TOPICS

- reckoning energy and power
- forms of energy
- energy balances – conservation of energy
- cellular energy production and storage
- how cells make ATP: substrate level oxidation and oxidative phosphorylation (respiration)

Energy and power dimensions and units

Energy is manifested in many forms.

Energy [=] mass•length^2/time^2 = force•distance = pressure•volume = surface tension•area…

The SI unit for energy is the joule (J).

1 J = 1 Newton•meter

Conversions: 1 J = 0.7373 lb_f•ft = 0.239 calories = 0.000948 British thermal units ("btu")

The total amount of energy that is liberated or consumed ("transferred") is important, but for living systems, in biomedical systems it is often the rate at which energy is transferred that is more important – life is a system of rate processes.

The rate at which energy is transferred is defined as **power**.

Power [=] energy/time = mass·length^2/time^3

The SI unit for power is the watt (W, named for J. Watt, another early pioneer of thermodynamics).

1 W = 1 joule/second

Conversions: 1 W = 0.00134 horsepower = 860.4 cal/hr = 3.414 btu/hr

Forms of energy

The first law of thermodynamics states that "energy can be converted from one form to another, but it is neither created nor destroyed, with the exception of nuclear processes."

This is similar to the law of conservation of mass. Just like mass, energy is a conserved quantity.

Note that energy can be converted among different forms. What are some of these different forms?

internal energy (U):	energy related to the bond vibrations in a material. It is a function of temperature.
potential energy (P.E.):	energy related to the elevation h of a mass m in a gravitational field. (P.E. = mgh)
kinetic energy (K.E.):	energy related to the velocity v of a moving mass m (K.E. = $mv^2/2$)
chemical energy:	energy released or absorbed by a chemical reaction; also the energy due to differences in solute concentration in different regions
electrochemical energy:	energy related to differences in charged solute (ion) concentrations

All of the above forms of energy reside within an object.
Of particular importance for biological systems is the chemical energy, particular the coupling between multiple chemical reactions and solute concentration gradients that store energy) and also its conversion to work.

There are other forms of energy that carry energy from one object to another:

work (W): mechanical, chemical, or electrical energy transferred from one object to another. Often we talk about work done on an object by its surroundings.

heat (Q): thermal energy transferred from one object (usually a warm object) to another object (usually a cool object). Often we talk about heat transferred between an object and its surroundings.

sensible heat effects versus **latent heat effects**

T versus Q, U(T) versus (T) {and Cv, Cp – heat capacities)…

Energy Balances

The mathematical application of the first law of thermodynamics is the **energy balance**. The energy balance concept is identical to the material balance concept, only we are doing an inventory accounting on energy entering or leaving a system in its numerous forms rather than mass entering or leaving a system, possibly in different chemical forms.

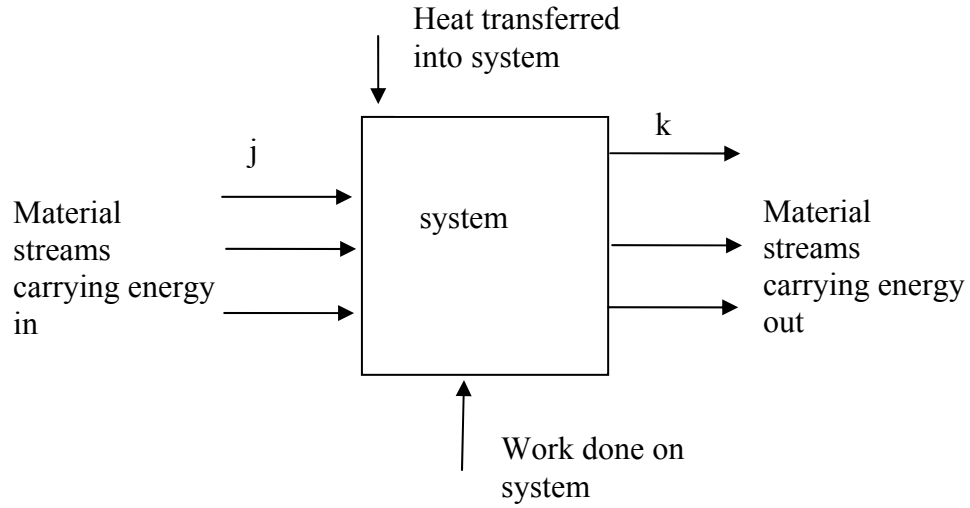
Note, again, in performing a balance, system definition is important.

Universe = System + Surroundings

Anything that is not part of the system is part of the surroundings.

Preparation for setting up the energy balance equation: think about all the ways energy can cross system boundaries…..

Now, the rate of energy accumulation in a system = the sum of all possible ways of putting energy into, or taking energy out of, the system



Let j and k represent separate material inlet streams and material outlet stream, respectively.

$$\frac{dE_{sys}}{dt} = \sum_{j}^{all\ inlets} \dot{E}_j - \sum_{k}^{all\ outlets} \dot{E}_k + \dot{Q} + \dot{W}$$

Where $\dot{E}$ represents the rate at which energy is carried by material inlet or outlet streams, $\dot{Q}$ is the net rate at which heat is transferred into the system, and $\dot{W}$ is the net rate at which work is done by the surroundings on the system. .

The energy in the system E_{sys} and the energy in any stream, has three components:

E = internal energy + kinetic energy + potential energy

$$E = mu + \frac{1}{2}mv^2 + mgh$$

where m is the mass, and u is the internal energy *per unit mass*, v is the velocity, g is the gravitational acceleration, and h is the height relative to some reference level.

