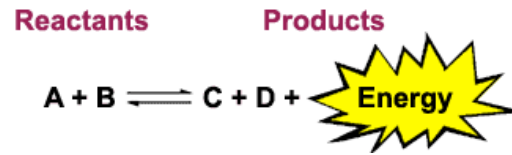


THERMODYNAMICS OF METABOLISM

- Overall process of catabolism **RELEASES** energy
- Overall process of anabolism **REQUIRES** energy input



How do we define amount of energy?

Let's look at a hypothetical spontaneous chemical reaction:

The quantity of usable energy (chemical potential) in a reaction is called the **Gibbs Free Energy (ΔG)**. ΔG is the difference between the energy contained in the products of a reaction and the reactants:

$$\Delta G = (\text{energy of products}) - (\text{energy of reactants})$$

Chemical reactions are classified as being either **exergonic** or **endergonic**. That just means that a reaction can either **release** energy useful for work (an **exergonic** reaction) or **requires** energy to proceed (an **endergonic** reaction).

The spontaneous reaction above is an **exergonic** reaction and **ΔG will be negative**. Thus, a negative ΔG value tells you that that reaction is possible

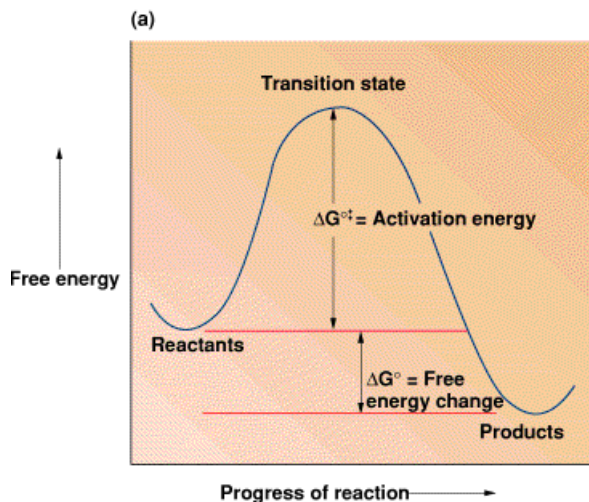


Table 14.5
Significance of ΔG° values

Value and Sign of ΔG°	Thermodynamic Consequences
$\Delta G^{\circ} = 0$	The reactants and the products are at the same energy level. The reaction under standard conditions is at equilibrium. No release of or requirement for energy.
$\Delta G^{\circ} < 0$ (negative values)	The reaction releases energy as it approaches equilibrium. The reactants are at a higher energy level than products. Useful energy is released and available to do work.
$\Delta G^{\circ} > 0$ (positive values)	The reactants are at a lower energy than products. The reaction requires an input of energy to proceed as written.

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- **Use ΔG – Thermodynamic term**
 - Measure of energy available to do useful work
 - ΔG is a constant for a reaction under a defined set of conditions
- We will use **ΔG° – The STANDARD free energy change**
 - Energy change occurring when a reaction proceeds under *standard biological conditions*
 - 1 ATM, 25°C and all reactants at 1M
 - Not really biologically relevant – so we define ΔG° as $\Delta G^{\circ'}$ at pH 7.0, 1 ATM, 25°C and all reactants at 1M
 - Since standard conditions DO NOT occur in cells, absolute values of $\Delta G^{\circ'}$ are not realistic. Can be used to COMPARE energy requirements.

TABLE 12-3 | Biochemical Standard State

Temperature	25°C (298 K)
Pressure	1 atm
Reactant concentration	1 M
pH	7.0 ([H⁺] = 10⁻⁷ M)
Water concentration	55.5 M

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When systems are not at equilibrium, the reactants experience a driving force to reach their equilibrium values. This force is the standard free energy of change for the reaction

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

- $\Delta G^{\circ'}$ is also defined the difference between the energy content of products and reactants

$$\Delta G^{\circ'} = G^{\circ'}_{\text{products}} - G^{\circ'}_{\text{reactants}}$$

$\Delta G^{\circ'}$ is a constant for a particular reaction. Can be positive or negative – indicates whether a reaction can proceed spontaneously under STANDARD CONDITIONS.

$\Delta G^{\circ'} > 0$; not spontaneous (Endergonic) ; $\Delta G^{\circ'} < 0$, spontaneous (exergonic).

