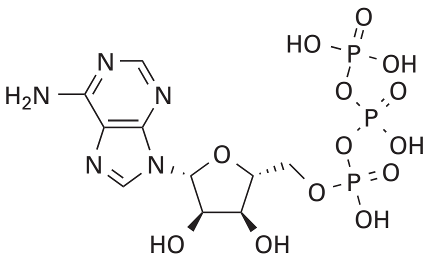
IMPACT 9 …ON BIOCHEMISTRY: Energy conversion in biological cells

The whole of life's activities depends on the coupling of exergonic and endergonic reactions, with oxidation of food the principal exergonic reaction driving other endoergic reactions forward. In biological cells, the energy released by the oxidation of foods is stored in adenosine triphosphate (ATP, **1**). The essence of the action of ATP is its ability to lose its terminal phosphate group by hydrolysis and to form adenosine diphosphate (ADP):

$$\mathrm{ATP(aq)} + \mathrm{H_2O(l)} \rightarrow \mathrm{ADP(aq)} + \mathrm{P_i^-(aq)} + \mathrm{H_3O^+(aq)}$$

where $\mathrm{P_i^-}$ denotes an inorganic phosphate group, such as $\mathrm{H_2PO_4^-}$.



1 ATP

The conventional standard state of hydrogen ions (unit activity, corresponding to pH = 0)[1] is not appropriate to normal biological conditions. Therefore, in biochemistry it is common to adopt the **biological standard state**, in which pH = 7 (an activity of 10^{-7}, neutral solution) and to label the corresponding standard thermodynamic functions as $G^{\oplus}$, $H^{\oplus}$, $\mu^{\oplus}$, and $S^{\oplus}$ (some texts use $X^{\circ\prime}$).

To find the relation between the thermodynamic and biological standard values of the chemical potential of hydrogen ions note that

$$\mu_{\mathrm{H^+}} = \mu_{\mathrm{H^+}}^{\ominus} + RT\ln a_{\mathrm{H^+}} = \mu_{\mathrm{H^+}}^{\ominus} - (RT\ln 10)\mathrm{pH}$$

It follows that

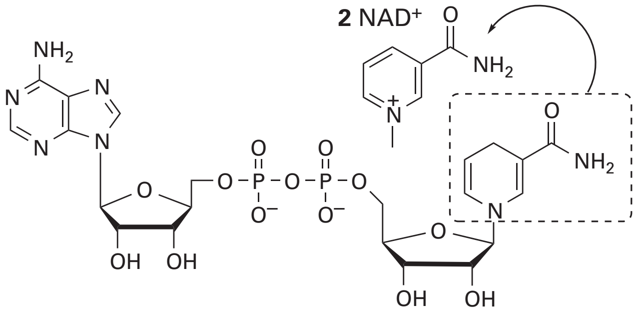
$$\mu_{\mathrm{H^+}}^{\oplus} = \mu_{\mathrm{H^+}}^{\ominus} - 7RT\ln 10$$

Then, in a reaction of the form $\mathrm{A} + 2\mathrm{H^+(aq)} \rightarrow \mathrm{B}$, the standard and biological standard Gibbs energies (at 25 °C) are related as follows:

$$\begin{aligned}\Delta_\mathrm{r}G^{\oplus} &= \mu_\mathrm{B}^{\oplus} - \{\mu_\mathrm{A}^{\oplus} + 2\mu_{\mathrm{H^+}}^{\oplus}\} = \mu_\mathrm{B}^{\ominus} - \{\mu_\mathrm{A}^{\ominus} + 2\mu_{\mathrm{H^+}}^{\ominus} - 14RT\ln 10\}\\ &= \mu_\mathrm{B}^{\ominus} - \{\mu_\mathrm{A}^{\ominus} + 2\mu_{\mathrm{H^+}}^{\ominus}\} + 14RT\ln 10 = \Delta_\mathrm{r}G^{\ominus} + 14RT\ln 10\\ &= \Delta_\mathrm{r}G^{\ominus} + 79.92\,\mathrm{kJ\,mol^{-1}}\end{aligned}$$

The biological standard reaction Gibbs energy for ATP hydrolysis at 37 °C (310 K, blood temperature) is $\Delta_\mathrm{r}G^{\oplus} = -31\,\mathrm{kJ\,mol^{-1}}$. The hydrolysis is therefore exergonic ($\Delta_\mathrm{r}G^{\oplus} < 0$) under these conditions, and $31\,\mathrm{kJ\,mol^{-1}}$ is available for driving other reactions forward. In view of its exergonicity, the ADP–phosphate bond has been called a 'high-energy phosphate bond'. The name is intended to signify a high tendency to undergo reaction, and should not be confused with 'strong' bond. In fact, even in the biological sense it is not of very 'high energy'. The action of ATP depends on it being intermediate in its 'energy'. Thus ATP acts as a phosphate donor to a number of acceptors (for example, glucose), but ADP is converted back to ATP by more powerful phosphate donors in a number of biochemical processes.

The oxidation of glucose to $\mathrm{CO_2}$ and $\mathrm{H_2O}$ by $\mathrm{O_2}$ is an example of how the breakdown of foods is coupled to the formation of ATP in the cell. The process begins with *glycolysis*, a partial oxidation of glucose by nicotinamide adenine dinucleotide ($\mathrm{NAD^+}$, **2**; its reduced form is NADH, **3**) to pyruvate ion, $\mathrm{CH_3COCO_2^-}$, continues with the *citric acid cycle*, which oxidizes pyruvate to $\mathrm{CO_2}$, and ends with *oxidative phosphorylation*, which reduces $\mathrm{O_2}$ to $\mathrm{H_2O}$. Glycolysis is the main source of energy during *anaerobic metabolism*, a form of metabolism in which inhaled $\mathrm{O_2}$ does not play a role. The citric acid cycle and oxidative phosphorylation are the main mechanisms for the extraction of energy from carbohydrates during *aerobic metabolism*, a form of metabolism in which inhaled $\mathrm{O_2}$ does play a role.



