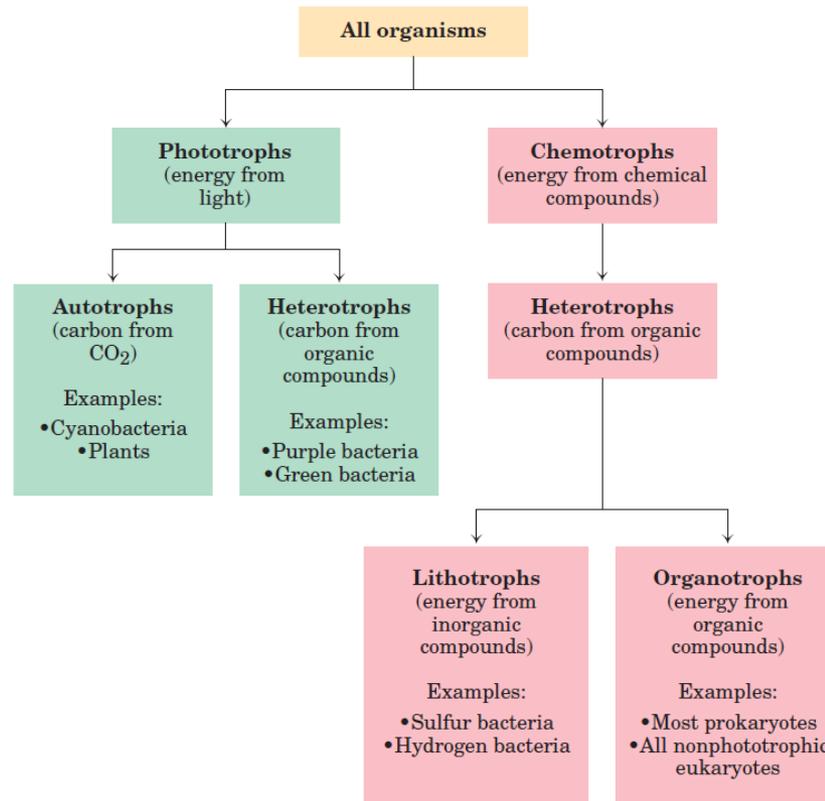


# Metabolismo e bioenergética

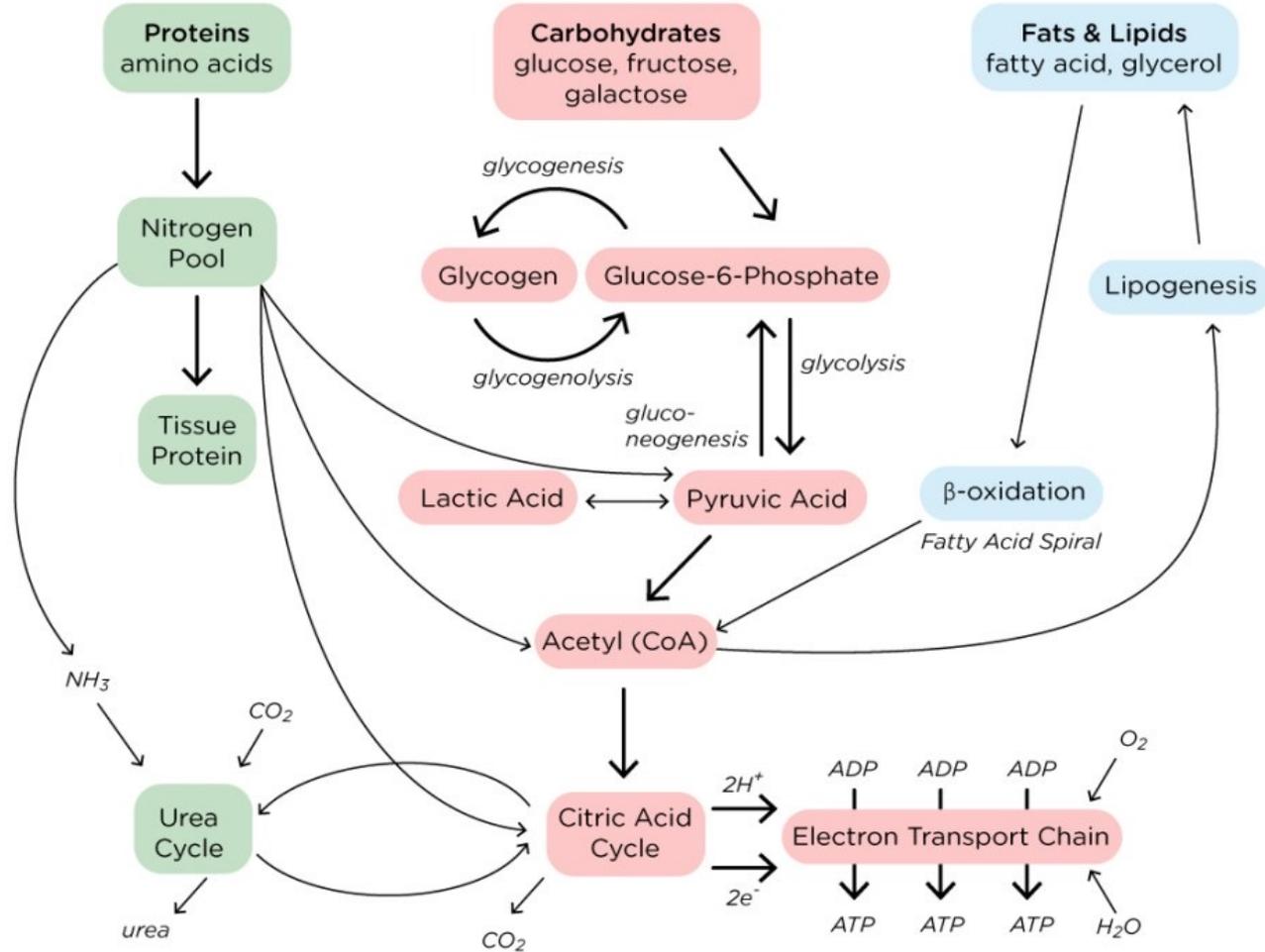
Sistemas biológicos são altamente organizados..... manter essa organização requer energia



