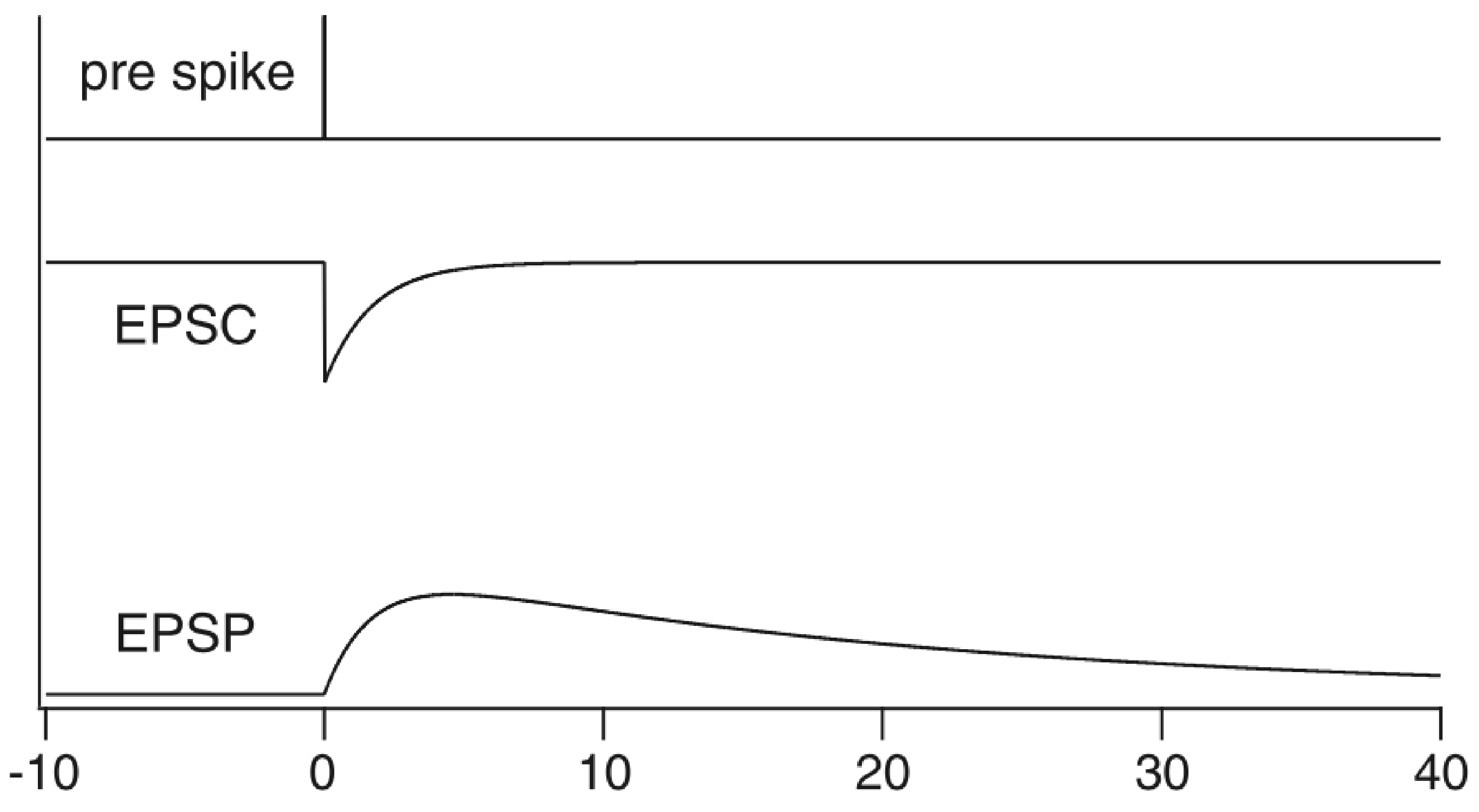
But how should we model s(t)?

