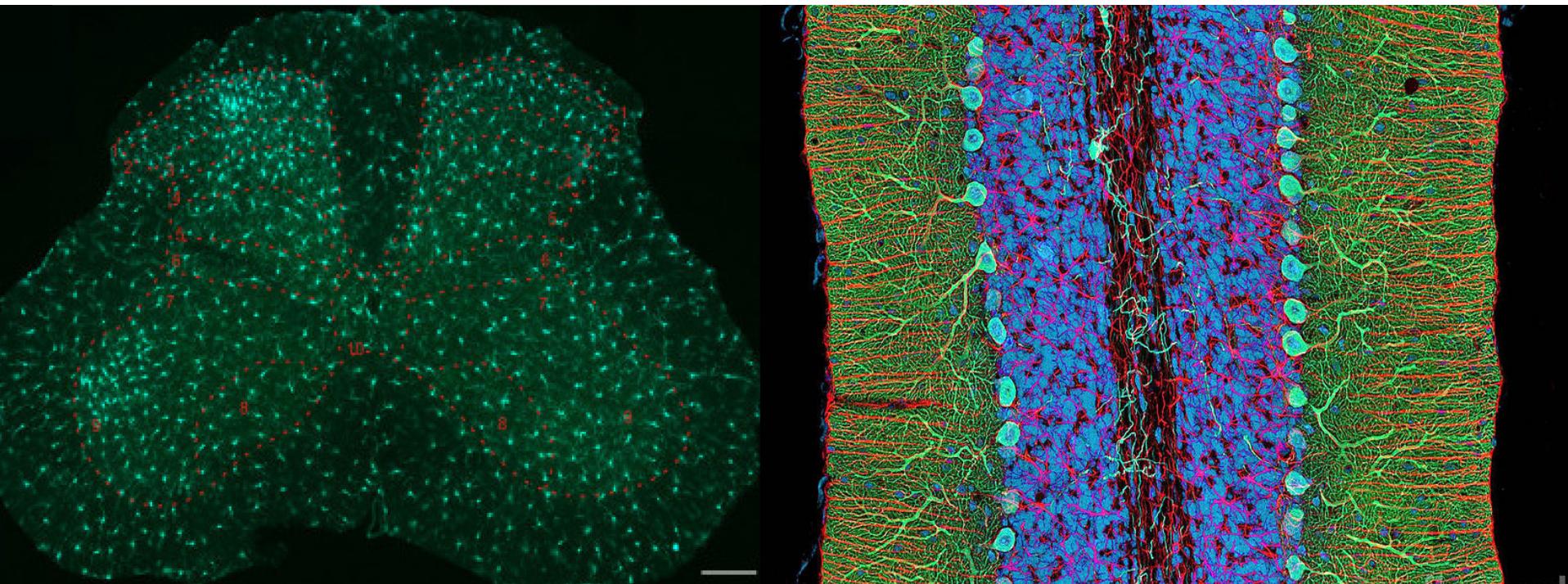


Synaptic Plasticity

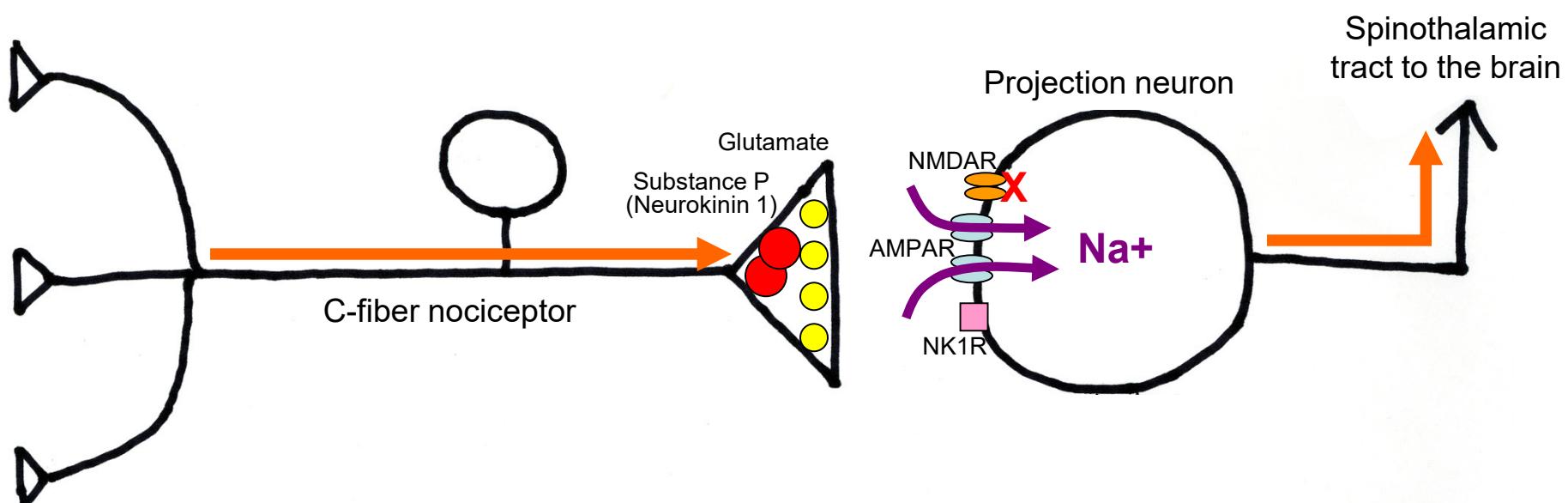
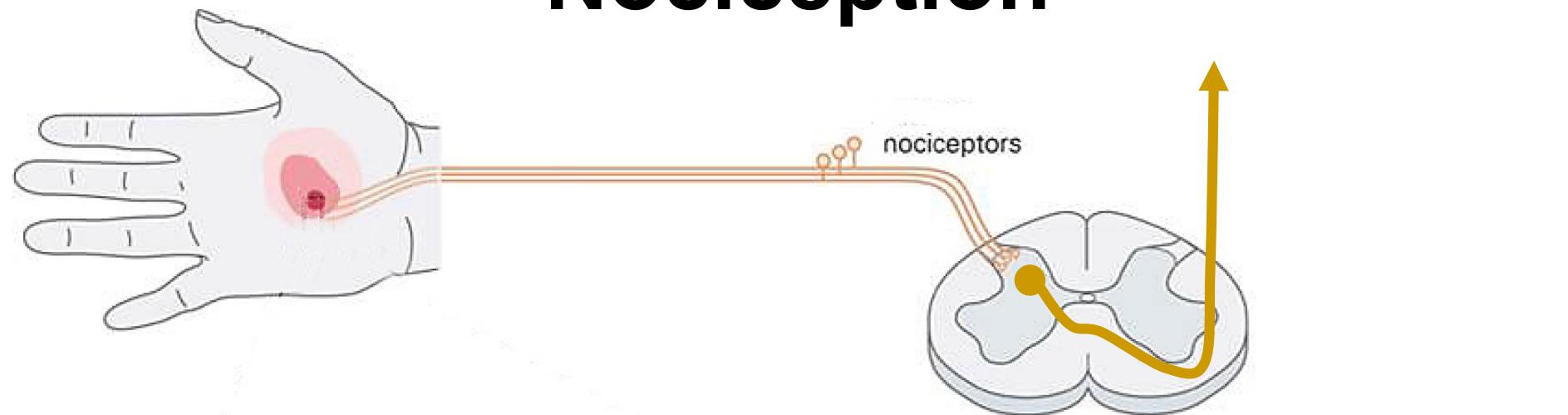


Chapter 20: Hyperalgesia (LTP in the spinal cord)

Chapter 42 & 53: Fear Conditioning (LTP in the amygdala)