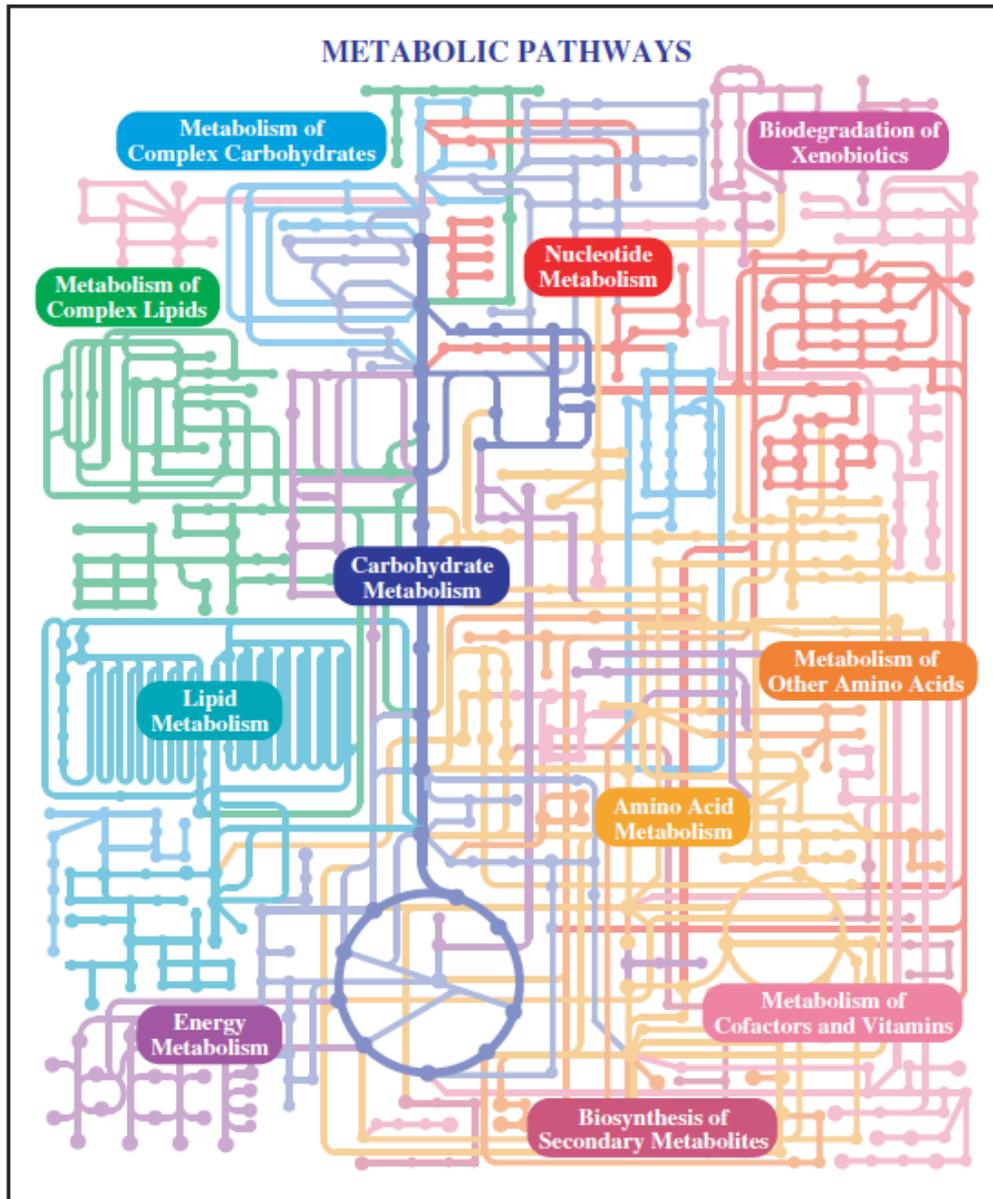
Organismos vivos são sistemas abertos; trocam energia e matéria com o ambiente



## Metabolism Summary

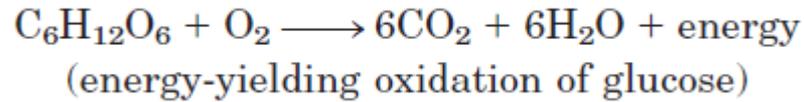
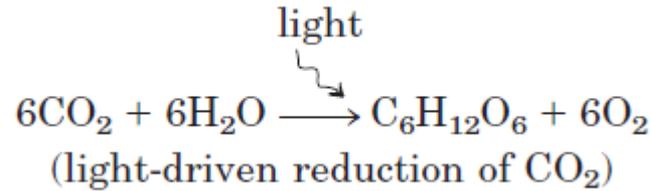


Jack Westin



**FIGURE 15-1 Metabolism as a three-dimensional meshwork.** A typical eukaryotic cell has the capacity to make about 30,000 different proteins, which catalyze thousands of different reactions involving many hundreds of metabolites, most shared by more than one “pathway.” This overview image of metabolic pathways is from the online KEGG (Kyoto Encyclopedia of Genes and Genomes) PATHWAY database ([www.genome.ad.jp/kegg/pathway/map/map01100.html](http://www.genome.ad.jp/kegg/pathway/map/map01100.html)). Each area can be further expanded for increasingly detailed information, to the level of specific enzymes and intermediates.

As reações químicas que convertem energia em organismos vivos são altamente conservadas

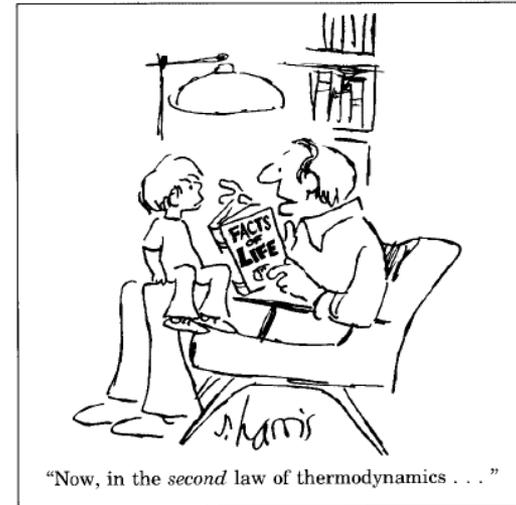


É o fluxo de elétrons, da água para a glicose, e de glicose para o  $\text{O}_2$ , que faz com que a energia captada do sol fique disponível aos organismos

<https://auspteespera.prg.usp.br/>

## Alguns princípios de Bioenergética:

### Biological Energy Transformations Obey the Laws of Thermodynamics



$G$  = a quantidade de energia necessária para uma reação em temperatura e pressão constantes

