BACKGROUND

BIOENERGETICS

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

ΔG = *Gibbs free energy*
energy available to do work
ΔH = *enthalpy*
energy associated with changes in bond energies, solvation
ΔS = *entropy*
changes in degree of disorder

If ΔG = - exergonic, rxn goes spontaneously
energy available to do work

If ΔG = + endergonic, rxn requies energy
no energy available to do work

$\Delta G^{o\prime}$ = Standard free energy at physiological pH 7.0

BACKGROUND

$$\boxed{A + B = C + D}$$

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

$$\Delta G = (G_{C} + G_{D}) - (G_{A} + G_{B}) = \Sigma G_{P} - \Sigma G_{R}$$

$$\Delta H = (H_{C} + H_{D}) - (H_{A} + H_{B}) = \Sigma H_{P} - \Sigma H_{R}$$

$$\Delta S = (S_{C} + S_{D}) - (S_{A} + S_{B}) = \Sigma S_{P} - \Sigma S_{R}$$

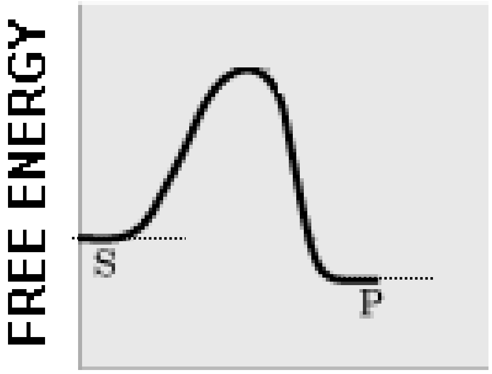
Standard versus Physiological Conditions

Quantity	Standard Conditions	Physiological Conditions
Solution	1.0 m	1.0 M
Gas	1.0 atm	1.0 atm
$[H^+]$	1.0 M pH 0.0	1.0×10^{-7} M pH 7.0
T	298K (25 °C)	298K (25 °C)
H_2O	1.0 M	1.0 M

R = 8.3145 J/mol/K (1.9872 cal/mol/K)

SIGN OF ΔG

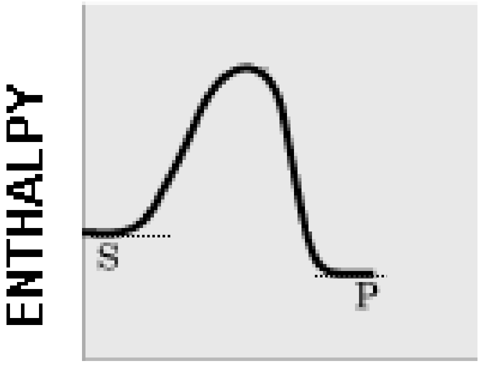
$$\Delta G = \Sigma G_P - \Sigma G_R$$



$\Delta G =$ [✓ -]

SIGN OF ΔH

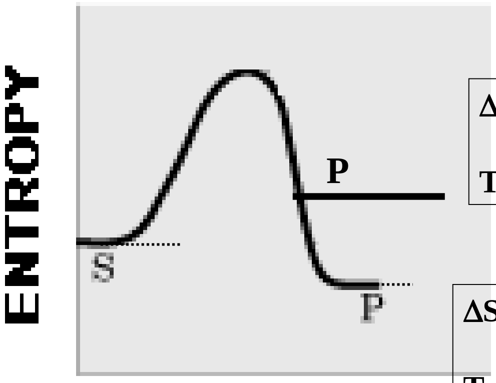
$$\Delta H = \Sigma H_P - \Sigma H_R$$



ΔH = ⊖

SIGN OF ΔS

$$\Delta S = \Sigma S_P - \Sigma S_R$$



ΔS = ⊕

T ΔS -

ΔS = ⊖

T ΔS +

TWO “TYPES” OF COUPLED REACTIONS

Hard!

ENERGY COUPLED REACTIONS

			$\Delta G^{o\prime}$ kJ/mole (kcal mole)
endergonic:	Pi + glucose	→ glucose-6-Pi + H_2O	+13.8 (+3.3)
exergonic:	ATP + H_2O	→ ADP + Pi	-30.5 (-7.5)
OVERALL:	ATP +glucose	→ ADP + glucose-6-Pi	-16.7 (-4.0)

(enzyme "coupling agent": hexokinase or glucokinase)

INTERMEDIATE COUPLED REACTIONS

Easy!

