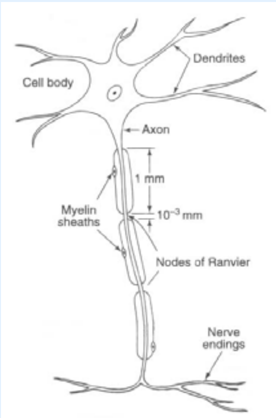
Mathematical Models of Nerves: Translating Biochemistry to Physics and Mathematics

Rebecca Lucast, Summer 2004 Young Scholars Grant

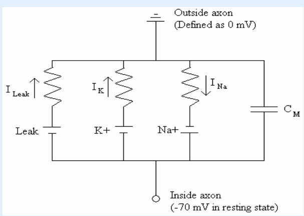
Nerves and Signals



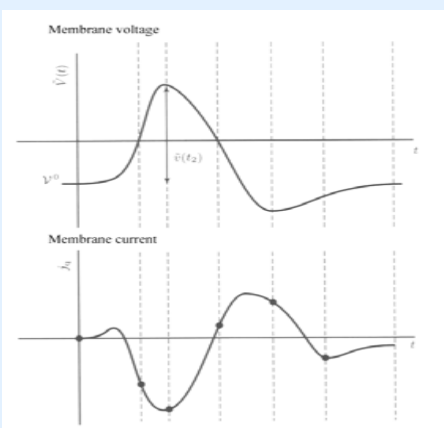
from Tuszynski and Dixon. 2002. Biomedical Applications of Introductory Physics. Wiley and Sons, NJ.

- Axon membrane surrounded by myelin sheath
- Signal is amplified at the nodes and passes without amplification in internode spaces
- Ion concentration differences across membrane
- Nernst equation explains potential difference of -70 mV across membrane

Simple circuit diagram as basic model of membrane



- The signal is a propagating change in membrane potential
- As the potential changes at a given point of exposed membrane:
  - Membrane permeabilities (resistances) change
  - Ions cross the membrane (current flows)
  - Nerve membrane shows non-Ohmic behavior



from Nelson. 2004. Biological Physics: Energy, Information, Life. Freeman, NY.

Alan Hodgkin and Andrew Huxley

- Experiments in the 1940s and 1950s using squid (*Loligo*) axons
- Published series of papers with equations to describe axon membrane that are still studied today

Why should we care?

- Many diseases affect nerves in different ways
  - Multiple Sclerosis is the planned focus of the project
    - Myelin sheath gets damaged
    - Signals get lost in the axon
  - Others include Parkinson's disease and ALS (Lou Gehrig's disease)
    - Include chemical and structural disruptions to the nerve

Circuit translated into equations

From the basic circuit model

$$I_M = C_M \frac{dV}{dt} + g_{Na}(V - V_{Na}) + g_K(V - V_K) + g_l(V - V_l)$$

To the Hodgkin-Huxley model

$$I_M = C_M \frac{dV}{dt} + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_K n^4 (V - V_K) + \bar{g}_l (V - V_l)$$

- Used gating variables to account for changing permeability
- Experimental results:
  - m^3h governs sodium conductance
  - n^4 governs potassium conductance
  - Defined as follows

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n \qquad \alpha_n = \frac{0.01(V+10)}{\left(e^{\frac{V+10}{10}}\right)-1} \qquad \beta_n = 0.125\, e^{\left(\frac{V}{80}\right)}$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m \qquad \alpha_m = \frac{0.1(V+25)}{\left(e^{\frac{V+25}{10}}\right)-1} \qquad \beta_m = 4e^{\left(\frac{V}{18}\right)}$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h \qquad \alpha_h = 0.07e^{\left(\frac{V}{20}\right)} \qquad \beta_h = \frac{1}{\left(e^{\frac{V+30}{10}}\right)+1}$$

Beyond Hodgkin and Huxley

- Basic simplifications
  - m as instantaneous: m0
  - n and h similar enough to be modeled together as w

$$I_M = C_M \frac{dV}{dt} + \bar{g}_{Na}(m_0)^3(w)(V - V_{Na}) + \bar{g}_K(w)^4(V - V_K) + \bar{g}_l(V - V_l)$$

- Fitzhugh-Nagumo model, 1960s
  - Took basic simplification and reduced it into two other functions F and G
  - Defined experimentally

$$\frac{dV}{dt} = \frac{1}{\tau}[F(V,w) + RI] \qquad F(V,w) = V - \frac{1}{3}V^3 - w$$

$$\frac{dw}{dt} = \frac{1}{\tau_w}G(V,w) \qquad G(V,w) = b_0 + b_1 V - w$$

- Morris-Lecar model
  - Reduced to voltage variation with time and a defined "recovery variable"

$$\frac{dV}{dt} = -g_1[\hat{m}_0(V)](V-1) - g_2(\hat{w})(V - V_2) - g_l(V - V_l) + I$$

$$\frac{d\hat{w}}{dt} = -\frac{1}{\tau(V)}[\hat{w} - w_0(V)]$$

Special thanks to:

- The University of St. Thomas Physics Department in helpful collaboration:
  - Dr. Paul Ohmann
  - Jimmy Thielen
  - Dr. Marty Johnston
  - Dr. Adam Green
  - Dr. Tom Tommet

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