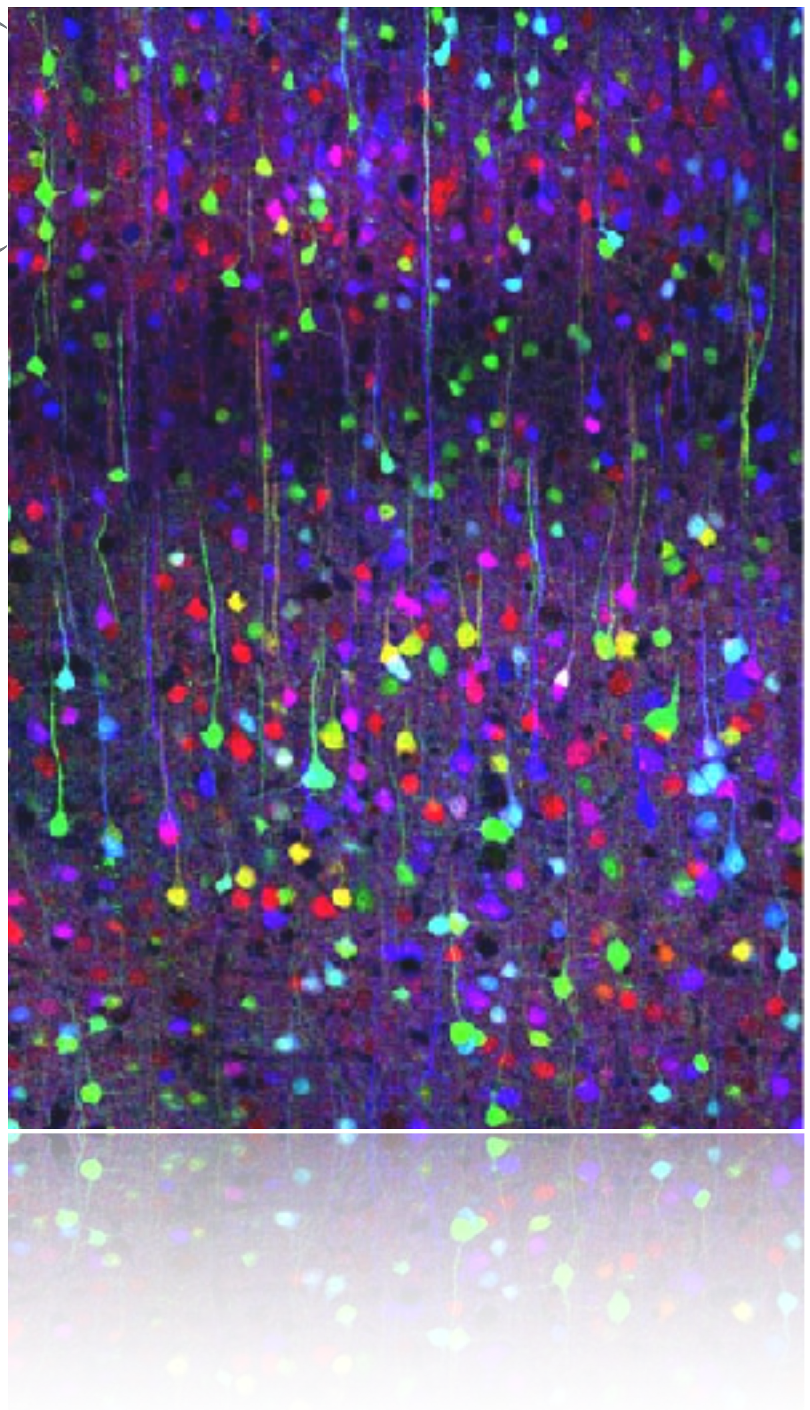
# Computational Neuroscience 2018/2019

University of BRISTOL

Brainbow (Litchman Lab)

