Metabolism encompasses degradative and biosynthetic pathways

- **Catabolism:** reactions that break down nutrients and collect released energy and reducing power
  - Catabolic pathways are convergent

- **Anabolism:** reactions that synthesize needed compounds, using stored energy and reducing power
  - Anabolic pathways are divergent

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

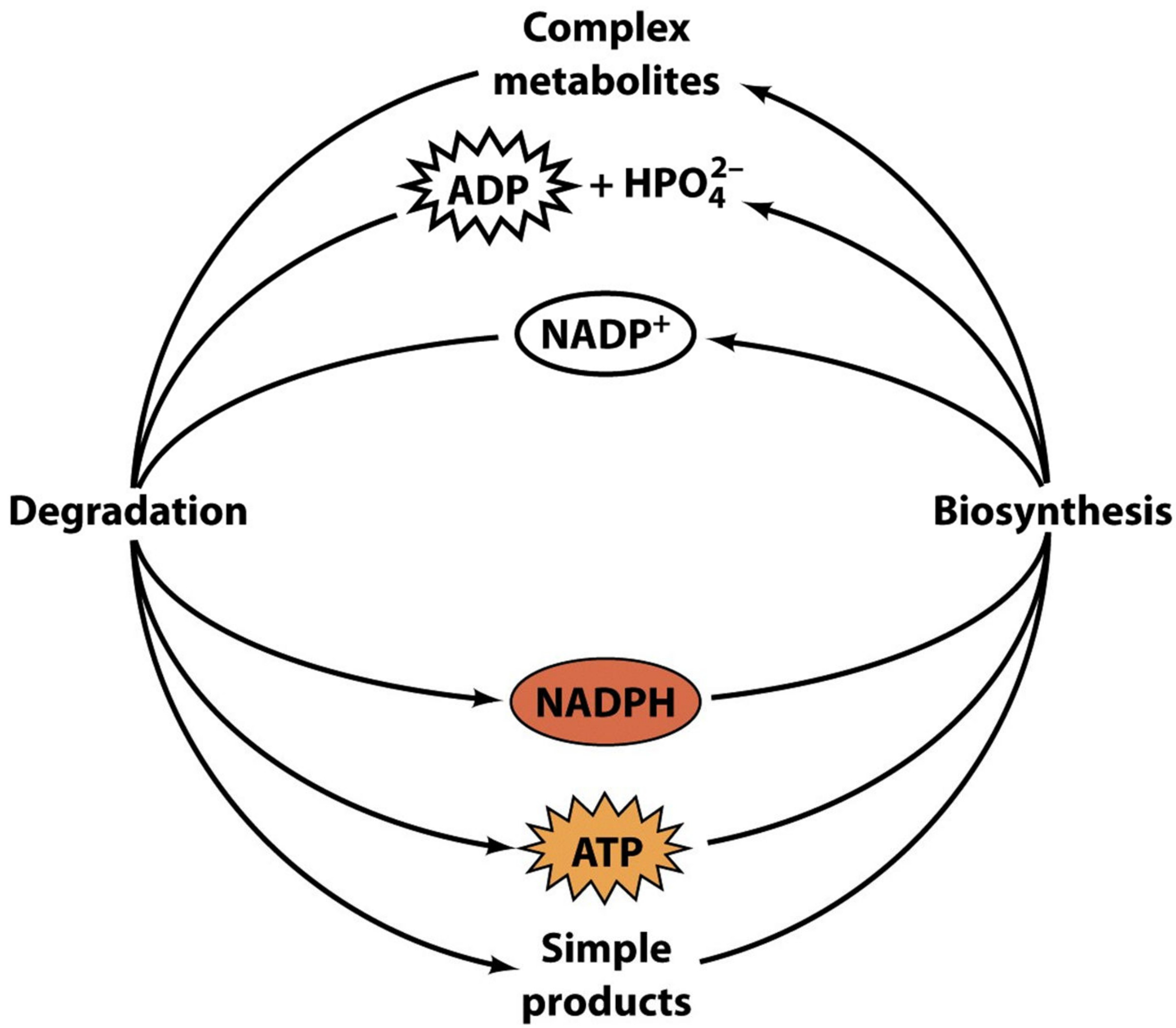
K'_{eq}	$\Delta G'^{\circ}$ (kJ/mol)	$\Delta G'^{\circ}$ (kcal/mol)*
10^3	−17.1	−4.1
10^2	−11.4	−2.7
10^1	−5.7	−1.4
1	0.0	0.0
10^{-1}	5.7	1.4
10^{-2}	11.4	2.7
10^{-3}	17.1	4.1
10^{-4}	22.8	5.5
10^{-5}	28.5	6.8
10^{-6}	34.2	8.2

TABLE 13–3 Relationships among K'_{eq}, $\Delta G'^\circ$, and the Direction of Chemical Reactions

When K'_{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

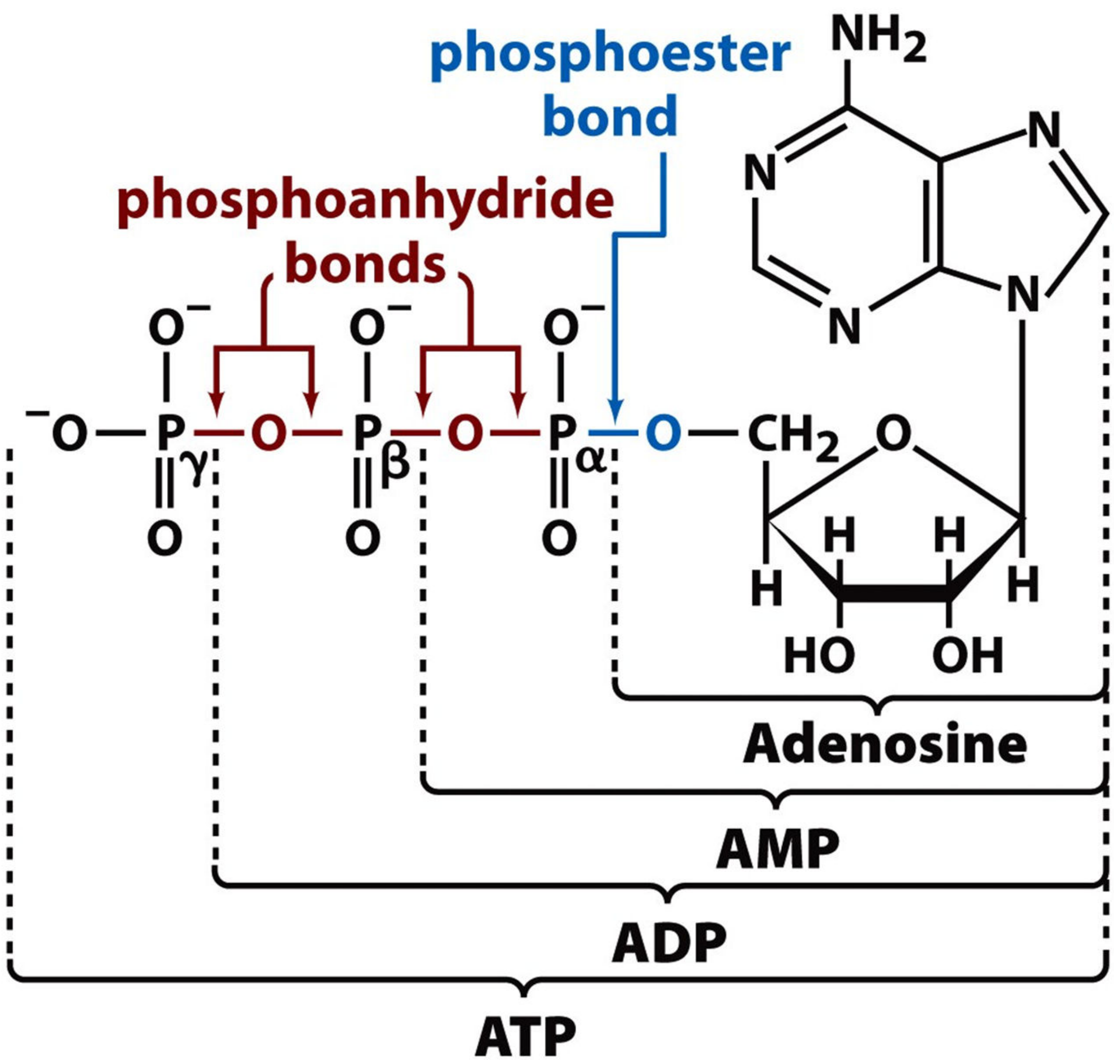
Table 13-3
Lehninger Principles of Biochemistry, Fifth Edition