Simple synapse models

Single exponential

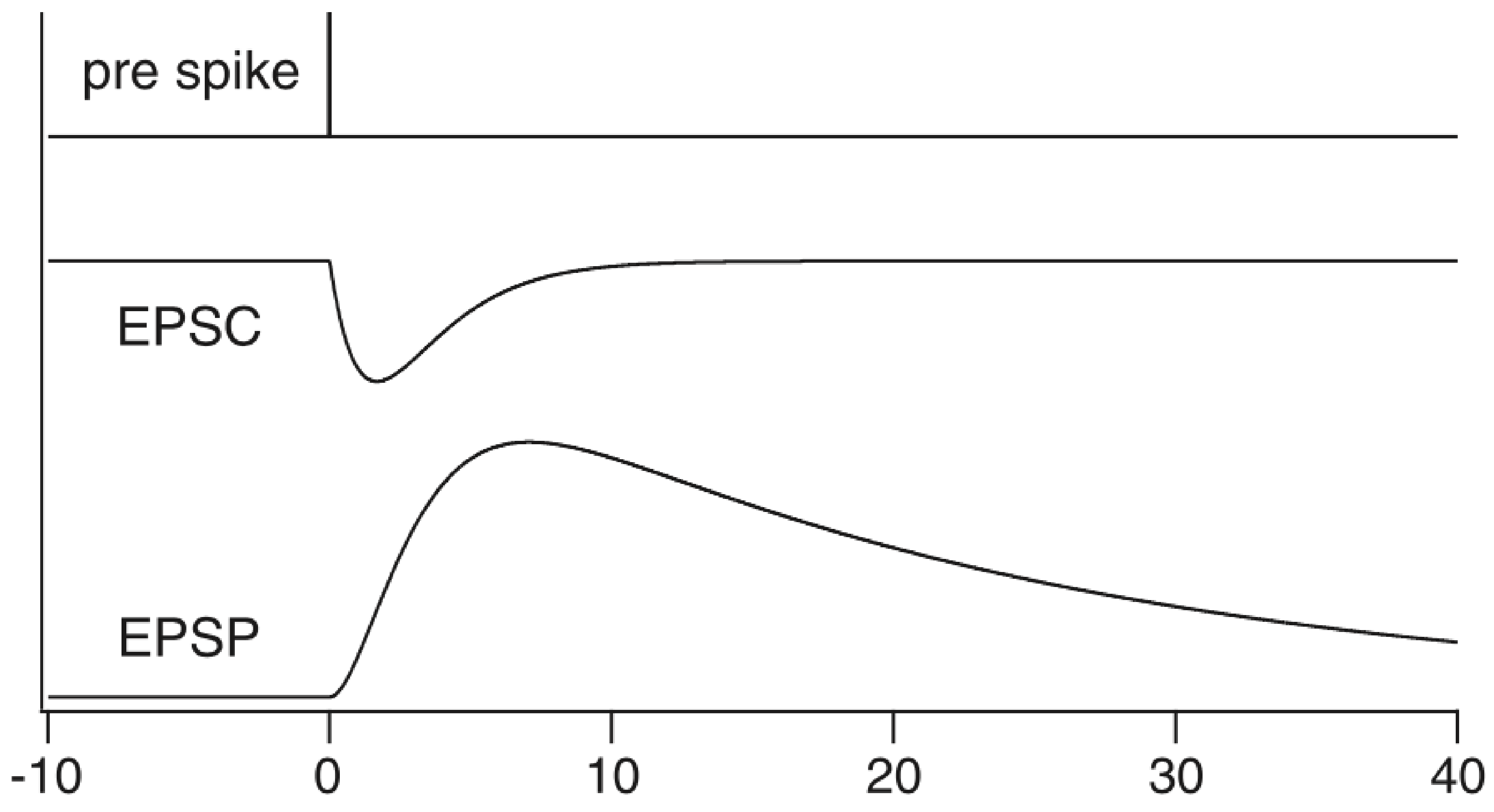
$$s(t) \rightarrow s(t) + 1$$

$$s(t) = e^{-t/\tau_s}$$



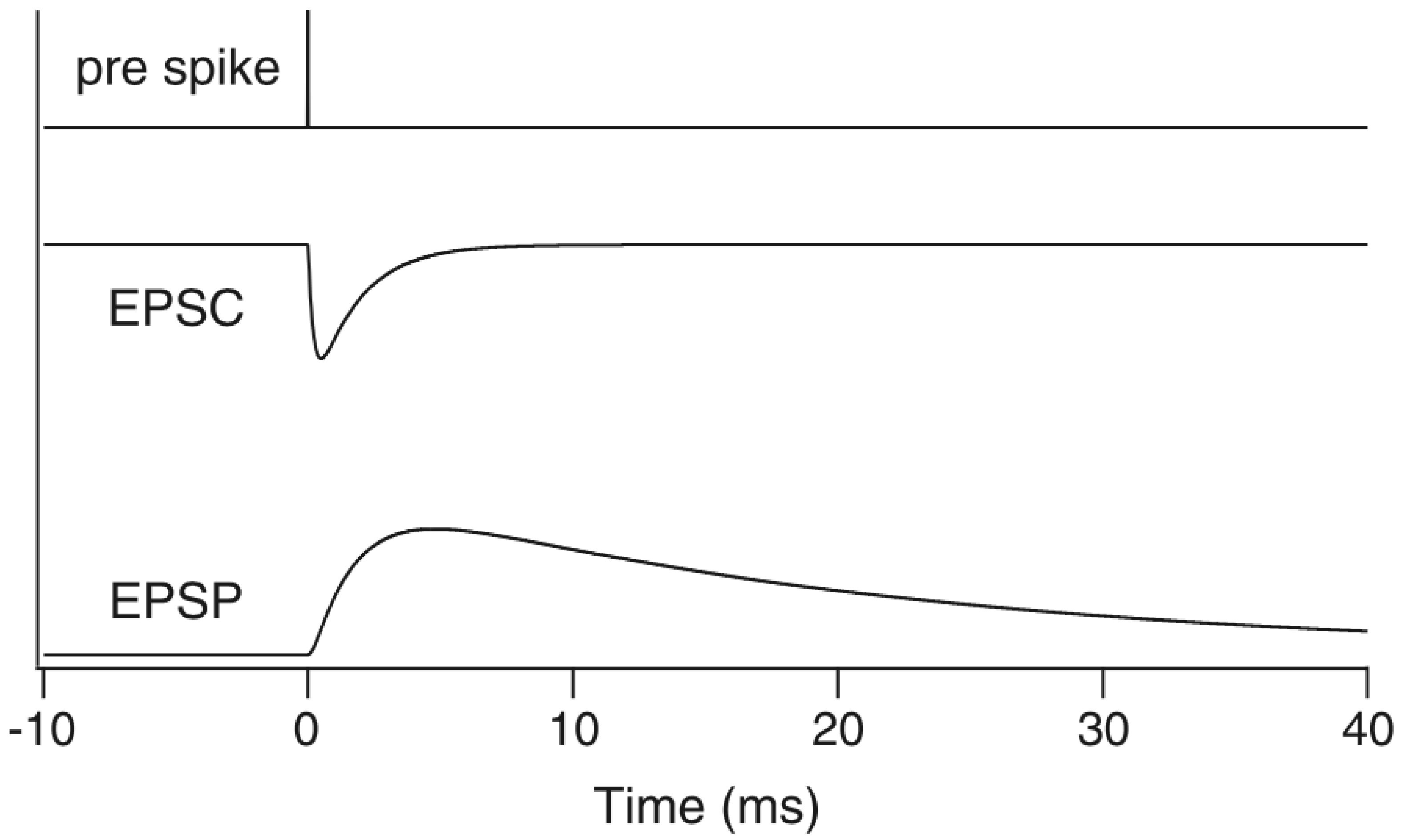
Alpha function

$$s(t) = te^{-t/\tau_s}$$



Difference of two exponentials

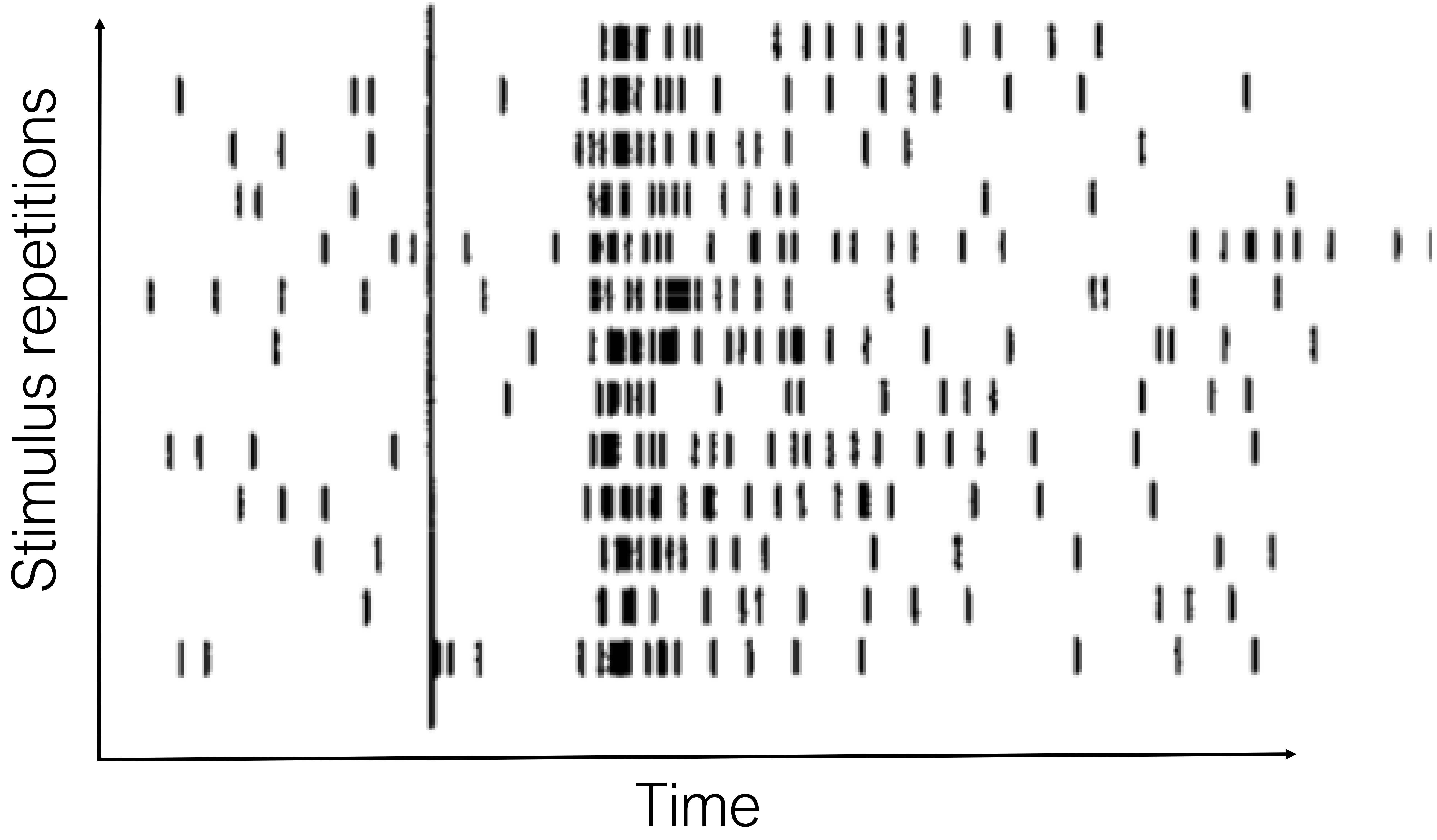
$$s(t) = e^{-t/\tau_{decay}} - e^{-t/\tau_{rise}}$$



