Biophysics

The energy around us

Forms of energy

In discussing the energy of a physiological system, the Gibbs free energy is most relevant. At its most fundamental level, the Gibbs free energy is

G = H – TS

Where (H) is the enthalpy, (T) is the absolute temperature and (S) is the entropy. Since the value of (S) cannot be known, the change in the Gibbs free energy (dG) is more commonly used:

$$dG = -SdT + Vdp + FdI + \sum_{i=}^{m} \mu_i dn_i \Psi\, dq$$

Where (V) is the volume, (dp) is the change in pressure, (F) is the mechanical force, (dl) is the change in length, (μ_i) is the chemical potential, (dn_i) is the change in the number of molecules, (ψ) is the electric potential and (dq) is the change in electric charge.
This daunting equation is more complex than the molar Gibbs free energy of reaction, familiar to many students from their biochemistry classes:

$$\Delta G = -RT\, InK_{eq}$$

Where R is the molar gas constant and Keq is the equilibrium constant.
The difference between the equations is illustrative. The smaller free energy of reaction equation is a subset of the larger Gibbs free energy of reaction equation, the reaction equation being derived by assuming that temperature, pressure, length and charge are all constant, reducing the free energy equation to a statement only relating to the chemical potential of the system.

In practical terms, this is the goal of experimental science: to hold all variables constant except the one we are interested in measuring.
Studies of thermal regulation focus only on (dT); respiration depends on (dp); muscle contraction measures (dl); and electrophysiology depends on (dq). All of these elements are always present, but using logic and control conditions we try to minimize the effect of outside forces that would alter our results.

Ambient energy

We live in a world where our body temperature is 98.6° F, 37° C or 310 K. We regulate this temperature closely, no matter the temperature around us.With the exception of a few molecules near our body surfaces, the constant temperature of the body produces an average energy that the molecules in the body are exposed to. This energy is the absolute temperature T (in degrees K) times the Boltzmann constant, k, 1.38 × 10−23 J/K. Except for those occasions when a molecule is involved in a reaction, molecules will be in equilibrium with the energy of the environment around us, Eo,

$$E_o = kT = 310K.1.38\,\text{x}10^{-23}\,J/K.molecule = 4.28\,\text{x}\,10^{-21}\,\text{J/molecule}$$

This is the equilibrium energy of a single molecule. When we deal with an ensemble of molecules, we measure molecules on the molar scale, using Avogadro's number (N_A), to convert Boltzmann's constant to the gas constant (R):

$$R = N_A.k = 6.02\,x\,10^{23}\,molecule\,/mol\,.1.38\,10^{-23}\,\frac{J}{K}.molecule$$
$$= 8.31\,J/K.mol$$

and the molar equilibrium energy to

$$E_m = RT = 8.31\,J/K.mol\,.310K = 2.58\,kJ/mol$$

Every ensemble of molecules at equilibrium will have the same average energy, but each individual molecule within the ensemble will not have the same energy. The Boltzmann function of energy distribution shows the number (n_i) of molecules that have a given energy level (E_i), according to the relationship

$$n_i = C\,e^{-E_i/kT}$$

Where C is a normalization constant. Because the exponent is negative, there will be fewer molecules with a given energy as Ei increases. Each molecule in the ensemble will be subject to local conditions, such as collisions with other molecules, which will constantly change its velocity and thus its energy.

Maxwell developed the equation of velocity distribution:

$$\frac{dn(\text{v})}{n_0\text{dv}} = \frac{4}{\sqrt{\pi}}\left(\frac{m}{2kT}\right)^{3/2}\text{v}^2\,e^{\frac{-m\text{v}^2}{2kT}}$$

In which the fraction of molecule (dn/n_0) is wthin a particular velocity range (dv). The velocity distribution is nearly symmetrical, as shown in the dashed line of figure.
in which the fraction of molecules (dn/no) is within a particular velocity range (dv). The velocity distribution is nearly symmetrical, as shown in the dashed line of Figure 1.2.

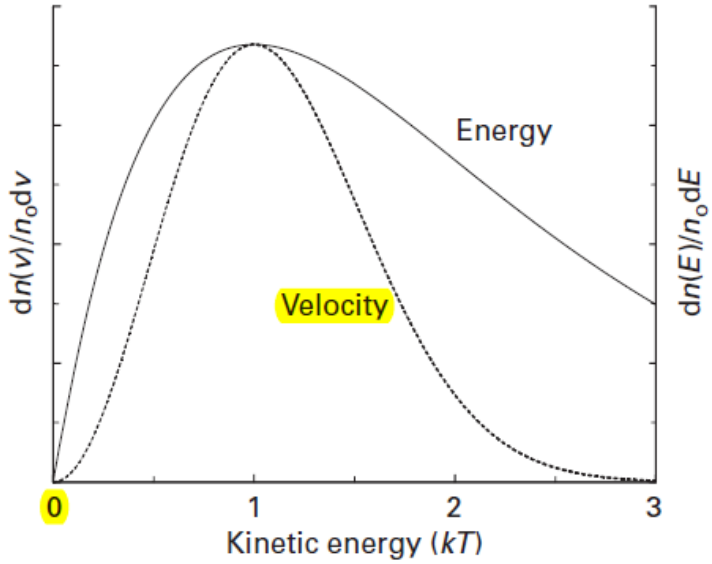
Look at the exponential term: $\frac{m\text{v}^2}{2}$ represents the kinetic energy of the molecule, divided by kT. Since the molecules are at equilibrium, there is no potential energy, only kinetic energy, and the energy of a molecule Em is

