ECE 796:

Models of the Neuron

Slides for Lecture #4

Friday, February 2, 2007

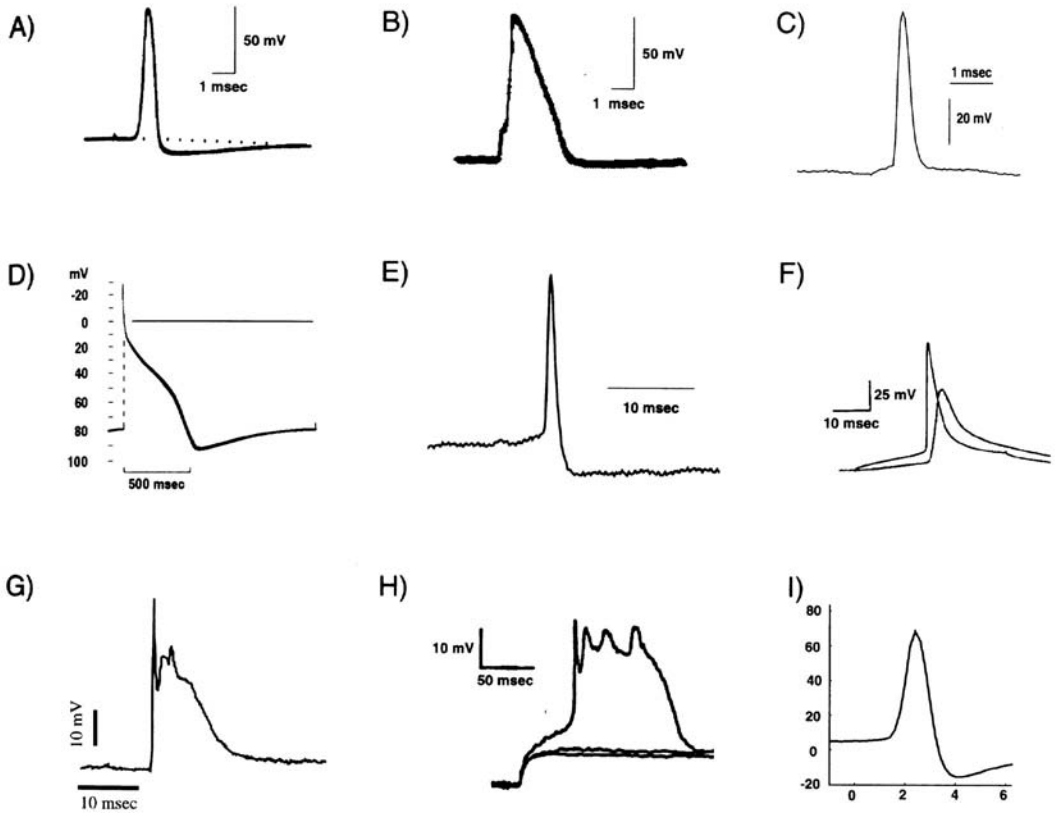

Fig. 6.1 ACTION POTENTIALS OF THE WORLD Action potentials in different invertebrate and vertebrate preparations. Common to all is a threshold below which no impulse is initiated, and a stereotypical shape that depends only on intrinsic membrane properties and not on the type or the duration of the input. **(A)** Giant squid axon at 16° C. Reprinted by permission from Baker, Hodgkin, and Shaw (1962). **(B)** Axonal spike from the node of Ranvier in a myelinated frog fiber at 22° C. Reprinted by permission from Dodge (1963). **(C)** Cat visual cortex at 37° C. Unpublished data from J. Allison, printed with permission. **(D)** Sheep heart Purkinje fiber at 10° C. Reprinted by permission from Weidmann (1956). **(E)** Patch-clamp recording from a rabbit retinal ganglion cell at 37° C. Unpublished data from F. Amthor, printed with permission. **(F)** Layer 5 pyramidal cell in the rat at room temperatures. Simultaneous recordings from the soma and the apical trunk. Reprinted by permission from Stuart and Sakmann (1994). **(G)** A complex spike—consisting of a large EPSP superimposed onto a slow dendritic calcium spike and several fast somatic sodium spikes—from a Purkinje cell body in the rat cerebellum at 36° C. Unpublished data from D. Jaeger, printed with permission. **(H)** Layer 5 pyramidal cell in the rat at room temperature. Three dendritic voltage traces in response to three current steps of different amplitudes reveal the all-or-none character of this slow event. Notice the fast superimposed spikes. Reprinted by permission from Kim and Connors (1993). **(I)** Cell body of a projection neuron in the antennal lobe in the locust at 23° C. Unpublished data from G. Laurent, printed with permission.