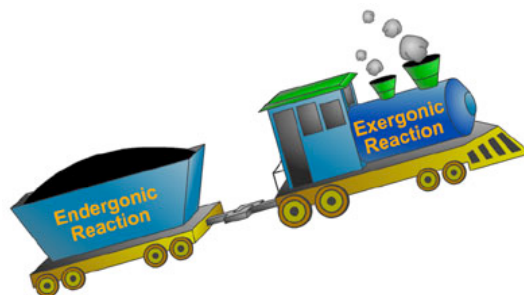
For reaction: $A + B \rightleftharpoons C + D$

Actual free energy change ΔG for a reaction is a function of the actual concentrations of the reactants and the temperature and is related to $\Delta G^{\circ'}$ by:

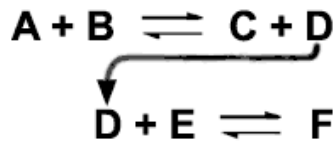
$$\Delta G = \Delta G^{\circ'} + RT \ln \frac{[C][D]}{[A][B]}$$

bracketed quantities are actual concentrations in cells

- Common in biological reactions to **COUPLE** unfavorable reactions with favorable ones to make the overall reaction favorable!
- We have already discussed that some reactions are, while others are endergonic. To get the energy to those endergonic reactions, they are **paired up** with energy-releasing exergonic reactions. Like a locomotive that gets the train car over the hill, an exergonic reaction can "pull" an endergonic reaction along to its destination (products). The reactions can be hooked together, or coupled, via a common intermediate.



- Thermodynamics lets us predict that the reaction will proceed if the overall ΔG° of the two reactions is negative. When two reactions are coupled, the overall ΔG° is the sum of the ΔG° 's of the component reactions.



ΔG° VALUES ARE ADDITIVE!

- Reactions that are not spontaneous can be coupled to spontaneous reactions
- Under these conditions, the overall reaction can be spontaneous (favorable)
- $\text{A} + \text{B} \rightarrow \text{C} + \text{D}$ ΔG° reaction 1
- $\text{D} + \text{E} \rightarrow \text{F}$ ΔG° reaction 2
- $\text{A} + \text{B} + \text{E} \rightarrow \text{C} + \text{F}$ ΔG° overall reaction
- ΔG° overall reaction = ΔG° reaction 1 + ΔG° reaction 2
- The coupling of metabolism, particularly to ATP hydrolysis, can drive thermodynamically unfavorable reactions forward.

	$\frac{\Delta G^{\circ}'}{\text{kJ/mol}}$
$\text{glucose} + \text{ATP} \rightleftharpoons \text{glucose-6-phosphate} + \text{ADP}$	-16.7
$\text{glucose-6-phosphate} + \text{H}_2\text{O} \rightleftharpoons \text{glucose} + \text{P}_i$	-13.8
Sum: $\text{ATP} + \text{H}_2\text{O} \rightleftharpoons \text{ADP} + \text{P}_i$	-30.5

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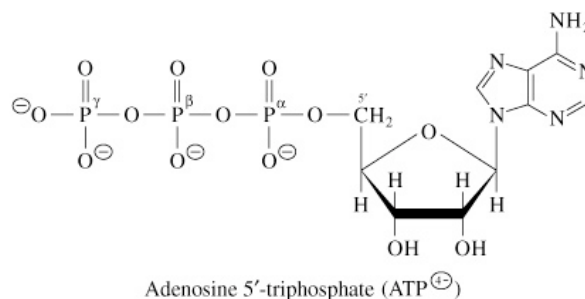
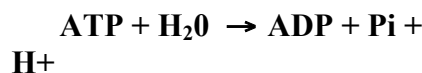
TABLE 12-4 | Standard Free Energy Change for Phosphate Hydrolysis

Compound	$\Delta G^{\circ} (\text{kJ} \cdot \text{mol}^{-1})$
Phosphoenolpyruvate	-61.9
1,3-Bisphosphoglycerate	-49.4
$\text{ATP} \rightarrow \text{AMP} + \text{PP}_i$	-45.6
Phosphocreatine	-43.1
$\text{ATP} \rightarrow \text{ADP} + \text{P}_i$	-30.5
Glucose-1-phosphate	-20.9
Glucose-6-phosphate	-13.8
Glycerol-3-phosphate	-9.2

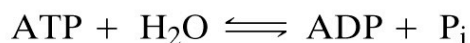
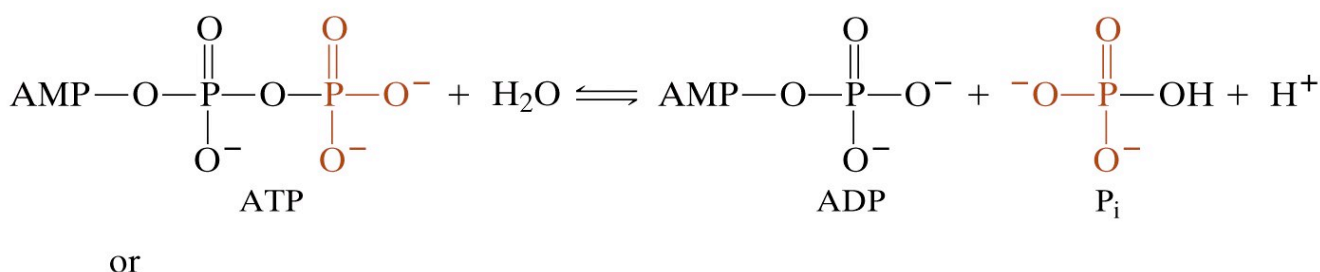
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ATP AS AN ENERGY SOURCE