		Free Energy	K_{eq}
	$A + B \rightleftharpoons C + D$	ΔG_1	K_1
	$C + D \rightleftharpoons E + F$	ΔG_2	K_2
OVERALL:	$A + B \rightleftharpoons E + F$	$\Delta G_{overall} = \Delta G_1 + \Delta G_2$	

$K_{overall} = K_1K_2$

INTERMEDIATE COUPLED REACTIONS

INTERMEDIATE COUPLED REACTIONS

		Free Energy	K_{eq}
	$A + B \rightleftharpoons C + D$	ΔG_1	K_1
	$C + D \rightleftharpoons E + F$	ΔG_2	K_2
OVERALL:	$A + B \rightleftharpoons E + F$	$\Delta G_{overall} = \Delta G_1 + \Delta G_2$	

A,B,C,D, etc are intermediates in metabolic pathways

$K_{overall} = K_1K_2$

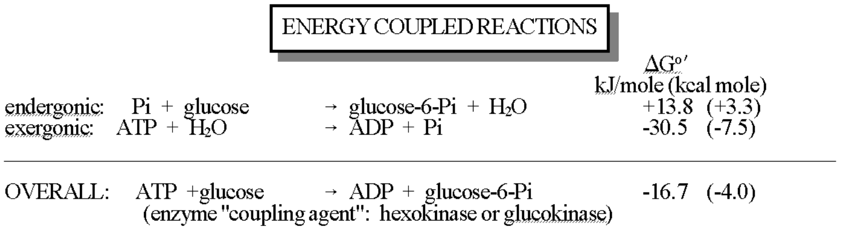
Glucose + ATP → ~~glucose-6-Pi~~ + ADP K_1

~~glucose-6-Pi~~ ⇌ ~~fructose-6-Pi~~ K_2

~~fructose-6-Pi~~ + ATP → fructose-1,6-bisphosphate (FBP) K_3

OVERALL: Glucose + 2 ATP → FBP + 2ADP $K_1K_2K_3$

ENERGY COUPLED REACTIONS



ENERGY COUPLED REACTIONS

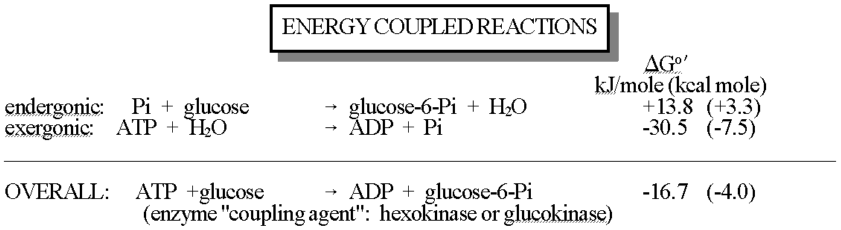
			$\Delta G^{o\prime}$ kJ/mole (kcal mole)
endergonic:	Pi + glucose	→ glucose-6-Pi + H_2O	+13.8 (+3.3)
exergonic:	ATP + H_2O	→ ADP + Pi	-30.5 (-7.5)
OVERALL:	ATP +glucose	→ ADP + glucose-6-Pi	-16.7 (-4.0)

(enzyme "coupling agent": hexokinase or glucokinase)

Note the following:

1. **Endergonic reaction as written is not occurring!**
2. **Exergonic reaction as written is not occurring!**
3. **OVERALL REACTION AS WRITTEN IS OCCURRING in the active site of an enzyme**
4. **THE ENZYME IS THE ‘COUPLING’ AGENT!**

ENERGY COUPLED REACTIONS



ENERGY COUPLED REACTIONS

			$\Delta G^{o\prime}$ kJ/mole (kcal mole)
endergonic:	Pi + glucose	→ glucose-6-Pi + H_2O	+13.8 (+3.3)
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OVERALL:	ATP +glucose	→ ADP + glucose-6-Pi	-16.7 (-4.0)