Figures from Roth & van Rossum
http://homepages.inf.ed.ac.uk/mvanross/reprints/roth_mvr_chap.pdf

Neural coding

Spike responses to a stimulus



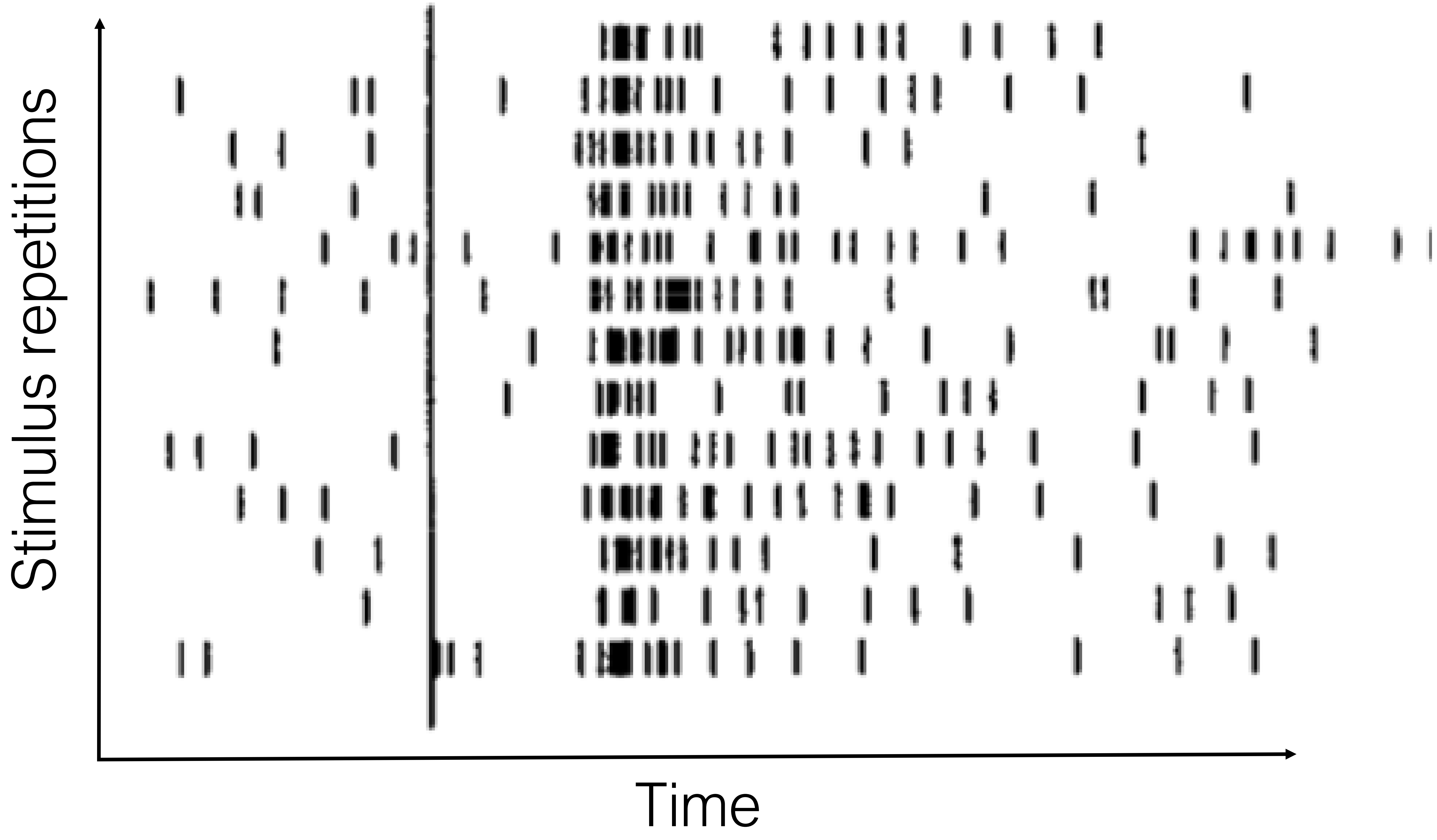
Raster plot of spikes from a single monkey visual cortex neuron from repeated presentations (each row) of a visual stimulus (oriented grating).

[Motter, J Neurophysiol, 1993]

Hubel and Wiesel cat visual cortex experiments

https://youtu.be/jw6nBWo21Zk

Spike times vs spike rates?