3 Nicotinamide adenine dinucleotide, reduced form (NADH)

At blood temperature, $\Delta_\mathrm{r}G^{\oplus} = -147\,\mathrm{kJ\,mol^{-1}}$ for the oxidation of glucose by $\mathrm{NAD^+}$ to pyruvate ions. The oxidation of one glucose molecule is coupled to the conversion of two ADP molecules to two ATP molecules, so the net reaction of glycolysis is

$$\begin{aligned}&\mathrm{C_6H_{12}O_6(aq)} + 2\,\mathrm{NAD^+(aq)} + 2\,\mathrm{ADP(aq)}\\ &\qquad + 2\,\mathrm{P_i^-(aq)} + 2\,\mathrm{H_2O(l)}\\ &\qquad\qquad \rightarrow 2\,\mathrm{CH_3COCO_2^-(aq)} + 2\,\mathrm{NADH(aq)}\\ &\qquad\qquad\qquad + 2\,\mathrm{ATP(aq)} + 2\,\mathrm{H_3O^+(aq)}\end{aligned}$$

The standard reaction Gibbs energy is $(-147) - 2(-31)\,\mathrm{kJ\,mol^{-1}} = -85\,\mathrm{kJ\,mol^{-1}}$: the reaction is exergonic and can be used to drive other reactions.

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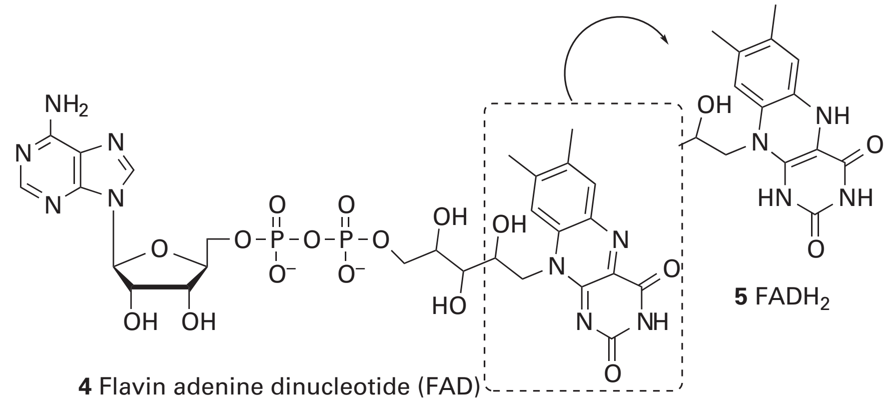
[1] Recall from introductory chemistry courses that $\mathrm{pH} = -\log a_{\mathrm{H_3O^+}}$.

The standard Gibbs energy of combustion of glucose is –2880 kJ mol^{-1}, so terminating its oxidation at pyruvate is a poor use of resources. In the presence of O_2, pyruvate is oxidized further during the citric acid cycle:

$$\begin{aligned}&2\,\mathrm{CH_3COCO_2^-(aq)} + 8\,\mathrm{NAD^+(aq)} + 2\,\mathrm{FAD(aq)}\\ &\quad + 2\,\mathrm{ADP(aq)} + 2\,\mathrm{P_i^-(aq)} + 8\,\mathrm{H_2O(l)}\\ &\quad\quad \rightarrow 6\,\mathrm{CO_2(g)} + 8\,\mathrm{NADH(aq)} + 4\,\mathrm{H_3O^+(aq)}\\ &\quad\quad\quad + 2\,\mathrm{FADH_2(aq)} + 2\,\mathrm{ATP(aq)}\end{aligned}$$

where FAD (and its reduced form $FADH_2$) is flavin adenine dinucleotide (**4**; its reduced form is **5**). The NADH and $FADH_2$ go on to reduce O_2 during oxidative phosphorylation, which also produces ATP. The citric acid cycle and oxidative phosphorylation generate as many as 38 ATP molecules for each glucose molecule consumed. Each mole of ATP molecules extracts 31 kJ from the 2880 kJ supplied by 1 mol $C_6H_{12}O_6$ (180 g of glucose), so 1702 kJ is stored for later use. Therefore, aerobic oxidation of glucose is much more efficient than glycolysis.

In the cell, each ATP molecule can be used to drive an endergonic reaction for which $\Delta_r G^{\ominus}$ does not exceed +31 kJ mol^{-1}. (In an actual cell, the composition may be far from standard and the ATP reaction much more potent.) For example, the biosynthesis of sucrose from glucose and fructose is endergonic to the extent $\Delta_r G^{\ominus}$ = +23 kJ mol^{-1} and so the formation of one sucrose molecule can be driven by the hydrolysis of a single ATP molecule, with the aid of plant enzymes. The biosynthesis of proteins is strongly endergonic, not only on account of the enthalpy change but also on account of the large decrease in entropy that occurs when many amino acids are assembled into a precisely determined sequence. For instance, the formation of a peptide link is endergonic, with $\Delta_r G^{\ominus}$ = +17 kJ mol^{-1}, but the biosynthesis occurs indirectly and requires the consumption of three ATP molecules for each link. In a moderately small protein like myoglobin, with about 150 peptide links, the construction alone requires 450 ATP molecules, and therefore about 12 mol of glucose molecules for 1 mol of protein molecules.



4 Flavin adenine dinucleotide (FAD)

5 $FADH_2$