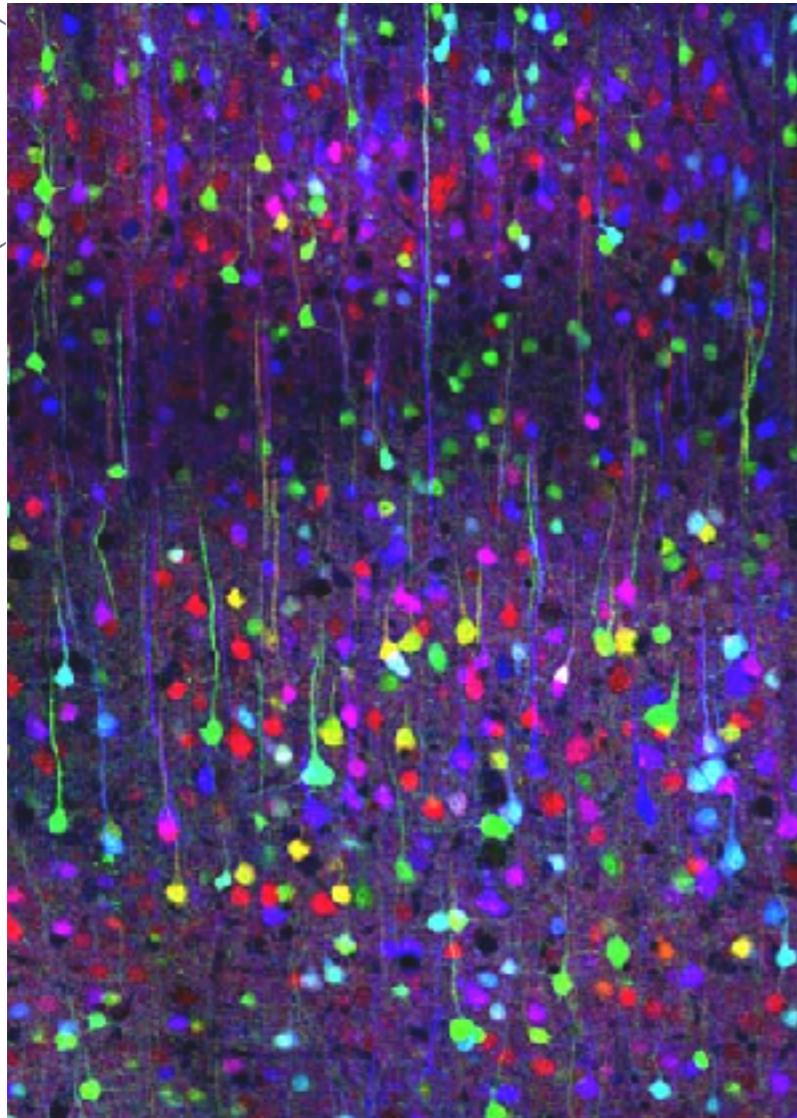


Computational Neuroscience 2018/2019



Brainbow (Litchman Lab)



Lecture 15 Synapses and synaptic plasticity

Outline

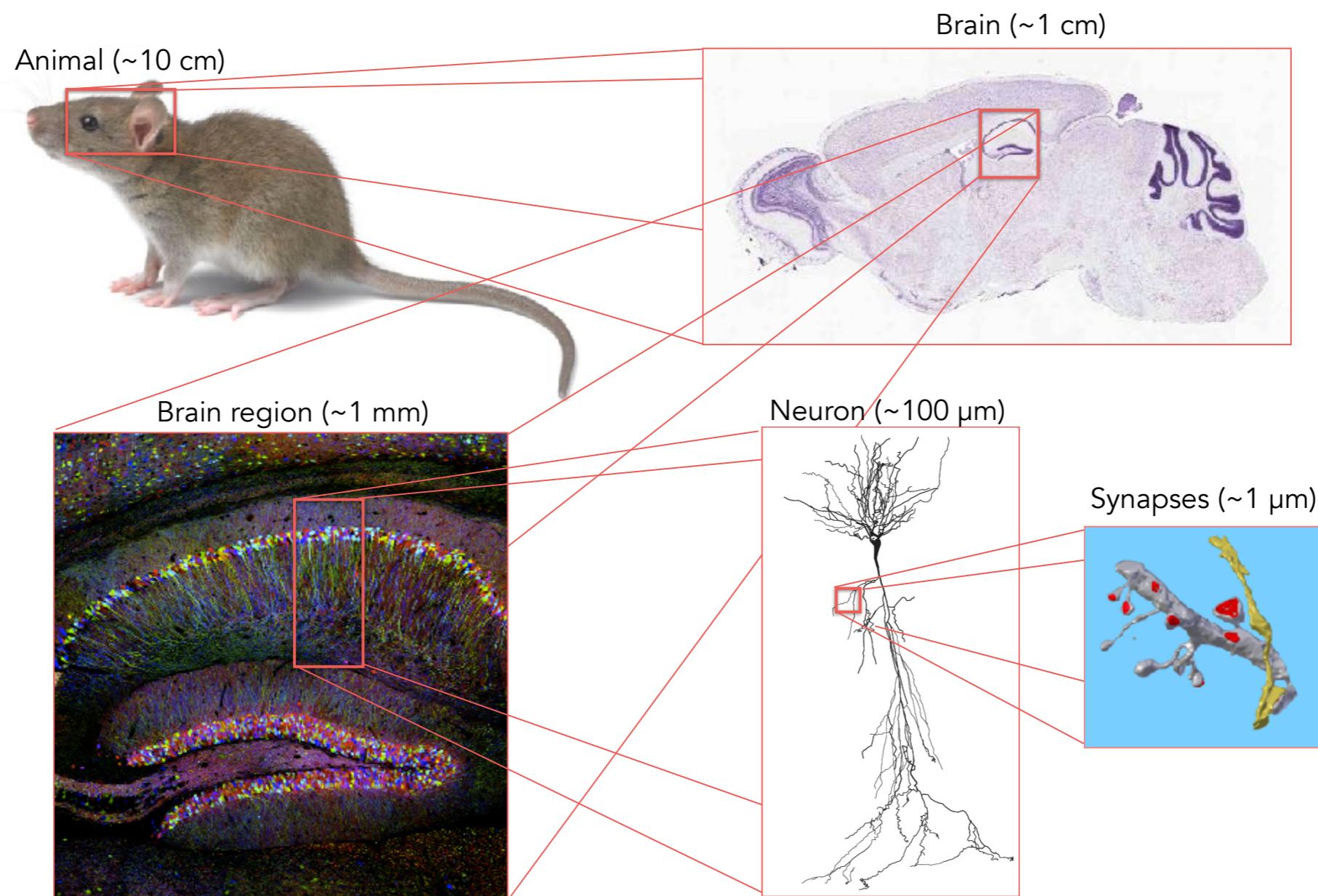
I. Synapses

1. **What are synapses?**
2. **How do they work?**
3. **Computational models of synapses:** static, stochastic, time-dependent, molecular

2. Synaptic plasticity

1. **Learning and memory**
2. **When and where**

Zooming in on the synapse



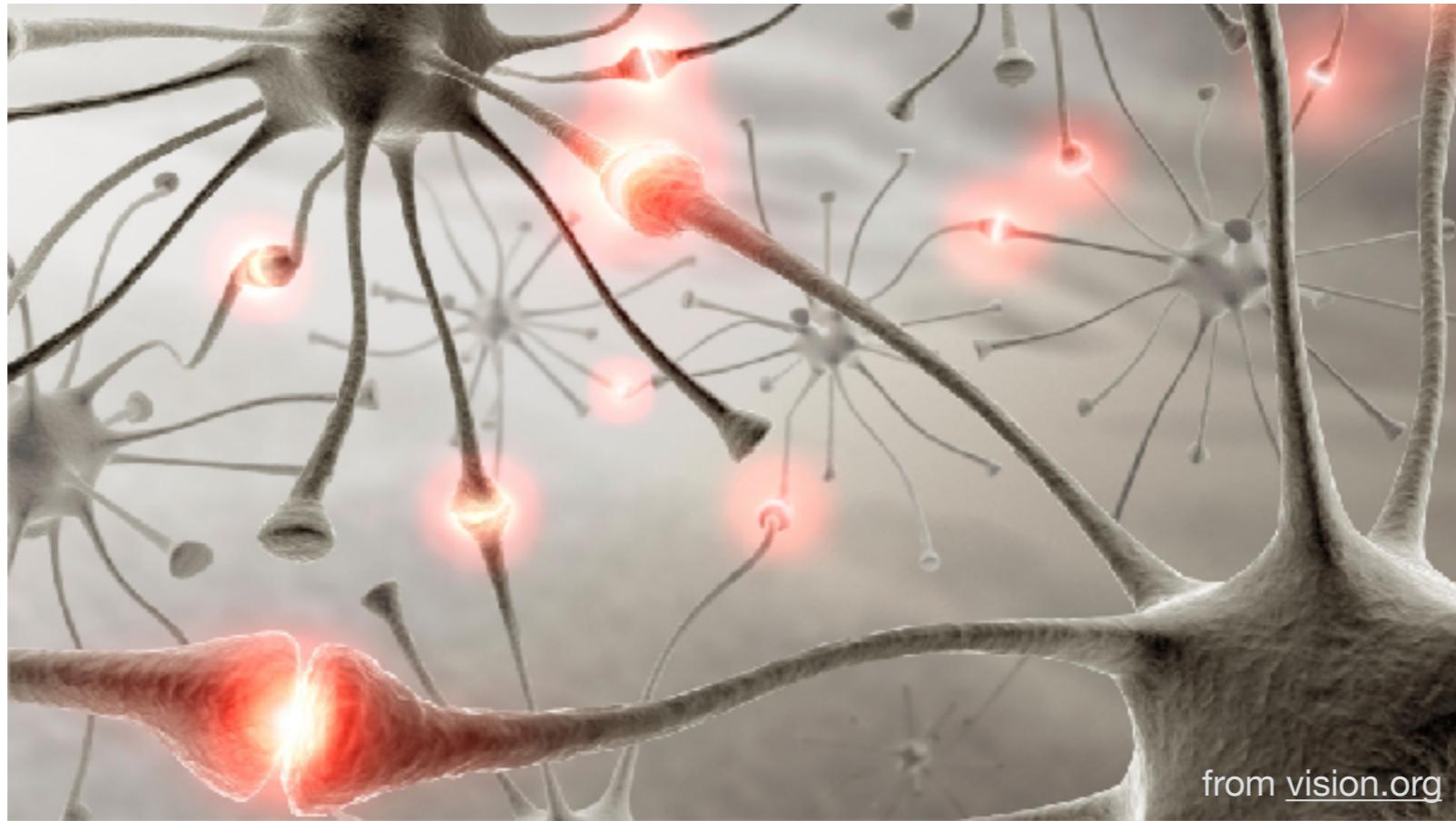
Adapted from Cian O'Donnell

Why build computer models of synapses?

There are ~ 100 billion neurons in an average human brain!

Each of connected to 10000 neurons, which leads to ~ 1000 trillion connections (or synapses)!