[Motter, J Neurophysiol, 1993]

Rate coding

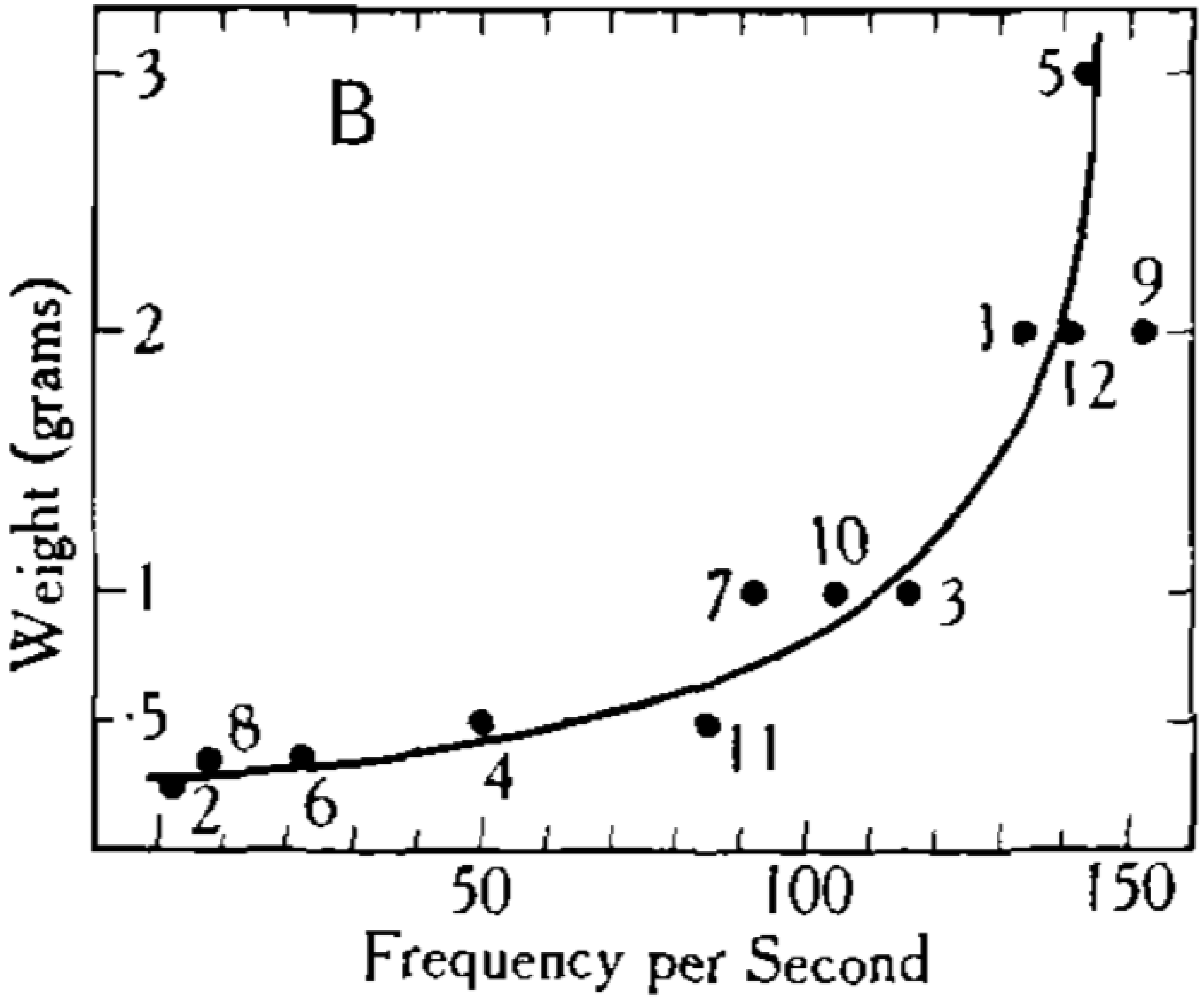


FIG. 25. FROG'S STERNO-CUTANEOUS PREPARATION. RELATION BETWEEN INTENSITY OF STIMULUS (WEIGHT ON MUSCLE) AND FREQUENCY OF DISCHARGE.

[The Basis of Sensation, Adrian, 1928]

Precise spike time coding

Responses of 10 neurons in primate somatosensory cortex to different textures applied to the fingertip. Authors found tha spike times had ~2 ms precision.

[Long et al, Nature Comms, 2022]

Neural decoding

- Up to now we have considered neural (en)coding: asking what the brain's response is to stimuli.

  $P(r|s) = ?$

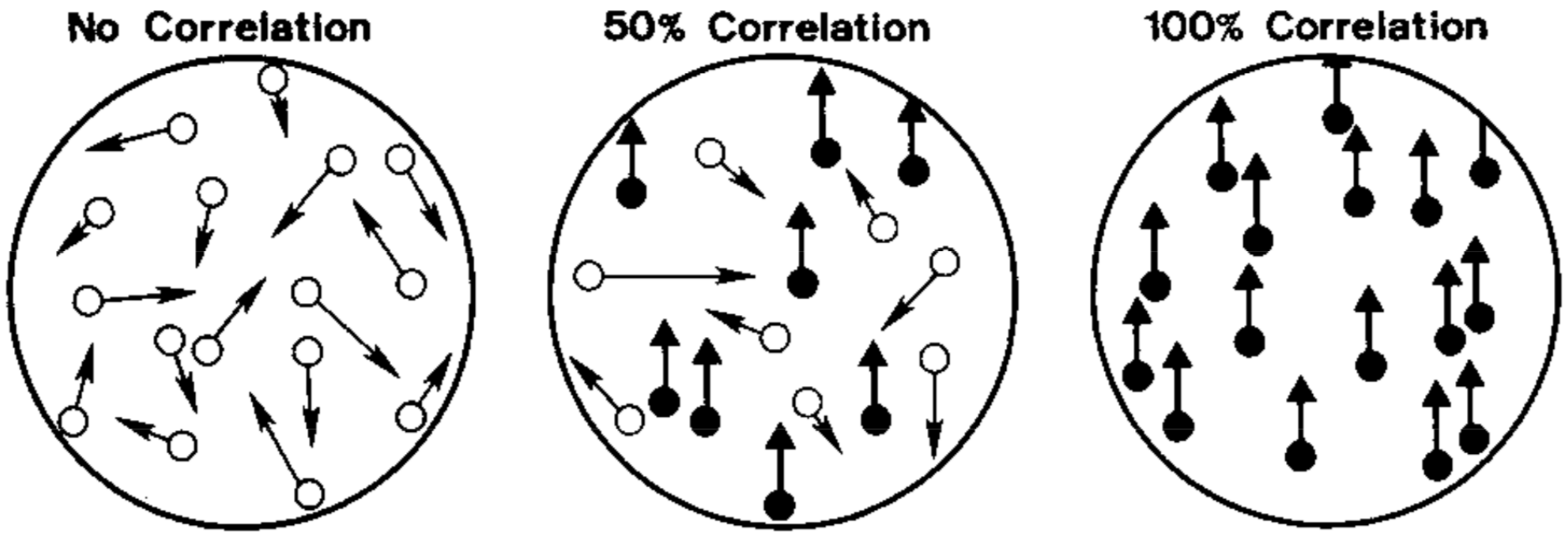
- Decoding is the opposite of encoding.

- Decoding takes the "brain's-eye view": trying to estimate the stimulus from the neural activity.

