COMS30127: Computational Neuroscience

Synapses

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Dr. [your name here]?

- Would you like to do a PhD in computational neuroscience?
- If so there are many good options in the UK and abroad. It's more or less a buyers market (you're buying).
- Here's 3 nice options:
    1. EPSRC DTP with one of Bristol's Computational Neuroscience Unit: Conor Houghton, Nathan Lepora, Naoki Masuda, Rosalyn Moran, Cian O'Donnell. Check out our research webpages and contact us directly if interested.
    2. Bristol's Neural Dynamics PhD program (joint experimental/computational). Webpage: http://www.bristol.ac.uk/neural-dynamics/
    3. Rafal Bogacz at Oxford is looking for a PhD student to start Oct 2017. "The topic of research could range from developing a formal theory of information processing in the brain to applying machine learning to the data recorded from the brains of patients."
       Rafal's page: https://www.ndcn.ox.ac.uk/team/rafal-bogacz
       PhD advert: https://www.findaphd.com/search/ProjectDetails.aspx?PJID=83868&LID=1239

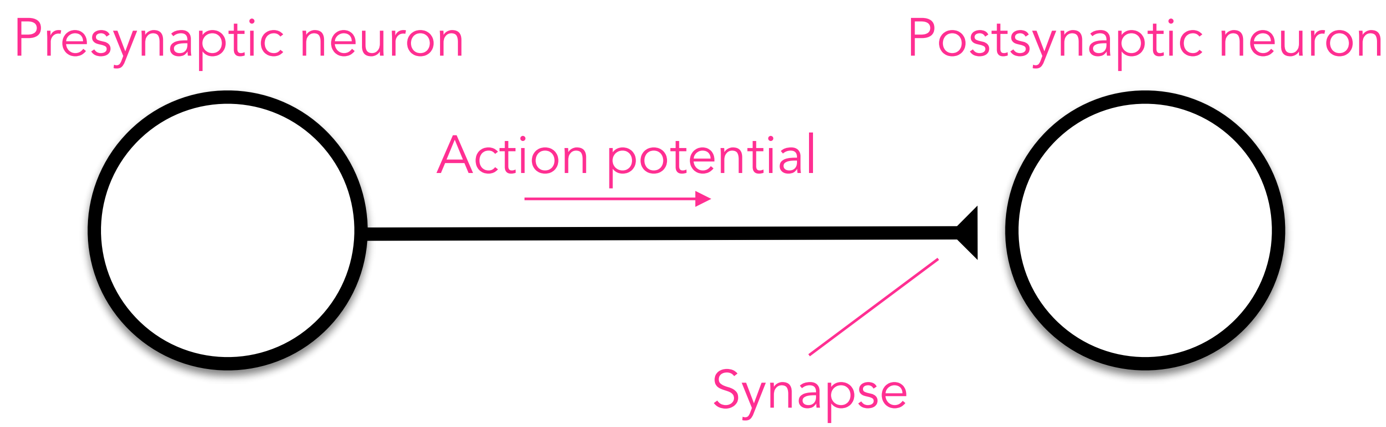
What we will cover today

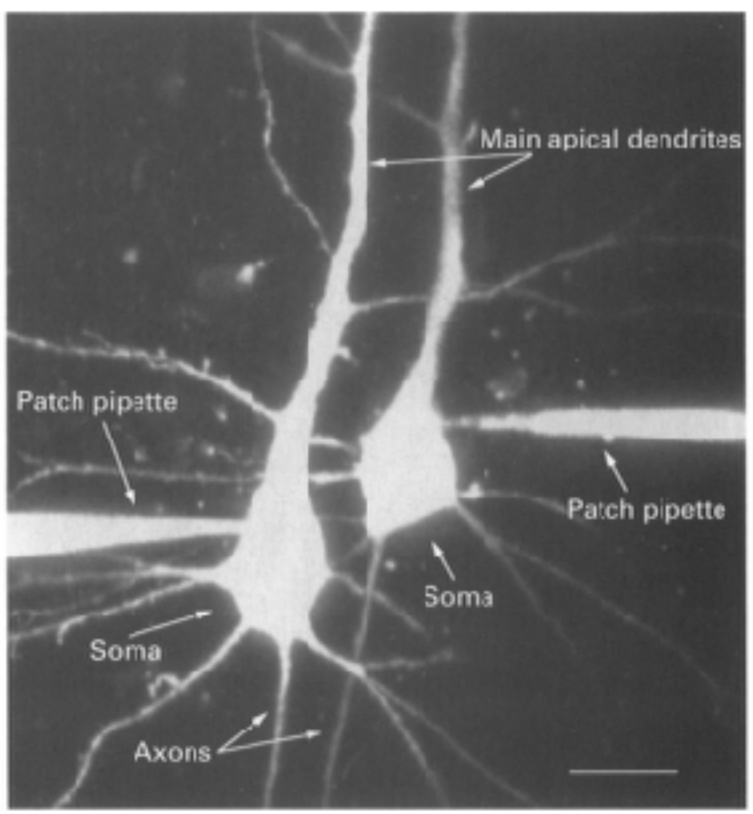
- What is a synapse?
- How do synapses work?
- How can we computationally model synapses?