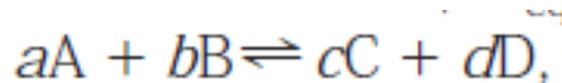
$H$  = entalpia, função do número e tipo de ligações químicas envolvidas na reação

$S$  = entropia, ou grau de liberdade molecular da energia em um sistema reacional

$\Delta G$  = variação de energia livre de um sistema reacional

$\Delta G^0$  =  $\Delta G$  de uma reação acontecendo em condições "padrão"  
(T 298K = 25°C; [ ] substratos e produto = 1 M)

$\Delta G^{0'}$  =  $\Delta G^0$  em pH 7 [H<sup>+</sup>] = 10<sup>-7</sup> M



$$\Delta G = \Delta G'^{\circ} + RT \ln \frac{[C][D]}{[A][B]}$$

$$K_{\text{eq}} = \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

$$\Delta G'^{\circ} = -RT \ln K_{\text{eq}}$$

A variação de energia livre "real" depende da concentração dos reagente e produtos, e muda à medida que a reação procede

É uma constante, característica para cada reação

A energia livre de uma reação ( $\Delta G^{\circ}$ ) é uma "maneira" matemática de expressar a constante de equilíbrio K

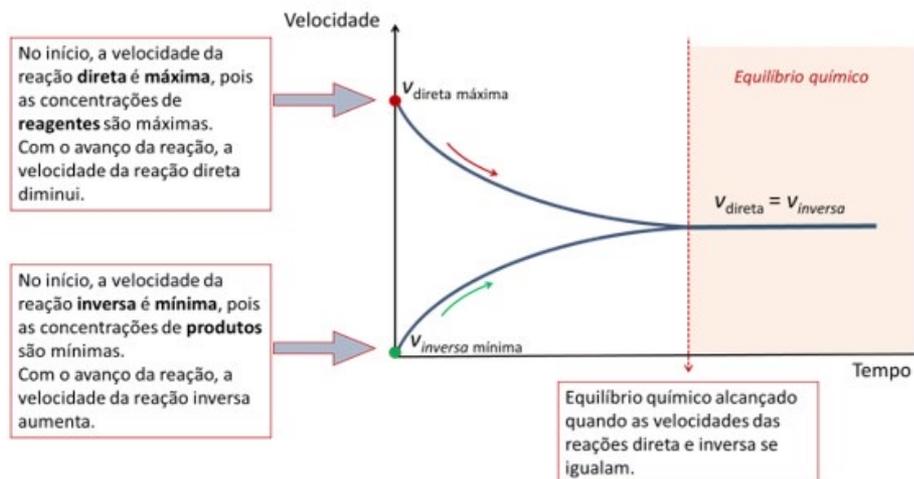
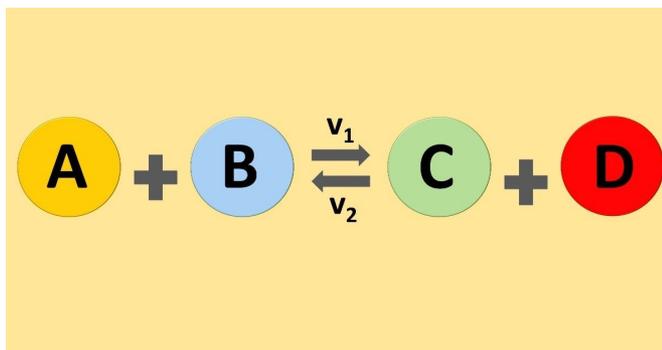
**TABLE 13-2** Relationship between the Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

$K'_{\text{eq}}$	$\Delta G^{\circ}$	
	(kJ/mol)	(kcal/mol)*
$10^3$	-17.1	-4.1
$10^2$	-11.4	-2.7
$10^1$	-5.7	-1.4
1	0.0	0.0
$10^{-1}$	5.7	1.4
$10^{-2}$	11.4	2.7
$10^{-3}$	17.1	4.1
$10^{-4}$	22.8	5.5
$10^{-5}$	28.5	6.8
$10^{-6}$	34.2	8.2

**TABLE 13-3** Relationships among  $K'_{\text{eq}}$ ,  $\Delta G^{\circ}$ , and the Direction of Chemical Reactions under Standard Conditions

When $K'_{\text{eq}}$ is ...	$\Delta G^{\circ}$ is ...	Starting with all components at 1 M, the reaction ...
>1.0	negative	proceeds forward
1.0	zero	is at equilibrium
<1.0	positive	proceeds in reverse

# O que é equilíbrio químico?



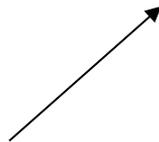
Por exemplo:



Se nós começarmos a reação com 20 mM de G1-P ou com 20 mM G6-P, no equilíbrio sempre teremos 19 mM de G6-P e 1 mM de G1-P

$$K'_{\text{eq}} = \frac{[\text{glucose 6-phosphate}]}{[\text{glucose 1-phosphate}]} = \frac{19 \text{ mM}}{1 \text{ mM}} = 19$$

$$\begin{aligned}\Delta G'^{\circ} &= -RT \ln K'_{\text{eq}} \\ &= -(8.315 \text{ J/mol} \cdot \text{K})(298 \text{ K})(\ln 19) \\ &= -7.3 \text{ kJ/mol}\end{aligned}$$

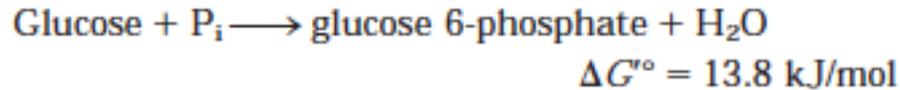


Isso significa que a reação procede, nesse sentido, espontaneamente

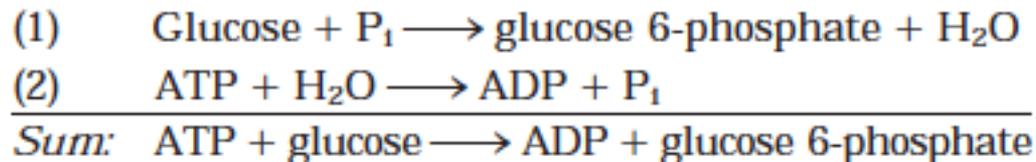
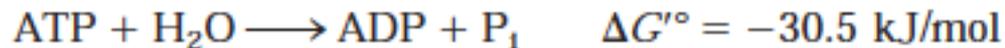
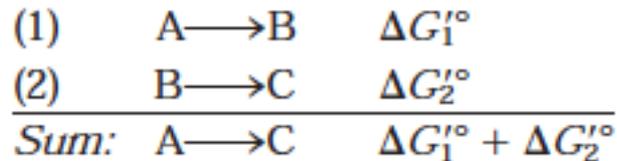
**TABLE 13–4** Standard Free-Energy Changes of Some Chemical Reactions at pH 7.0 and 25 °C (298 K)