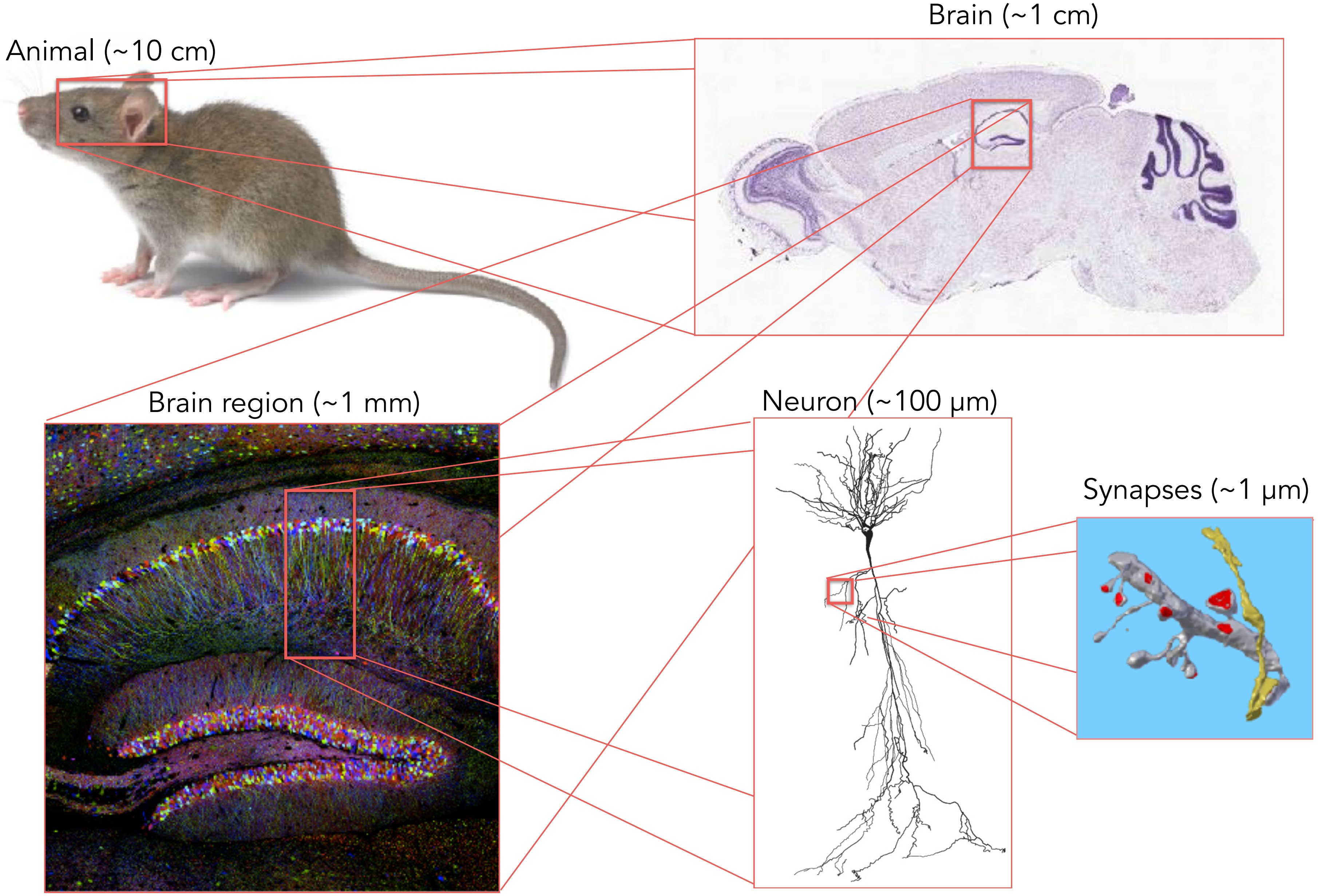


## Lecture 15
## Synapses and synaptic plasticity

# Outline

1. **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**

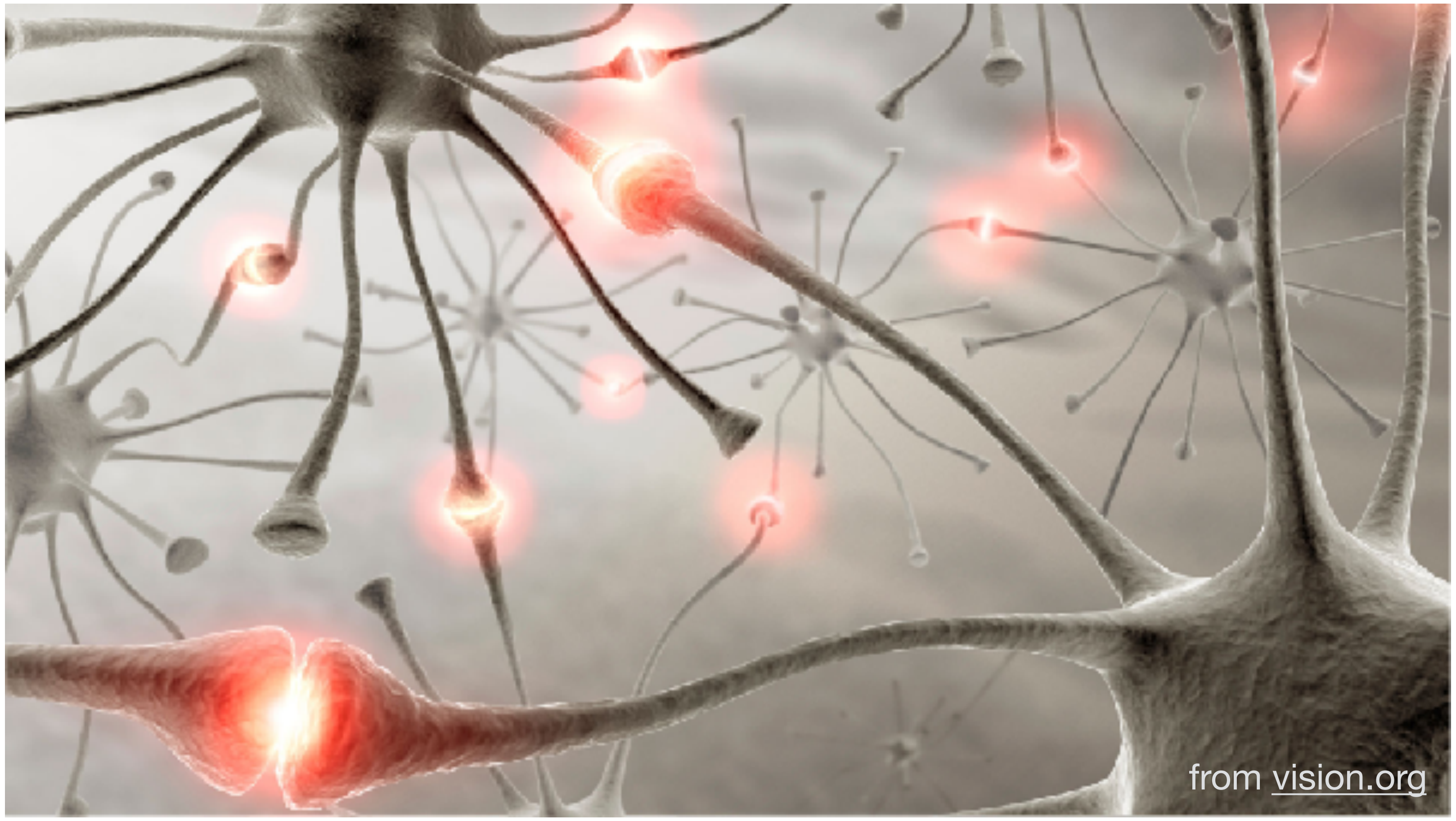
# Zooming in on the synapse




Adapted from Cian O'Donnell

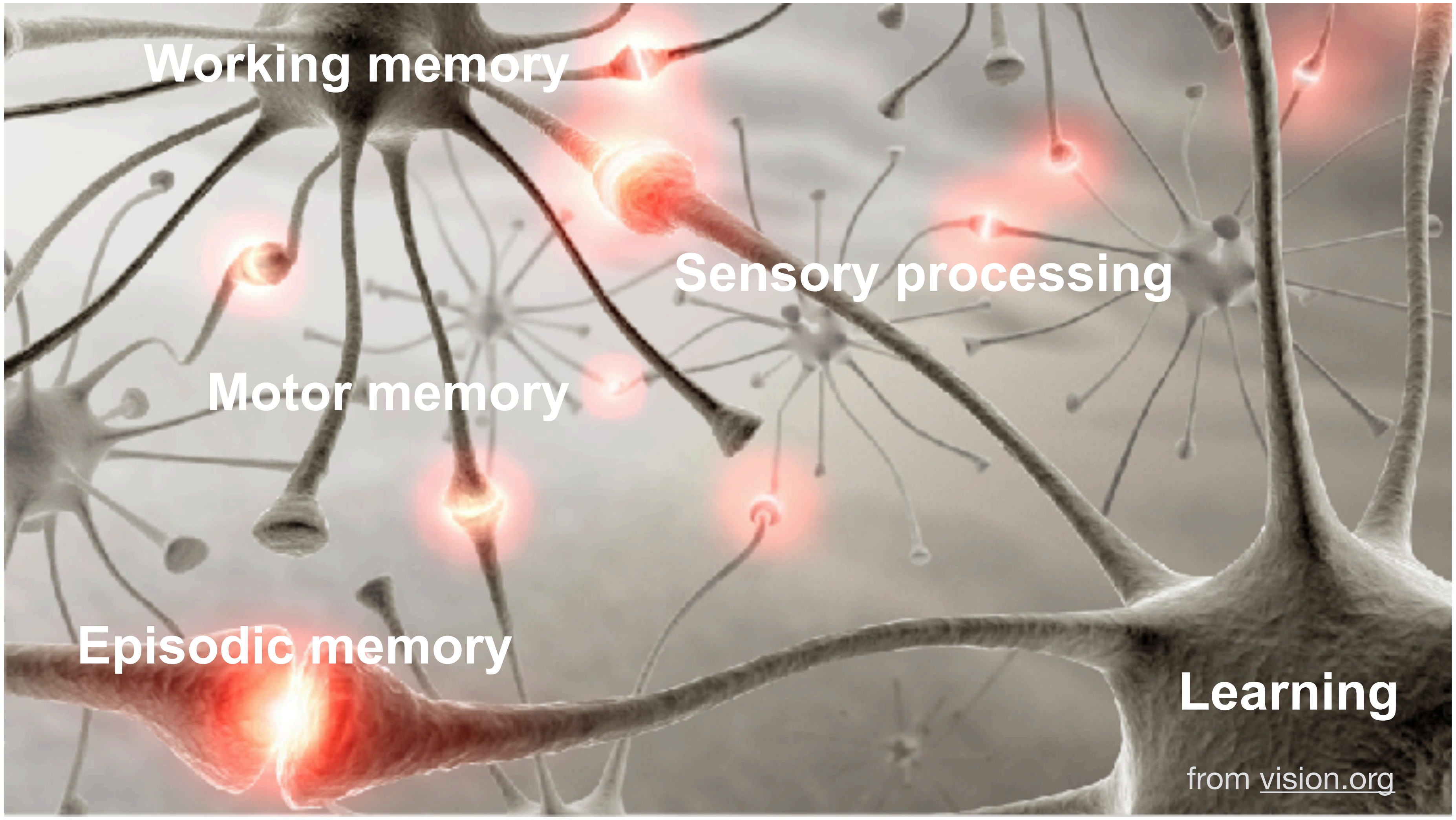
# Why build computer models of synapses?

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!*

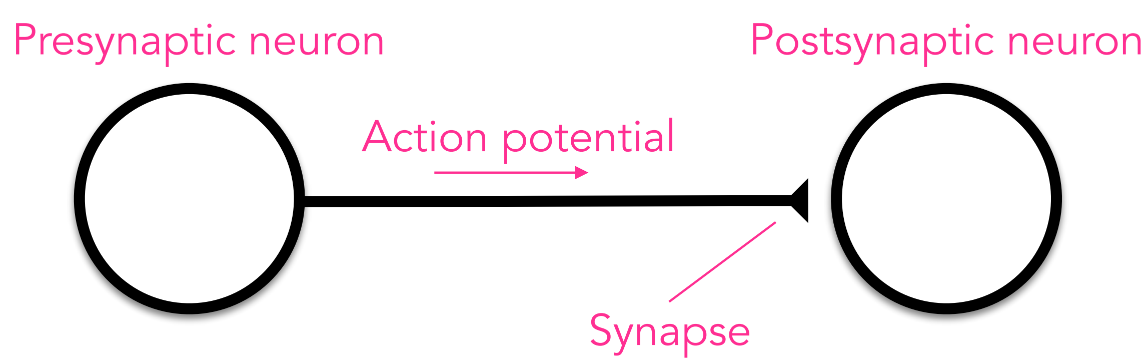


# Why build computer models of synapses?

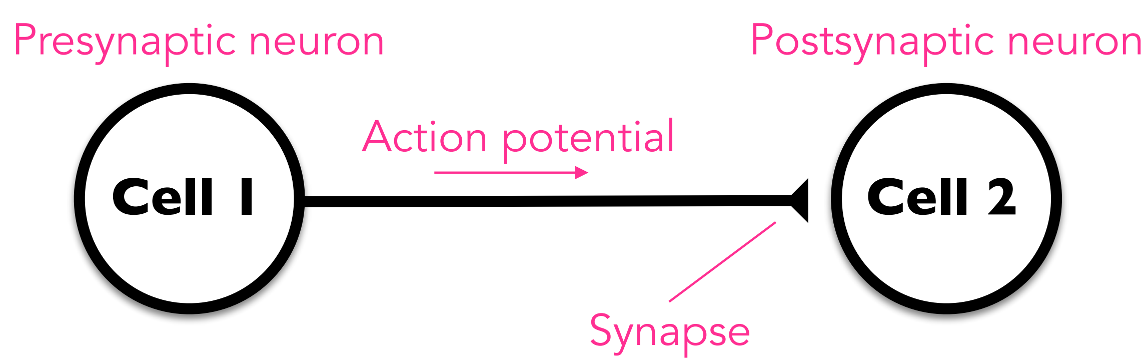
**Synapses are crucial for brain function, for example:**

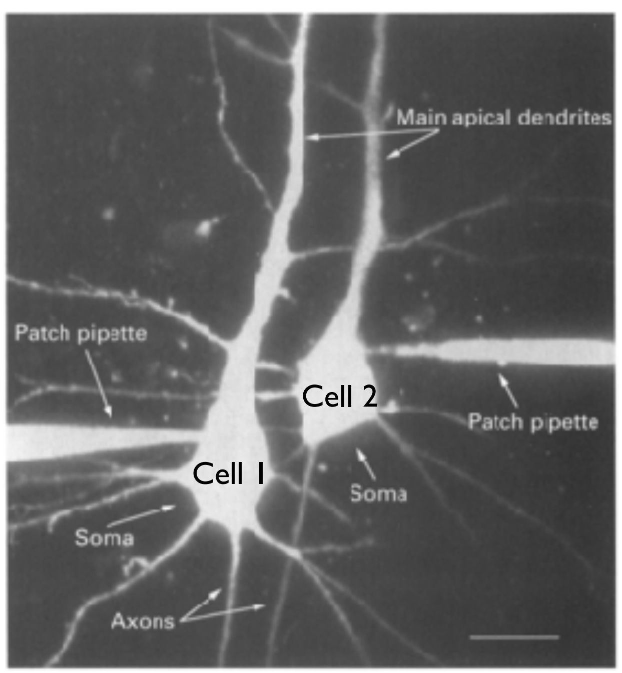


# What are synapses?



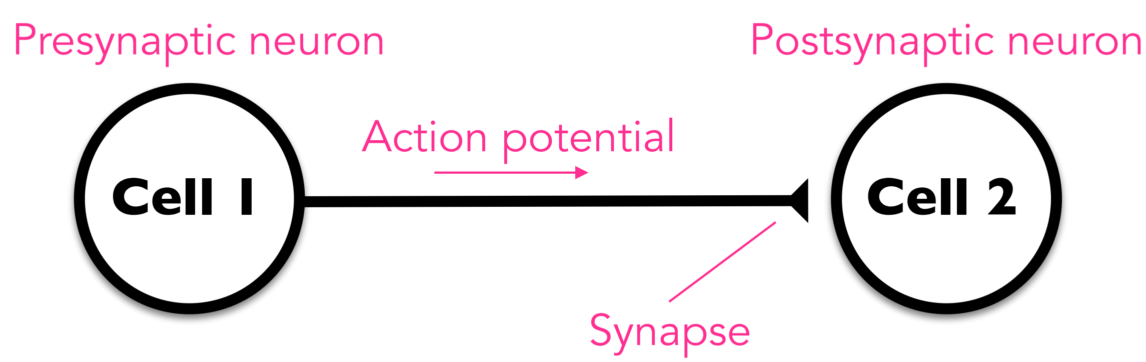
# What is a synapse?

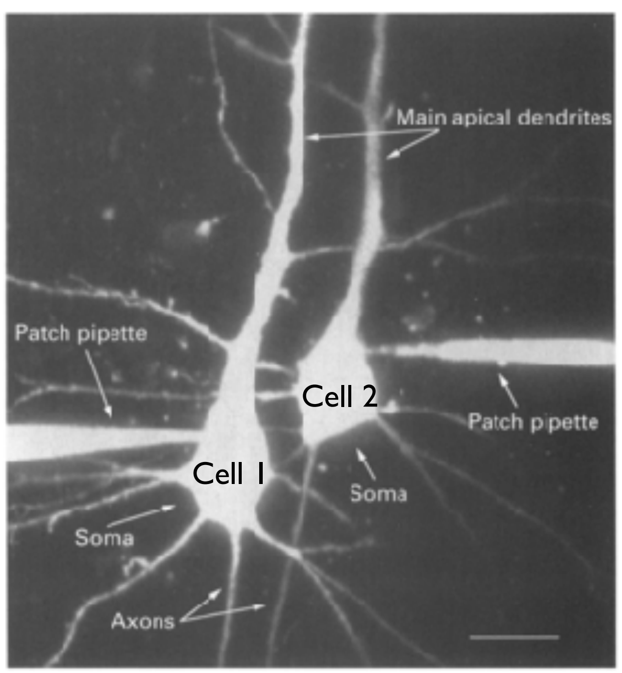


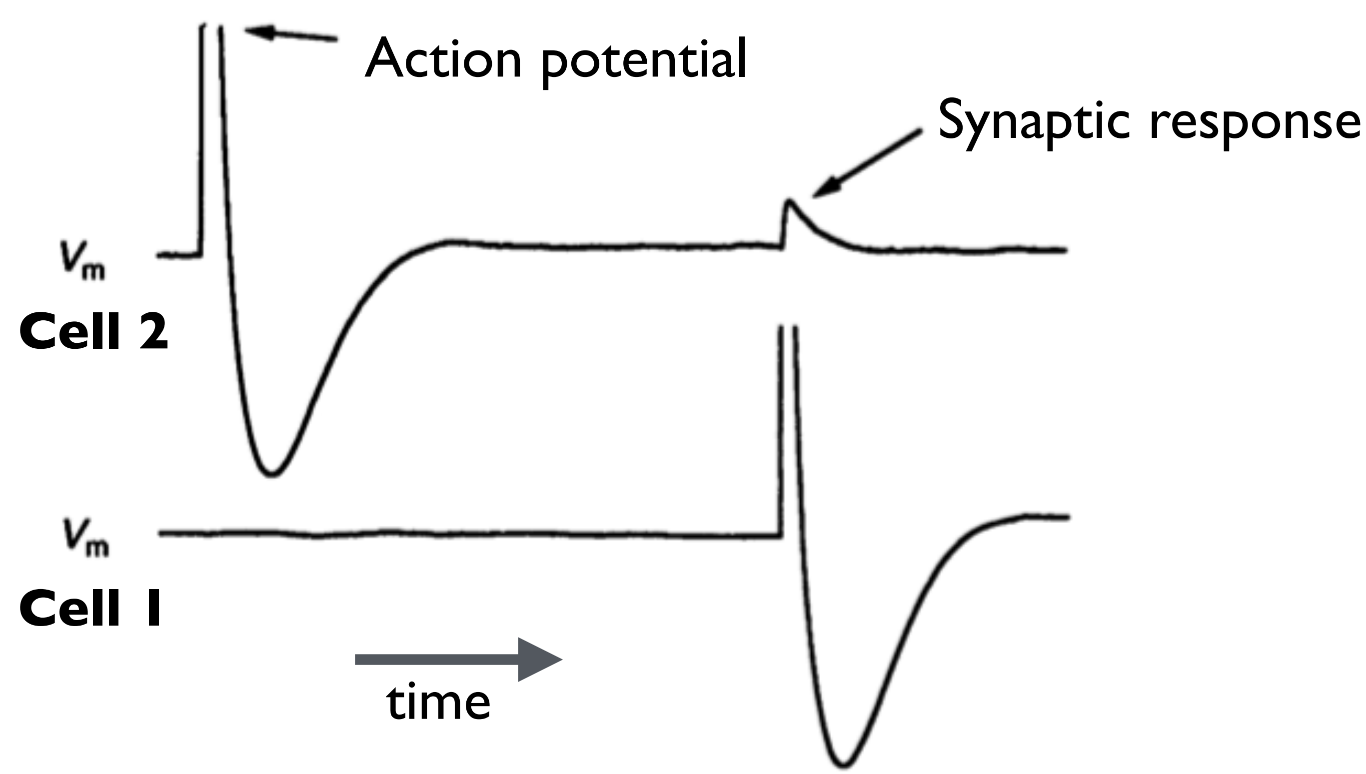




Markram et al, *J Physiol* (1997)