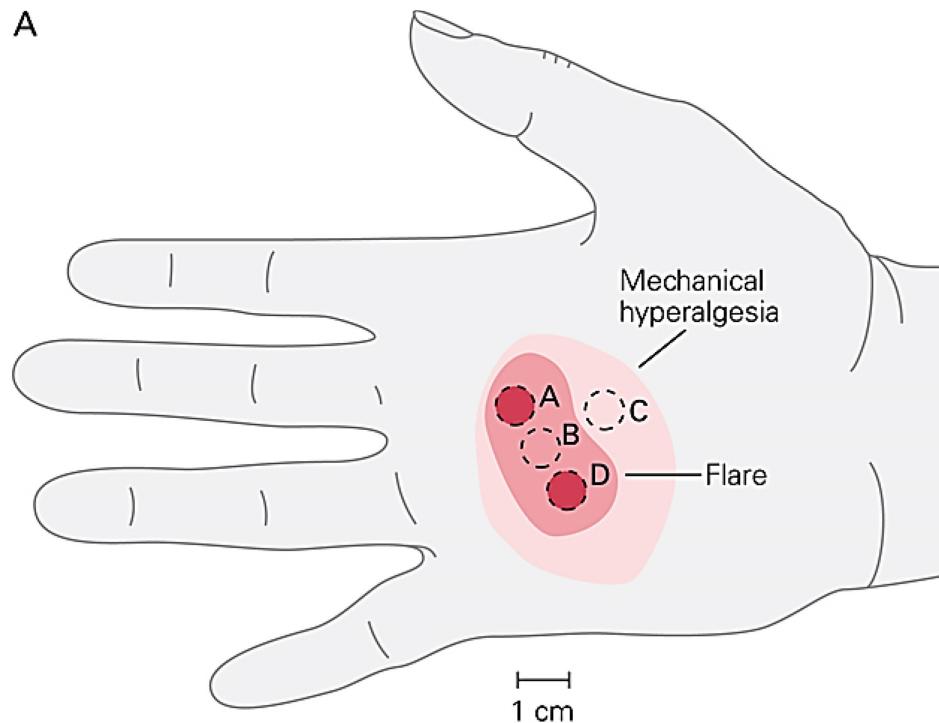
Chapter 37: Behavioral Conditioning (LTD in the cerebellum)

Nociception

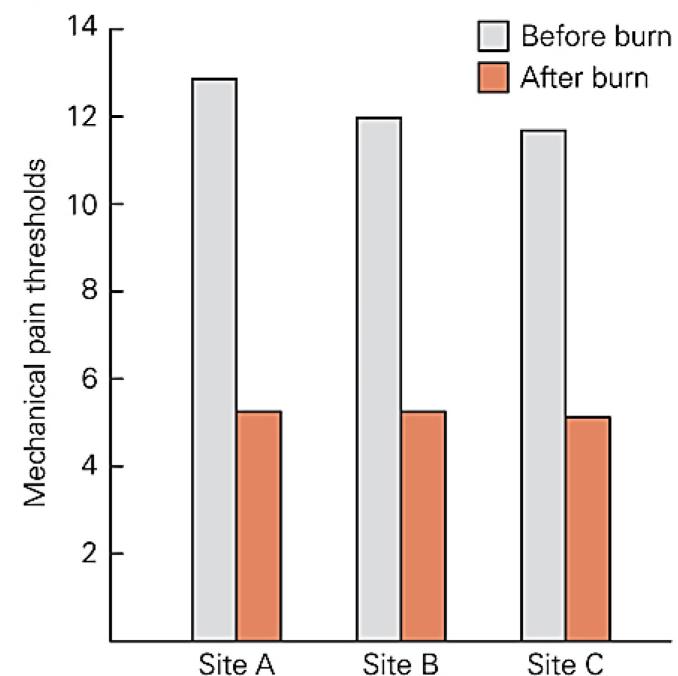


Hyperalgesia

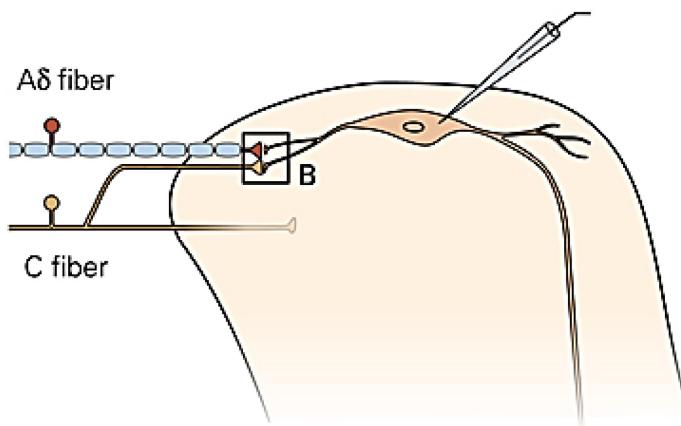
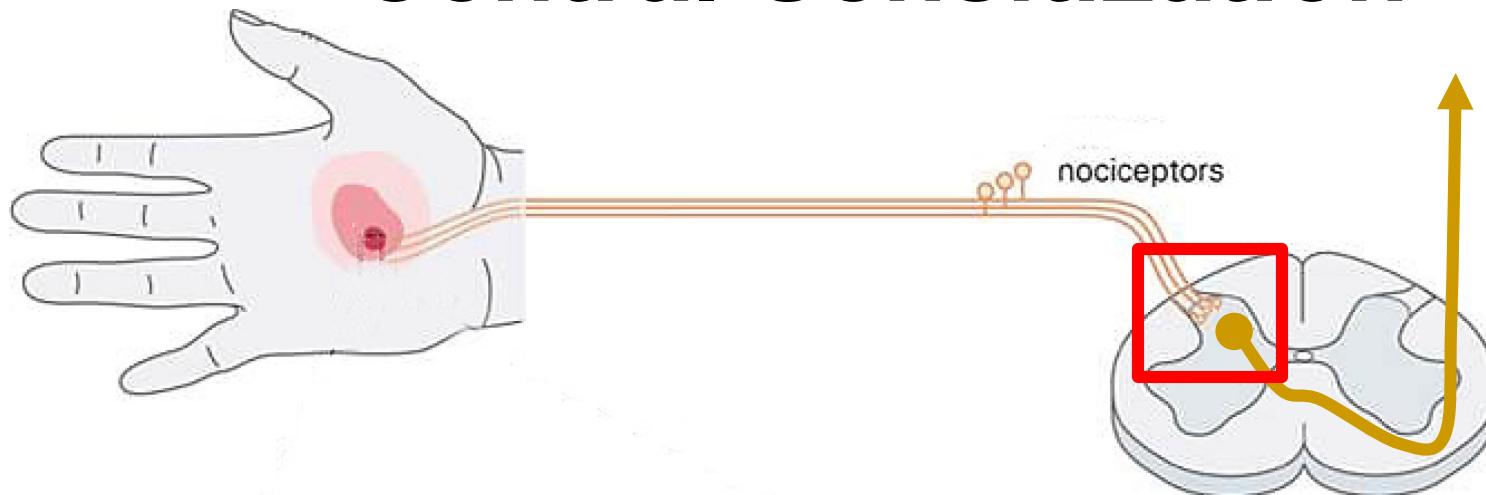
A