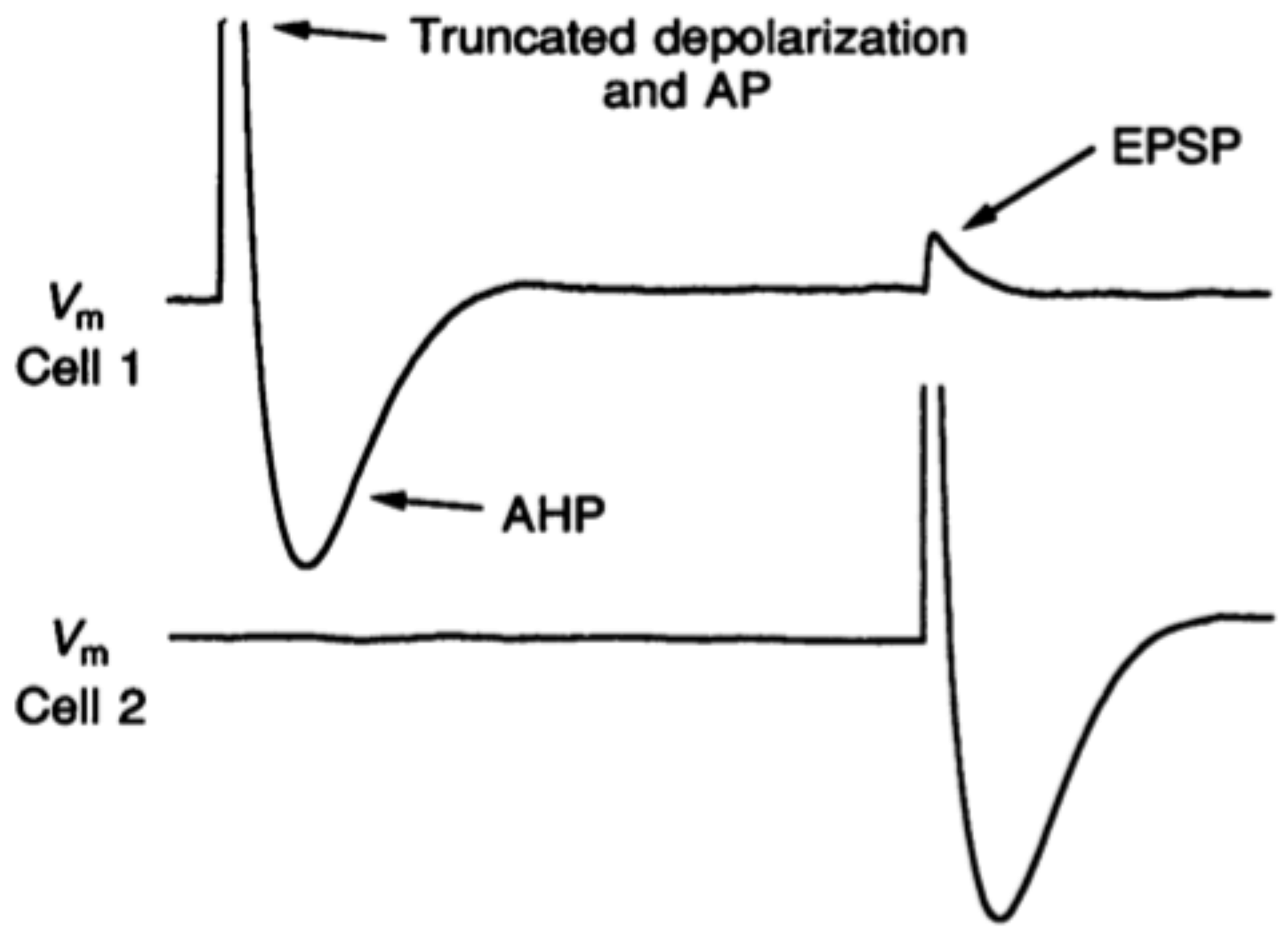
What is a synapse?

- Synapses are the connections between neurons.
- They convert the action potential from one neuron's axon into a 'post-synaptic-potential' in the dendrite of another neuron.
- Although both a synapse's input and output signals are electrical, the most common type of synapse converts the signal into chemical form at an intermediate stage.
- There are also purely electrical synapses (called 'gap junctions') but in this course we will focus on chemical synapses.
- From a functional point of view, synapses are interesting for two reasons:
    1. they are nonlinear, so can perform computations.
    2. they are plastic, so can store information (memories).

What is a synapse?

