WELCOME TO
Biochemistry II (BI/CH 422 & BI/CH 622)

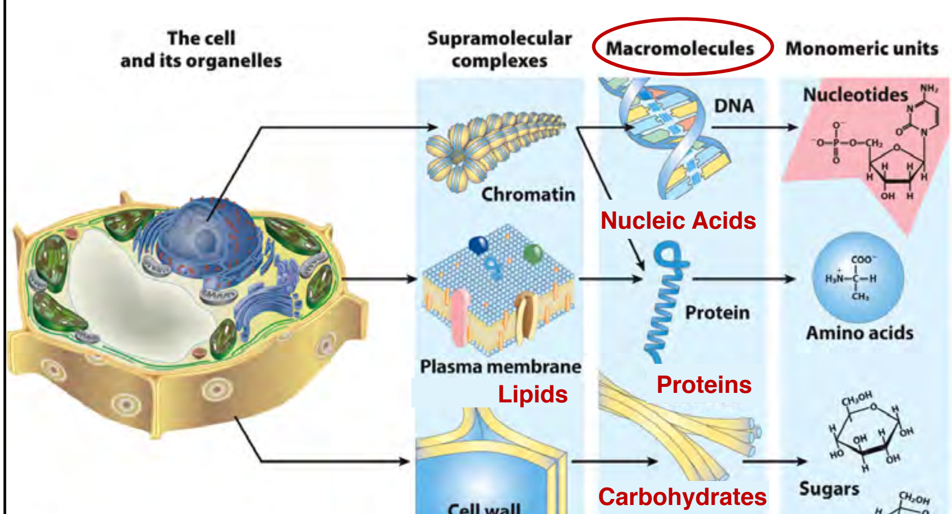
This course is Dedicated to the memory of Sir Hans Kornberg

January 14, 1928 ~ December 16, 2019

- Review of 421
- Goals of 422
- Review of chemical principles
  - Thermo
  - C/O cycles
  - overview
  - ATP cycles
  - Coupling
- Chemistry
- Bioenergetics

Dr. Kornberg: **Lecture 01.20.17 (35:58-42:12)**
(6 min)

Macromolecules are Key to Cellular Structures



Problem: A simple *E. coli* cell need only salts and a simple carbon source like acetic acid for growth. How is that possible?

Goals for Biochem II:

Problem: A simple *E. coli* cell need only salts and a simple carbon source like acetic acid for growth. How is that possible?

This semester we will answer this question, which relates all these macromolecular components:

- How are they interrelated?
- How are they synthesized from each other?
- What are the common chemical reactions and unique enzyme mechanisms?
- How is all this accomplished without breaking any of the rules of thermodynamics and organic chemistry?

All of these questions are answered, thus making **LIFE** possible, by what is termed **INTERMEDIARY METABOLISM**

FIRST, lets review some chemical principles and reactions…

Energetics of Life

The **laws of thermodynamics** apply to all matter and all energy transformations in the universe.

1st & 2nd Laws of Thermodynamics:

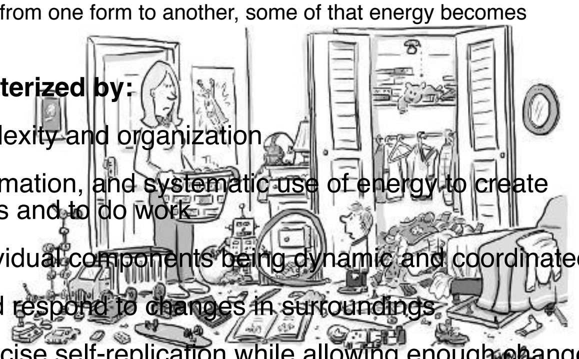
1) Energy can never be created or destroyed, but can be interconverted.

2) The universe tends toward more disorder (randomness)

[When energy is converted from one form to another, some of that energy becomes unavailable to do work.]

