

## Chapter 2

# Energy in Biology—Demand and Use

*A coupled energy source is a prerequisite of sustained dynamics in thermodynamically open systems.*

**Abstract** From the point of view of energy management in biological systems, a fundamental requirement is to ensure spontaneity. **Process spontaneity** is necessary since in a thermodynamically open system—such as the living cell—only spontaneous reactions can be catalyzed by enzymes. Note that enzymes do not, by themselves, contribute additional energy. Spontaneity of biological processes may be expressed by the following correlation:

$\Delta G = \Delta H - T\Delta S$  where  $\Delta G$  means the change of free energy,  $\Delta H$ —change of enthalpy,  $\Delta S$ —change of entropy,  $T$ —temperature. Desirable processes which do not occur on their own must be coupled to other highly spontaneous mechanisms serving as energy sources. In biology, the fundamental sources of energy involve synthesis of water and photosynthesis. Since both processes are rather complex and cannot be exploited directly, they are used to synthesize ATP which acts as an energy carrier. Approaching biology from the point of view of elementary physics and chemistry reveals important mechanisms and enhances our understanding of various phenomena.

**Keywords** Spontaneity · Source of energy · Entropy-driven processes · Enthalpy-driven processes · Direct and indirect use of energy

### 2.1 General Principles of Thermodynamics

Physical and chemical processes may only occur spontaneously if they generate energy, or non-spontaneously if they consume it. However, **all processes occurring in a cell must have a spontaneous character because only these processes may be catalyzed by enzymes. Enzymes merely accelerate reactions; they do not provide energy.**

In the inanimate world non-spontaneous (endergonic) reactions, including most synthesis processes, consume thermal energy. In a cell, chemical energy can be derived from exergonic (energy-producing) processes. An important source of energy in living organisms is sunlight—the driving force in photosynthesis.

Due to high susceptibility of living organisms to heat damage, thermal energy is inconvenient.

Catalysis of inherently non-spontaneous processes becomes possible only when they are thermodynamically coupled to other, spontaneous processes in such a way that the resulting complex process dissipates energy.

Examples of inherently non-spontaneous processes which acquire spontaneity by relying on exergonic reactions include:

1. synthesis;
2. structural rearrangement of proteins (e.g. in muscle contraction).

Processes related to degradation are usually spontaneous by nature and most of their stages do not require additional exergonic processes as a source of energy.

In physical terms, spontaneity is subject to Gibb's definition, where  $\Delta G$  (change in free energy) corresponds to  $\Delta H$  (change in enthalpy) and  $\Delta S$  (change in entropy), according to the following equation

$$\Delta G = \Delta H - T \Delta S$$

T temperature in °K

The change in enthalpy associated with a chemical process may be calculated as a net difference in the sum of molecular binding energies prior to and following the reaction.

Entropy is a measure of the likelihood that a physical system will enter a given state. Since chaotic distribution of elements is considered the most probable, physical systems exhibit a general tendency to gravitate towards chaos. Any form of ordering is thermodynamically disadvantageous.

According to the presented formula, energy loss and the corresponding increase in entropy ( $\Delta H$  and  $\Delta S$ ) are the hallmarks of a spontaneous process.

For specific processes, the change in free energy may be determined without referring to the presented mechanism and instead relying on reaction dynamics; specifically—on the ratio of product and substrate concentrations:

$$\Delta G = \Delta G^0 + RT * \ln\{([C] * [D])/([A] * [B])\}$$

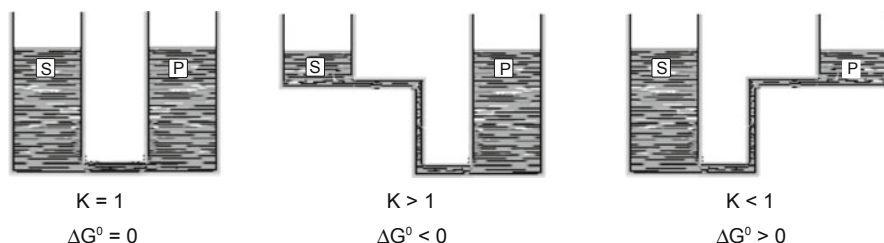
R Gas constant

T Absolute temperature

The  $\Delta G^0$  parameter is a measure of spontaneity. It depends on the properties of process elements and is therefore a function of the state of equilibrium. It may be derived from the ratio of product and substrate concentrations once a state of equilibrium has been reached.