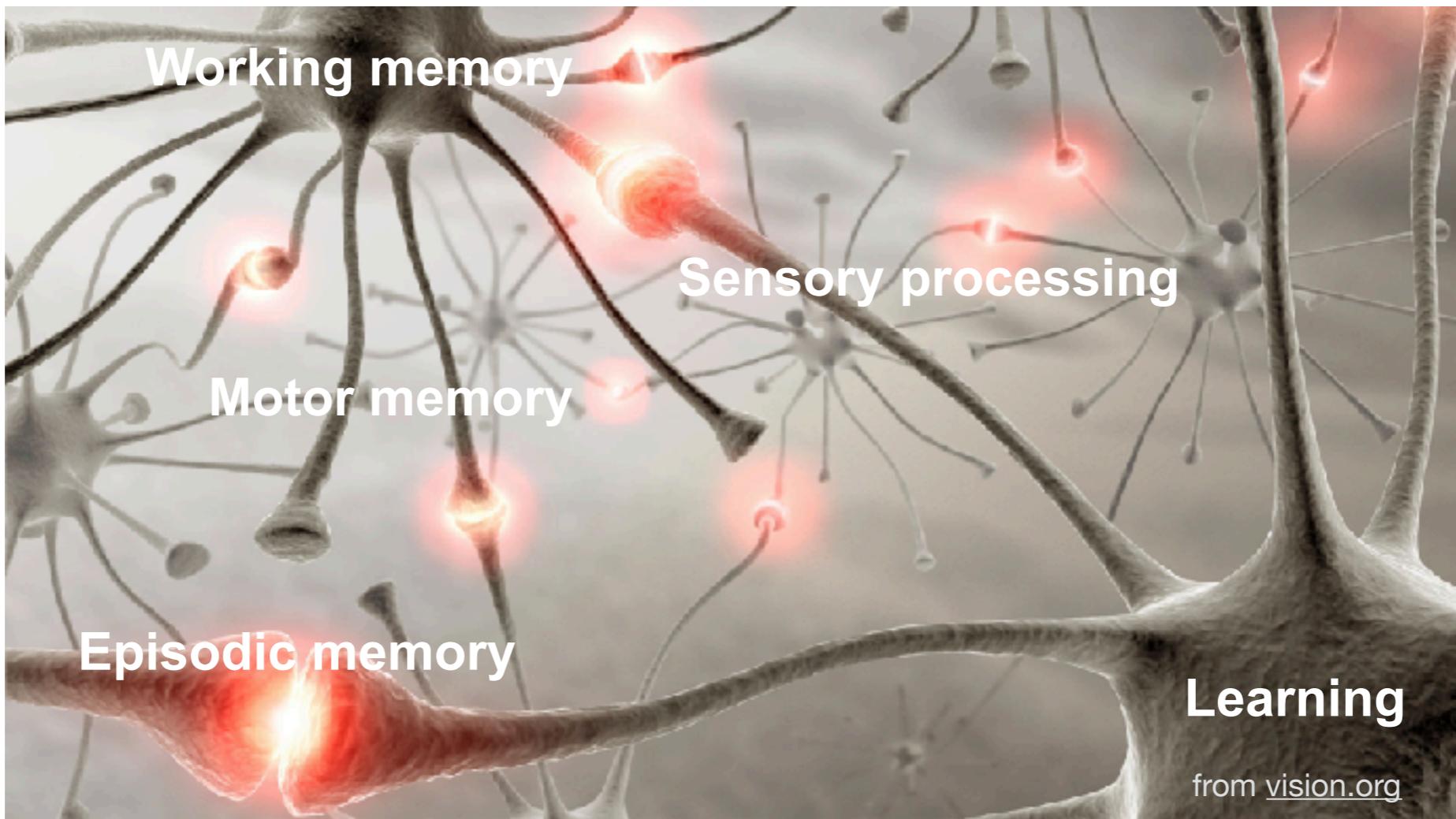
More synapses in your brain than stars in the universe!



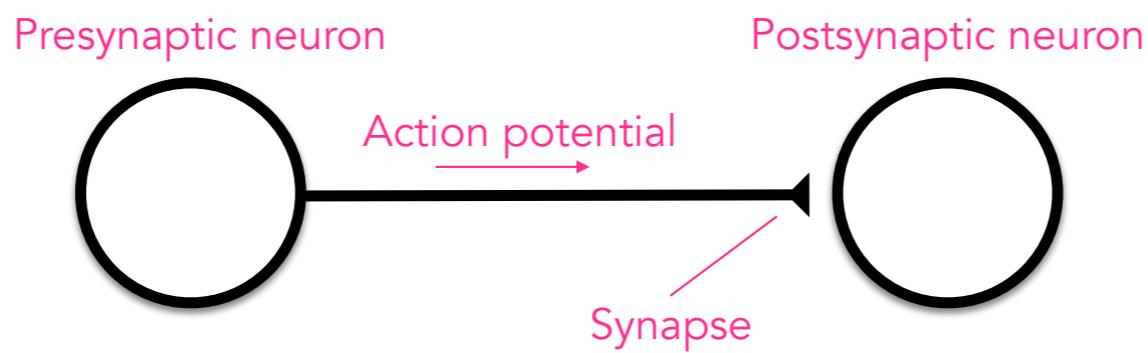
from vision.org

Why build computer models of synapses?

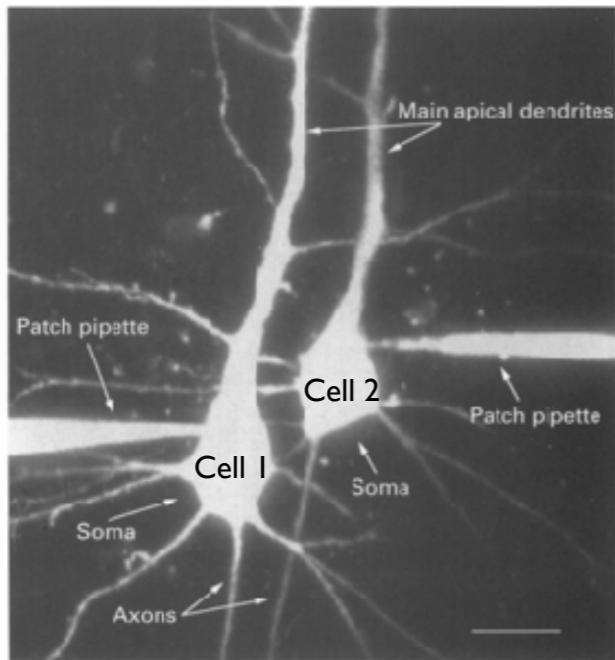
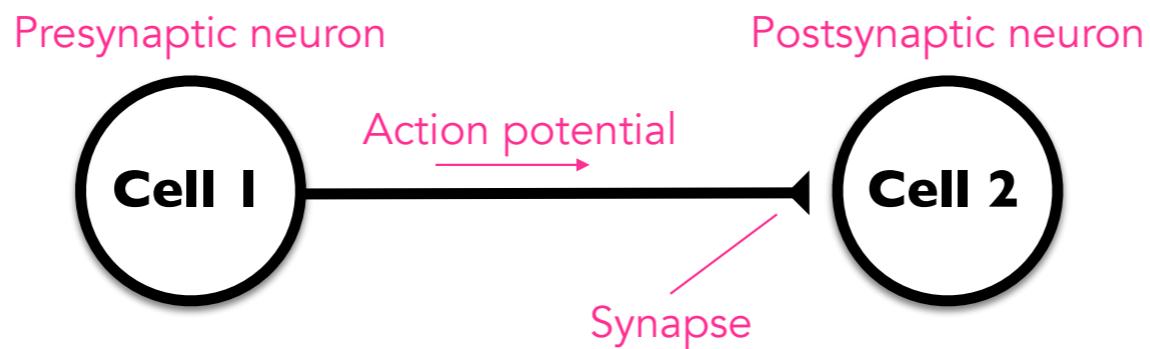
Synapses are crucial for brain function, for example:



What are synapses?

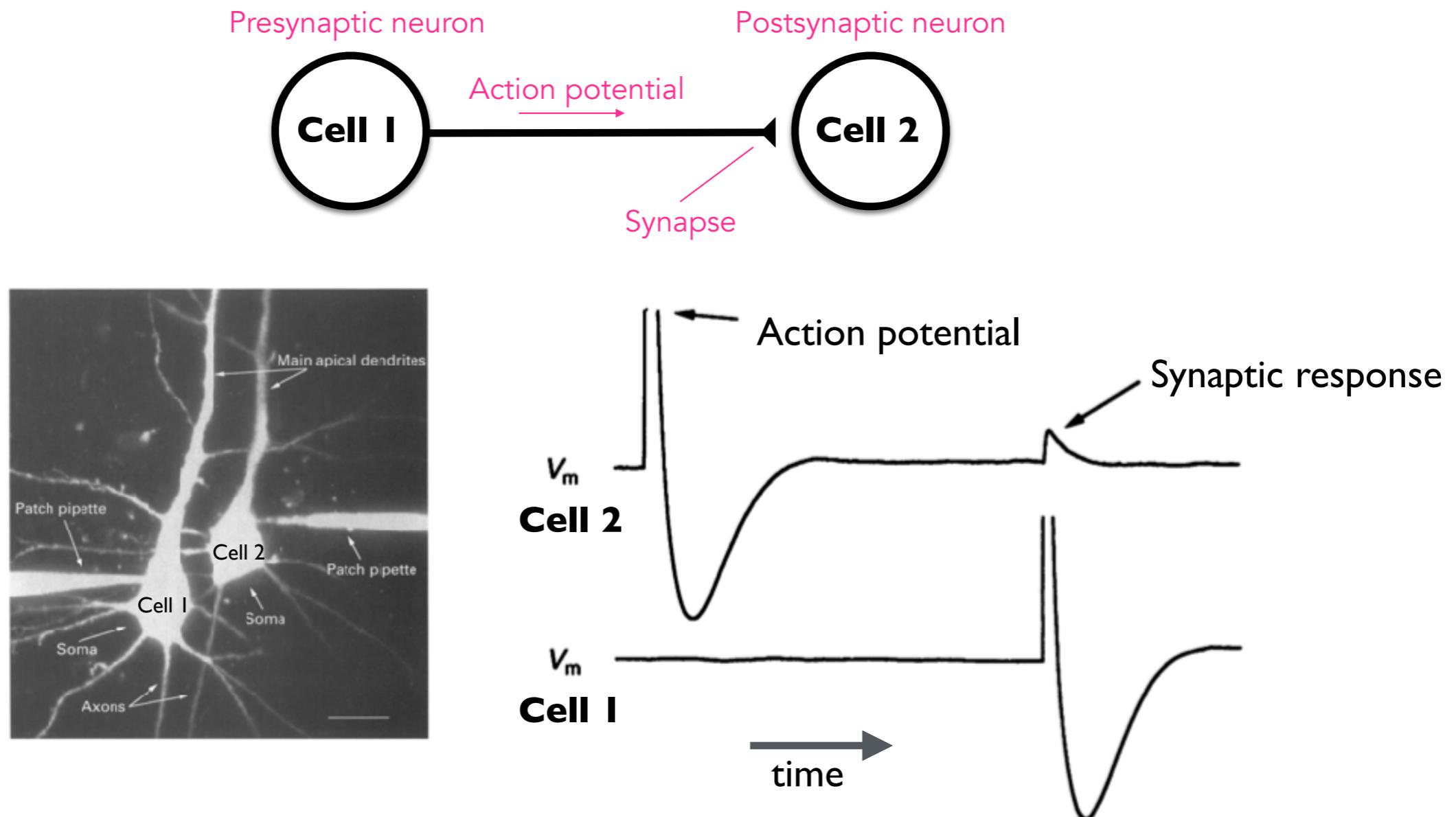


What is a synapse?



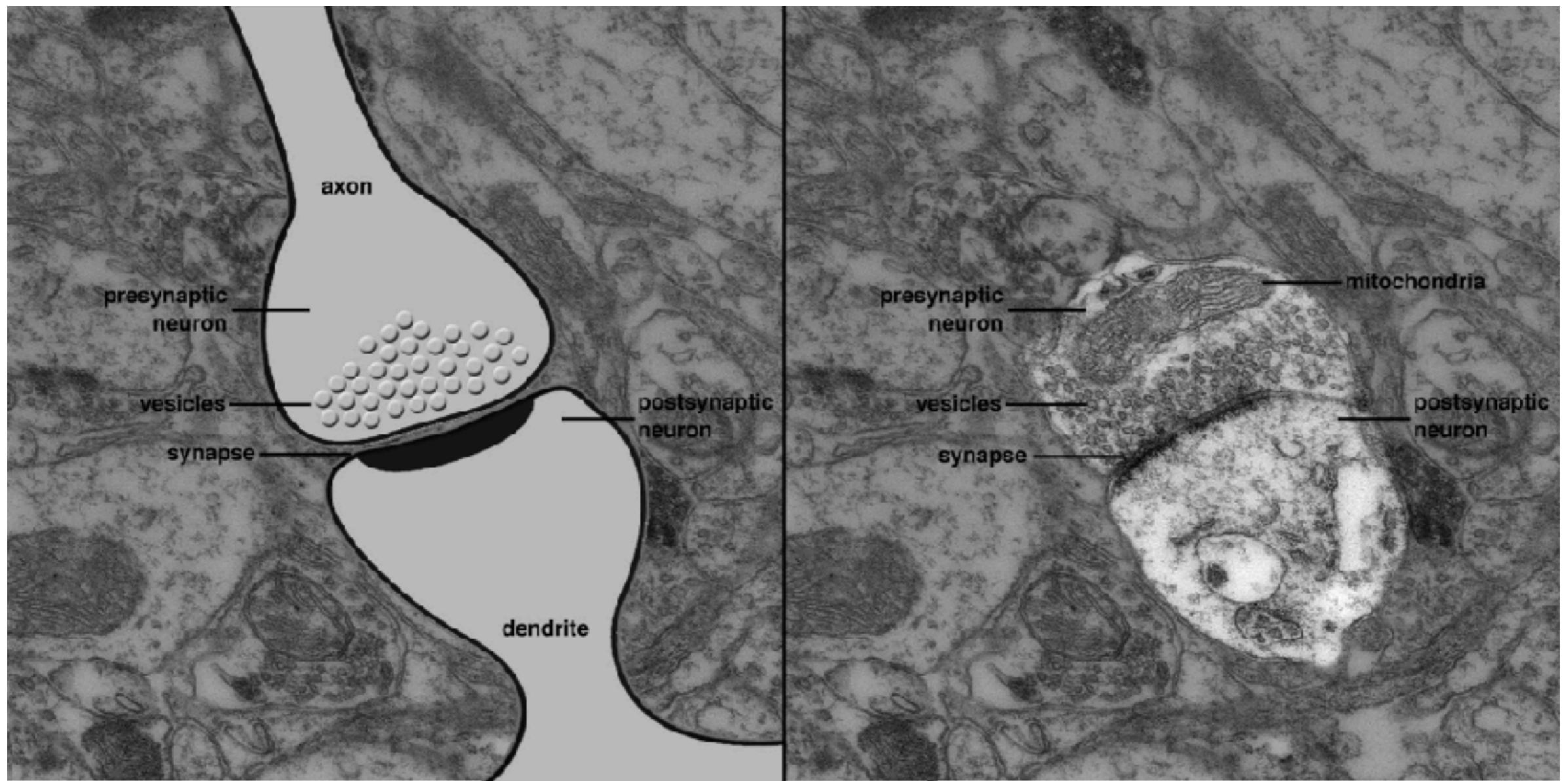
Markram et al, *J Physiol* (1997)

What is a synapse?