$$E_m = \frac{m\,v^2}{2}$$

The Maxwell velocity distribution equation can be modified, multiplying the non exponential part by 2/m · m/2 and converting mv2/2 to Em to give the energy distribution:

$$\frac{dn(\text{E})}{n_0\text{dE}} = \frac{8}{m\sqrt{\pi}}\left(\frac{m}{2kT}\right)^{3/2}E_m\,e^{\frac{-E_m}{kT}}$$

This allows us to plot the energy distribution of the molecules in Figure, The important concept here is that even at equilibrium there will be a distribution of the energy of the molecules.



The energy and velocity distributions of molecules at equilibrium. The abscissa is plotted in units of kT relative to the ambient energy. The velocity distribution will have its peak when the $mv^2/2kT = 1$. The energy distribution will have its peak when $E_m/kT = 1$.

Molecular energy

The energy associated with each atom and each bond is not continuous, but quantal, based on the electron shells occupied in the electron cloud around the nucleus. For a given atom, there would be a quantal energy distribution, with the lowest energy configuration being the most common, as Boltzmann demonstrated.
In a molecule, however, not every bond will be at its lowest energy: instead, the molecule as a whole will seek its lowest overall energy, out of the many possible configurations of attractions and repulsions that will alter bond angles and the energy in the bonds.
The ambient energy in the human body is 2.58 kJ/mol. This energy is far below that of any covalent bond in the body. This means that it is statistically unlikely that any covalent bond would spontaneously break due to the random thermal fluctuations around it.

Molecular energy absorbance

Despite the thermal stability of covalent bonds in physiological systems, some of these bonds are sensitive to energy input from external sources. When energy is absorbed by a molecule, it will either release the energy as heat, returning to its original configuration, or trap some of the energy within the molecule by altering its structure, as shown in Figure (2)
In the first case, the molecule can absorb heat from the environment without changing its chemical structure, as will occur when there is a local temperature increase.
In the second case, shown in the lower part of Figure 1.3, a molecule will absorb energy, alter the electrons of the bonds of the molecule, and change its chemical structure.

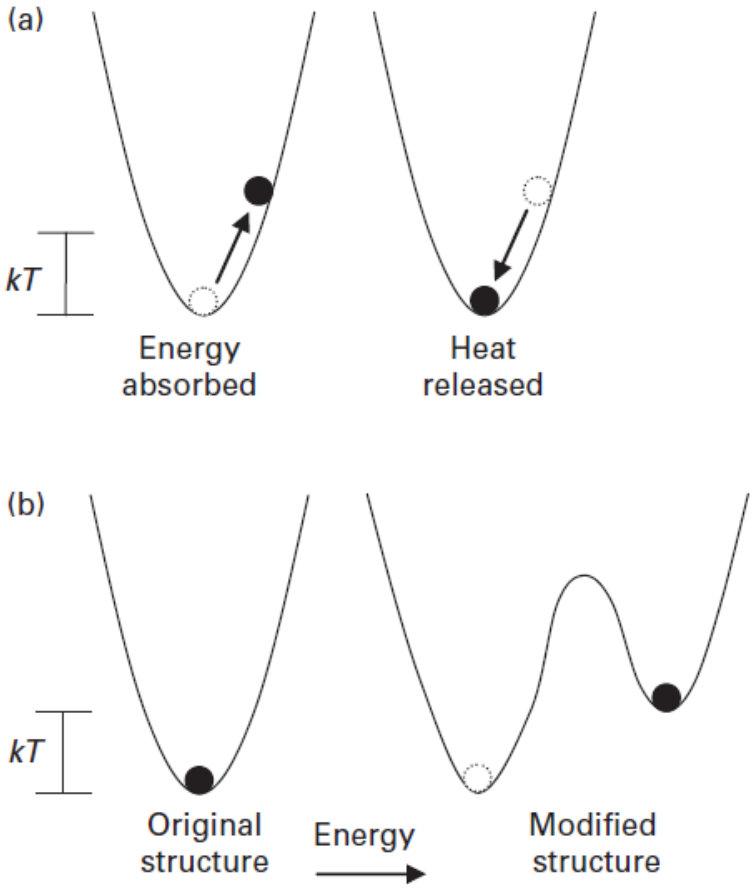


Figure 1.2 Energy absorbance within molecules. The molecule may absorb energy and radiate heat (a), or alter its chemical structure (b). The effect of kT on any state is measured from its local minimum relative to the lowest local energy barrier.

