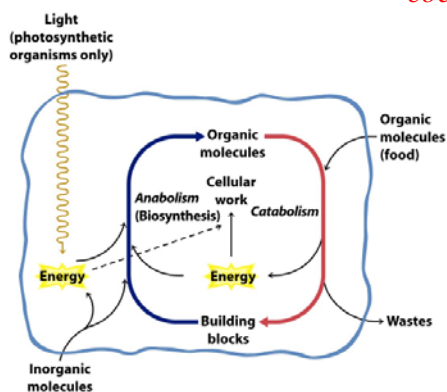
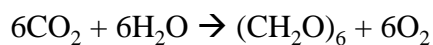


## Chapters 7 & 10    Bioenergetics

To live, organisms must obtain **energy** from their environment and use it to do the **work** of building and organizing cell components such as proteins, enzymes, nucleic acids, membranes, organelles ..... (*Ch. 10 on metabolism, Ch. 7 on coenzymes and vitamins*)



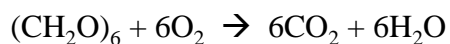
Photosynthetic **autotrophs** use the energy of sunlight to convert low-*G* CO<sub>2</sub> and H<sub>2</sub>O into energy-rich complex sugar molecules (*Ch. 10 p. 302*).



This reaction has a large positive  $\Delta H$  and a large negative  $\Delta S$ .

The products have more enthalpy and are more ordered than the reactants.

**Heterotrophs** extract the chemical potential energy stored in sugars and other organic compounds and release CO<sub>2</sub> and H<sub>2</sub>O.



This reaction has a large negative  $\Delta H$  and a large positive  $\Delta S$ .  
The products have lost energy and are less ordered.

The  $G$  is released slowly in many steps using several metabolic pathways.

For any (bio)chemical reaction recall that  $\Delta G = -RT \ln(K_{eq})$

where  $\Delta G = G_p - G_s$

$R = \text{Gas Constant} = 8.31 \text{ J/mol} \cdot \text{K}$ .       $T = \text{Temp in K}$ .

Under “*standard*” conditions:  $\Delta G^\circ = -RT \ln(K_{eq})$

$^\circ$  refers to  $25^\circ \text{C}$ ,  $55 \text{ M H}_2\text{O}$ ,  $[\text{reactant}] = 1\text{M}$

Biochemists prefer pH 7 to pH 0 where  $[\text{H}^+] = 1\text{M}$

$$\Delta G'^{\circ} = -RT \ln(K'_{eq})$$

where ' refers to pH = 7.

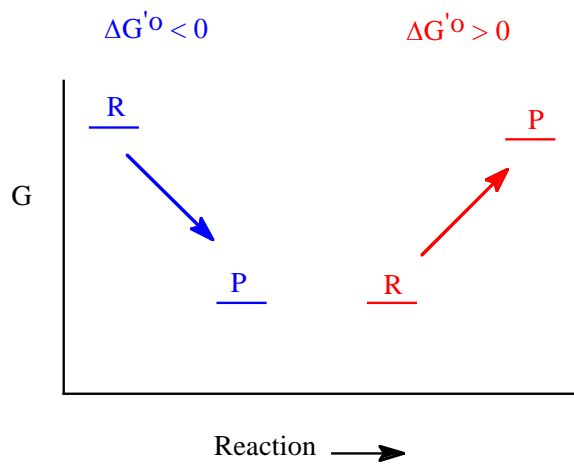
If  $K'_{eq} = 19$  at  $25^\circ\text{C}$  then,  $-RT \ln(K'_{eq}) =$

$$-(8.315 \text{ J/mol K})(298 \text{ K})(\ln 19) = -7,296 \text{ J/mol} = -7.3 \text{ kJ/mol}$$

If reactants and products are present at 1M we can predict the direction of the reaction:

$K'_{eq}$	$\Delta G'^{\circ}$	Direction
$> 1$	negative	Forward
$< 1$	positive	Reverse
$= 1$	0	–

When  $\Delta G'^o$  is **negative**, the products contain less  $G$  than the reactants.



When  $\Delta G'^o$  is **positive** the products contain more  $G$  than the reactants.

For a chemical reaction **at** equilibrium, the rates of the forward and reverse reactions are equal and no net change is occurring but no work can be done and  $\Delta G = 0$ .

For this reaction,  $\text{Glc-1-P} \xrightleftharpoons{\text{phosphoglucomutase}} \text{Glc-6-P}$

$$K'_{eq} = \frac{[\text{Glc-6-P}]}{[\text{Glc-1-P}]} = 19 \quad \Delta G'^o = -7.3 \text{ kJ/mol}$$

When  $[\text{Glc-6-P}] = [\text{Glc-1-P}] = 1 \text{ M}$ , the reaction will spontaneously convert Glc-1-P into Glc-6-P until equilibrium is established.



What if we add [Glc-1-P] @ 1 mM to [Glc-6-P] @ 100 mM?

The reaction will convert Glc-6-P into Glc-1-P to re-establish equilibrium.