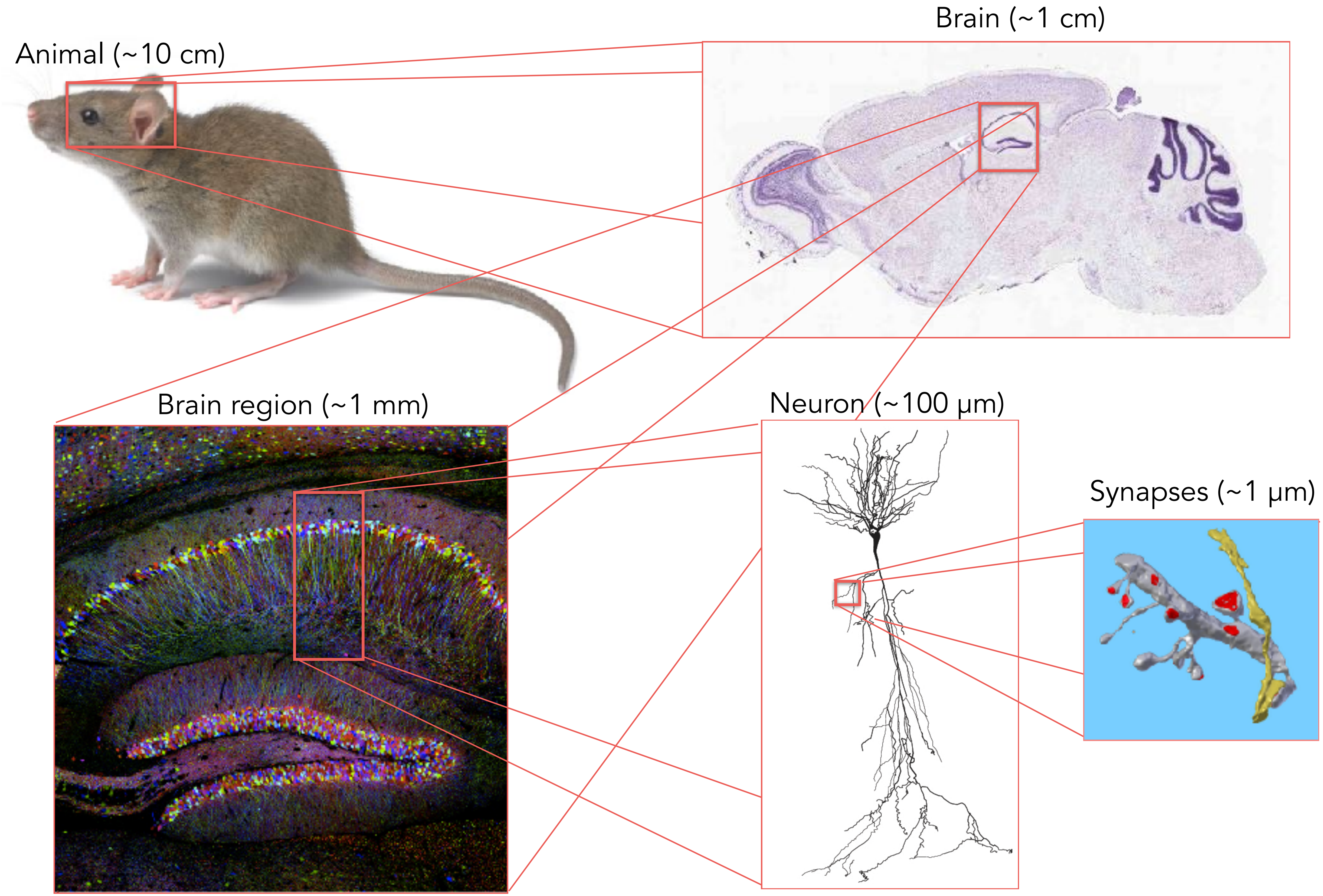






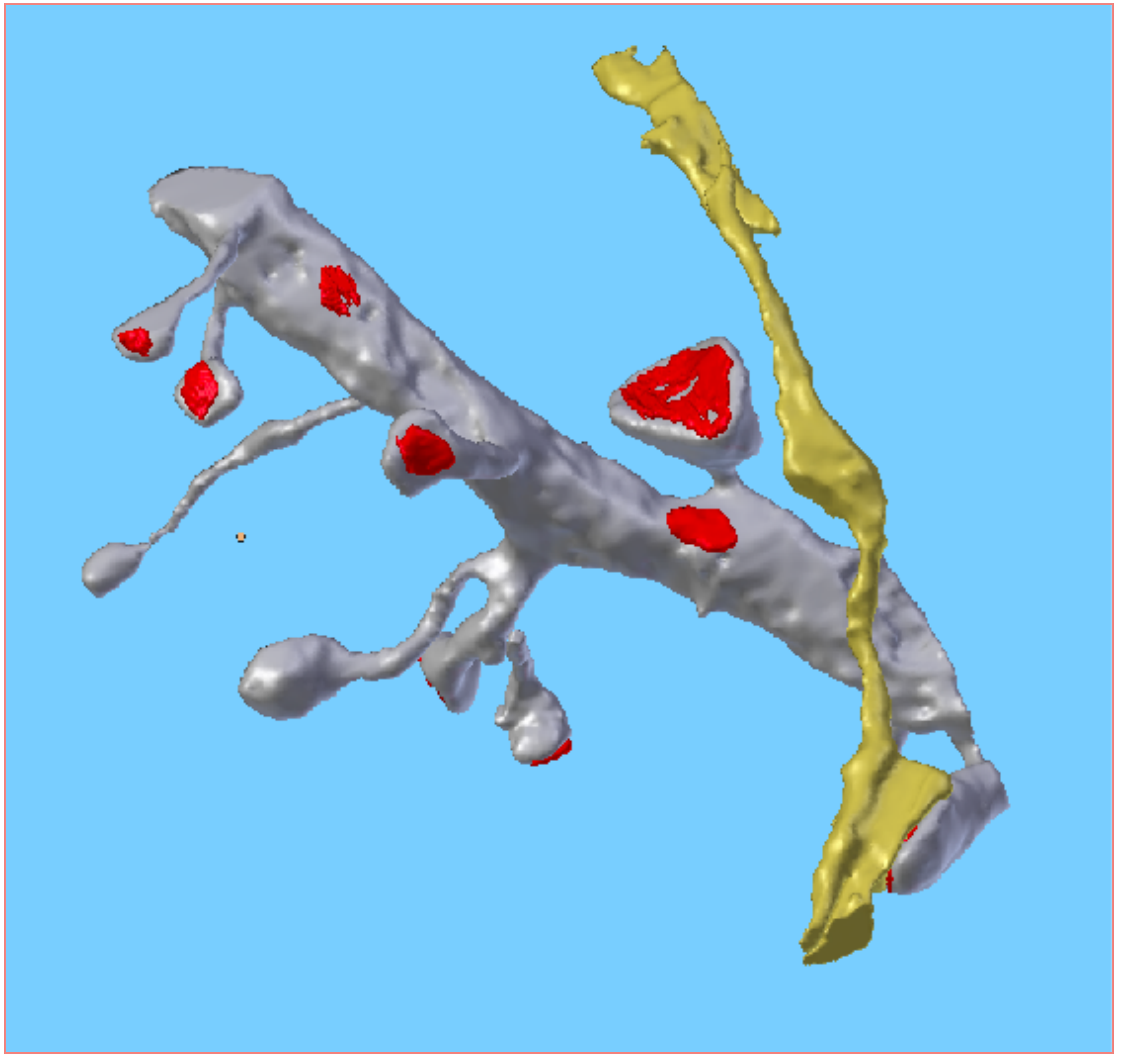
Markram et al, *J Physiol* (1997)

Zooming in on synapses



What is a synapse?

Dendrite and axon from mouse somatosensory cortex.



Electron microscopy data from Graham Knott (EPFL)

Blender demo & Youtube video (https://www.youtube.com/watch?v=FZT6c0V8fW4&t)

How do synapses work?

Axon
(presynaptic action potential)

Chemical
signalling

Dendrite
(postsynaptic potential)