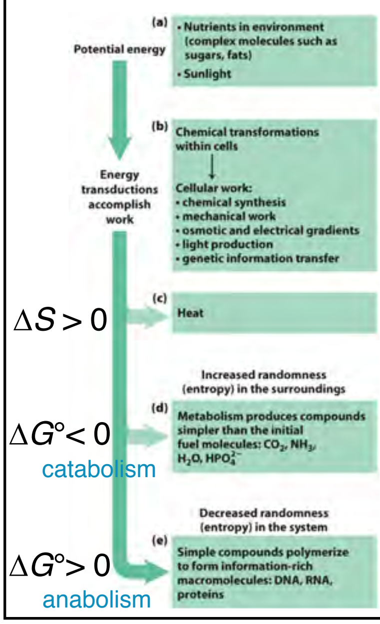
Living matter is characterized by:

- a high degree of complexity and organization
- the extraction, transformation, and systematic use of energy to create and maintain structures and to do work
- the interactions of individual components being dynamic and coordinated
- the ability to sense and respond to changes in surroundings
- a capacity for fairly precise self-replication while allowing enough change for evolution



"I blame entropy."

Energetics of Life



Life uses the First Law, performing energy transformations to Stay Alive

Favorable and Unfavorable Reactions

- The breakdown of some metabolites releases a significant amount of energy (**exergonic**).
  - Their cellular concentration is far higher than their equilibrium concentration.
  - Metabolites, such as ATP, NADH, NADPH, can be synthesized using the energy from sunlight and fuels…..
- Synthesis of complex molecules and many other metabolic reactions requires energy (**endergonic**).
  - A reaction might be thermodynamically unfavorable ($\Delta G^\circ > 0$).
    - Creating order requires work and energy.

Energetics of Life

- Living organisms cannot create energy from nothing.
- Living organisms cannot destroy energy into nothing.
- Living organism may transform energy from one form to another.

- In the process of transforming energy, living organisms must increase the entropy of the universe.

- In order to maintain organization within themselves, living systems must be able to extract useable energy from their surroundings and release useless energy (heat) back to their surroundings.

Overview of Metabolism

Metabolism

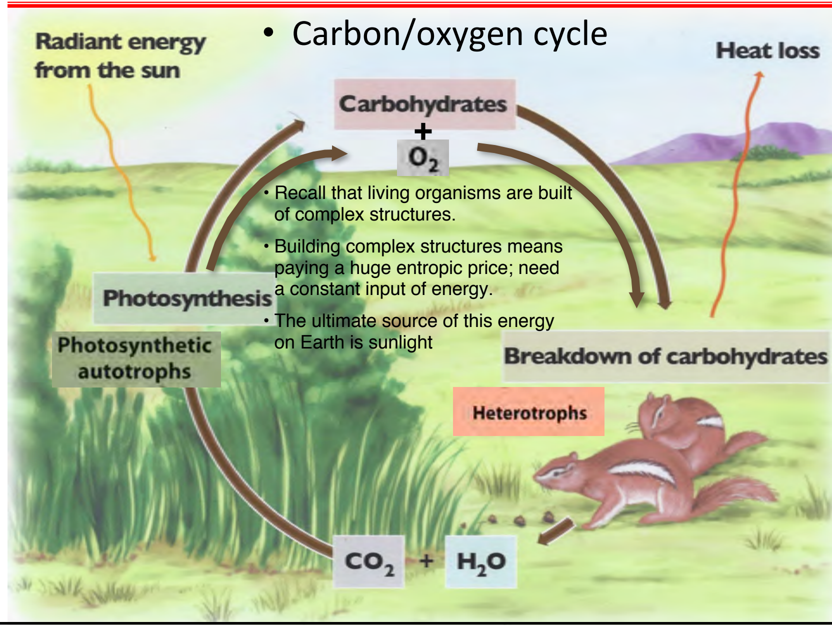
Issues:

- Thermodynamics and biochemistry; carbon/oxygen cycle & nitrogen cycle
- Some biomolecules are “high energy” with respect to their hydrolysis and group transfers.
- Energy stored in reduced organic compounds can be used to reduce cofactors such as NAD^+ and FAD, which serve as universal electron carriers and lead to ATP formation.