# What is a synapse?

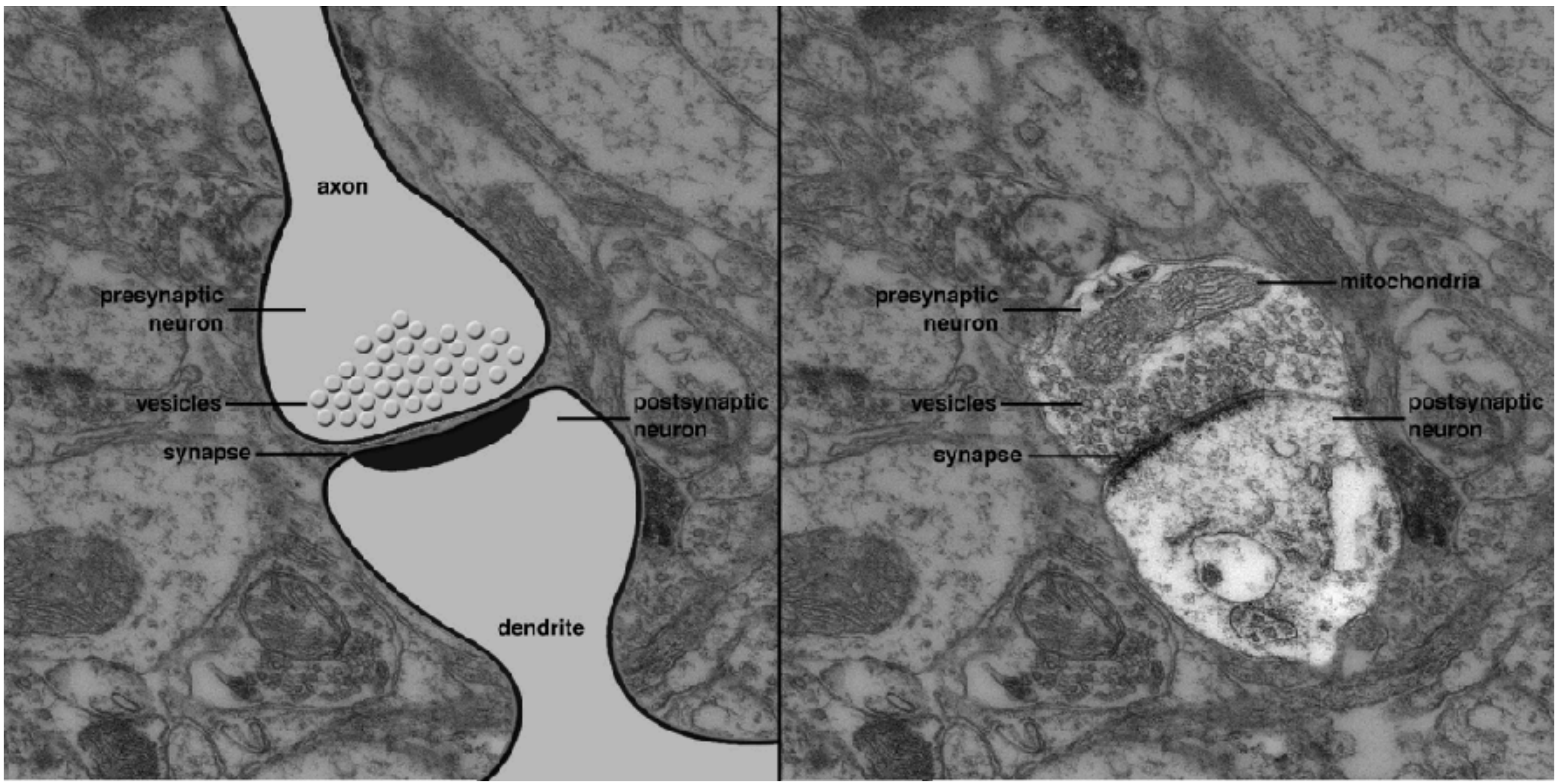


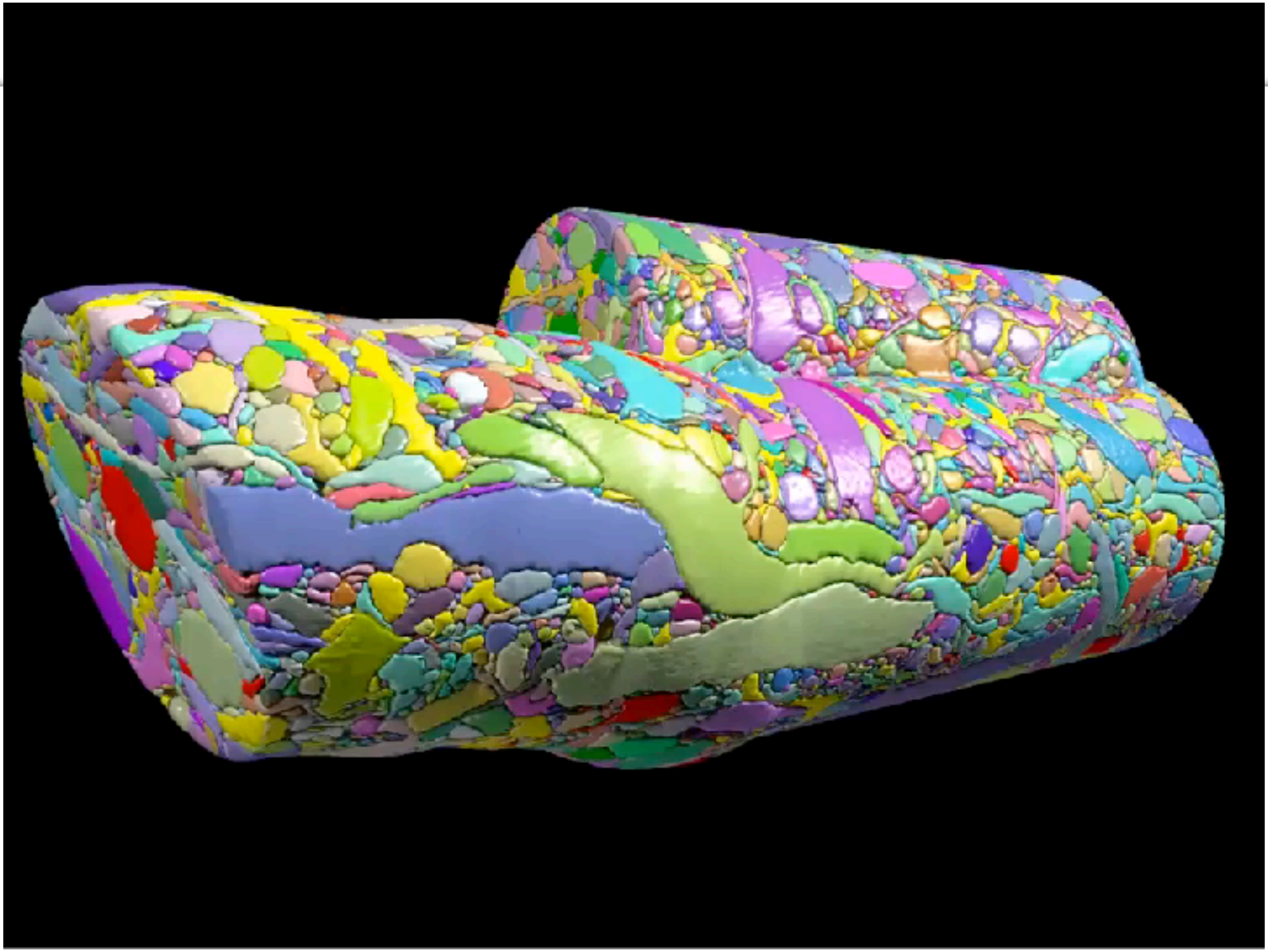

Markram et al, *J Physiol* (1997)

# A closer look into synapses:
## electron microscopy



# Finding synapses in the brain

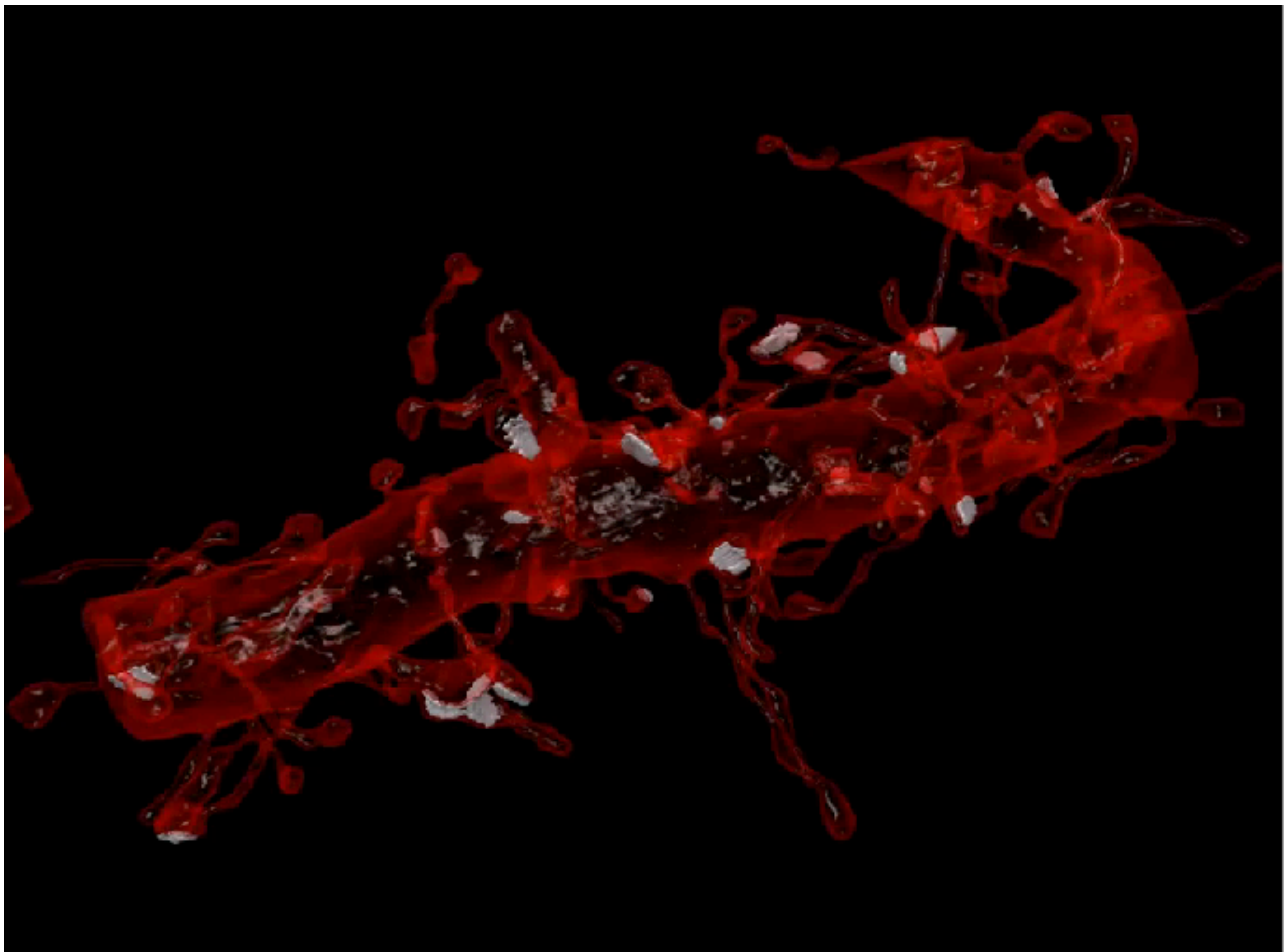
or a few micrometers of it



Using a combination of automatic and manual image segmentation.