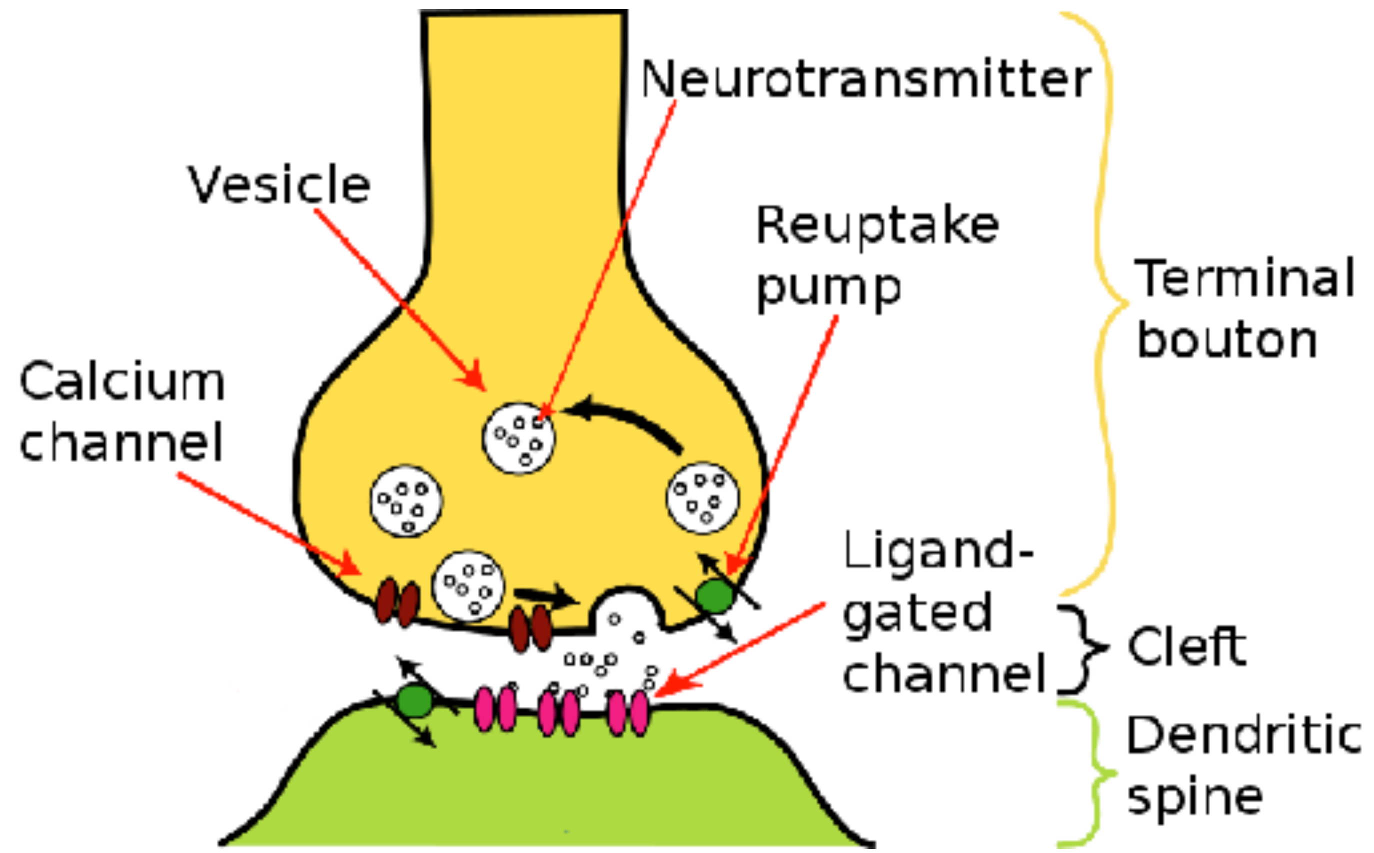
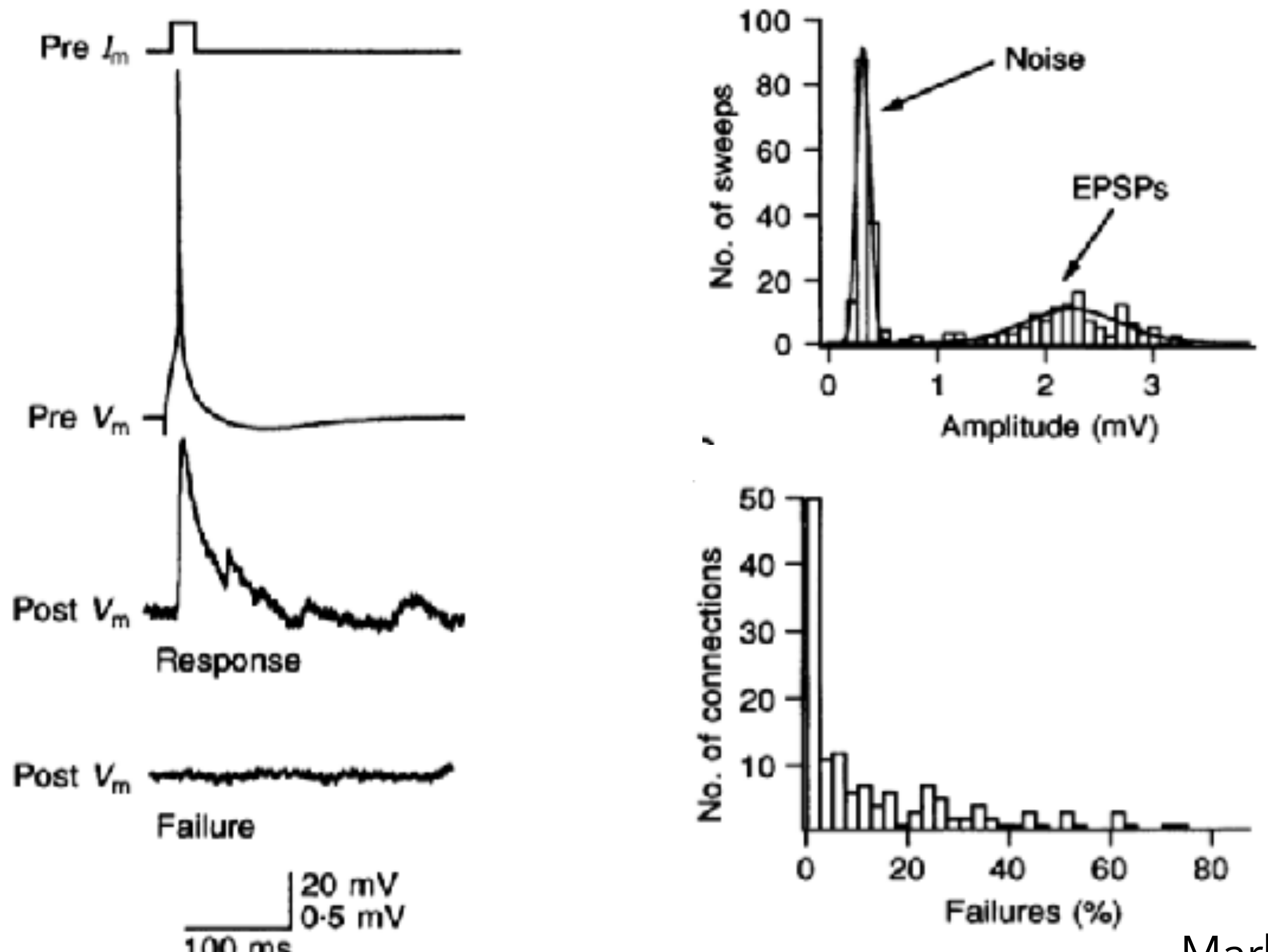


Image from Wikipedia (modified by C Houghton)