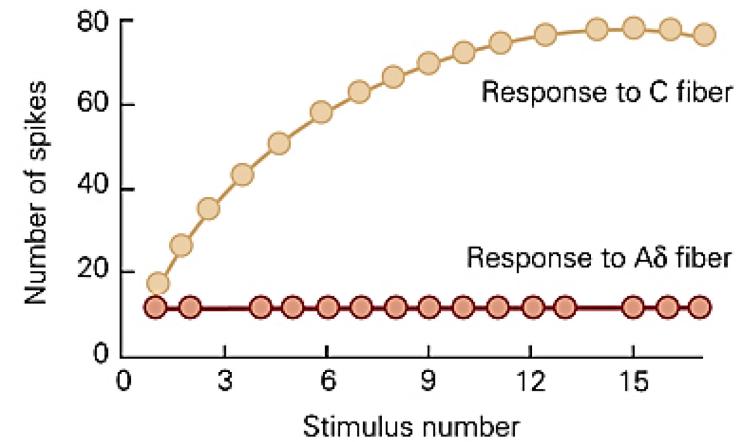
B



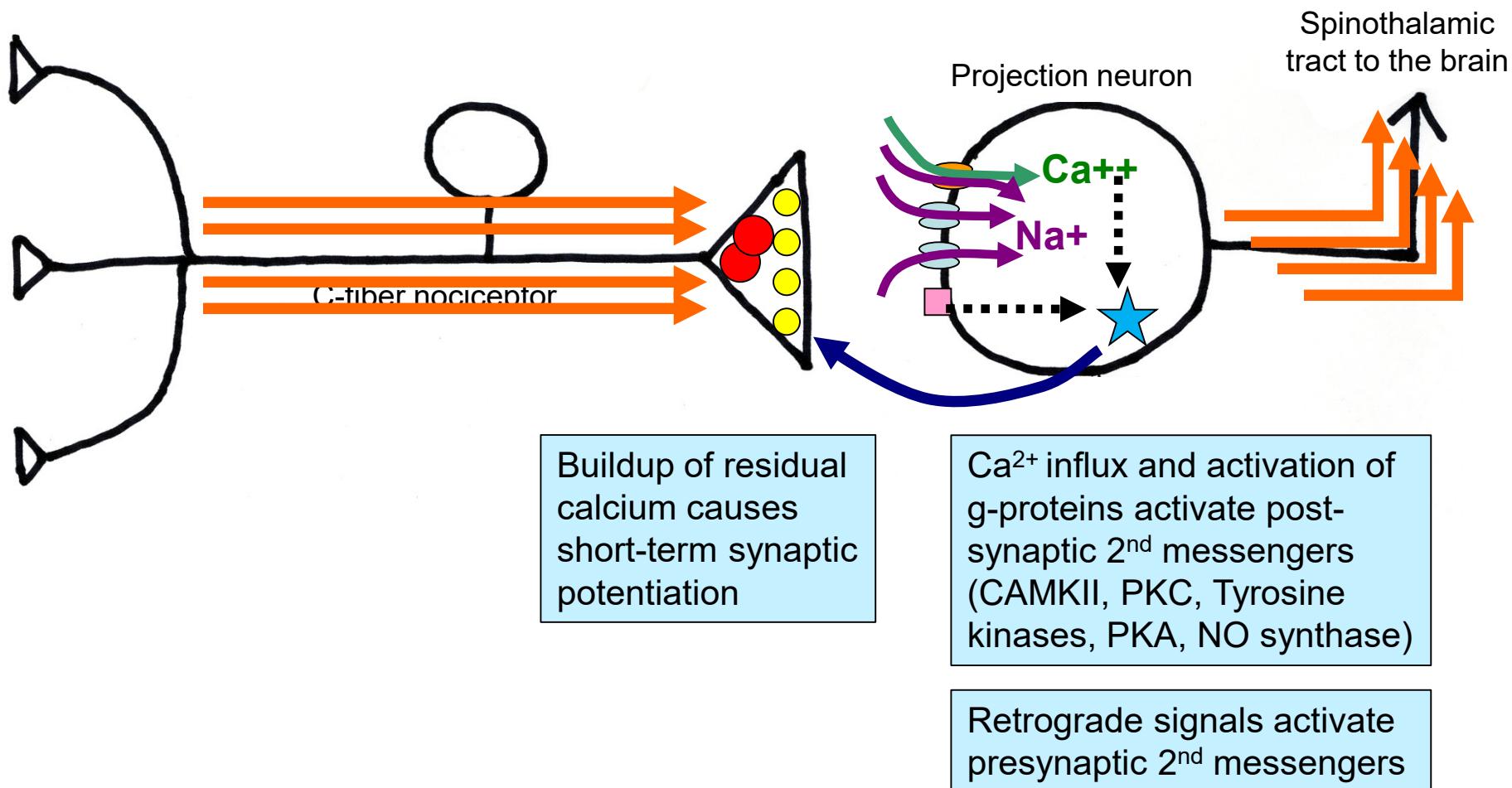
Hyperalgesia – Central Sensitization



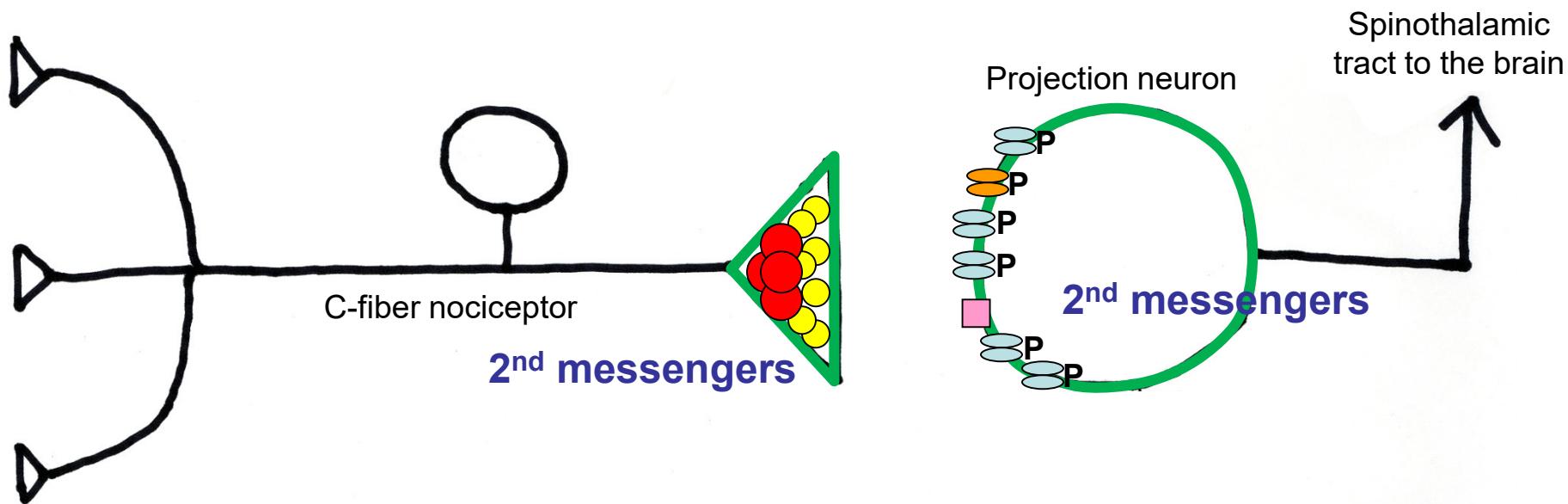
A Repetitive stimulation of C and A fibers



