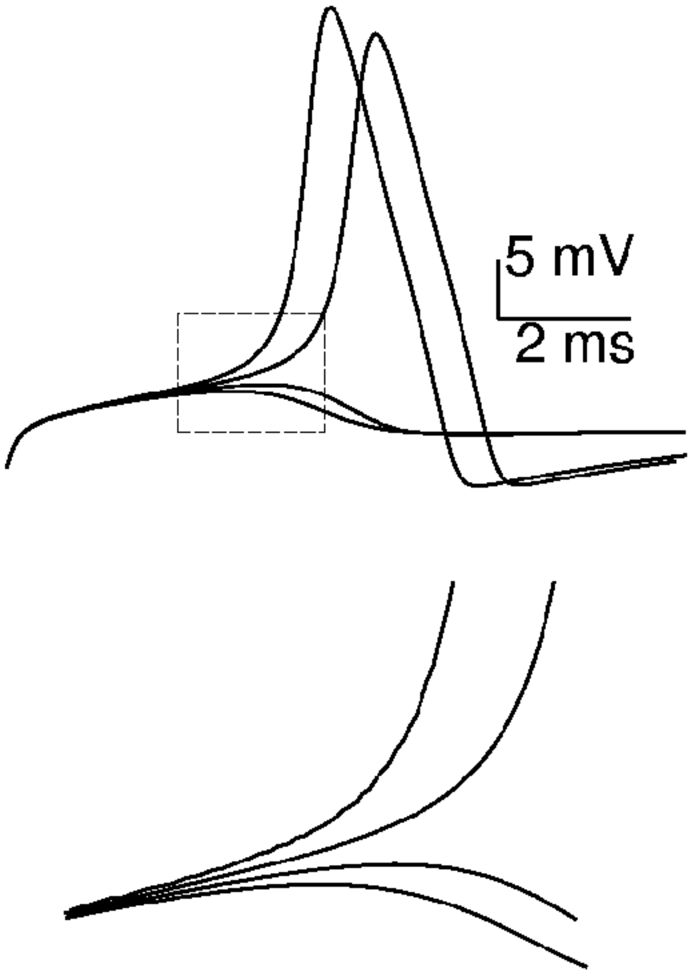
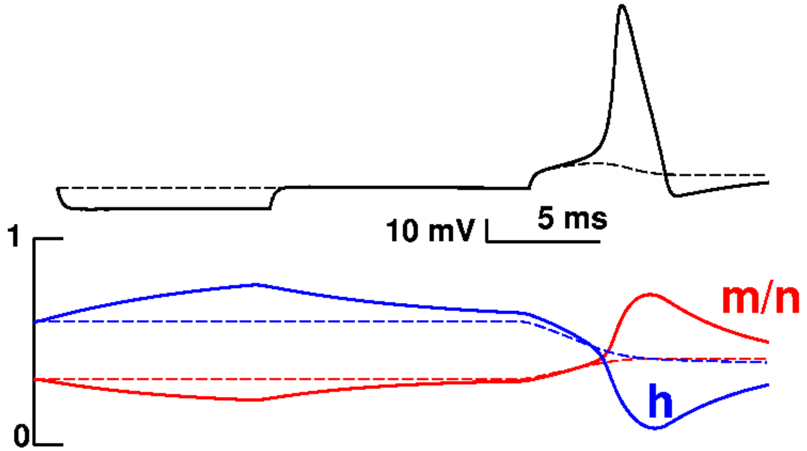
9.7.4 The threshold and channel memory



- 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.



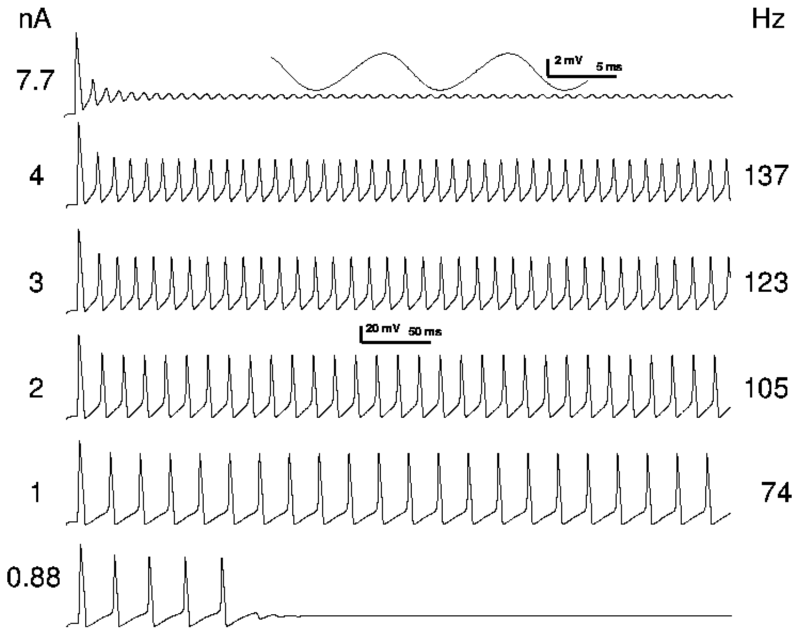
- A subsequent depolarization will open the sodium channel more, and the potassium channel less, than it otherwise would.
- Similarly, a preceding depolarization, which is immediately excitatory, will have a late effect that is inhibitory.