Energy currencies provide a common intermediate in energy transductions



The adenylates (ATP, ADP, AMP) are the primary energy currency

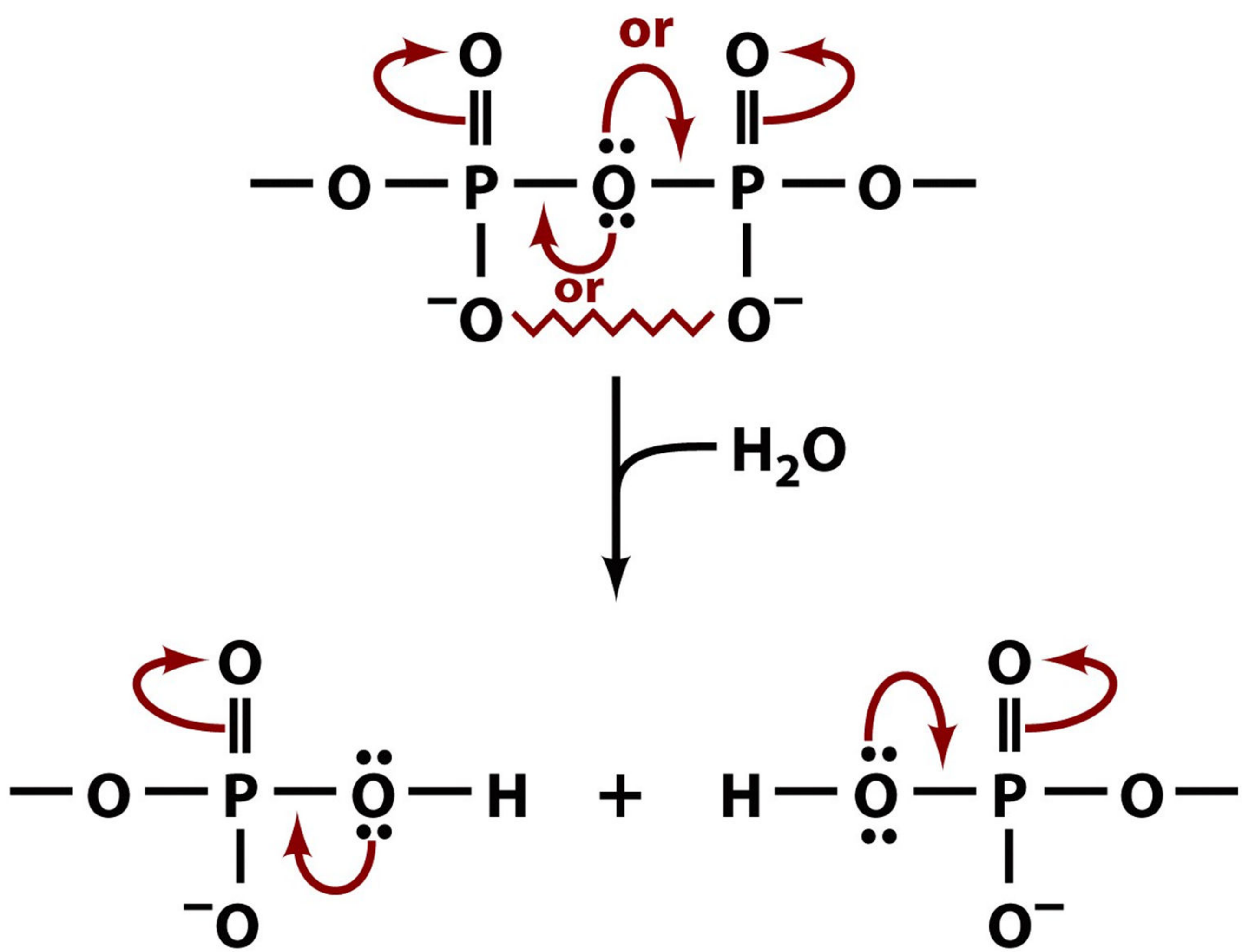
Why?



The ΔG of ATP hydrolysis is large and negative

- Reduced charge repulsion in products
- Better resonance stabilization of products

Products of phosphoanhydride hydrolysis have better resonance stabilization



The ΔG of ATP hydrolysis is large and negative

- Reduced charge repulsion in products
- Better resonance stabilization of products
- More favored solvation of products