The *actual*  $\Delta G$  under **non**-standard conditions for:



Is

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

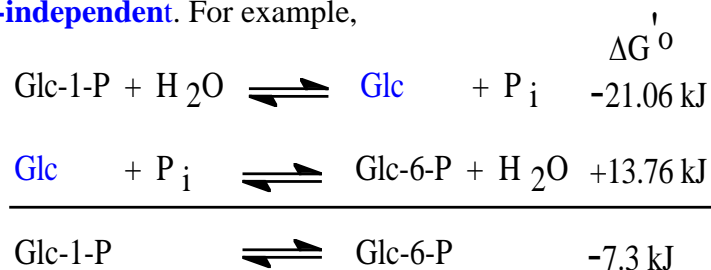
where the concentrations are “*actual*”.

**Notes:**

1. Both  $\Delta G$  and  $\Delta G'^{\circ}$  are *theoretical* maxima. Some G is always lost as heat.

2. Even if  $\Delta G'^{\circ}$  is positive, the reaction can go forward if  $\Delta G$  is negative. *i.e.* if the second term is negative and bigger than  $\Delta G'^{\circ}$ .

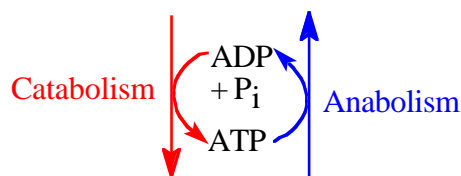
3.  $\Delta G$ 's of **sequential** reactions are additive because  $\Delta G$  is **path-independent**. For example,



The  $G$  released in 1 reaction can be used to drive a 2<sup>nd</sup> reaction as long as the two share a common intermediate. *E.g.* **Glc**

Nearly all of the  $G$  stored in carbohydrates, lipids, and AA transits through **ATP**, the cell's "*energy currency*", for use in building cell constituents and doing cellular work such as muscle contraction and active transport of molecules against concentration gradients.

So ATP is the common intermediate between **catabolism** and **anabolism**. ATP is **not** an energy storage molecule.



The **synthesis** of ATP is a highly endergonic reaction and the **hydrolysis** of ATP is a highly exergonic reaction.

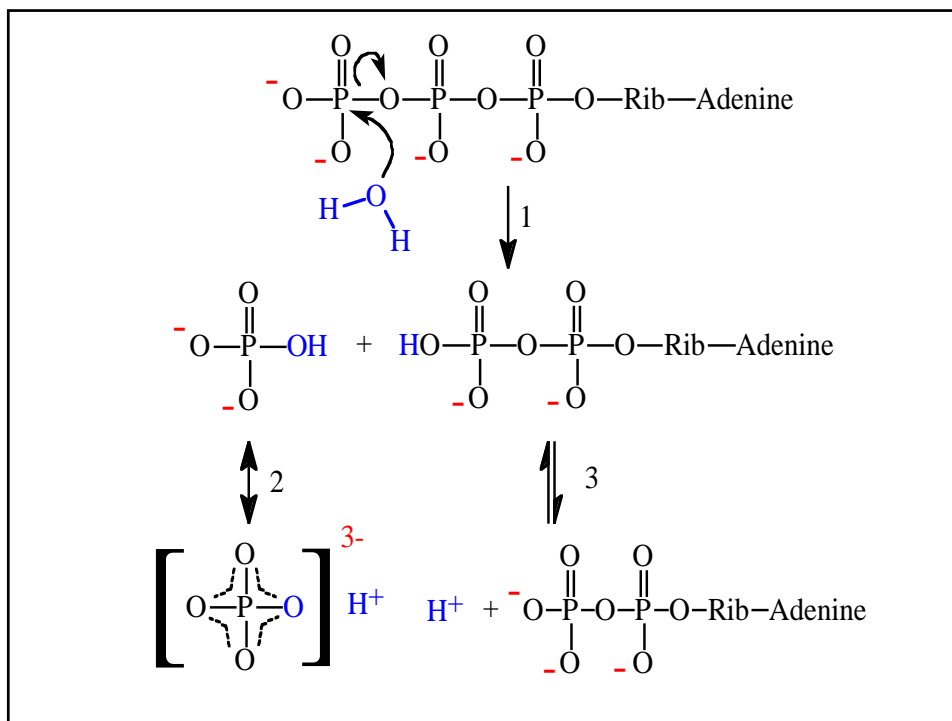


$$\Delta G'^0 = -30 \text{ kJ / mole}$$

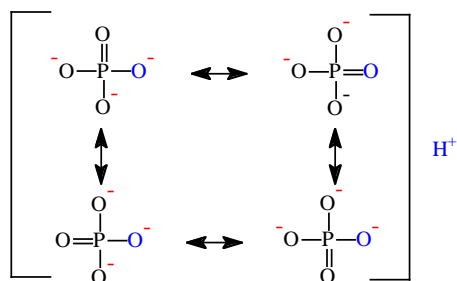
How does ATP store **chemical potential energy** or why does hydrolysis release this energy? There are 4 parts to the answer:

1. Relief of charge repulsion.

One molecule with 4 negative charges is converted into 2 molecules with 2 negative charges each.