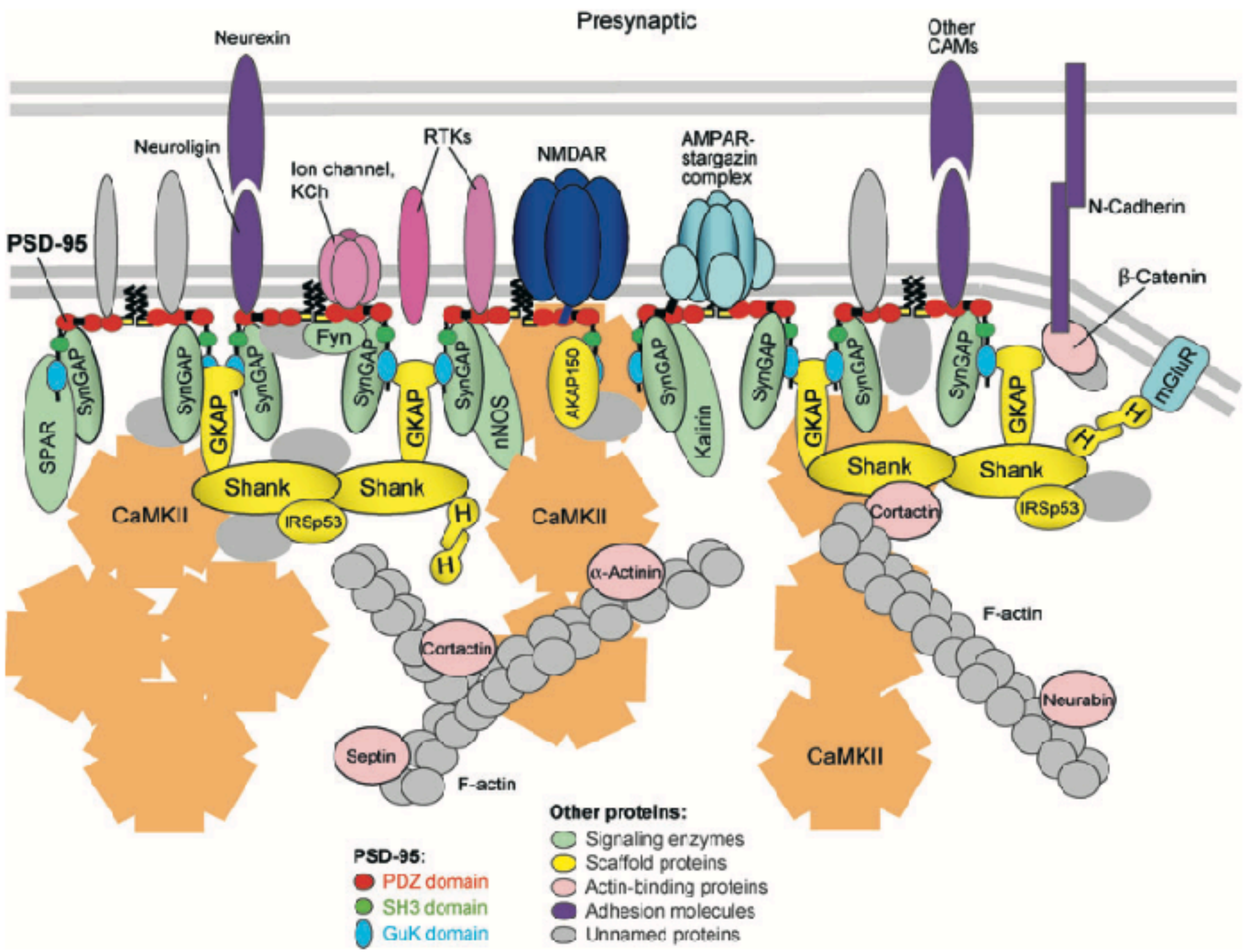
Synapses are probabilistic

- When an action potential arrives at a synapse, it may or may not lead to release of neurotransmitter.
- The 'release probability' p is often quantified experimentally, $0<p<1$.



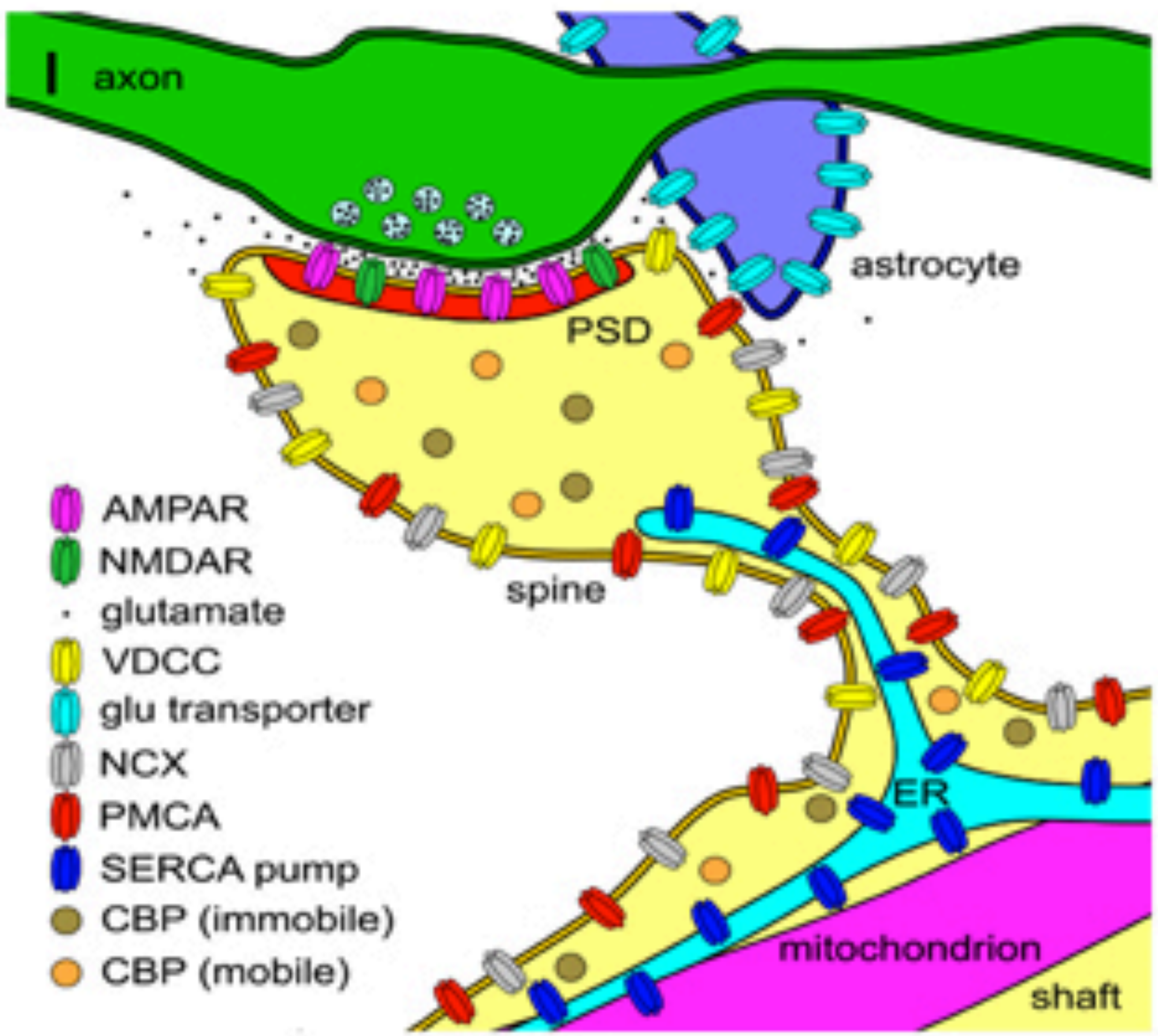
Markram et al, *J Physiol* (1997)