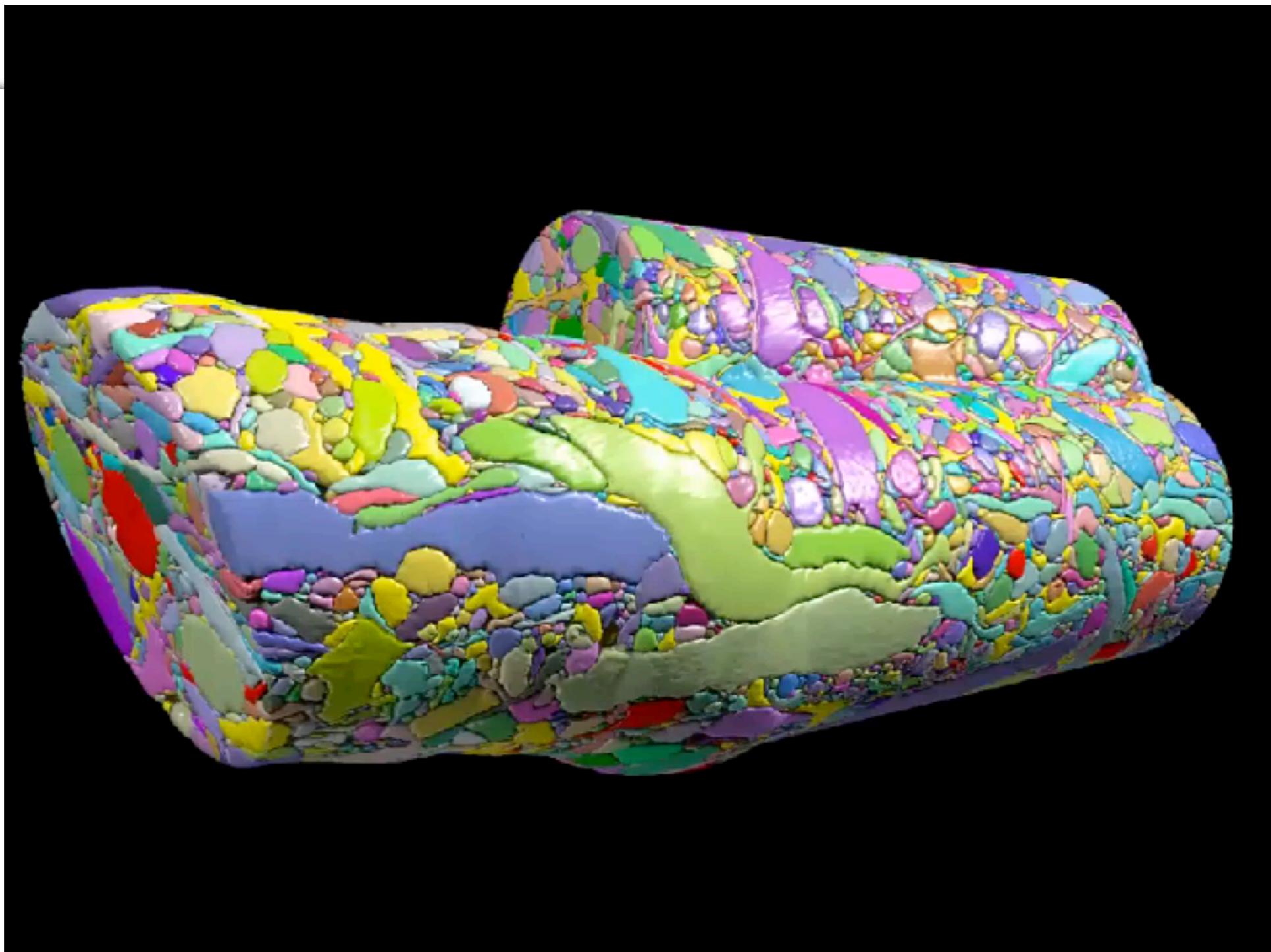
Markram et al, *J Physiol* (1997)

A closer look into synapses: electron microscopy



Finding synapses in the brain

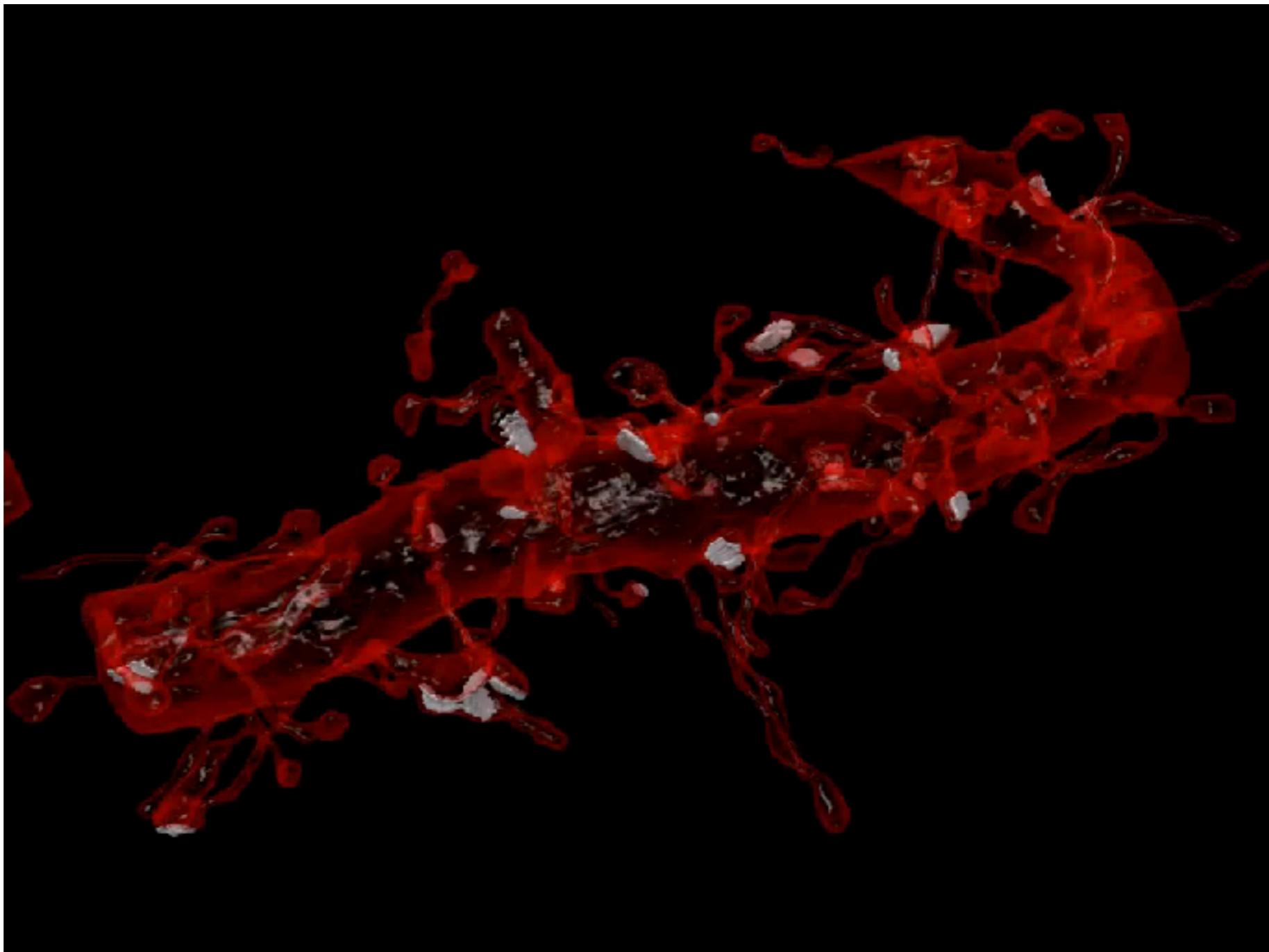
or a few micrometers of it



Using a combination of automatic and manual image segmentation.

Kasthuri et al. Cell 2015

Synapse reconstruction in a few micrometers!



Computational models of synapses

I. **Phenomenological** (abstracted out from molecular details)

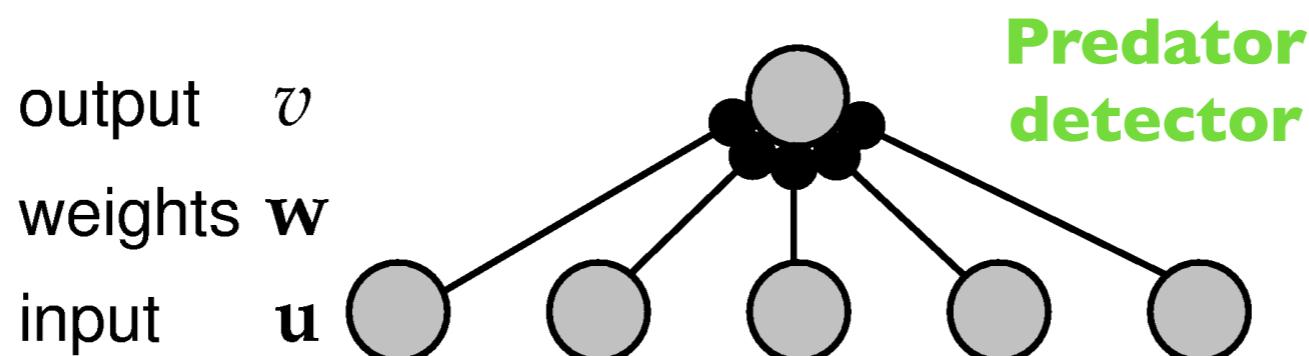
I.1. **Static**

I.2. **Stochastic**

I.3. **Time-dependent**

2. **Molecular**

Mathematical models of synapses: Static model



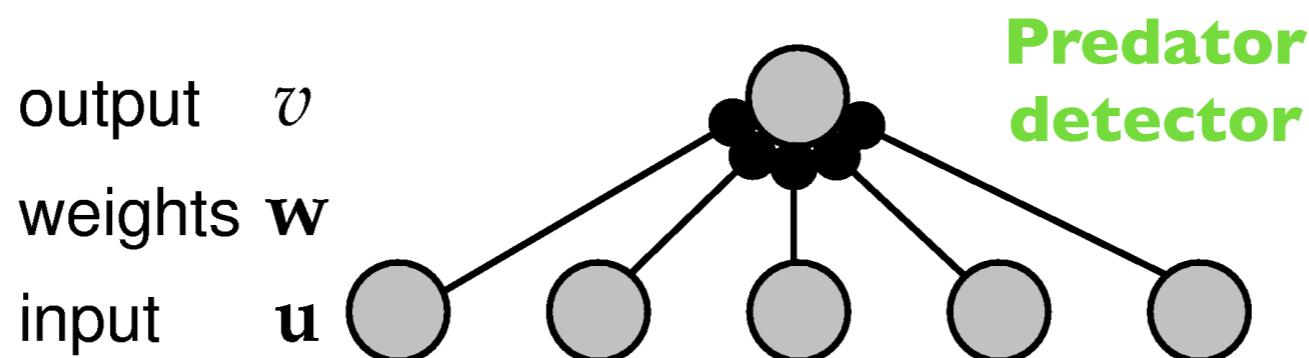
Task: Adjust w to detect predators given visual input u

