In 1905 he published four key papers. The one relevant to neuroscience (and many other fields) is that he was the first to provide the quantitative relation between the diffusion constant \( D \) and the mobility constant \( \mu \).

\[ D = \frac{kT}{q\mu} \]

This relation is known as the Einstein relation. It is equally important to the semiconductor industry where it allows one to find the nonlinear relation of the current conducted through the diode, as a function of voltage across a diode.

Hodgkin and Huxley were the first to work out the mechanism between spike propagation in nerve fibers.

Helmholtz was the first to measure the speed of a spike in a frog nerve, which he found to be \( \approx 27 \) m/s, around 1850.

For the space-clamp a wire is pushed down into the plasma core of the squid axon. The low output impedance of the amplifier drives the wire, which holds the internal voltage of the axon constant over several space-constants. When the output voltage of the amplifier is set to the rest voltage of the axon, the displacement current \( J = C \frac{dv}{dt} = 0 \) because the voltage drop across the membrane is zero.

The basic equations are

\[ V_o = G(v_+ - v_-) \]

with \( G = 10^6 \).
2 Thermodynamics

Problem # 3: Thermodynamics of the cell membrane. Set up the equations to estimate the equilibrium sodium and potassium concentrations.

- 3.1: Define the three membrane currents that are most important to action potentials (spikes).

\[ J_{\text{ion}} = C_e \frac{d}{dt} v(t) \]

\[ J_i(s) = q_{\text{ion}}[\text{Na}^+] E = -q_{\text{ion}}[\text{Na}^+] \frac{dV}{dx} \]

\[ J_d = -q_{\text{ion}} \frac{d}{dx}[\text{Na}^+] \]

**Sol:** the displacement current \( J_{\text{ion}} \), the conduction current \( J_i \), and the diffusion current \( J_d \).

- 3.2: What is the relation between the conduction and diffusion currents under equilibrium conditions?

**Sol:** The two currents sum to zero.

- 3.3: Derive the relation between the voltage and [Na\(^+\)] when the system is in the equilibrium condition?

**Sol:** When the two currents are equal \( J_i = J_d = 0 \), thus

\[ q_{\text{ion}}[\text{Na}^+] \frac{dV}{dx} = -q_{\text{ion}} \frac{d}{dx}[\text{Na}^+] \]

- 3.4: Integrate the differential equation and derive the relation between the Na\(^+\) concentrations on the two sides of the membrane and the voltage across the membrane \( V = V_i - V_o \). Hint: see pp. 57-59.

**Sol:** Rewriting and consolidating the equilibrium equation gives

\[ \frac{1}{\text{Na}^+} \frac{d[\text{Na}^+]}{dx} = - \frac{\mu_{\text{ion}}}{D_{\text{Na}}} \frac{dV}{dx} \]

\[ \int V \ln[\text{Na}^+] = \ln[\text{Na}^+] \]

Thus finally we find

\[ \frac{[\text{Na}^+]_i}{[\text{Na}^+]_o} = e^{\frac{-\mu_{\text{ion}} V}{D_{\text{Na}}}} \]

- 3.5: Analyze a \( \Delta \) long patch of membrane. Set up the equations to estimate the properties of a myelinated nerve fiber.

**Figure 1:** Diagram of the Frog axon showing the physical and electrical circuit (Scott, p. 142).

- 4.1: Assume the following

\[ \lambda = 23 \text{ [m/s]} \]

\[ \lambda = \lambda_0/2 \text{ [mm]} \]

From a previous homework we assumed that \( \Delta = \lambda/2 \) and \( \tau = RC \). Here \( \Delta = s \) is taken to be the distance between nodes.

Find \( f_{\text{max}} \).

**Sol:** Since \( f_{\text{max}} = v_c/\lambda_0 \) with \( v_c = 23 \text{ [m/s]} \) and \( \lambda_0 = 2s = 4 \times 10^{-3} \text{ [m]} \). Thus \( f_{\text{max}} = 23/4 = 5.75 \text{ [kHz]} \).

- 4.2: Find the time constant (\( \tau = RC \)) and the cutoff frequency \( f_c = 1/2\pi\tau \). Compare \( f_c \) to \( f_{\text{max}} \).

**Sol:** The internal \( R = 142 \times 10^8 \text{ [F/m]} \) and the membrane capacitance is \( C = 1,300 \text{ [pF/m]} \). Thus \( \tau = RC = 18.46 \times 10^{-6} \text{ [s/m]} \). Expressed in terms of the area \( s^2 = 4 \times 10^{-4} \text{ this is } \tau \cdot s^2 = (4 \times 18.46) \times 10^{-6} = 73.84 \text{ [u s]} \).

The corresponding cutoff frequency is \( \omega = 1/\tau \cdot s^2 \), which in [Hz] is \( f_c = 1/2\pi\tau \cdot s^2 = 2.155 \text{ [kHz]} \) which is 37.5% of \( f_{\text{max}} = 5.75 \text{ [kHz]} \).

- 4.3: The two figures below show the parameters \( n(t), m(t), h(t) \) used in Hodgkin–Huxley’s model of spike generation. Their equation for the current is:

\[ I(t) = C_m \frac{d}{dt} V + g_{\text{ion}} n(t)(V - V_{\text{ion}}) + g_{\text{K}} m^2(t) h(t)(V - V_{\text{ion}}) \]

The generally accepted but unproven form of the spike voltage is the solution to the linear wave equation

\[ V(t) = S(x - vt) \]

where \( x \) is the axial distance down the fiber and \( v_c \) is the velocity. A number of models have attempted to replace the phenomenological H–H model with a physical model into closer agreement with the data, however H–H is still the generally accepted explanation.

Explain in your own words why the nonlinear model would have the same property as the wave equation, where the spikes travel at the fixed velocity \( v_c \) (see the above equation). **Sol:** See the relevant discussion from Scott in §4.5. These two attached pages from Cole’s book (p. 84-85) (Scott’s ref. 8, p. 92) give the HH view of spike propagation. The model described in class using Matlab’s simulink with three diodes, seems to provide the physical model we need.

**Figure 2:** Parameters measured for the Frog axon (Scott, p. 142).