- Common organic chemistry principles in biochemistry

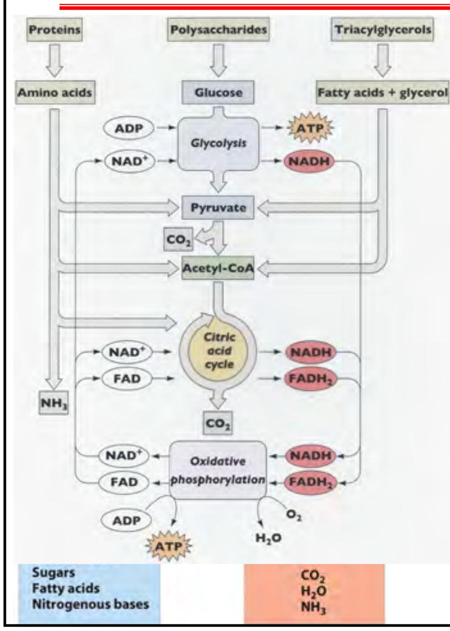
Metabolism

- Carbon/oxygen cycle

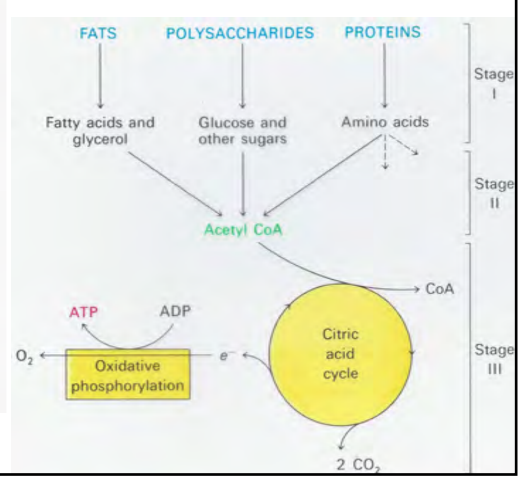


- Recall that living organisms are built of complex structures.
- Building complex structures means paying a huge entropic price; need a constant input of energy.
- The ultimate source of this energy on Earth is sunlight

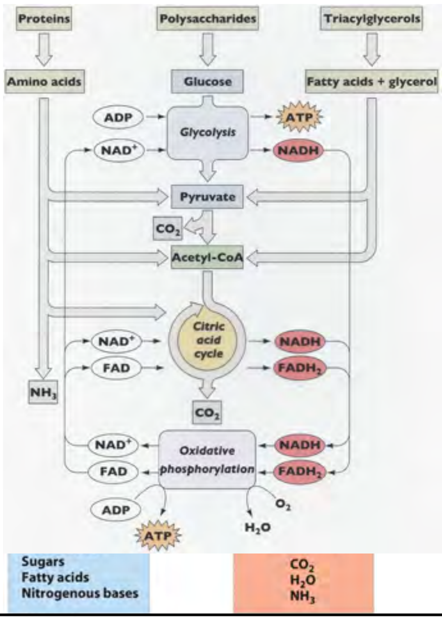
Metabolism



- In biochemistry, the oxidation of reduced fuels with O_2 is stepwise and controlled.
- Recall that being thermodynamically favorable is not the same as being kinetically rapid.