Molecular transduction

Between the cases in which the molecule that changes its structure can spontaneously revert to its original conformation and in which it is denatured so that no return is possible, there are particular alterations in physiological systems that can revert with the assistance of enzymes. In these cases, a particular bond can absorb energy from the surrounding environment and alter its structure. Unlike the case in which all parts of the molecule see a higher local temperature, here a particular bond is sensitive to a particular wavelength of electromagnetic radiation, due to a match of the electron oscillation frequency of the bond and the external radiation frequency.
The energy of an individual bond is not continuous, but has specific quantum energy levels. Planck postulated that the energy (ε) of the quantum is not fixed, but will increase as the frequency ν of the oscillation increases, with Planck's constant h as the proportionality factor:

$$\varepsilon = h\nu$$

ν: frequency
The frequency of electromagnetic radiation is inversely proportional to the wavelength λ of the electromagnetic wave, with the product equal to the speed of light c in a vacuum:

$$C = \lambda\nu$$

Thus, the energy, frequency and wavelength of electrons are all connected.

The electromagnetic spectrum (Figure 1.3) has been subdivided from gamma rays to radio waves. Since gamma waves have the highest frequency, they will have the highest energy. Radio waves, with the lowest frequency, will have the lowest energy.

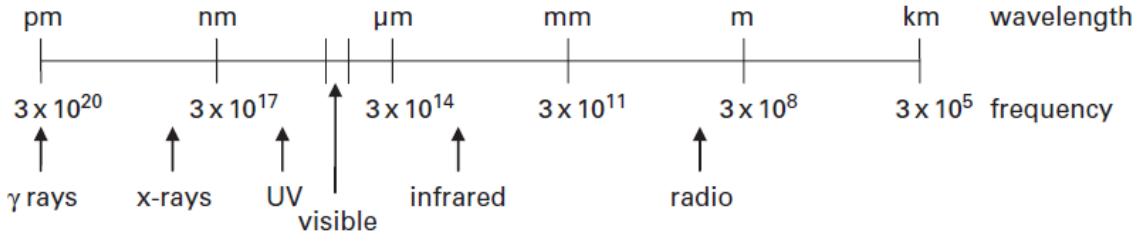


Figure 1.3 Electromagnetic spectrum. Wave energy is directly proportional to frequency and inversely proportional to wavelength.

Ionizing radiation

DNA damage can also occur from exposure to x-rays. X-rays have wavelengths in the nanometer range, shorter than the visible and UV-B wavelengths. X-rays produce ionizing radiation, in which molecules are altered by ionization of one of their electrons. The usefulness of x-ray radiation for medical diagnosis lies in the ability of the x-rays to interact with tissue: if there were no interactions, all the x-rays coming from the x-ray source would uniformly pass through tissue, and the x-ray film would have no contrast. Damage to the tissue with diagnostic x-rays is slight, and in most cases can be repaired enzymatically. In contrast, radiation therapy to kill cancer cells is much more intense, with the goal of eliminating the cancerous tissue.
X-rays are highly energetic, and can ionize many different molecules. Every molecule has an energy of ionization: in the case of water, that energy is 1200 kJ/mol, 100–1000 times less than the energy of x-rays. The collision of an x-ray with a water molecule will result in the ionization of the water molecule. The ionization of water leads to the formation of the destructive radicals that are a product of ionizing radiation. There are multiple reaction sequences generated by this initial reaction. An example of one of these leading to a chain reaction of destructive reactions is as follows:

$H_2O + h\nu \rightarrow H_2O^+ + e^-$	Ionization of water
$H_2O^+ + e^- \rightarrow H_2O^*$	Excited water molecule
$H_2O^* \rightarrow H^\bullet + OH^\bullet$	Dissociation to radicals
$R_1H + OH^\bullet \rightarrow R_1^\bullet + H_2O$	Generation of organic radical R_1
$R_1^\bullet + O_2 \rightarrow R_1O_2^\bullet$	Generation of oxygen radical R_1

which leads to the chain reaction:

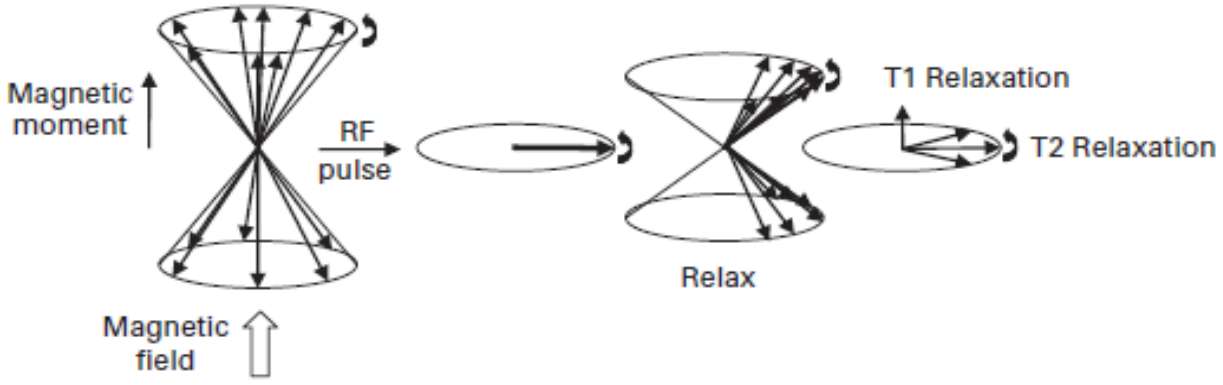
$R_1O_2^\bullet + R_2 \rightarrow R_1O_2H + R_2^\bullet$	Covalent change in R_1, generation of radical R_2
$R_2^\bullet + O_2 \rightarrow R_2O_2^\bullet \ldots$	Generation of oxygen radical R_2, etc.