Approach often taken when modelling complex neural networks [for simplicity]

$$v = f(wu), w \in \mathbb{R}$$

where f is some (non)linear function, and w a real number

Mathematical models of synapses: Static model



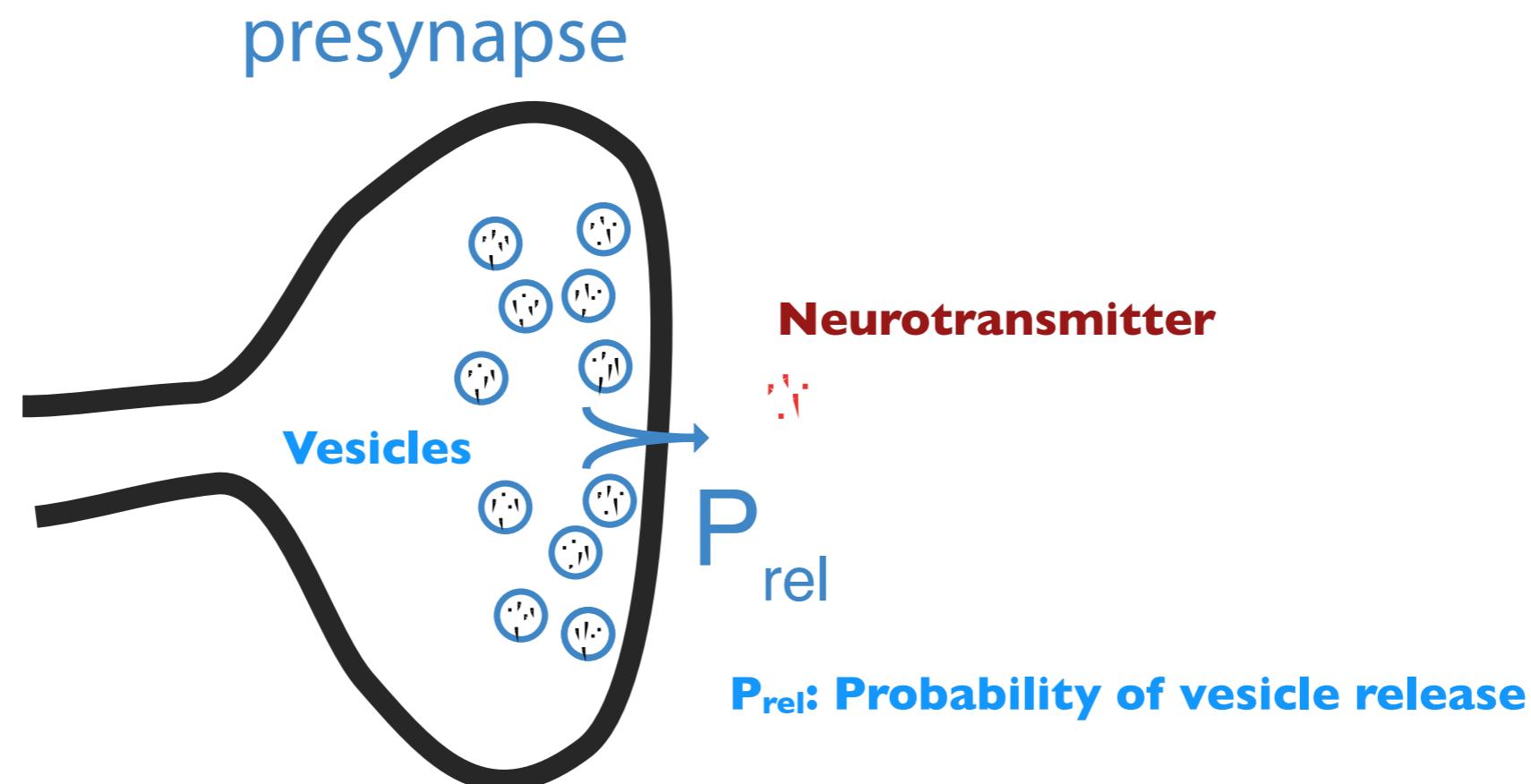
Task: Adjust w to detect predators given visual input u

$$v = f(wu), w \in \mathbb{R}$$

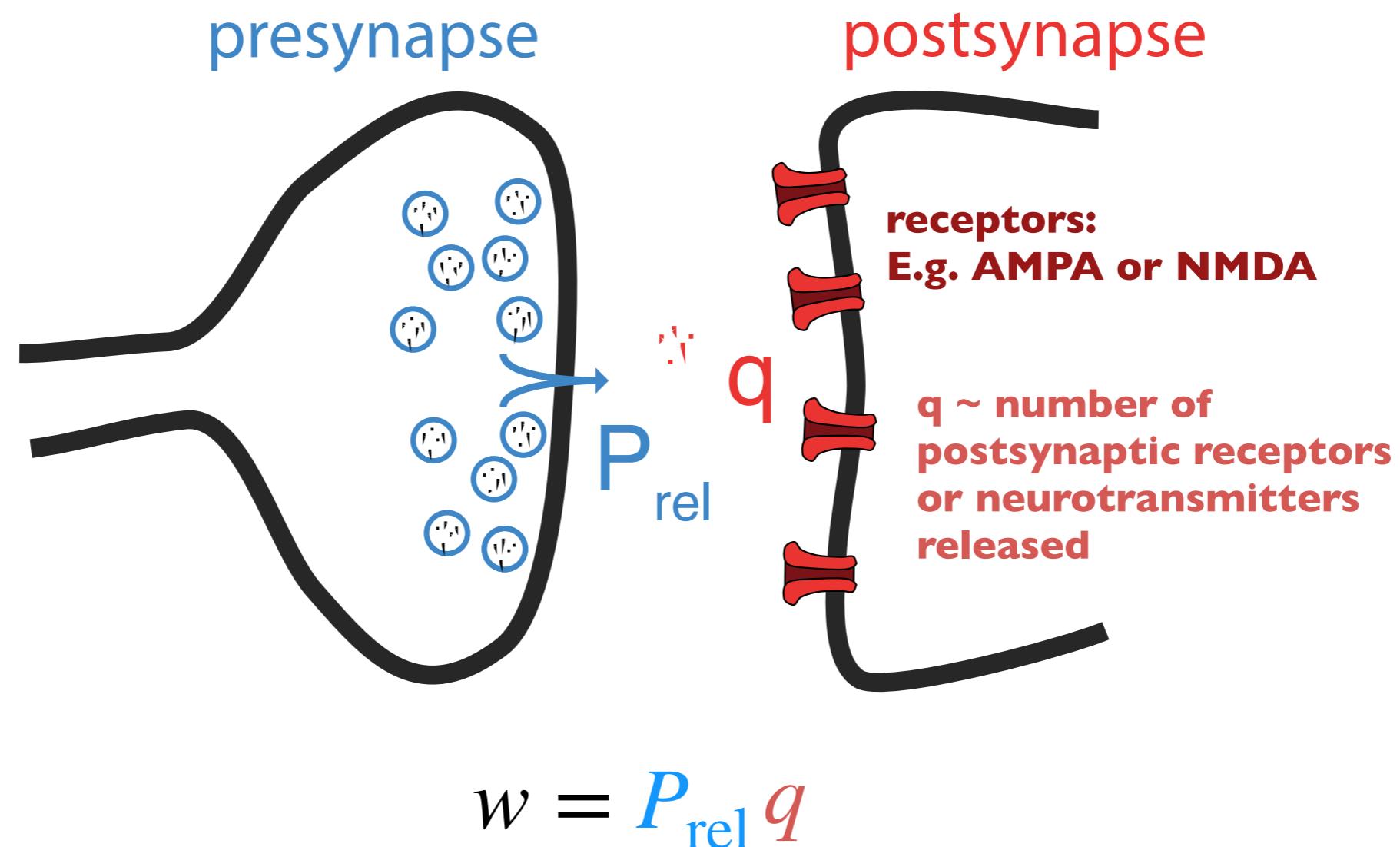
for excitatory synapses $w > 0$

for inhibitory synapses $w < 0$

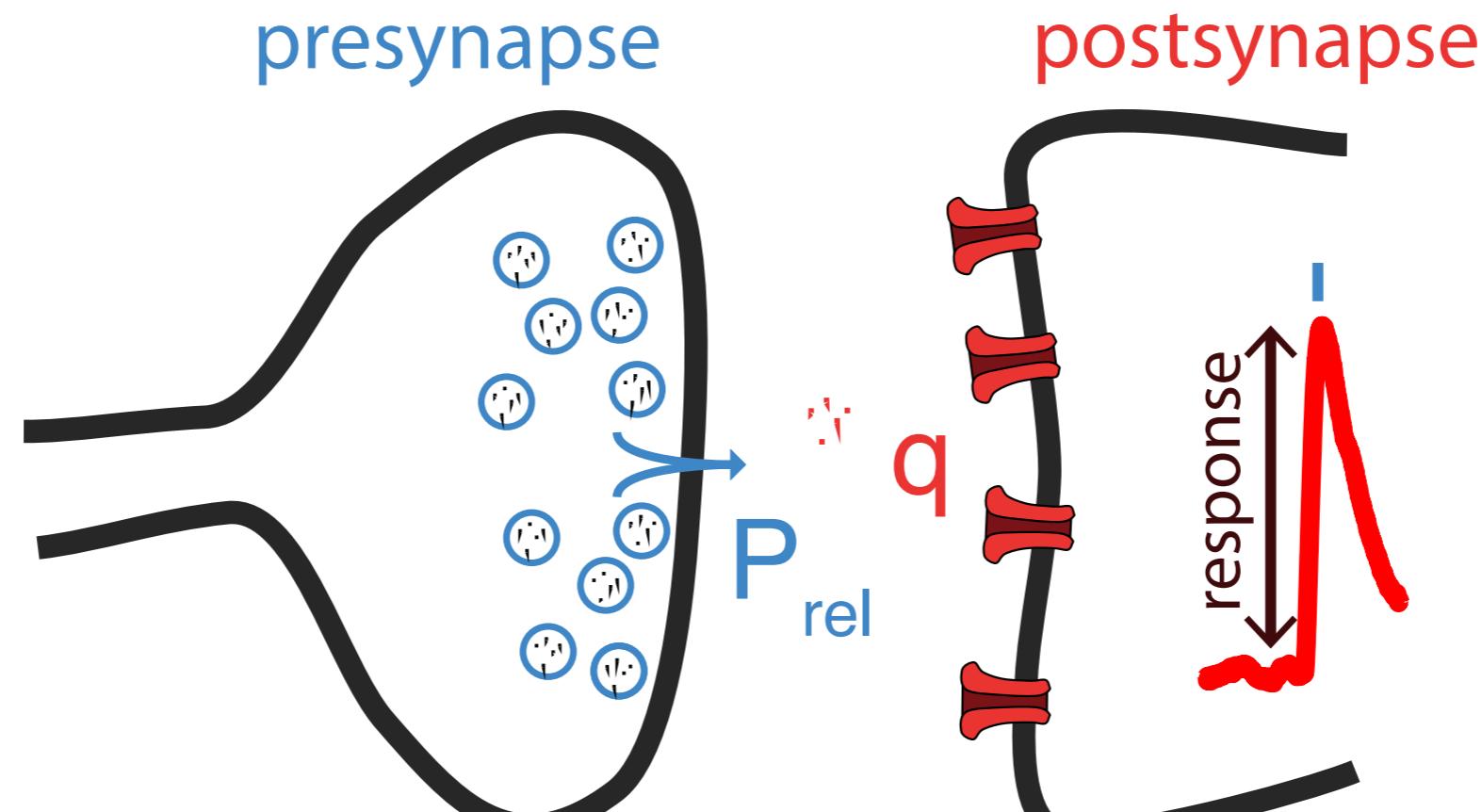
But synapses are more complex
than a simple real number



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than a simple real number



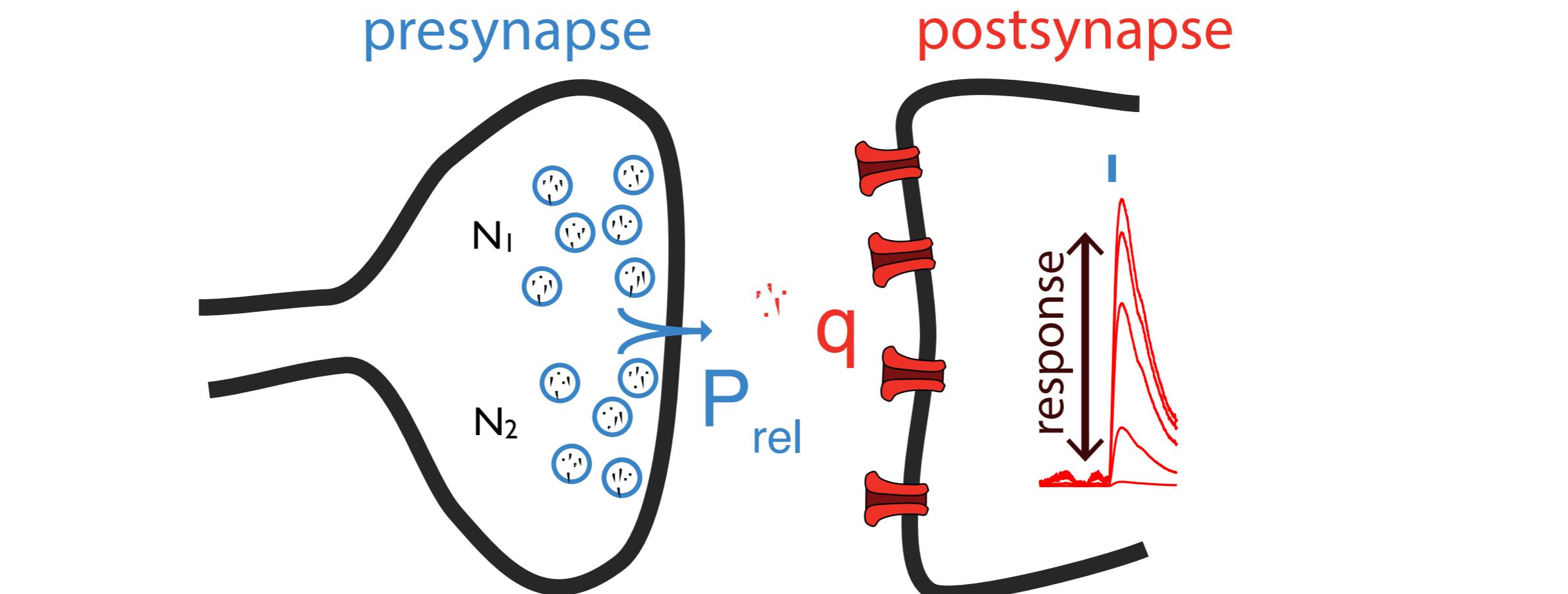
But synapses are more complex
than a simple real number



$$\text{response} \sim w = P_{\text{rel}} q$$

Mathematical models of synapses: Stochastic model

Synapses are stochastic, synaptic release may or may not occur, this leads to variability in the synaptic response.