Kasthuri et al. Cell 2015

# Synapse reconstruction in a few micrometers!



Kasthuri et al. Cell 2015

# Computational models of synapses

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

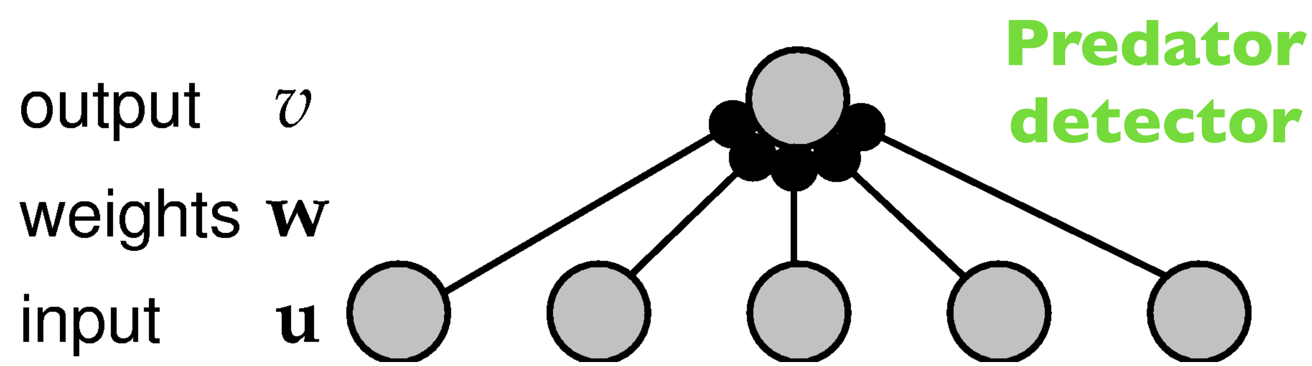
   1.1. **Static**

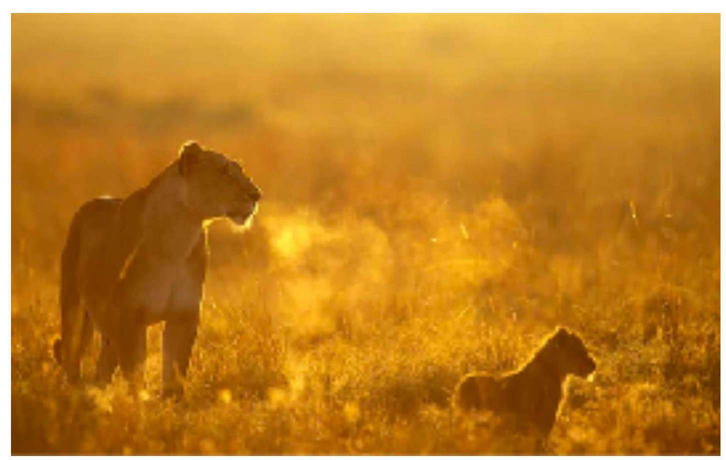
   1.2. **Stochastic**

   1.3. **Time-dependent**

2. **Molecular**

# Mathematical models of synapses: Static model



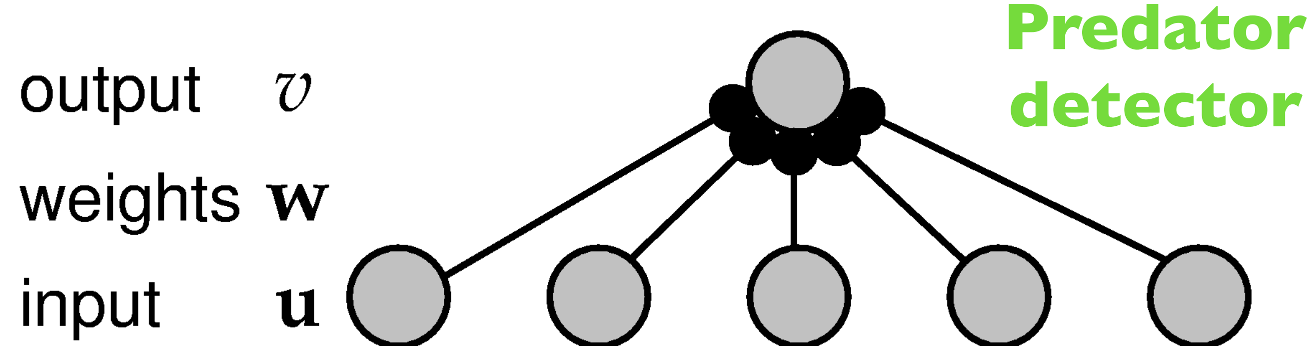
**Task**: Adjust ***w*** to detect predators given visual input ***u***