Synapses are complex

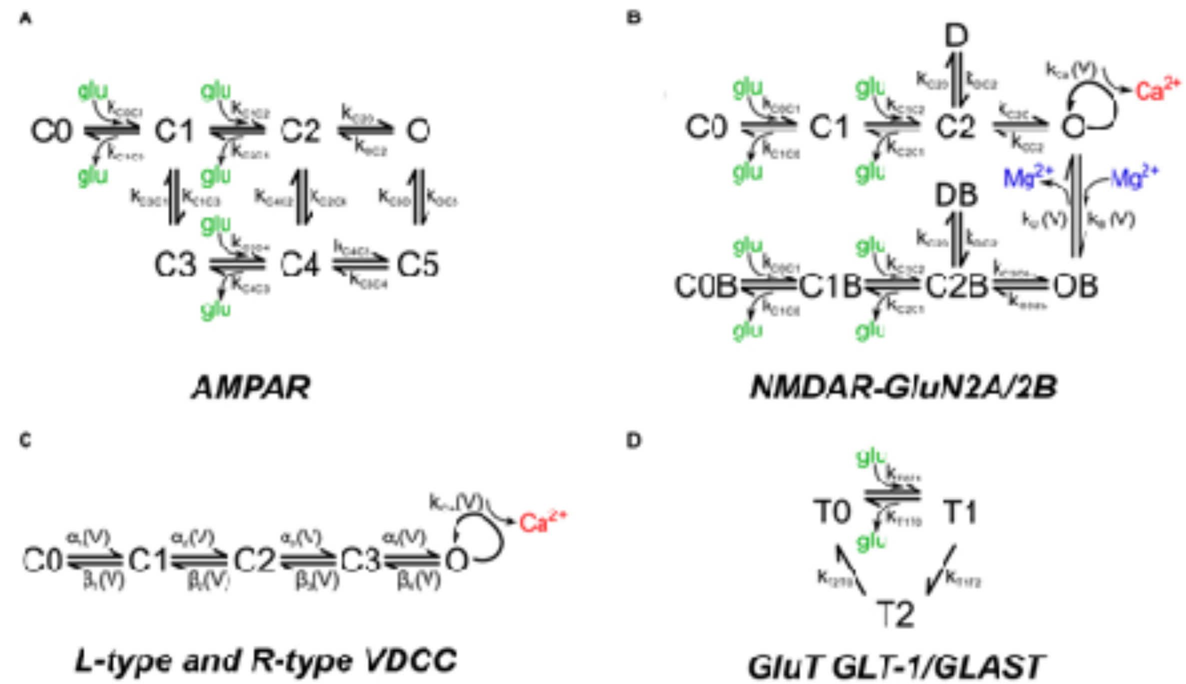


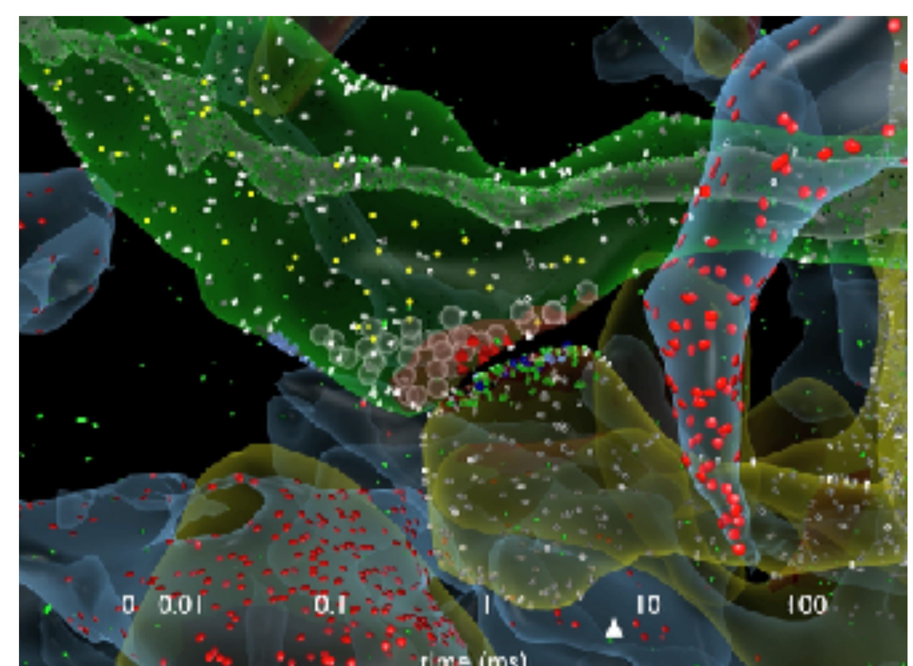
Sheng & Hoogenraad, *Annu Rev Neurosci* (2007)

MCell simulation of synaptic release



Bartol et al, *Frontiers Syn Neuro* (2015)





Video courtesy of Tom Bartol (Salk Institute, California)