So we can write

$$E_{sys} = m_{sys}\left(u + \frac{1}{2}v^2 + gh\right)$$
$$\dot{E}_{in} = \dot{m}_{in}\left(u_{in} + \frac{1}{2}v_{in}^2 + gh_{in}\right)$$
$$\dot{E}_{out} = \dot{m}_{out}\left(u_{out} + \frac{1}{2}v_{out}^2 + gh_{out}\right)$$

The complete energy balance equation is thus

$$\frac{dE_{sys}}{dt} = \sum_{j}^{all\ inlets} \dot{m}_{in,j}\left(u_{in,j} + \frac{1}{2}v_{in,j}^2 + gh_{in,j}\right) - \sum_{k}^{all\ outlets} \dot{m}_{out,k}\left(u_{out,k} + \frac{1}{2}v_{out,k}^2 + gh_{out,k}\right) + \dot{Q} + \dot{W}$$

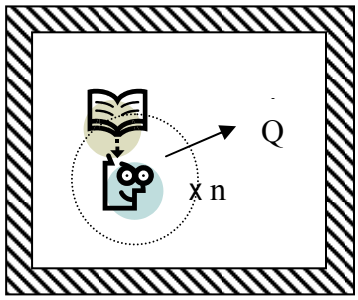
Just as with the material balance, there are special cases. If the system is at steady state, the time derivative is zero. If the system is *closed* (i.e., there are no material inlet or outlet streams), the two summations are not included. The simplest case is the closed, steady-state system for which $\dot{Q} + \dot{W} = 0$

If the system is closed, but not at steady-state, then

$$\frac{dE_{sys}}{dt} = \dot{Q} + \dot{W}$$

Example: Energy balance on classroom full of students…

Consider a class with n people sitting in a room with the door closed. Assume the room is well insulated (= room is adiabatic, no heat crosses room boundaries). Calculate how fast the temperature in the room would rise if each person gave off heat at a rate of 72 kcal/hr (the basal metabolic rate).



Choose system carefully!

We want the T change in the air in the room ⇒ our system is going to be the air in the room, i.e., everything outside of the students, but within the room.

We write the energy balance for our closed system as follows:

$$\frac{dE_{room}}{dt} = \dot{Q} + \dot{W}$$

We will neglect kinetic energy and potential energy, since the room air does not experience any significant change in velocity due to the students' thinking, nor does the elevation of the room air change. So, we only will concern ourselves with internal energy.

Furthermore, the students do no significant amount of work on the air by sitting and thinking – work on the air would require a volume change or pressure change. So the energy balance becomes

$$\frac{dU_{room}}{dt} = \dot{Q}$$

Let's define $\dot{q}$ as the rate of heat transfer from one student to the surrounding air, +72 kcal/hr.

Then, $\dot{Q} = n\dot{q}$.

Also, we will express U as $m_{air}u$ where m_{air} is the mass of the air in the room, and u is the internal energy per unit mass of air.

The change in internal energy of the air that corresponds to a certain change in temperature at a constant volume is described by $du = C_v dT$, where C_v is the heat capacity of the air at constant volume (a constant).

Substituting this into our energy balance gives

$$\frac{d(m_{air}C_vT)}{dt} = m_{air}C_v\frac{dT}{dt} = n\dot{q}$$

$$\frac{dT}{dt} = \frac{n}{m_{air} C_v} \dot{q}$$

Let's take n = 30 and C_v = 1000 J/kg·K. To find m_{air}, we need to use the density of air at 300K, ρ_{air} = 1.18 kg/m^3. Let's take the volume of the room air to be 3m x 10m x 15m = 450m^3. So,

$$m_{air} = V\rho_{air} = \left(450m^3\right)\left(1.18\frac{kg}{m^3}\right) = 530kg$$

Let's convert the basal metabolic rate to SI energy units:

$$\dot{q} = \left(72\frac{kcal}{hr}\right)\left(\frac{1J}{0.239cal}\right)\left(\frac{1000cal}{kcal}\right) = 3.0\times10^5\,\frac{J}{hr}$$

Thus,

$$\frac{dT}{dt} = \frac{40}{\left(530kg\right)\left(1000\frac{J}{kgK}\right)}\left(3.0\times10^5\,\frac{J}{hr}\right) = 23\frac{K}{hr}\ \text{!!}$$

It will get pretty hot in an hour! Of course, if we leave the door open, or if we have air conditioning, some of that heat can be carried away from the room – i.e., it will leave the system.

If we wanted to find the temperature of the air in the room at any point in time, we'd have to integrate our energy balance to convert the rate of temperature change to a temperature.

We can rearrange this differential equation to take advantage of separation of variables…

