

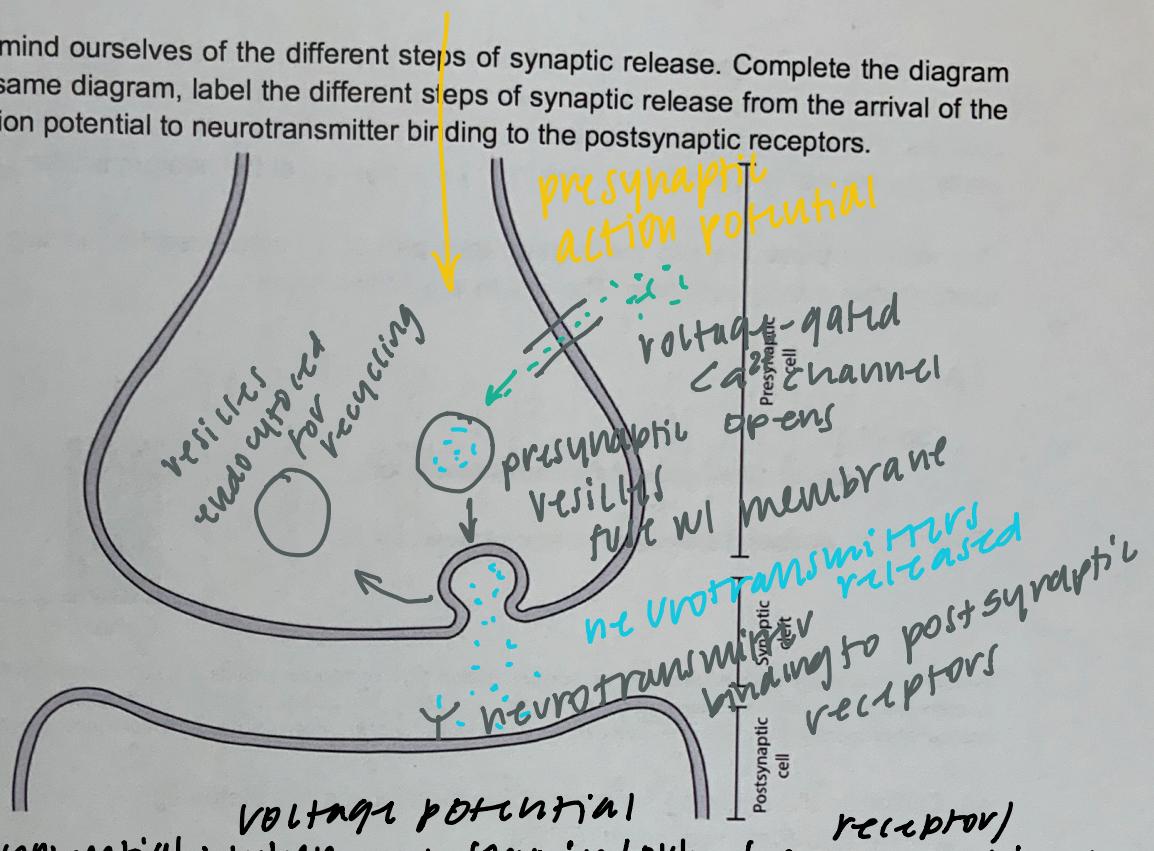
Neuro 80 Section 4

October 4, 2019

Section 4 (week 09/30 - 10/04)

MCB/Neuro 80, Fall 2019

1. First, let's remind ourselves of the different steps of synaptic release. Complete the diagram below. On the same diagram, label the different steps of synaptic release from the arrival of the presynaptic action potential to neurotransmitter binding to the postsynaptic receptors.

