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Lecture 7
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Solution 7.1: Components of the synaptic delay

1. The four traces are (in the order of appearance):

   (A) the presynaptic action potential
   (B) the presynaptic Ca^{2+}-current
   (C) the postsynaptic current
   (D) the postsynaptic potential

   Explanation: The action potential in the presynaptic neuron leads to a presynaptic Ca^{2+}-current. Intracellular Ca^{2+} triggers the release of vesicles of neuro-transmitter which diffuses through the synaptic cleft, giving rise – mediated by receptors – to a postsynaptic current that changes the postsynaptic potential.

2. The components of the synaptic delay are:

   (a) This component is approx. 0.8 ms long and comprises
   - Gating of presynaptic Ca^{2+}-channels

   (b) This component is approx. 0.2 ms long and comprises all the processes from the Ca^{2+}-current to the subsequent steps leading to the postsynaptic potential. Concretely:
   - Ca^{2+}-dependent vesicle fusion (exocytosis)
   - Transmitter diffusion in the synaptic cleft
   - Gating of postsynaptic ligand-gated channels

   One can easily see that the component (a) (time dependence for the onset of the calcium current) makes the larger part of the synaptic delay. It is much slower than all the processes that are combined in the component (b).

Solution 7.2: Quantal release I

1. A trial when 0 quanta are released is called a failure. The expression $P[X = x]$ denotes the probability that x vesicles are released in a trial. Here, the mean number of vesicles released per trial (expectation value of the Poisson distribution) is $m = 5$. Therefore, the expected number of failures in 500 trials N_0 is:

$$N_0 = 500 \cdot P[X = 0] = 500 \cdot \frac{5^0}{0!} e^{-5} = 500 \cdot 0.0067 = 3.37$$

   Note that $0! = 1$.

2. Similarly, the expected number of trials with two released quanta in 500 trials N_2 is:

$$N_2 = 500 \cdot P[X = 2] = 500 \cdot \frac{5^2}{2!} e^{-5} = 500 \cdot \frac{25}{2} \cdot 0.0067 = 42.1$$

Solution 7.3: Quantal release II

1. They denote the observations where 0 (failure of transmission, A), 1 (B), 2 (C) and 3 (D) vesicles are released.

2. It can be seen from the graph that the quantal amplitude Q is 0.4mV.

3. The mean number of vesicles released per observation is

$$m = \frac{0.93\text{mV}}{0.4\text{mV}} = 2.3.$$

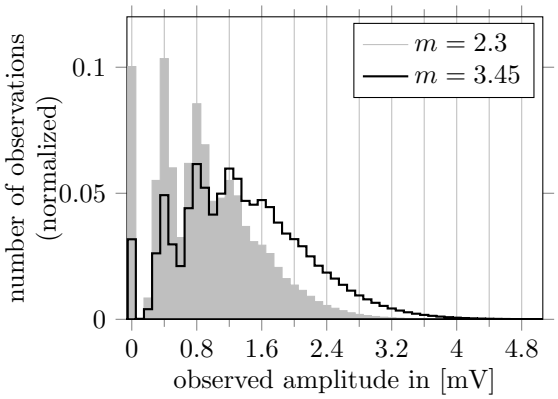
   Knowing that $P[X = x]$ follows a Poisson distribution, we can also read out the value at $x = 0$ from the plot and put it into the formula of the Poisson distribution:

$$P[X = 0] = \frac{m^0}{0!} e^{-m} = 18/200.$$

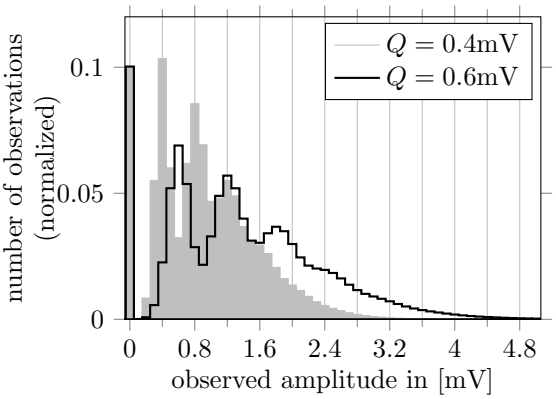
   This gives

$$m = -\ln\left(\frac{18}{200}\right) = 2.41.$$

4. An increase in release probability (is a pre-synaptic change) increases the value of m, whereas the value of Q remains the same (examples are shown in fig. 1). On the other hand, post-synaptic modifications lead to a change of Q (the amplitude of the end-plate potential when one vesicle is released), whereas m stays the same.