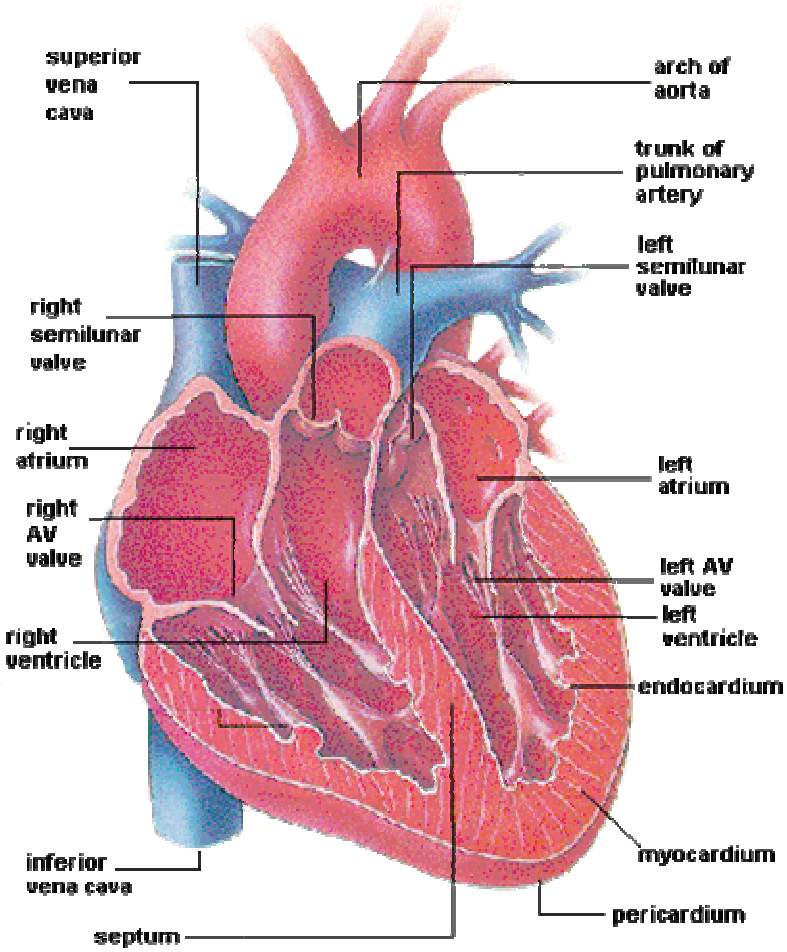
$$dT_{ait} = 23(K/hr)dt$$

And then integrate from some starting time (t=0) to some later time t…

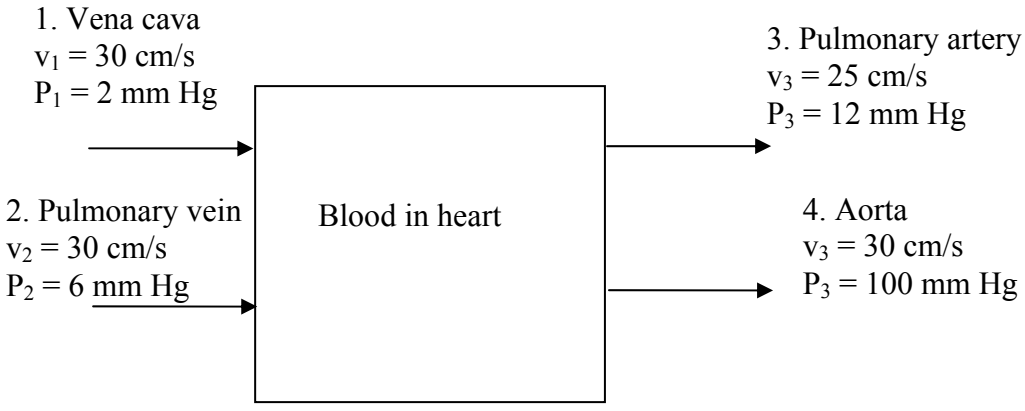
$$\int_{T_{air}(t=0)}^{T_{air}(t)} dT_{air} = 23(K/hr)\int_0^t dt$$

So, $T_{air} = T_{air}(0) + 23t$ where t has units of hours.

Example: Power expenditure of human heart (in horsepower)



= engineering representation of system



We will choose the blood in the heart as the system.

Energy Balance

$$\frac{dE_{sys}}{dt} = \sum_{j}^{all\ inlets} \dot{m}_{in,j}\left(u_{in,j} + \frac{1}{2}v_{in,j}^2 + gh_{in,j}\right) - \sum_{k}^{all\ outlets} \dot{m}_{out,k}\left(u_{out,k} + \frac{1}{2}v_{out,k}^2 + gh_{out,k}\right) + \dot{Q} + \dot{W}$$

First, let's assume steady-state operation – even though we know the heart is beating, we will be interested in the average work done by the heart over many heart beats. Then, the time derivative is zero.

$$0 = \dot{m}_1\left(u_1 + \frac{1}{2}v_1^2 + gh_1\right) + \dot{m}_2\left(u_2 + \frac{1}{2}v_2^2 + gh_2\right) - \dot{m}_3\left(u_3 + \frac{1}{2}v_3^2 + gh_3\right) - \dot{m}_4\left(u_4 + \frac{1}{2}v_4^2 + gh_4\right) + \dot{Q} + \dot{W}$$

Let's take this apart term by term.

$\dot{Q}$: The heart does not lose much heat as it pumps, so we will set $\dot{Q} = 0$.

$\dot{W}$: Mechanical work is done on the blood to squeeze it out of the heart. We'll call this non-flow work, $\dot{W}_{nonflow}$

There is also **flow work** – blood must push itself into the atria of the heart as it flows in and it must push blood ahead of it in the pulmonary artery and aorta out of the way as it pushes out of the heart.

Recall that work = force**x**distance = pressure**x**volume. Then, power must be force**x**velocity = pressure**x**volumetric flowrate.

So, we can express $\dot{W}_{flow}$, the rate at which flow work is done, or the flow power, as

$\dot{W}_{flow,i} = \dot{V}_i P_i = \frac{\dot{m}_i P_i}{\rho}$ for any stream i, where ρ is the density of the blood.

So the total rate at which work is done (power) is

$$\dot{W} = \dot{W}_{nonflow} + \dot{W}_{flow} = \dot{W}_{nonflow} + \frac{\dot{m}_1 P_1}{\rho} + \frac{\dot{m}_2 P_2}{\rho} - \frac{\dot{m}_3 P_3}{\rho} - \frac{\dot{m}_4 P_4}{\rho}$$

Note that we have used the fact that the entering streams (streams 1 and 2) do work on the system (blood in the heart, positive sign on associated flow work), while the system (blood in the heart, negative sign on associated flow work) does work on the surroundings at the outlet streams (3 and 4).

The energy balance is now

$$0 = \dot{m}_1\left(u_1 + \tfrac{1}{2}v_1^2 + gh_1\right) + \dot{m}_2\left(u_2 + \tfrac{1}{2}v_2^2 + gh_2\right) - \dot{m}_3\left(u_3 + \tfrac{1}{2}v_3^2 + gh_3\right)$$
$$- \dot{m}_4\left(u_4 + \tfrac{1}{2}v_4^2 + gh_4\right) + \frac{\dot{m}_1 P_1}{\rho} + \frac{\dot{m}_2 P_2}{\rho} - \frac{\dot{m}_3 P_3}{\rho} - \frac{\dot{m}_4 P_4}{\rho} + \dot{W}_{nonflow}$$

The mass flowrate in all the streams is equal. So $\dot{m}_1 = \dot{m}_2 = \dot{m}_3 = \dot{m}_4 = \dot{m}$

And the energy balance simplifies to

$$0 = \dot{m}\left[\begin{array}{l}\left(u_1 + u_2 - u_3 - u_4\right) + \left(\tfrac{1}{2}v_1^2 + \tfrac{1}{2}v_2^2 - \tfrac{1}{2}v_3^2 - \tfrac{1}{2}v_4^2\right) + \\ \left(gh_1 + gh_2 - gh_3 - gh_4\right) + \dfrac{1}{\rho}\left(P_1 + P_2 - P_3 - P_4\right)\end{array}\right] + \dot{W}_{nonflow}$$

The temperature of the blood is pretty much the same as it enters and leaves the heart. Therefore, the internal energy (u) is not changed, so $u_1=u_2=u_3=u_4$. So, the first term is the square brackets is zero.

