

9 Generation of Action Potential — Hodgkin-Huxley Model

(based on chapter 12, W.W. Lytton, *Hodgkin-Huxley Model*)

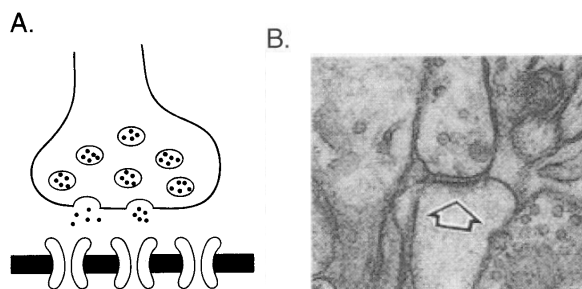
9.1 Passive and active membrane models

- In the previous lecture we have considered a **passive model** of the neuronal **membrane** and applied this model to predict the change of the **Post-Synaptic Potential** in response to pulses arriving at the synapse.
- Now we extend the synapse model to include active elements, namely, **batteries** and **variable resistors/conductors**.
- Such an **active model** will be used to explain generation of pulses known as the **action potential** at the axon of a neuron.
- In the 1950s Alan Hodgkin and Andrew Huxley worked out the ionic basis of the action potential and developed a mathematical model that successfully predicted the speed of spike propagation.
- Their work can be regarded in retrospect as the beginning of computational neuroscience.
- It remains the touchstone for much neural modeling today.

Since then hundreds have been described and some of the basic parameterization has been updated, but the Hodgkin–Huxley model is still considered to be the standard model.

9.2 Ion channels

- Ion channels (pores) are proteins that span the cell membrane allowing the flow of ions through the membrane.
- Ion channels have three important properties:
 1. They conduct ions,
 2. they recognize and select specific ions, e.g. sodium Na^+ ions
 3. they open and close in response to specific electrical or chemical signals.
- Consider the following example of a neurotransmitter-gated, or chemical-sensitive channels in the dendritic spine:

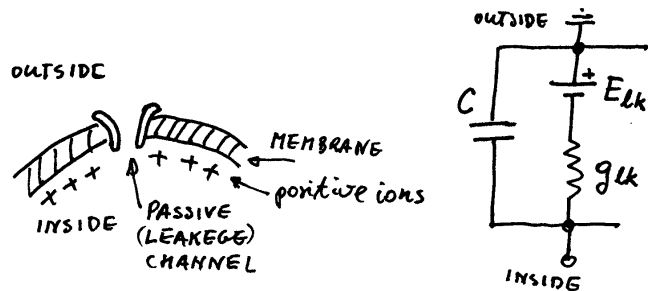


from Trappenberg, *Fundamentals of Computational Neuroscience*

- Schematic illustration of a chemical synapse and an electron microscope photo of a synaptic terminal
- Neurotransmitter-gated ion channels open and close under the regulation of neurotransmitters, such as GABA, glutamate and dopamine.
- The flow of ions results in the **postsynaptic potential** (PSP).
- It is good to remember that the synaptic cleft, that is, the gap between the axon terminal and the dendritic spine is only a few μm wide.

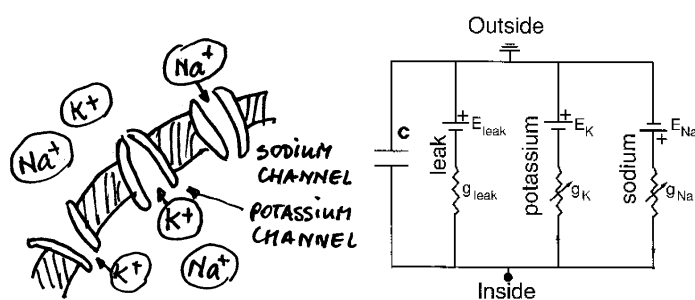
9.3 From passive to the active membrane model

- In the passive model the membrane was modeled as a leakage conductance g_{lk} and a capacitance, C .
 - Such a model assumed that the resting membrane potential was 0 mV.
 - In reality the **resting membrane potential** (RMP) is negative and approximately equal to -70 mV.
 - To account for that we have to add a battery E_{lk} associated with the leakage conductance.
 - The battery implies that there is a constant excess of positive ions inside the cell.
 - These positive ions flow through the always open leakage channel.
 - Such a model does not explain the magic of having the excess of positive ions despite of their constant outflow from the cell.
- To understand that we have to consider a few more mechanisms present in the cell.
- First, we have to consider the presence of (at least) two types of positive ions: **sodium**, Na^+ , and **potassium**, K^+ , ions.
 - There are **voltage-sensitive** channels and related batteries associated with each type of ions.