**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



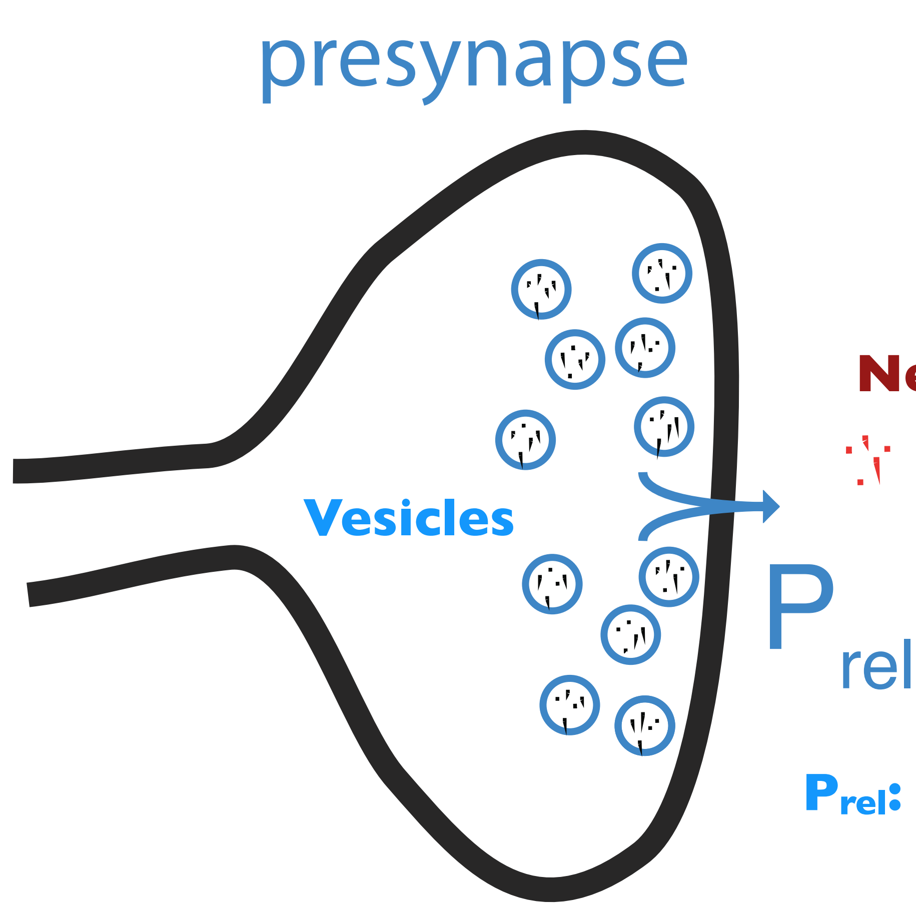

**Task**: Adjust ***w*** to detect predators given visual input ***u***

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

for **excitatory** synapses $w > 0$

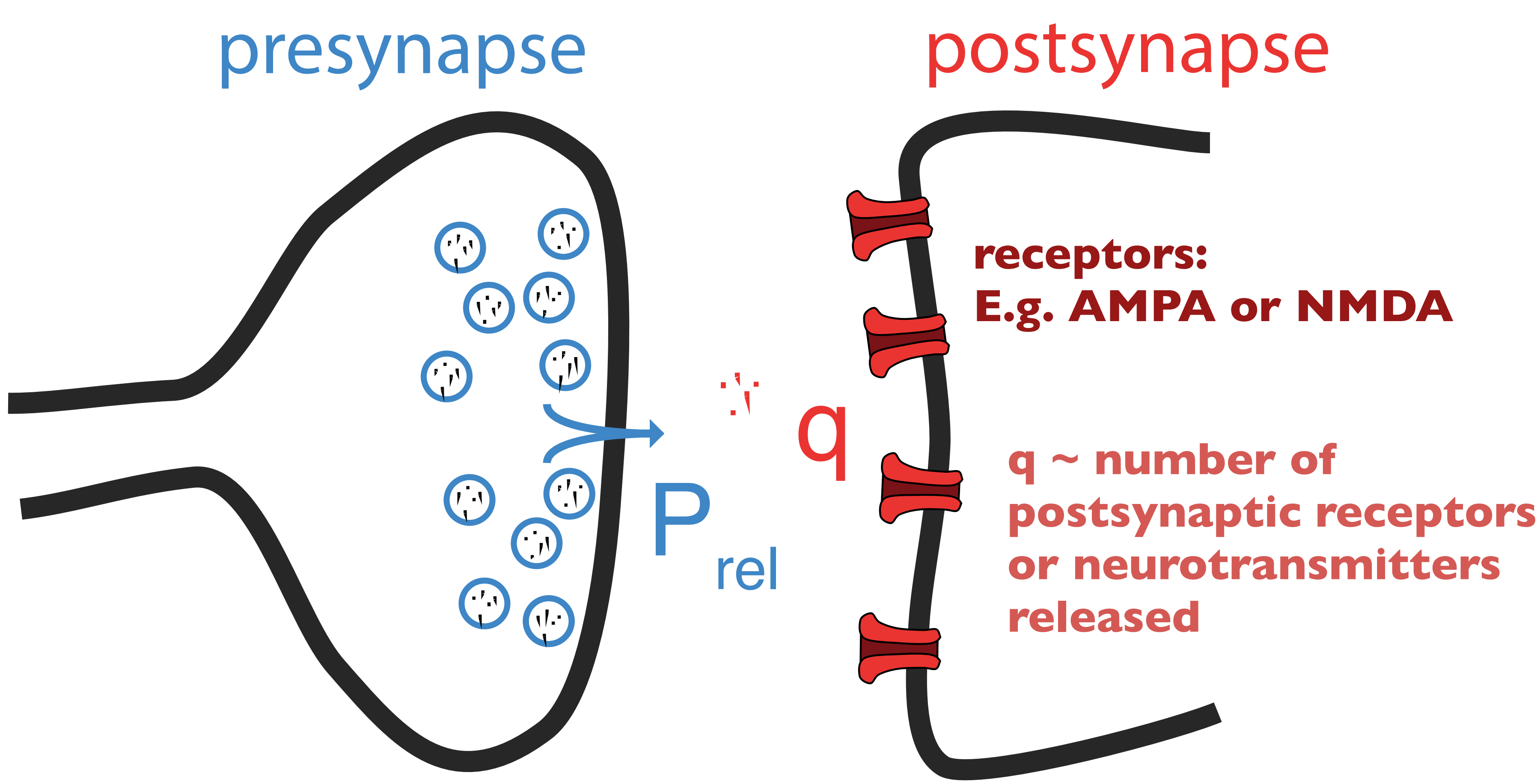
for **inhibitory** synapses $w < 0$

# But synapses are more complex than a simple real number



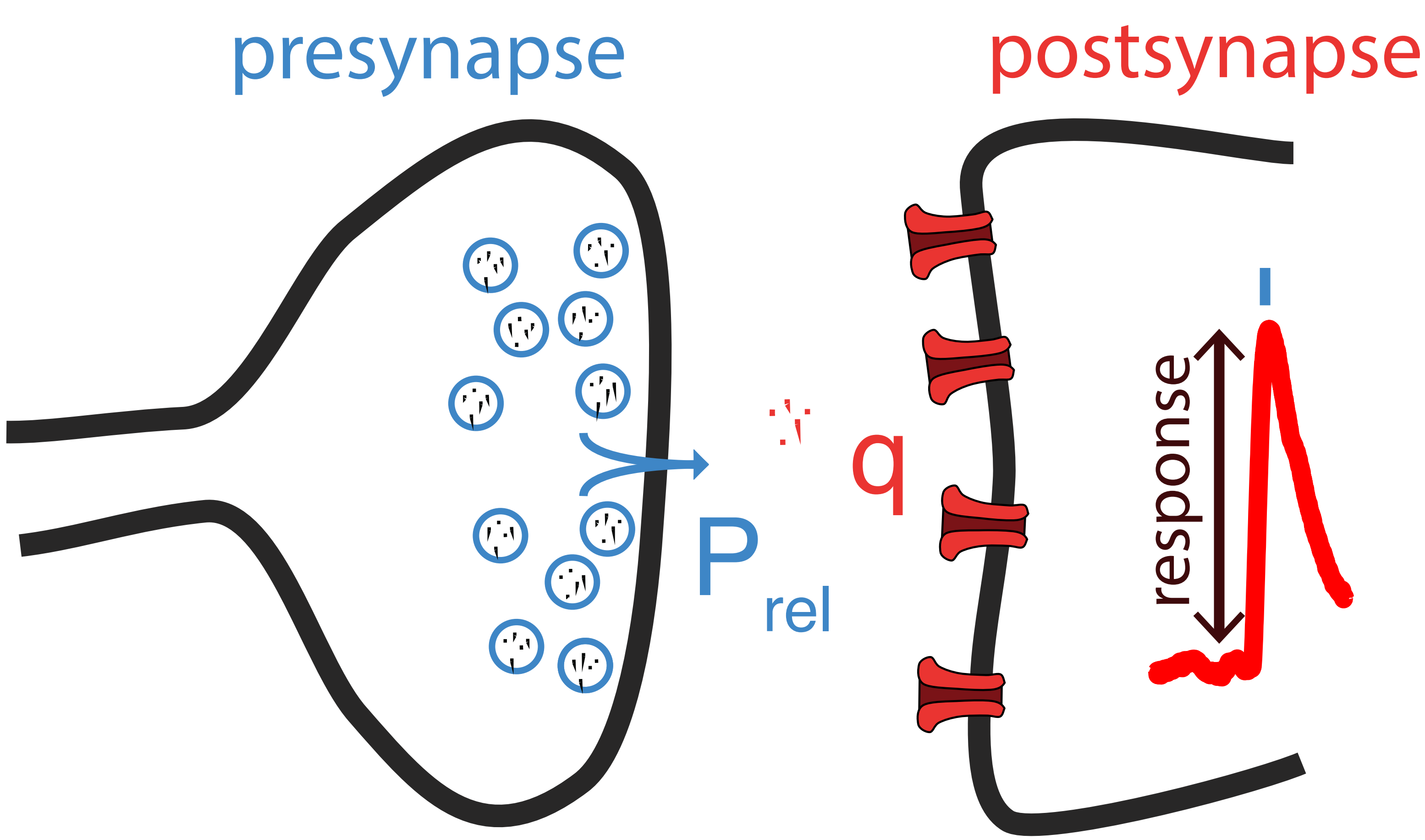

**$P_{rel}$: Probability of vesicle release**

# But synapses are more complex than a simple real number




$$w = P_{\text{rel}}\, q$$

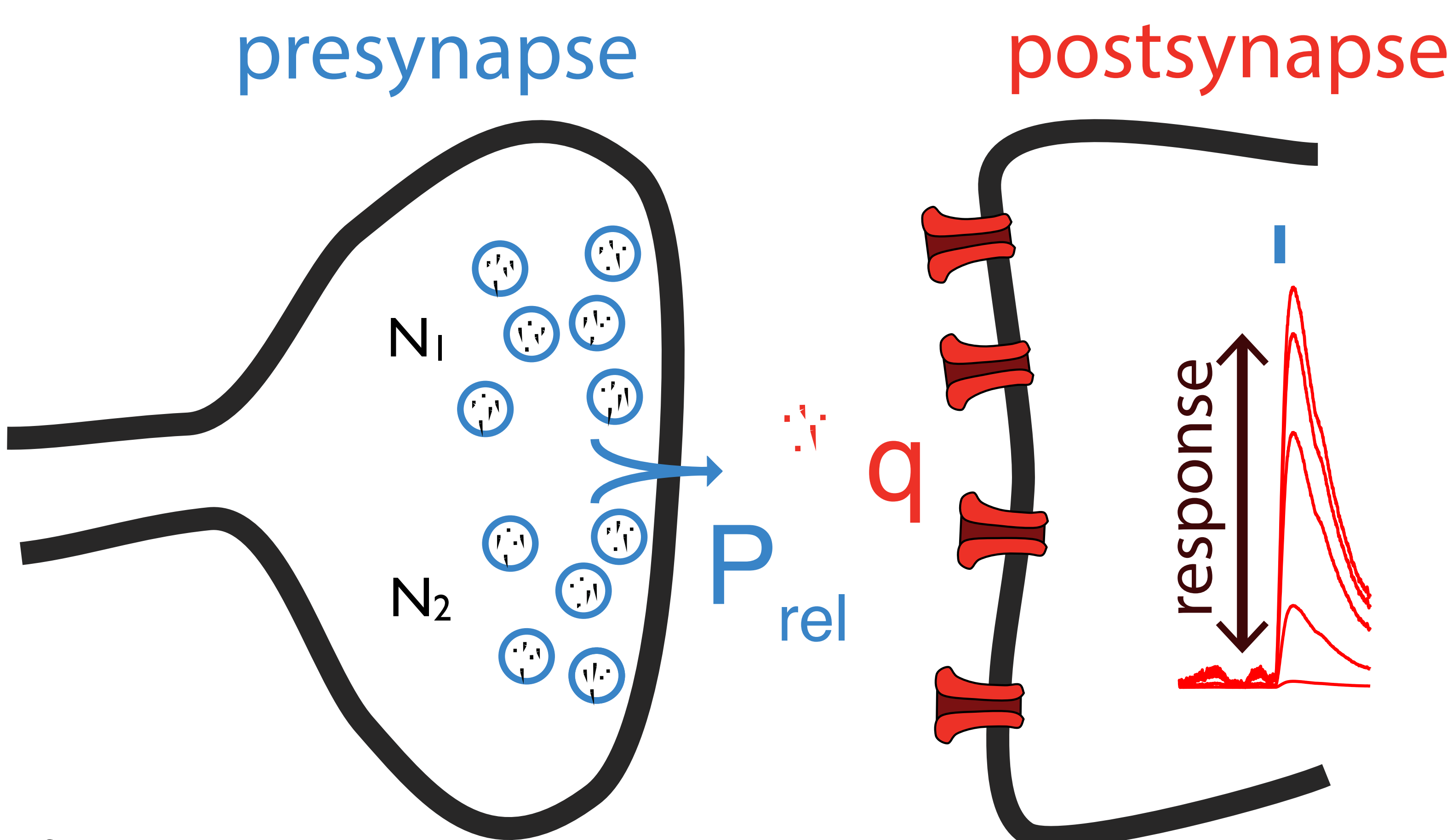
# But synapses are more complex than a simple real number




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

# Mathematical models of synapses: Stochastic model

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



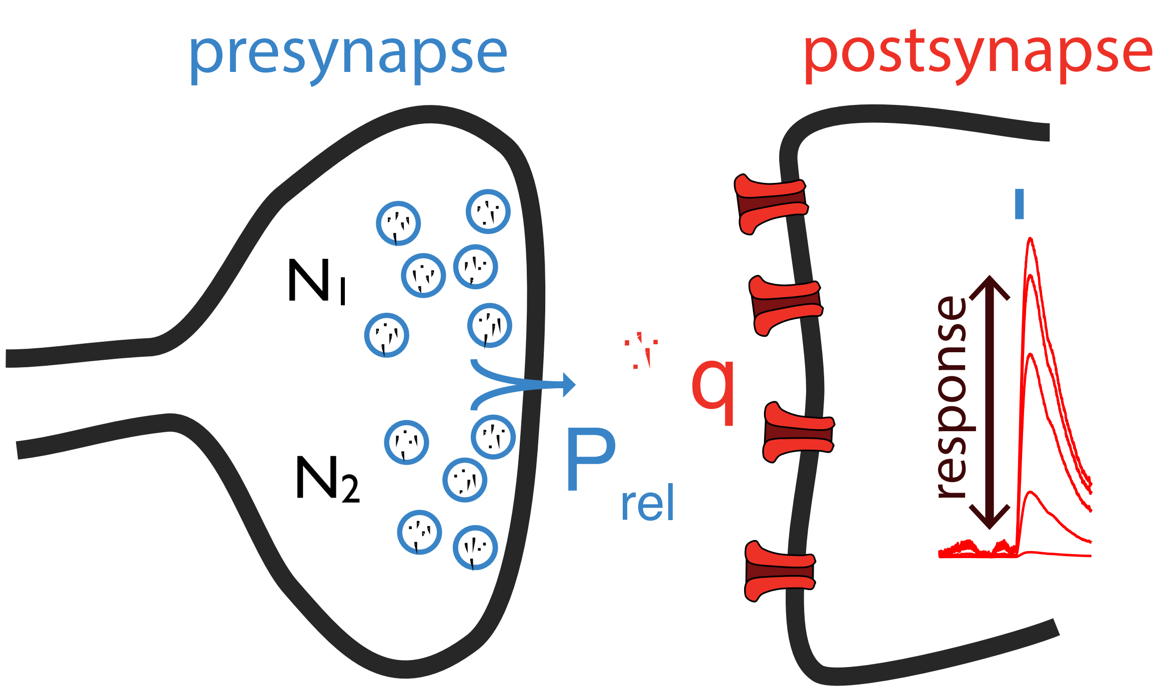

N: number of release sites

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

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*:

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

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

$P_{rel}$: release probability (of vesicles)

N: Number of release sites

k: Possible responses [0,…,N]

Principles of Computational Modelling in Neuroscience (2012)

# Mathematical models of synapses: Binomial release model

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

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

Principles of Computational Modelling in Neuroscience (2012)

# Mathematical models of synapses: Binomial release model

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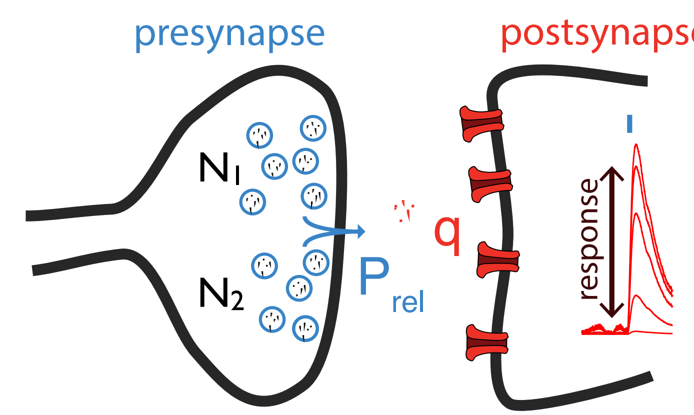
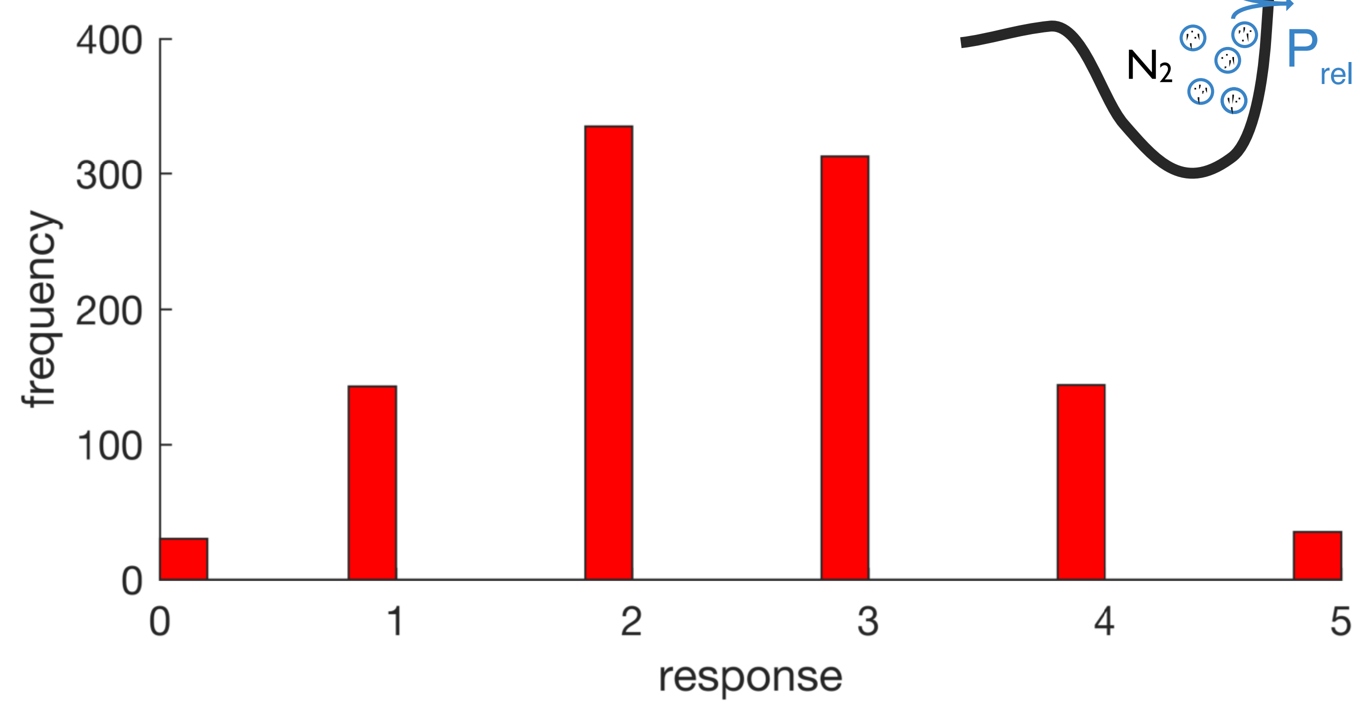