2. There are more resonance forms of ADP + P<sub>i</sub> than of ATP, so there is an **entropy increase** due to hydrolysis.



3. Solvation of ADP + P<sub>i</sub> > the solvation of ATP which stabilizes the products relative to the reactants.

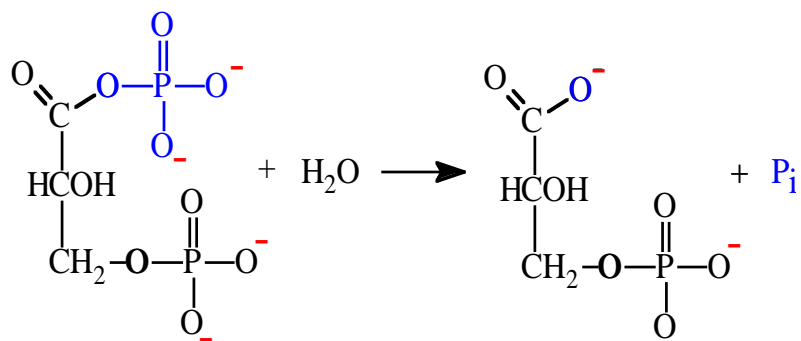
**Note:**

In cells, [ATP] ~ 2.25 mM; [ADP] ~ 0.25 mM; [P<sub>i</sub>] ~ 1.65 mM

These concentrations are far from standard. So “*actual*”  $\Delta G = -50$  to  $-65$  kJ / mole.

Other compounds have large negative  $\Delta G$  of hydrolysis for reasons similar to ATP:

## 1. 1,3 bis-phosphoglycerate

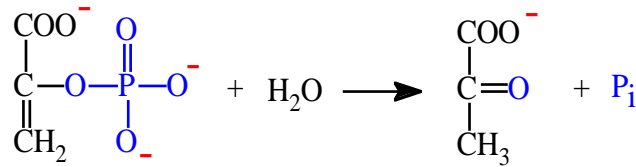


1,3 bis-phosphoglycerate

3-phosphoglycerate

$$\Delta G^{\circ} = -49 \text{ kJ/mol}$$

2.



Phosphoenolpyruvate

Pyruvate

$$\Delta G'^0 = -62 \text{ kJ/mol}$$

There is more than enough  $G$  released in the above two reactions to form ATP from ADP +  $\text{P}_i$ .

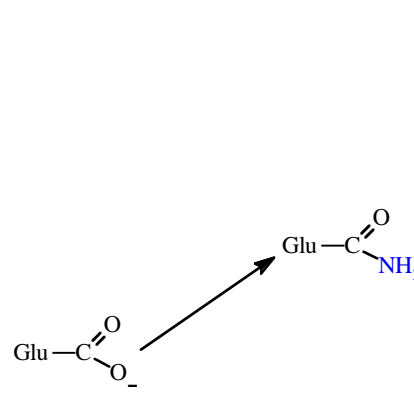
1. So cells use high- $G$  compounds to make ATP. This is called: **“Substrate Level Phosphorylation”**.

Two other processes for regenerating ATP are:

2. **Photophosphorylation** in chloroplasts.

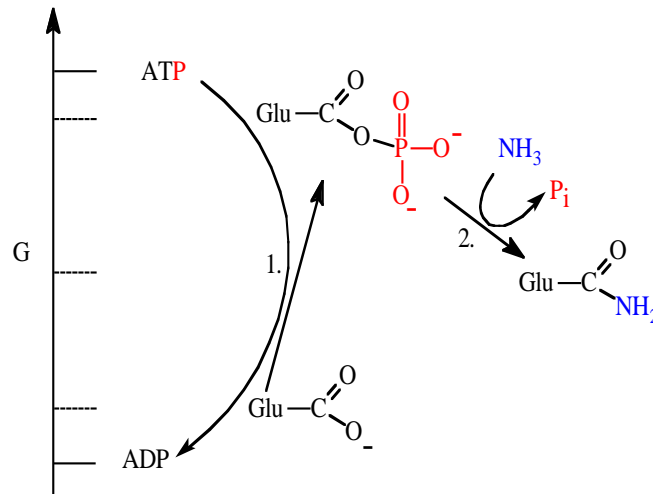
3. **Oxidative phosphorylation** in mitochondria.

How are reactions coupled?  
For *e.g.* how can ATP hydrolysis be used to convert  
 $\text{Glu} + \text{NH}_3 \rightarrow \text{Gln}$ ,  
an endergonic process?  
 $+14 \text{ kJ/mol}$



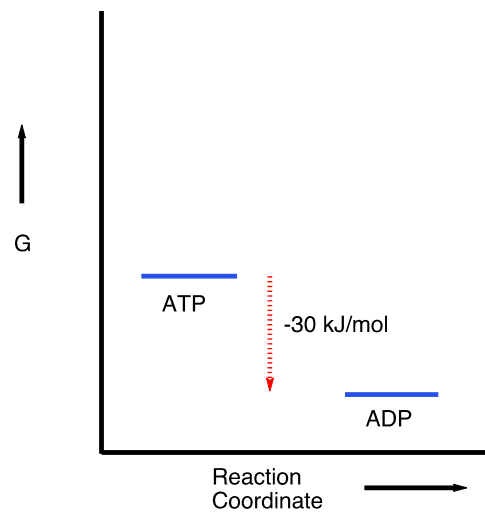


1. The phosphate from ATP is transferred to an enzyme or to a substrate which becomes **activated**. In this case, the  $G$  of Glu is raised by phosphorylation.