If the process is in equilibrium,  $\Delta G$  becomes equal to 0 and thus, according to the formula,  $\Delta G^0$  is given as:

$$\Delta G^0 = -RT\{\ln(K)\}$$



**Fig. 2.1** The relationship between  $\Delta G^0$  and the equilibrium constant  $K$  in a model system

**Table 2.1** An integral part of Fig. 2.1

$K$	$\Delta G^0$ (kJ/mol)—temp. 25°C
$10^4$	− 22.8
$10^1$	− 5.7
$10^0$	0.0
$10^{-1}$	5.7
$10^{-4}$	22.8

where:

$K$  Equilibrium constant (Fig. 2.1 and Table 2.1).

The figure depicts three types of communicating vessels in which the liquid has reached a state of equilibrium corresponding to various ratios of “products” (right vessel) and “substrates” (left vessel). The table (in Fig. 2.1) presents some numerical examples of the relation between  $K$  and  $\Delta G^0$ .

The true measure of spontaneity is therefore not  $\Delta G^0$  but  $\Delta G$ , which expresses the capability to perform work for a reaction which is not in a state of equilibrium. In contrast,  $\Delta G^0$  merely indicates the reactivity of substrates as a consequence of their physical and chemical nature.

**A reaction which is in a state of equilibrium cannot perform useful work.** Energy can only be extracted from processes which have not yet reached equilibrium.

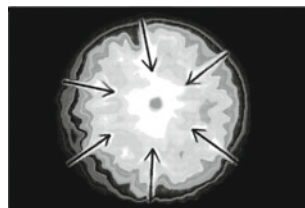
Maintaining a steady state of nonequilibrium is possible only in a thermodynamically open environment where energy and reaction components may flow through the system. This, in turn, calls for an external source of energy as well as a means of automatic control (see Fig. 2.1).

Any spontaneous reaction can be treated as a source of energy as long as its spontaneity is sufficient for the thermodynamically disadvantageous reaction to occur and provided that both processes are thermodynamically coupled. In practice, synthesis reactions may only draw energy from highly spontaneous processes due to the need to form covalent bonds.

The chemical reactions which power biological processes are characterized by varying degrees of efficiency. In general, they tend to be on the lower end of the efficiency spectrum, compared to energy sources which drive matter transformation processes in our universe.

In search for a common criterion to describe the efficiency of various energy sources, we can refer to the net loss of mass associated with a release of energy,

**Fig. 2.2** Pictorial representation of the efficiency of selected energy sources, including stellar collapse, nuclear reactions and chemical processes



$$\frac{\Delta M}{M} \leq 40\%$$



$$\frac{\Delta M}{M} = 0,8\%$$



$$\frac{\Delta M}{M} = 10^{-7} \%$$

according to Einstein's formula:

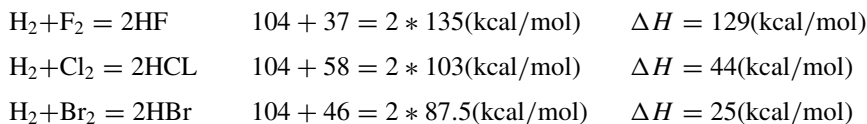
$$E = mc^2$$

The  $\Delta M/M$  coefficient (relative loss of mass, given e.g. in %) allows us to compare the efficiency of energy sources. The most efficient processes are those involved in the gravitational collapse of stars. Their efficiency may reach 40 %, which means that 40 % of the stationary mass of the system is converted into energy. In comparison, nuclear reactions have an approximate efficiency of 0.8 %.

The efficiency of chemical energy sources available to biological systems is incomparably lower and amounts to approximately  $10^{-7} \%$  (Fig. 2.2).

Among chemical reactions, the most potent sources of energy are found in oxidation processes, commonly exploited by biological systems. Oxidation tends

to result in the largest net release of energy per unit of mass, although the efficiency of specific types of oxidation varies. For instance, the efficiency of hydrogen-halogen reactions (expressed in kcal/mol), calculated as the balance of binding energies, is as follows:



Under similar conditions the reaction between hydrogen and oxygen yields an average of 56.7 kcal/mol. It should come as no surprise that—given unrestricted access to atmospheric oxygen and to hydrogen atoms derived from hydrocarbons—the combustion of hydrogen (i.e. the synthesis of water;  $\text{H}_2 + 1/2\text{O}_2 = \text{H}_2\text{O}$ ) has become a principal source of energy in nature, next to photosynthesis, which exploits the energy of solar radiation.

