

## Chemical Reactivity

Re-dox

### Oxidation-Reduction Reactions

Reduced organic compounds serve as **fuels** from which electrons can be stripped off during oxidation.

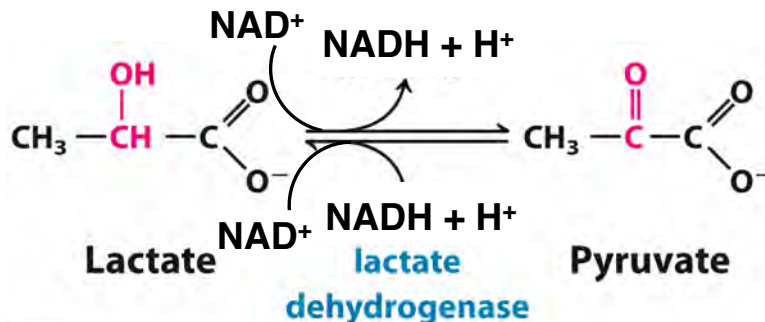
$-\text{CH}_2 - \text{CH}_3$	Alkane	Most energy	Relative $\Delta G^{\circ}$ of oxidation per carbon (kcal/mol)
$-\text{CH}_2 - \text{CH}_2\text{OH}$	Alcohol		-196
$-\text{CH}_2 - \text{C}(=\text{O})\text{H(R)}$	Aldehyde (ketone)		-168
$-\text{CH}_2 - \text{C}(=\text{O})\text{OH}$	Carboxylic acid		-125
$\text{O}=\text{C}=\text{O}$	Carbon dioxide	Least energy	-68
			0

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### EXAMPLE: Reversible Oxidation of a Secondary Alcohol to a Ketone

- Many biochemical oxidation-reduction reactions involve transfer of **two electrons**.
- In order to keep charges in balance, proton transfer often accompanies electron transfer.
- In many **dehydrogenases**, the reaction proceeds by a stepwise transfers of **proton** ( $\text{H}^+$ ) and **hydride** ( $:\text{H}^-$ ).



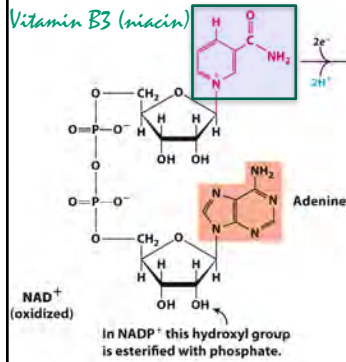
# Chemical Reactivity

Re-dox

## Common Redox Cofactors: NADH, NADPH, and FADH<sub>2</sub>

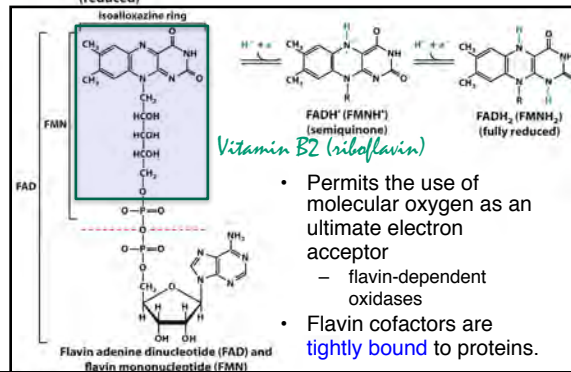
- Niacin Cofactors allow Hydride (2 e<sup>-</sup>) Electron Transfers
- Flavin Cofactors allow single Electron Transfers

Vitamin B3 (niacin)



- These are commonly called pyridine nucleotides.
- They can dissociate from the enzyme after the reaction.
- In a typical biological oxidation reaction, hydride from an alcohol is transferred to NAD<sup>+</sup>, giving NADH.

- Measure the change of absorbance at 340 nm
- Very useful signal when studying the kinetics of NAD-dependent dehydrogenases



Vitamin B2 (riboflavin)

- Permits the use of molecular oxygen as an ultimate electron acceptor
  - flavin-dependent oxidases
- Flavin cofactors are tightly bound to proteins.