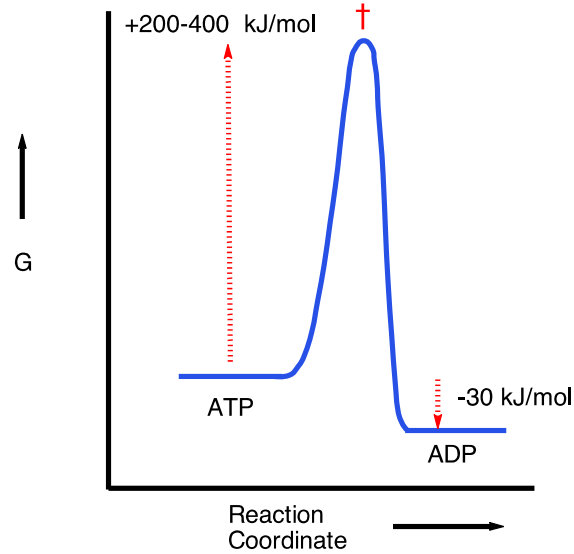


2. The reaction is completed by displacement of the  $\text{P}_i$  by  $\text{NH}_3^+$ , which is a "downhill"  $G$ -releasing reaction.

If ATP has so much  $G$ , why does it not spontaneously decompose?



The reaction is spontaneous, but very slow because it has a very high **activation energy**  $\Delta G^\ddagger$ .



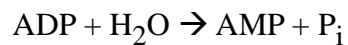
So **enzymes** lower the activation energy and allow the  $G$  release.

Other nucleoside triphosphates are energetically equivalent to ATP and are also used by cells. *e.g.* GTP

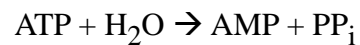
These are usually made by the following reactions catalysed by **nucleoside diphosphate kinases**:



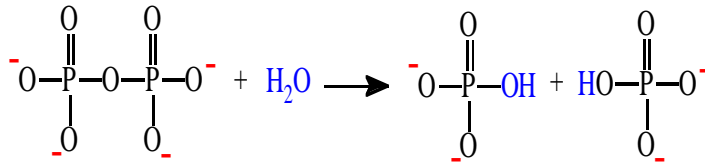
The following reactions release about the same amount of  $G$  as ATP hydrolysis and also can be used as energy “*currency*”:



$$\Delta G'^{\circ} \sim -33 \text{ kJ/mole}$$



$$\Delta G'^{\circ} \sim -46 \text{ kJ/mole}$$

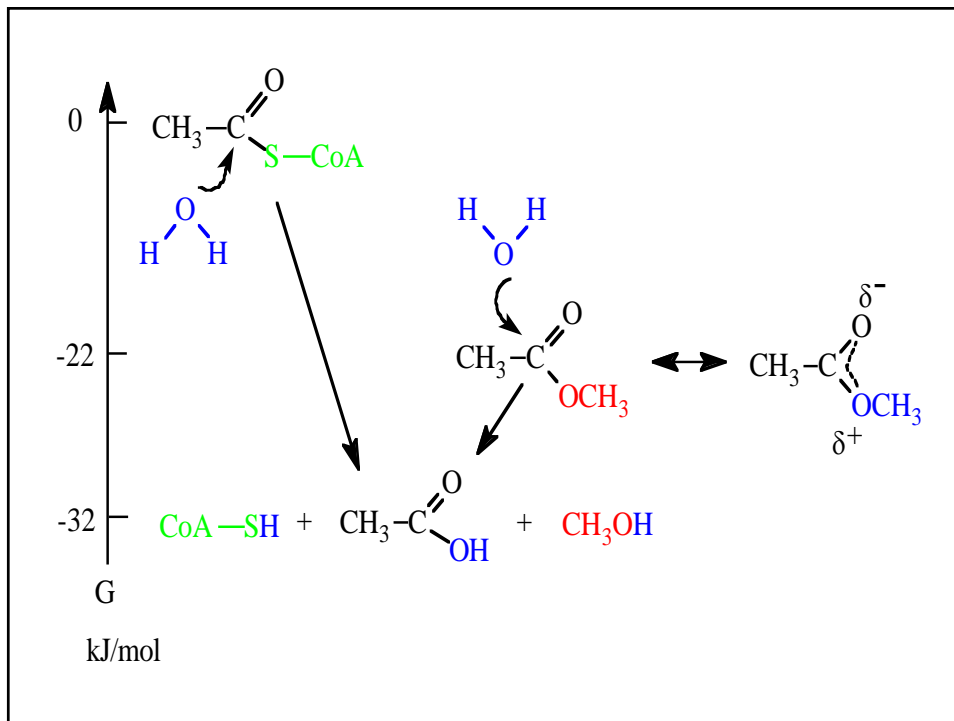


PP<sub>i</sub> is inorganic pyrophosphate.  $\Delta G'^0 \sim -19$  kJ/mole

Another type of energy storage is provided by **thioester bonds**.