9.4 Parallel-conductance model of the membrane

- Now we have all elements to form the parallel-conductance model that was first formulated by Hodgkin and Huxley in 1950s



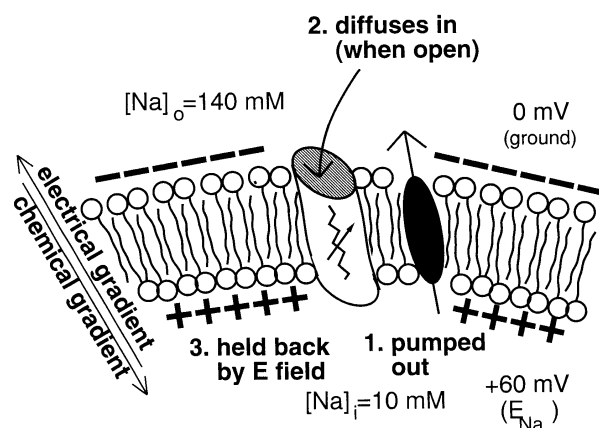
- Note that all points on the inside of the membrane are electrically connected via the cytoplasm. This is the point where we measure potential.
- Similarly the outside of the membrane is connected via the extracellular fluid (horizontal line at top) and is grounded, keeping it at 0 mV.

- The potassium channel is modeled by a variable resistor, g_K and a battery, E_K .
- Similarly, sodium channel is modeled by a variable resistor, g_{Na} and a battery, E_{Na} .
- The variable resistor is voltage-sensitive and varies its conductance depending on the voltage across the resistor.
- Note that the potassium battery pushes the positive potassium ions out off the membrane.
- Conversely, the sodium battery pushes the positive sodium ions inside the cell.
- At rest, the sodium and potassium conductances are zero, that is, the channels are closed and the flow of ions through the respective channels are turned off.

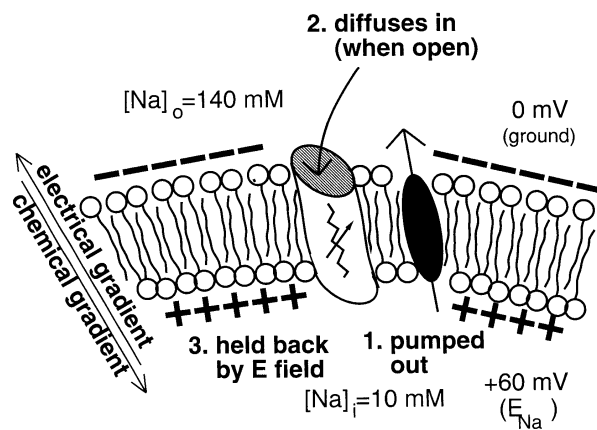
9.5 Where do the batteries come from?

- The batteries are an indirect result of proteins that pump ions across the membrane.
- These ions then try to flow back “downhill,” in the direction of their **chemical gradient** from high concentration to low concentration (diffusion process).
- Only a little current has to flow in order to set up an equal and opposite electrical gradient.
- The electrical gradient, opposite in direction to the chemical gradient, is the battery.
- This electrical potential is called the Nernst potential. Each ion has its own Nernst potential.
- It can be precisely calculated by knowing the **concentrations** of a particular ion inside and outside of the cell.
- The value in millivolts of the Nernst potential is the strength of the battery that we use in the circuit diagram.

9.5.1 Sodium battery — Nernst potential



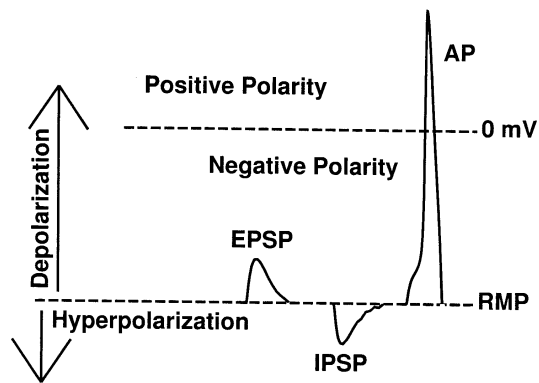
- Concentration of sodium ions Na^+ outside the cell is higher than it is in the cytoplasm, that is, inside the cell.
 - The concentration difference creates the chemical gradient forcing the inward diffusion of sodium ions.
 - Sodium is pumped from inside to outside (#1 in figure) by a protein that uses energy from ATP (adenosine triphosphate).
- The pumping leaves sodium concentration outside of the cell ($[Na]_o \approx 140$ millimoles) higher than it is in the cytoplasm ($[Na]_i \approx 10$ millimoles).
(1 mole = $6.02 \cdot 10^{23}$ atoms — the Avogadro number — is a measure of amount of substance)
 - The concentration difference across the membrane does not in itself lead to any charge separation, since sodium ions on both sides are appropriately matched with negatively charged proteins.
 - Since there is more sodium outside, it “wants” to flow inside due to diffusion (#2 in Fig. 12.3).
 - (Diffusion is what makes a drop of ink spread out in a glass of water; it wants to go where no ink has gone before.)



- As long as the selective channels for sodium remain closed, sodium cannot diffuse and the sodium concentration gradient has no effect on membrane potential.
- When the sodium channel opens, sodium rushes down its concentration gradient.
- The negative proteins that are paired with the sodium ions cannot follow; they are not allowed through the sodium channel.

- This diffusion of sodium across the membrane leads to charge separation across the membrane, with unmatched sodium ions on the inside and unmatched negative protein molecules on the outside.
- The unmatched sodium ions inside the membrane will stay near the membrane, in order to be close to their lost negative brethren.
- This bunching of positives next to the inside of the membrane, with a corresponding bunching of negatives next to the outside, creates an electric field (#3 in Fig. 12.3) that opposes inward diffusion through the ion channels.
- This outward electric field is the sodium battery.

