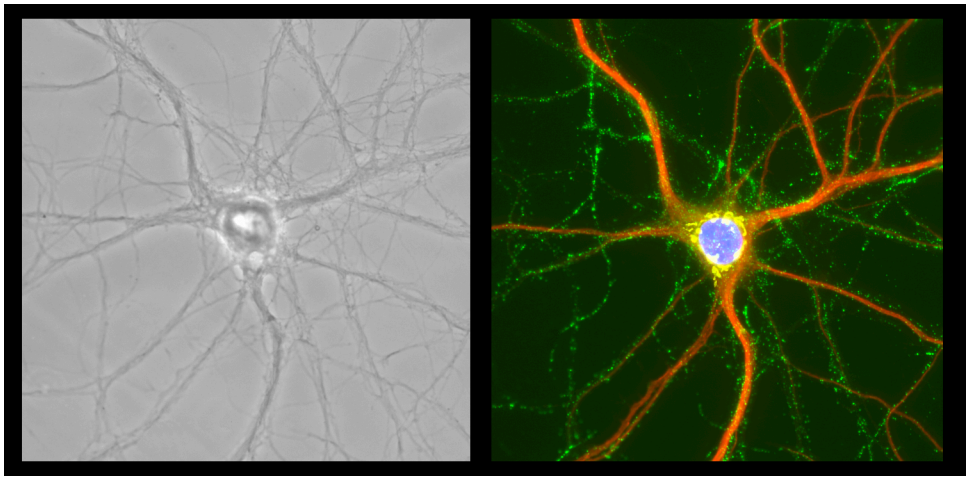
PHYS 4xx Mem 7 - The action potential in nerves

Shapes of nerve cells are exotic: from the main cell body extend branched dendrites for gathering sensory input and an elongated axon for dispatching a signal.



Staining: nuclear DNA (blue), Golgi apparatus (yellow), dendrites (red), secretory vesicles (green).

Axons. Length: up to a few meters. Diameter: ~0.5 - 1.5 μm (no myelin sheath) to 10 - 20 microns for myelinated axons are not uncommon.
Role: signal propagation and chemical delivery to its terminus at a synapse (through secretory vesicles in the axon's interior).

Signals are propagated at a benchmark speed of 30 m/s (30 cm in 10 ms). Compare:
Diffusion: $\langle r_{ee}^2 \rangle = 2Dt$. For $D \sim 10^{-12}$ m^2/s, $t = 10$ ms, $\langle r_{ee}^2 \rangle^{1/2} = 0.14$ μm (tiny!)
Molecular motors: at $v = 2$ μm/s, distance of 0.02 μm in 10 ms (tiny!).

Because of their hydrophobic interiors, pure lipid bilayers are relatively impermeable to charged molecules, even if they are small. However, two classes of proteins aid in the passage of charged species: *channel* proteins and *transporters*. Examples:

Channel proteins
(a) passive when open; flow driven by concentration gradient or electric field
Transporters
(b) passive; gate opens randomly; flow driven by electrochemical gradient
(c) active; pumps against an electrochemical gradient using light as an energy source (mainly found in bacteria and archaea) or using ATP hydrolysis. *Uniporters* pump in a single direction.
(d) *Coupled* transporters move two species at once and come in two variants: symporters move two species in the same direction (in or out) while antiporters are

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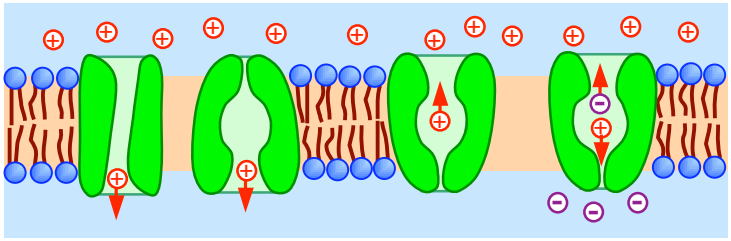
bidirectional in that they carry one species into the cell and a different species in the opposite direction. *E.g.*, the sodium-potassium pump removes 3 Na^+ ions from the cell and brings 2 K^+ ions into the cell per ATP hydrolysis; both ionic species are moved against their electrochemical gradient.



The solute species are only loosely associated with the pore in a channel protein, whereas the solute occupies one of the binding sites (there may be several) in a transporter. The bound solute is moved by an active change in conformation of a transporter; although many types of pumps require only one ATP hydrolysis per step, some require two.

Concentrations of ions commonly found in the cytosol and the surrounding environment for mammalian cells. Approximate concentrations of these ions found in sea-water are shown for comparison; SO_4^{2-} is present in sea water at higher concentrations than Ca^{2+}. Units are milliMolar. There are more charged objects in the cell than just solvated ions - DNA and a number of phospholipids are also charged.