$\Rightarrow$ $\Delta G'^{\circ}$ is -30.5 kJ/mol

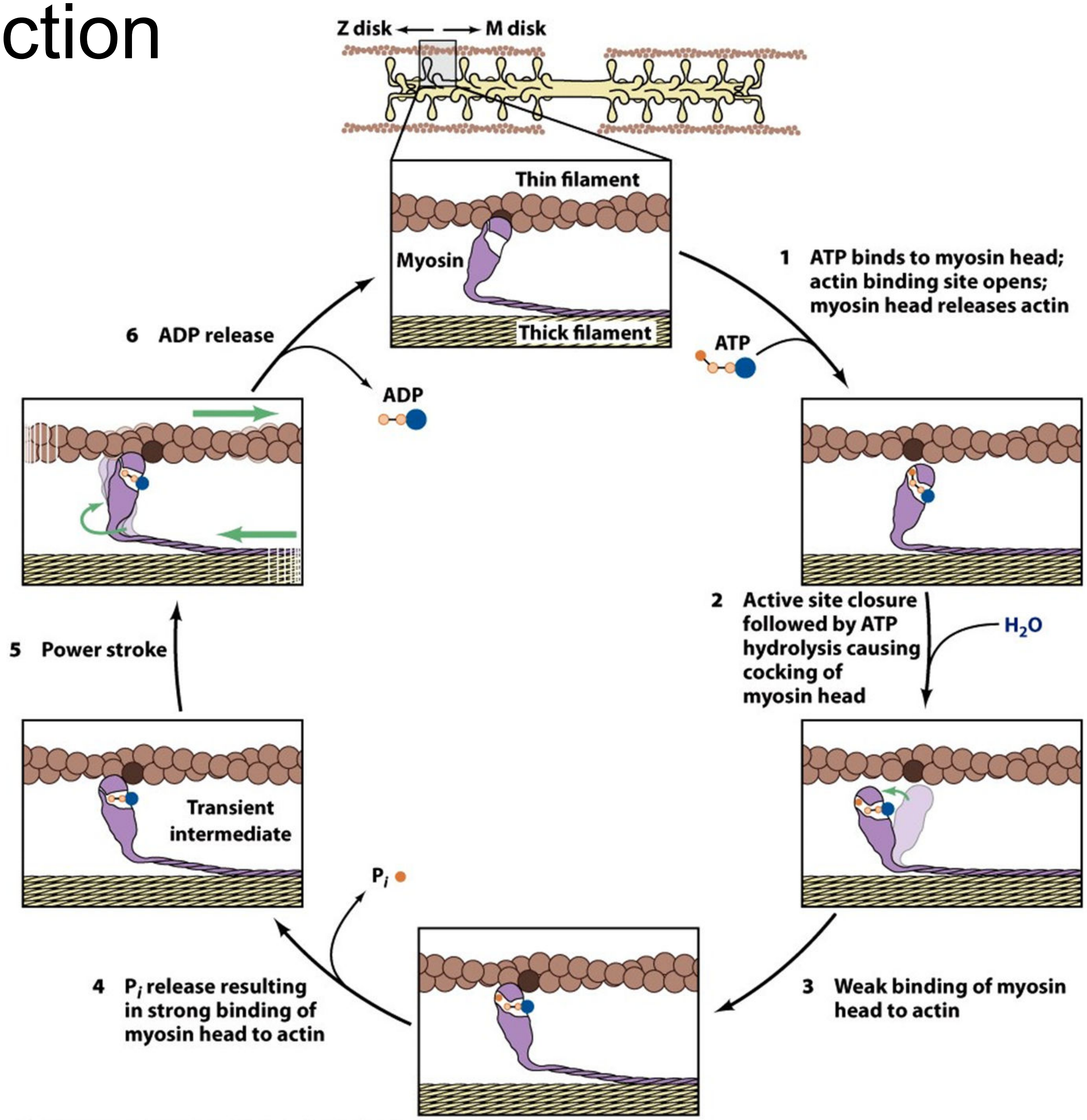
- Cells keep [ATP] relatively high

$\Rightarrow$ $\Delta G < -30.5$ kJ/mol

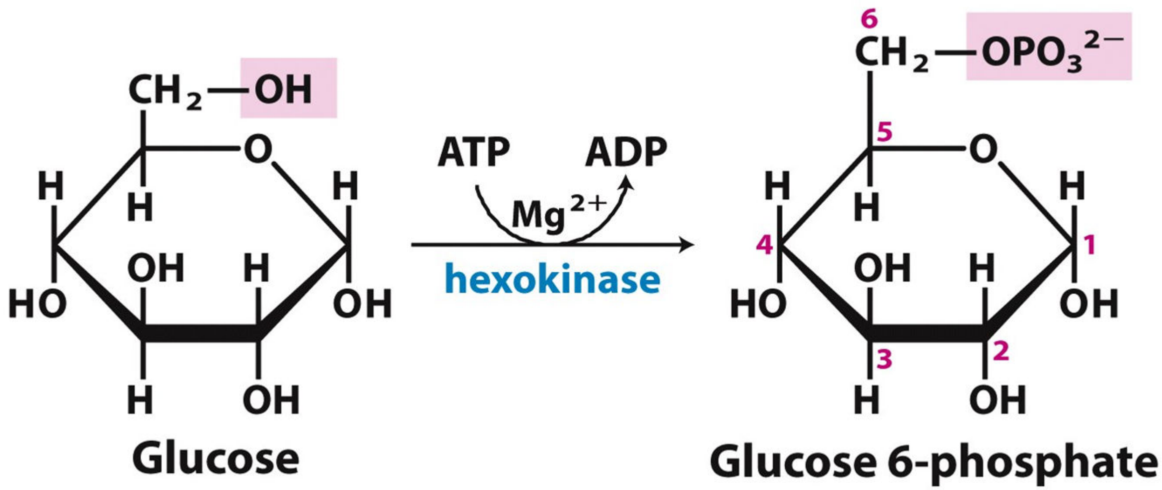
TABLE 13–5	Adenine Nucleotide, Inorganic Phosphate, and Phosphocreatine Concentrations in Some Cells				
	Concentration (mM)*				
	ATP	ADP†	AMP	P_i	PCr
Rat hepatocyte	3.38	1.32	0.29	4.8	0
Rat myocyte	8.05	0.93	0.04	8.05	28
Rat neuron	2.59	0.73	0.06	2.72	4.7
Human erythrocyte	2.25	0.25	0.02	1.65	0
E. coli cell	7.90	1.04	0.82	7.9	0

For practice: Calculate the ΔG of ATP hydrolysis in *E. coli*

ATP binding and hydrolysis drives muscle contraction



Phosphoryl transfer from ATP drives many reactions (via coupling)

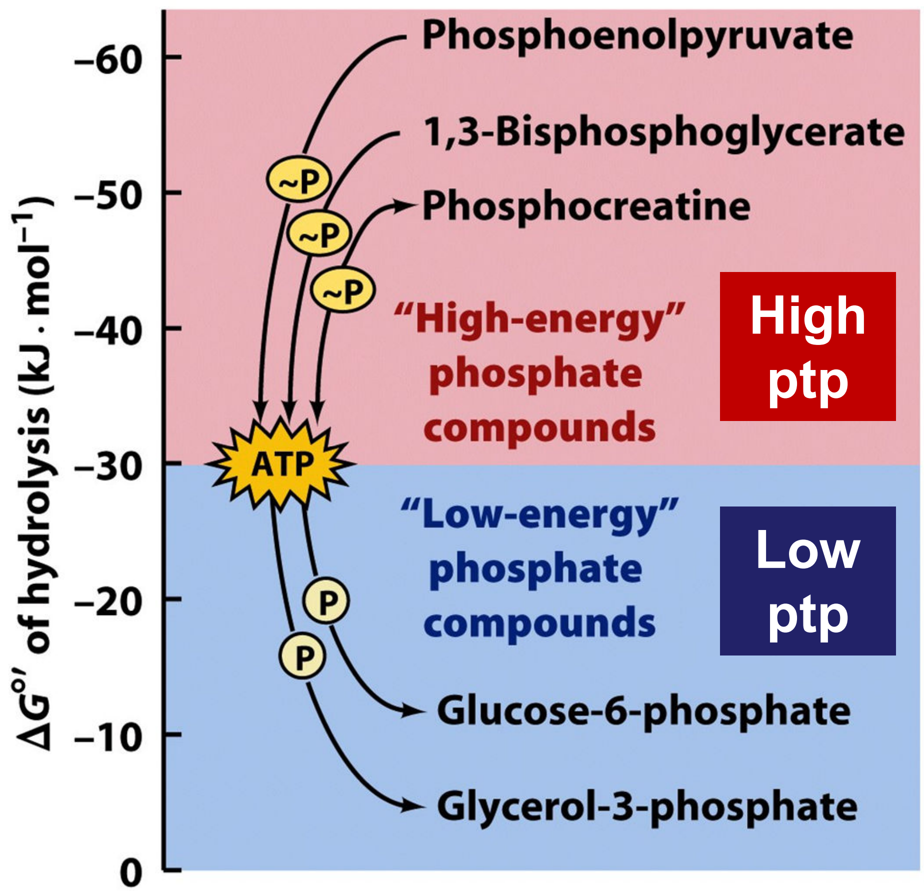


ΔG's are additive

				$G^{\circ\prime}$ (kJ·mol^{-1})
Endergonic half-reaction 1	P_i + glucose	$\rightleftharpoons$	glucose-6-P + H_2O	+13.8
Exergonic half-reaction 2	ATP + H_2O	$\rightleftharpoons$	ADP + P_i	–30.5
Overall coupled reaction	ATP + glucose	$\rightleftharpoons$	ADP + glucose-6-P	–16.7

