

1.a. Explain the positive feedback involved in producing an action potential in the Hodgkin-Huxley model.

The cell membrane of a neuron has voltage-gated sodium (Na^+) and potassium (K^+) ion channels. These channels open and close based on changes in membrane potential. When a neuron is at rest, a stimulus can lead to a slight increase in membrane potential (depolarization) and start to open some voltage-gated sodium channels. As sodium channels open, positively charged sodium ions (Na^+) rush into the cell, making the inside of the cell even more positive. This further depolarizes the membrane. The increased depolarization causes even more voltage-gated sodium channels to open, leading to an even greater influx of Na^+ . This cycle repeats, with more sodium channels opening and more sodium ions entering, creating a rapid, self-reinforcing depolarization towards a positive membrane potential. This is the primary positive feedback component.

2.b. Describe how three different terms produce negative feedback in the Hodgkin-Huxley equations.

The positive feedback cycle continues until the membrane potential reaches a threshold. At this point Sodium channels begin to close (inactivate). This limits further sodium influx and counteracts the positive feedback loop, slowing down or even preventing excessive depolarization. Similar to the sodium channel inactivation, potassium channel activation increases with depolarization. As more potassium channels open, they allow K^+ efflux, which opposes further depolarization and pushes the potential back towards the resting state. Slower voltage-gated potassium channels start to open, allowing positively charged potassium ions (K^+) to flow out of the cell. These actions eventually lead to repolarization and the return of the membrane potential to the resting state, completing the action potential.

2. In the Hodgkin-Huxley model, the potassium activation variable, n , impacts the conductance as n^4 , which is equivalent to the effect of four independent subunits, with each one in the state necessary for channel-opening with probability, n . Would the exponent change from 4, and if so, in what direction, if the subunits were not independent but had some degree of cooperativity to produce a positive correlation between their states? Explain your reasoning.

Yes, the exponent would change if the potassium channel subunits exhibited cooperativity instead of being entirely independent. The dependency means that the state of one subunit affects the probability of the other subunits being in the open state. If we consider having positive cooperativity, one open subunit makes it more likely for the others to open as well. Therefore, the overall probability of the channel being open would increase more rapidly than it would with independence. This is because an open subunit boosts the likelihood of others following suit. As a result, the exponent in the conductance term would need to be less than 4 to produce the same overall gating behavior. If we consider having negative cooperativity meaning that once one subunit is activated, the probability of the other subunits being activated decreases. This negative cooperativity would result in a lower conductance than expected from the independent activation of each subunit.

3. What is the key similarity between anode break in the Hodgkin-Huxley model and postinhibitory rebound in the thalamocortical model neuron? What differences are there between the two?

Both of them have the ability to generate a burst of activity following a period of reduced activity (action potential firing). But Anode break occurs on a faster timescale compared to postinhibitory rebound due to the simpler interplay of intrinsic membrane properties in the Hodgkin-Huxley model. The other

difference is that Anode break involves the activation of voltage-gated sodium channels and the inactivation of voltage-gated potassium channels. Postinhibitory rebound involves the activation of T-type calcium channels.