The chain reaction nature of radical formation means many molecules will be destroyed and the cell potentially killed. In the case of radiation therapy on a cancerous growth, this is the desired outcome; in the case of healthy tissue, it is not. Antioxidant molecules such as Vitamin C can stop this chainreaction.

X-rays are of course not the only imaging technology. Computerized tomography (CT) images produce two-dimensional images using Radon transforms of multiple x-ray scans. Closely related to CT is positron emission tomography scanning, or PET.
PET scans use a metabolic tracer radio-labeled with a positron-emitting nuclide.

Magnetic resonance

Other imaging technologies, such as magnetic resonance imaging (MRI) and ultrasound, use different methods of energy absorbance. (MRI) takes advantage of a different properties of molecules, the spin associated with the nucleus. The nucleus is charged due to the presence of protons, and a spinning charge generates a magnetic field.
Different atomic nuclei (H1, F19, P32, C13) have different spin rates, and therefore have different magnetic moments. When an external magnetic field is applied to the nuclei of a tissue, two spin states exists: one in which some magnetic moments line up with the applied field (the low energy spin state), and one in which some magnetic moments line up against the applied field (the high energy state) as shown in Figure.
There will always be more spins in the low energy state than in the high energy state, creating a net magnetic moment along the z-axis in the direction of the magnetic field.
The stronger the applied magnetic field, the greater the energy difference and the stronger the potential signal. When a radio frequency signal is applied that matches the spin frequency of the protons, the energy states are equilized. When the radio field is turned off, the spins will re-equilibrate, releasing a radio frequency signal that can be detected.
This is T1 relaxation. In addition to the energy difference between the states, the magnetic moments, spread out in the shape of a cone when no radio frequency energy is applied, will be lined up together at a single angle of the cone in the x–y plane when the radio waves are applied.



Magnetic moments precess, or spin, around the nucleus. When atoms are placed in a magnetic field, the magnetic moments of the atoms will align with or against the field, with the greater number aligned with the field. An applied radio frequency pulse will equalize the magnetic moments. When the radio frequency field is removed, the magnetic moments will re-equilibrate using T1 and T2 relaxations, and generate a signal that produces MR images and MR spectra. The smaller cones on the right show the signals in the middle of relaxation.

Sound

There is a range of sound waves that can be detected by the human ear. Sound waves, unlike electromagnetic radiation, require a medium for the waves to pass through. The frequency of a sound wave is its pitch, and the amplitude of the sound wave is its loudness. Sound waves produce cyclic compressions of the medium, whether gas, liquid or solid. All of these media are part of the sound transduction system of the human ear:
The sound waves arrive through the air, pass though the solid structures of the tympanic membrane, bones of the middle ear, and the oval window, the liquid of the inner ear, and the solid basilar membrane before being transduced into electrical signals.
The relation between the speed of sound in a medium C_m, the frequency of the sound wave ν, and the wavelength of the sound wave λ is

$$C_m = \nu \lambda$$

The speed of sound is not constant. It is faster in solid than liquids, and faster in liquids than in air. In addition, the physical properties of the medium will change what the speed of sound is in that medium, such as the density of the material or the humidity of the air.
The relationship between the speed of sound, the stiffness of the medium K, and the density of the medium δ is

$$C_m = \sqrt{\frac{K}{K\,\delta}}$$

The stiffness of the medium is in part determined by how much physical change is retained by the material as it absorbs sound energy, a significant property of solids but unimportant in fluid and air. In the ear, this aspect of hearing is manifested by changes in the bones of the middle ear as people age and the slight thickening of the oval window end of the basilar membrane over time, resulting in the gradual loss of high frequency hearing with age.
Sound pressure can be measured on an absolute scale in units of pascals. This is not, however, how differences is the sound pressure that humans can detect is normally presented. The different sound levels are compared with an arbitrary standard: the lowest sound detectable by the human ear at 1 kHz. This sound pressure, P_0, is 20 μPa, and is defined as 0 decibels. The decibel units use a logarithmic scale. The relationship between sound intensity L and pressure p is