By comparison, oxygen esters are resonance stabilized, and thus store less *G* than thioesters.

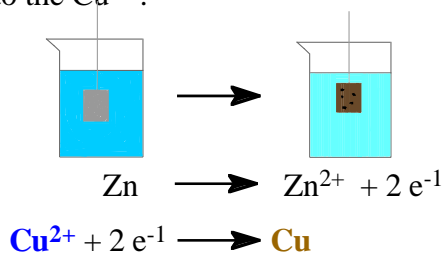
*E.g.* Acetyl-Coenzyme A (Acetyl-CoA)



**Electron flow** can also do work.



1.  $\text{Cu}^{2+}$  has a higher electron affinity than  $\text{Zn}^{2+}$ , so when Zn is placed in a copper sulphate solution, electrons flow spontaneously from the Zn to the  $\text{Cu}^{2+}$ :



The Zn metal erodes and  $\text{Zn}^{2+}$  goes into the solution.

**Cu** deposits on the Zn.  $\text{Cu}^{2+}\text{SO}_4^{2-}$  is blue.

As  $\text{Cu}^{2+}$  is converted into **Cu**, the blue colour of the solution fades.

The zinc is “**oxidized**” (loses electrons) and the copper is “**reduced**” (gains electrons). Overall, the Redox reaction is:



By separating the two half reactions, and permitting the electrons to flow through a conductor, the  $G$  released can be used to do work.

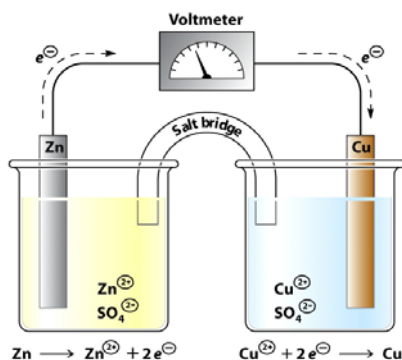
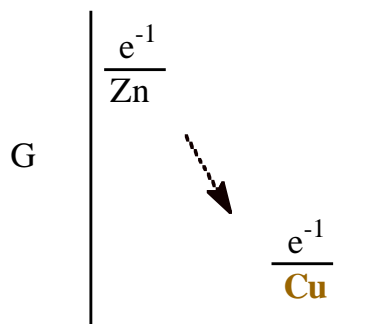
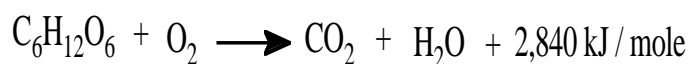


Figure 10-14 Principles of Biochemistry, 4/e  
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The electrons fall down the  $G$  hill from Zn to **Cu**.



2. A second type of electron flow involves  $O_2$ .



$O_2$  has a higher electron affinity than glucose, so electrons flow from glucose to  $O_2$  releasing  $G$ .

The C is oxidized and the O is reduced.

In  $O_2$ , bonding  $e^{-1}$  are shared equally by the 2 O.

In  $CO_2$  and  $H_2O$  the electronegative O pulls  $e^{-1}$  away from C and H.

In  $CO_2$ , the C's have lost a share of the  $e^{-1}$  they had in glucose.

In living cells, this oxidation is a multi-step process involving [glycolysis](#), [tricarboxylic acid cycle](#), and mitochondrial [respiration](#).

At various points,  $e^{-1}$  are transferred to electron carriers, and then to  $O_2$ .

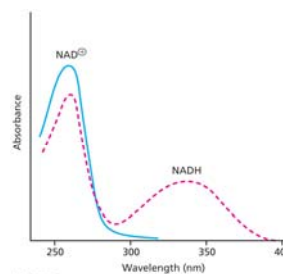
The electron flow is used to do the work of making ATP.

1. A water-soluble, diffusible electron carrier is:  $\text{NAD}^+$   
Nicotinamide Adenine Dinucleotide.

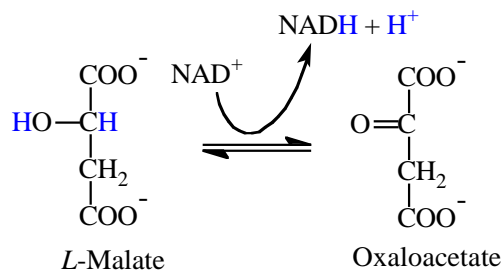
Nicotinamide is also known as Niacin and Vitamin B6.

$\text{NAD}^+$  = Adenine-1'-Ribose-5'-P-P-5'-Ribose-1'-Nicotinamide

Electrons are transferred in the form of  $\text{H}^-$ ,  
a hydride ion.