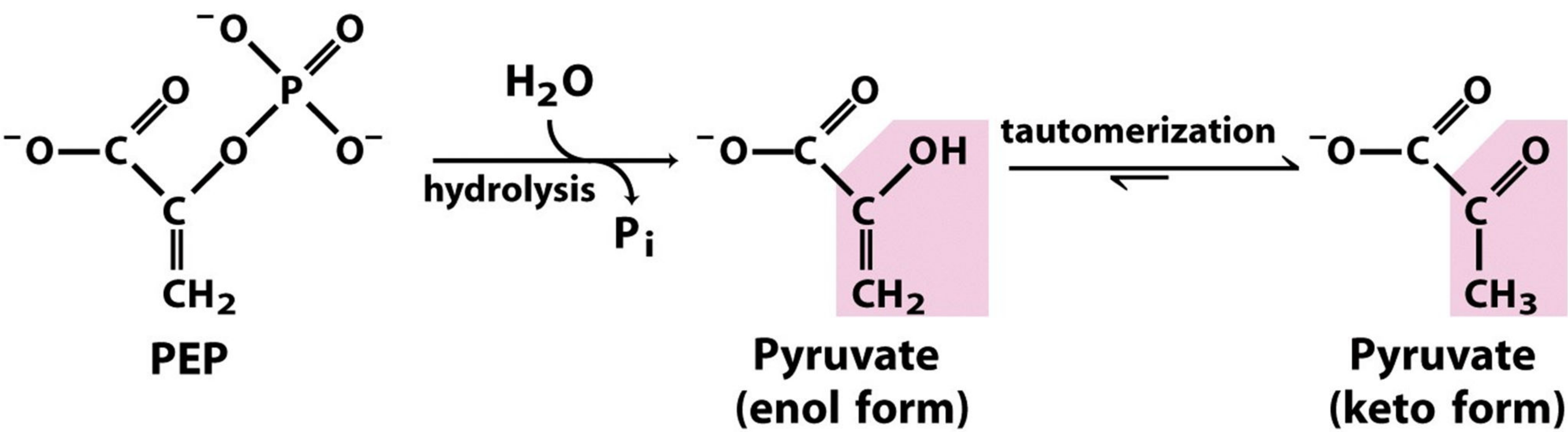
ΔG'° values of phosphate hydrolysis reflect ‘phosphoryl transfer potential’ (ptp)

Compound	$\Delta G^{\circ\prime}$ (kJ · mol^{-1})
Phosphoenolpyruvate	−61.9
1,3-Bisphosphoglycerate	−49.4
ATP (→ AMP + PP_i)	−45.6
Acetyl phosphate	−43.1
Phosphocreatine	−43.1
ATP (→ ADP + P_i)	−30.5
Glucose-1-phosphate	−20.9
PP_i	−19.2
Fructose-6-phosphate	−13.8
Glucose-6-phosphate	−13.8
Glycerol-3-phosphate	−9.2



Other ‘high-energy phosphate’ compounds have great stabilization of hydrolysis products

Reduced charge repulsion and tautomerization:

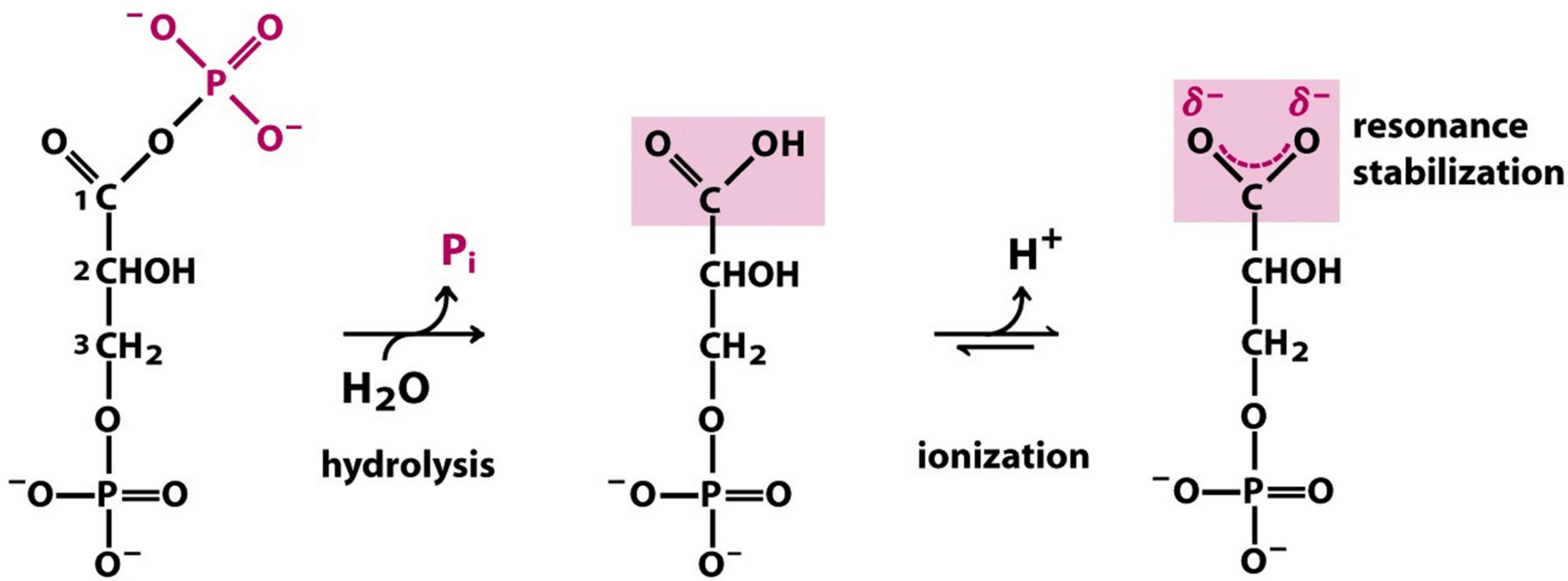


$$PEP^{3-} + H_2O \longrightarrow pyruvate^{-} + P_i^{2-}$$

$$\Delta G'^{\circ} = -61.9\ kJ/mol$$

Other ‘high-energy phosphate’ compounds have great stabilization of hydrolysis products

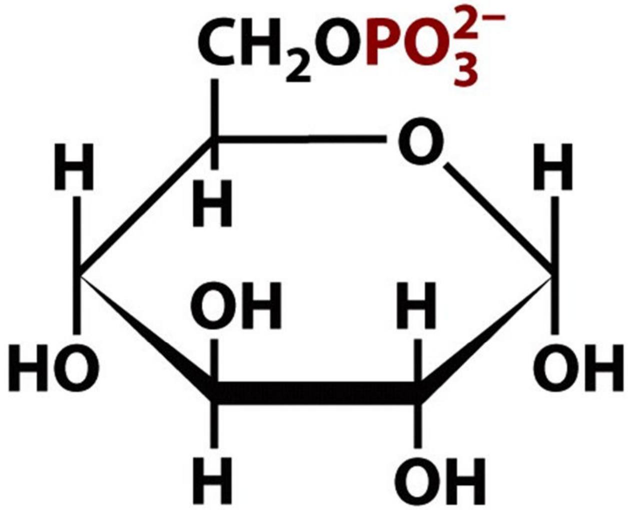
Reduced charge repulsion and resonance stabilization:



1,3-Bisphosphoglycerate — 3-Phosphoglyceric acid — 3-Phosphoglycerate

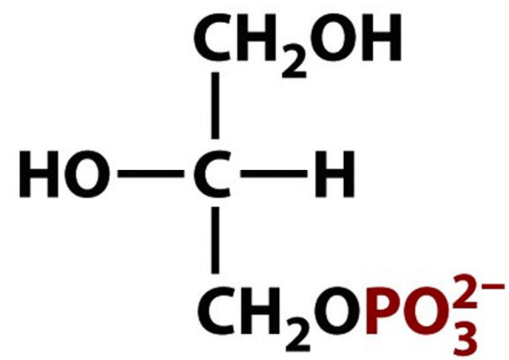
$$\text{1,3-Bisphosphoglycerate}^{4-} + H_2O \longrightarrow \text{3-phosphoglycerate}^{3-} + P_i^{2-} + H^+$$
$$\Delta G'^{\circ} = -49.3\ \text{kJ/mol}$$

‘Low-energy phosphate’ compounds have less stabilization of hydrolysis products



α-D-Glucose-6-phosphate

ΔG'° of hydrolysis:
-13.8 kJ/mol



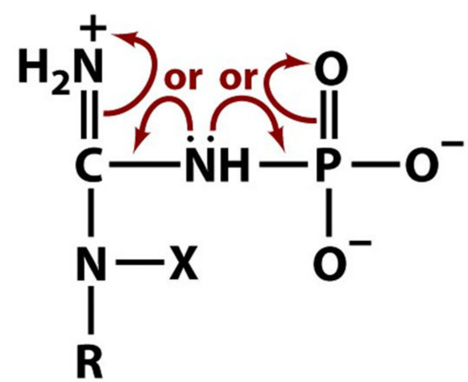
L-Glycerol-3-phosphate

ΔG'° of hydrolysis:
-9.2 kJ/mol

Phosphagens are ‘high-energy phosphate’ compounds used to quickly regenerate ATP

ex: **ADP + phosphocreatine ↔ ATP + creatine**

$\Delta G'° = -12.5$ kJ/mol



$R = CH_2—CO_2^-$; $X = CH_3$ **Phosphocreatine**

$R = CH_2—CH_2—CH_2—CH(NH_3^+)—CO_2^-$; $X = H$ **Phosphoarginine**

ATP may transfer additional functional groups (pyrophosphoryl or adenylyl)

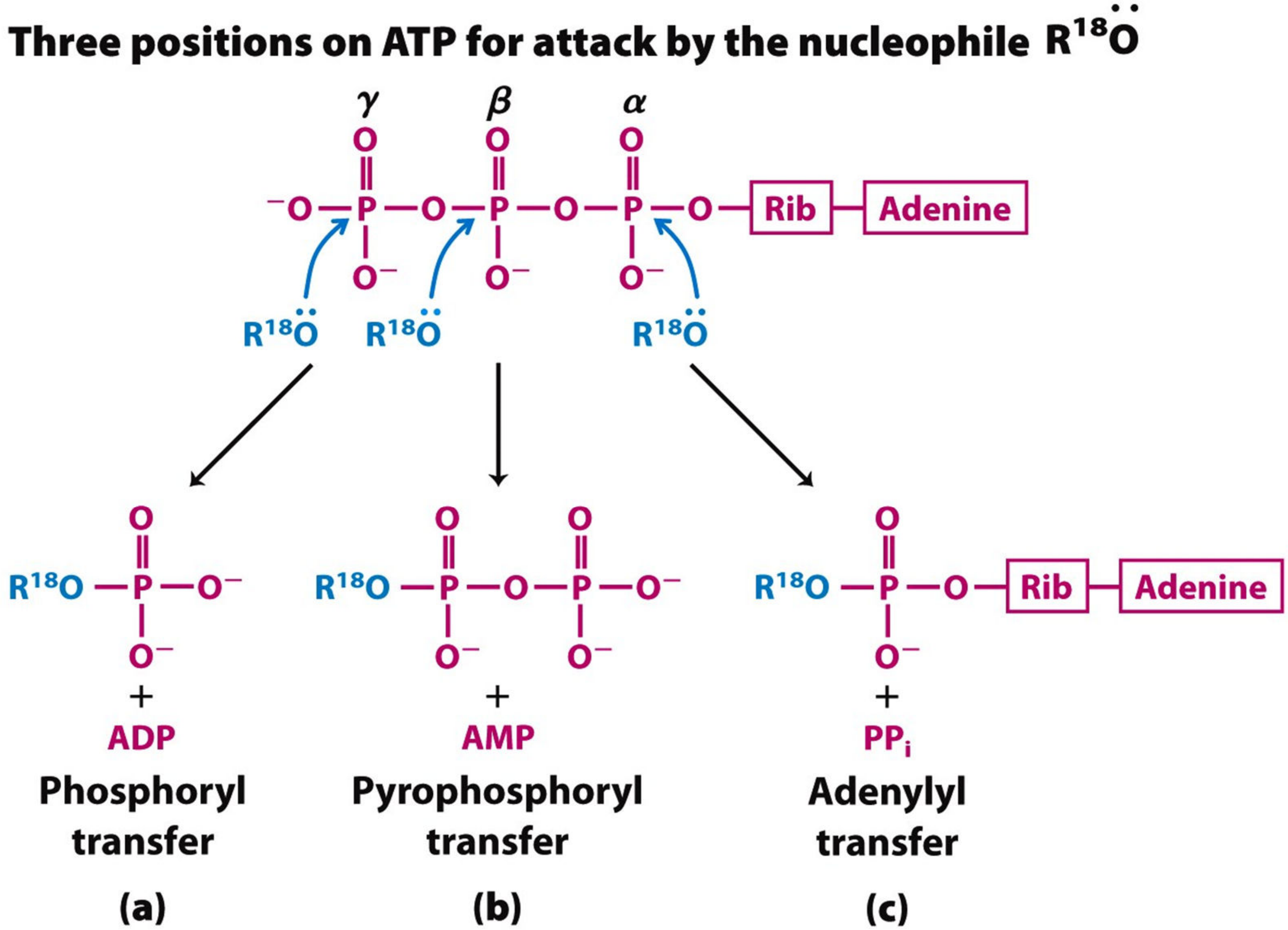
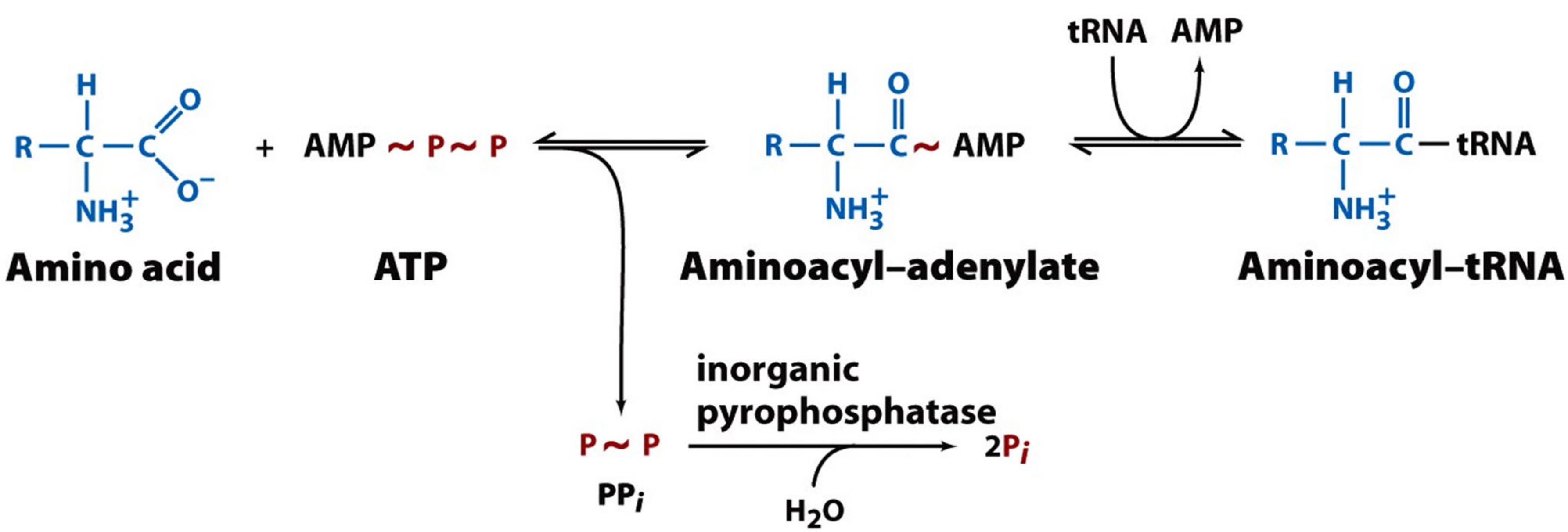