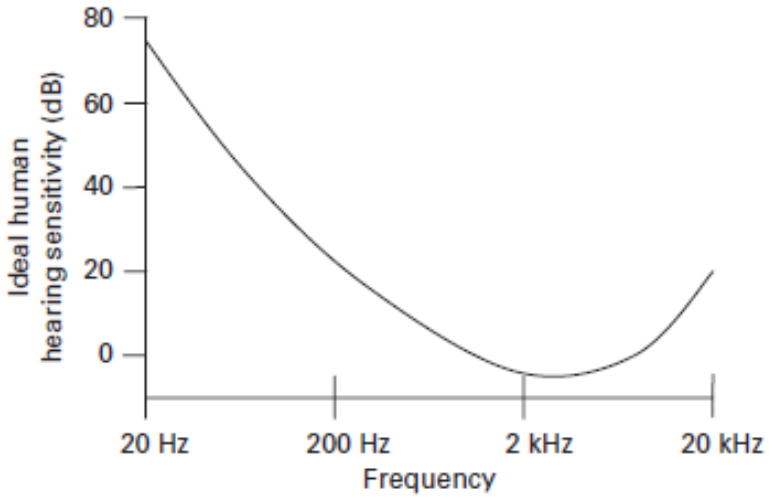
$$L = 10 \log \frac{P^2}{P_0^2} = 20 \log \frac{p}{p_0}$$

This is the decibel scale. For a sound equal to p_0, the ratio $\frac{p}{p_0}$ is 1 and the log is 0, so L = 0 .
This sound has zero decibels. Because there is a squared relationship between sound intensity and sound pressure, a tenfold change in sound pressure produces a sound intensity change of 20 decibels.

When sound waves enter the ear canal, they produce vibrations of the tympanic membrane, or eardrum. The tympanic membrane separates the outer ear from the middle ear. The first of the three bones of the middle ear, the malleus, spans the tympanic membrane and receives its vibrations from it. The oscillations of the tympanic membrane have a displacement of about 100 nm up to a frequency of 1 kHz, and decrease to less than 10 nm at 10 kHz. The vibrations are conducted through the middle ear bones, the malleus, incus and stapes to the oval window, the membrane that separates the middle ear from the inner ear.

The combination of all the sound transmission structures in the ear results in a frequency range of 20–20 000 Hz. The peak of the range occurs at 1–3 kHz (Figure).

Ultrasound imaging uses sound waves, not electromagnetic radiation, with frequencies of 1–5MHz penetrating tissue, a higher frequency range than that of human hearing (20 Hz to 20 kHz). As the ultrasound waves pass through tissue, they reach boundaries between tissues of different densities. When this occurs, some of the waves are reflected back, while some continue on to the next boundary, where again some waves are reflected back. The image is constructed based on the differential reflections, so that the areas of different densities appear with different intensities. Current developments in this field allow three-dimensional construction of images, as well as Doppler images, in which the flow of blood allows imaging of blood vessels.



Frequency dependence of ideal human hearing sensitivity. The standard of human hearing is set at 0 decibels at 1 kHz. Humans have their most sensitive hearing at about 3 kHz. The limitations on hearing are set by the sensitivity of the tympanic membrane, the ear bones, and the vibrations of the basilar membrane.

The ultrasound waves are not absorbed by specific molecules, so that the energy dissipation is in the form of heat. In all types of imaging the applied energy must interact with molecules to produce the image. This will cause an increase in heat during image production. The side effect of increased local temperature has to be considered whenever an image is produced, regardless of the imaging technology. In the development of each imaging modality, the increase in temperature is measured to determine the safety of the procedure. Routine procedures only use energies that produce insignificant changes in

temperature. The destructive properties of ultrasound are medically applied in the fracturing of
kidney stones, a process called lithotripsy. Kidney stones will shatter when specific wavelengths of sound impart a force on a stone. The force F applied to the stone is

$$F = \frac{W}{C}$$

Diffusion and directed transport

The movement of material within the cell and across membranes always requires a driving force. For diffusive processes, the driving force is the electrochemical gradient. The electrical component of this force requires a separation of charge: the negative and positive charges must be kept from one another until a conductive channel opens and the charged species can flow down their electrical gradient. Intact membranes, whether the cell membrane or those of organelles, are needed to provide the voltage buildup that will allow current to flow when conduction becomes possible.

Forces and flows
Students are exposed to this concept in their initial exposure to
electrical physics, in the relation between current I, resistance R, conductance C and voltage V:

$$I = \frac{V}{R} = CV$$

The voltage is the force, and the current is the flow. An analogous equation applies to the flow of blood F, the blood pressure P and the resistance R:

$$F = \frac{P}{R}$$

and the relationship of cardiac output CO, total peripheral resistance, TPR, and blood pressure BP:

$$CO = \frac{BP}{TPR}$$

Each of these relates a flow to a particular driving force. Newton defined the relation of force, mass and acceleration for an object in a vacuum with no friction,

f = ma

conditions that do not apply to physiological systems. When friction is also considered, the relation becomes

f =ma + hv

with the force f having both acceleration and velocity components. When the acceleration is damped out or the mass is so small as to make ma insignificant, the relation relates a flow v and a force f. The h factor, as seen in the equations above, is a resistance or frictional factor.