Likewise, the elevation difference between the entrances and exits is not significant, so $h_1=h_2=h_3=h_4$, and the term with the h's becomes zero.

So, now we are left with

$$0 = \dot{m}\left[\frac{1}{2}\left(v_1^2 + v_2^2 - v_3^2 - v_4^2\right) + \frac{1}{\rho}\left(P_1 + P_2 - P_3 - P_4\right)\right] + \dot{W}_{nonflow}$$

Now, $\dot{m} = \dot{V}\rho$, where $\dot{V}$ is the volumetric flowrate, 5 L/min (at rest).
The density ρ = 1.1 kg/m^3.

Now, let's work on some units.

$$\left(5\frac{L}{\min}\right)\left(\frac{1000cm^3}{L}\right)\left(\frac{1m}{100cm}\right)^3\left(\frac{1\min}{60s}\right)=8.3\times10^{-5}\,\frac{m^3}{s}$$

Thus, $\dot{m}=\left(8.3\times10^{-5}\ m^3/s\right)\left(\frac{1100kg}{m^3}\right)=0.092kg/s$

Our pressures, converted into Pa (using 1 mm Hg = 133 Pa) are

P_1 = 266 Pa P_2 = 800 Pa P_3 = 1600 Pa P_4 = 13300 Pa

Plug these into the energy balance and solve for $\dot{W}_{nonflow}$

$$\dot{W}_{nonflow}=-\dot{m}\left[\frac{1}{2}\left(v_1^2+v_2^2-v_3^2-v_4^2\right)+\frac{1}{\rho}\left(P_1+P_2-P_3-P_4\right)\right]$$

$$\dot{W}_{nonflow}=-\left(0.092kg/s\right)\left[\begin{array}{l}\left(0.3m/s\right)^2+\left(0.3m/s\right)^2-\left(0.25m/s\right)^2-\left(0.3m/s\right)^2\\+\dfrac{1}{1100kg/m^3}\left(266Pa+800Pa-1600Pa-13300Pa\right)\end{array}\right]$$

$$\dot{W}_{nonflow}=1.2W$$

Convert from Watts to hp:

$$1.2W\left(\frac{0.00134hp}{1W}\right)=0.0016hp$$

Cellular Energy Production and Storage

Considering energy as the capacity to do work, we keep track of the energy at the cellular level in terms of the **Gibbs energy** or **free energy**, G

$$G = U + PV - TS$$

where U is internal energy, P is pressure, V is volume, T is absolute temperature, and S is the **entropy**. U represents the thermal energy content related to the temperature of the species. The product PV represents the capacity of the species to do pressure-volume work or flow work. Entropy represents the state of disorder in the system. (Systems tend to change in a way that either increases entropy or leaves it unchanged. This is the 2nd Law of Thermodynamics.)

Again, these are the most common forms of energy that a chemical species can have at constant temperature and pressure. There are other forms of energy – energy can be contained in species concentration differences (as we'll see later) and, for charged species, species present with electrical potential differences (as we'll also see later). G accounts for the total energy content of the molecules making up our system.

In the cell, and for reactions in general, energy is liberated or consumed by chemical reactions. We consider an arbitrary reversible chemical reaction

$aA + bB \Leftrightarrow cC + dD$, for which we define an equilibrium constant

$$K = \prod_{i=1}^{n_{species}} [i]^{\nu_i}$$

In this expression, the capital Π represents a product, [i] is the concentration of species *i* in mol/L, ν_i is the stoichiometric coefficient (see below), and $n_{species}$ is the total number of different chemical species that take part in the reaction.

Stoichiometric coefficients are negative for reactants and positive for products of reactions. For the reaction above

$$K = \prod_{i=1}^{n_{species}} [i]^{\nu_i} = [A]^{-a}[B]^{-b}[C]^{c}[D]^{d} = \frac{[C]^{c}[D]^{d}}{[A]^{a}[B]^{b}}$$

This is related to the change in Gibbs Energy that happens as a result of the reaction, ΔG_{rxn}, as

$$\Delta G^{o}_{rxn}' = -RT \ln K$$

ΔG^{o}_{rxn}' is the free energy change as "biological standard state conditions", R is the *gas constant* (8.314 J/(mol•K)), and T is the absolute temperature.

The superscript o and prime marks indicate the biological standard state conditions, which are T = 298K, , and all concentrations are 1 M except for protons, H^+, which are constant at pH = 7.

We noted earlier in the course that ATP is the biological "currency" for energy. How does ATP store or liberate energy? It releases energy via the *hydrolysis* reaction

$ATP + H_2O \rightarrow ADP + P_i + 7.3$ kcal/mole ATP at std. state conditions.

P_i represents *inorganic phosphate* HPO_4^{2-}.