- ATP is a common form of “energy currency” within cells
- Commonly use ATP hydrolysis to drive unfavorable reactions

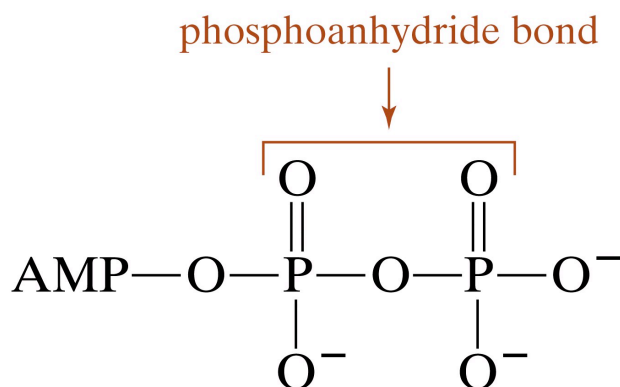


- ATP hydrolysis has a high ΔG° (-30.5 kJ mol⁻¹)
- The equilibrium for this reaction lies heavily towards the products



$$K'_{eq} = \frac{[ADP][P_i]}{[ATP][H_2O]}$$

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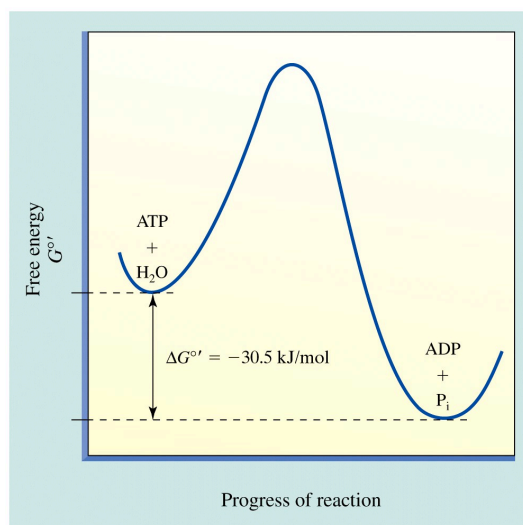


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Energy Diagram for ATP hydrolysis:

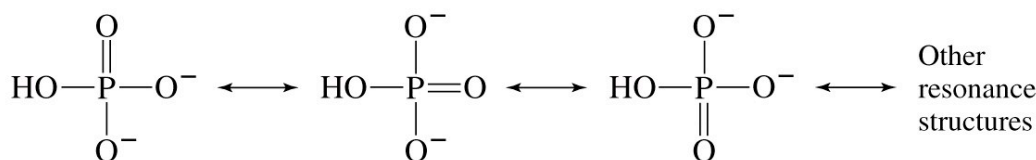
The products (ADP and Pi) are at a lower energy level than the reactants. ADP and Pi are made less reactive by **resonance stabilization**. Higher degree of electron delocalization – more stable.

Phosphoanhydride bonds are relatively reactive. Release energy upon cleavage. A large amount of energy is released in the hydrolysis of the phosphoanhydride bonds of ATP

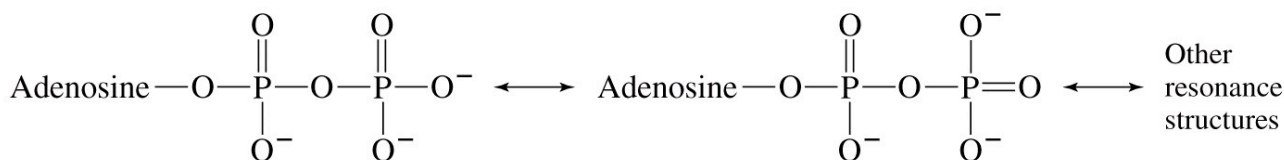
Energy of phosphoanhydrides

- (1) Electrostatic repulsion among partially positively charged phosphorus atoms of ATP
- (2) Solvation of products (ADP and P_i) or (AMP and PP_i) is better than solvation of reactant ATP
- (3) Products are more stable than reactants
There are more delocalized electrons on ADP, P_i or AMP, PP_i than on ATP