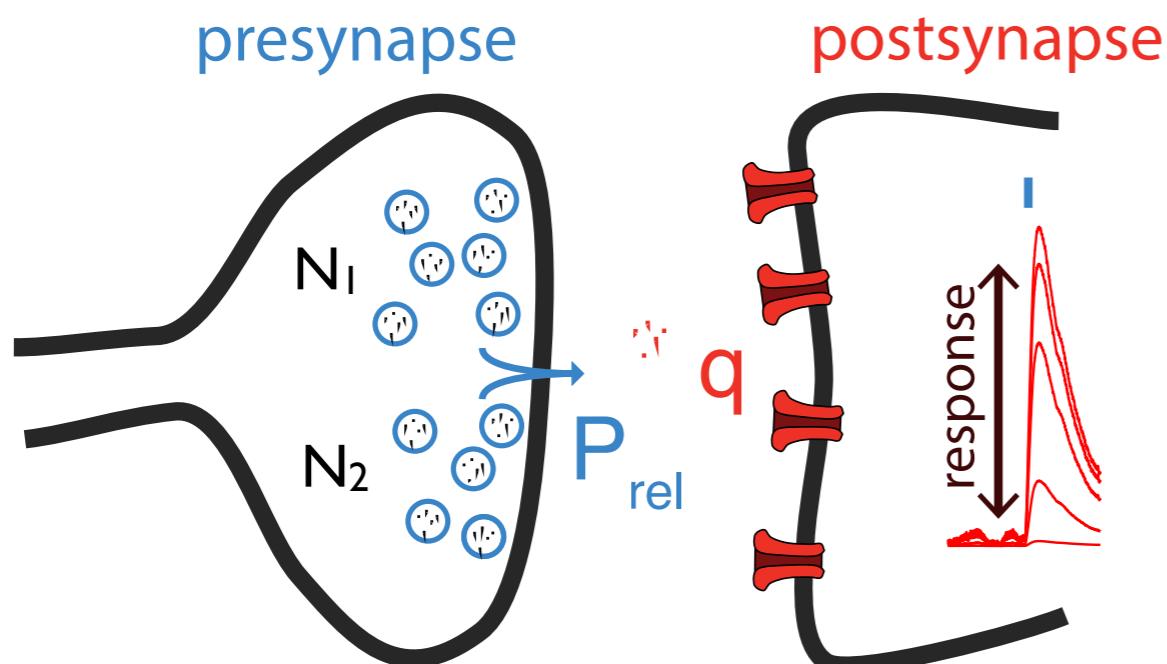


$$W \sim \text{Prob}(N, P_{\text{rel}}, q)$$

Del Castillo and Katz 1954 JPhysiology

Mathematical models of synapses: Stochastic model

Synapses are stochastic, synaptic release may or may not occur.



Binomial release model for response, W :

$$W \sim \text{Bin}(N, P_{\text{rel}})$$

$$P(W = k) = \binom{N}{k} P_{\text{rel}}^k (1 - P_{\text{rel}})^{N-k}$$

P_{rel} : release probability (of vesicles)

N : Number of release sites

k : Possible responses $[0, \dots, N]$

Mathematical models of synapses: Binomial release model

Binomial release model for response, W
scaled by the number of postsynaptic receptors q :

$$P(W = qk) = P(X = k) = \binom{N}{k} P_{\text{rel}}^k (1 - P_{\text{rel}})^{N-k}$$

Mathematical models of synapses: Binomial release model

Binomial release model for response, W
scaled by the number of postsynaptic receptors q :

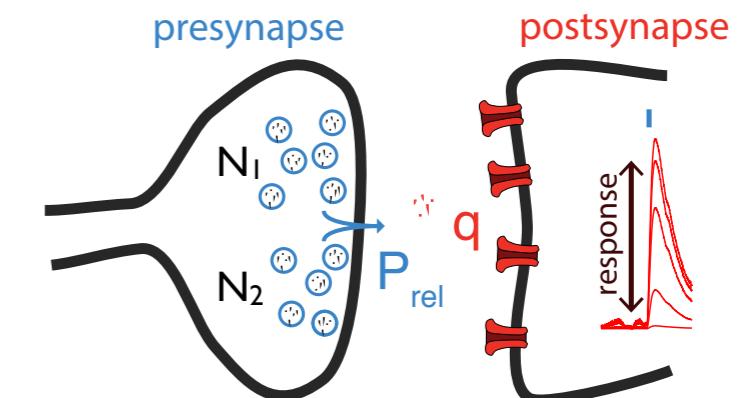
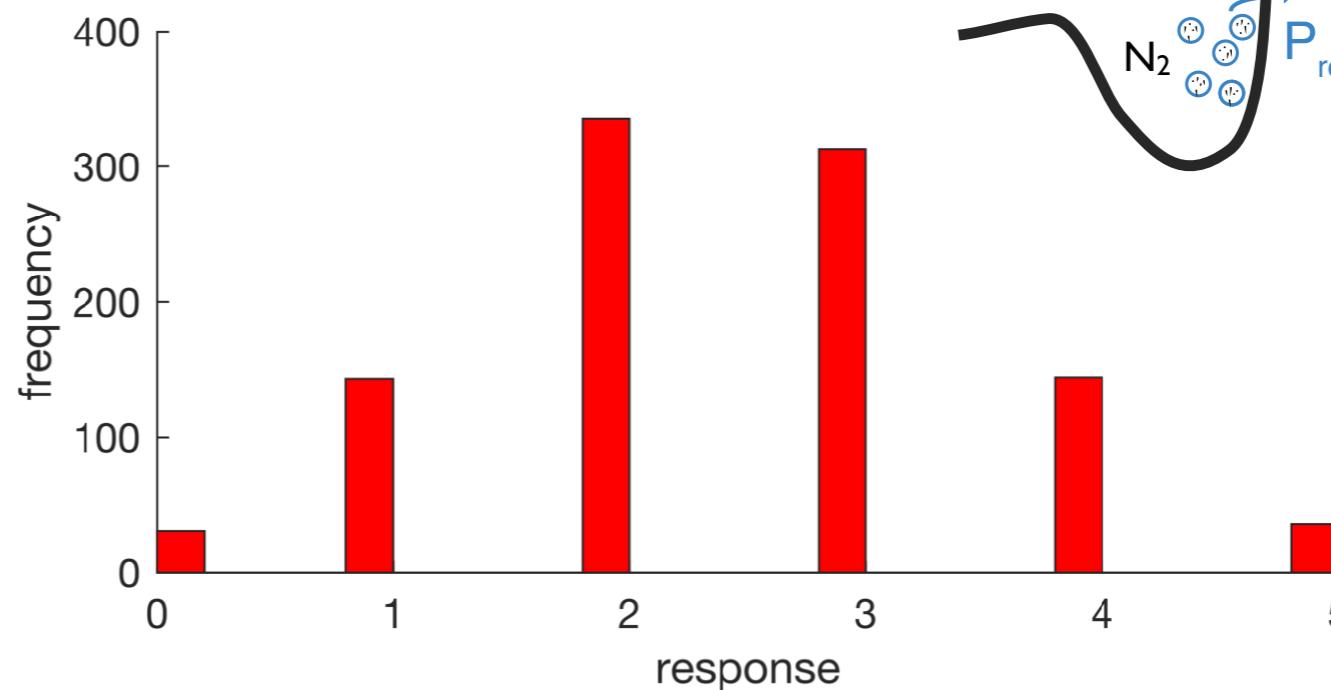
$$P(W = qk) = P(X = k) = \binom{N}{k} P_{\text{rel}}^k (1 - P_{\text{rel}})^{N-k}$$

$P_{\text{rel}}: 0.5$

$q: 1$

$N: 5$

$k: [0, \dots, 5]$



demo!

Mathematical models of synapses: Time-dependent models

These type of models are commonly used!

Recall the simple leaky integrate-and-fire neuron from the previous lecture:

$$\frac{dV}{dt} = V_{\text{rest}} - V + I_{\text{syn}}(t)$$

Mathematical models of synapses: Time-dependent models

These type of models are commonly used!

Recall the simple leaky integrate-and-fire neuron from the previous lecture:

$$\frac{dV}{dt} = V_{\text{rest}} - V + I_{\text{syn}}(t)$$

$$V_{\text{rest}} \sim -60 \text{ mV}$$

Current-based models:

$$I_{\text{syn}}(t) = \bar{g}_{\text{syn}} s(t)$$

Conductance-based models:

$$I_{\text{syn}}(t) = \bar{g}_{\text{syn}} s(t)(E_{\text{syn}} - V)$$

where g is the maximum synaptic strength.

and E_{syn} is the reversal potential, which determines the ‘sign’ of a synapse:

for **excitatory** synapses $E_{\text{syn}} \sim 0 \text{ mV} \sim I_{\text{syn}} > 0$

for **inhibitory** synapses $E_{\text{syn}} \sim V_{\text{rest}} \sim I_{\text{syn}} < 0$

Mathematical models of synapses: Time-dependent models

$s(t)$ defines the shape of the synaptic input, how can we model it?

Single exponential:

$$s(t) = \exp^{-\frac{(t - t_{\text{spike}})}{\tau_{\text{decay}}}}$$

Mathematical models of synapses: Time-dependent models

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Mathematical models of synapses: Time-dependent models