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

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

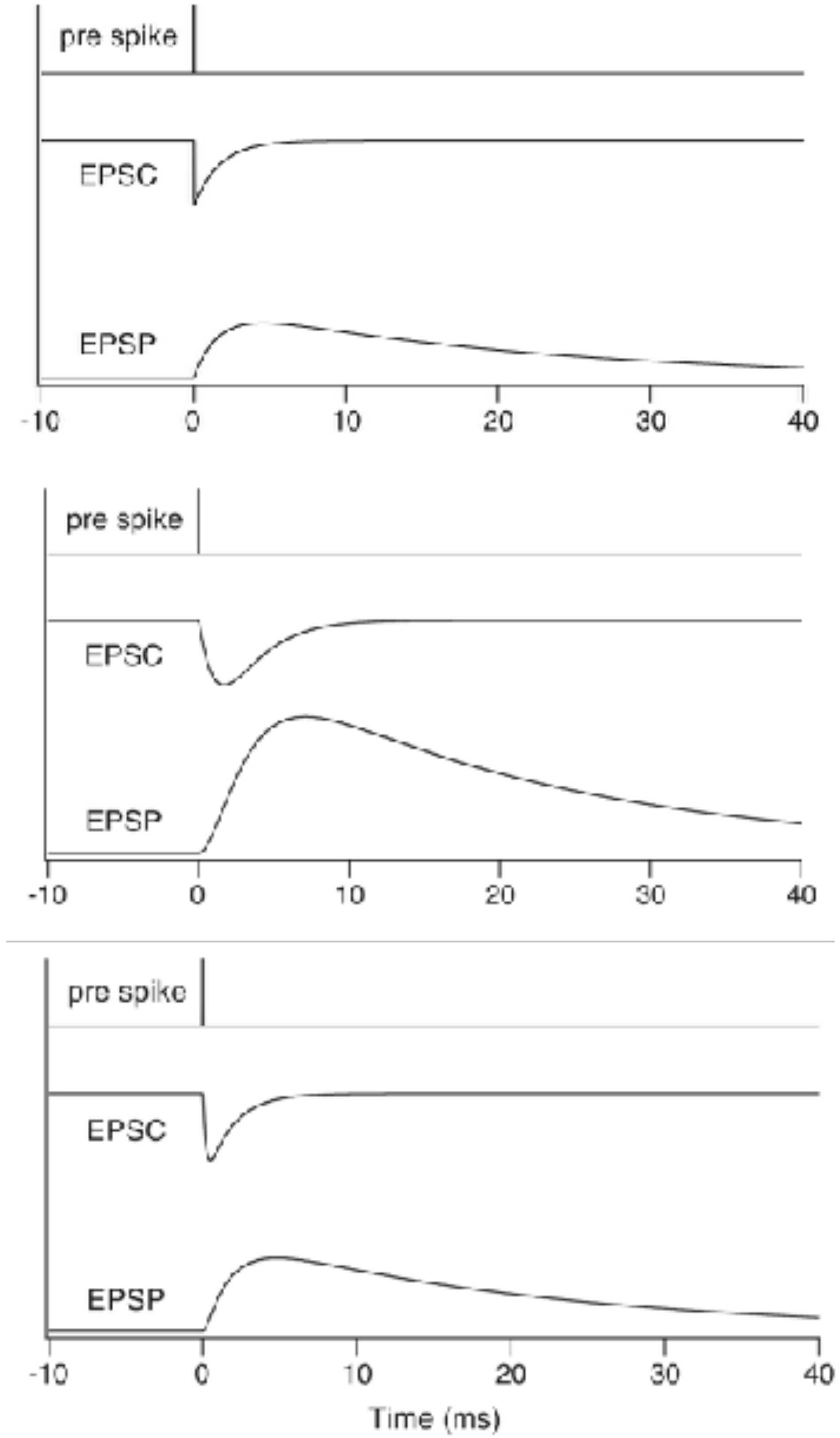
$$s(t) = e^{-t/\tau_s}$$

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

Plastic synapses

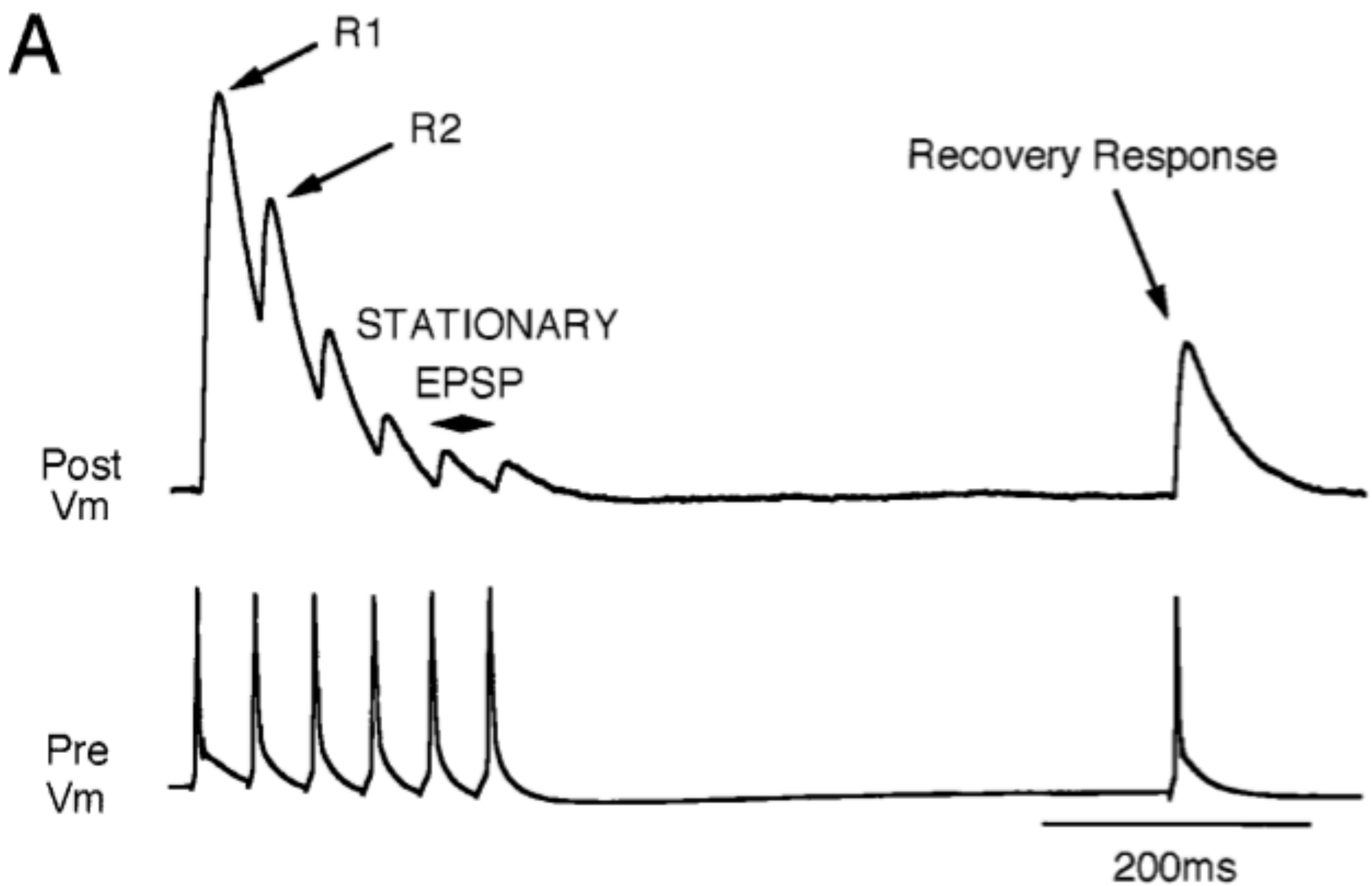
- The magnitude of a synapse's electrical response to an action potential can change depending on the activity history of the synapse (known as plasticity).

- These changes can be fast or slow, and short-lasting (ms—s) or long-lasting (hours—years).

- Short-term synaptic plasticity is thought to aid fast cognitive processing (much like the spikes themselves).

- Long-term synaptic plasticity, in contrast, is thought to mediate long-term memory (more on this next lecture).

Dynamical synapses



Short-term synaptic depression due to a use-dependent decrease in release probability.

Tsodyks & Markram, *PNAS* (1997)

Dynamical synapse models

- Think of the synaptic efficacy as being determined by the available amount of some resource.
- The resource has 3 states: Effective (*E*), Inactive (*I*) and Recovered (*R*).