- The inward diffusive force and the outward electrical force reach a steady state (Nernst equilibrium) so that there is no net flow of ions and little need for continued pumping to maintain equilibrium.
- The concentration difference between inside and outside can be directly translated into an electrical potential by using the Nernst equation.
- The resulting battery voltage E_{Na} is approximately +60 mV between the battery plates.
- By contrast, **potassium** is at high concentration inside and low concentration outside.
- The potassium chemical gradient is outward so the electrical gradient is inward.
- The positive inward electrical gradient would be +90 mV if measured from the outside of the membrane, relative to a grounded inside.
- However, we always measure the potential on the inside, relative to ground outside, so the potassium potential (E_K) is about -90 mV.
- Before we write Hodgkin-Huxley equations some comments regarding a standard nomenclature to describe voltage deviations from resting potential

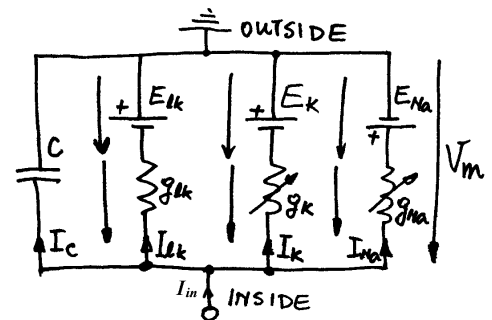


- Resting membrane potential (RMP) is typically about -70 mV (inside negative).
- Negative deviations, which make the membrane even more negative than at rest, are called **hyperpolarizing** (hyper means more).
- Positive deviations, which make the membrane less negative than it is at rest, reducing its polarization, are called **depolarizing**.

- Excitatory postsynaptic potentials (EPSPs) depolarize. Inhibitory postsynaptic potentials (IPSPs) hyperpolarize.
- Action potentials (APs) are depolarizations that can overshoot 0 mV, temporarily reversing membrane polarity.
- The membrane can be naturally depolarized by about 120 mV, (approximately the value of the sodium battery) from -70 mV to $+50$ mV
- Natural activity will only hyperpolarize the cell by about 20 to 30 mV (approximately the value of the potassium battery) to -100 mV
- Artificial depolarization with injected current is limited by the tendency of prolonged depolarization to kill the cell.

9.6 The membrane voltage equation

- The calculations for the parallel-conductance model are similar to those for the RC model except that we have to add in the batteries.
- The membrane voltage, V_m , is the same for each parallel branch of the circuit. Hence we can write:



- For the Sodium branch: $V_m = E_{Na} + \frac{I_{Na}}{g_{Na}}$. Hence the current: $I_{Na} = g_{Na} \cdot (V_m - E_{Na})$

- For the Potassium branch: $V_m = E_K + \frac{I_K}{g_K}$. Hence the current: $I_K = g_K \cdot (V_m - E_K)$

- For the leak branch: $V_m = E_{lk} + \frac{I_{lk}}{g_{lk}}$. Hence the current: $I_{lk} = g_{lk} \cdot (V_m - E_{lk})$

- The current through the capacitor is proportional to the time derivative of the voltage across the capacitor

$$I_C = C \cdot \frac{dV_m}{dt}$$

- According to Kirchoff's law the input current must balance the outgoing currents:

$$I_C + I_{lk} + I_K + I_{Na} = I_{in}$$

- This is typically written in the following form

$$I_C = -I_{lk} - I_K - I_{Na} + I_{in}$$

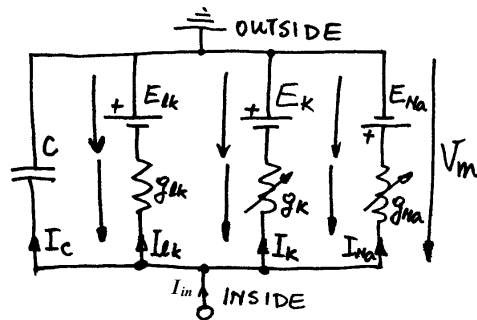
- Substituting the currents gives the first **Hodgkin-Huxley equation for the membrane voltage**:

$$C \cdot \frac{dV_m}{dt} = -g_{lk} \cdot (V_m - E_{lk}) - g_K \cdot (V_m - E_K) - g_{Na} \cdot (V_m - E_{Na}) + I_{in} \quad (9.1)$$

- It is a first-order differential equation for the membrane voltage V_m , that can be also written as:

$$C \cdot \frac{dV_m}{dt} = g_{lk} \cdot (E_{lk} - V_m) + g_K \cdot (E_K - V_m) + g_{Na} \cdot (E_{Na} - V_m) + I_{in} \quad (9.2)$$

- The fact that the sodium and potassium conductances also depends on the membrane voltage. This makes the equation difficult to analyze.
- First, some comments on the directions of current and voltages involved in the model:



- Typically the conventional direction of currents is towards the ground, that is, zero potential.
- If the current is positive, than it indicates the direction of movement of positive charges.
- The conventional direction of voltages is “against the current”. Such voltages can be positive or negative.

- In the literature, the phrase “membrane current” is used as a synonym for conductive (ionic) current.
- Therefore, negative current flows in and depolarizes; positive current flows out and hyperpolarizes.

9.6.1 Calculating the resting potential

- The resting potential can be calculated assuming that there is voltage change, that is, the time derivative of the membrane voltage is zero.
- In addition the external current $I_{in} = 0$.