$P_{rel}$: 0.5

q: 1

N: 5

k: [0,…,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:

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

Principles of Computational Modelling in Neuroscience (2012)

# 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:

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

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

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 $\boldsymbol{E_{syn}}$ is the reversal potential, which determines the 'sign' of a synapse:

for **excitatory** synapses $E_{syn}$ ~ 0 mV ~ $I_{syn} > 0$

for **inhibitory** synapses $E_{syn}$ ~ $V_{rest}$ ~ $I_{syn} < 0$

Principles of Computational Modelling in Neuroscience (2012)

# Mathematical models of synapses:
# Time-dependent models

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

Single exponential:

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

Principles of Computational Modelling
in Neuroscience (2012)

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Principles of Computational Modelling
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# Mathematical models of synapses: Time-dependent models

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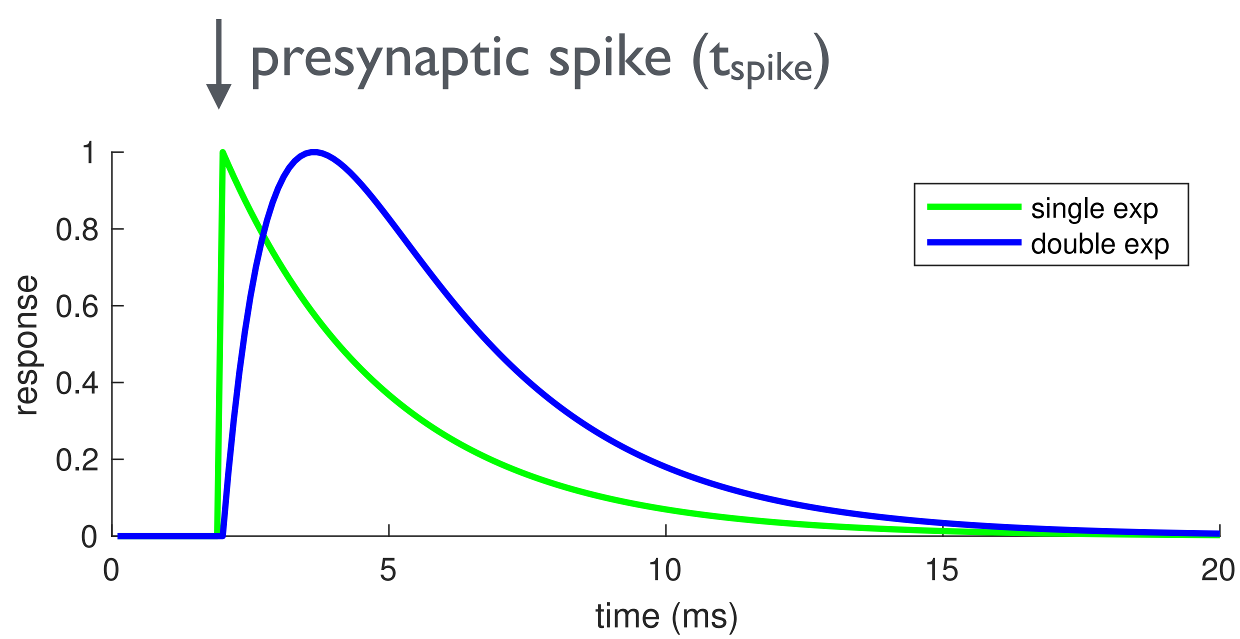
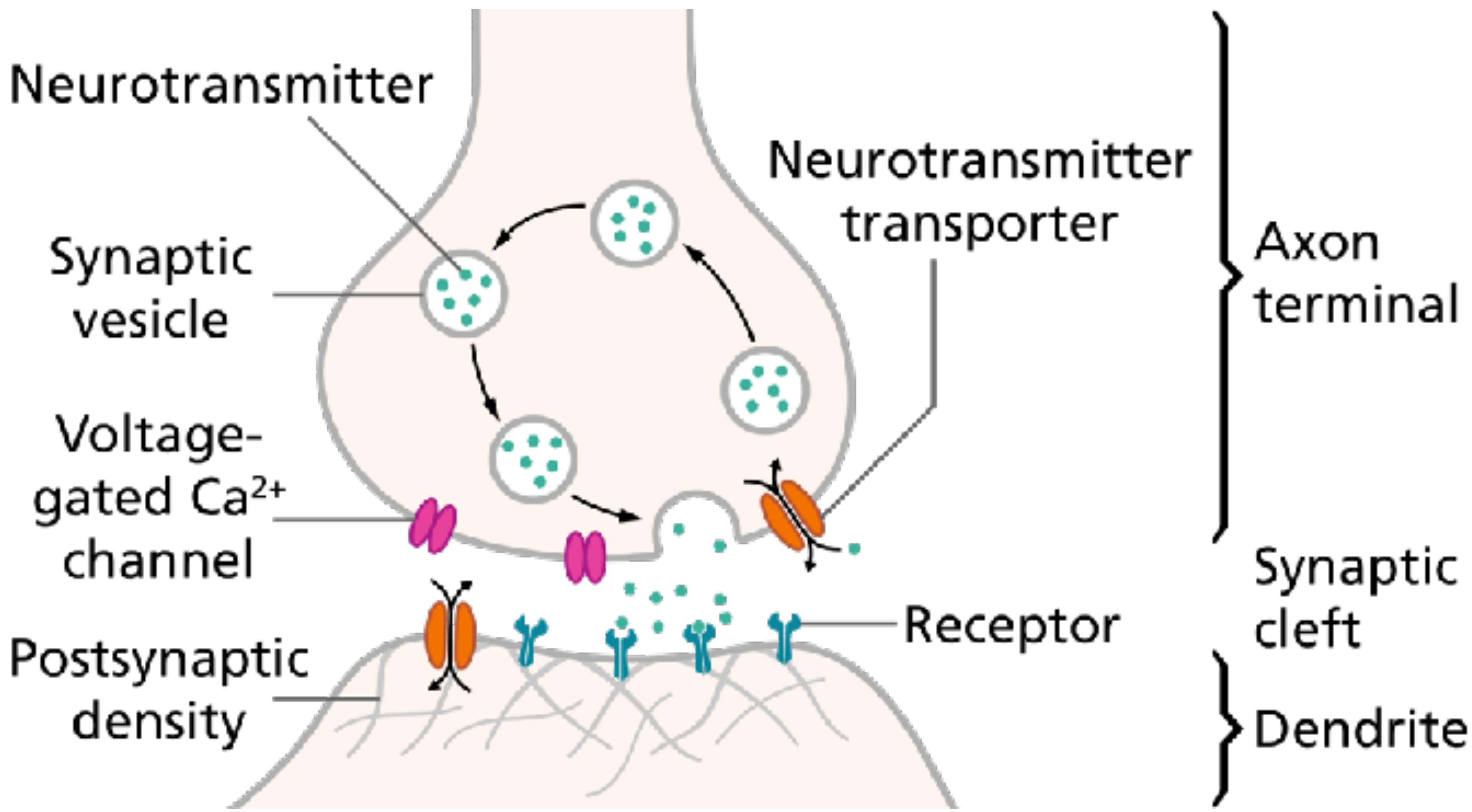


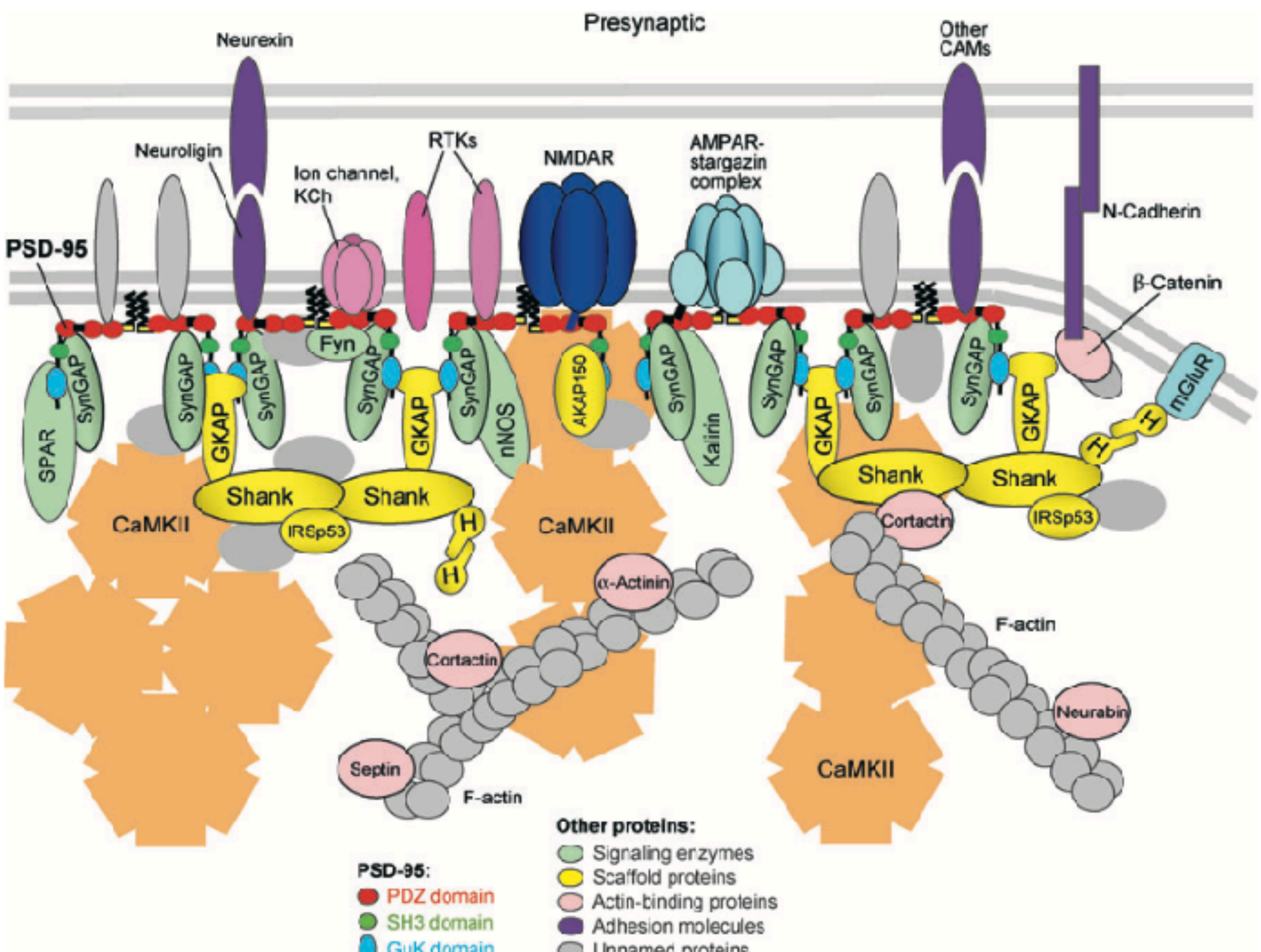

Principles of Computational Modelling in Neuroscience (2012)