Hyperalgesia – Central Sensitization



Hyperalgesia – Central Sensitization



Presynaptic axon terminal produces and stores more transmitter

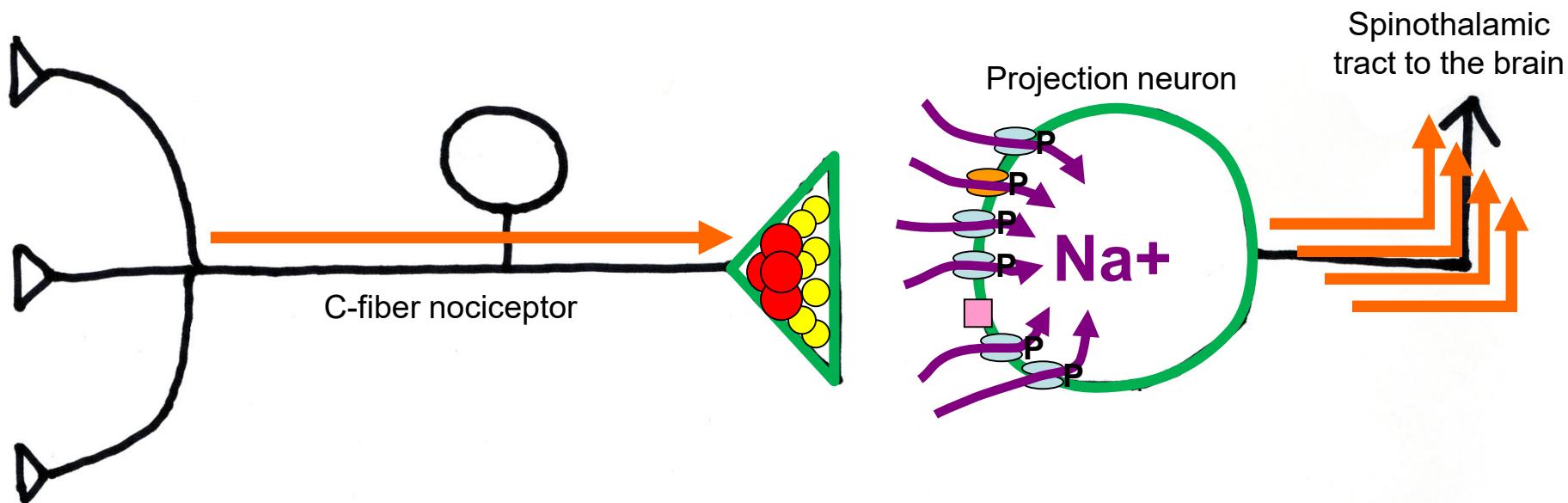
Alterations in ion channels increase inward currents and reduce outward currents in presynaptic and postsynaptic cells

Phosphorylation of NMDAR and AMPAR changes their threshold and activation kinetics

Additional AMPAR are placed into the post-synaptic membrane.

Post-synaptic AMPAR subunits are switched to be Ca^{2+} permeable

Hyperalgesia – Central Sensitization



The resulting increase in membrane excitability and potentiation of the synapse cause...

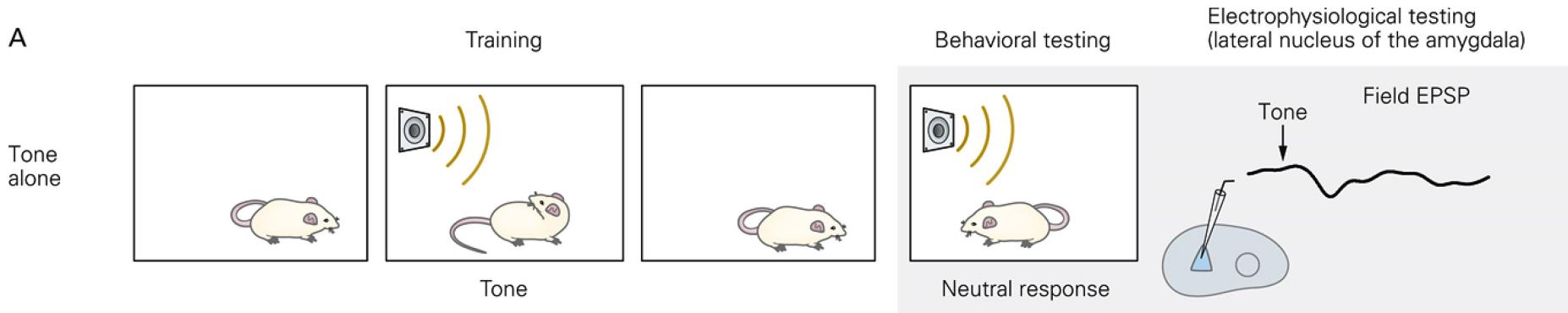
A reduction in the threshold for activation by peripheral stimuli

The development of or an increase in spontaneous neural activity

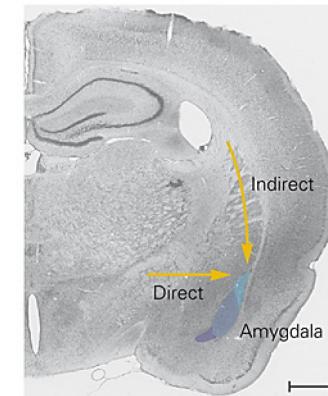
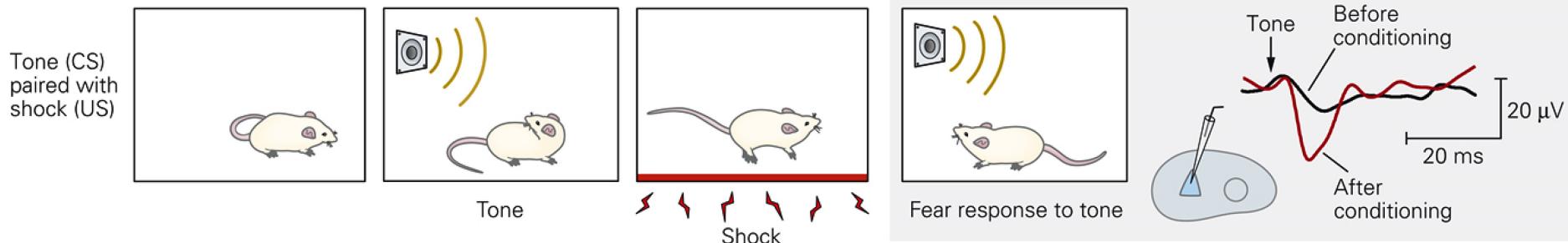
An enlargement of nociceptor receptive fields