Since energy is liberated, we say $\Delta G^o_{rxn}' = -7.3$ kcal/moleATP

The reverse reaction can happen as well:

$ADP + P_i + 7.3$ kcal/moleATP $\rightarrow ATP + H_2O$

$\Delta G^o_{rxn}' = +7.3$ kcal/moleATP

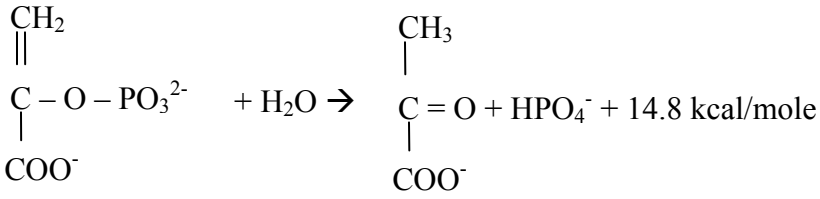
The sign of $\Delta G^o_{rxn}'$ (or ΔG_{rxn} if not at standard state conditions) indicates whether or not a reaction will happen spontaneously at biological standard state conditions:

If $\Delta G^o_{rxn}' < 0$: spontaneous
If $\Delta G^o_{rxn}' = 0$: system is at equilibrium
If $\Delta G^o_{rxn}' > 0$: reaction will not happen spontaneously

Cells have two ways of producing ATP when nutrients are metabolized…

1) Substrate-Level ATP Formation. Chemical energy is stored in ATP by coupling ATP production reaction directly with the reactions that break down nutrients.

Considering glucose as the nutrient, one of the last steps in the process of glycolysis (glucose breakdown) is



phosphoenol pyruvate (PEP) | pyruvate (Pyr) | inorganic phosphate (P_i)

This reaction liberates energy. It is directly coupled to the reaction

$ADP + P_i + 7.3$ kcal/moleATP $\rightarrow ATP + H_2O$

Adding these two reactions together we have the net chemical reaction:

$PEP + ADP \rightarrow Pyr + ATP + 7.5$ kcal/mole

$\Delta G^o_{rxn}' = -7.5$ kcal/mole

Although the ATP production by itself is non-spontaneous, by coupling it with PEP hydrolysis, the net reaction is spontaneous. Note that 7.3 kcal of energy were stored in ATP (per mole of PEP). This corresponds to an efficiency of 7.3/14.8 = 49%. Only 49% of the energy is stored. The rest is given off as heat. This may not sound so efficient, but compare it to a typical coal-burning electrical generation plant, which has an efficiency of approximately 30%. Living systems are more efficient. It turns out that the laws of thermodynamics do not allow for 100% efficiency.

Notice that glycolysis happens in the absence of oxygen (or other so-called "terminal electron acceptors"). This is the process that anaerobic organisms use. It is also used in our own bodies sometimes, e.g. muscles doing very hard work. PEP has three carbons and yielded 1 ATP. Since glucose has six carbons, it is converted to two PEP molecules and yields 2 ATP:

$C_6H_{12}O_6 + 2\ P_i + 2\ ADP \rightarrow 2\ C_3H_6O_3 + 2\ ATP + 2\ H_2O + 32.4$ kcal/mole
(lactic acid)

$\Delta G^o_{rxn} = -32.4$ kcal/mole

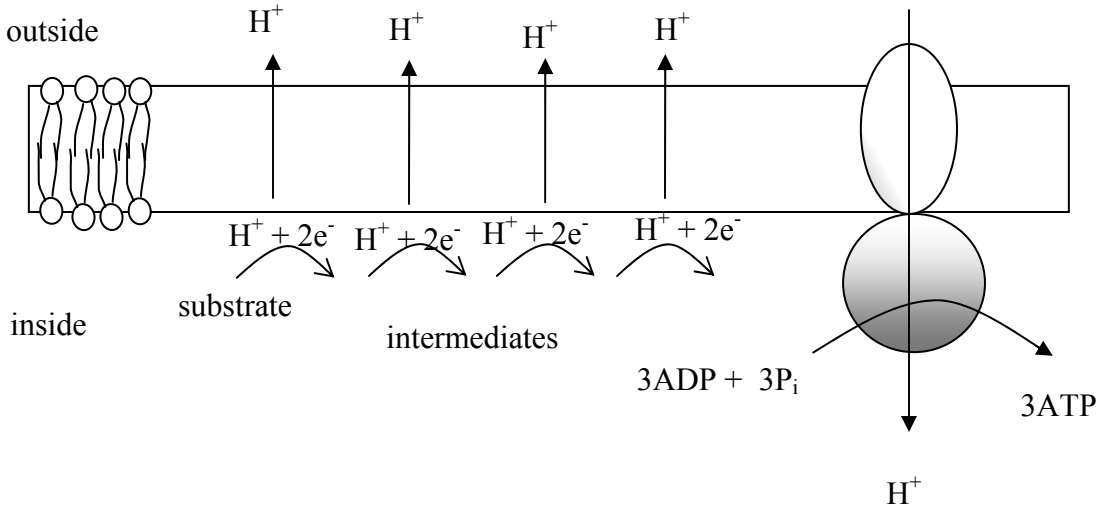
Since two ATP molecules are produced, 2x7.3 kcal/mole = 14.6 kcal/mole of energy is stored.

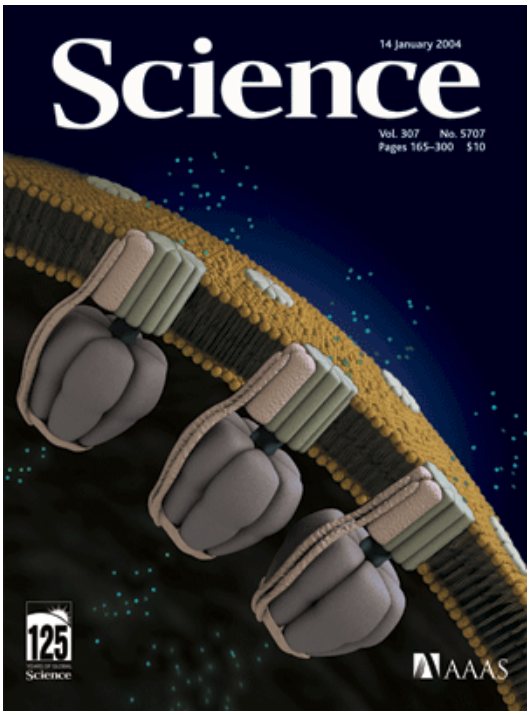
The second way to produce ATP stores far more energy per mole of glucose….