Now eqn (9.1) can be re-written as:

$$g_{lk} \cdot (V_m - E_{lk}) + g_K \cdot (V_m - E_K) + g_{Na} \cdot (V_m - E_{Na}) = 0 \quad (9.3)$$

- Solving equation (9.3) for V_m gives the **resting membrane potential (RMP)**:

$$V_m = \frac{g_{lk} \cdot E_{lk} + g_K \cdot E_K + g_{Na} \cdot E_{Na}}{g_{lk} + g_{Na} + g_K} \quad (9.4)$$

- This is a version of the Goldman-Hodgkin-Katz (GHK) equation.
- It says that steady-state membrane voltage is the weighted sum of the batteries, weights being the conductances associated with respective batteries.
- Since g_{lk} is the dominant conductance at rest, it will have the greatest effect on determining RMP.
- If a conductance is turned off completely (e.g., $g_{Na} = 0$), the corresponding battery has no influence.
- If, on the other hand, a conductance is very high, then the other batteries will have very little influence, e.g., if $g_{Na} \gg g_K$ and $g_{Na} \gg g_{lk}$, then $V_m \approx \frac{g_{Na} \cdot E_{Na}}{g_{Na}} = E_{Na}$

9.7 Modelling the active channels

- To complete the Hodgkin-Huxley model, we have to describe the behavior of the **sodium** and **potassium** channels.
- These channels are modeled as voltage-sensitive conductances controlled by **three types of “activation particles”**.
- These conceptual activation particles are voltage-dependant time-evolving quantities describing gradual switching on and off the potassium and sodium channels.
- These quantities associated with the conceptual particles change their values between 0 (channel off) and 1 (channel fully on).

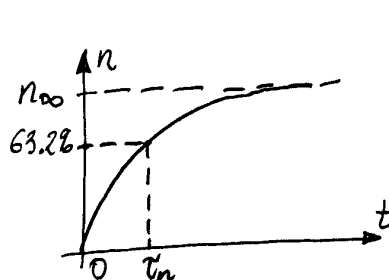
9.7.1 The potassium channel — n particles

- The variation of the conductance of the potassium channel, g_K , is modeled by one type of time-varying activation particles called n .
- Firstly, there is the following non-linear relationship between the channel conductance and the activation particles

$$g_K = G_K \cdot n^4 \quad (9.5)$$

where G_K is the maximum value of the conductance, for $n = 1$.

- Secondly, the particles vary in time between 0 and its maximum, or steady-state value, n_∞



$$\tau_n \frac{dn}{dt} = n_\infty - n \quad (9.6)$$

Assuming that n_∞ is constant (which it is NOT), this equation would have a well-known solution in the form of a saturating exponential growth

$$n(t) = n_\infty (1 - e^{-\frac{t}{\tau_n}}) \quad (9.7)$$

governed by the time constant τ_n .

- Thirdly, the time constant, τ_n and the steady-state value n_∞ depends on the membrane voltage through the following experimentally verified equations:

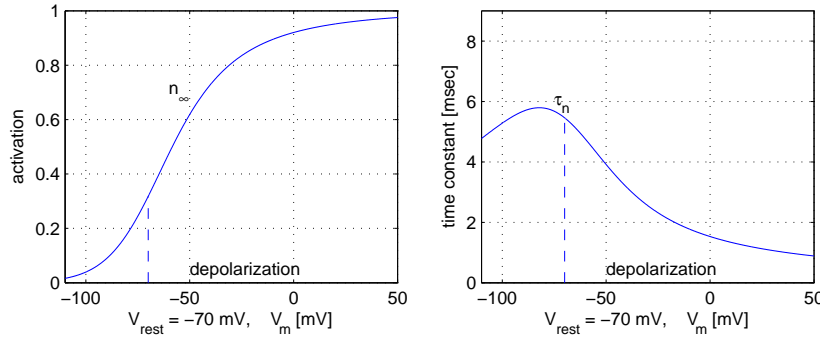
$$\tau_n = \frac{1}{\alpha_n + \beta_n}, \quad n_\infty = \alpha_n \cdot \tau_n = \frac{\alpha_n}{\alpha_n + \beta_n} \quad (9.8)$$

where the rate constants are:

$$\alpha_n(V) = \frac{10 - V}{100(e^{(10-V)/10} - 1)}, \quad \beta_n(V) = 0.125e^{-V/80} \quad (9.9)$$

where V is the membrane potential relative to the axon's resting potential in millivolts.

- The voltage dependence of n_∞ and τ_n is illustrated by the following plots



- Note that when the membrane is depolarized ($V_m > V_r$) the steady-state value of the activation particles n increases, and the time constant decreases.

9.7.2 The sodium channel — m and h particles

- The variation of the conductance of the sodium channel, g_{Na} , is modeled by two types of activation particles, m and h also called inactivation particle due to its role of switching off the channel.
- The relationship between the channel conductance and the activation particles is now as follows

$$g_{Na} = G_{Na} \cdot m^3 \cdot h \quad (9.10)$$

where G_{Na} is the maximum value of the conductance, for $m = 1$ and $h = 1$.