  $P(s|r) = ?$

Decoding from a single neuron

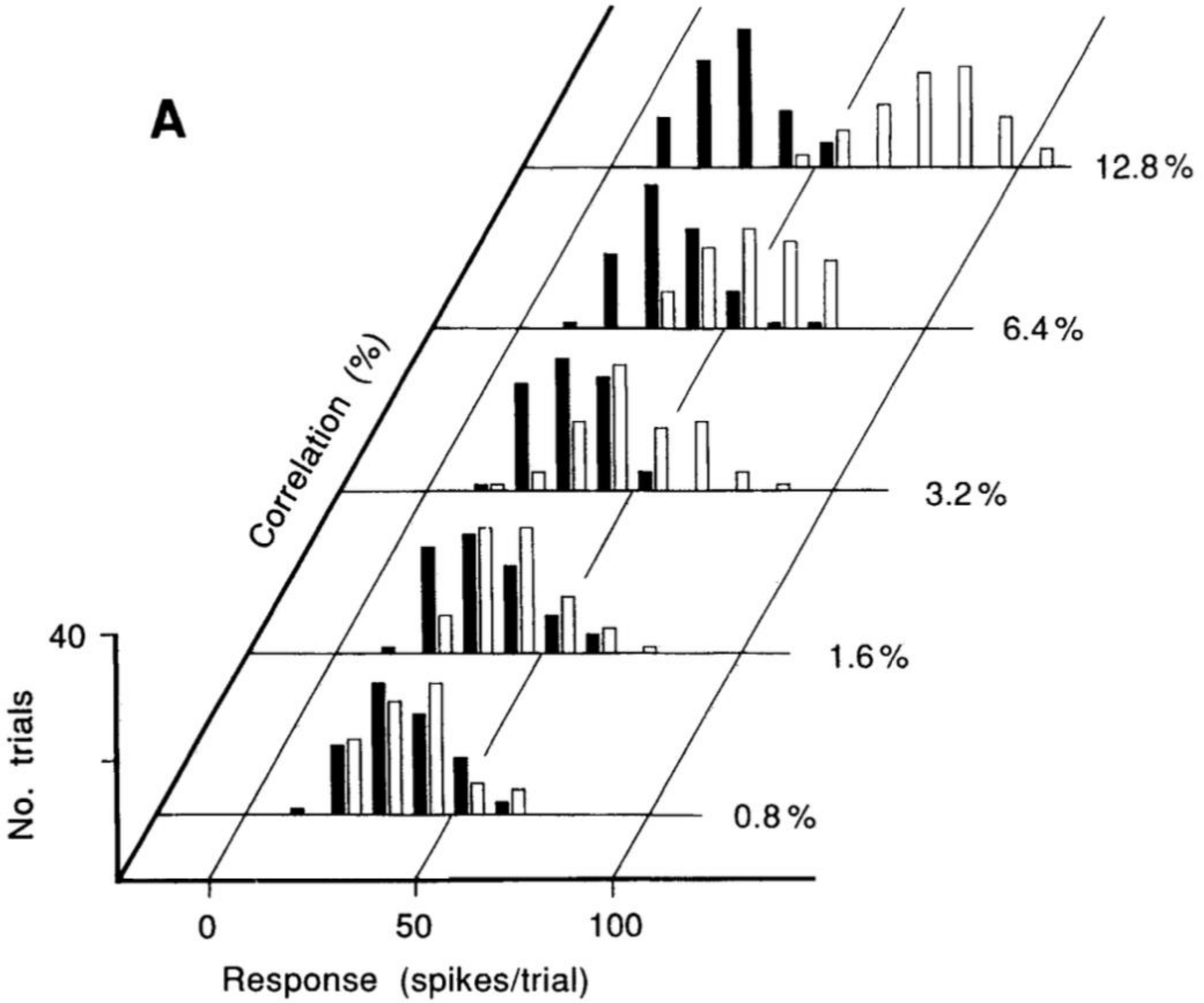
- Decoding is the process of inferring a stimulus from a neuron's spiking.
- This can give us insight into the neural code: how the brain represents information.
- As an example we can use signal detection theory to compute decoding quality for a moving dots task.



Example video: https://youtu.be/xUcwbjaGGNM?t=48

Britten, K.H., Shadlen, M.N., Newsome, W.T., Movshon, J.A., (1992). Journal of Neuroscience 12, 4745–4765.

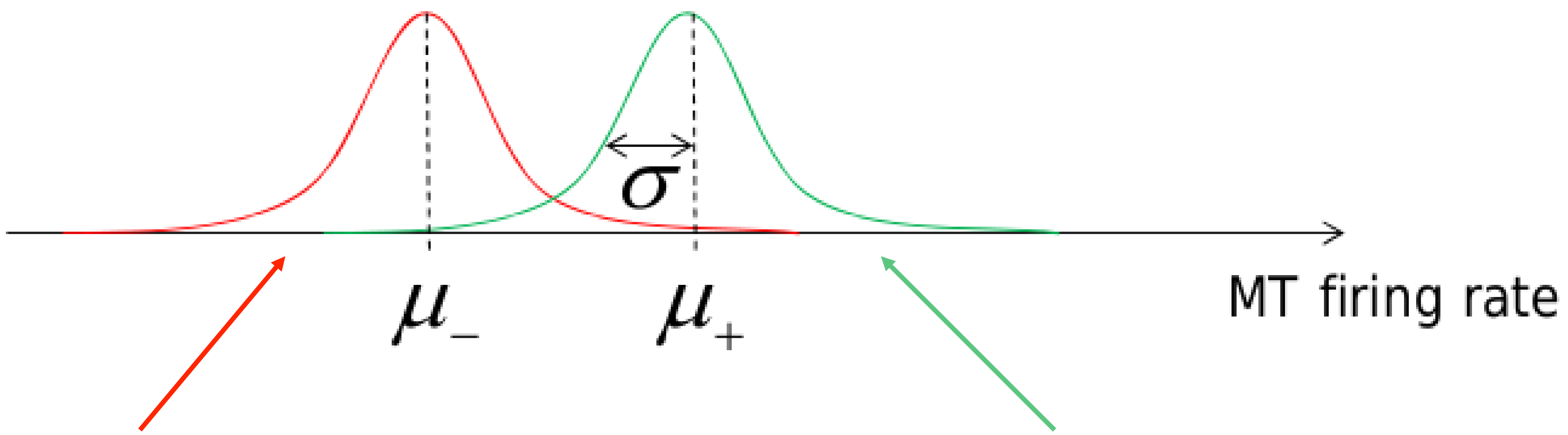
Decoding from a single neuron



The firing rate responses become more separated for higher moving dot image correlation levels.

Britten, K.H., Shadlen, M.N., Newsome, W.T., Movshon, J.A., (1992). Journal of Neuroscience 12, 4745–4765.

Decoding from a single neuron



$$P(\text{rate}|\text{corr} = 0) = \mathcal{N}(\mu_-, \sigma) \qquad P(\text{rate}|\text{corr} > 0) = \mathcal{N}(\mu_+, \sigma)$$

- Fit a probability distribution to each response per stimulus condition: $P(\text{response}|\text{stimulus})$
- Now, if we are given a neural response for a trial where we don't know the stimulus, we ask the question: "Under which stimulus condition was that response more probable?"
- In this 2-choice task, the decision making rule simplifies to putting a decision boundary at the crossover point in the two probability distributions.