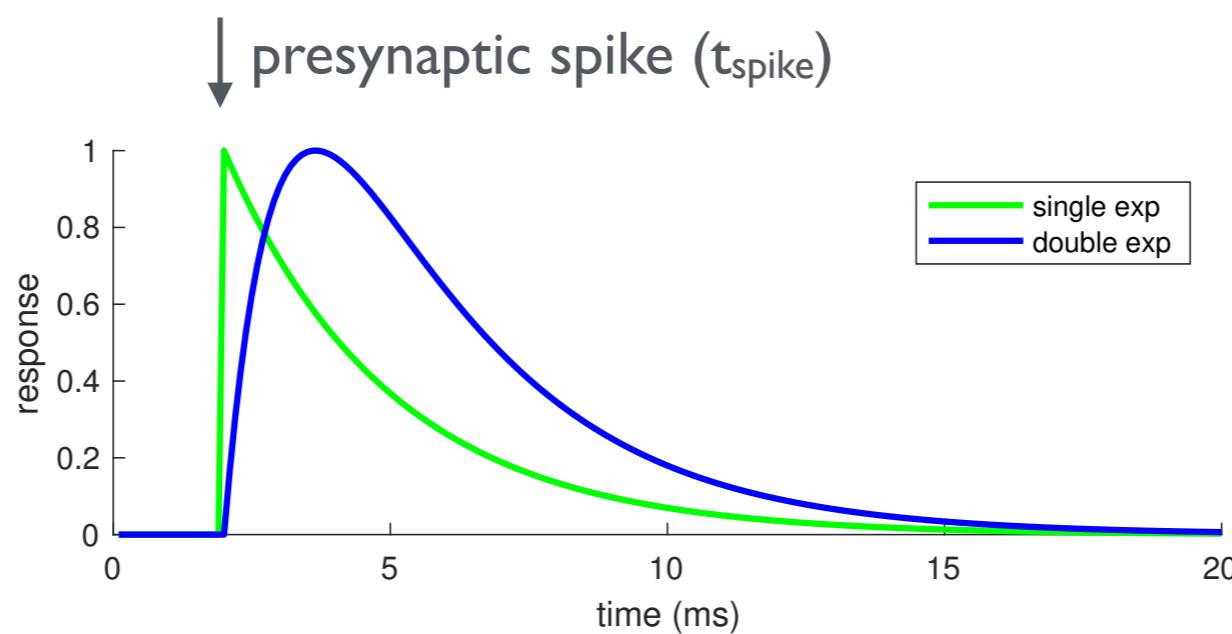
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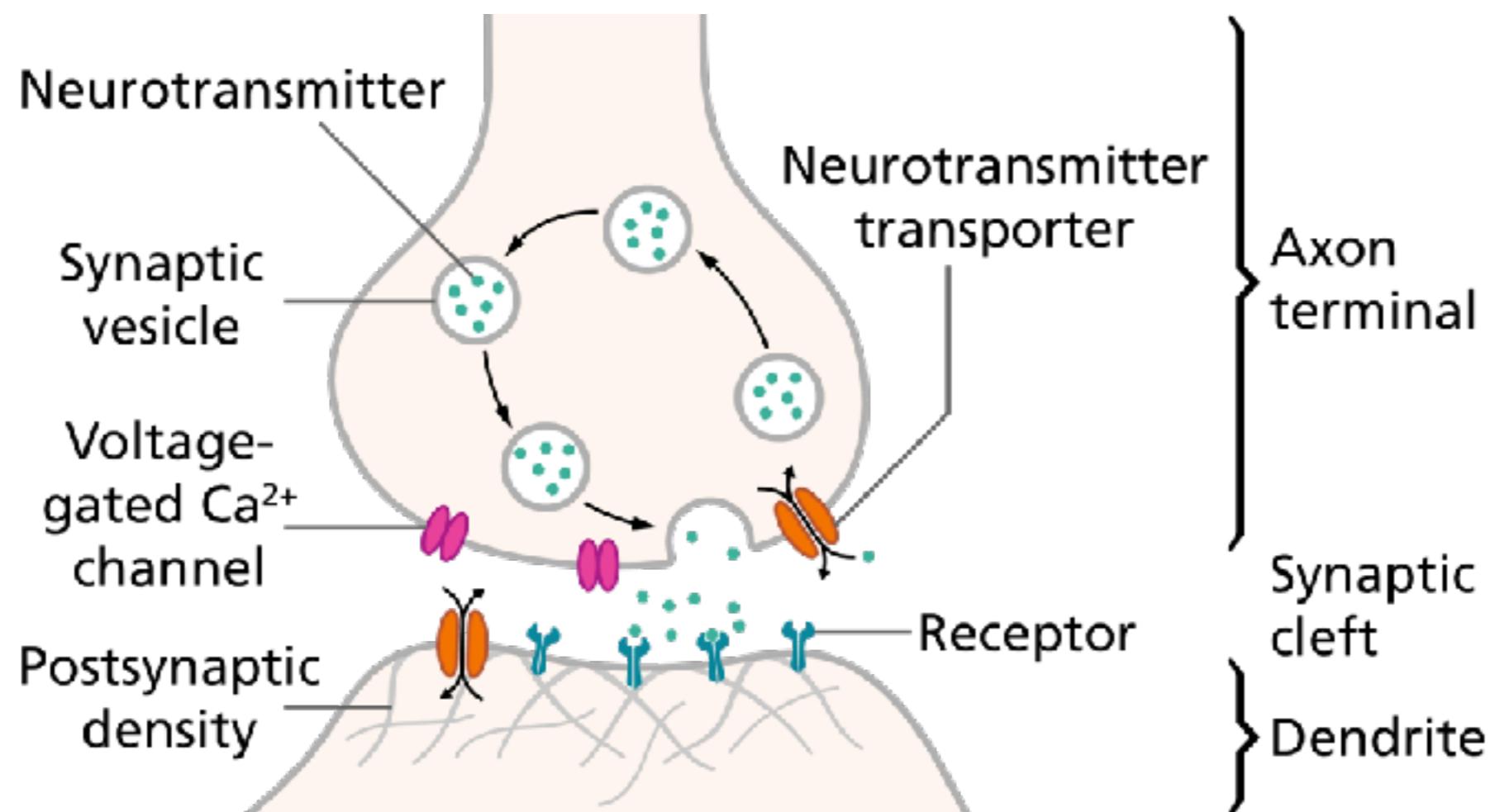
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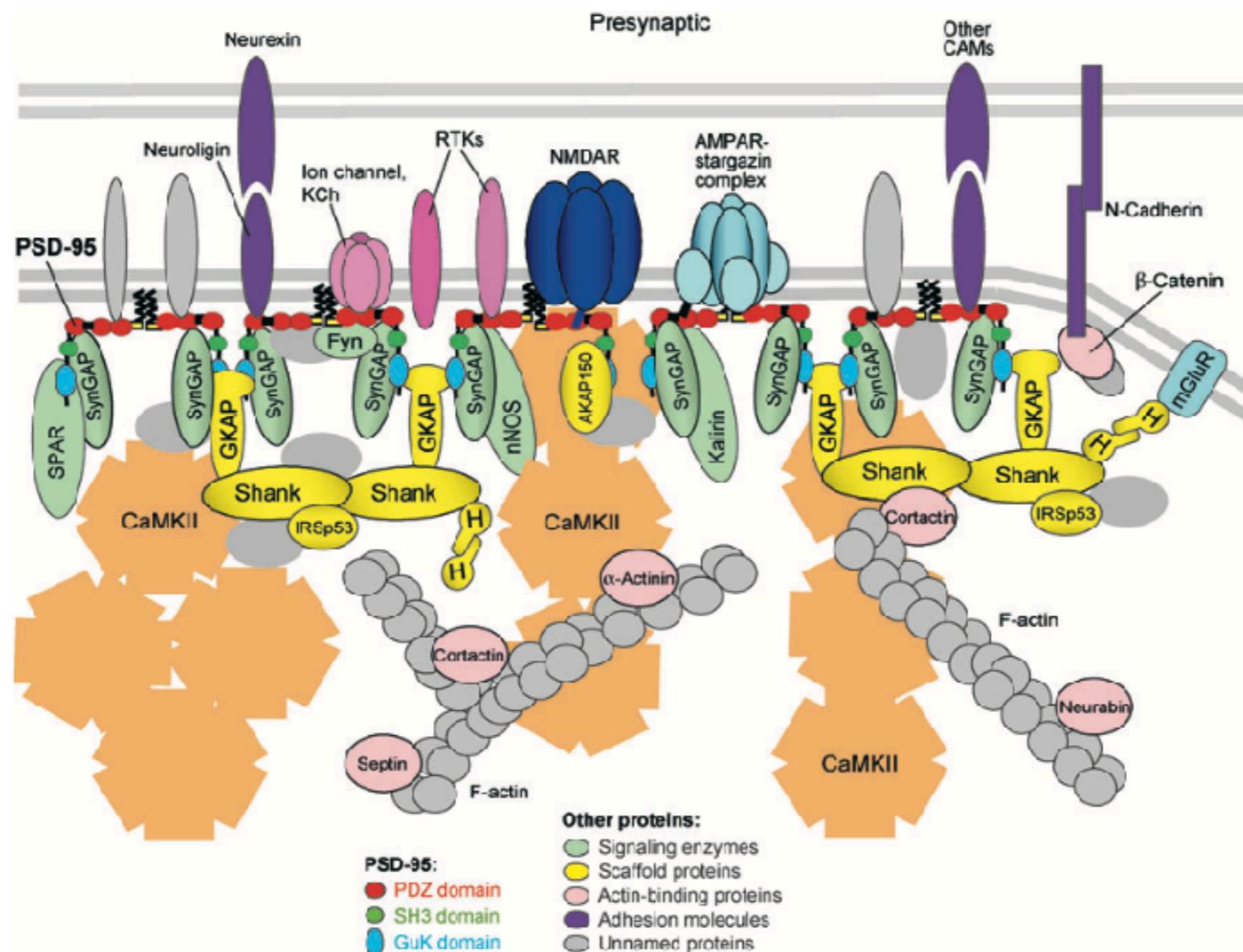


Synapses as dynamic/complex systems?



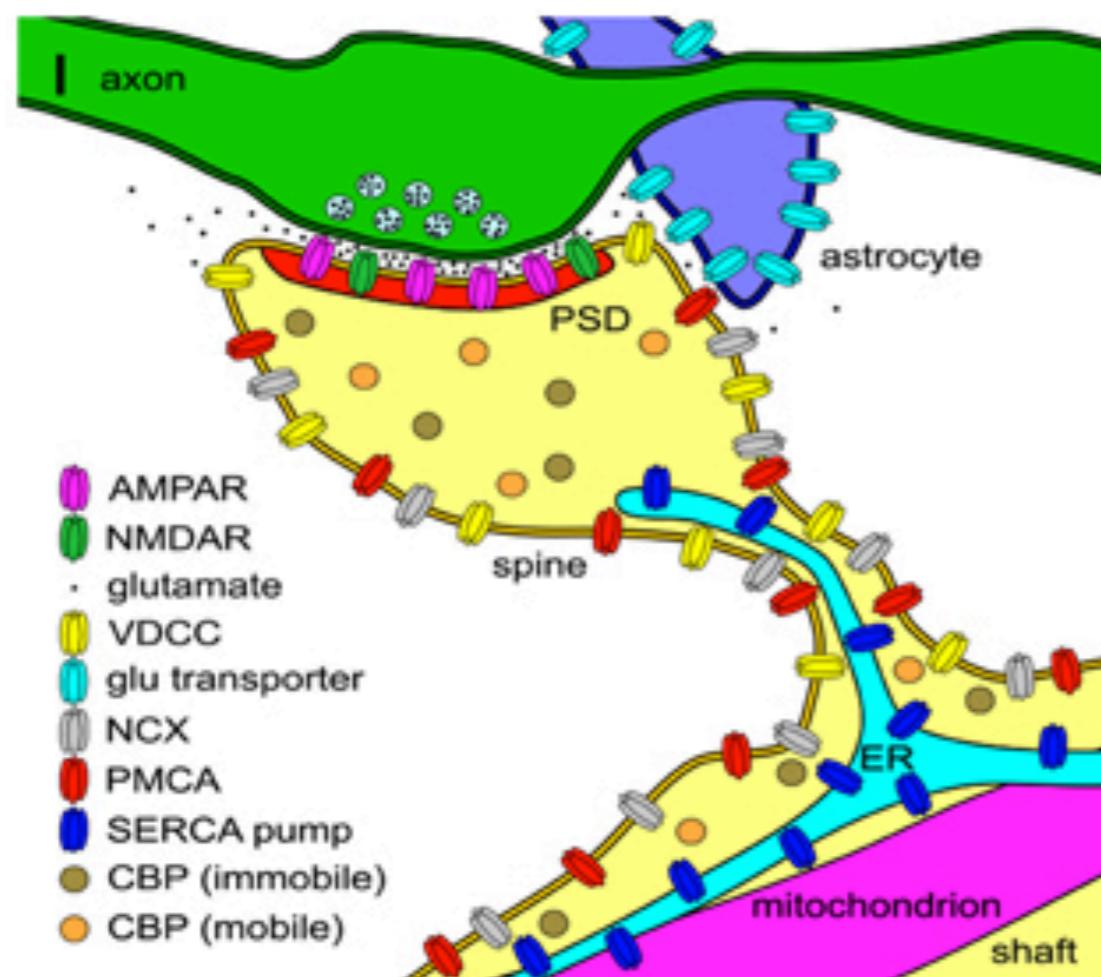
wikipedia.org;
Kandel, Schwartz and Jessell 2012

Mathematical models of synapses: Molecular models



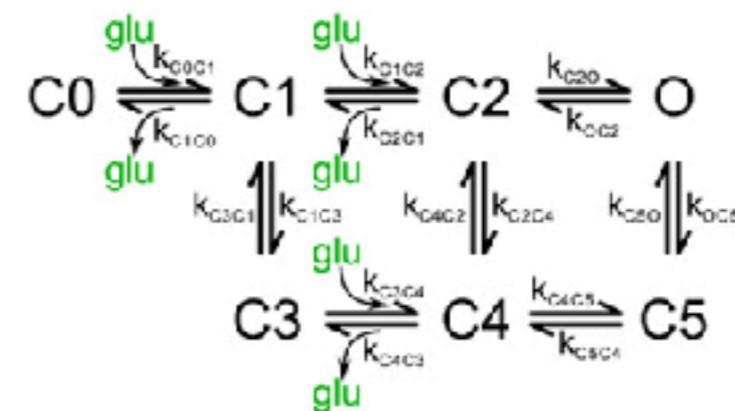
Sheng and Hoogenraad, Annu Rev Neurosci (2007)

Mathematical models of synapses: Molecular models



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

Markov model of AMPA receptor:



AMPAR

video!

by Tom Bartol (Salk Institute, California)

Summary: synapses

1. Synapses are crucial for brain functioning
2. Synapses have two components: *presynapse* and *postsynapse*
3. Each is a complex system in itself
4. Different levels of abstraction for synaptic modelling:
static, stochastic, time-dependent and *molecular*.

Group discussion

[groups of 2-3 (5 min)]

- What are the **advantages** and **disadvantages** of the different synaptic models?