2. Oxidative-Level ATP Formation: Respiration

Aerobic respiration employs oxygen as the oxidizing agent (removes electrons from other reactants). An organic substrate is oxidized in a series of steps, involving the transfer of electrons. At each step protons H^+ are pumped across the membrane. This sets up a concentration gradient across the membrane (with a higher H^+ concentration outside the membrane than inside). This concentration gradient stores energy. That stored energy is captured by ATP bonds by allowing them to flow back across the membrane (relieving the concentration gradient, therefore releasing stored energy) via H^+ transport proteins in the membrane called ATPases.

The important feature of this is that H^+ cannot freely diffuse across the nonpolar lipid bilayer. Its only pathway back through the membrane is to be transported via the ATPases. This provides the direct coupling between proton transport and ATP production.





The enzyme adenosine triphosphate (ATP) synthase spanning a bacterial cell membrane. A promising new diarylquinoline drug interacts with the transmembrane portion of this enzyme in the bacteria that cause tuberculosis, killing the microbe by shutting down ATP synthesis. See page 223. [Image: W. Junge and MediTech Media]

This occurs in the mitochondria. The transport of protons across the membrane involves the action of membrane proteins. The energy content in the concentration gradient between the outside (C_1) and the inside (C_2) is

$$\Delta G^o = RT \ln \frac{C_1}{C_2} + ZF\Delta\psi$$

Z is the valence (charge) on the ion. If the species is not an ion, then Z = 0. F is the Faraday constant, which is the charge on one mole of electrons (9.65×10^4 C/mole). $\Delta\psi$ is the difference in electrical potential between the outside and inside ($\psi_1 - \psi_2$). A typical potential difference across a mitochondrial membrane, for example, would be -200 mV.

There are several molecules that act as electron carriers:

Reduced substrate + FAD ↔ oxidized substrate + $FADH_2$ + H^+

or	or
NAD^+	NADH
or	or
$NADP^+$	NADPH

(NAD = nicotinamide adenine dinucleotide.) Two H are removed from the substrate as $2H^+ + 2e^-$, giving $2e^- + H^+$ to NAD^+ or $NADP^+$ as carriers. As these carriers accept and handoff electrons (ultimately donating them to O_2), one H^+ is pumped outside membrane.

Each mole of NADH or HADPH formed yields 3 moles ATP. Each mole of $FADH_2$ formed yields ~ 1 mole ATP. The overall reaction for glucose oxidation via aerobic respiration is

$C_6H_{12}O_6 + 36\ P_i + 36\ ADP + 6O_2 \rightarrow 6CO_2 + 6H_2O + 36ATP + 263$ kcal/mole

Compare this to the 2 moles of ATP created by glycolysis.

Thoughts on the trans-membrane potential

Where does the trans-membrane potential $\Delta\psi$ come from?

We discussed how this potential affects the energy content of the proton gradient. Other ions are pumped to maintain this potential gradient – the sodium-potassium pump (a protein embedded in the membrane) is the key player.

Because of the action of this pump, there is a gradient (difference across space) of Na^+ and K^+ ion concentrations across the membrane.

$$\psi_1 - \psi_2 = \frac{RT}{ZF} \ln \frac{C_2}{C_1}$$ This is called the Nernst potential.

Molecular Biology of the Cell ➔**IV. Internal Organization of the Cell** ➔11. Membrane Transport of Small Molecules and the Electrical Properties of Membranes ➔Carrier Proteins and Active Membrane Transport

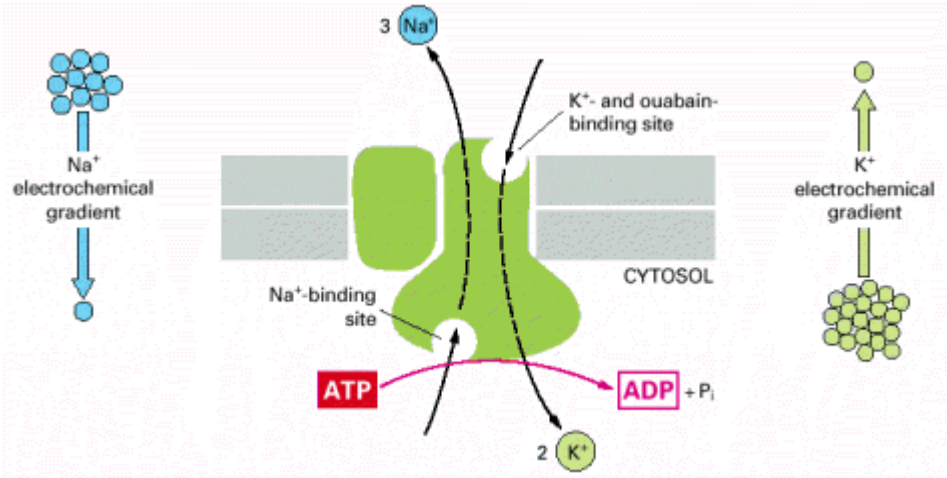


Figure 11-13. The Na^+-K^+pump. This carrier protein actively pumps Na^+ out of and K^+ into a cell against their electrochemical gradients. For every molecule of ATP hydrolyzed inside the cell, three Na^+ are pumped out and two K^+ are pumped in. The specific inhibitor ouabain and K^+ compete for the same site on the extracellular side of the pump.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.2014