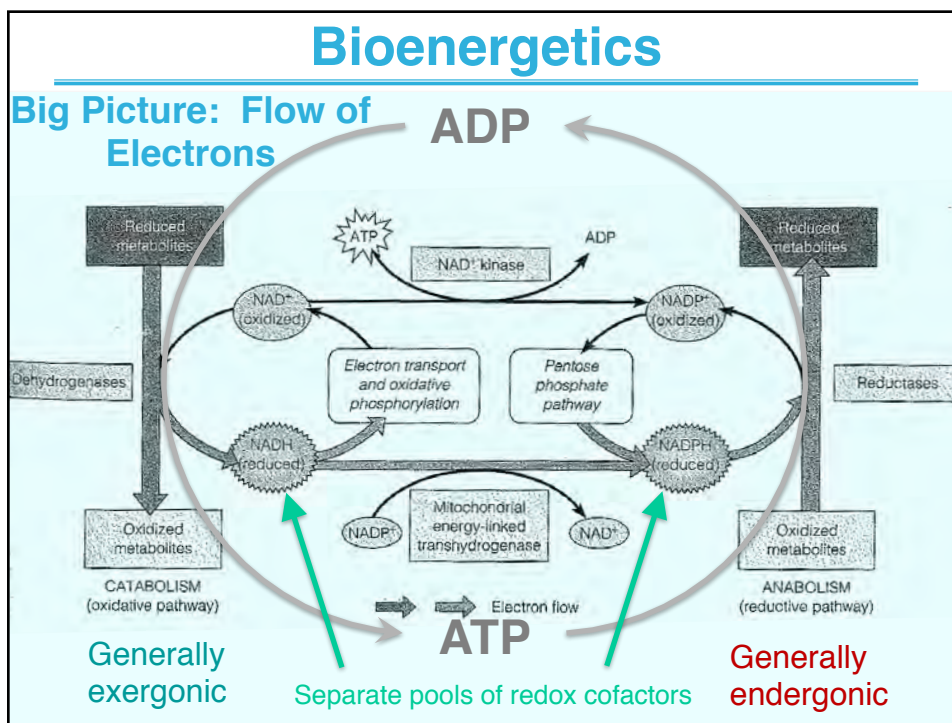
# Bioenergetics

## Energetics of Biochemical Reactions:

# Bioenergetics

## Energetics of Some Chemical Reactions:

- **Hydrolysis reactions** tend to be strongly favorable (spontaneous).
  - Recall that being thermodynamically **favorable** is not the same as being kinetically rapid.
- **Isomerization reactions** have smaller free-energy changes.
  - isomerization between enantiomers:  $\Delta G^\circ = 0$
- Complete oxidation of reduced compounds (redox reactions) is strongly favorable.
  - This is how chemotrophs obtain most of their energy.
  - In biochemistry, the oxidation of reduced fuels with  $O_2$  is **stepwise and controlled**.



# Bioenergetics

## Reduction Potential determines the Flow of Electrons

- Reduction potential (E)
  - affinity for electrons; higher E, higher affinity
  - electrons transferred from lower to higher E

$$\Delta E^{\circ'} = E^{\circ'}_{(e^- \text{ acceptor})} - E^{\circ'}_{(e^- \text{ donor})}$$

(that which is reduced)                      (that which is oxidized)

$$\Delta E^{\circ'} = -(RT/n\mathcal{F}) \ln(K_{eq}) = \Delta G^{\circ'}/n\mathcal{F}$$

$$\Delta G^{\circ'} = -n\mathcal{F}\Delta E^{\circ'}$$

- For negative  $\Delta G$ , need positive  $\Delta E$

$$E^{\circ'}_{(\text{acceptor})} > E^{\circ'}_{(\text{donor})}$$

# Bioenergetics

## Reduction Potential determines the Flow of Electrons

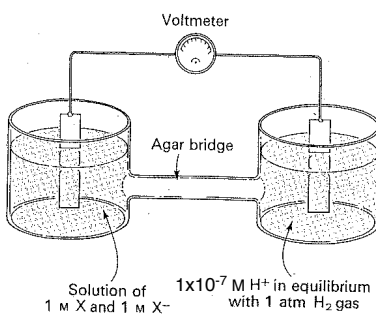


TABLE 13-7a Standard Reduction Potentials of Some Biologically Important Half-Reactions