# Synapses as dynamic/complex systems?



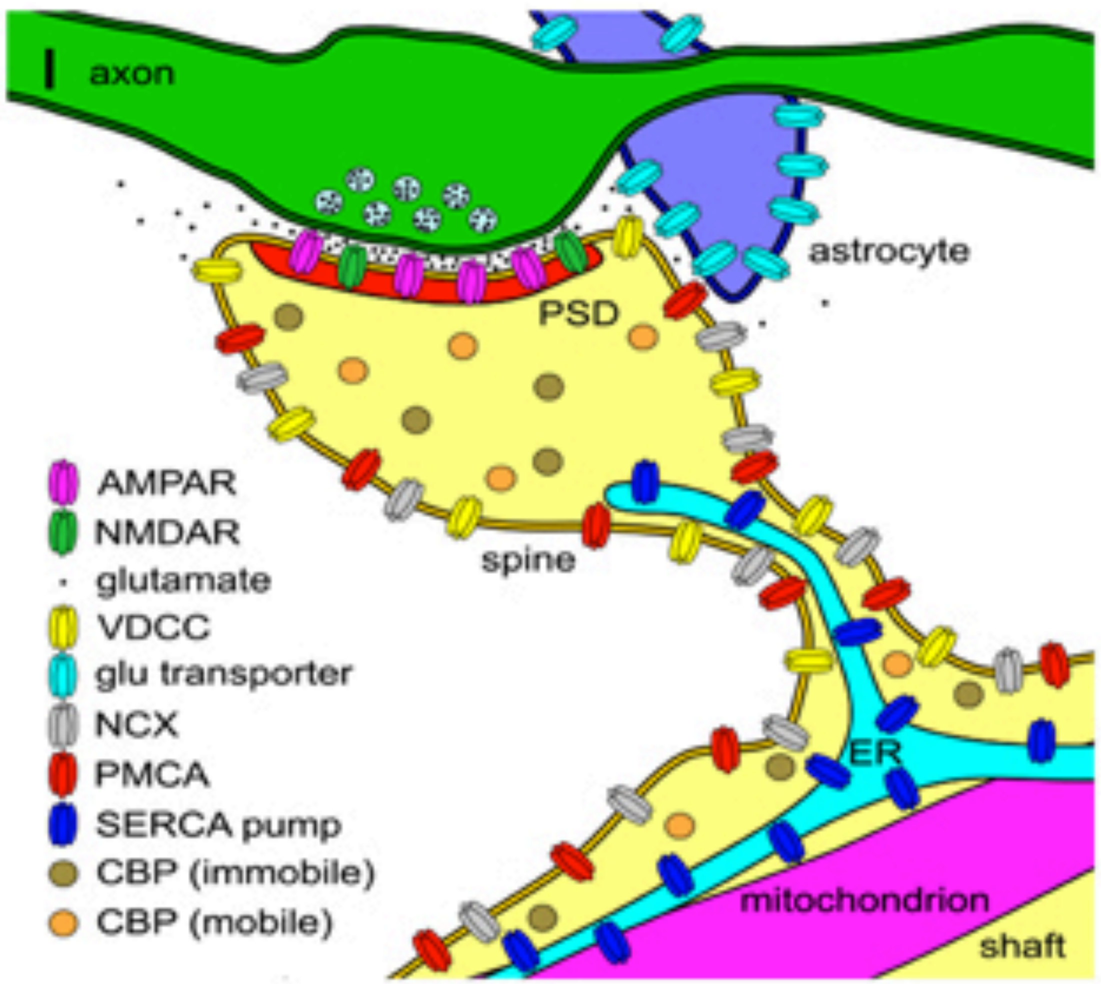

wikipedia.org;
Kandel, Schwartz and Jessell 2012

# Mathematical models of synapses: Molecular models



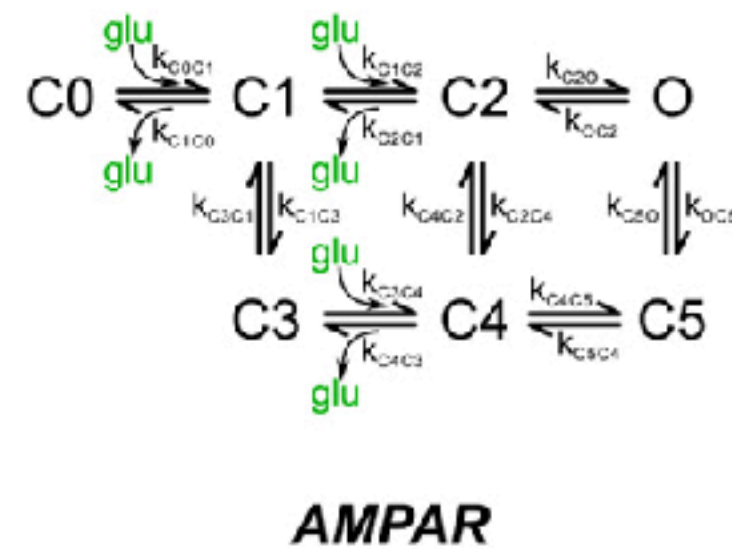

Sheng and Hoogenraad, Annu Rev Neurosci (2007)

# Mathematical models of synapses: Molecular models




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

Markov model of AMPA receptor:




**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?

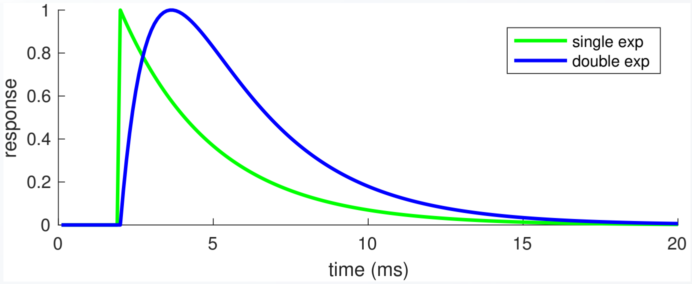
**Hint**: Think of the biological detail vs computational costs

1. Phenomenological

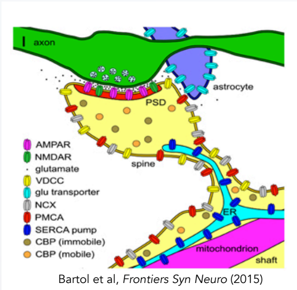
   1.1. Static $w \in \mathbb{R}$

   1.2. Stochastic $W \sim \mathrm{Bin}(N, P_{\mathrm{rel}})$

   1.3. Time-dependent




2. Molecular

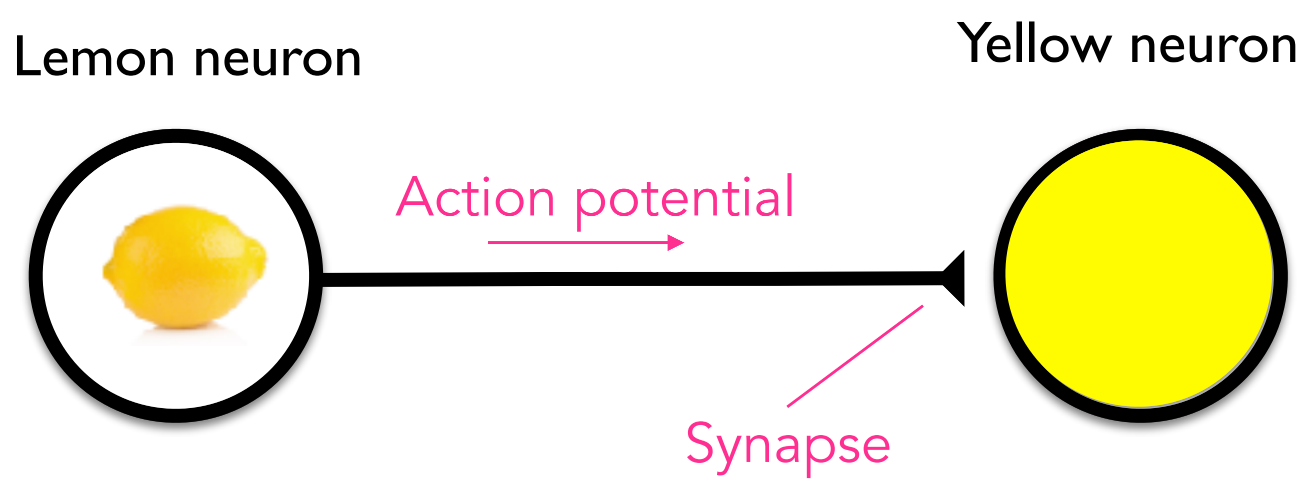



Bartol et al, *Frontiers Syn Neuro* (2015)

# 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*.

# Synaptic plasticity

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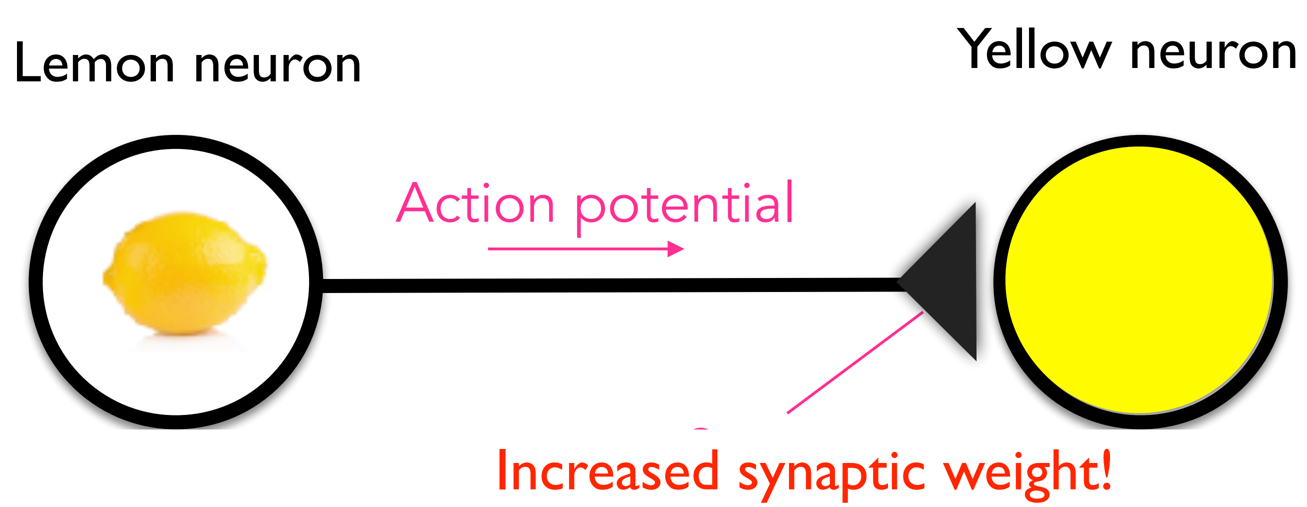