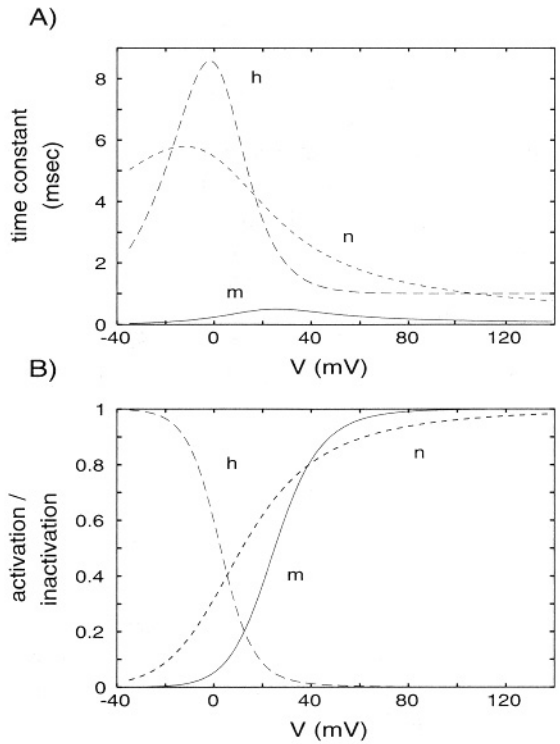

Fig. 6.3 VOLTAGE DEPENDENCY OF THE GATING PARTICLES Time constants **(A)** and steady-state activation and inactivation **(B)** as a function of the relative membrane potential V for sodium activation m (solid line) and inactivation h (long dashed line) and potassium activation n (short, dashed line). The steady-state sodium inactivation h_∞ is a monotonically decreasing function of V, while the activation variables n_∞ and m_∞ increase with the membrane voltage. Activation of the sodium and potassium conductances is a much steeper function of the voltage, due to the power-law relationship between the activation variables and the conductances. Around rest, G_{Na} increases e-fold for every 3.9 mV and G_{K} for every 4.8 mV. Activating the sodium conductance occurs approximately 10 times faster than inactivating sodium or activating the potassium conductance. The time constants are slowest around the resting potential.