Reaction type	$\Delta G'^{\circ}$	
	(kJ/mol)	(kcal/mol)
<b>Hydrolysis reactions</b>		
Acid anhydrides		
Acetic anhydride + H <sub>2</sub> O → 2 acetate	−91.1	−21.8
ATP + H <sub>2</sub> O → ADP + P <sub>i</sub>	−30.5	−7.3
ATP + H <sub>2</sub> O → AMP + PP <sub>i</sub>	−45.6	−10.9
PP <sub>i</sub> + H <sub>2</sub> O → 2P <sub>i</sub>	−19.2	−4.6
UDP-glucose + H <sub>2</sub> O → UMP + glucose 1-phosphate	−43.0	−10.3
Esters		
Ethyl acetate + H <sub>2</sub> O → ethanol + acetate	−19.6	−4.7
Glucose 6-phosphate + H <sub>2</sub> O → glucose + P <sub>i</sub>	−13.8	−3.3
Amides and peptides		
Glutamine + H <sub>2</sub> O → glutamate + NH <sub>4</sub> <sup>+</sup>	−14.2	−3.4
Glycylglycine + H <sub>2</sub> O → 2 glycine	−9.2	−2.2
Glycosides		
Maltose + H <sub>2</sub> O → 2 glucose	−15.5	−3.7
Lactose + H <sub>2</sub> O → glucose + galactose	−15.9	−3.8
Rearrangements		
Glucose 1-phosphate → glucose 6-phosphate	−7.3	−1.7
Fructose 6-phosphate → glucose 6-phosphate	−1.7	−0.4
Elimination of water		
Malate → fumarate + H <sub>2</sub> O	3.1	0.8
Oxidations with molecular oxygen		
Glucose + 6O <sub>2</sub> → 6CO <sub>2</sub> + 6H <sub>2</sub> O	−2,840	−686
Palmitate + 23O <sub>2</sub> → 16CO <sub>2</sub> + 16H <sub>2</sub> O	−9,770	−2,338

Muitas reação biológicas são endergônicas....como elas acontecem *in vivo*?



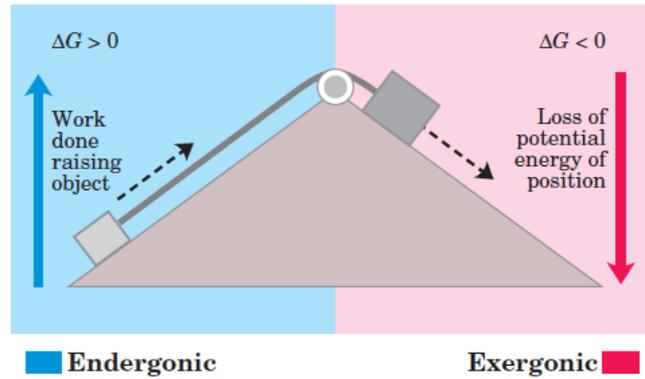
As energias livres de reações sequenciais são aditivas



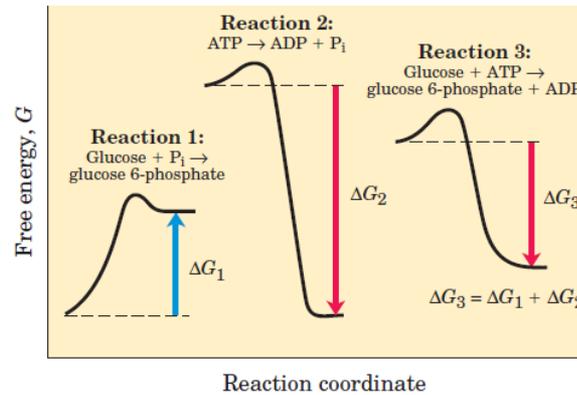
$$\Delta G'^{\circ} = 13.8 \text{ kJ/mol} + (-30.5 \text{ kJ/mol}) = -16.7 \text{ kJ/mol}$$

# Acoplamento energético

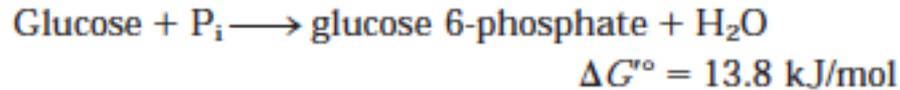
(a) Mechanical example



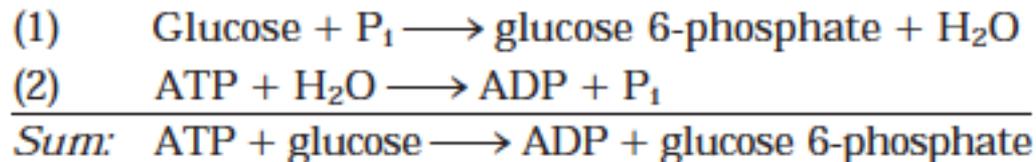
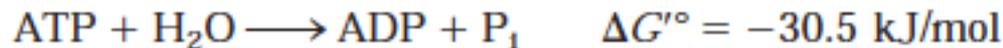
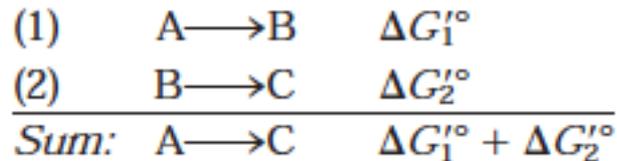
(b) Chemical example



Muitas reação biológicas são endergônicas....como elas acontecem *in vivo*?