Metabolism



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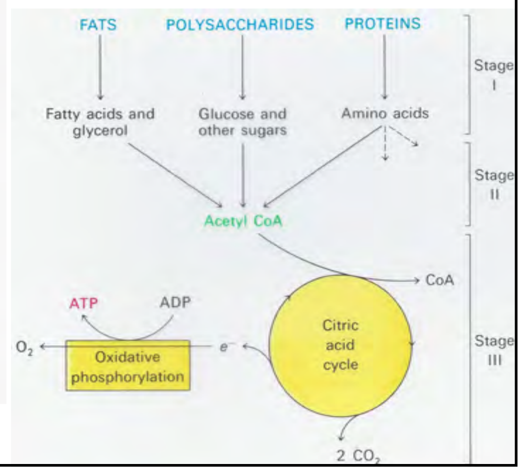
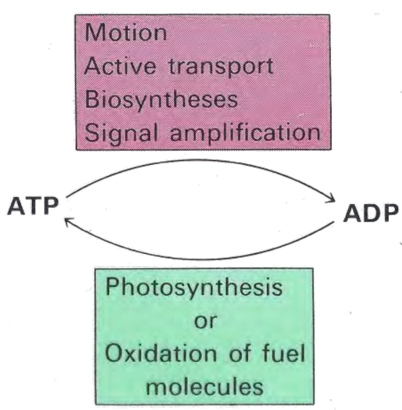
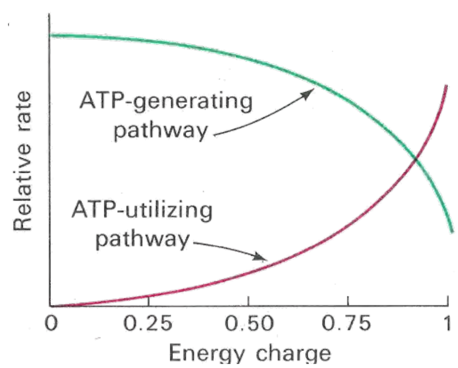


Metabolism

THE ATP CYCLE

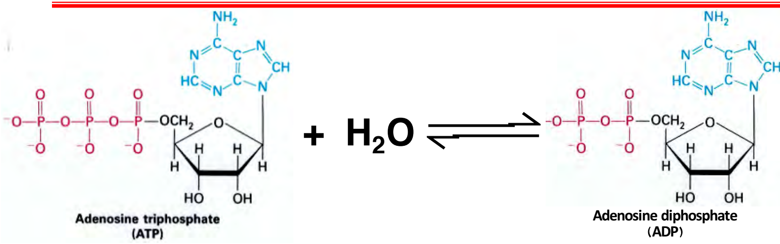




This "buffering" of energy in the cell keeps the [ATP] high enough to keep fighting the second law of thermodynamics.

$$\text{Energy Charge} = \frac{[ATP^{-4}] + \frac{1}{2}[ADP^{-3}]}{[ATP^{-4}] + [ADP^{-3}] + [AMP^{-2}]}$$

Metabolism



+ HPO_4^{2-}
+
H^+
(at pH 7)

If this reaction is allowed to come to equilibrium, what is the ΔG?

Recall, at equilibrium, ΔG=0

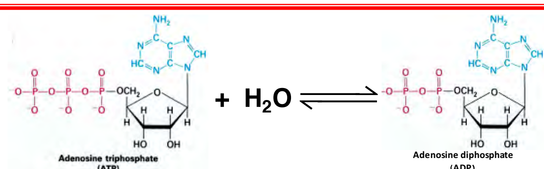
Also, recall that the actual free-energy change of a reaction depends on:

- A constant (the standard change in free energy, ΔG°)
- actual concentrations of products and reactants
- For the reaction aA + bB ⇌ cC + dD:

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

[In biochemistry, we add a prime (′) because we pull [H+] out of the expression and set it to 10^{-7}, not 1 M]

Metabolism



+ HPO_4^{-2} + H^+
(at pH 7)

At equilibrium, ΔG=0

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

BUT, if we are at equilibrium, this equation becomes:

$$\Delta G' = \Delta G^{\circ\prime} + RT \ln K'_{eq}$$

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

For the above reaction (hydrolysis of ATP):

$$\Delta G^{\circ\prime} = -7.3 \text{ kcal/mole}$$

But, what is the actual $\Delta G'$ of ATP Hydrolysis IN THE CELL?

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

	$\Delta G'^{\circ}$	
K'_{eq}	(kJ/mol)	(kcal/mol)[a]
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

[a] Although joules and kilojoules are the standard units of energy and are used throughout this text, biochemists and nutritionists sometimes express $\Delta G'^{\circ}$ values in kilocalories per mole. We have therefore included values in both kilojoules and kilocalories in this table and in Tables 13-4 and 13-6. To convert kilojoules to kilocalories, divide the number of kilojoules by 4.184.