- As for the potassium channel there is a differential equation for each particle:

$$\tau_m \frac{dm}{dt} = m_\infty - m \quad \tau_h \frac{dh}{dt} = h_\infty - h \quad (9.11)$$

- The time constants and steady state values are defined in terms of the rate constants:

$$\tau_m = \frac{1}{\alpha_m + \beta_m} \quad \tau_h = \frac{1}{\alpha_h + \beta_h} \quad (9.12)$$

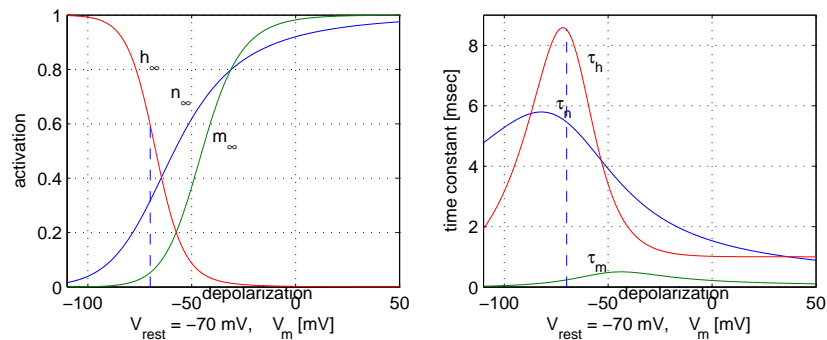
$$m_\infty = \alpha_m \cdot \tau_m = \frac{\alpha_m}{\alpha_m + \beta_m} \quad h_\infty = \alpha_h \cdot \tau_h = \frac{\alpha_h}{\alpha_h + \beta_h} \quad (9.13)$$

- The voltage-dependant rate constants are experimentally derived to be equal to

$$\alpha_m(V) = \frac{25 - V}{10(e^{(25-V)/10} - 1)} \quad \alpha_h(V) = 0.07e^{-V/20} \quad (9.14)$$

$$\beta_m(V) = 4e^{-V/18} \quad \beta_h(V) = \frac{1}{e^{(30-V)/10} + 1}$$

- The voltage dependence of the steady-state values and time constants are illustrated by the following plots. The potassium parameters are included for comparison.



- The steady-state value, m_∞ , of the sodium activation particle m behaves similarly to its potassium counterpart: when the membrane voltage increases, m_∞ also increases.
- The steady-state value, h_∞ , of the sodium in-activation particle h behaves in the opposite direction: when the membrane voltage increases, h_∞ decreases, switching off the sodium channel.
- **Four first-order differential equations** (9.2), (9.6) and (9.11) together with the supporting algebraic equations for the **potassium conductance** (9.5), (9.8), (9.9) and for the **sodium conductance** (9.10), ..., (9.14) form the **complete Hodgkin-Huxley model of action potential generation**.

9.7.3 Action potential — the pulse

- The Hodgkin-Huxley equations cannot be solved analytically due to non-linear relationship between the conductances and the unknown membrane voltage, and must be solved using recursive approximation of derivatives.

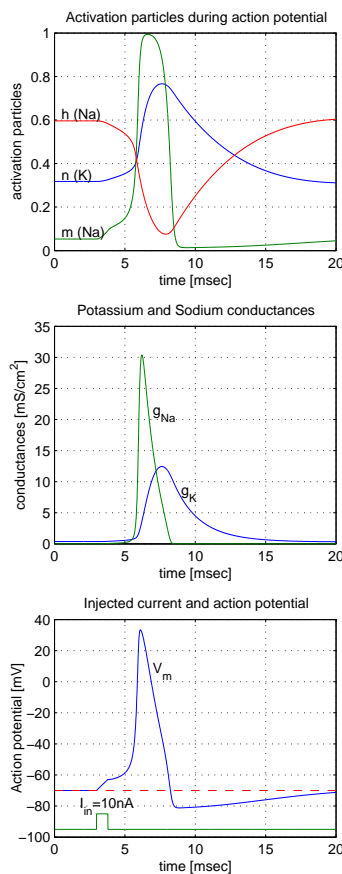
- Each first-order differential equation of the form $\frac{dx}{dt} = f$ approximated by $\Delta x = \Delta t \cdot f$

is replaced with the recursive relationship for the next value of the unknown variable x in the following form:

$$x(k+1) = x(k) + \Delta t \cdot f$$

where Δt is the time step, and k is the time step number.

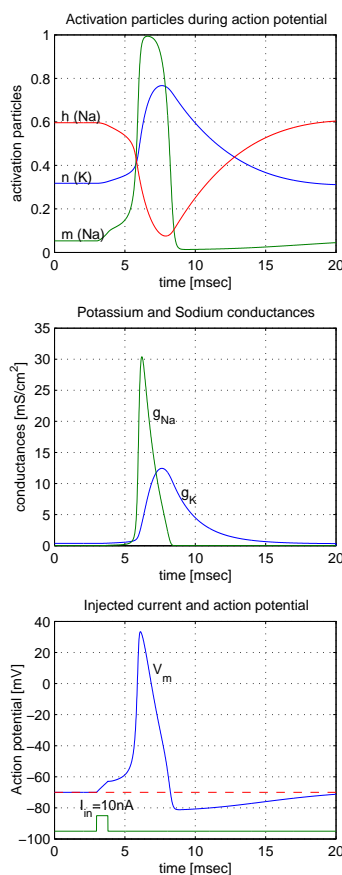
- Now we can calculate the membrane voltage and associated quantities step by step.
- To calculate the membrane voltage (action potential) we have used the following parameters:
 Membrane capacitance: $C = 1 \mu\text{F}/\text{cm}^2$
 Potassium battery: $E_K = -12$ mV relative to the resting potential of the axon.
 Maximal Potassium conductance: $G_K = 36$ mS/cm²
 Sodium battery: $E_{Na} = 115$ mV sodium reversal potential relative to the resting potential of the axon.
 Maximal Sodium conductance: $G_{Na} = 120$ mS/cm²
 Leakage conductance: $g_{lk} = 0.3$ mS/cm² is voltage-independent.
 Leakage battery $E_{lk} = 10.613$ mV is calculate from the membrane equilibrium condition.