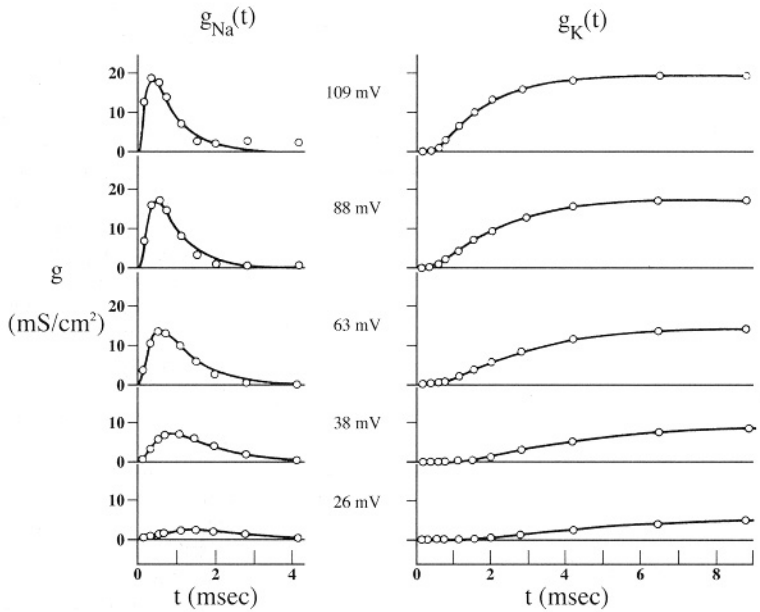

Fig. 6.4 K^+ AND Na^+ CONDUCTANCES DURING A VOLTAGE STEP Experimentally recorded (circles) and theoretically calculated (smooth curves) changes in G_{Na} and G_K in the squid giant axon at 6.3° C during depolarizing voltage steps away from the resting potential (which here, as throughout this chapter, is set to zero). For large voltage changes, G_{Na} briefly increases before it decays back to zero (due to *inactivation*), while G_K remains activated. Reprinted by permission from Hodgkin (1958).

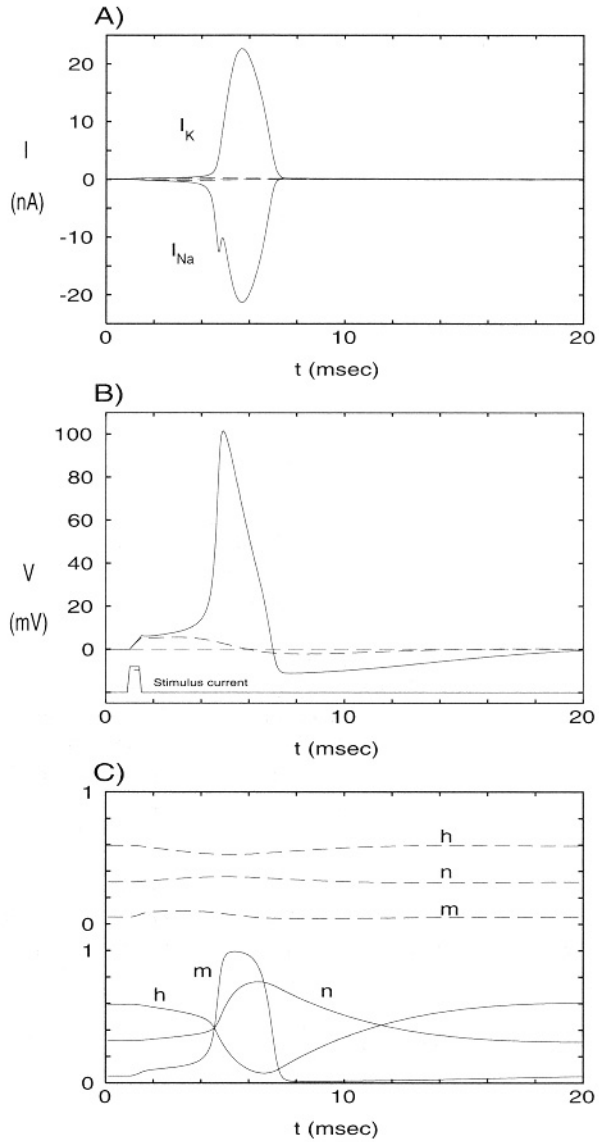

Fig. 6.5 HODGKIN-HUXLEY ACTION POTENTIAL Computed action potential in response to a 0.5-msec current pulse of 0.4-nA amplitude (solid lines) compared to a subthreshold response following a 0.35-nA current pulse (dashed lines). **(A)** Time course of the two ionic currents. Note their large sizes compared to the stimulating current. **(B)** Membrane potential in response to threshold and subthreshold stimuli. The injected current charges up the membrane capacity (with an effective membrane time constant $\tau = 0.85$ msec), enabling sufficient I_{Na} to be recruited to outweigh the increase in I_K (due to the increase in driving potential). The smaller current pulse fails to trigger an action potential, but causes a depolarization followed by a small hyperpolarization due to activation of I_K. **(C)** Dynamics of the gating particles. Sodium activation m changes much more rapidly than either h or n. The long time course of potassium activation n explains why the membrane potential takes 12 msec after the potential has first dipped below the resting potential to return to baseline level.