Figure 13-20
Lehninger Principles of Biochemistry, Fifth Edition

Adenylyl transfer is used to drive particularly disfavored reactions

Ex: activating amino acids for protein synthesis



ATP hydrolysis to AMP & PP_i: $\Delta G'° = -45.6$ kJ/mol

PP_i hydrolysis to $2P_i$: $\Delta G'° = -19.2$ kJ/mol

Transphosphorylations between nucleotides control relative concentrations

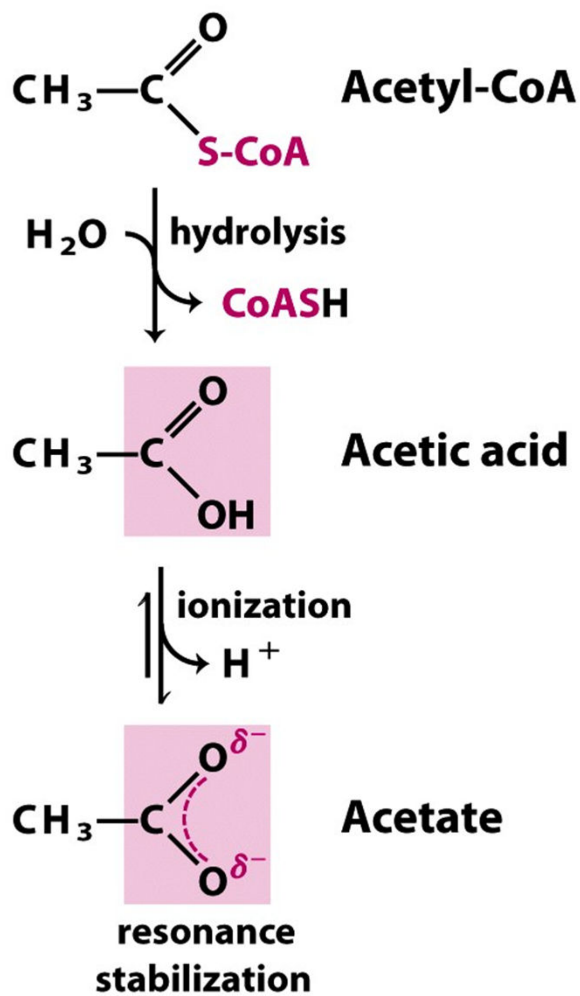
Nucleoside diphosphate kinase:

$$\underset{}{ATP} + \underset{(dNDP)}{NDP} \leftrightarrow ADP + \underset{(dNTP)}{NTP} \qquad \Delta G'^{\circ} \approx 0 \text{ kJ/mol}$$

Adenylate kinase:

$$2ADP \leftrightarrow ATP + AMP \qquad \Delta G'^{\circ} \approx 0 \text{ kJ/mol}$$

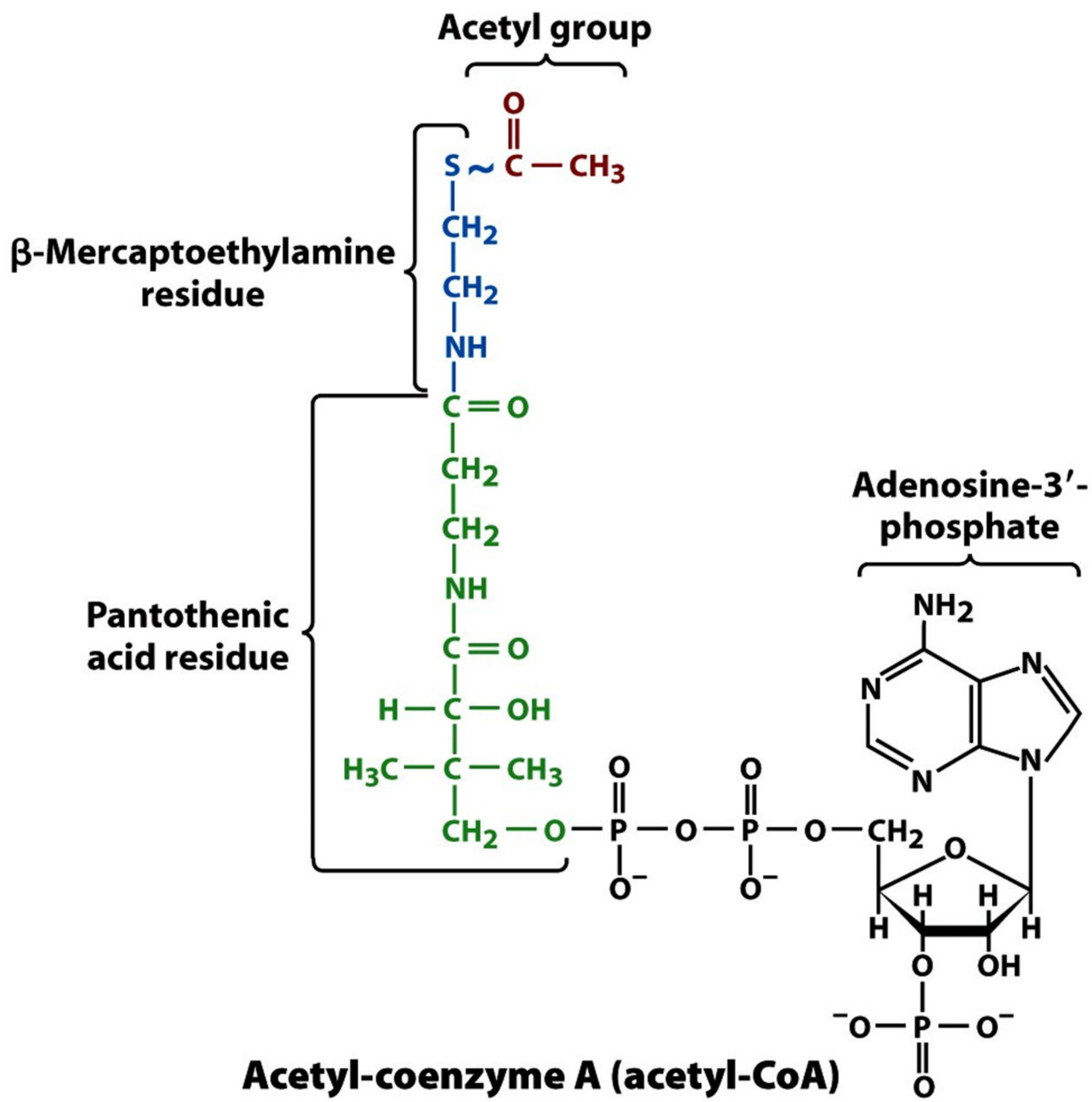
Thioesters also serve as energy currencies, due to large, negative ΔG'° of hydrolysis