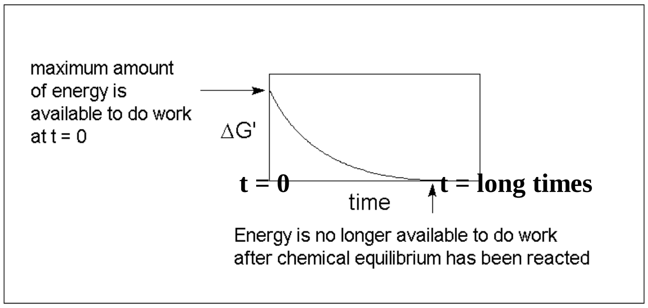
(enzyme "coupling agent": hexokinase or glucokinase)

Note the following:

Without the enzyme, the energy provided by ATP would be lost as heat and entropy as the ATP is hydrolyzed!!!

Maximum Energy Available: t = 0

FREE ENERGY CHANGES



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

$$\Delta G' = \Delta G^{\circ\prime} + 2.303 \cdot R \cdot T \cdot \log \frac{[C][D]}{[A][B]}$$

Energy to do work	Standard Energy (pH 7.0)	Correction term for nonstandard starting conditions

---

Difference between $\Delta G'$ and $\Delta G^{0'}$

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

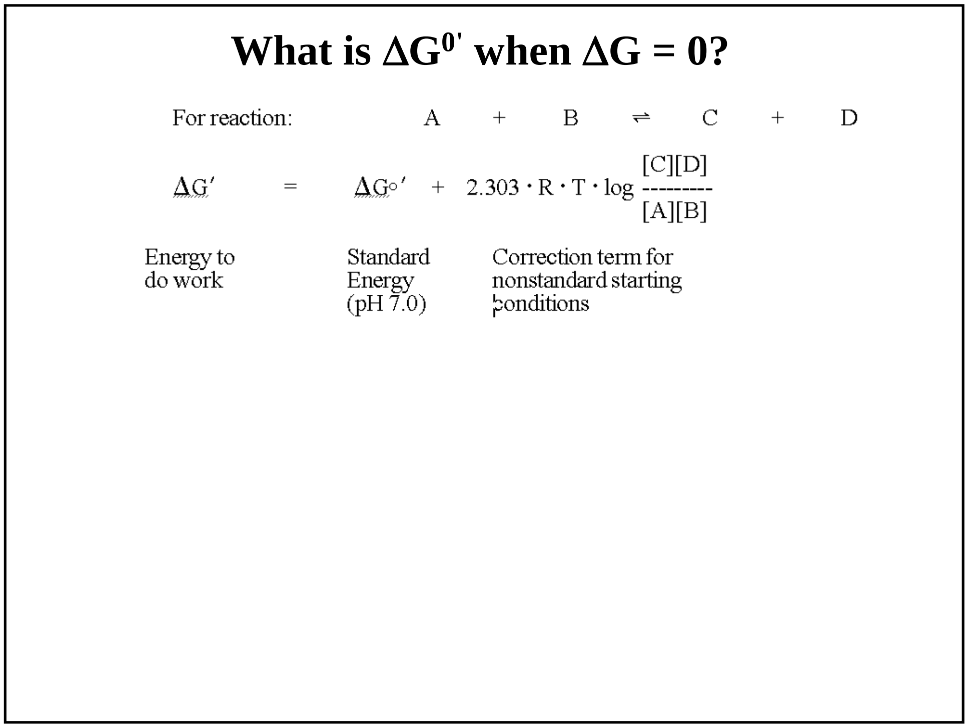
$$\Delta G' = \boxed{\Delta G^{\circ\prime} +} \boxed{2.303 \cdot R \cdot T \cdot \log \frac{[C][D]}{[A][B]}}$$

Energy to do work	Standard Energy (pH 7.0)	Correction term for nonstandard starting conditions

$\Delta G^{0'}$ determined in the laboratory

Don’t memorize!