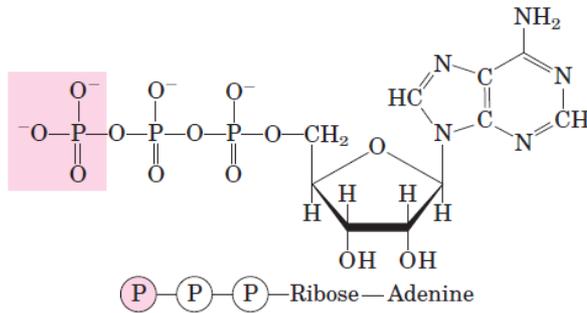


As energias livres de reações sequenciais são aditivas

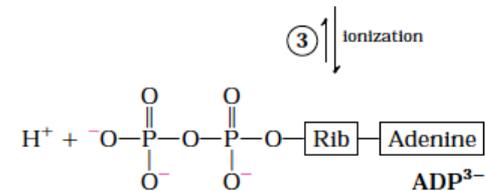
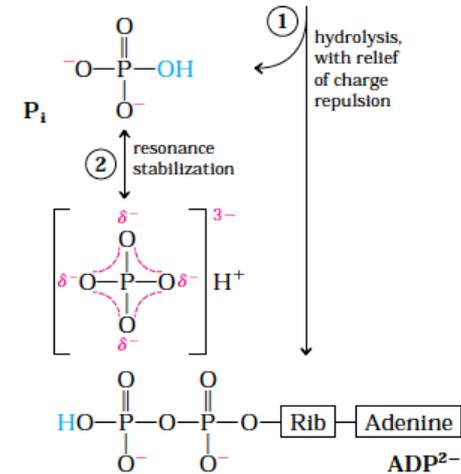
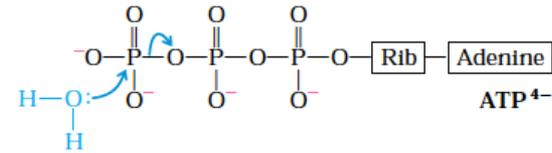
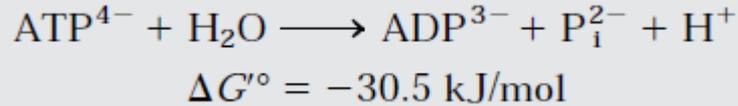


$$\Delta G'^{\circ} = 13.8 \text{ kJ/mol} + (-30.5 \text{ kJ/mol}) = -16.7 \text{ kJ/mol}$$

# Adenosina trifosfato é a grande "moeda energética" da célula



**FIGURE 1-25** Adenosine triphosphate (ATP). The removal of the terminal phosphoryl group (shaded pink) of ATP, by breakage of a phosphoanhydride bond, is highly exergonic, and this reaction is coupled to many endergonic reactions in the cell (as in the example in Fig. 1-26b).



A liberação de produtos cuja concentração intracelular é baixa, favorece a hidrólise

A energia livre de hidrólise de ATP em células é diferente do  $\Delta G^{\circ}$

TABLE 13-5 Adenine Nucleotide, Inorganic Phosphate, and Phosphocreatine Concentrations in Some Cells

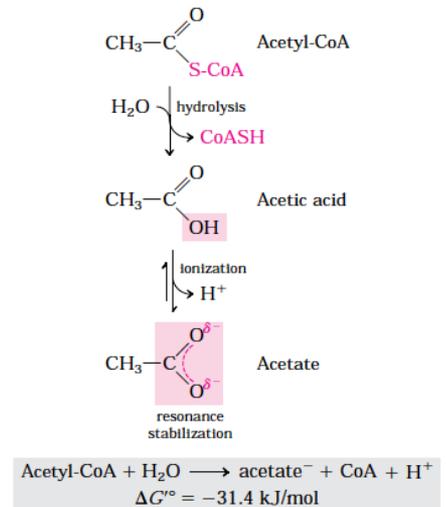
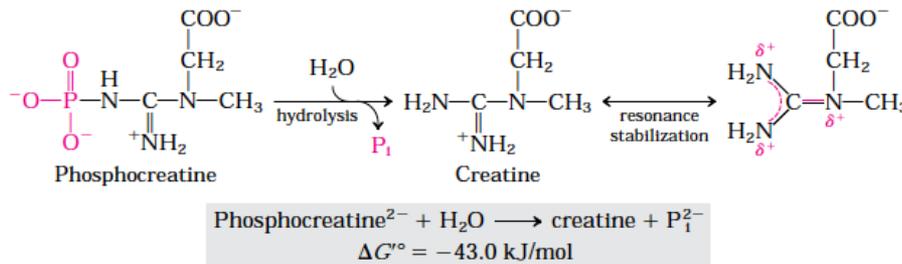
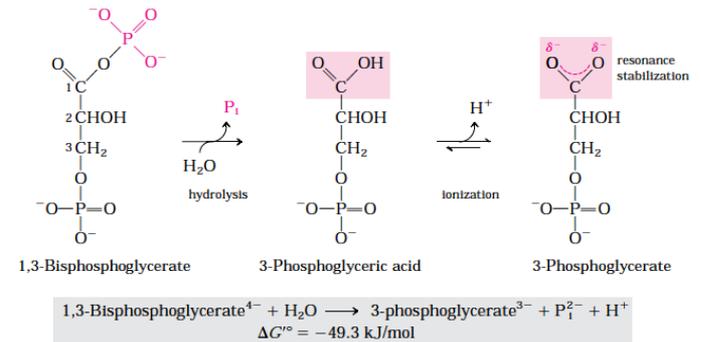
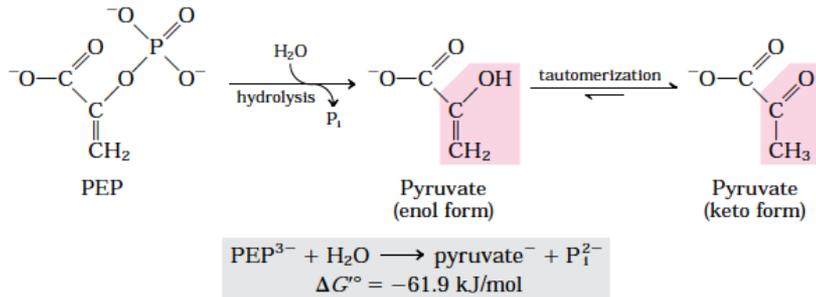
	Concentration (mM)*				
	ATP	ADP <sup>i</sup>	AMP	P <sub>i</sub>	PCr
Rat hepatocyte	3.38	1.32	0.29	4.8	0
Rat myocyte	8.05	0.93	0.04	8.05	28
Rat neuron	2.59	0.73	0.06	2.72	4.7
Human erythrocyte	2.25	0.25	0.02	1.65	0
<i>E. coli</i> cell	7.90	1.04	0.82	7.9	0

$$\Delta G_p = \Delta G'^{\circ} + RT \ln \frac{[ADP][P_i]}{[ATP]}$$

$$\begin{aligned} \Delta G_p &= -30.5 \text{ kJ/mol} + \\ &\left[ (8.315 \text{ J/mol} \cdot \text{K})(298 \text{ K}) \ln \frac{(0.25 \times 10^{-3})(1.65 \times 10^{-3})}{2.25 \times 10^{-3}} \right] \\ &= -30.5 \text{ kJ/mol} + (2.48 \text{ kJ/mol}) \ln 1.8 \times 10^{-4} \\ &= -30.5 \text{ kJ/mol} - 21 \text{ kJ/mol} \\ &= -52 \text{ kJ/mol} \end{aligned}$$