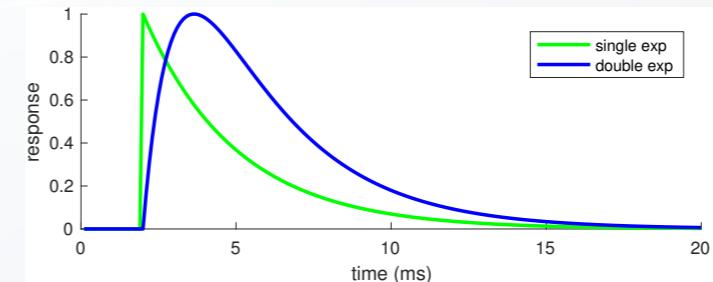
Hint: Think of the biological detail vs computational costs

I. Phenomenological

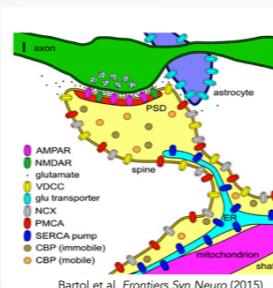
I.1. Static $w \in \mathbb{R}$

I.2. Stochastic $W \sim \text{Bin}(N, P_{\text{rel}})$

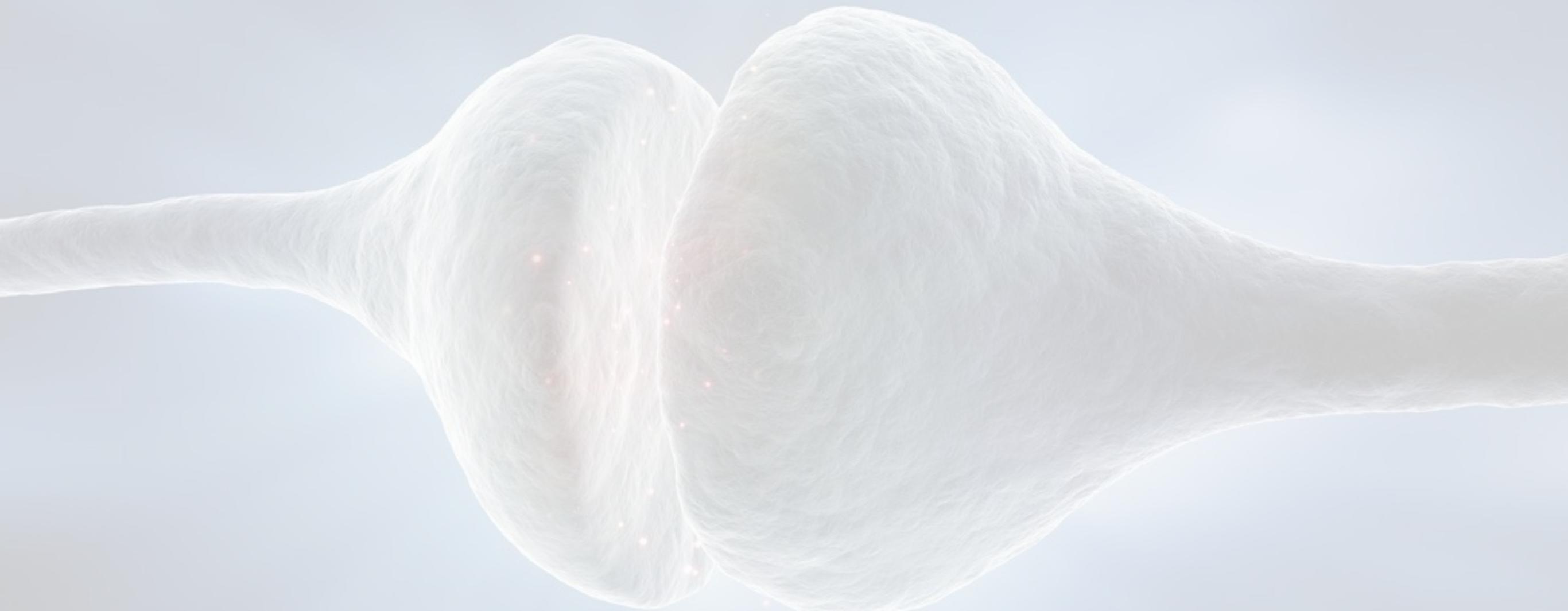
I.3. Time-dependent



2. Molecular

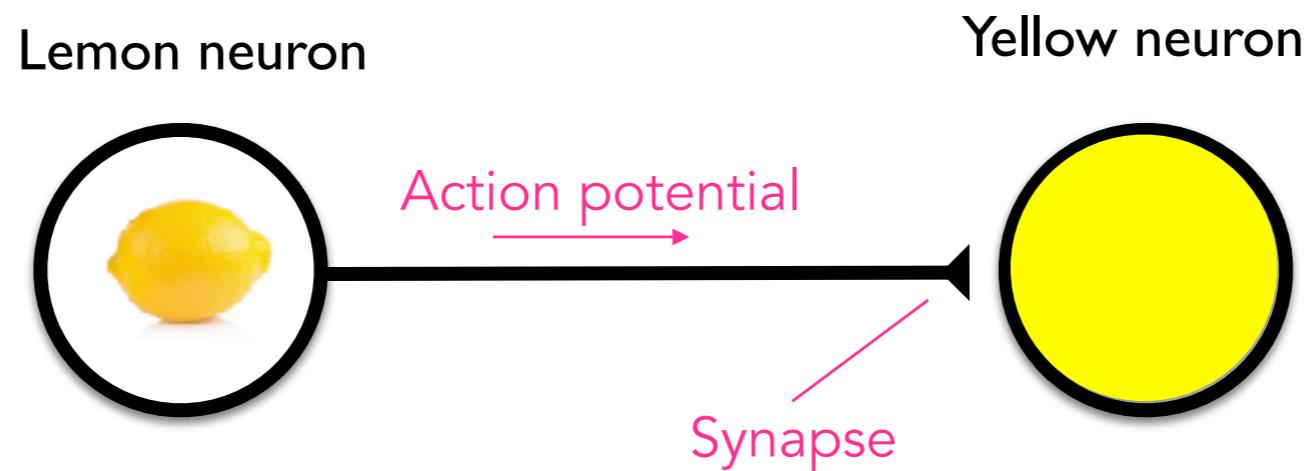


Questions?



Synaptic plasticity

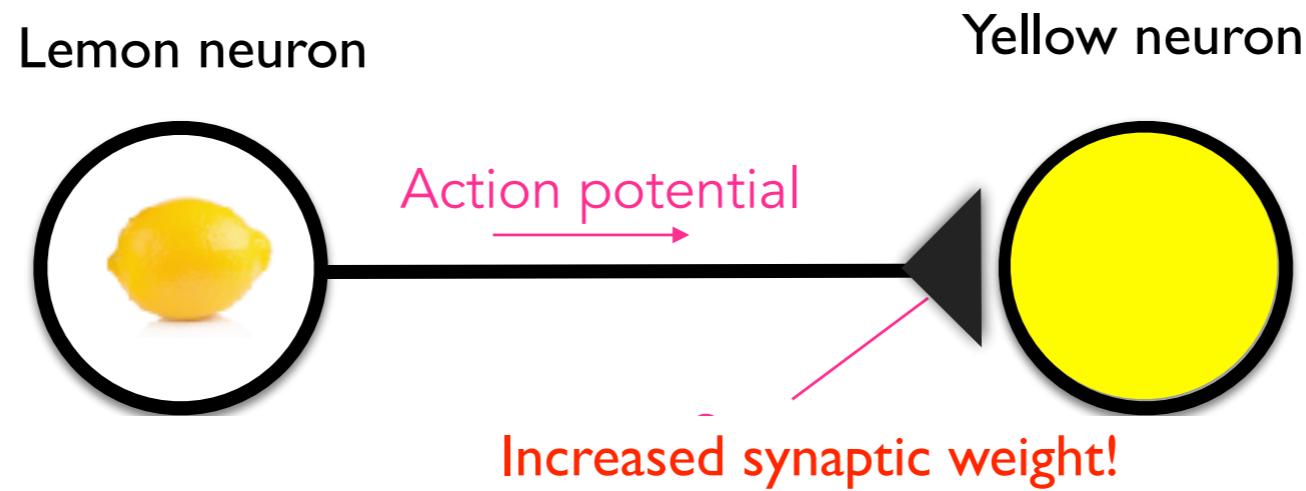
- *Synaptic plasticity* refers to changes to the synaptic properties (typically synaptic weight, W)
- Such changes are believed to underlie *learning* and *memory*



- Because **lemon** and **yellow** tend to occur together, it is likely that when you see yellow you think of lemons (or the sun, etc.). It is useful for the brain to capture these features in the world, and store them through changes in the *synaptic weights*.

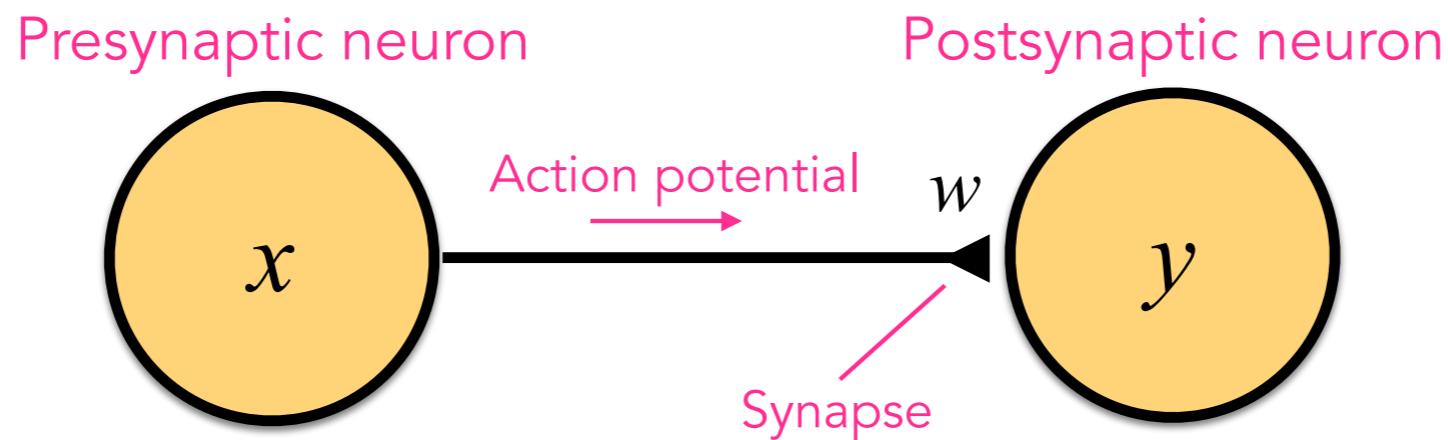
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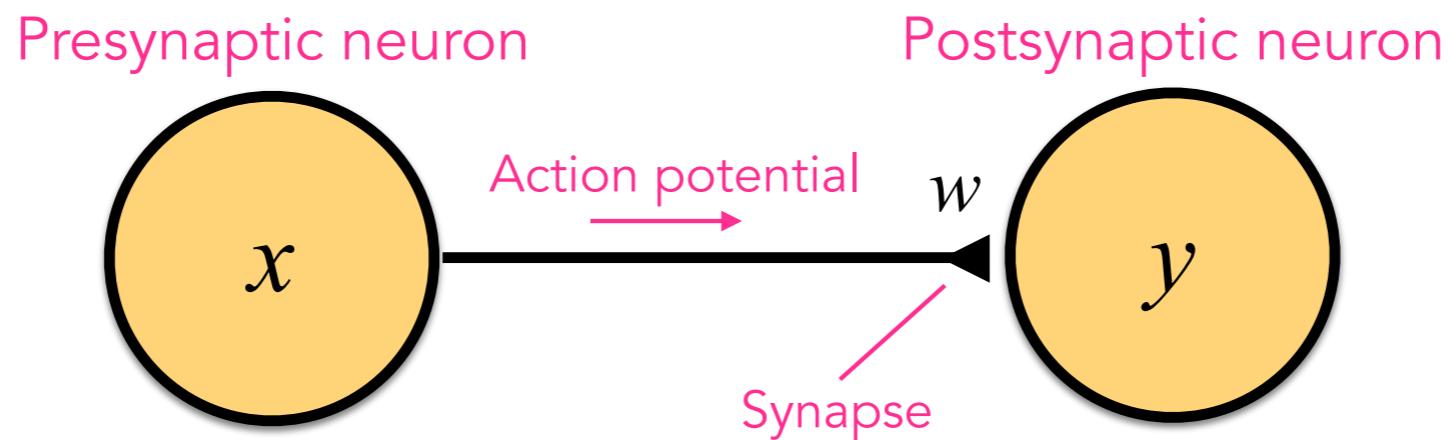
Synaptic plasticity



- *Synaptic plasticity can be formulated as a change in W (ΔW), which is a function of pre- and postsynaptic activity (x and y , respectively):*

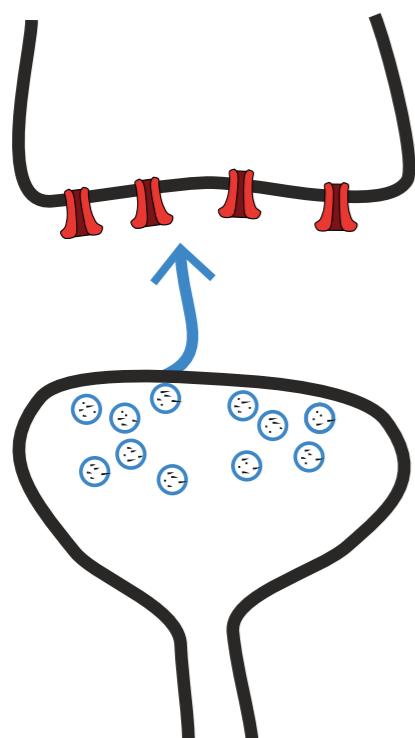
$$\Delta w = f(x, y) = ???$$

Synaptic plasticity



- *Synaptic plasticity can be formulated as a change in W (ΔW), which is a function of pre- and postsynaptic activity (x and y , respectively):*
$$\Delta w = f(x, y) = xy$$
- This is a very simple form of *correlation-based* or *Hebbian learning rules* [see next lectures].