Use conditions of reaction to find the sign and magnitude of this correction term

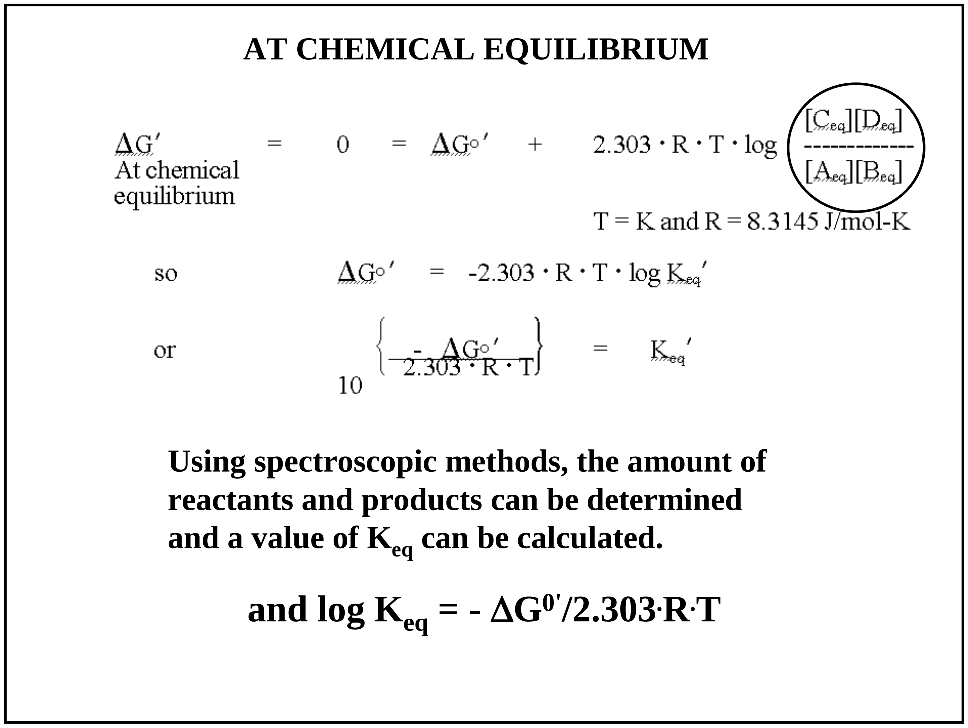


What is $\Delta G^{0'}$ when $\Delta G = 0$?

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

$$\Delta G' = \Delta G^{\circ\prime} + 2.303 \cdot R \cdot T \cdot \log \frac{[C][D]}{[A][B]}$$

Energy to do work	Standard Energy (pH 7.0)	Correction term for nonstandard starting conditions



AT CHEMICAL EQUILIBRIUM

$$\Delta G' = 0 = \Delta G^{\circ\prime} + 2.303 \cdot R \cdot T \cdot \log \frac{[C_{eq}][D_{eq}]}{[A_{eq}][B_{eq}]}$$

$\Delta G'$ At chemical equilibrium

T = K and R = 8.3145 J/mol-K

so $$\Delta G^{\circ\prime} = -2.303 \cdot R \cdot T \cdot \log K_{eq}'$$

or $$10^{\left\{\frac{-\Delta G^{\circ\prime}}{2.303 \cdot R \cdot T}\right\}} = K_{eq}'$$

Using spectroscopic methods, the amount of reactants and products can be determined and a value of K_{eq} can be calculated.

and $\log K_{eq} = -\Delta G^{0'}/2.303 \cdot R \cdot T$

SIGN OF $\Delta G^{0'}$ AND MAGNITUDE OF K_{eq}

or $$10^{\left\{\frac{-\Delta G^{\circ\prime}}{2.303 \cdot R \cdot T}\right\}} = K_{eq}'$$

Case I:
If $\Delta G^{\circ\prime}$ is ⊖, then $\{\log K_{eq}'\}$ is ⊕ and $K_{eq}' > 1.0$

Case 2:
If $\Delta G^{\circ\prime}$ is ⊕, then $\{\log K_{eq}'\}$ is ⊖ and $K_{eq}' < 1.0$

EXTENT OF REACTION

EXTENT OF REACTION
$A + B \rightleftharpoons C + D$

$\Delta G^{\circ\prime}$ kJ/mol	K_{eq}' (no units for reaction above)	Extent of Reaction is toward.....
+17.1	10^{-3}	.....toward reactants
+11.4	10^{-2}	.....toward reactants
+5.7	10^{-1}	.....toward reactants
0	1.0	.....equal products and reactants
-5.7	10^{1}	.....toward products
-11.4	10^{2}	.....toward products
-17.1	10^{3}	.....toward products