Fear Conditioning in the Amygdala

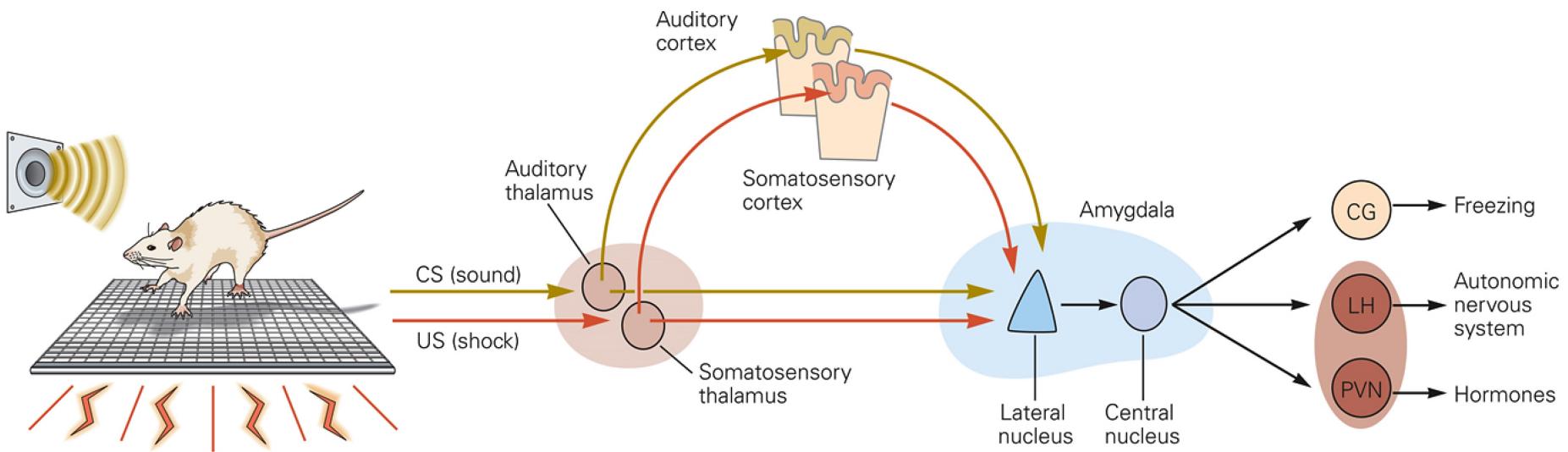
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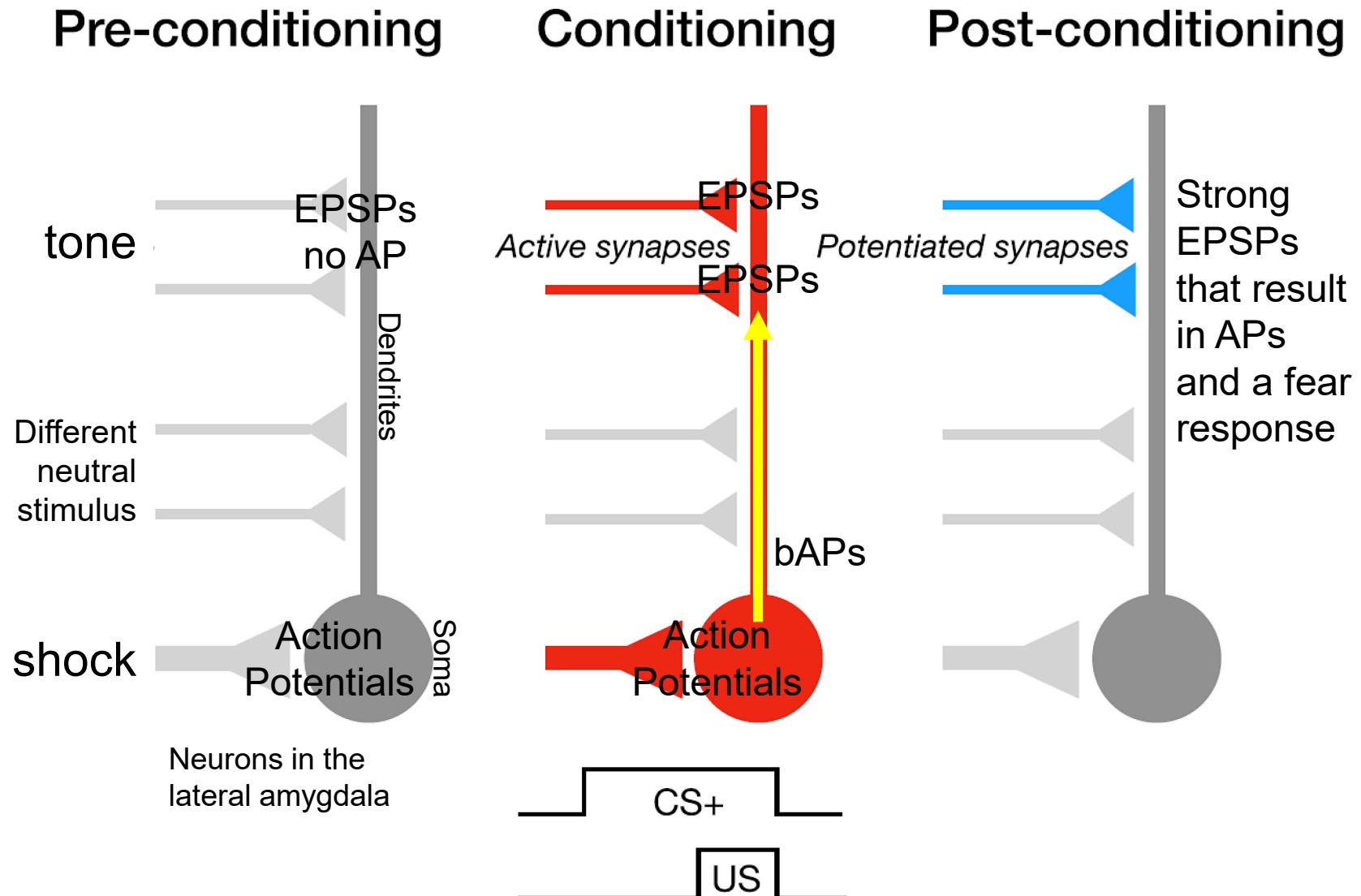
B



Fear Conditioning in the Amygdala



Fear Conditioning in the Amygdala



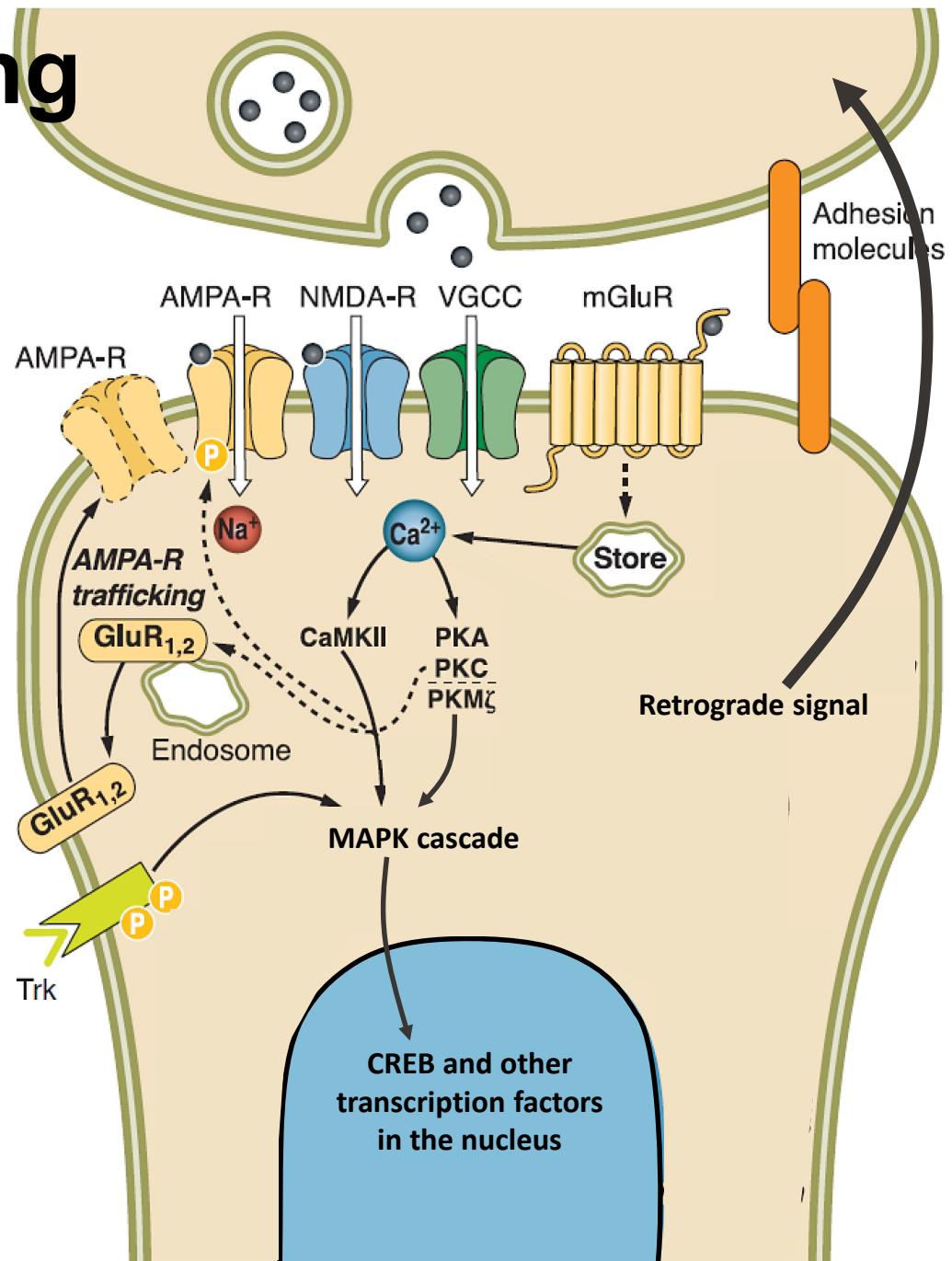
Fear Conditioning in the Amygdala

$[Ca^{2+}]_{\text{inside}}$ rises
(because of NMDAR, VGCC, and mGluR activation of PLC)