Energia livre de hidrólise de ATP na célula é maior do que a energia livre padrão

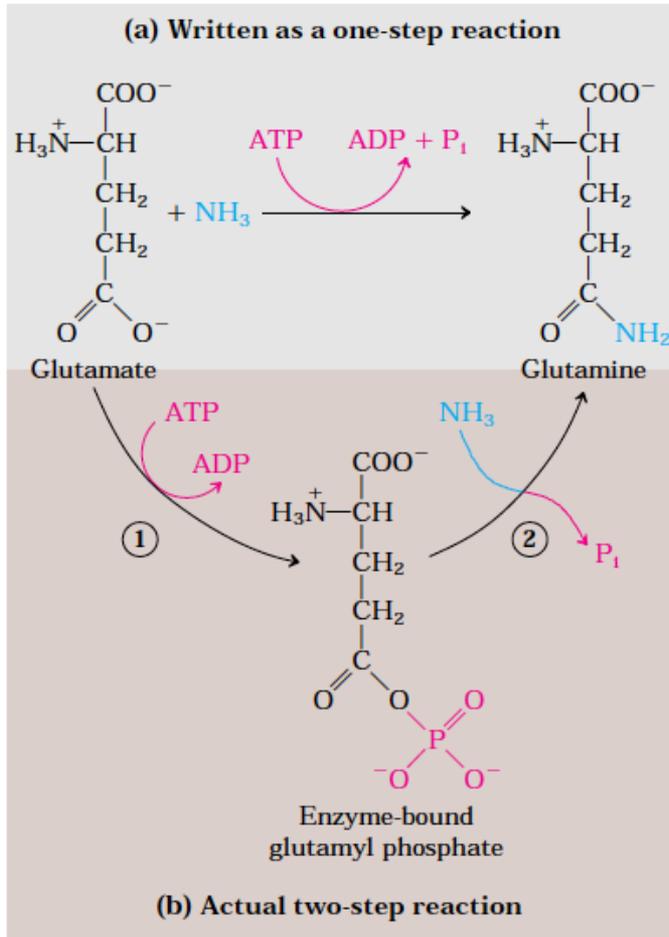
# A hidrólise de outras moléculas fosforiladas também pode "dirigir" reações desfavoráveis



**TABLE 13–6** Standard Free Energies of Hydrolysis of Some Phosphorylated Compounds and Acetyl-CoA (a Thioester)

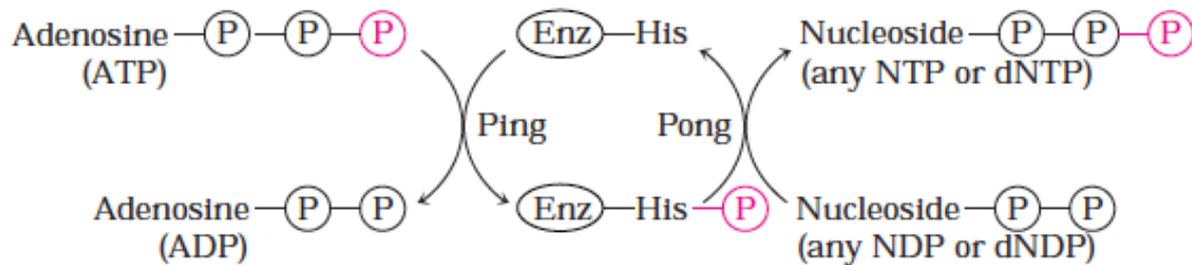
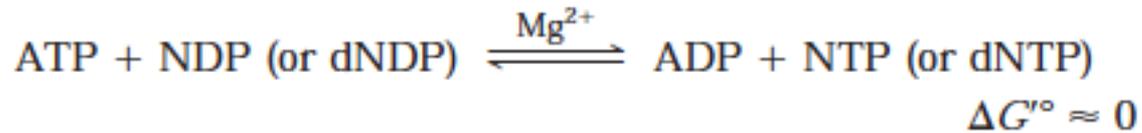
	$\Delta G'^{\circ}$	
	(kJ/mol)	(kcal/mol)
Phosphoenolpyruvate	−61.9	−14.8
1,3-bisphosphoglycerate ( $\rightarrow$ 3-phosphoglycerate + $P_i$ )	−49.3	−11.8
Phosphocreatine	−43.0	−10.3
ADP ( $\rightarrow$ AMP + $P_i$ )	−32.8	−7.8
ATP ( $\rightarrow$ ADP + $P_i$ )	−30.5	−7.3
ATP ( $\rightarrow$ AMP + $PP_i$ )	−45.6	−10.9
AMP ( $\rightarrow$ adenosine + $P_i$ )	−14.2	−3.4
$PP_i$ ( $\rightarrow$ 2 $P_i$ )	−19.2	−4.0
Glucose 1-phosphate	−20.9	−5.0
Fructose 6-phosphate	−15.9	−3.8
Glucose 6-phosphate	−13.8	−3.3
Glycerol 1-phosphate	−9.2	−2.2
Acetyl-CoA	−31.4	−7.5

A hidrólise de ATP fornece energia através de reações acopladas, com intermediários fosforilados



**FIGURE 13-8 ATP hydrolysis in two steps.** (a) The contribution of ATP to a reaction is often shown as a single step, but is almost always a two-step process. (b) Shown here is the reaction catalyzed by ATP-dependent glutamine synthetase. ① A phosphoryl group is transferred from ATP to glutamate, then ② the phosphoryl group is displaced by NH<sub>3</sub> and released as P<sub>i</sub>.