	Intracellular concentration	Extracellular concentration	Sea water
Na^+	5 - 15	145	470
K^+	140 - 155	4 - 5	10
Mg^{2+}	0.5	1 - 2	50
Ca^{2+}	10^{-4}	1 - 2	10
Cl^-	5 - 15	110 - 120	550

The local charge density of each species is related to the potential difference across the membrane. From the definition of electrostatic potentials, the energy of an ion of charge ze when placed in an electric potential V is zeV, where e is the elementary unit of charge (1.6×10^{-19} C) and z is the number of charges on the ion, including its sign. Suppose now that the potential varies from place to place as $V(x)$. Then the probability of finding the ion at location x is proportional to the usual Boltzmann factor $\exp(-zeV / k_B T)$. Comparing the probabilities P_1 and P_2 at two locations 1 and 2,

$$P_1/P_2 = \exp(ze[V_2 - V_1] / k_B T), \qquad (1)$$

where the proportionality constant has been eliminated. Now, the concentration of an ionic species is proportional to the probability P, so Eq. (1) can be rewritten as

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$$V_2 - V_1 = (k_B T/ze) \ln(c_1/c_2)$$ Nernst equation (2)

This expression, called the Nernst equation, relates concentration ratios at two locations to their potential differences. The prefactor $k_B T/ze$ sets the physical scale for the potential difference, and is equal to 25 mV for $z = 1$ and $k_B T = 4 \times 10^{-21}$ J at room temperature. Examination of the ionic concentrations of Na^+, K^+ and Cl^- shows that potential differences V are commonly in the -60 to -80 mV range according to Eq. (2) where $V = V_{inside} - V_{outside}$. A minus sign for V means that the inside location is more negative than the outside.

The immediate effect on V is small if the protein pumps are turned off; we call this quasi-steady state potential V_{qss}. At V_{qss}, the net current transiting the membrane for all species must be zero. For an ionic species with the label α, its current density (current per unit area of the membrane) is

$$\mathcal{I}_\alpha = \gamma_\alpha (V_\alpha - V_{qss}),$$

where γ_α is its conductivity through the membrane and V_α is the Nernst potential for species α according to Eq. (2). The conductivity γ_α is the (two-dimensional) conductance per unit area with units of $\Omega^{-1}m^{-2}$, such that the conductance G of a membrane patch of area A is

$$G = \gamma_\alpha A, \quad (3)$$

for a single ionic species. The total conductivity of a number of species transiting a membrane is just the sum of the individual contributions

$$\gamma_{tot} = \Sigma_\alpha \gamma_\alpha. \quad (4)$$

Recall that the conductance is the reciprocal of the resistance R

$$G = 1/R. \quad (5)$$

The condition that there is no net current density then reads

$$\Sigma_\alpha \gamma_\alpha (V_\alpha - V_{qss}) = 0. \quad (6)$$

Restricting our attention to the movement of only three ionic species, Na^+, K^+ and Cl^-, Eq. (6) can be rearranged to yield

$$V_{qss} = (\gamma_{Na} V_{Na} + \gamma_K V_K + \gamma_{Cl} V_{Cl}) / (\gamma_{Na} + \gamma_K + \gamma_{Cl}). \quad (7)$$

Knowing the ionic concentrations maintained by the ion pumps, Eq. (7) yields $V_{qss} = -74$ mV for the mid-range of the concentrations given in Table 1; this estimate is very close to the measured potential of the membrane.

Propagation of a signal along an axon (without a myelin sheath). Under resting conditions, concentration gradients are maintained by transporters (Na high outside, K

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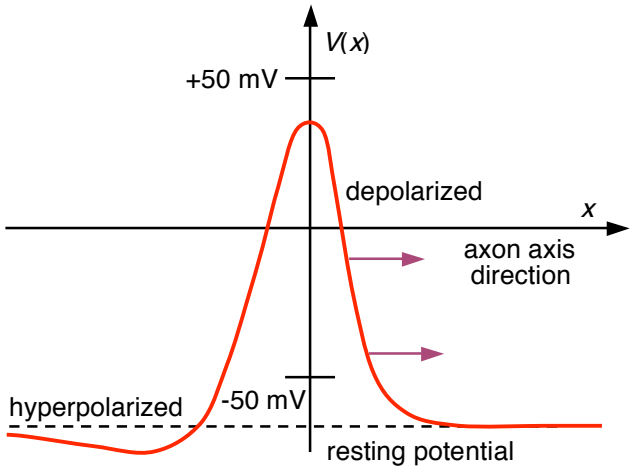
high inside the cell). When a signal passes along the axon, Na and K ions are (unequally) exchanged across the plasma membrane in a local region and the membrane potential swings from its rest value by roughly 100 mV, to +30 mV or more, before falling back toward the rest value as the axon recovers. The swing in the membrane potential is called the action potential. The time scale for the change in the potential is ~ 10^{-3} s for Na-based potentials, but much longer for Ca-based ones. Once the membrane potential has swung positive, sodium channels close, helping prevent the back-propagation of the signal.



The mechanism for depolarization of the membrane must come from channel proteins. Now, there are many different types of channel proteins: mechanically-gated channels, ligand-gated channels and, of importance here, voltage-gated channels.

To be useful in a thermal environment, the channel must require a minimum voltage in order to open; otherwise the channel would open at random. The typical threshold for activation is ~15 mV; below this threshold, a stimulus does not propagate along the axon but simply decays away, also on a time scale of milliseconds.

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