Physiological systems do not exist in isolation. There is linkage between the hydrolysis of ATP and the movement of ions against their gradient, the movement of ions down their gradient and the production of second messengers, or the contraction of muscle cells and the movement of blood. The principles of linked forces and flows were formalized by Onsager (1931). He modeled the relation between a flow J and force X as

J = LX

with L as a numerically positive phenomenological coefficient, a relationship applicable when the system is near equilibrium and the coefficient is independent of the flow. As systems move away from equilibrium, the total coefficient L_T will change as a function of the flow

$$J = L_T\mathrm{X} = \left(L_0 + L_J\mathrm{J}\right)\mathrm{X}$$

where L_0 is the equilibrium coefficient and L_J is the flow-dependent coefficient. Rearranging the non-linear equation to solve for J,

$$J = \frac{L_0\, X}{1 - L_J X}$$

it is clear that the system is linear when X is small, and becomes non-linear as the driving force X increases. Figure 1 shows that energy systems are linear near equilibrium, but become increasingly non-linear the farther the system is from equilibrium.

Friction is the ratio of force/flow, X/J, and the dependence of friction on the flow rate is shown in Figure 2. At low flow rates, LJ has little influence, and the system is linear. As the flow rate increases, the system becomes progressively more non-linear. The degree of non-linearity is determined by the ratio of the coefficients L_J/L_0, with the friction produced increasing as the ratio increases.

For coupled systems, the relation between two forces and two flows is

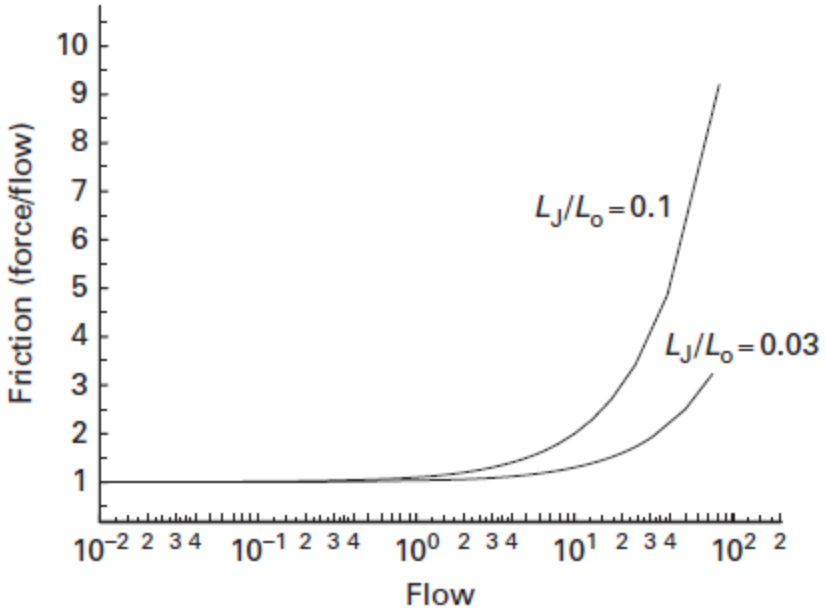
$$J_1 = L_{11}X_1 + L_{12}X_2$$

$$J_2 = L_{21}X_1 + L_{22}X_2$$

where the flows J_1 and J_2 are driven by forces X_1 and X_{12}, with the relationships connected by the phenomenological coefficients Lik. L_{11} and L_{22} are the direct coefficients linking the flow and force of systems 1 and 2, respectively, as the conductance linked voltage and current above. In systems that interact, force X_1 will have an influence on flow J_2, and force X_2 will have an influence on flow J1. The linkage is described by the coupling coefficients L_{12} and L_{21}. The higher the value of the coupling coefficients, the stronger the linkage between the systems. If the systems are not linked, the coupling coefficients will be zero, and the paired equations above will reflect two entirely separate systems.

The filled circle state is within *kT*, but removed from the lowest energy state. The force returning it to the lowest energy state will be small, with a linear Onsager coefficient. The open circle state is far from equilibrium. It will have large force and a non-linear Onsager coefficient.

Figure 1



Non-linearity of force/flow system. Increased force produces increased flow away from near-equilibrium conditions, resulting in increased friction within the system.

Figure 2

Onsager proved that in coupled systems, the value of

$$\boldsymbol{L_{12} = L_{21}}$$

as long as the local entropy production σ of the two-equation system is

$$\boldsymbol{\sigma = J_1 X_1 + J_2 X_2}$$

Nerve cells

Each cell has a cell body containing a nucleus, endoplasmic reticulum, ribosomes, Golgi apparatus, mitochondria, and other organelles that are essential to the function of all cells (see fig.1). Specific for nerve cells, is their dendritic structure (see fig. 2). The dendrites (together with the cell body) provide sites for the synaptic contacts made by the terminals of other nerve cells and can thus be regarded as specialized for receiving information.