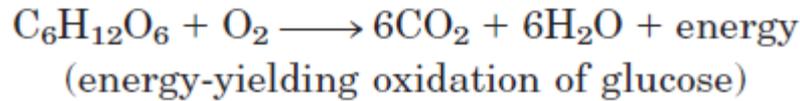
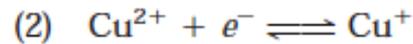
Reações de transfosforilação acontecem entre todos os nucleotídeos, com  $\Delta G^{\circ}$  próximo de 0



# Reações de oxido-redução são fundamentais no metabolismo energético



can be described in terms of two half-reactions:



Estados de oxidação do C  $\longrightarrow$

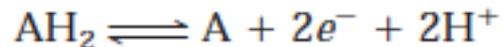
Methane	$\begin{array}{c} \text{H} \\   \\ \text{H} : \text{C} : \text{H} \\   \\ \text{H} \end{array}$	8
Ethane (alkane)	$\begin{array}{c} \text{H} \quad \text{H} \\   \quad   \\ \text{H} : \text{C} : \text{C} : \text{H} \\   \quad   \\ \text{H} \quad \text{H} \end{array}$	7
Ethene (alkene)	$\begin{array}{c} \text{H} \quad \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C} : : \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \quad \text{H} \end{array}$	6
Ethanol (alcohol)	$\begin{array}{c} \text{H} \quad \text{H} \\   \quad   \\ \text{H} : \text{C} : \text{C} : \text{O} : \text{H} \\   \quad   \\ \text{H} \quad \text{H} \end{array}$	5
Acetylene (alkyne)	$\text{H} : \text{C} : : \text{C} : \text{H}$	5
Formaldehyde	$\begin{array}{c} \text{H} \\   \\ \text{H} : \text{C} : \text{O} \\   \\ \text{H} \end{array}$	4
Acetaldehyde (aldehyde)	$\begin{array}{c} \text{H} \quad \quad \text{H} \\   \quad \quad   \\ \text{H} : \text{C} : \text{C} : \text{O} \\   \quad \quad   \\ \text{H} \quad \quad \text{O} \end{array}$	3
Acetone (ketone)	$\begin{array}{c} \text{H} \quad \text{O} \quad \text{H} \\   \quad    \quad   \\ \text{H} : \text{C} : \text{C} : \text{C} : \text{H} \\   \quad \quad   \\ \text{H} \quad \quad \text{H} \end{array}$	2
Formic acid (carboxylic acid)	$\begin{array}{c} \text{O} \\    \\ \text{H} : \text{C} : \text{O} \\   \\ \text{H} \end{array}$	2
Carbon monoxide	$: \text{C} : : \text{O} :$	2
Acetic acid (carboxylic acid)	$\begin{array}{c} \text{H} \quad \quad \text{O} \\   \quad \quad    \\ \text{H} : \text{C} : \text{C} : \text{O} \\   \quad \quad   \\ \text{H} \quad \quad \text{O} \end{array}$	1
Carbon dioxide	$\text{O} : : \text{C} : : \text{O} :$	0

Reações de oxido-redução podem ocorrer de diferentes maneiras:

1. Directly as *electrons*. For example, the  $\text{Fe}^{2+}/\text{Fe}^{3+}$  redox pair can transfer an electron to the  $\text{Cu}^+/\text{Cu}^{2+}$  redox pair:



2. As *hydrogen atoms*. Recall that a hydrogen atom consists of a proton ( $\text{H}^+$ ) and a single electron ( $e^-$ ). In this case we can write the general equation



where  $\text{AH}_2$  is the hydrogen/electron donor.

← Não é um próton ionizável, o átomo de H foi removido

3. As a *hydride ion* ( $\text{:H}^-$ ), which has two electrons. This occurs in the case of NAD-linked dehydrogenases, described below.

4. Through direct *combination with oxygen*. In this case, oxygen combines with an organic reductant and is covalently incorporated in the product, as in the oxidation of a hydrocarbon to an alcohol:



The hydrocarbon is the electron donor and the oxygen atom is the electron acceptor.

O potencial redox padrão ( $E^0$ ) é uma medida da afinidade de um acceptor de elétrons por esses

↑  
Determinado experimentalmente

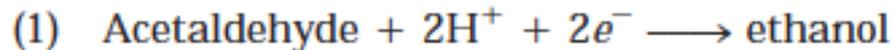
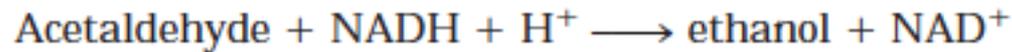
O potencial redox ( $E$ ) de uma reação de transferência de elétrons é determinado pela relação entre o  $E^0$  e a concentração das espécies do par redox

$$E = E^{\circ} + \frac{RT}{nF} \ln \frac{[\text{electron acceptor}]}{[\text{electron donor}]}$$

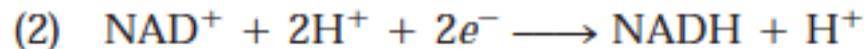
A energia disponível em reações de transferência de elétrons é proporcional ao  $\Delta E$

$$\Delta G = -nF \Delta E \quad \text{or} \quad \Delta G^\circ = -nF \Delta E^\circ$$

Ex:



$$E^\circ = -0.197 \text{ V}$$



$$E^\circ = -0.320 \text{ V}$$

By convention,  $\Delta E^\circ$  is expressed as  $E^\circ$  of the electron acceptor minus  $E^\circ$  of the electron donor. Because acetaldehyde is accepting electrons from NADH in our example,  $\Delta E^\circ = -0.197 \text{ V} - (-0.320 \text{ V}) = 0.123 \text{ V}$ , and  $n$  is 2. Therefore,

$$\begin{aligned} \Delta G^\circ &= -nF \Delta E^\circ = -2(96.5 \text{ kJ/V} \cdot \text{mol})(0.123 \text{ V}) \\ &= -23.7 \text{ kJ/mol} \end{aligned}$$