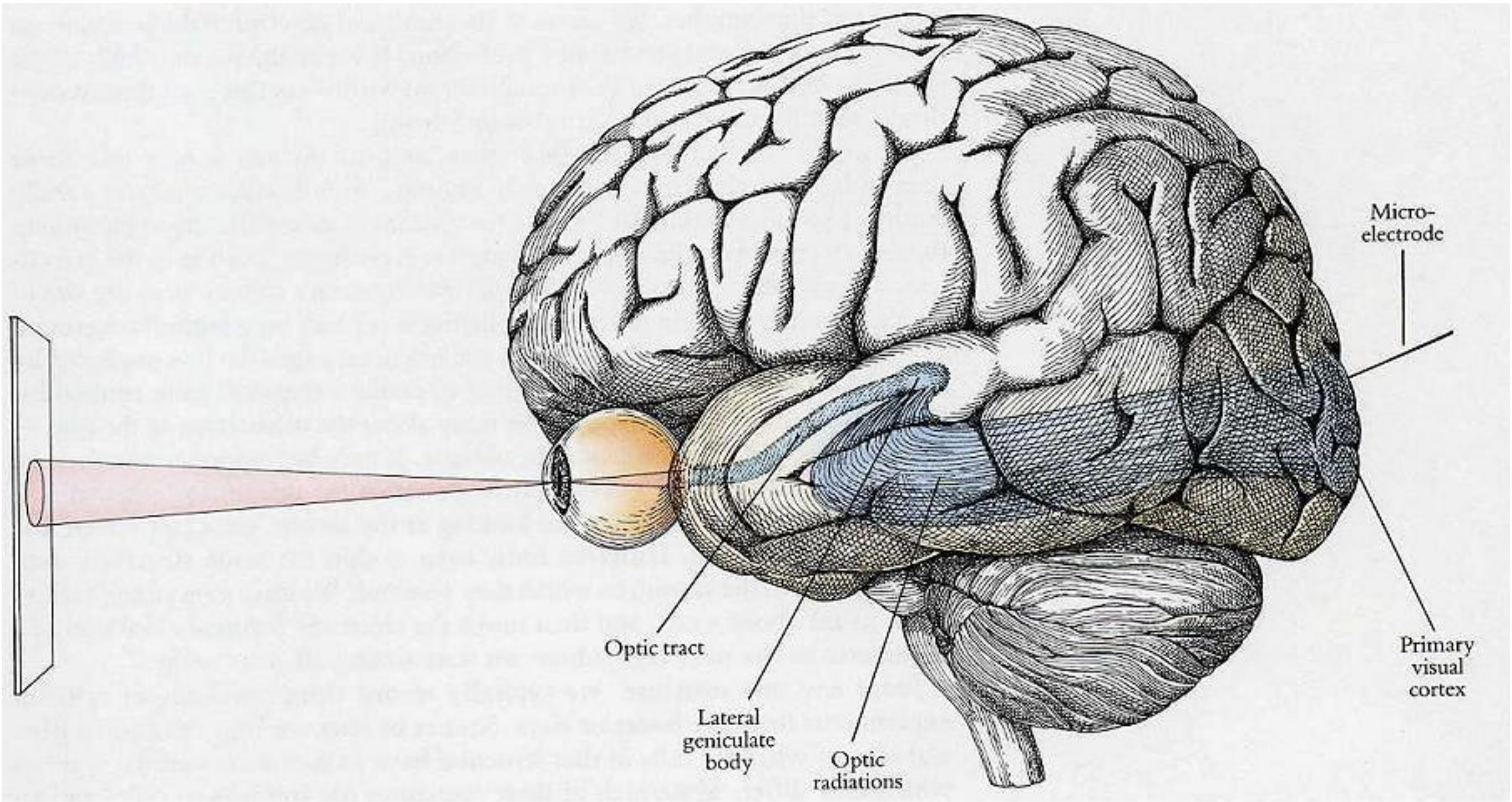
Figure from Rafal Bogacz

Feedforward neural network models of the visual system

The visual system

- As a first approximation, the visual system comprises:

Retina → LGN (Thalamus) → Primary visual cortex (V1) → V2/V4/MT etc



http://hubel.med.harvard.edu/book/b3.htm

- However, reality is much more complicated
  (tens of visual regions, lots of heterogeneity, feedback connections)

Coding along the visual hierarchy

Receptive fields tend to change from level to level up the visual processing hierarchy.

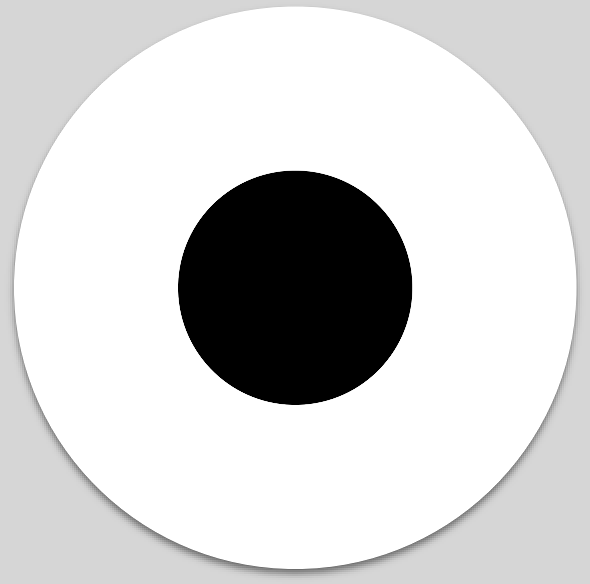
They:

- Become larger.
- Become sensitive to complicated aspects of the visual stimulus.
- Become more sensitive to top-down, contextual information (e.g. task context, animal’s behavioural state, attention)

Coding along the visual hierarchy: retinal ganglion cells/LGN

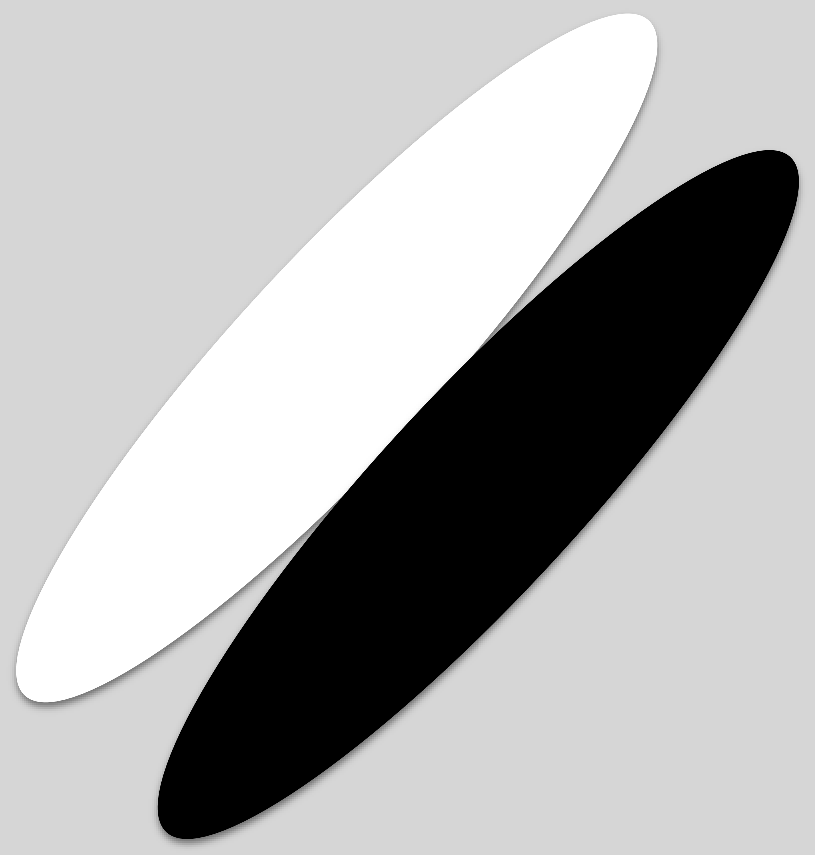
"ON centre"