A.P. Papiński, L. Gustafsson

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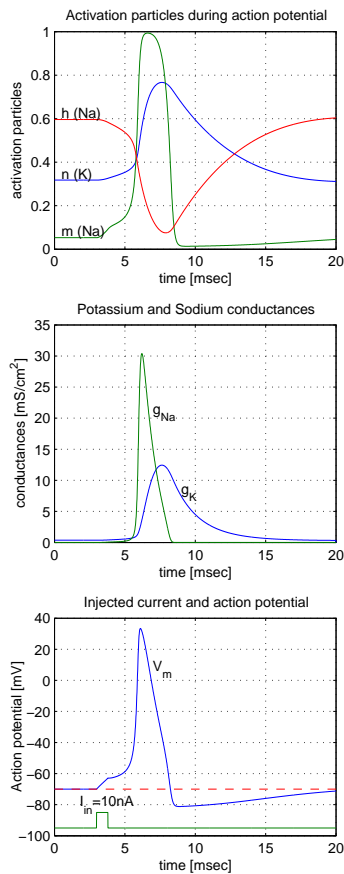
- At rest, the membrane potential is $V_r = -70\text{mV}$.
- Both potassium and sodium channels were almost completely switched off as indicated by the small values of potassium and sodium conductances.
- Note the resting values of particles: K: $n = 0.32$, Na: $m = 0.05, h = 0.6$.
- At some stage the injected current pulse ($I_{in} = 10\text{nA}$ in the example) that emulates the Post-Synaptic Potential (PSP) **depolarizes** the cytoplasm, that is, the inside of the cell.
- This initial depolarization (before 5ms in the example) results in a slow increase of the membrane potential, which results in the increase of the values of the particles m (Na) and n (K) and decrease of the value of h .
- As a result both sodium and potassium channels start to open up.
- At some stage, (just after 5ms when all particle values are equal) the **conductance of the sodium channel increases rapidly**.
- The rapid increase of the sodium channel conductance results in **rapid depolarization**, that is, increase of the voltage potential, creating the **rising edge of the action potential**.



A.P. Papiński, L. Gustafsson

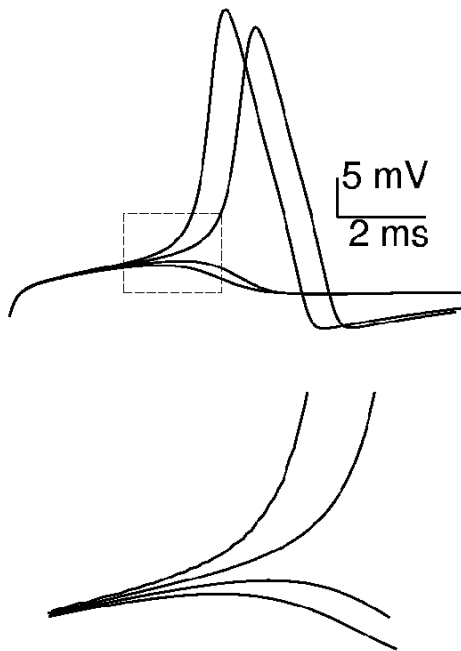
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- **During the rising edge of the action potential**, the slower process of opening the potassium channel begins.
- This process is driven by the slow increase of the value of m particles and corresponding increase of the potassium channel conductance.
- At the same time the sodium channel conductance increases to its maximum value due to increase of the value of the n particles and the decrease of the value of the h particles.
- **After the action potential reaches its maximum**, the opening of the potassium channel and closing of the sodium channel starts the **rapid process of re-polarization** when the membrane voltage goes quickly towards the resting potential.
- Switching off the sodium channel (its conductance is close to zero) with the potassium channel being still open and supplying the outward current, results in **hyperpolarization** when the membrane voltage drops below the resting potential.



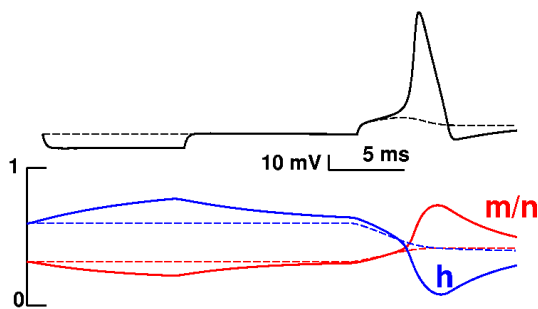
- After the membrane voltage reaches its minimum, a slow process of **After-HyperPolarization** (AHP) begins.
- During after-hyperpolarization the potassium channel slowly switches off as indicated by reduced channel conductance g_K and corresponding particle n .
- In addition a very slow process of partial opening of the sodium channel takes place as indicated by the channel particles h and m slowly moving towards their resting values.
- The after-hyperpolarization is always present after the neuron fires.
- It reflects a short term firing history and, as we will investigate it further, provides immediate inhibition.