Special case where $\Delta G^{0'} = 0$ so $K_{eq} = 1.0$ **Does not mean that $\Delta G'$ has to be zero nor that rxn is at chemical equilibrium**

FIRST NOTE

Reactions that have $\Delta G^{\circ\prime}$ values of greater and more negative than -17.1 are highly exergonic. They are said to be HIGHLY FAVORABLE and most likely to go extensively to product even under physiological conditions that may reduce the magnitude of $\Delta G'$

Example in glycolysis:

pyruvate + NADH + H^+ → lactate + NAD^+ $\Delta G^{\circ\prime}$ = -25 kJ/mole

(Important in anaerobic glycolysis to regenerate NAD^+)
(Pyruvate is directed into citric acid cycle under aerobic conditions)

SECOND NOTE

Reactions that have $\Delta G^{\circ\prime}$ values of greater and and more positive than +17.1 are highly endergonic. They are said to be HIGHLY UNFAVORABLE. However, this does not mean that no product forms. It means that only a small of product forms. These types of reactions can be driven to completion by removing the product(s) in a subsequent reaction or reactions that are hightly favorable.

Example in glycolysis:

Fructose-1,6-bisphosphate ⇌ DHAP + 3GAP $\Delta G^{\circ\prime}$ = +23.8 kJ/mole

(This is a highly unfavorable reaction that is essentially “driven” to completion by removing the DHAP and 3GAP in the subsequent more favorable steps in glycolysis)

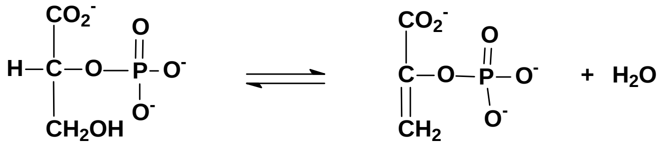
THIRD NOTE

When a reaction has a value of $\Delta G^{\circ\prime} = 0$, it does not mean that that reaction is at equilibrium. It only means that the value for K_{eq}' for that reaction is 1.0. The reaction has no energy available to do work under standard conditions, but may have energy available to do work under physiological conditions as long as the value of $\Delta G'$ is negative!

---

1 - Problem illustrating the difference between $\Delta G'$ and $\Delta G^{0'}$

$$2PG \rightleftharpoons PEP + H_2O \quad K_{eq} = 0.476\ M$$



2-phosphoglycerate
2PG

phosphoenol pyruvate
PEP

What is $\Delta G^{0'}$?

R = 8.3145 J/mol/K

T = 298 K

$$\text{What is } \Delta G^{0'} = -2.303 \cdot R \cdot T \cdot \log K_{eq}$$

$$= -2.303 \cdot R \cdot T \cdot (-0.3223)$$

Carry extra digit

$$= +\ 1839\ \text{J/mol}\ \ (1840\ \text{J/mol if answer})$$

Carry extra digit if used in another calculation

2 - Problem illustrating the difference between $\Delta G'$ and $\Delta G^{0'}$

$$2PG \rightleftharpoons PEP + H_2O \quad K_{eq} = 0.476\ M$$

Given: 5.00 mM 1.00 mM

What are the 2PG and PEP concentrations at equilibrium and what is $\Delta G'$ (+ or -)? Is there net synthesis of product?

---

3 - Problem illustrating the difference between $\Delta G'$ and $\Delta G^{0'}$

$$2PG \rightleftharpoons PEP + H_2O \quad K_{eq} = 0.476\ M$$

Given: 5.00 mM 1.00 mM

let X = new PEP at equilibrium

At Eq: 5.00 mm –X 1.00 mm + X

$$K_{eq} = \frac{[PEP][H_2O]}{[2PG]} = 0.476\ M$$

$$K_{eq} = \frac{[1\ mM + X][1.0\ M]}{[5\ mm - X]} = 0.476\ M$$

4 - Problem illustrating the difference between $\Delta G'$ and $\Delta G^{0'}$

2PG ⇌ PEP + H_2O $K_{eq} = 0.476$ M

Given: 5.00 mM 1.00 mM

let X = new PEP at equilibrium

At Eq: 5.00 mm –X 1.00 mm + X

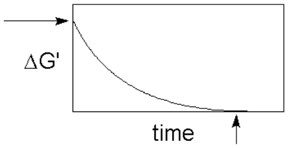
X = + 0.935 mM
positive solution
indicates net synthesis
of product

What must be sign of $\Delta G'$? –

5 - Problem illustrating the difference between $\Delta G'$ and $\Delta G^{0'}$

2PG ⇌ PEP + H_2O $K_{eq} = 0.476$ M

Given: 5.00 mM 1.00 mM



Calculate the value of $\Delta G'$!