Coding along the visual hierarchy: retinal ganglion cells/LGN



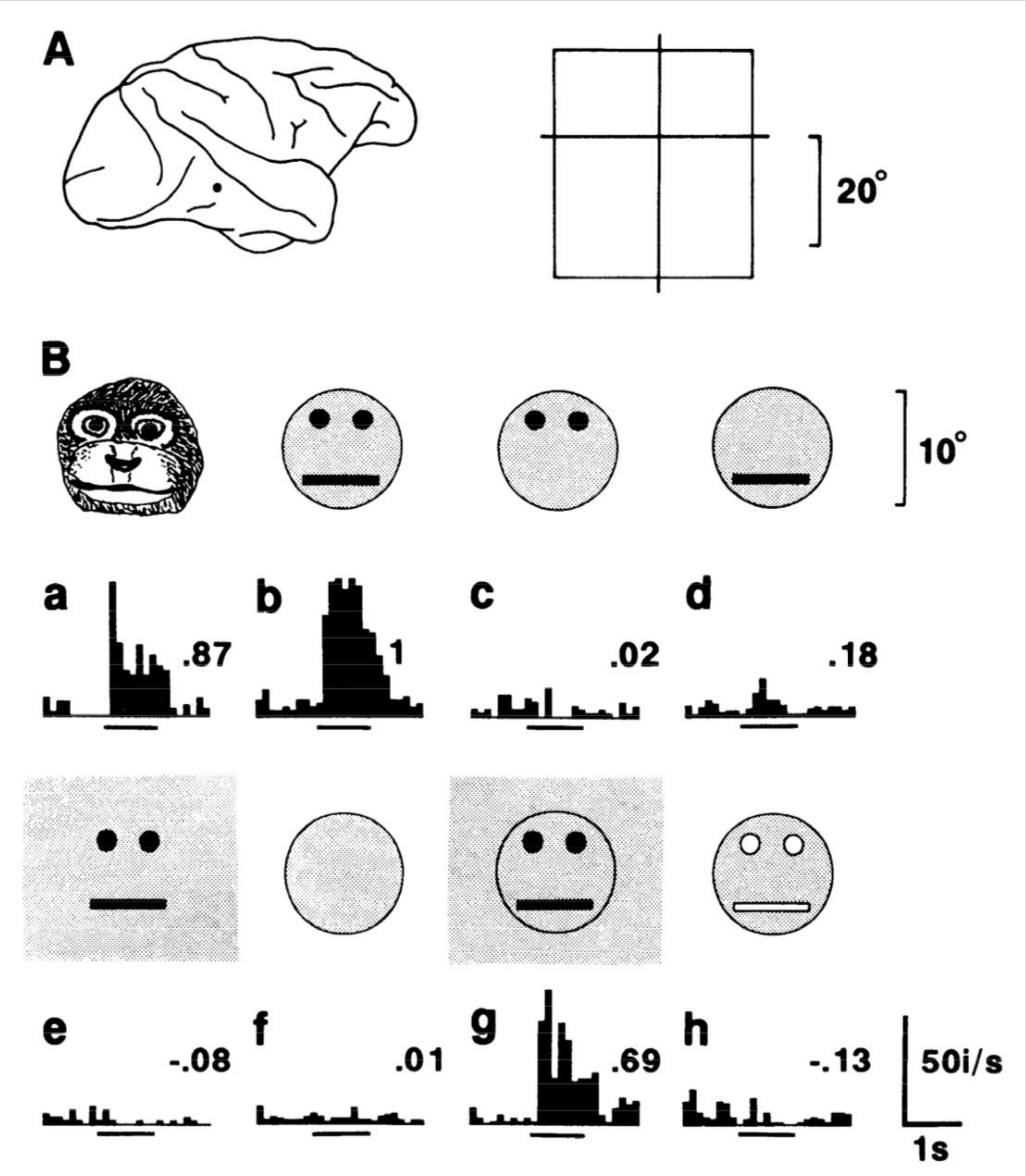
“OFF centre”

Coding along the visual hierarchy: V1



Orientation tuning,
Gabor-like.

Coding along the visual hierarchy: higher visual areas



Objects, e.g. faces

[Kobatake and Tanaka, J Neurophysiol (1994)]