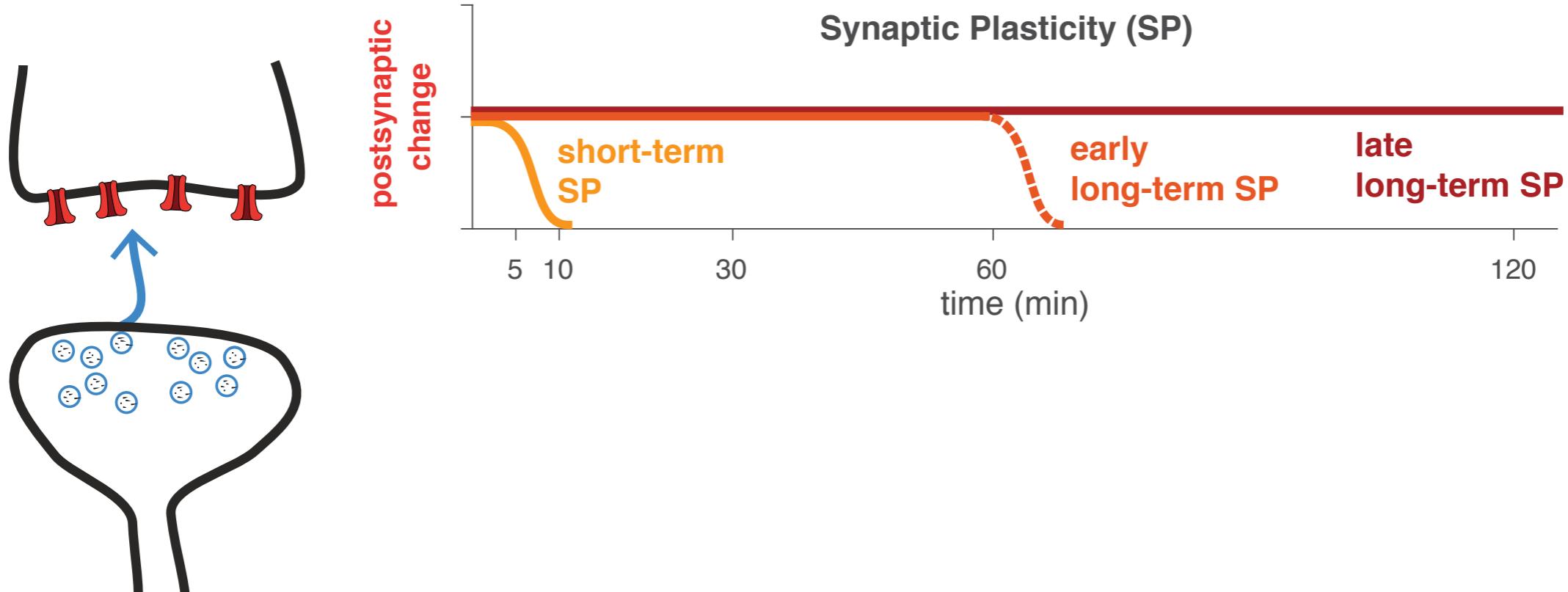
Synaptic plasticity: when and where?



Synaptic plasticity: Multiple timescales and locations

Synapses can change **postsynaptically**

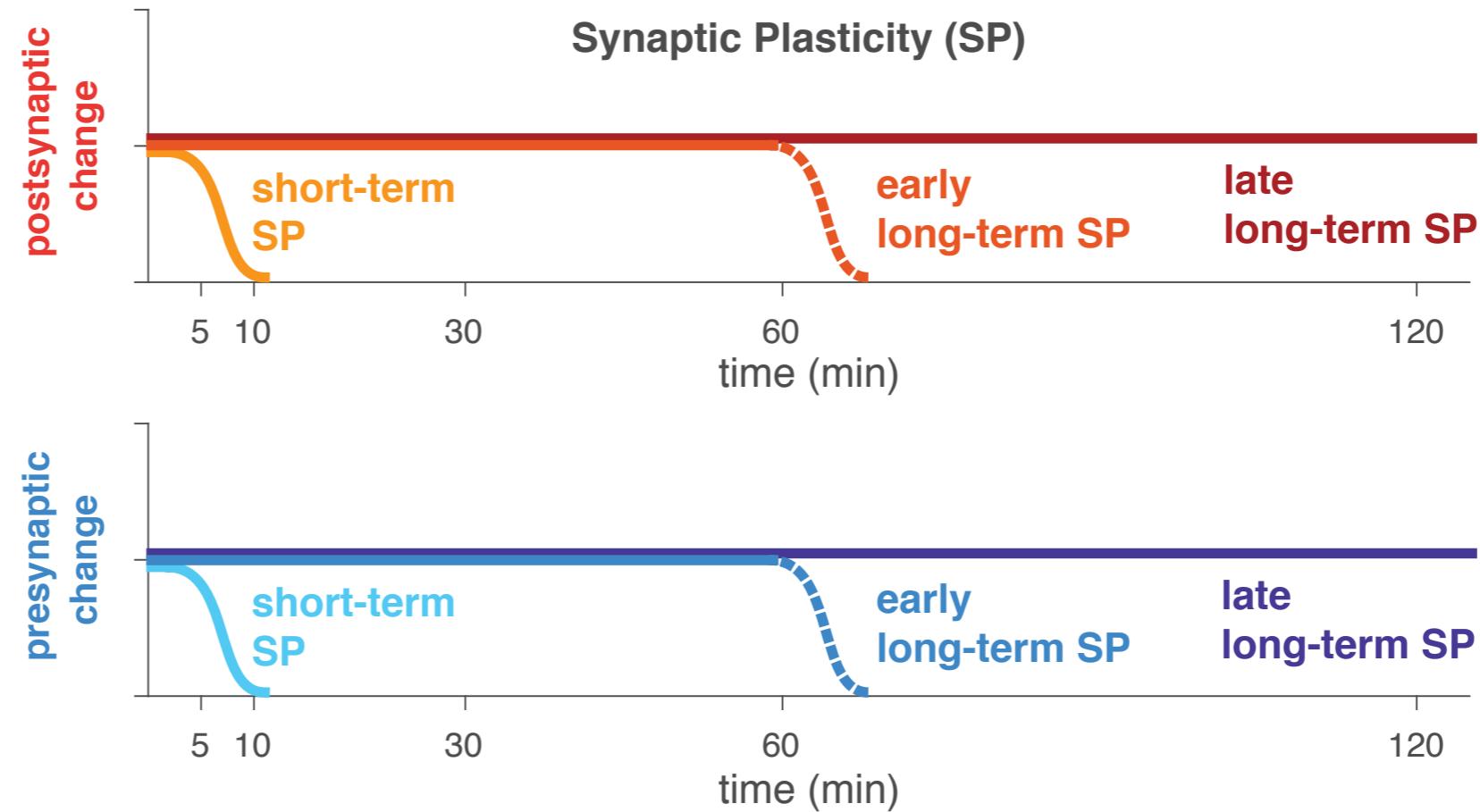
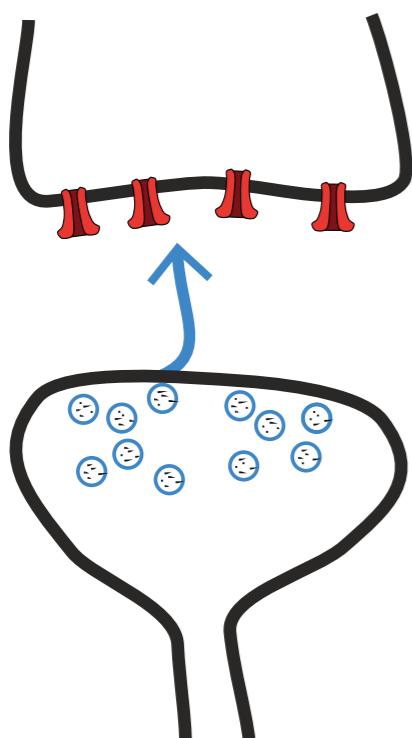
(from a few seconds (**short-term**) to tens of minutes, hours (**long-term**) or even days/years!):



Synaptic plasticity: Multiple timescales and locations

But they can also change **presynaptically**

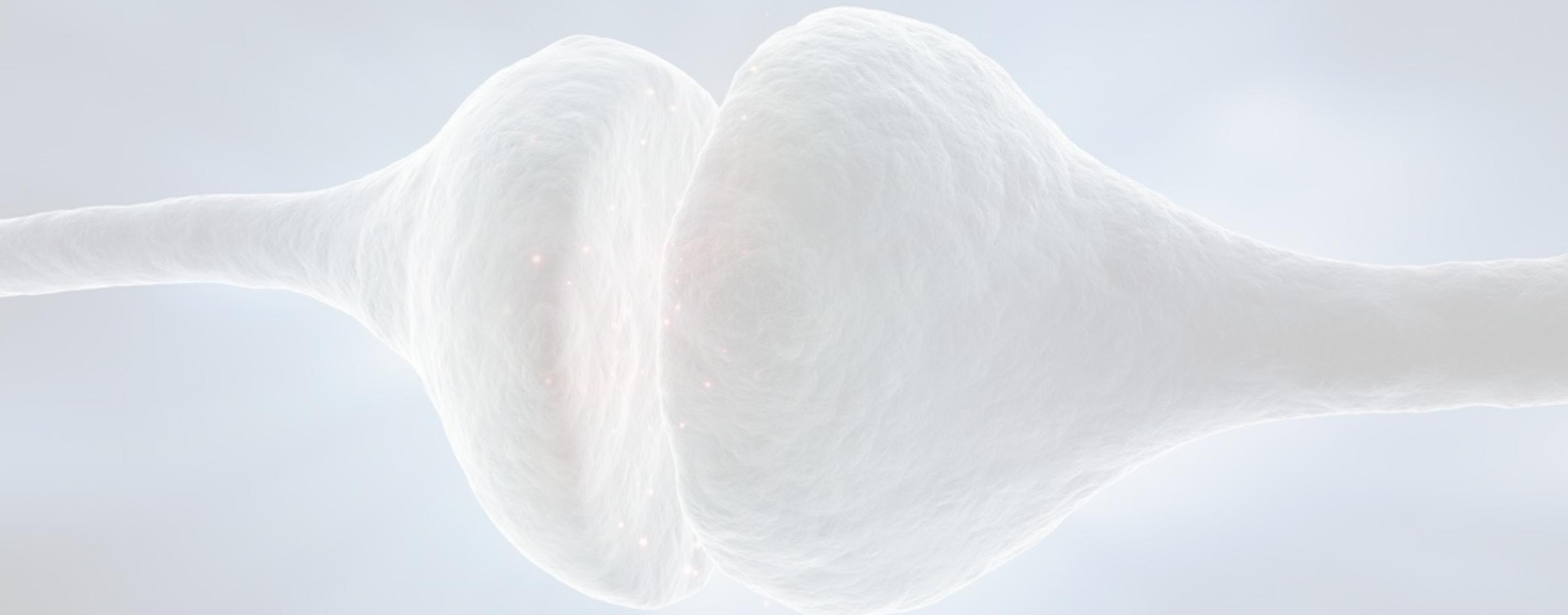
(from a few seconds (**short-term**) to tens of minutes, hours (**long-term**) or even days/years!):



Summary: synaptic plasticity

1. Synaptic plasticity underlies learning & memory
2. Different models can be formulated to adjust the synaptic weights
3. Occurs across multiple locations and timescales
4. Next lecture: Short-term synaptic plasticity

Questions?



References

Text books:

General neuroscience: Wikipedia/Principles of neuroscience by Kandel, Schwartz and Jessell 2012 [neuroscience bible]

Computational Neuroscience: Neuronal Dynamics by Gerstner, Kistler, Naud and Paninski

Computational Neuroscience: Principles of Computational Modelling in Neuroscience by Sterratt, Gillies, Graham and Willshaw

[Chapter on Synaptic modelling: http://dai.fmph.uniba.sk/courses/comp-neuro/reading/Sterratt_CH7_synapse.pdf]