9.7.4 The threshold and channel memory



- The action potential has a threshold.
- In figure the area around threshold is expanded (rectangle).
- A current injection that does not reach the threshold does not generate a spike.
- In the example, the threshold for firing is about -51 mV.
- At the threshold, inward (sodium) current exceeds outward (Potassium) current and positive feedback kicks in.
- From the perspective of neural network theory, this threshold could be taken to be the sharp threshold of a binary activation function.
- This would allow the neuron to add up its inputs and then provide a rapid signal indicating whether or not sufficient excitation had been received.
- However, in contrast to standard neural network theory, the Hodgkin and Huxley threshold is not a fixed value.

- The three channel particles, m , h , and n , all respond with a lag (first-order differential equation).
- This lag provides a simple form of memory.
- Something that happened in the past can be “remembered” while the m , h , or n , state variables catch up with their steady-state values.
- The afterhyperpolarization is an example of this.
- The AHP reflects firing history — it is only present after the neuron has fired.
- This history is not always immediately reflected in the membrane potential but can be held hidden in the state variables, inaccessible to experimental detection.
- For example, a hyperpolarizing input provides immediate inhibition.
- The hyperpolarization opposes any depolarization that would push the potential up to threshold.
- However, after the hyperpolarization ends, h is left at a relatively high and n at a relatively low value for a brief period of time.
- This pushes the effective threshold down closer to rest, making it easier to fire the cell.



- A subsequent depolarization will open the sodium channel more, and the potassium channel less, than it otherwise would.
- Similarly, a preceding depolarization, which is immediately excitatory, will have a late effect that is inhibitory.

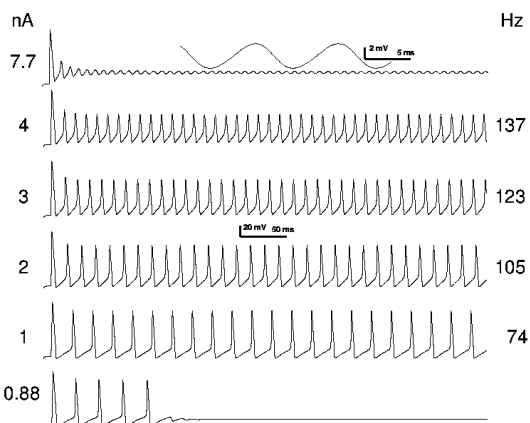
- Note that with preceding hyperpolarization (solid line), h is elevated and n is depressed allowing a small depolarization to fire the cell 10 ms later.

In the absence of the hyperpolarization, the same small stimulus is subthreshold (dashed line).

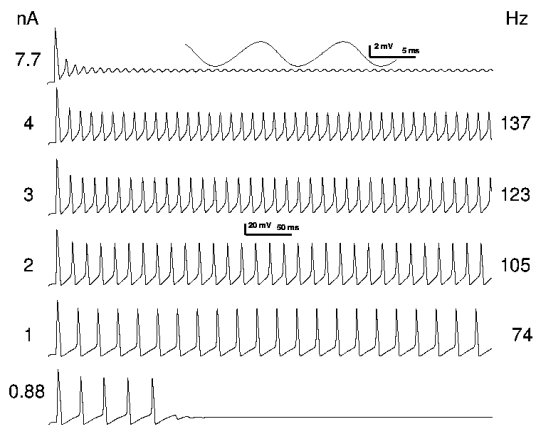
- From a neural network perspective, this membrane memory could be tuned to allow the neuron to respond preferentially to certain sequences of inputs.
- In this simple case, an optimal stimulation would involve an IPSP followed by an EPSP after an interval of two to three times τ_n at RMP.
- A neuron has dozens of channel types, allowing the construction of more complex responses that can build up over relatively long periods of time.
- A novel firing pattern could be the result of some combination of inputs occurring over several seconds.
- This would allow the use of very complex, hard-to-interpret coding schemes.

9.7.5 Rate coding redux

- Having speculated about complex history-dependent coding schemes, I now wish to return to the comforting simplicity of rate coding.
- We have shown that slow potential theory explains the transduction from a presynaptic rate code to a postsynaptic depolarization plateau:
- increasing input rate gave an increased depolarization, due to increasing current flow.
- Using the Hodgkin-Huxley model, we can complete the sequence of signal transductions by showing that a depolarizing current injection converts to increasing firing rate within a certain range.