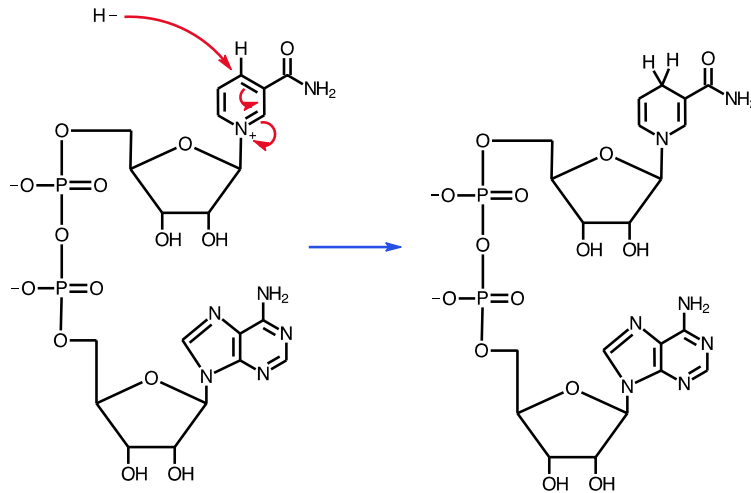


For *e.g.*, the enzyme *malate dehydrogenase* removes electrons from *L*-malate producing oxaloacetate and reducing  $\text{NAD}^+$  to  $\text{NADH}$ .



Malate is **dehydrogenated** and **oxidized**. It loses 2 electrons in the form of **2H**.

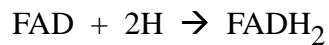
$\text{NAD}^+$  accepts  $\text{H}^-$  and is **reduced**. A **proton** is released (*Ch. 7*).



Over 200 **dehydrogenase** enzymes are known that use  $\text{NAD}^+$ .

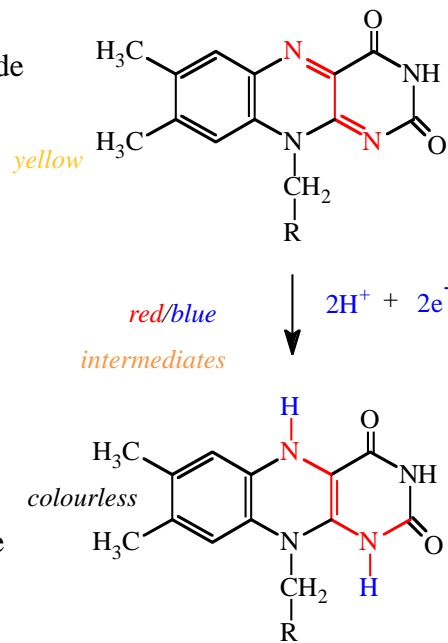
2. Two water-soluble, covalently-bound electron carriers are:

FMN, Flavine Mononucleotide  
and FAD, Flavine Adenine  
Dinucleotide



Here, 1 or 2 H are transferred

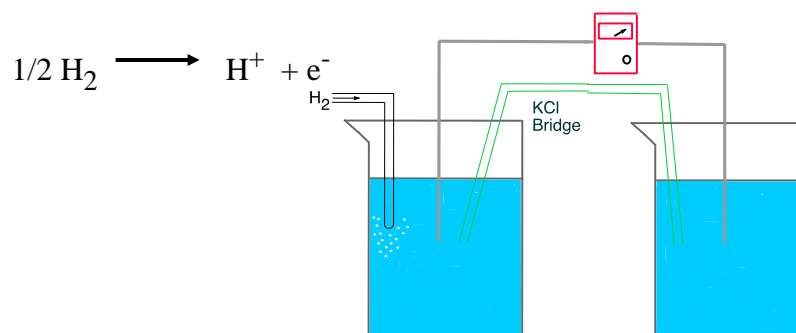
Flavin + Ribitol =  
Riboflavin = Vit B<sub>2</sub>  
FMN = Riboflavin + phosphate



The relative affinity of an atom or molecule for electrons can be measured.

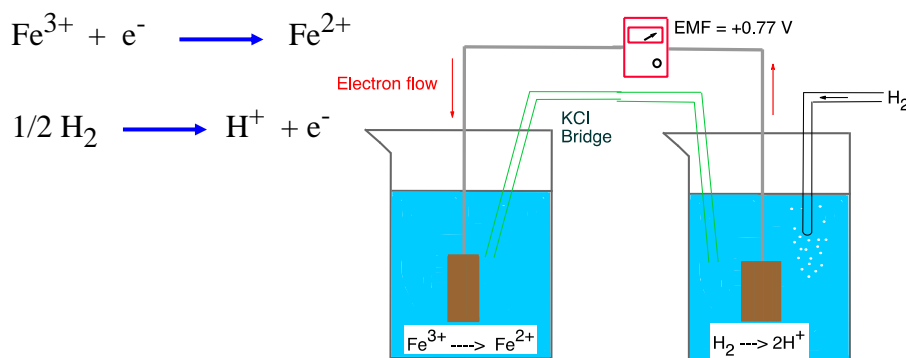
The **reference** point is a solution containing:

$\text{H}_2$  at 101 kPa +  $1 \text{ M H}^+$  (pH = 0)

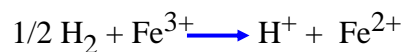


If the reference cell and test cell both contain this solution, no electrons will flow so the electromotive force, emf, will be 0 Volts.