- 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

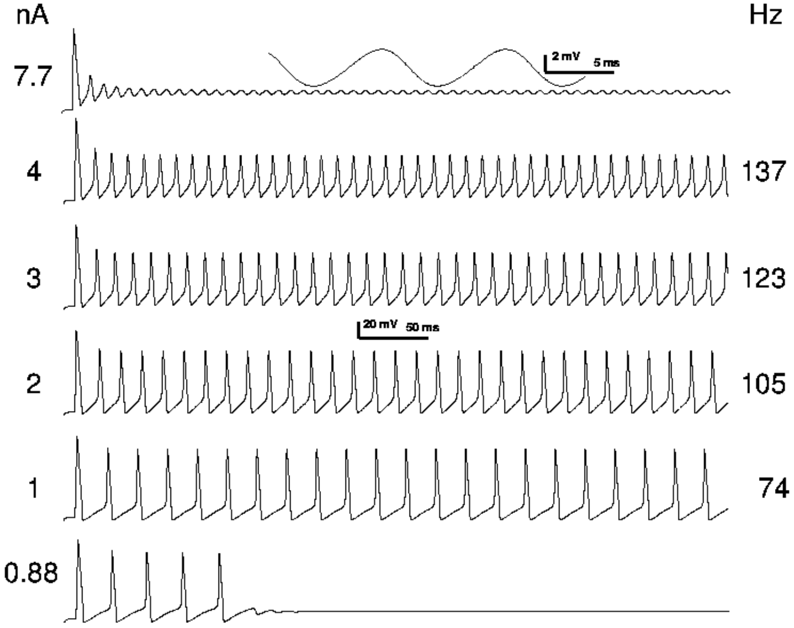
- Having speculated about complex history-dependent coding schemes, I now wish to return to the comforting simplicity of rate coding.
- We have shown that slow potential theory explains the transduction from a presynaptic rate code to a postsynaptic depolarization plateau:
- increasing input rate gave 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

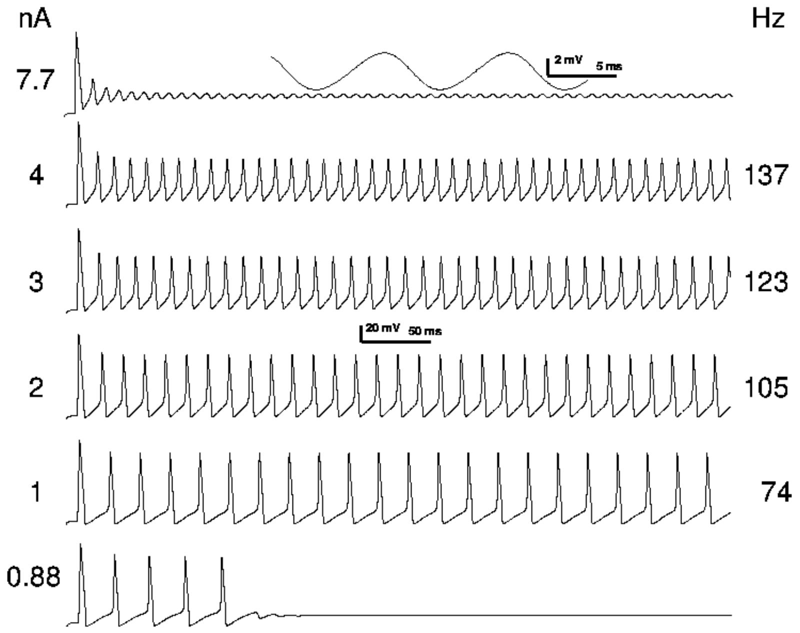
  At and below 0.88 nA, there is no continuous repetitive spiking.

  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.



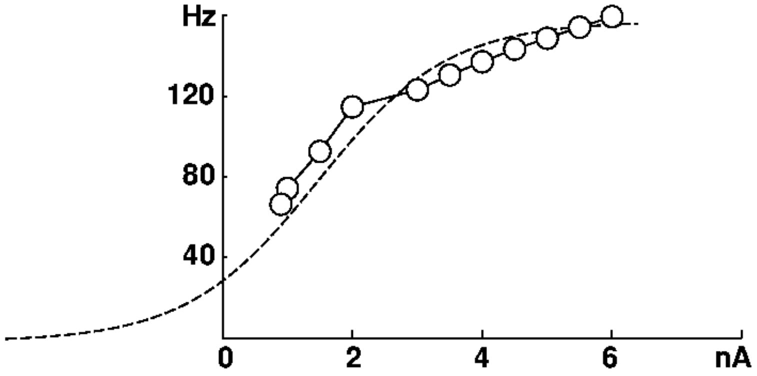
- Below 0.84 nA, down to the spiking threshold, about 0.2 nA this Hodgkin-Huxley model produces only one spike.
- The spikes become smaller and smaller.
- This contradicts what I said earlier about spikes being stereotyped and of constant amplitude.
- In fact, spike size does carry information about 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.