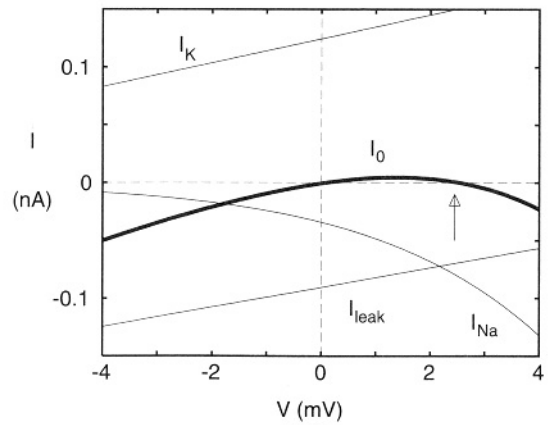

Fig. 6.6 CURRENT-VOLTAGE RELATIONSHIP AROUND REST Instantaneous I–V relationship, I_0, associated with the standard patch of squid axon membrane and its three components: $I_0 = I_{Na} + I_K + I_{leak}$ (Eq. 6.21). Because m changes much faster than either h or n for rapid inputs, we computed G_{Na} and G_K under the assumption that m adapts instantaneously to its new value at V, while h and n remain at their resting values. I_0 crosses the voltage axis at two points: a stable point at $V = 0$ and an unstable one at $V_{th} \approx 2.5$ mV. Under these idealized conditions, any input that exceeds V_{th} will lead to a spike. For the "real" equations, m does not change instantaneously and nor do n and h remain stationary; thus, I_0 only crudely predicts the voltage threshold which is, in fact, 6.85 mV for rapid synaptic input. Note that I_0 is specified in absolute terms and scales with the size of the membrane patch.

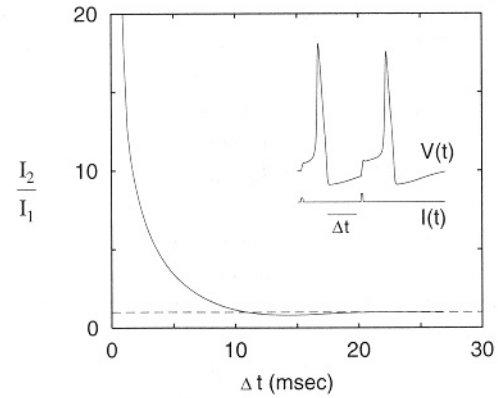

Fig. 6.7 Refractory Period A 0.5-msec brief current pulse of $I_1 = 0.4$ nA amplitude causes an action potential (Fig. 6.5). A second, equally brief pulse of amplitude I_2 is injected Δt msec after the membrane potential due to the first spike having reached $V = 0$ and is about to hyperpolarize the membrane. For each value of Δt, I_2 is increased until a second spike is generated (see the inset for $\Delta t = 10$ msec). The ratio I_2/I_1 of the two pulses is here plotted as a function of Δt. For several milliseconds following repolarization, the membrane is practically inexcitable since such large currents are unphysiological (*absolute refractory period*). Subsequently, a spike can be generated, but it requires a larger current input (*relative refractory period*). This is followed by a brief period of reduced threshold (hyperexcitability). No more interactions are observed beyond about $\Delta t = 18$ msec.

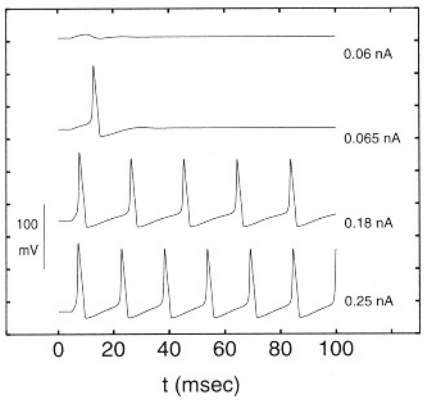

Fig. 6.8 Repetitive Spiking Voltage trajectories in response to current steps of various amplitudes in the standard patch of squid axonal membrane. The minimum sustained current necessary to initiate a spike, termed *rheobase*, is 0.065 nA. In order for the membrane to spike indefinitely, larger currents must be used. Experimentally, the squid axon usually stops firing after a few seconds due to secondary inactivation processes not modeled by the Hodgkin–Huxley equations (1952d).