If  $1 \text{ M Fe}^{3+} + \text{Fe}^{2+}$  are in one cell,  $\text{Fe}^{3+}$  will draw electrons from  $\text{H}_2$  and the emf will be +0.77 Volts. This is called the **standard reduction potential,  $\mathcal{E}^0$** .

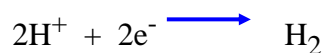


The net reaction is:

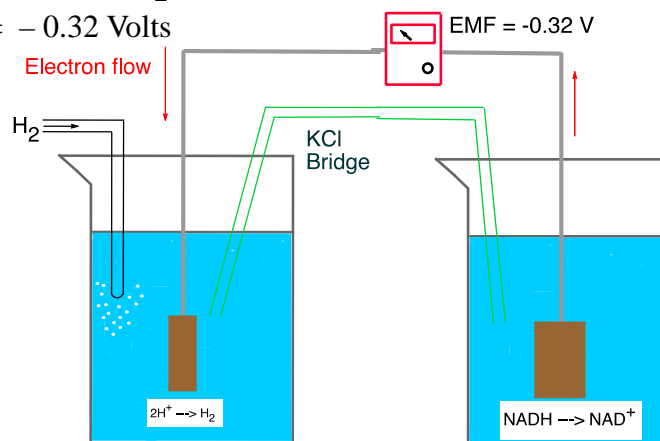




If the iron is replaced by 1 M NADH + NAD<sup>+</sup>, e<sup>-</sup> will flow from the test cell to the reference cell. H<sup>+</sup> will draw e<sup>-</sup> from NADH:



$$\mathcal{E}^0 = \text{emf} = -0.32 \text{ Volts}$$



For biochemists, the test cells are always kept at pH 7 and reported as:  $\mathcal{E}'^0$

A Table of  $\mathcal{E}'^0$  values, where the half reactions are written as reductions, can be used to predict the directions of Redox reactions.

The more positive is the  $\mathcal{E}'^0$  (bottom of the Table) the stronger is the oxidizing agent. *i.e.* The reactions go as written in the Table.

In combining pairs of half reactions the more positive  $\mathcal{E}'^0$  reactions are written as reductions ( $e^-$  on the left) and the more negative  $\mathcal{E}'^0$  are written as oxidations ( $e^-$  on the right).

**TABLE 10.4** Standard reduction potentials of some important biological half-reactions

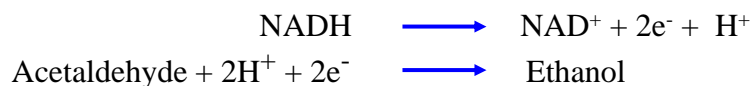
Reduction half-reaction	$\mathcal{E}'^0$ (V)
Acetyl CoA + CO <sub>2</sub> + H <sup>+</sup> + 2e <sup>-</sup> → Pyruvate + CoA	-0.48
Ferredoxin (spinach), Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	-0.43
2 H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> (at pH 7.0)	-0.42
α-Ketoglutarate + CO <sub>2</sub> + 2 H <sup>+</sup> + 2e <sup>-</sup> → Isocitrate	-0.38
Lipoyl dehydrogenase (FAD) + 2 H <sup>+</sup> + 2e <sup>-</sup> → Lipoyl dehydrogenase (FADH <sub>2</sub> )	-0.34
NADP <sup>+</sup> + 2 H <sup>+</sup> + 2e <sup>-</sup> → NADPH + H <sup>+</sup>	-0.32
NAD <sup>+</sup> + 2 H <sup>+</sup> + 2e <sup>-</sup> → NADH + H <sup>+</sup>	-0.32
Lipoic acid + 2 H <sup>+</sup> + 2e <sup>-</sup> → Dihydrolipoic acid	-0.29
Glutathione (oxidized) + 2 H <sup>+</sup> + 2e <sup>-</sup> → 2 Glutathione (reduced)	-0.23
FAD + 2 H <sup>+</sup> + 2e <sup>-</sup> → FADH <sub>2</sub>	-0.22
FMN + 2 H <sup>+</sup> + 2e <sup>-</sup> → FMNH <sub>2</sub>	-0.22
Acetaldehyde + 2 H <sup>+</sup> + 2e <sup>-</sup> → Ethanol	-0.20
Pyruvate + 2 H <sup>+</sup> + 2e <sup>-</sup> → Lactate	-0.18
Oxaloacetate + 2 H <sup>+</sup> + 2e <sup>-</sup> → Malate	-0.17
Cytochrome b <sub>5</sub> (microsomal), Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.02
Fumarate + 2 H <sup>+</sup> + 2e <sup>-</sup> → Succinate	0.03
Ubiquinone (Q) + 2 H <sup>+</sup> + 2e <sup>-</sup> → QH <sub>2</sub>	0.04
Cytochrome b (mitochondrial), Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.08
Cytochrome c <sub>1</sub> , Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.22
Cytochrome c, Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.23
Cytochrome a, Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.29
Cytochrome f, Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.36
Plastocyanin, Cu <sup>2+</sup> + e <sup>-</sup> → Cu <sup>+</sup>	0.37
NO <sub>3</sub> <sup>-</sup> + 2 H <sup>+</sup> + 2e <sup>-</sup> → NO <sub>2</sub> <sup>-</sup> + H <sub>2</sub> O	0.42
Photosystem I (P700) Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.77
$\frac{1}{2}$ O <sub>2</sub> + 2 H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> O	0.82
Photosystem II (P680)	1.1