## 2.2 Biological Energy Sources—Synthesis of Water

Hydrogen is combined with oxygen on inner mitochondrial membrane, while the conversion of hydrogen carriers (lipids, sugars and proteins) into forms appropriate for water synthesis occurs in the cytoplasm and the mitochondrial matrix. Major energy-generating metabolic pathways include glycolysis,  $\beta$ -oxidation and degradation of aminoacids.

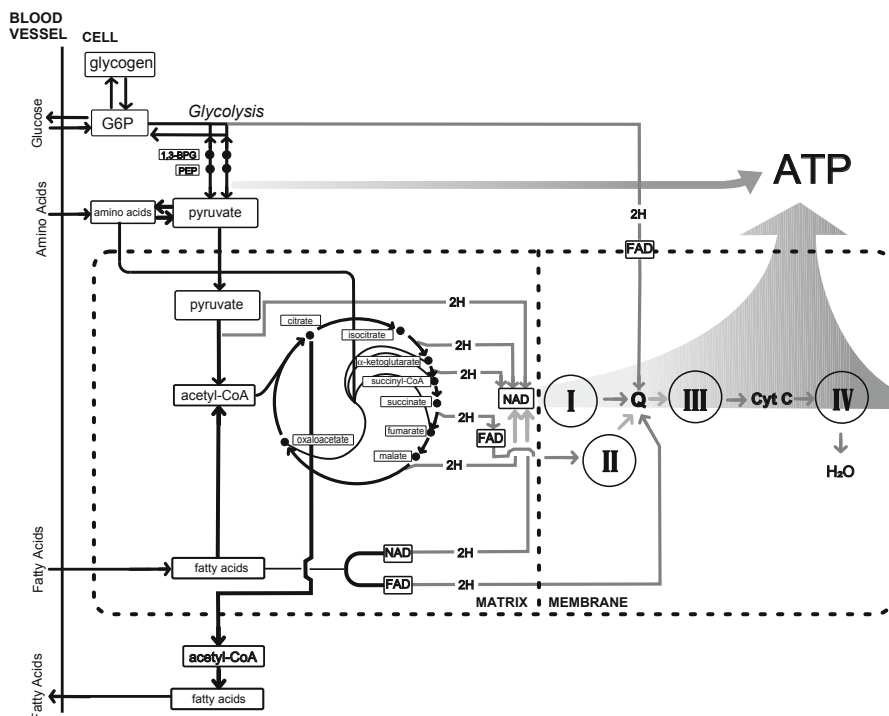
The basic process associated with the release of hydrogen and its subsequent oxidation (called the Krebs cycle) is carried by processes which transfer electrons onto oxygen atoms (Fig. 2.3).

Oxidation occurs in stages, enabling optimal use of the released energy. An important byproduct of water synthesis is the universal energy carrier known as ATP (synthesized separately).

As water synthesis is a highly spontaneous process, it can be exploited to cover the energy debt incurred by endergonic synthesis of ATP, as long as both processes are thermodynamically coupled, enabling spontaneous catalysis of anhydride bonds in ATP.

Water synthesis is a universal source of energy in heterotrophic systems. In contrast, autotrophic organisms rely on the energy of light which is exploited in the process of photosynthesis. Both processes yield ATP along with reduced pyridine nucleotides.

As mentioned above, linking the spontaneous process of water synthesis with non-spontaneous creation of anhydride bonds in ATP is a prerequisite for achieving a thermodynamically unified system. This is done by introducing a hydrogen ion gradient which affects both processes, although in different ways:



**Fig. 2.3** A schematic depiction of energy conversion processes in living cells

A. The respiratory chain—by carrier proteins which transfer hydrogen atoms and electrons, and must therefore be able to dissociate or attach hydrogen ions, enabling their transduction across the mitochondrial membrane and giving rise to an ion gradient;

B. ATP synthesis—by exploiting the energy released in the spontaneous discharge of the hydrogen ion gradient.

The hydrogen atoms used to synthesize water in the respiratory chain are derived from nutrients and can directly participate in the chain by way of the Krebs cycle (TCA). Nutrients include sugars (mostly glucose), amino acids and lipids, which reach hepatocytes following absorption from the small intestine. The energy they carry is exploited in sequestration processes (mainly fatty acid synthesis and lipogenesis) (Fig. 2.4).

During periods of starvation, hydrogen carriers can be retrieved from storage: glucose comes from glycogen while fatty acids are extracted from adipose tissue.

Under conditions of high physical exertion or inadequate food intake, the extraction of lipids increases and most of the released energy is used to resynthesize glucose from amino acids (Fig. 2.5).