$$\frac{dR}{dt} = \frac{I}{\tau_{rec}}$$

$$\frac{dE}{dt} = -\frac{E}{\tau_{inact}} + U_{SE} \cdot R \cdot \delta(t - t_{AP})$$

$$I = 1 - R - E,$$

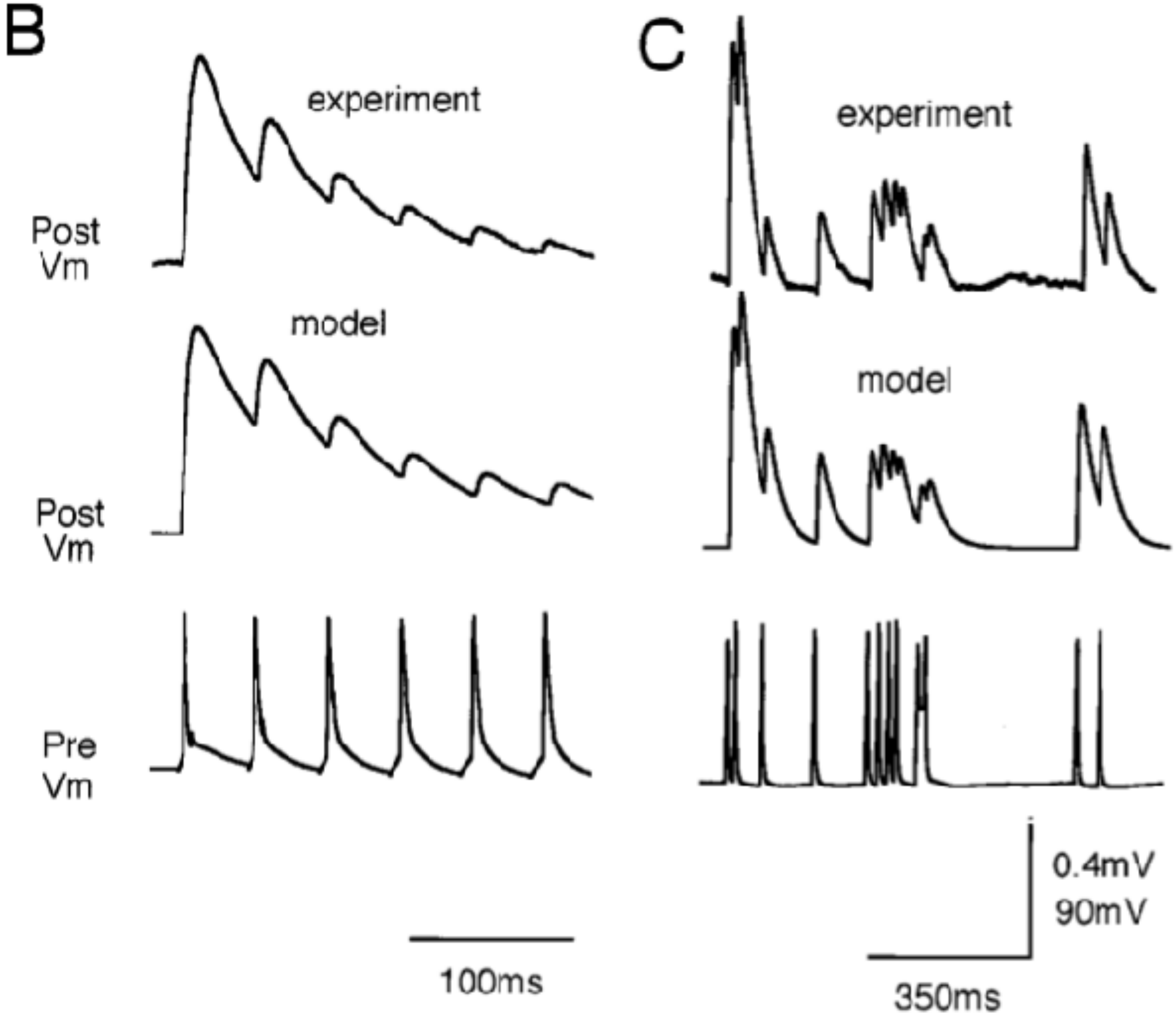
- U_{SE} is a parameter that determines how much resources get depleted with each spike.

$$EPSC_{n+1} = EPSC_n(1 - U_{SE})e^{-\Delta t/\tau_{rec}} + A_{SE} \cdot U_{SE}(1 - e^{-\Delta t/\tau_{rec}}),$$

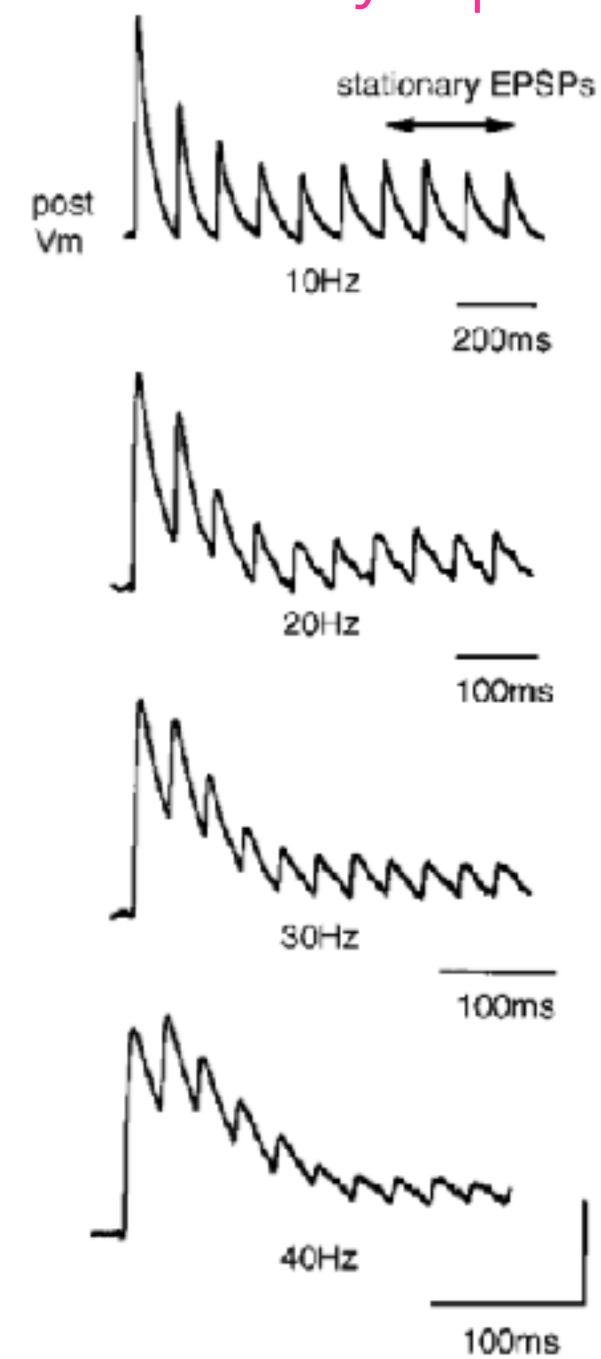
Tsodyks & Markram, *PNAS* (1997)

Dynamical synapses

Model matches data



Faster stimulation = weaker synapses



Tsodyks & Markram, *PNAS* (1997)

Summary

- Synapses are the connections between neurons.
- The convert the pre-synaptic action potential to a (excitatory or inhibitory) post-synaptic potential via a chemical intermediate stage.
- They are highly stochastic (noisy).
- They are also complicated molecular machines.
- We can model them at multiple levels of granularity, as appropriate for the task at hand.

End