**Table 10-4 Principles of Biochemistry, 4/e**  
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*e.g.* Acetaldehyde / NAD<sup>+</sup> From the Table:

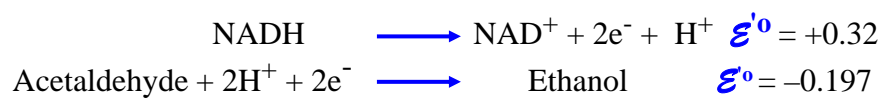


So the coupled reaction is:



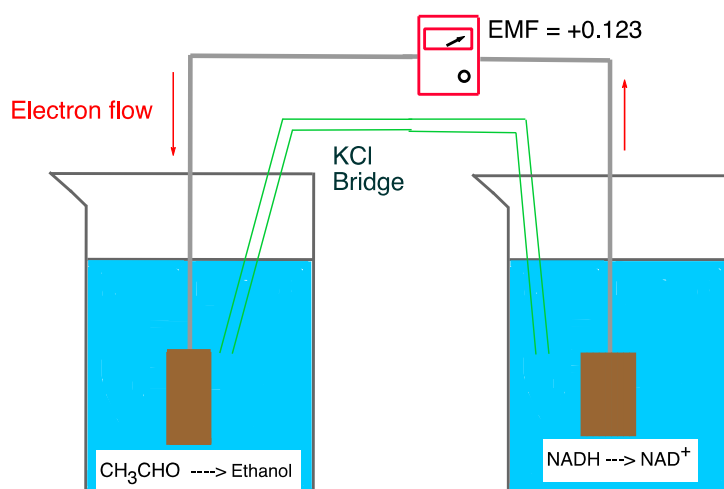
$$\Delta\mathcal{E}'^0 = -0.197 \text{ V} - (-0.32 \text{ V}) = +0.123 \text{ V} \quad (\text{acceptor} - \text{donor})$$

Another way to do this is to reverse the sign of the  $\mathcal{E}'^0$  value for the reaction that is written as an oxidation, and then add the  $\mathcal{E}'^0$  values.



$$\Delta\mathcal{E}'^0 = +0.32 \text{ V} + (-0.197 \text{ V}) = +0.123 \text{ V}$$

$$\Delta\mathcal{E}'^0 = +0.32 \text{ V} + (-0.197 \text{ V}) = +0.123 \text{ V}$$

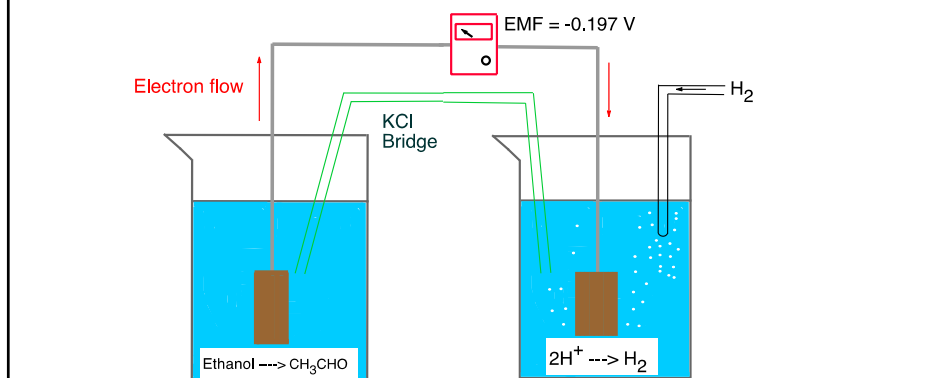


For any pair of 1/2 reactions the  $\Delta G$  can be calculated from the difference in emf:

$$\Delta G'^o = -nF\Delta\mathcal{E}'^o \quad n = \# \text{ of moles of } e^- \text{ transferred}$$

$F$  = Faraday constant = 96.48 kJ / Volt mole

$$\Delta G'^o = -2 (96.5) (0.123) = -23.7 \text{ kJ / mole}$$



Under non-standard conditions:

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

Remember,  $\Delta\mathcal{E}'^o = \mathcal{E}'^o_{\text{acceptor}} - \mathcal{E}'^o_{\text{donor}}$