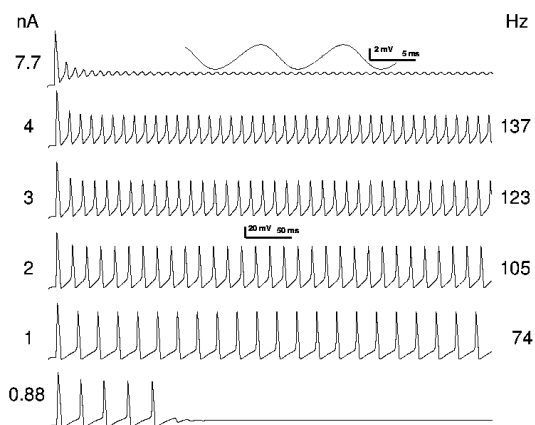


- Note that the firing frequency increases with increased current injection between 0.88 nA and 7.7 nA. At and below 0.88 nA, there is no continuous repetitive spiking. At and above 7.7 nA depolarization blockade is seen.
- The trace at the bottom of figure (0.88 nA) illustrates activity just below the threshold for continuous repetitive spiking.



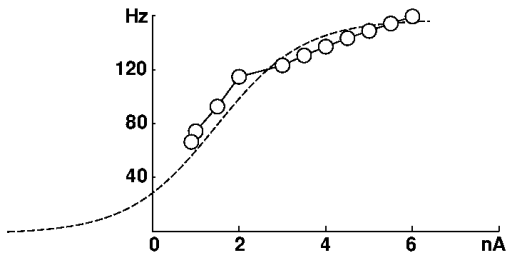
- Below 0.84 nA, down to the spiking threshold, about 0.2 nA this Hodgkin-Huxley model produces only one spike.
- The spikes become smaller and smaller.
- This contradicts what I said earlier about spikes being stereotyped and of constant amplitude.
- In fact, spike size does carry information about spike rate. It does not appear that this amplitude information is used however.

- A 4-nA current injection gives a measurable 137-Hz spike frequency.
- The spikes at this rate are only about half the size of the spikes produced by a 1-nA current injection.
- As we go to higher and higher injections, the spikes get less and less spike-like as we gradually pass over to the low-amplitude oscillation that is characteristic of depolarization blockade.
- Depolarization blockade occurs when the voltage gets so high that the h particle remains near 0.
- This means that the sodium channel does not deinactivate.
- Since the sodium channel is continuously inactivated, it is not possible to generate spikes.



- For example, in the top trace, with 7.7 nA of injected current, the tiny oscillation has an amplitude of about 4 mV and frequency of about 165 Hz.
- Examination of state variables demonstrates that this oscillation is based on an interaction between V and m without substantial contribution from n and h .
- This is the dynamics of depolarization blockade, not the dynamics of neural spiking.

Using the Hodgkin and Huxley model of neuron spiking, we can compare this realistic input/output (I-f) curve with the sigmoid (squashing) curve, the idealized input/output curve used in artificial neural network modeling:



- Both curves are monotonically increasing, meaning they only go up.
 - Although it does not asymptote, the realistic I-f (current-frequency) curve, like the sigmoid curve, does show some reduction in slope with higher input values.
 - However, the sigmoid curve covers all input values, while the realistic I-f curve (current-frequency curve) only has outputs for a certain range of inputs.
- By altering the Hodgkin and Huxley parameters we can move the ceiling, the floor, and the precise relationship between current and frequency.
 - However, these measures are not independent, so that if you try to move the floor down, the ceiling and slope of the I-f relation (the gain) will change as well.
 - This means that it is not possible to precisely tune a Hodgkin-Huxley model to produce exactly the response one might want for a particular network model.

9.8 Summary and thoughts

- The Hodgkin-Huxley model of the action potential is the most influential computer model in neuroscience and as such remains a touchstone of computational neuroscience.
- It's a dynamical model that arises from the interaction of four time-dependent state variables — V , m , h , and n .
- Of these only V , voltage, is directly measurable.
- The others are putative populations of switches that turn sodium and potassium channels on and off.
- Electrically, the Hodgkin-Huxley model is the basic membrane RC circuit with two conductances added in parallel.
- Hence the circuit is called the parallel-conductance model.
- The two added conductances are the active sodium and potassium conductances.
- These conductances are active because they change with change in voltage.
- A controllable resistance (conductance) is called a rheostat.
- Each of the conductances, including the passive “leak” conductances is attached to a battery.
- The battery potential (voltage) depends on the distribution of the particular ion that flows through its own selective conductances.

- This Nernst potential is the electrical field that holds back the chemical flow of the ion across the membrane down its concentration gradient.
- The spike is the result of a set of interacting feedback loops.
- Depolarization activates sodium channels ($\uparrow m$) producing positive feedback with further depolarization.
- This is the upswing of the spike.
- Following this, two negative feedback influences kick in.
- The sodium channel starts to inactivate ($\downarrow h$).
- Additionally, activation of the potassium channel actively pulls the potential back toward and past the resting membrane potential.
- The Hodgkin-Huxley model can be used to see how action potential behavior will influence neural signal processing and signal transduction.
- For example, the neuron has a threshold for action potential generation that can be altered by preceding inputs in a paradoxical way.
- An earlier excitatory input will raise the threshold, producing a late inhibitory influence.
- A preceding inhibitory input will lower the threshold, resulting in a relatively excitable state.
- Repetitive action potential firing is possible over only a limited range of inputs.

- Too little input produces no spikes or only a few spikes.
- Too much input produces depolarization blockade with a low amplitude oscillation.
- This limited range makes it difficult to use standard Hodgkin-Huxley model dynamics for rate coding in neural network models.
- Adding in the dynamics of other channels that are present in neurons makes it possible to get a wider range of firing frequency.