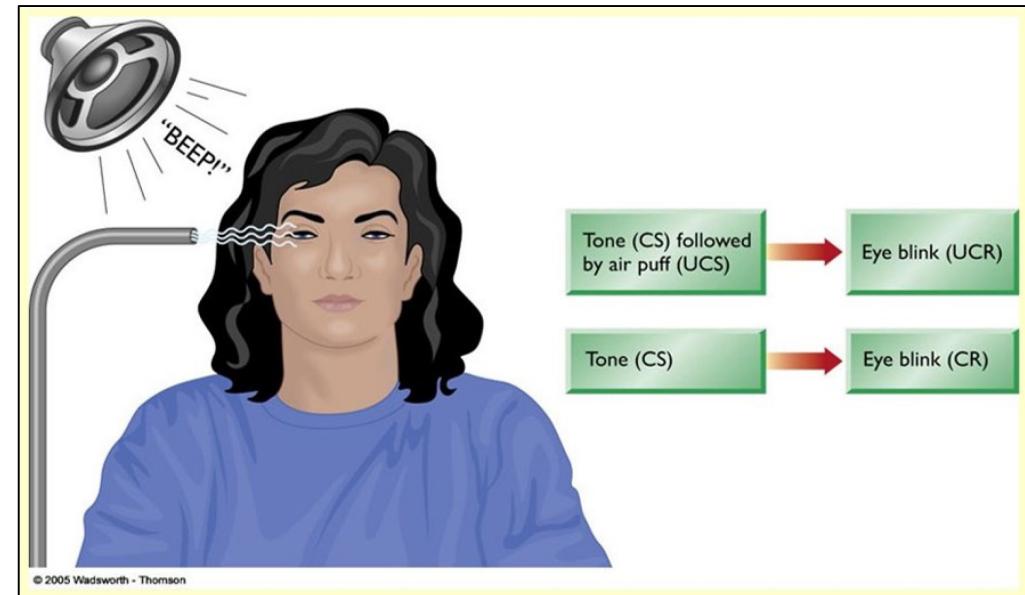
Activation of 2nd messengers
(CAMKII, PKC, Tyrosine kinases, PKA, PKM ζ , MAPK)

Short-term potentiation
(Phosphorylation of ionotropic glutamate receptors, insertion of additional AMPA receptors)

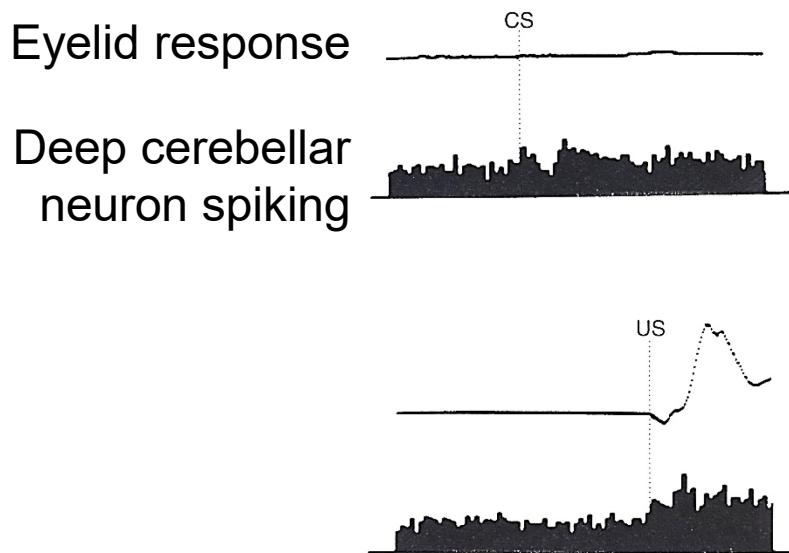
Long-term potentiation
(Changes in gene transcription, new protein synthesis, larger synapses, more synapses)



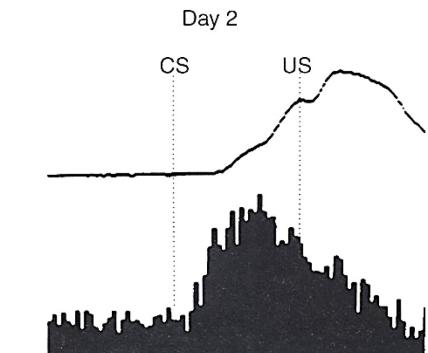
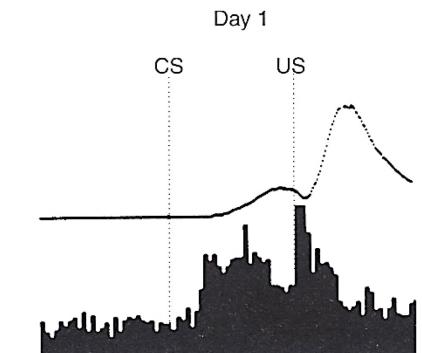
Behavioral Conditioning (Eyeblink Model)



Unpaired



Paired



Cerebellar Circuitry

Two loop circuits

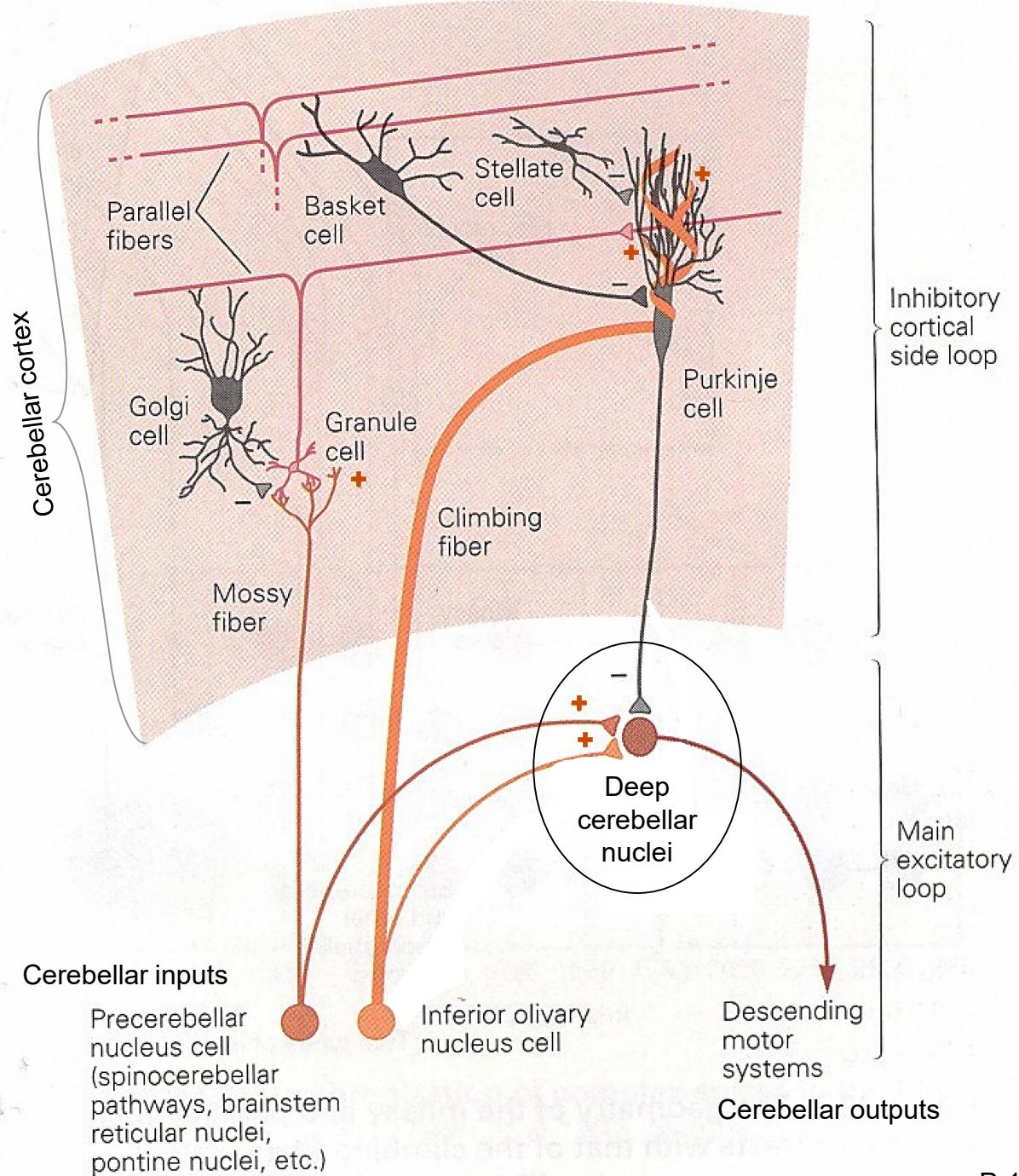
- Main excitatory loop
- Inhibitory cortical side loop