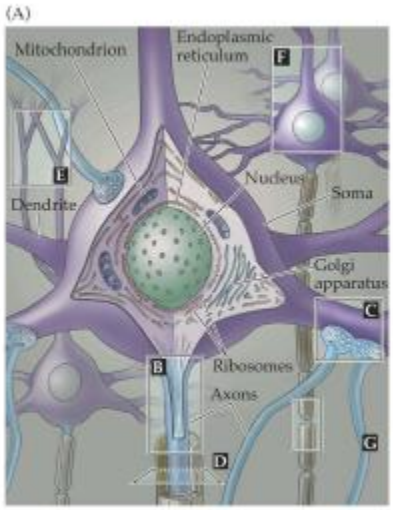


Figure 1 Diagram of nerve cells and their component parts.

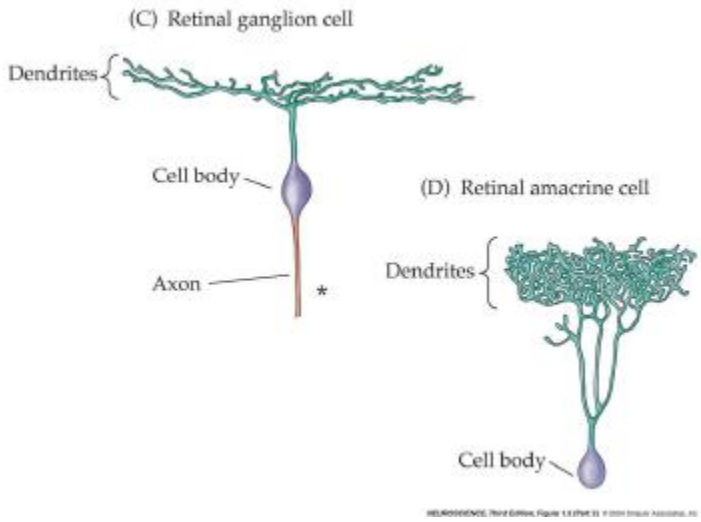


Figure 2: Cells stained with silver salts

The nervous system

The nervous system is traditionally divided into a central and peripheral component (see fig. 3). The peripheral system contains the sensory neurons, which receive information

from the outside world, and the motor neurons, that connect to muscles and glands. Sensory information is processed in the brain.

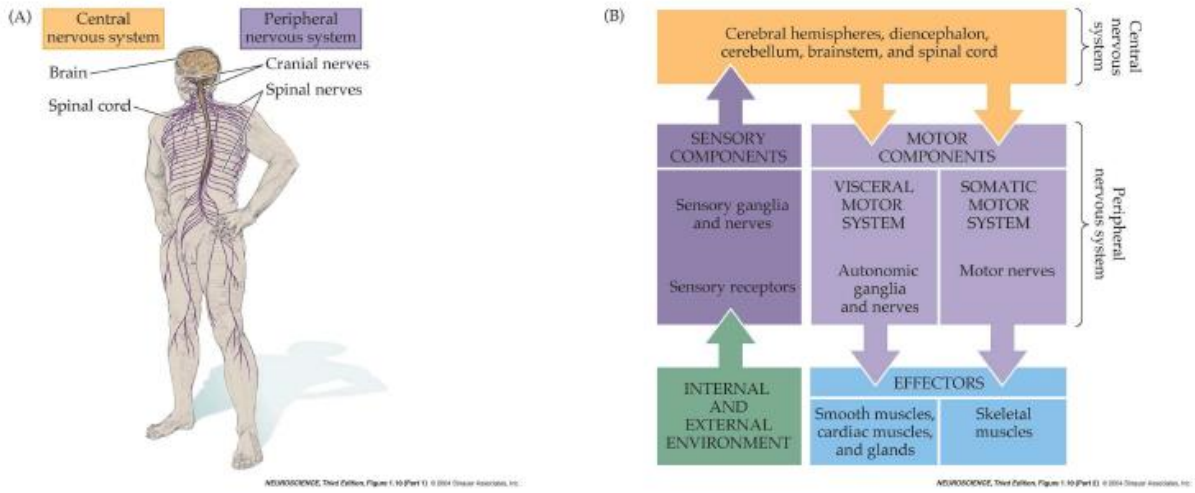


Figure 4: The major components of the nervous system and their functional relationships. A) The CNS (brain and spinal cord) and the PNS (spinal and cranial nerves). B) The peripheral nervous system receives sensory input and outputs motor commands. The central nervous system provides the 'mapping' from sensory input to motor output.

Electrical properties of cells

Nerve cells generate electrical signals that transmit information. Neurons are not good conductors of electricity, but have evolved elaborate mechanisms for generating electrical signals based on the ow of ions across their membranes. Ordinarily, neurons generate a negative potential, called the resting membrane potential , that can be measured by intracellular recording.
The action potential is a short spike in the membrane potential, making the membrane potential temporarily positive. Action potentials are propagated along the length of axons and are the fundamental electrical signal of neurons.
The best way to observe an action potential is to use an intracellular microelectrode to record directly the electrical potential across the neuronal membrane (fig. 5).