Half-reaction	E <sup>o'</sup> (V)
1/2 O <sub>2</sub> + 2H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> O	0.816
Fe <sup>3+</sup> + e <sup>-</sup> → Fe <sup>2+</sup>	0.771
NO <sub>3</sub> <sup>-</sup> + 2H <sup>+</sup> + 2e <sup>-</sup> → NO <sub>2</sub> <sup>-</sup> + H <sub>2</sub> O	0.421
Cytochrome f (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome f (Fe <sup>2+</sup> )	0.365
Fe(CN) <sub>6</sub> <sup>3-</sup> (ferricyanide) + e <sup>-</sup> → Fe(CN) <sub>6</sub> <sup>4-</sup>	0.36
Cytochrome a <sub>3</sub> (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome a <sub>3</sub> (Fe <sup>2+</sup> )	0.35
O <sub>2</sub> + 2H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> O <sub>2</sub>	0.295
Cytochrome a (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome a (Fe <sup>2+</sup> )	0.29
Cytochrome c (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome c (Fe <sup>2+</sup> )	0.254
Cytochrome c <sub>1</sub> (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome c <sub>1</sub> (Fe <sup>2+</sup> )	0.22
Cytochrome b (Fe <sup>3+</sup> ) + e <sup>-</sup> → cytochrome b (Fe <sup>2+</sup> )	0.077
Ubiquinone + 2H <sup>+</sup> + 2e <sup>-</sup> → ubiquinol	0.045
Fumarate <sup>2-</sup> + 2H <sup>+</sup> + 2e <sup>-</sup> → succinate <sup>2-</sup>	0.031
2H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> (at standard conditions, pH 0)	0.000
Crotonyl-CoA + 2H <sup>+</sup> + 2e <sup>-</sup> → butyryl-CoA	-0.015
Oxaloacetate <sup>2-</sup> + 2H <sup>+</sup> + 2e <sup>-</sup> → malate <sup>2-</sup>	-0.166
Pyruvate + 2H <sup>+</sup> + 2e <sup>-</sup> → lactate <sup>-</sup>	-0.185
Acetaldehyde + 2H <sup>+</sup> + 2e <sup>-</sup> → ethanol	-0.197
FAD + 2H <sup>+</sup> + 2e <sup>-</sup> → FADH <sub>2</sub>	-0.219 <sup>a</sup>
Glutathione + 2H <sup>+</sup> + 2e <sup>-</sup> → 2 reduced glutathione	-0.23
S + 2H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> S	-0.243
Lipoic acid + 2H <sup>+</sup> + 2e <sup>-</sup> → dihydrolipoic acid	-0.29
NAD <sup>+</sup> + H <sup>+</sup> + 2e <sup>-</sup> → NADH	-0.320
NADP <sup>+</sup> + H <sup>+</sup> + 2e <sup>-</sup> → NADPH	-0.324
Acetoacetate + 2H <sup>+</sup> + 2e <sup>-</sup> → β-hydroxybutyrate	-0.346
α-Ketoglutarate + CO <sub>2</sub> + 2H <sup>+</sup> + 2e <sup>-</sup> → isocitrate	-0.38
2H <sup>+</sup> + 2e <sup>-</sup> → H <sub>2</sub> (at pH 7)	-0.414
Ferredoxin (Fe <sup>3+</sup> ) + e <sup>-</sup> → ferredoxin (Fe <sup>2+</sup> )	-0.432

# Bioenergetics

## Reduction Potentials with higher affinity at bottom

Standard reduction potentials of some reactions

Oxidant	Reductant	n	$E^{\circ}$ (V)
Succinate + CO <sub>2</sub>	$\alpha$ -Ketoglutarate	2	-0.67
Acetate	Acetaldehyde	2	-0.60
Ferredoxin (oxidized)	Ferredoxin (reduced)	1	-0.43
2 H <sup>+</sup>	H <sub>2</sub>	2	-0.42
NAD <sup>+</sup>	NADH + H <sup>+</sup>	2	-0.32
NADP <sup>+</sup>	NADPH + H <sup>+</sup>	2	-0.32
Lipoate (oxidized)	Lipoate (reduced)	2	-0.29
Glutathione (oxidized)	Glutathione (reduced)	2	-0.23
Acetaldehyde	Ethanol	2	-0.20
Pyruvate	Lactate	2	-0.19
Fumarate	Succinate	2	0.03
Cytochrome b (+3)	Cytochrome b (+2)	1	0.07
Dehydroascorbate	Ascorbate	2	0.08
Ubiquinone (oxidized)	Ubiquinone (reduced)	2	0.10
Cytochrome c (+3)	Cytochrome c (+2)	1	0.22
Fe (+3)	Fe (+2)	1	0.77
$\frac{1}{2}$ O <sub>2</sub> + 2 H <sup>+</sup>	H <sub>2</sub> O	2	0.82