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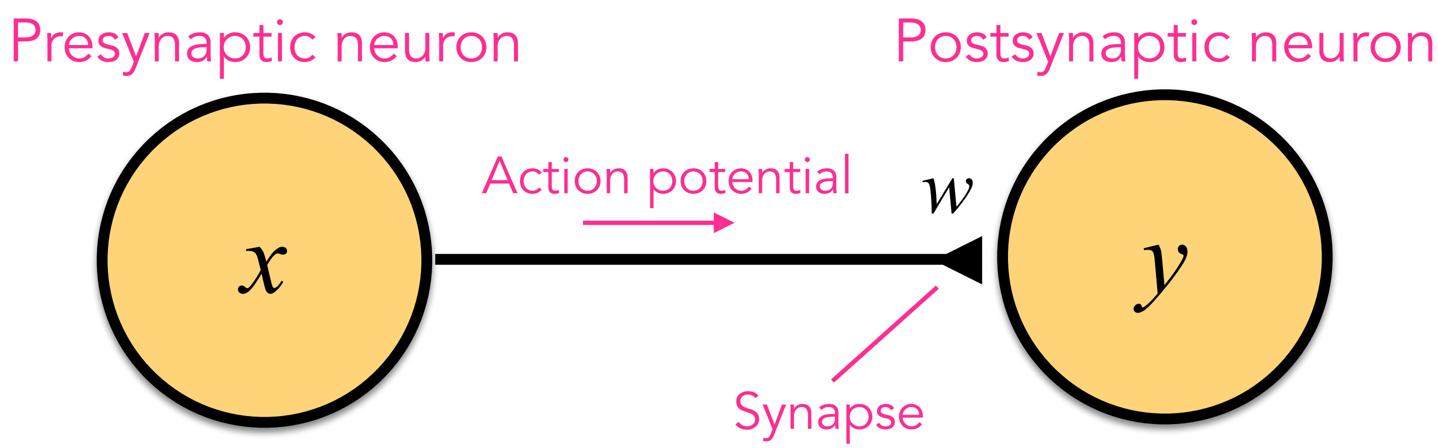
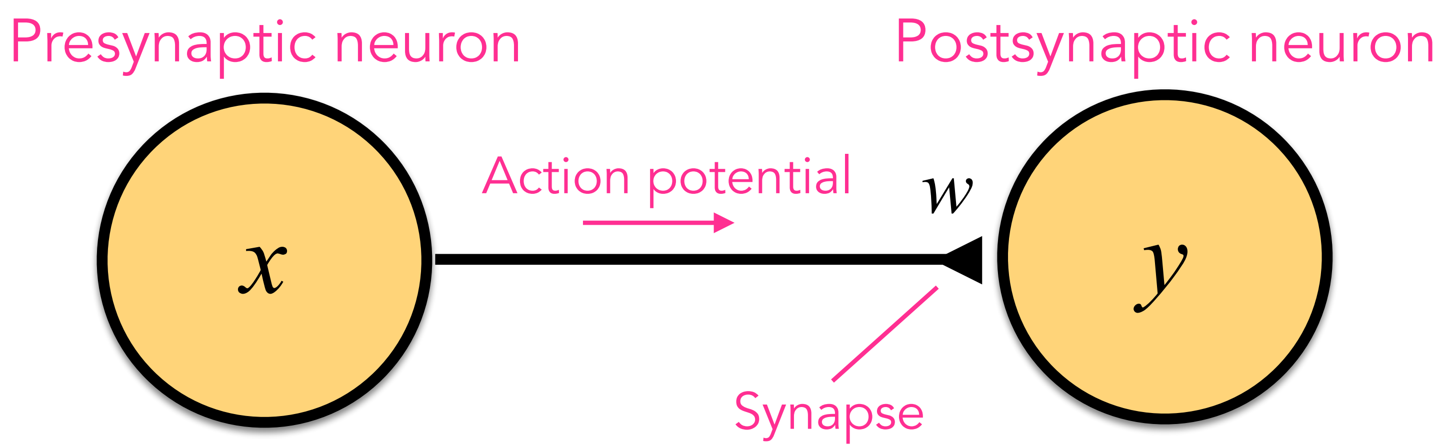
# Synaptic plasticity




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

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

# Synaptic plasticity

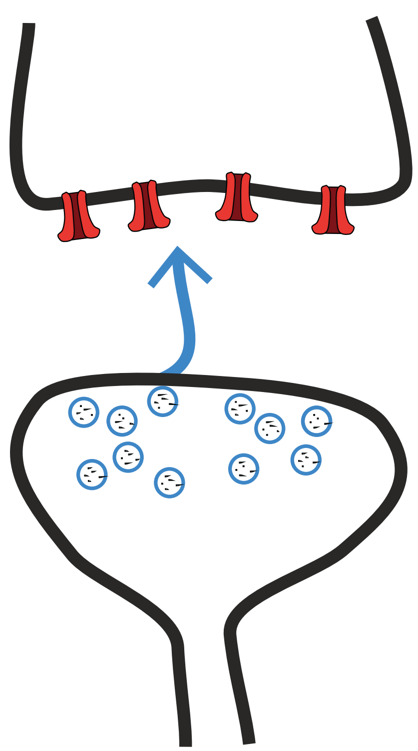



- *Synaptic plasticity can be formulated as a change in W ($\Delta W$), which is a function of pre- and postsynaptic activity (x and y, respectively):*

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

- This is a very simple form of *correlation-based* or *Hebbian learning rules* [see next lectures].

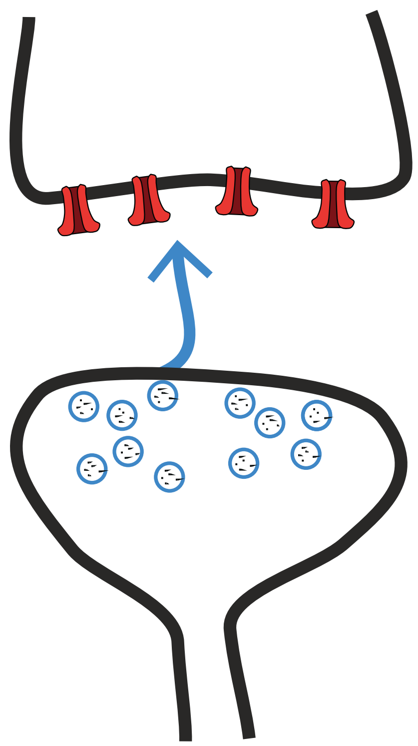
# Synaptic plasticity: when and where?

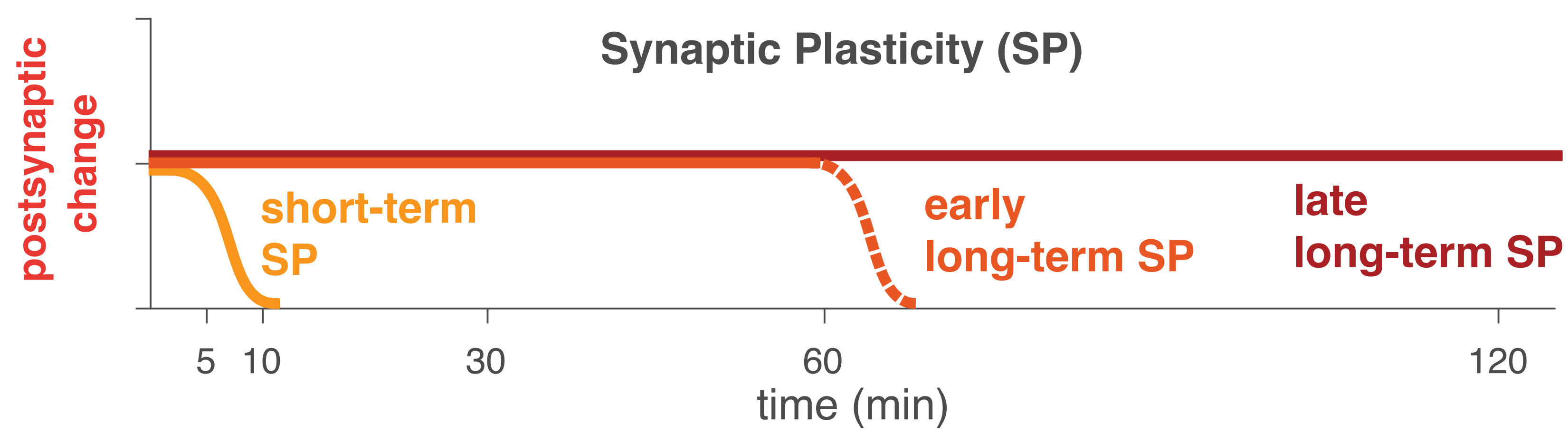


# Synaptic plasticity: Multiple timescales and locations

Synapses can change **postsynaptically**

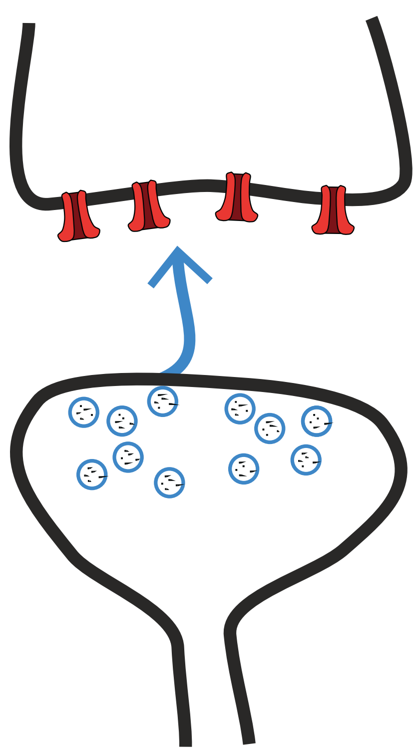
(from a few seconds (**short-term**) to tens of minutes, hours (**long-term**) or even days/years!):

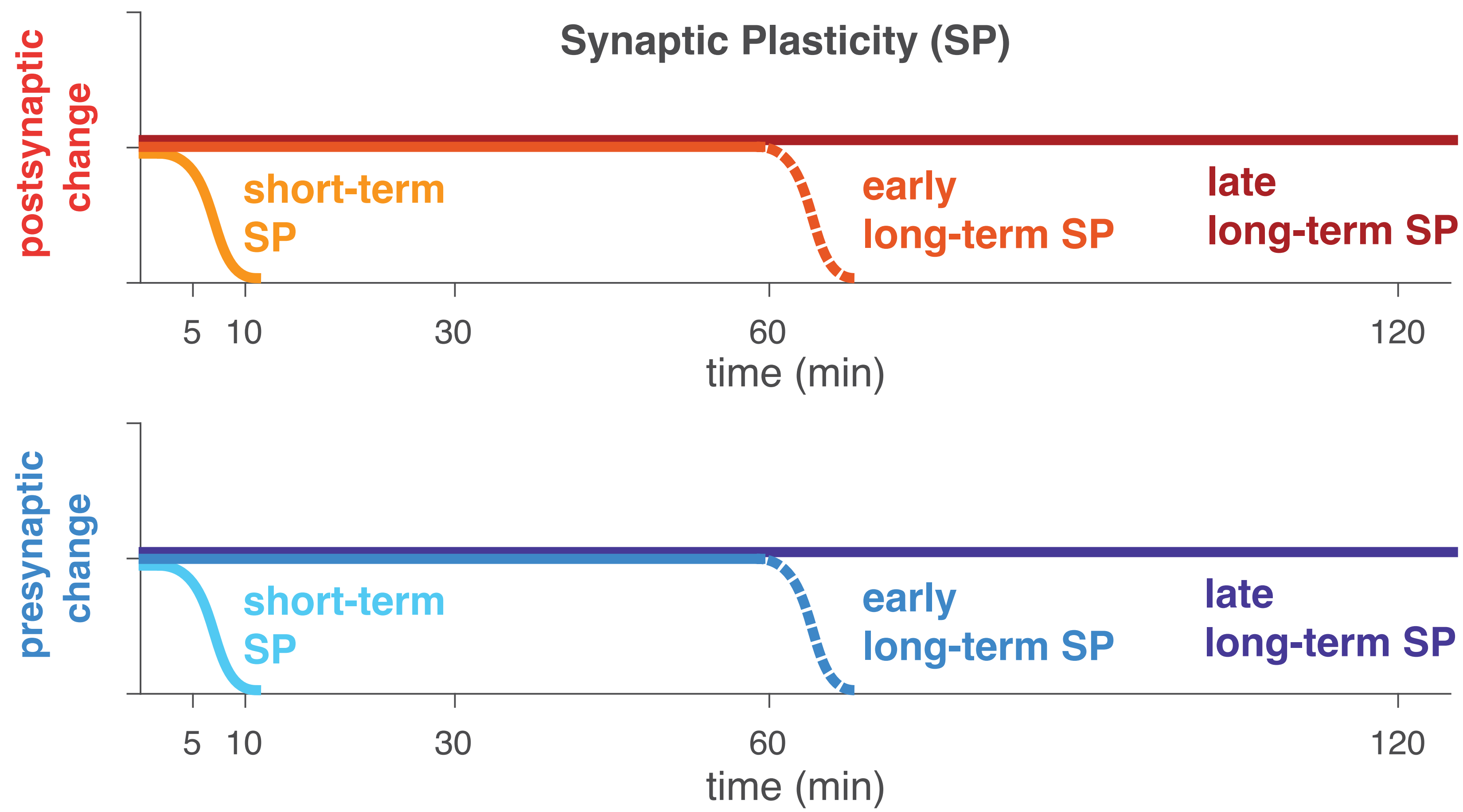




# Synaptic plasticity: Multiple timescales and locations

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. <u>Next lecture</u>: *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]