Similar ΔG'° of hydrolysis as ATP

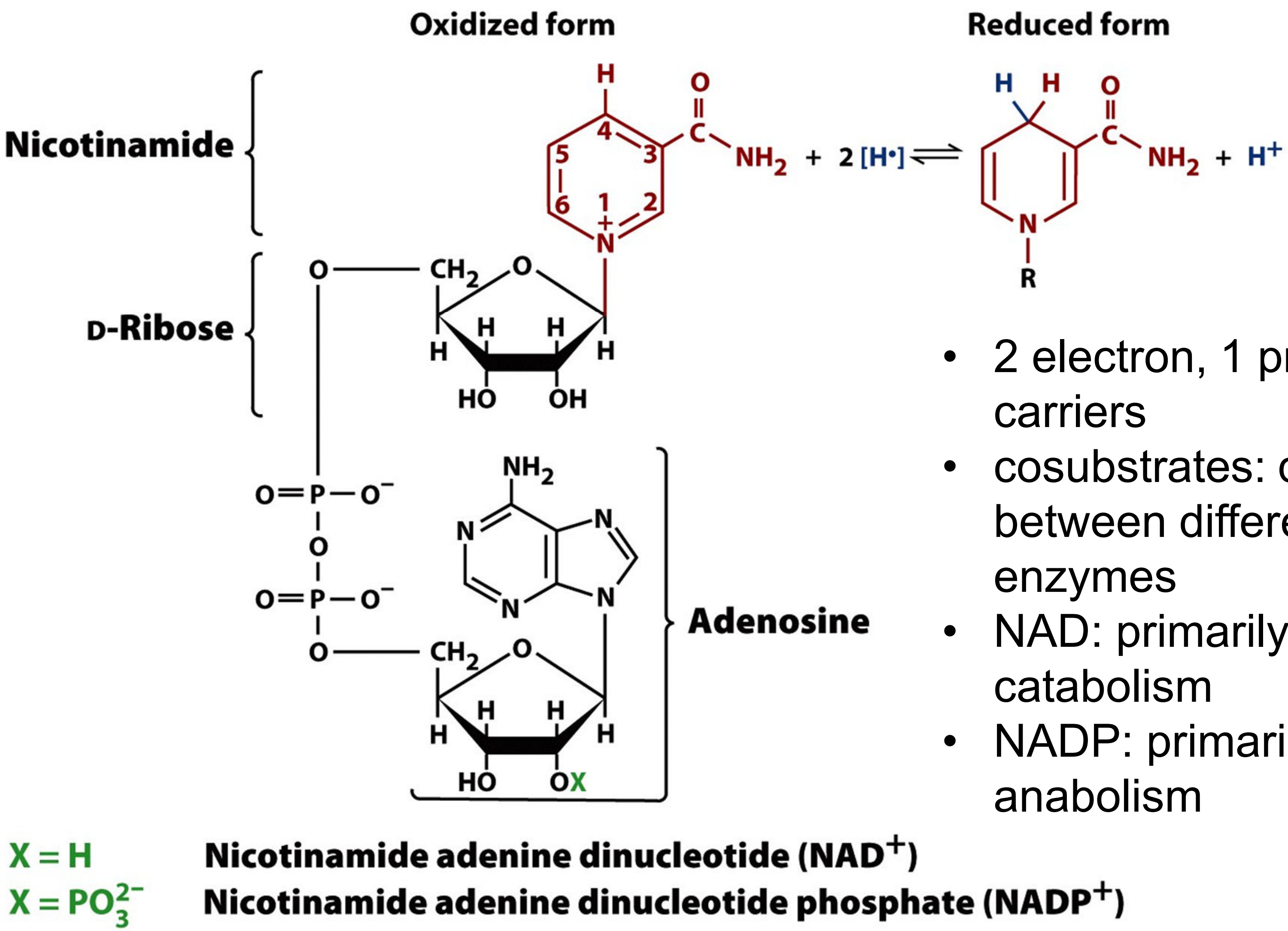
$$\text{Acetyl-CoA} + H_2O \longrightarrow \text{acetate}^- + \text{CoA} + H^+$$
$$\Delta G'^\circ = -31.4 \text{ kJ/mol}$$

Coenzyme A functions as an acyl-carrier cofactor and thioester energy currency



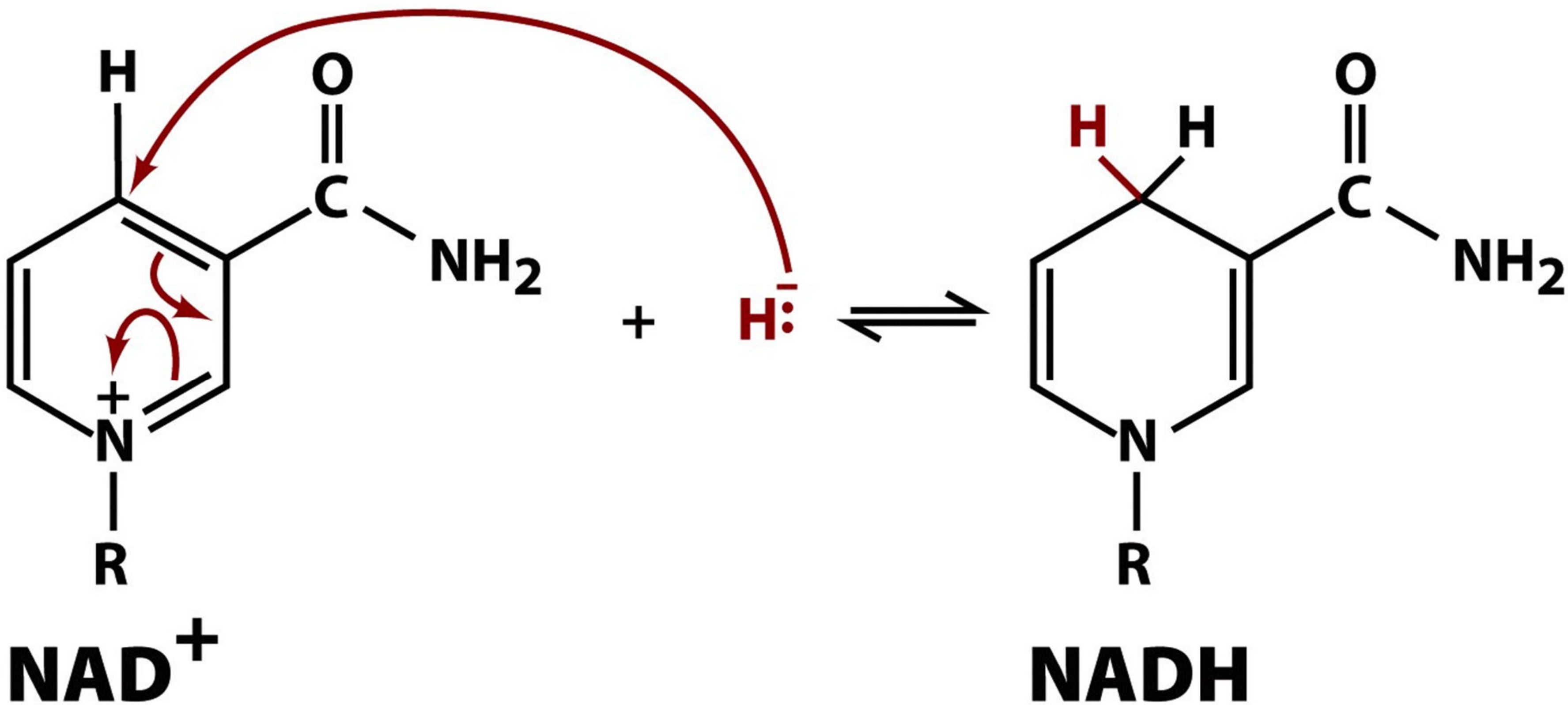
Acetyl-coenzyme A (acetyl-CoA)