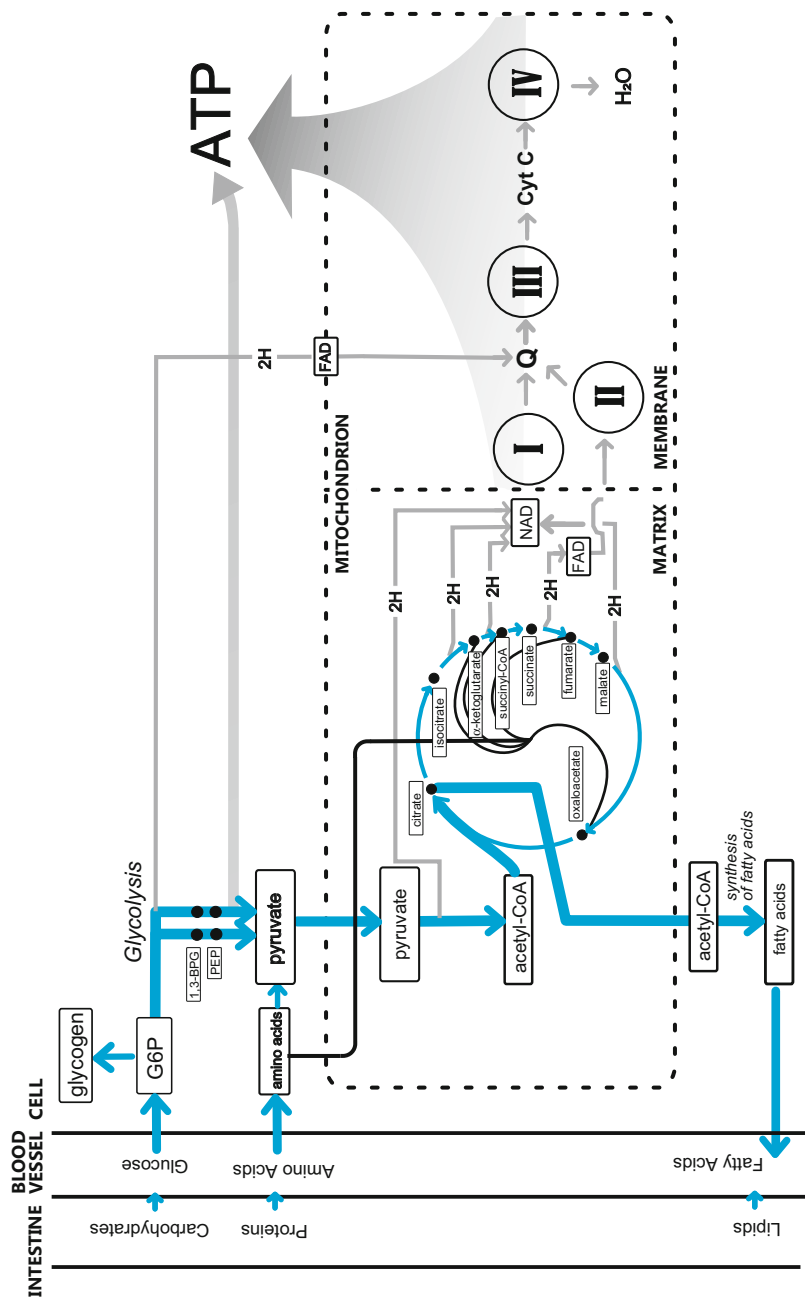
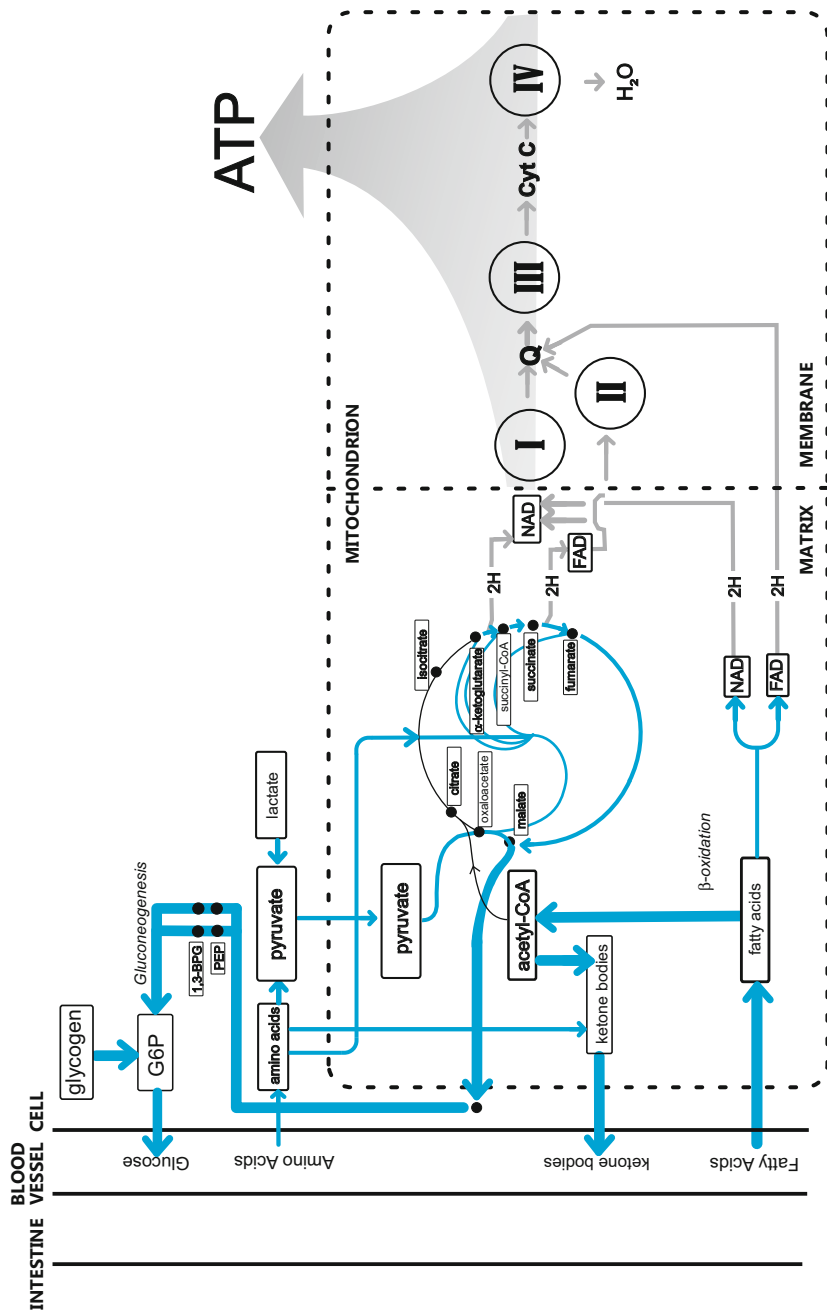