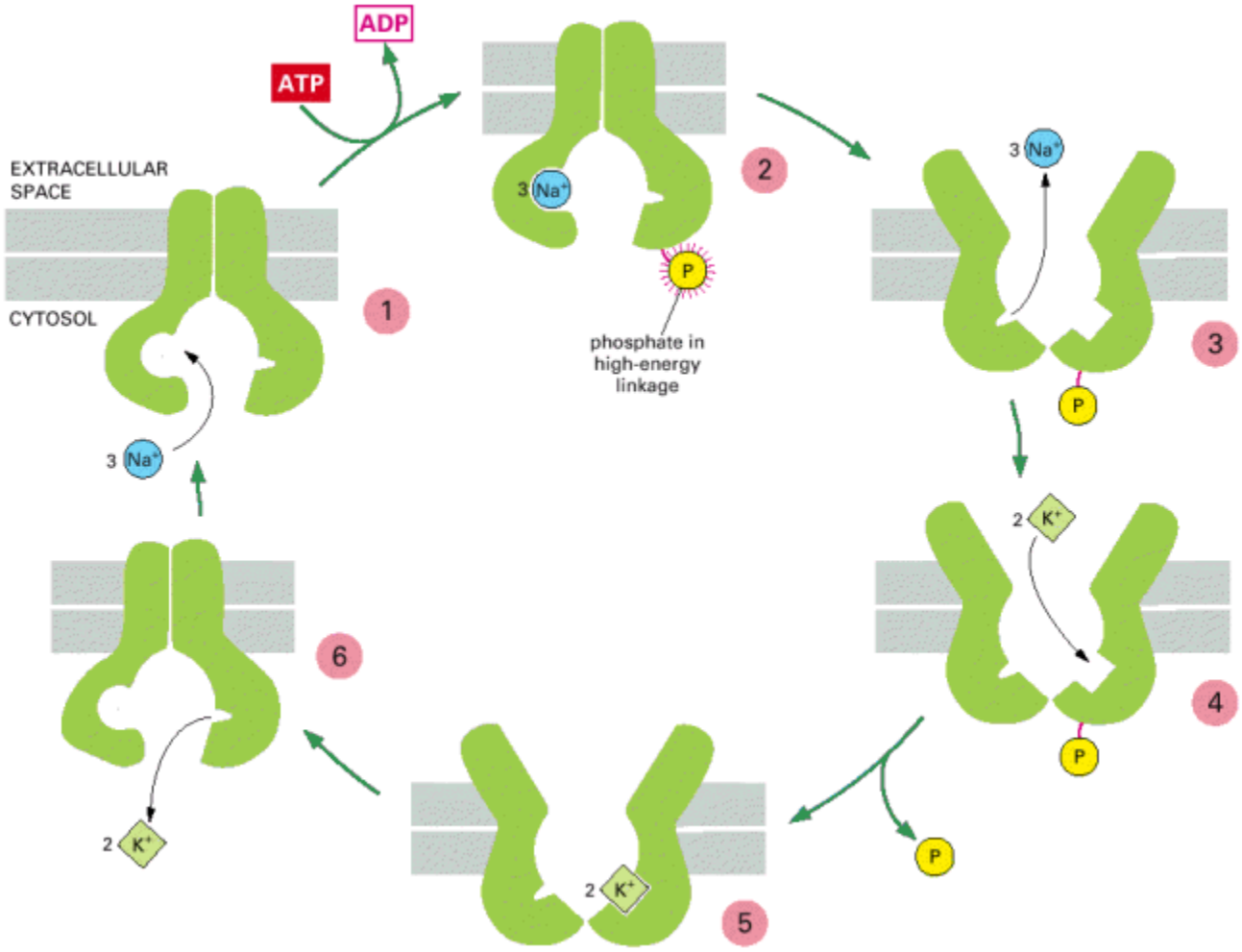


Figure 11-14. A model of the pumping cycle of the Na^+ -K^+ pump. (1) The binding of Na^+ and (2) the subsequent phosphorylation by ATP of the cytoplasmic face of the pump induce the protein to undergo a conformational change that (3) transfers the Na^+ across the membrane and releases it on the outside. (4) Then, the binding of K^+ on the extracellular surface and (5) the subsequent dephosphorylation return the protein to its original conformation, which (6) transfers the K^+ across the membrane and releases it into the cytosol. These changes in conformation are analogous to the A ⇔B transitions shown in Figure 11-6, except that here the Na^+ -dependent phosphorylation and the K^+ -dependent dephosphorylation of the protein cause the conformational transitions to occur in an orderly manner, enabling the protein to do useful work. Although for simplicity only one Na^+ - and one K^+ -binding site are shown, in the real pump there are thought to be three Na^+ - and two K^+ -binding sites. Moreover, although the pump is shown as alternating between two conformational states only, there is evidence that it goes through a more complex series of conformational changes during the pumping cycle.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.2015

These pumps are important because of the low permeability of ions in membranes:

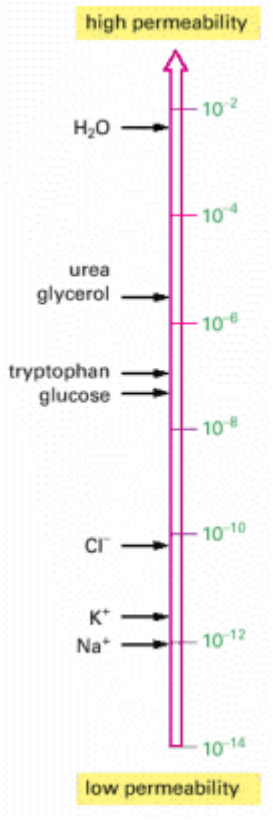


Figure 11-2. Permeability coefficients for the passage of various molecules through synthetic lipid bilayers

Notice that the action of ion pumps such as this can be overwhelmed by large salt concentration gradients, if the free energy contained in that gradient is larger than the free energy of ATP hydrolysis. Pumps such as this are often harnessed to transport other solutes, such as glucose, into a cell. A glucose pump acts in parallel with the Na-K pump. This is called "co-transport" as the transport of glucose is directly coupled to sodium and potassium transport.

Ion concentration gradients are vital to the life of cells. Certain bacteria have evolved mechanisms to compete with other organisms for nutrients by releasing *ionophores* into their environments. Ionophores are small molecules that bind to ions and carry them by passive diffusion across a cell membrane, thereby relaxing the concentration gradients that produced the trans-membrane potential. This can kill other cells.