Use initial values since $\Delta G' = 0$ at equilibrium!

$$\Delta G' = \Delta G^{0'} + 2.303\ R\ T \log \{[PEP][H_2O]/[2PG]\}$$

$$\Delta G' = \Delta G^{0'} + 2.303 * 8.3145 J/mol/K * 298K\ (-0.6990)$$

$$= +1839\ J/mol + (-3988\ J/mol) = -2150\ J/mol$$

Use extra sig fig as previously calc’d

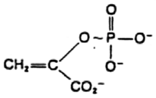
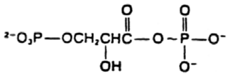
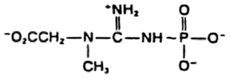
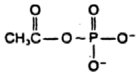
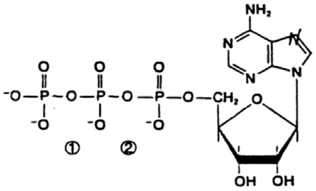
Correct sig fig

$\Delta G'$ = -

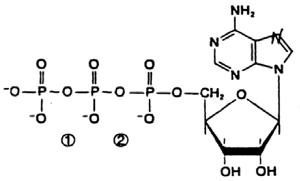
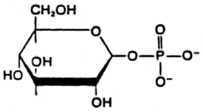
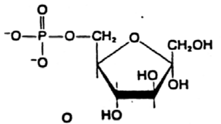
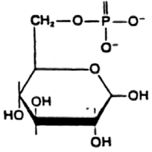
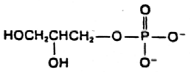
HIGH ENERGY PHOSHPATE COMPOUNDS

Some Organophosphates in Metabolism

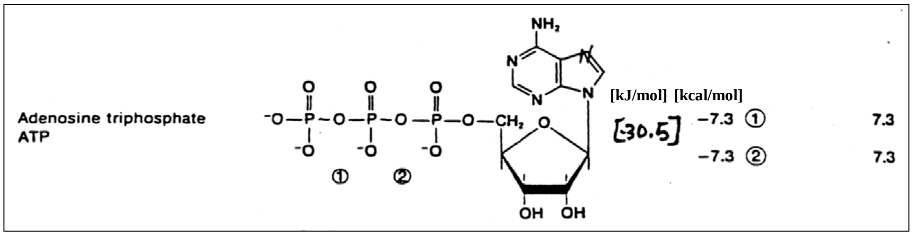
4.184 J = 1 cal

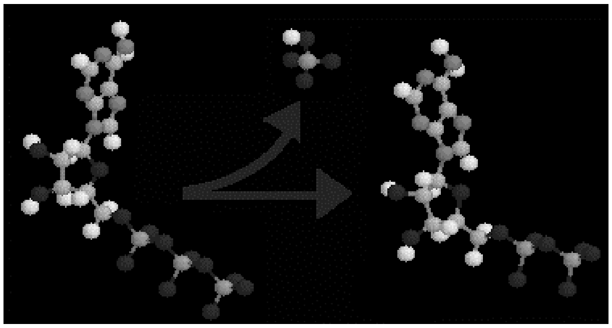
Phosphate	Structure^a	kJ/mol	Free Energy of Hydrolysis (ΔG°')^b (kcal/mol)	Phosphate Group Transfer Potential^c
Phosphoenolpyruvate		[-61.9]	−14.8	14.8
1,3-Diphosphoglycerate		[-49.4]	−11.8	11.8
Creatine phosphate		[-43.1]	−10.3	10.3
Acetyl phosphate			−10.1	10.1
Adenosine triphosphate ATP		[30.5]	−7.3 ①	7.3
			−7.3 ②	7.3