Two major pathways to Purkinje cells

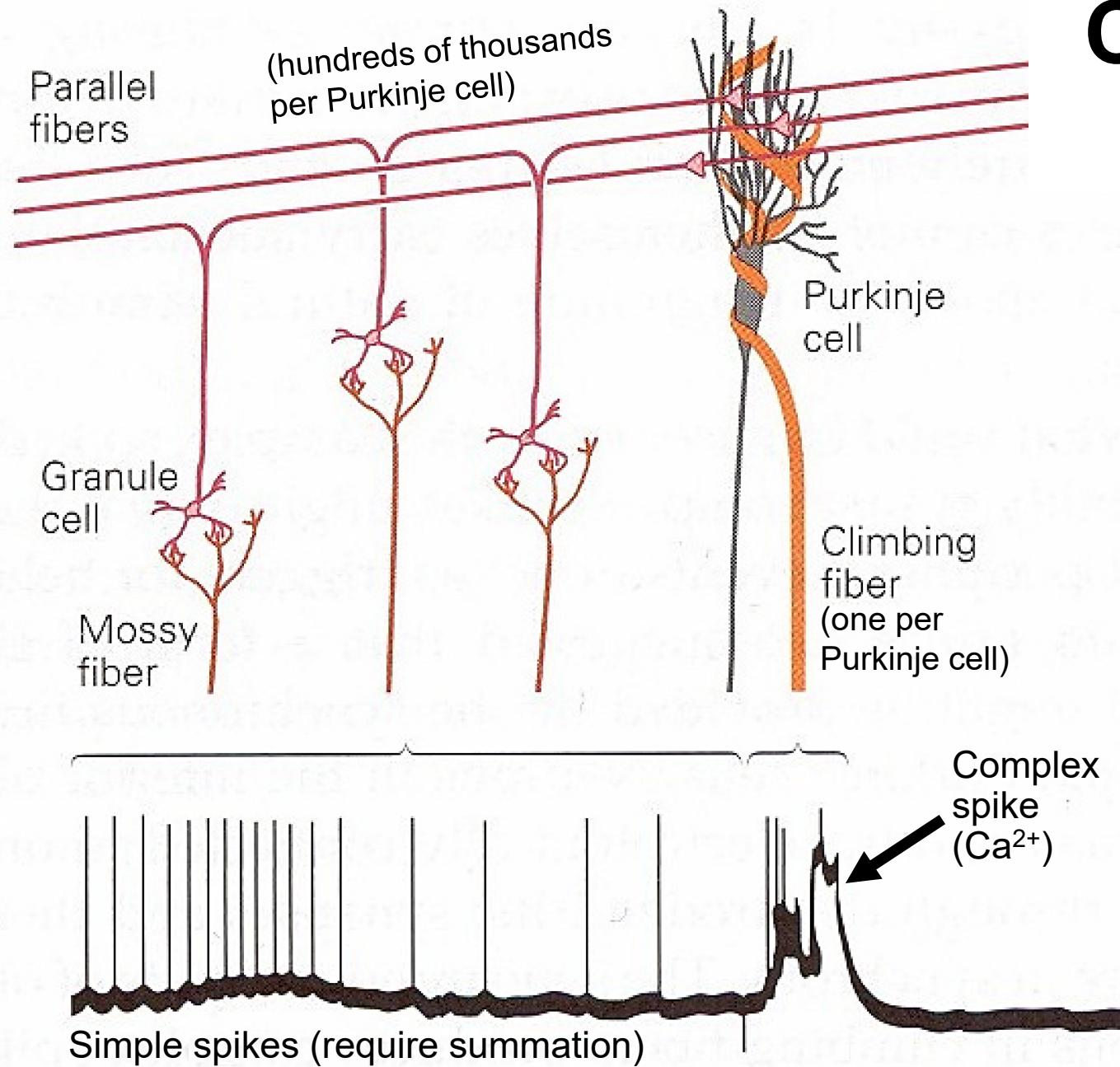
- Mossy fiber – Granule cell – Parallel fiber
- Climbing fiber

Local interneurons

- Golgi cells
- Basket cells
- Stellate cells

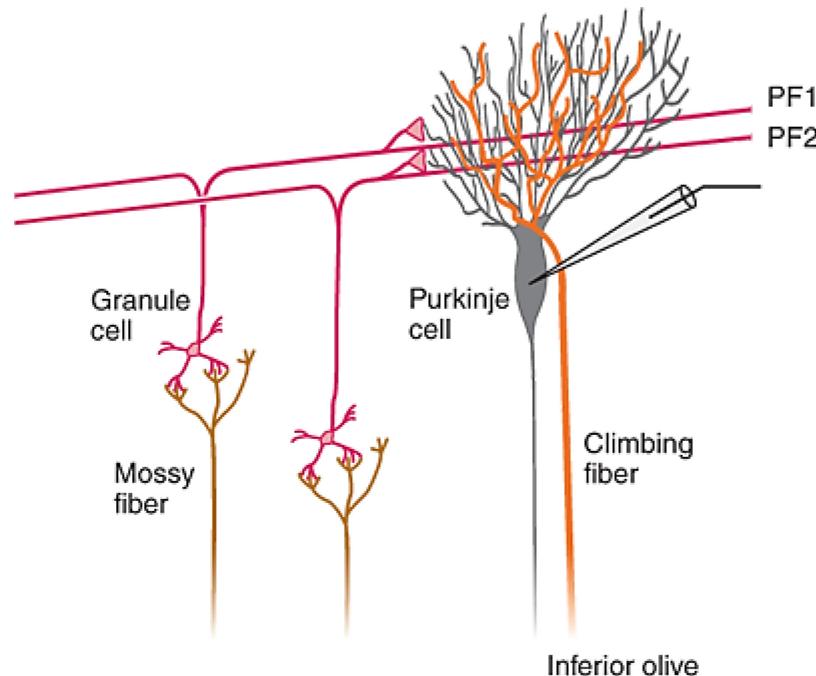


Cerebellar Circuitry



When the climbing fiber fires, all parallel fiber synapses that are active at the same time undergo long-term depression (LTD).