(a) Change in the histogram with **pre**-synaptic modifications (m changes and $Q = 0.4$mV stays the same). As $m = n \cdot p$ (n is the numbers of vesicles at the presynaptic site and p is the release probability for each vesicle), an increase in release probability p corresponds to an increased m.

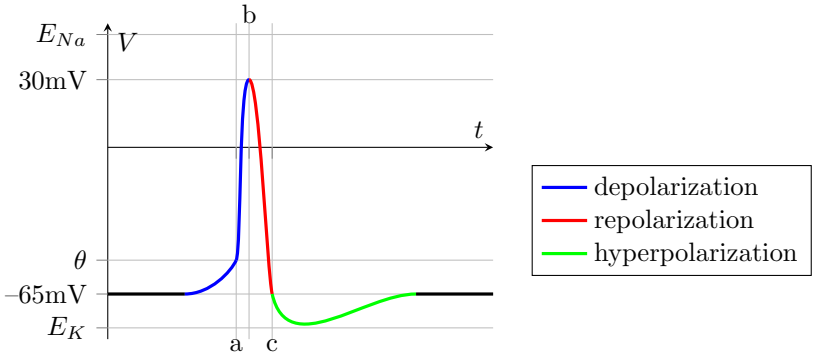


(b) Change in the histogram with **post**-synaptic modifications (Q changes and $m = 2.3$ stays the same). Note that the value of Q does not have an effect on the number of observed transmission failures.

Figure 1: Examples for how the histogram of observed amplitudes can be changed. Note that for both examples with the thick black line the mean amplitude of all events is the same ($m \cdot Q = 3.45 \cdot 0.4\text{mV} = 1.38\text{mV} = 2.3 \cdot 0.6\text{mV}$), but their shape is different.

Solution 7.4: Back to Basics

At (a) and shortly before Na^+ channels open and K^+ channels start to open
At (b) Na^+ channels close (inactivation!)
At (c) K^+ channels start to close



Note that the threshold θ depends also on the history of the membrane potential, *e.g.* how fast it is depolarized, so it is not a fixed quantity as the figure could suggest. Moreover, not all the channels open and close at exactly the same time, it is still a stochastic process.

Solution 7.5: Influence of Ion Concentrations

The more permeable a membrane is to a particular ion, the more that ion will control the value of the membrane potential as the concentration gradient for that ion is varied. This is expressed quantitatively in the Goldman-Hodgkin-Katz equation. If $P_{ion} = 0$, then the membrane potential will not change as the concentration of that ion varies across the membrane, *i.e.* the membrane potential will no longer depend on that particular ion. Further the slopes of figures 2(b) tell us that RP mainly depends on potassium and AP peak mainly on calcium.

1. We know that $[K^+]$ dominates the RP. By way of the GHK equation this implies that $P_K > P_{Ca}$.

2. The AP peak is dominated by $[Ca^{++}]$, therefore $P_K < P_{Ca}$.

3. The RP is dominated by $[K^+]$ and V_m is negative at RP, thus from Nernst equation: $[K^+]_{in} > [K^+]_{out}$. Since V_m must be above the reversal potential E_K, K^+ ions have the tendency to flow outward. However, since the membrane is close to E_K, the K^+ current is only weak. Furthermore, P_{Ca} is negligible, which implies that there is no Ca^{++} current.
   At the peak of the AP, P_{Ca} is high, so we are closer to E_{Ca} at positive membrane potentials, therefore, again from Nernst equation $[Ca^{++}]_{in} < [Ca^{++}]_{out}$. The calcium current has the opposite direction of the potassium current. The rising of the AP is generated by Ca^{++} influx, which depolarizes the cell.

4. Since $[K^+]$ dominates the RP, in rest V_m is close to E_K. Therefore E_K is negative and hyperpolarisation is mainly caused by an increasing P_K. You also could think of decreasing P_{Ca}, but as we know from 1, at the RP there is not much room for P_{Ca} to decrease more.

Please note that this was a general example of a cell membrane permeable only to K^+ and to Ca^{++} ions. In the particular case of many types of *neurons*, of course, Na^+ permeability (not Ca^{++}) plays an important role for the generation of their action potential.