← Em condições padrão

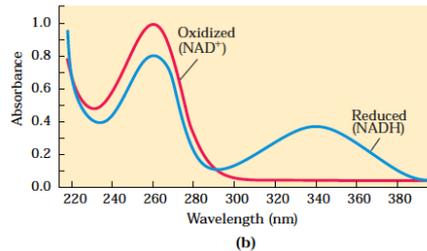
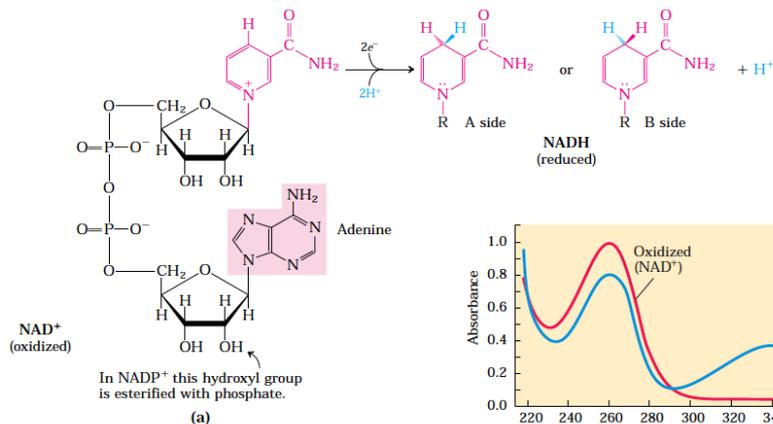
Se as concentrações de acetaldeído/etanol e  $\text{NAD}^+/\text{NADH}$  não fossem as mesmas:

$$\begin{aligned}E_{\text{acetaldehyde}} &= E^\circ + \frac{RT}{n\mathcal{F}} \ln \frac{[\text{acetaldehyde}]}{[\text{ethanol}]} \\ &= -0.197 \text{ V} + \frac{0.026 \text{ V}}{2} \ln \frac{1.00}{0.100} = -0.167 \text{ V} \\ E_{\text{NADH}} &= E^\circ + \frac{RT}{n\mathcal{F}} \ln \frac{[\text{NAD}^+]}{[\text{NADH}]} \\ &= -0.320 \text{ V} + \frac{0.026 \text{ V}}{2} \ln \frac{1.00}{0.100} = -0.350 \text{ V}\end{aligned}$$

Then  $\Delta E$  is used to calculate  $\Delta G$  (Eqn 13-5):

$$\begin{aligned}\Delta E &= -0.167 \text{ V} - (-0.350) \text{ V} = 0.183 \text{ V} \\ \Delta G &= -n\mathcal{F} \Delta E \\ &= -2(96.5 \text{ kJ/V} \cdot \text{mol})(0.183 \text{ V}) \\ &= -35.3 \text{ kJ/mol}\end{aligned}$$

# Muitas reações redox em sistemas biológicos utilizam coenzimas como transportadores de elétrons



**TABLE 13-7** Standard Reduction Potentials of Some Biologically Important Half-Reactions, at pH 7.0 and 25 °C (298 K)

Half-reaction	$E'^{\circ}$ (V)
$\frac{1}{2}\text{O}_2 + 2\text{H}^+ + 2e^- \longrightarrow \text{H}_2\text{O}$	0.816
$\text{Fe}^{3+} + e^- \longrightarrow \text{Fe}^{2+}$	0.771
$\text{NO}_3^- + 2\text{H}^+ + 2e^- \longrightarrow \text{NO}_2^- + \text{H}_2\text{O}$	0.421
Cytochrome <i>f</i> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>f</i> ( $\text{Fe}^{2+}$ )	0.365
$\text{Fe}(\text{CN})_6^{3-}$ (ferricyanide) + $e^- \longrightarrow \text{Fe}(\text{CN})_6^{4-}$	0.36
Cytochrome <i>a</i> <sub>3</sub> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>a</i> <sub>3</sub> ( $\text{Fe}^{2+}$ )	0.35
$\text{O}_2 + 2\text{H}^+ + 2e^- \longrightarrow \text{H}_2\text{O}_2$	0.295
Cytochrome <i>a</i> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>a</i> ( $\text{Fe}^{2+}$ )	0.29
Cytochrome <i>c</i> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>c</i> ( $\text{Fe}^{2+}$ )	0.254
Cytochrome <i>c</i> <sub>1</sub> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>c</i> <sub>1</sub> ( $\text{Fe}^{2+}$ )	0.22
Cytochrome <i>b</i> ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ cytochrome <i>b</i> ( $\text{Fe}^{2+}$ )	0.077
Ubiquinone + $2\text{H}^+ + 2e^- \longrightarrow$ ubiquinol + $\text{H}_2$	0.045
$\text{Fumarate}^{2-} + 2\text{H}^+ + 2e^- \longrightarrow \text{succinate}^{2-}$	0.031
$2\text{H}^+ + 2e^- \longrightarrow \text{H}_2$ (at standard conditions, pH 0)	0.000
Crotonyl-CoA + $2\text{H}^+ + 2e^- \longrightarrow$ butyryl-CoA	-0.015
Oxaloacetate <sup>2-</sup> + $2\text{H}^+ + 2e^- \longrightarrow$ malate <sup>2-</sup>	-0.166
Pyruvate <sup>-</sup> + $2\text{H}^+ + 2e^- \longrightarrow$ lactate <sup>-</sup>	-0.185
Acetaldehyde + $2\text{H}^+ + 2e^- \longrightarrow$ ethanol	-0.197
$\text{FAD} + 2\text{H}^+ + 2e^- \longrightarrow \text{FADH}_2$	-0.219*
Glutathione + $2\text{H}^+ + 2e^- \longrightarrow$ 2 reduced glutathione	-0.23
$\text{S} + 2\text{H}^+ + 2e^- \longrightarrow \text{H}_2\text{S}$	-0.243
Lipoic acid + $2\text{H}^+ + 2e^- \longrightarrow$ dihydrolipoic acid	-0.29
$\text{NAD}^+ + \text{H}^+ + 2e^- \longrightarrow \text{NADH}$	-0.320
$\text{NADP}^+ + \text{H}^+ + 2e^- \longrightarrow \text{NADPH}$	-0.324
Acetoacetate + $2\text{H}^+ + 2e^- \longrightarrow \beta$ -hydroxybutyrate	-0.346
$\alpha$ -Ketoglutarate + $\text{CO}_2 + 2\text{H}^+ + 2e^- \longrightarrow$ isocitrate	-0.38
$2\text{H}^+ + 2e^- \longrightarrow \text{H}_2$ (at pH 7)	-0.414
Ferredoxin ( $\text{Fe}^{3+}$ ) + $e^- \longrightarrow$ ferredoxin ( $\text{Fe}^{2+}$ )	-0.432

A oxidação completa de glicose fornece a energia que é utilizada para sintetizar ATP



$\Delta G'^{\circ}$  of  $-2,840$  kJ/mol.



Metabolismo energético

# Differences Between Catabolism And Anabolism