HIGH ENERGY PHOSHPATE COMPOUNDS

Phosphate	Structure	[kJ/mol]	[kcal/mol]	
Adenosine triphosphate ATP		[30.5]	−7.3 ①	7.3
			−7.3 ②	7.3
Glucose 1-phosphate		[20.9]	−5.0	5.0
Fructose 6-phosphate		[-15.9]	−3.8	3.8
Glucose 6-phosphate		[-13.8]	−3.3	3.3
Glycerol 3-phosphate		[-9.2]	−2.2	2.2

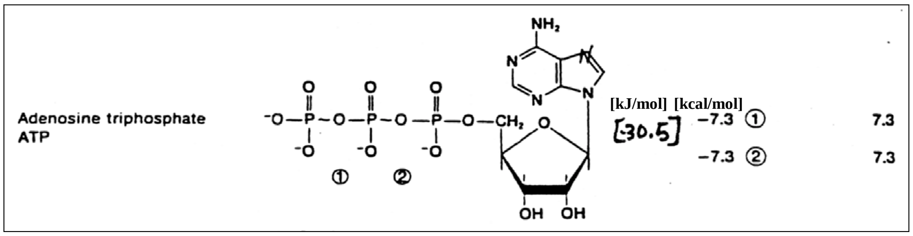
Why is $\Delta G^{0'}$ for ATP hydrolysis so large and negative?





http://www.life.uiuc.edu/crofts/bioph354/images/atp_adp.gif

Why is $\Delta G^{0'}$ for ATP hydrolysis so large and negative?



$$ATP^{-4} + H_2O \rightarrow ADP^{-3} + Pi^{-2} + H^+$$

$HATP^{3-} \rightleftharpoons ATP^{4-} + H^+$ $pK_1' = 6.95$

$HADP^{2-} \rightleftharpoons ADP^{3-} + H^+$ $pK_2' = 6.88$

Compare to:

6.75

$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$ $pK_a' =$ ~~7.20~~

http://www.life.uiuc.edu/crofts/bioph354/atp_hydrolysis.html

Why is $\Delta G^{0'}$ for ATP hydrolysis so large and negative?

$$ATP^{-4} + H_2O \rightarrow ADP^{-3} + Pi^{-2} + H^+$$

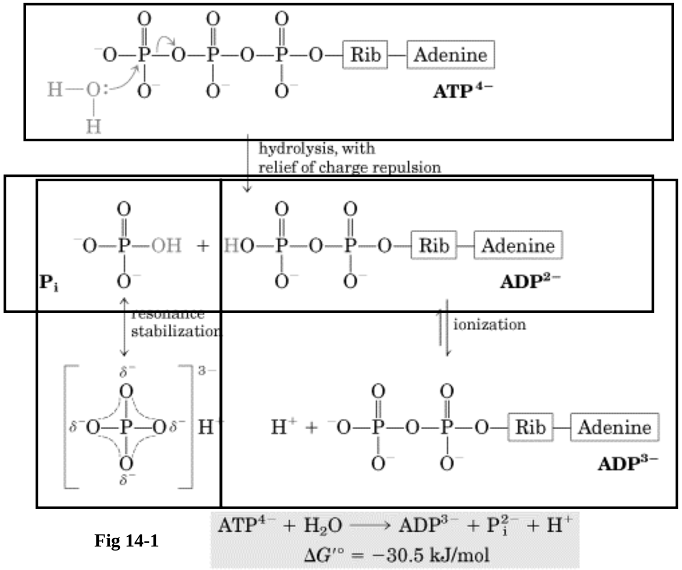
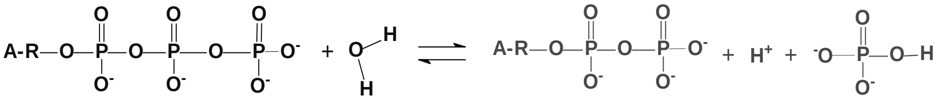