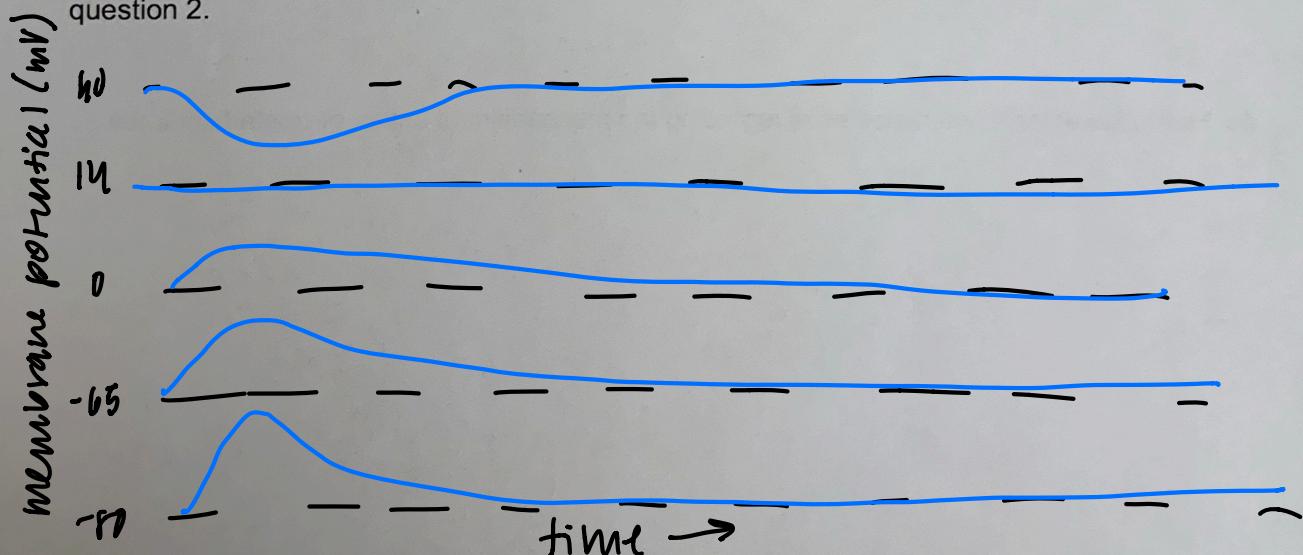


2. Now, let's focus on the postsynaptic receptor. This is a new receptor - a promiscuous cation so net channel with twice higher conductivity to Na^+ than to K^+ . Define the term "reversal potential", then $I_{\text{Na}} + I_{\text{K}} = 0$, then $I_{\text{Na}} = -I_{\text{K}}$, then $I_{\text{Na}}(V_m - E_{\text{Na}}) = -I_{\text{K}}(V_m - E_{\text{K}})$.

$$I_{\text{Na}} + I_{\text{K}} = 0 \quad I_{\text{Na}} = -I_{\text{K}} \quad g_{\text{Na}}(V_m - E_{\text{Na}}) = -g_{\text{K}}(V_m - E_{\text{K}})$$

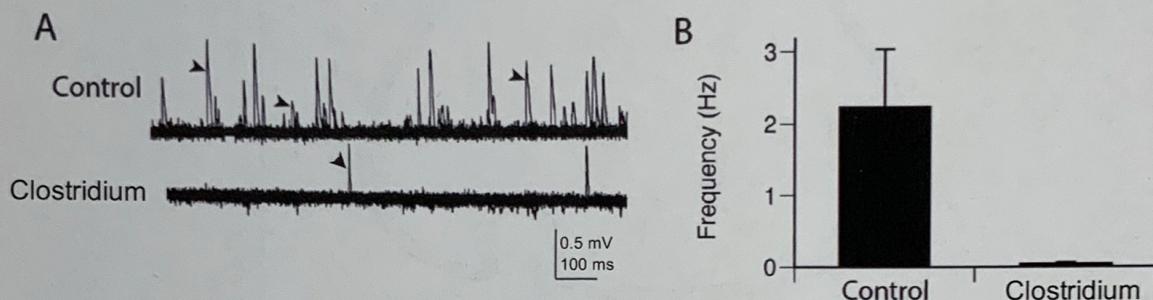
$$2(V_m - 60) = -(V_m + 77) \quad 3V_m = 42 \quad V_m = 14 \quad \text{mV}$$

3. Draw EPSPs after activating the synapse with the ligand, when you "hold the cell" (artificially use electricity to change the "resting potential" temporarily without affecting the chemical gradients) at the following 5 potentials: +40, 0, -65, -80 mV and whatever potential you found in question 2.



4. *Clostridium* are a genus of bacteria commonly found in the soil, yet some species produce various toxins and neurotoxins. You are helping with research that has identified a new bacterial species. The neurotoxin causes weakness and paralysis as well as numbness, so you want to study the mechanism of action of this toxin by studying it at the neuromuscular junction.

You stick an electrode into the postsynaptic part of a neuromuscular junction and record the spontaneous activity over time. The results are shown below:



Effects of clostridium toxin on the neuromuscular junction. (A) Exemplar recordings at the postsynaptic part of the neuromuscular junction before and after application of conotoxin. Arrows: "blips" (see questions below). (B) Frequency of "blips" before vs after application of conotoxin. The graph gives the mean \pm standard error of the mean (20 neuromuscular junctions recorded per condition).

4a. Complete the following sentence: "The small "blips" visible on figure A are..."

- (A) End Plate Potentials (EPPs)
- (B) Action Potentials
- (C) Miniature End Plate Potentials (mEPPs)
- (D) Electrical noise / experimental artifacts
- (E) None of the above

Explain your answer.

M EPPs are caused by spontaneous releases of neurotransmitter.

4b. Describe and interpret the results.

Describe: there are more spikes in the control, shown qualitatively in A and quantitatively in B

Interpret: Clostridium decreases # of APs (and therefore frequency)

4c. Formulate at least two hypotheses regarding the mechanism of action of clostridium toxin.

1. Blocks voltage-gated Ca^{2+} channels, preventing release of ACh into the NMJ. \therefore Fewer APs.
2. Competitive inhibition of ligand-gated ion channels in postsynaptic membrane, so signal conduction is halted.
3. prevent intravacuole w/ SNARE proteins