LTD in the Cerebellum



Training

PF1 PF2

Test

PF1/CF PF2

Adapt

PF1 PF2

Test

Parallel fiber EPSPs recorded in Purkinje cell

Paired (PF1)

Unpaired (PF2)

Before training

After
training

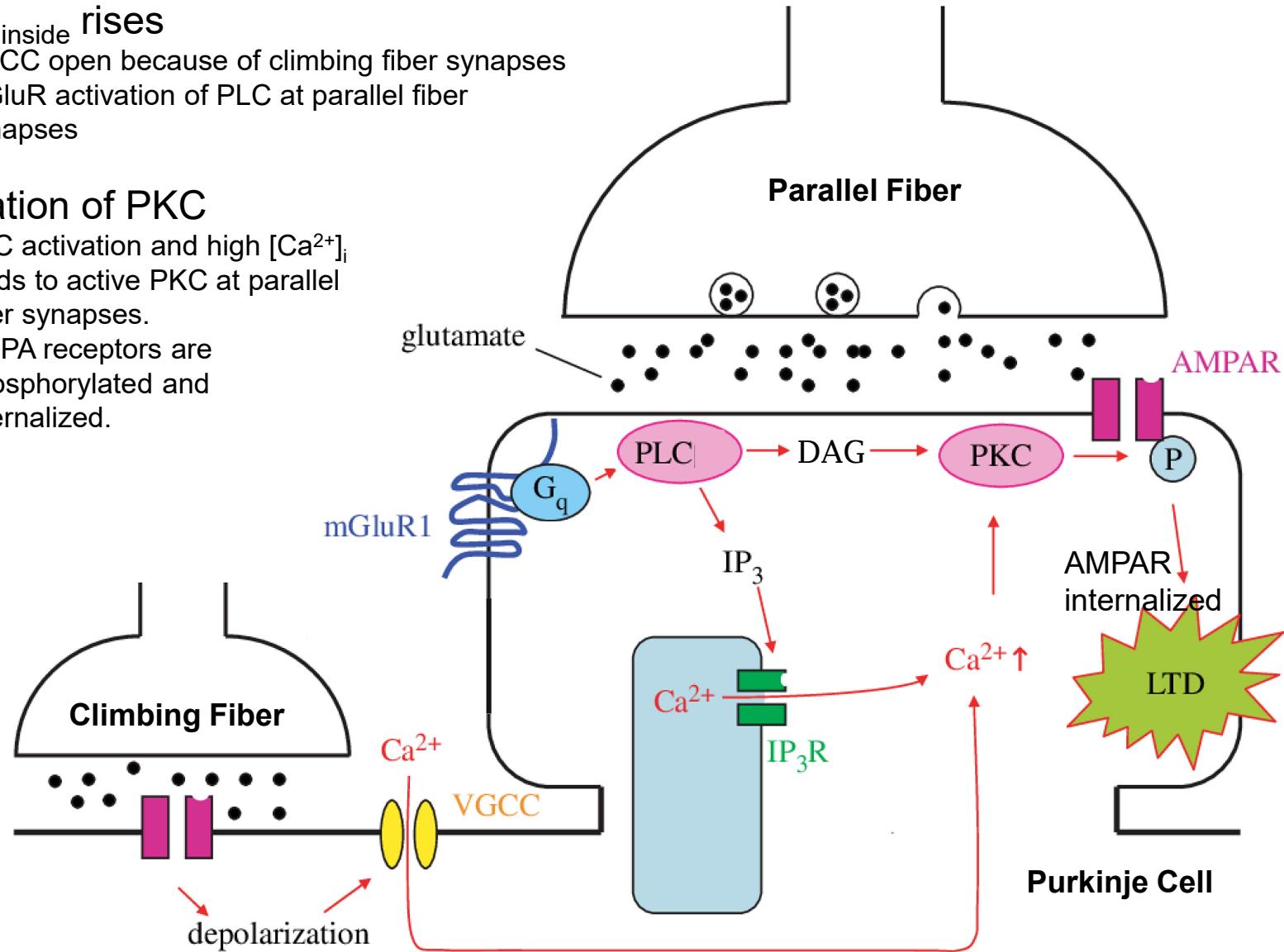
LTD in the Cerebellum

$[Ca^{2+}]_{\text{inside}}$ rises

- VGCC open because of climbing fiber synapses
- mGluR activation of PLC at parallel fiber synapses

Activation of PKC

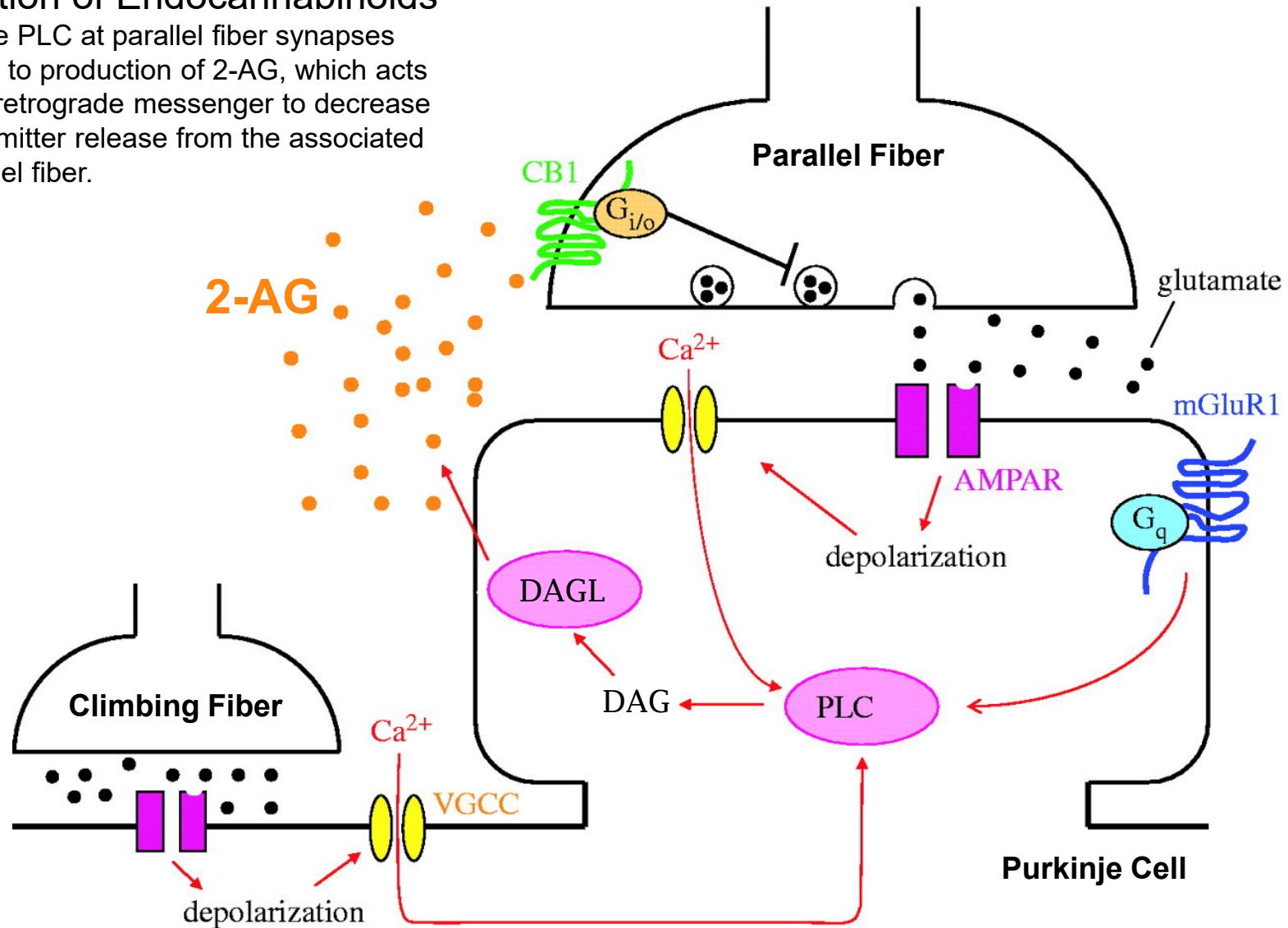
- PLC activation and high $[Ca^{2+}]_i$ leads to active PKC at parallel fiber synapses.
- AMPA receptors are phosphorylated and internalized.



LTD in the Cerebellum

Production of Endocannabinoids

- Active PLC at parallel fiber synapses leads to production of 2-AG, which acts as a retrograde messenger to decrease transmitter release from the associated parallel fiber.



Eyeblink Behavioral Conditioning Circuitry