Feedforward neural network models of the visual system

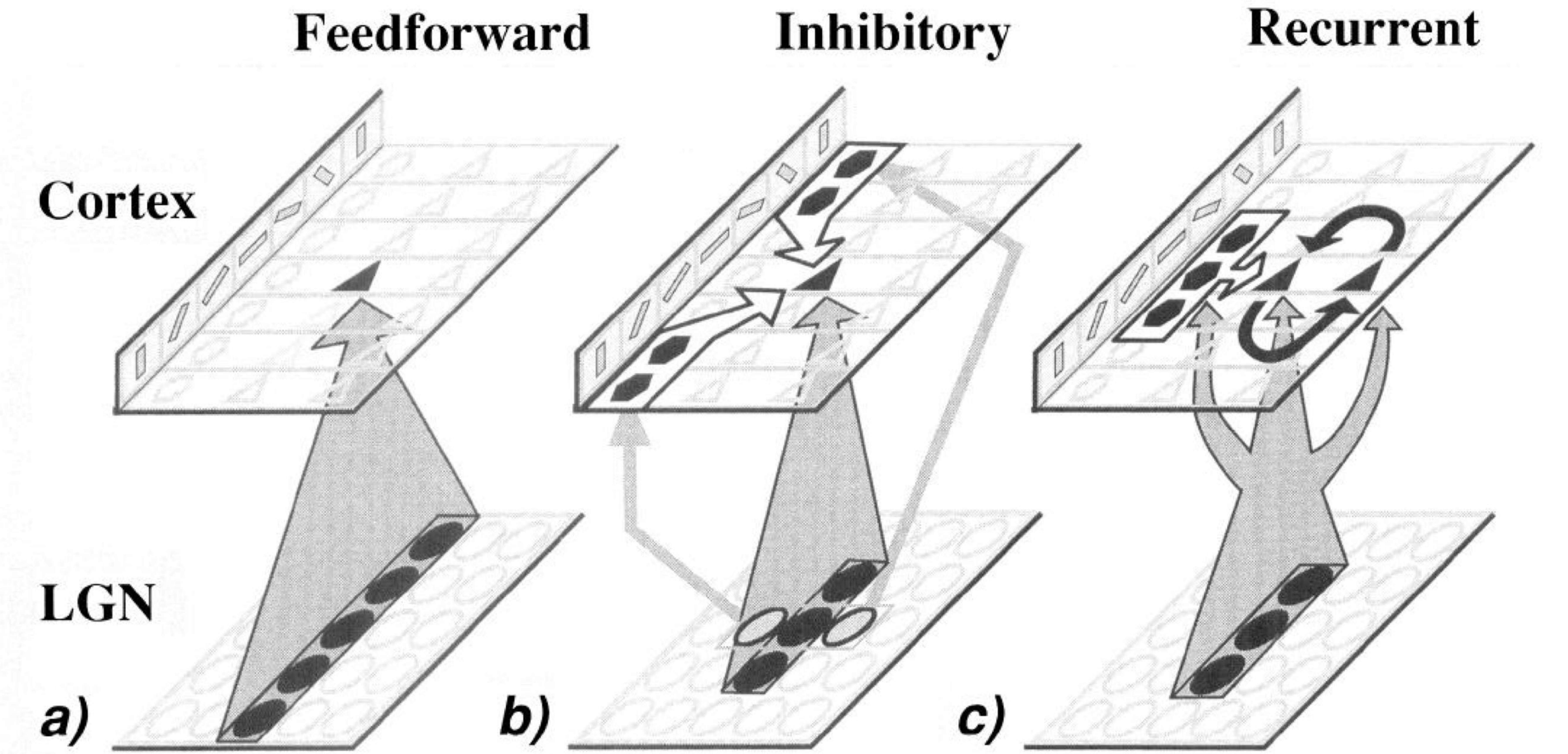
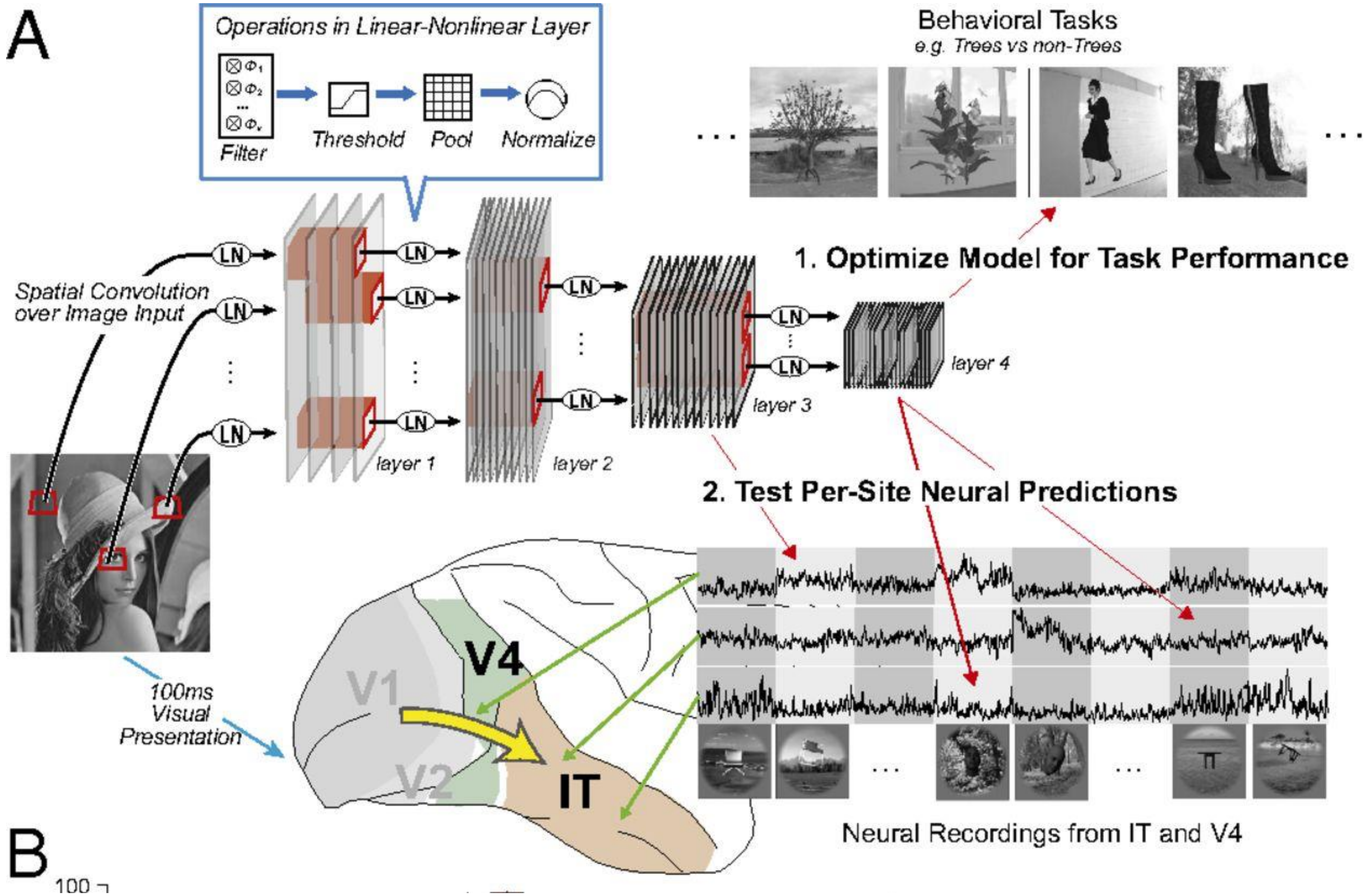


Figure 1. Models of visual cortical orientation selectivity. *a*, In feedforward models all "first-order" cortical neurons (*triangle*, excitatory; *hexagon*, inhibitory) receive converging input (*gray arrow*) from a population of LGN neurons that cover a strongly oriented region of visual space. The bandwidth or sharpness of a cortical cell's orientation tuning is determined by the aspect ratio of its LGN projection. *b*, Many inhibitory models employ a mild feedforward bias to establish the initial orientation preference of cortical neurons and utilize inhibitory inputs (*white arrows*), from cortical neurons preferring different orientations, to suppress nonpreferred responses. Here, we present a model, *c*, in which recurrent cortical excitation (*black arrows*) among cells preferring similar orientations, combined with iso-orientation inhibition from a broader range of orientations, integrates and amplifies a weak thalamic orientation bias, which is distributed across the cortical columnar population.

Somers, Nelson & Sur, J Neurosci (1995)

Artificial neural network models of the visual system



Yamins et al, PNAS (2014)

Summary of part 1

- We can mathematically and computationally model neurons and synapses at various levels of detail.
- The Hodgkin-Huxley model linked sodium and potassium currents to the action potential.
- Neurons covey information in both spike timing and spike rates — your model choice will reflect your assumptions about the target phenomenon.
- Feedforward network models give a decent approximation of the mammalian visual system.
- But we are still many decades away from a 'complete model of the human brain'!