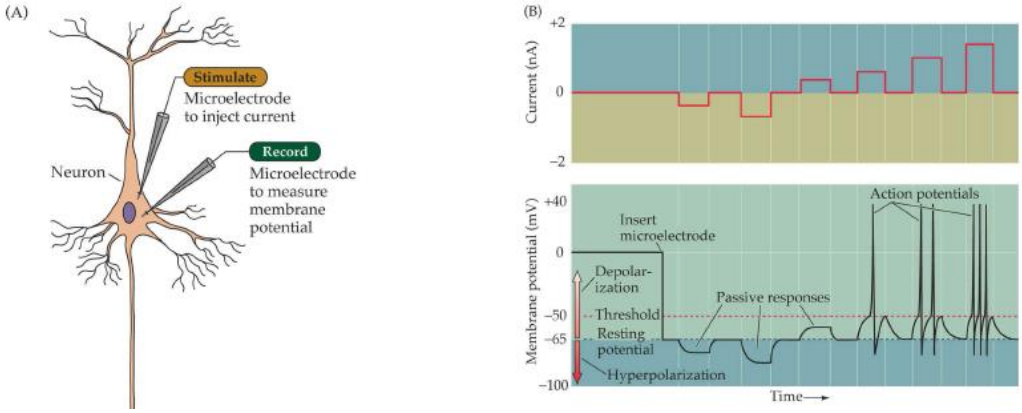


Figure 5: Recording passive and active electrical signals in a nerve cell.

Inserting the voltage-measuring microelectrode into the neuron reveals a negative potential, the resting membrane potential. Typical values are 60-80 mV.

Ion channels

Electrical potentials are generated across the membranes of neurons (in fact of all cells) because (1) there are di_erence in the concentrations of speci_c ions across nerve cell membranes and (2) the membranes are selectively permeable to some of these ions (fig. 6).

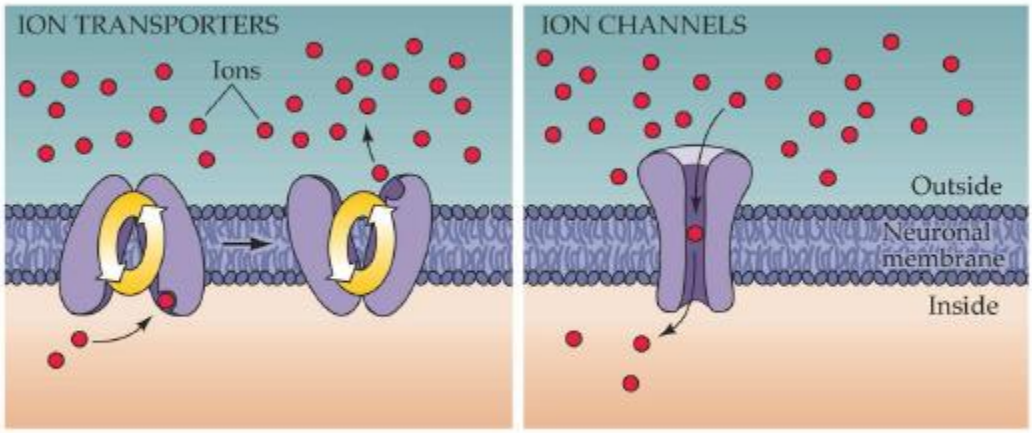


Figure 6: Ion pumps and ion channels are responsible for ionic movements across neuronal membranes.

The ion concentration gradients are established by proteins known as ion pumps, which actively move ions into or out of cells against their concentration gradients. The selective permeability of membranes is due largely to ion channels, proteins that allow only certain kinds of ions to cross the membrane in the direction of their concentration gradients. Thus, channels and pumps basically work against each other, and in so doing they generate cellular electricity.

Membrane channels can open or close in response to changes in their direct vicinity, such as a change in the membrane potential, changes in the concentration of neurotransmitters, or sensory input. For instance, hair cells in the cochlea (inner ear) mechanically deform in response to sound, and this mechanical deformation changes the permeability of certain channels.

Channels open and close rapidly in a stochastic manner (fig. 7). The macroscopically observed permeability of the membrane is related to the probability that the channel is open.

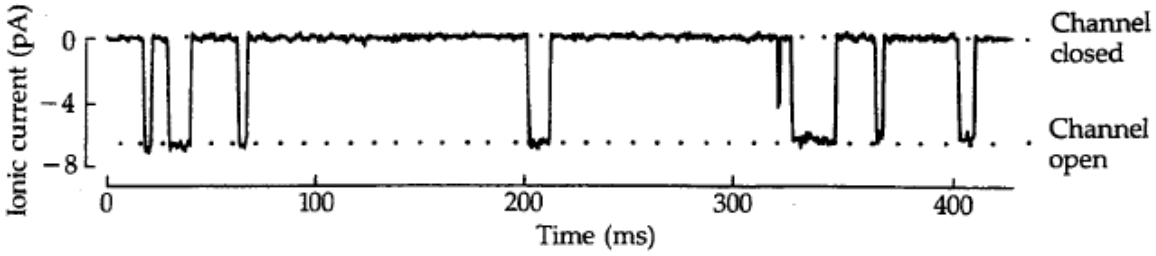


Figure 7: Open-shut gating of an ionic channel showing 8 brief openings.