Fig. 2.4 Directed energy transfer occurring in a living cell when nutrients (hydrogen carriers) are freely available. (Fed state)



**Fig. 2.5** Directed energy transfer occurring in a living cell whenever stored resources must be expended to maintain appropriate level of glucose in blood. (Fasted state)



Dehydrogenation of substrates is catalyzed by pyridine- and flavin-linked dehydrogenases. Respiratory chain proteins integrated in the mitochondrial membrane transport hydrogen atoms and electrons onto oxygen ( $O_2$ ) molecules across the potential gradient, via complexes I, III and IV—namely NADH dehydrogenase (complex I) and coenzyme Q; cytochrome  $bc_1$  complex reductase (complex III); cytochrome c and finally cytochrome c oxidase (complex IV). Hydrogen atoms released by dehydrogenation of succinate are introduced to the respiratory chain via complex II (succinate dehydrogenase) and coenzyme Q, skipping complex I (Figs. 2.3, 2.4 and 2.5).

Complexes I, III and IV are integrated in the membrane. In contrast, coenzyme Q (mediating capture of electrons by complex III) and cytochrome c are mobile, although the former is located within the membrane while the latter is found in the intermembrane space. The double-electron NAD dehydrogenase initiator changes to a conduit for univalent electron carriers (iron-sulfur proteins, cytochromes) and a four-electron channel in the last phase of oxygen reduction.

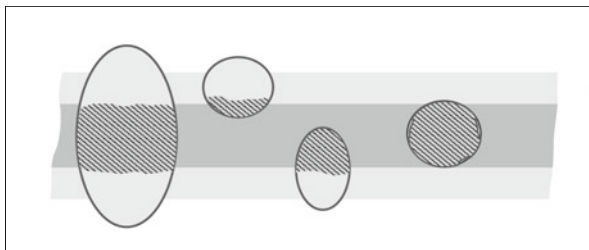
Water synthesis ultimately results in phosphorylation, which (in this case) converts ADP to ATP. Since an anhydride bond must be created, there is a need of energy. ATP synthesis must therefore be coupled to the synthesis of water if spontaneity is to be maintained. The link is effected by introducing a hydrogen ion gradient between the mitochondrial matrix and the intermembrane space, which, requires ejecting of hydrogen ions into the inter-membrane space in the course of electron transportation for synthesis of water. The structures responsible for transporting ions must do so in a predetermined direction and maintain functional specificity. This task, like many others, is performed by dedicated proteins.