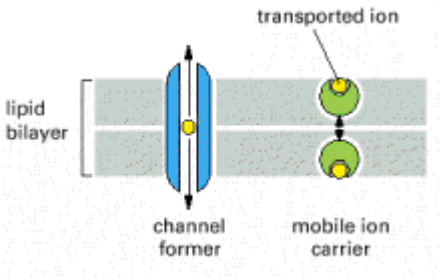


Figure 11-5. Ionophores: a channel-former and a mobile ion carrier. In both cases, net ion flow occurs only down an electrochemical gradient.

Another interesting example of an ion pump is bacteriorhodopsin, a H^+ pump in the membrane of the bacterium *halobacterium halobium*. It harvests solar energy and pumps H^+ across its membrane as a way to produce ATP.

The general working principle of all H^+ pumps is thought to be the following:

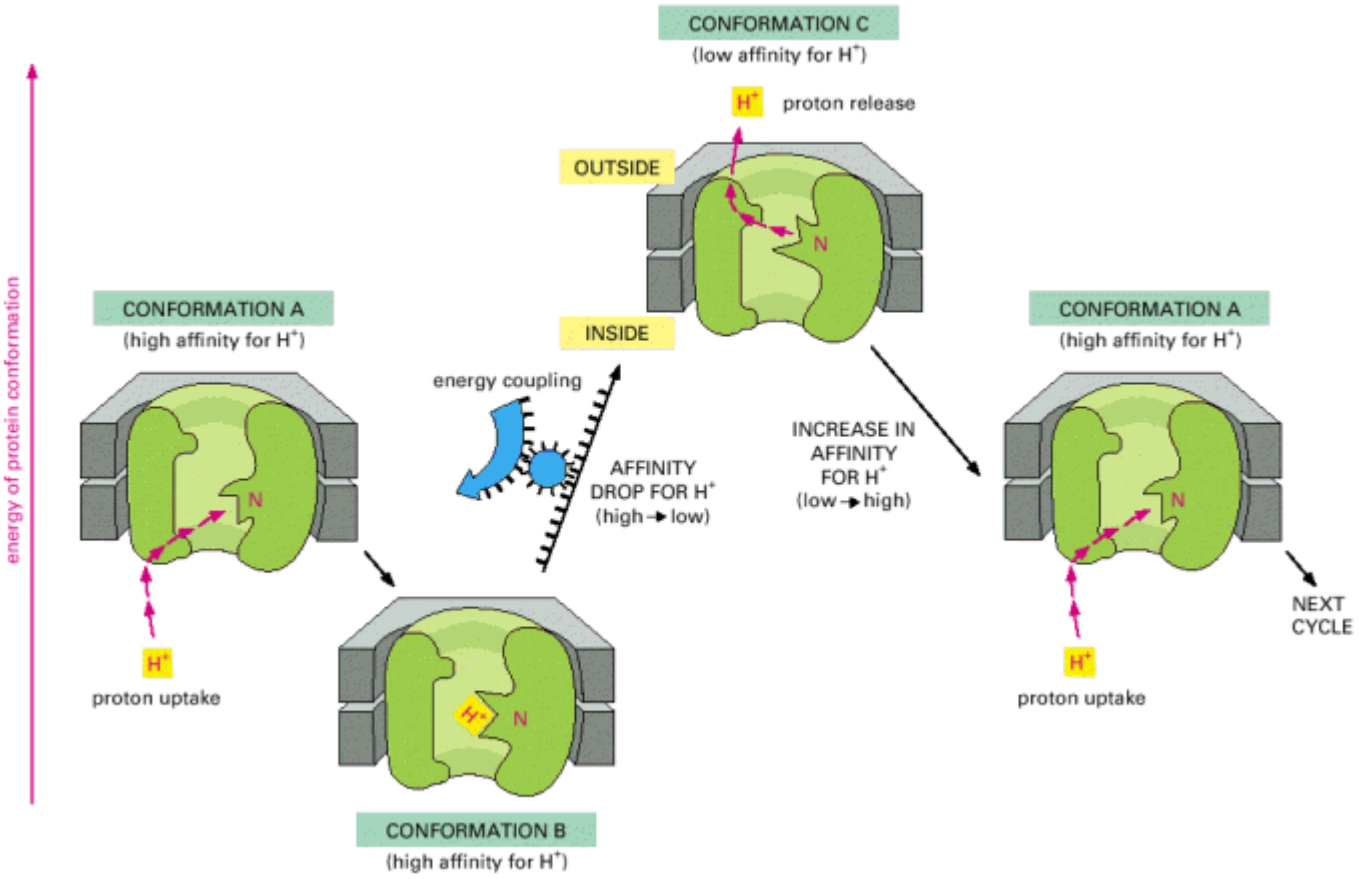


Figure 14-31. A general model for H^+ pumping. This model for H^+ pumping by a transmembrane protein is based on mechanisms that are thought to be used by both cytochrome oxidase and the light-driven procaryotic proton pump, bacteriorhodopsin. The protein is driven through a cycle of three conformations: A, B, and C. As indicated by their vertical spacing, these protein conformations have different energies. In conformation A, the protein has a high affinity for H^+, causing it to pick up a H^+ on the inside of the membrane. In conformation C, the protein has a low affinity for H^+, causing it to release a H^+ on the outside of the membrane. The transition from conformation B to conformation C that releases the H^+ is energetically unfavorable, and it occurs only because it is driven by being allosterically coupled to an energetically favorable reaction occurring elsewhere on the protein *(blue arrow)*. The other two conformational changes, A $\rightarrow$B and C $\rightarrow$A, lead to states of lower energy, and they proceed spontaneously. Because the overall cycle A $\rightarrow$B $\rightarrow$C $\rightarrow$A $\rightarrow$B $\rightarrow$C releases free energy, H^+ is pumped from the inside (the matrix in mitochondria) to the outside (the intermembrane space in mitochondria). For cytochrome oxidase, the energy required for the transition B $\rightarrow$C is provided by electron transport, whereas for bacteriorhodopsin, this energy is provided by light (see Figure 10-37). For yet other proton pumps, the energy is derived from ATP hydrolysis.