Note:  $E^{\circ}$  is the standard oxidation-reduction potential (pH 7, 25°C) and  $n$  is the number of electrons transferred.  $E^{\circ}$  refers to the partial reaction written as

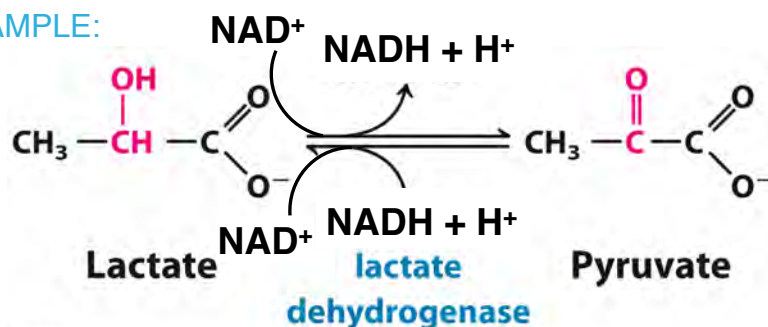
Oxidant + e<sup>-</sup> → reductant

Hates e<sup>-</sup>

Loves e<sup>-</sup>

# Bioenergetics

EXAMPLE:



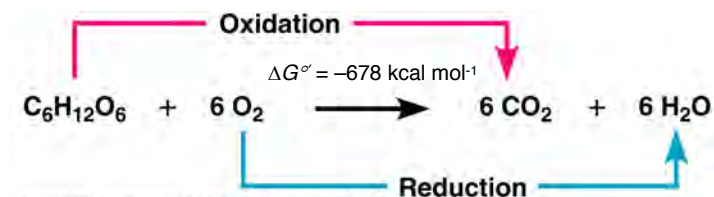
$$\begin{aligned}\Delta E^{\circ} &= E^{\circ}_{(\text{reduction})} - E^{\circ}_{(\text{oxidation})} \\ &= -0.32 \text{ V} - (-0.19 \text{ V}) \\ &= -0.13 \text{ V}\end{aligned}$$

$$\begin{aligned}\Delta G^{\circ} &= -n \mathcal{F} \Delta E^{\circ} \\ &= -(2)(23.06 \text{ kcal V}^{-1} \text{ mol}^{-1})(-0.13 \text{ V}) \\ &= +6 \text{ kcal mol}^{-1}\end{aligned}$$

This is why we always ran the reaction the other way!

## Bioenergetics

EXAMPLE:



What is the  $\Delta E^\circ$  for the complete oxidation of glucose?

$$\Delta G^\circ = -n \mathcal{F} \Delta E^\circ$$

$$-678 \text{ kcal mol}^{-1} = -(24)(23.06 \text{ kcal V}^{-1} \text{ mol}^{-1})(x \text{ V})$$

$$\Delta E^\circ = +1.25 \text{ V}$$

What is the reduction potential ( $E^\circ$ ) for Glc  $\rightarrow$   $\text{CO}_2$ ?

$$\Delta E^\circ = E^\circ_{(\text{reduction})} - E^\circ_{(\text{oxidation})}$$

$$+1.25 \text{ V} = +0.82 \text{ V} - (E^\circ_{(\text{Glc oxidation})})$$

$$E^\circ_{(\text{Glc oxidation})} = -0.43 \text{ V}$$

## Summary

We learned that:

- The rules of thermodynamics and organic chemistry still apply to living systems
- **Reactions** are favorable when the free energy of products is much lower than the free energy of reactants
- Biochemical phosphoryl transfer reactions are favorable when:
  - the phosphate donors are destabilized by electrostatic repulsion
  - the reaction products are often stabilized by resonance
- **Unfavorable reactions can be made possible** by chemically coupling a highly favorable reaction to the unfavorable reaction
- **Oxidation-reduction reactions** commonly involve **transfer of electrons** from reduced organic compounds to specialized redox cofactors
  - Reduced cofactors can be used in biosynthesis, or may serve as a source of energy for ATP synthesis.