Ion transport is usually effected by a protein-specific change in pK of selected proton-binding groups, similar to the Bohr effect which occurs in hemoglobin. Transduction of hydrogen ions from the mitochondrial matrix to the intermembrane space works against the emerging ion gradient. Thus, protein ion channels must also fulfill the role of a sluice gate. Electron carriers participating in the highly spontaneous process of water synthesis in the membrane also act as transverse carriers of hydrogen ions. Thus owing to the mutual dependence of both ways of transport, the non-spontaneous formation of an ion gradient may draw energy from the oxidation process.

A suitable direction of transduction is ensured by maintaining proper alignment and integration of hydrogen and electron carrier proteins in the membrane so that protons are captured and released on specific sides (either within the mitochondrial matrix or in the intermembrane space). The structure of membrane proteins and their localization in the membrane is well suited to this task. Their apolar aminoacids and their shape enforce the correct alignment and integration of protein molecules in the membrane (Fig. 2.6).

The ability to transport hydrogen ions is a property of proteins forming complexes I and IV. In complex III a similar function is most likely performed by coenzyme Q. Its specific structure and integration with the membrane, as well as its interaction with proteins ensures unidirectional ion transfer. Coenzyme Q is an apolar, non-protein mobile molecule, consisting of a quinone derivative ring and a polyisoprenyl chain

**Fig. 2.6** Various forms of protein-membrane integration (gray zones indicate hydrophobic surfaces)



which, in humans, contains 10 elements. The carbonyl groups of the quinone ring may undergo reduction by a hydrogen ion or by an electron (Fig. 2.7).

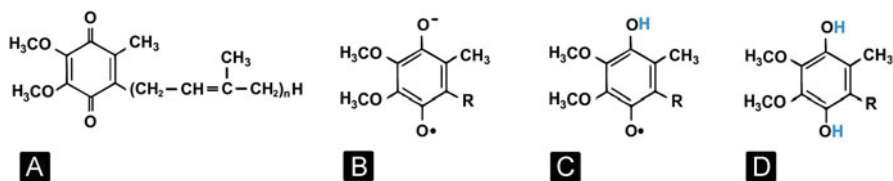
A proton may also dissociate from the hydroxyl group, leaving behind an anionic residue.

According to the most widely accepted hypotheses, the ubiquinone molecule (coenzyme Q) is able to rotate in the hydrophobic area of the membrane, coming into contact with integrated respiratory chain proteins and mediating the transduction of electrons and hydrogen ions. Through reduction (with an electron) the carboxyl group assumes a polar form and migrates from the membrane to the aqueous environment where it immediately attracts a proton (as its pK precludes the existence of a dissociated form in a non-alkaline environment). Subsequently, a protonated ubiquinone again becomes apolar and returns to the hydrophobic zone of the membrane. While rotating it encounters cytochrome b and releases an electron, converting to semiquinone or quinone.

The presence of iron-sulfur proteins within the mitochondrial matrix, and of cytochrome b in the intermembrane space, results in a situation where the shortest proton transport route across the membrane is the one provided by ubiquinone. The source of energy powering this process is the electrons transport carried by the respiratory chain (Fig. 2.8). A suitable arrangement of respiratory chain proteins is therefore crucial for coupling ATP synthesis to the synthesis of water.

The process depends on respiratory chain proteins being integrated and properly aligned in the membrane (either on the side of the matrix or in the intermembrane space) as well as on the presence of mobile ubiquinone molecules.

The arrangement of proteins which participate in binding hydrogen ions and transporting electrons across the membrane is such that electron transduction follows



**Fig. 2.7** Ubiquinone oxidation and reduction products: **a** Ubiquinone, **b, c** Semiquinone intermediates, **d** Ubiquinol

Systems Biology

Functional Strategies of Living Organisms

Konieczny, L.; Roterman-Konieczna, I.; Spólnik, P.

2014, XIII, 204 p. 157 illus., 91 illus. in color., Hardcover

ISBN: 978-3-319-01335-0