Redox energy currencies transfer reducing power (ex: NAD and NADP)

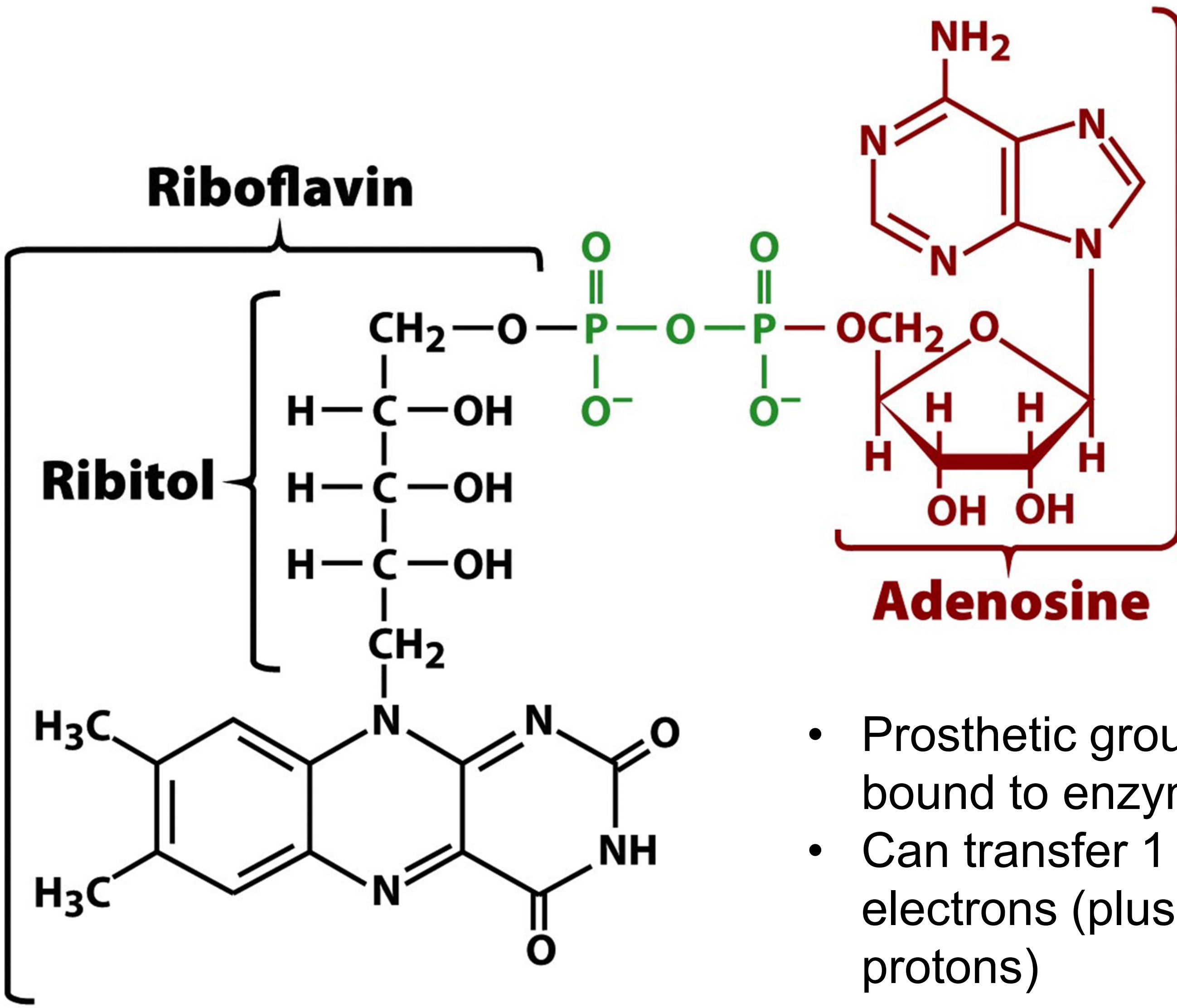


- 2 electron, 1 proton carriers
- cosubstrates: diffuse between different enzymes
- NAD: primarily used in catabolism
- NADP: primarily used in anabolism

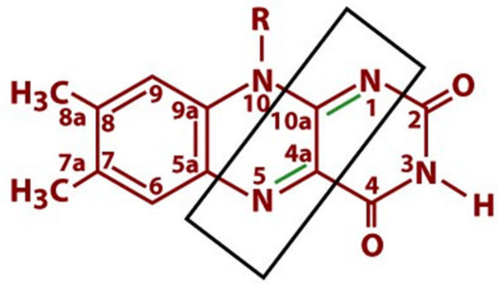
NAD+ accepts a hydride ion to become NADH



FAD and FMN are other redox currencies

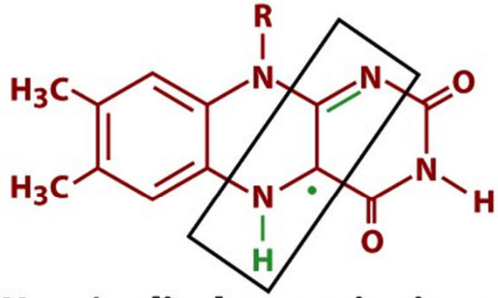


- Prosthetic groups: tightly bound to enzyme
- Can transfer 1 or 2 electrons (plus 1 or 2 protons)



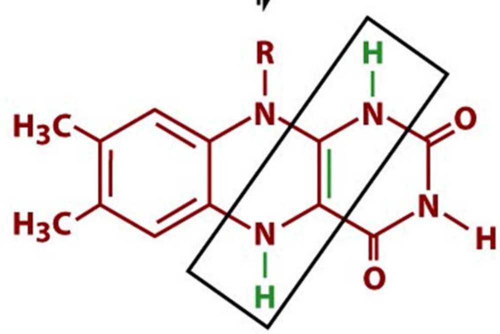
Flavin adenine dinucleotide (FAD)
(oxidized or quinone form)

⇌ H•



FADH · (radical or semiquinone form)

⇌ H•



$FADH_2$ (reduced or hydroquinone form)