Fig 14-1

Summary of why $\Delta G^{0'}$ for ATP hydrolysis so large and negative

$$ATP^{-4} + H_2O \rightarrow ADP^{-3} + Pi^{-2} + H^+$$



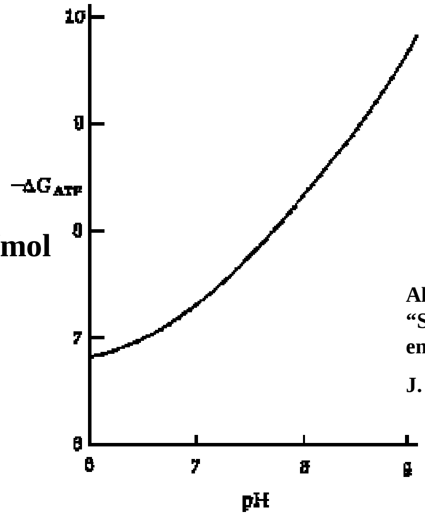
$$\text{A-R—O—}\overset{O}{\underset{O^-}{P}}\text{—O—}\overset{O}{\underset{O^-}{P}}\text{—O—}\overset{O}{\underset{O^-}{P}}\text{—O}^- + H_2O \rightleftharpoons \text{A-R—O—}\overset{O}{\underset{O^-}{P}}\text{—O—}\overset{O}{\underset{O^-}{P}}\text{—O}^- + H^+ + {}^-O\text{—}\overset{O}{\underset{O^-}{P}}\text{—O—H}$$

$\Delta H_{\text{charge repulsion}}$	Higher charge repulsion	Lower charge repulsion because of separation of charge	$\Delta H = -$
$\Delta H_{\text{solvation}}$	Fewer H_2O (24)	More H_2O (26)	$\Delta H = -$
ΔS	24 frozen H_2O	26 frozen H_2O	$\Delta S = -$
ΔS	One molecule	Two molecules + H^+	$\Delta S = +$
ΔS	Fewer ways to distribute negative charge	More ways to distribute negative charge	$\Delta S = +$

$+\Delta S$ contributes to $-\Delta G$ ($-T\Delta S$); $-\Delta S$ contributes to $+\Delta G$ ($-(T)(-\Delta S) = +$)

Explain the pH dependence of $\Delta G^{0'}$ for ATP

$ATP^{-4} + H_2O \rightarrow ADP^{-3} + Pi^{-2} + H^{+}$



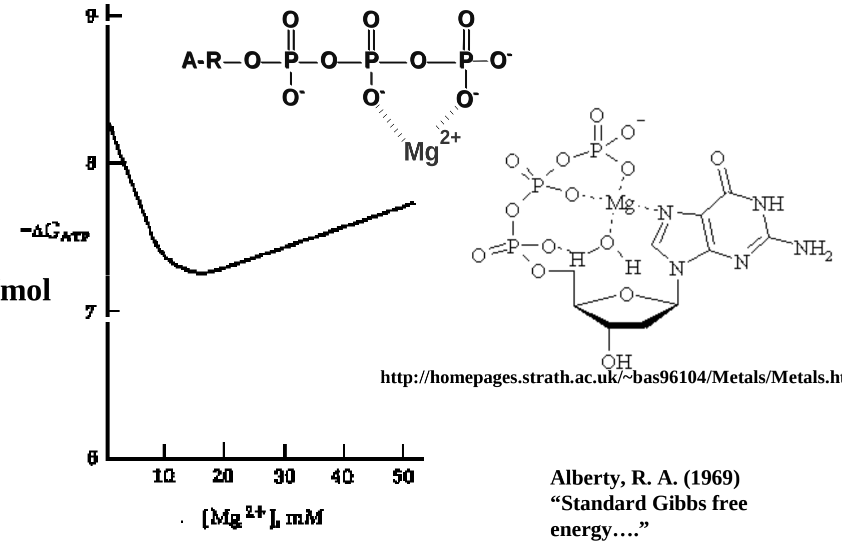
kcal/mol

Alberty, R. A. (1969) “Standard Gibbs free energy….”

J. Biol. Chem. 244, 3290-3302

http://www.life.uiuc.edu/crofts/bioph354/atp_ph.gif

Explain the Mg^{2+} dependence of $\Delta G^{0'}$ for ATP



kcal/mol

http://homepages.strath.ac.uk/~bas96104/Metals/Metals.htm

http://www.life.uiuc.edu/crofts/bioph354/atp_hydrolysis.html

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