Stabilized Resonance Structures of P_i and ADP



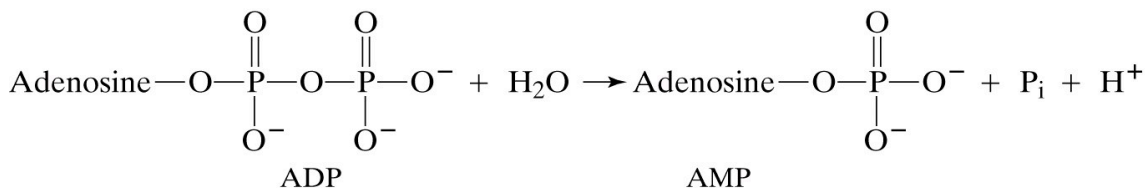
(a) P_i



(b) ADP

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ADP is also energy rich (high potential to transfer phosphate) can also be further cleaved to AMP + P_i & energy is released:

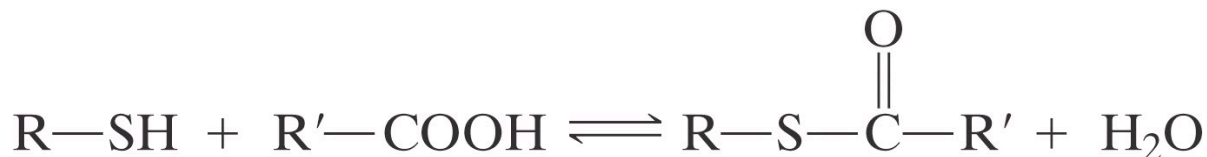


where: $\Delta G^{\circ'} = -30.5 \text{ kJ/mol}$

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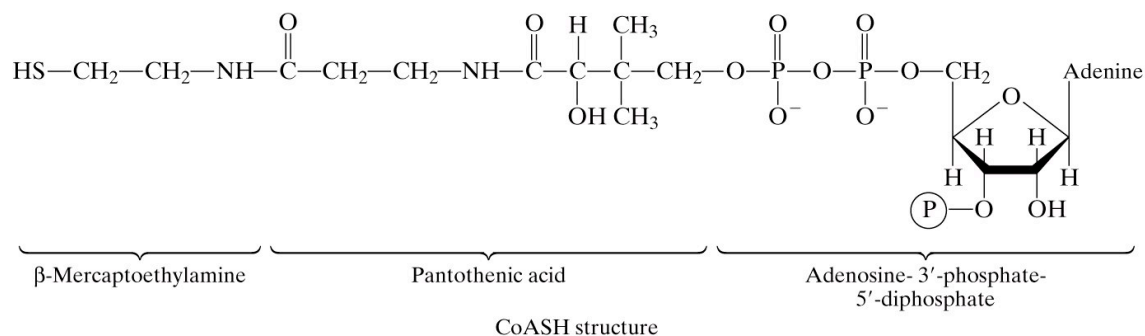
THIOESTERS: Other “highly reactive” or “energy rich” molecule.

Thioesters formed when a thiol (R – SH) joins with a carboxylic acid (R'COOH)



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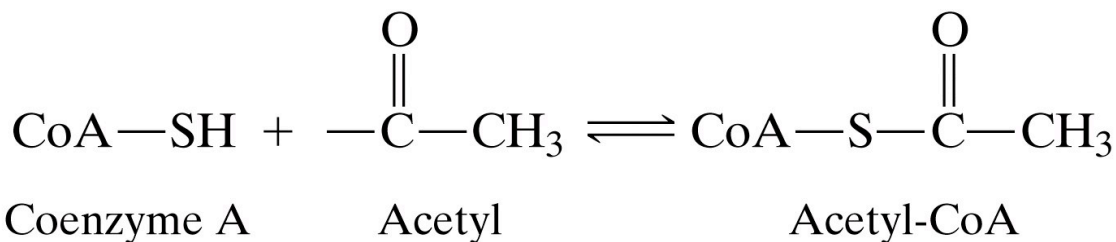
Most common thioesters in cells are produced from the thiol Coenzyme A (CoA-SH)



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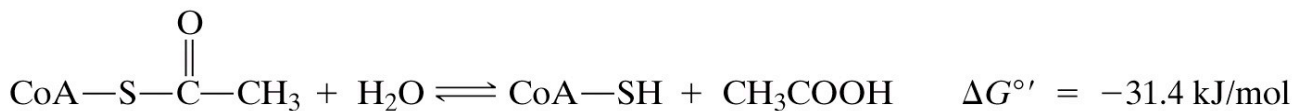
CoA-SH is a common carrier of activated acetyl or other acyl groups. Used a lot in metabolism.

Derived from the vitamin pantothenic acid (B₅)



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Cleavage of thioester releases energy!



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