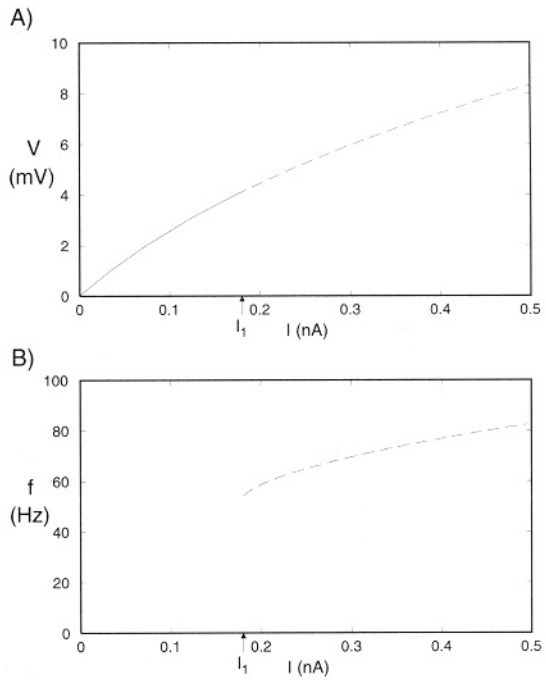

Fig. 6.9 Sustained Spiking in the Hodgkin-Huxley Equations **(A)** Steady-state I–V relationship and **(B)** f–I or discharge curve as a function of the amplitude of the sustained current I associated with the Hodgkin-Huxley equations for a patch of squid axonal membrane. For currents less than 0.18 nA, the membrane responds by a sustained depolarization (solid curve). At I_1, the system loses its stability and generates an infinite train of action potentials: it moves along a stable limit cycle (dashed line). A characteristic feature of the squid membrane is its abrupt onset of firing with nonzero oscillation frequency. The steady-state I–V curve can also be viewed as the sum of all steady-state ionic currents flowing at any particular membrane potential V_m.

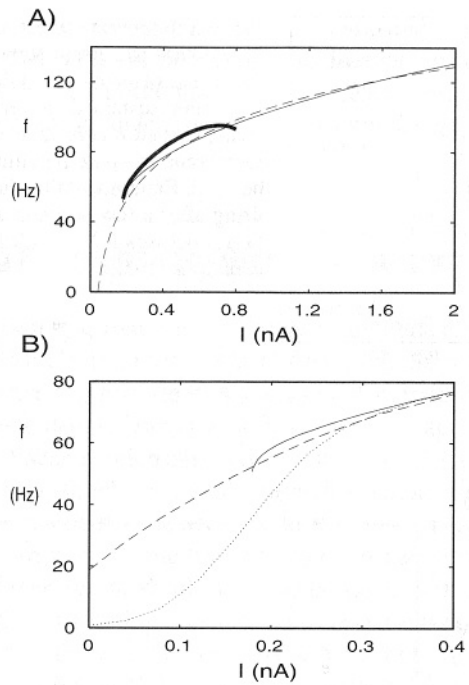

Fig. 6.10 HODGKIN-HUXLEY f–I CURVE AND NOISE **(A)** Relationship between the amplitude of an injected current step and the frequency of the resultant sustained discharge of action potentials (f–I curve) for a membrane patch of squid axon at 6.3° C (solid line) and its numerical fit (dashed line) by $f = 33.2 \log I + 106$. Superimposed in bold is the f–I curve for the standard squid axon cable (using normalized current). Notice the very limited bandwidth of axonal firing. **(B)** f–I curve for the membrane patch case around its threshold (rheobase) in the presence of noise. White (2000-Hz band-limited) current noise whose amplitude is Gaussian distributed with zero mean current is added to the current stimulus. In the absence of any noise (solid line) the f–I curve shows abrupt onset of spiking. The effect of noise (dotted curve—standard deviation of 0.05 nA; dashed curve—0.1 nA) is to linearize the threshold behavior and to increase the bandwidth of transmission (stochastic linearization). Linear f–I curves are also obtained when replacing the continuous and deterministic Hodgkin-Huxley currents by discrete and stochastic channels (see Sec. 8.3).