#8: Fundamental Topics in Metabolism BIOCHEM2280

Gibbs Free Energy (ΔG)

The free energy available to do work in a chemical system

Depends on:
- **Chemical nature** of the molecule
  - Can vary
- **Environmental conditions** (T, P, conc.)
  - Cannot vary
  - Increased conc. = increased ΔG

Defining environmental conditions:
Chemical ΔG°
- T = 298 K
- P = 1 bar

Biochemical ΔG°
- pH = 7
- [H_2O] = 55.5 M

Defined Conditions:
- All molecules at 1 mol/L
- Values are constant if the reaction doesn't involve H_2O or protons
  - *Thus, ΔG will only depend on the nature of the molecules*

Predicting Reactions

ΔG = Gproducts - Greactants < 0
Spontaneous reaction
Forward reaction is energetically favorable
Continue to react until ΔG = 0

ΔG = Gproducts - Greactants = 0
Equilibrium
Forward rate = reverse rate
No net reaction

ΔG = Gproducts - Greactants > 0
Reverse reaction is energetically favorable
Continue to react until ΔG = 0

Irreversible reactions: ΔG<<0

- Not sensitive to concentration changes

How to target reactions for **regulation:**
- Couple the reaction with ATP hydrolysis (ATP and H_2O → ADP + Pi)
  - Allows negative charges to separate (spontaneous process)
  - Increased surface area = distribute products = increased stability (phosphate products have more resonance to spread out the negative charge)
  - Highly solvated → interact more with solvent

Regulated Reactions

- **ATP:**
  - A nucleotide
  - Building block for RNA

ATP-driven Glutamine Formation
- Glutamine gets phosphate group
- Ammonia reacts with intermediate

Alternative Reactions
- ATP + $2H_2O$ → AMP + 2Pi
- Phosphocreatine –(H_2O → Pi)→ Creatine
- Hydrolysis Reaction

Controlling Enzymatic Activity

1. Amount of enzyme
- Gene expression regulation: rate of transcription, translation, degradation

2. Enzyme location
3. Catalytic ability
- Allosteric or covalent modifications

Allosteric Enzymes
- Bind to effectors (NOT active site of enzyme)
- Reversible
- Conformational change
- Multiple subunits
- Distinct catalytic and regulatory sites
- NOT non-competitive inhibition

Ex: PFK
- PEP decrease activity
- ADP increase activity

Ex: muscle glycogen phosphatase
- AMP increase activity
- ATP decrease activity

Covalent Modifications
- Post-translational modification
- Carried out by enzymes → add chemical group, change enzyme confirmation
- Site of addition usually different from the active site
- Ex: phosphorylation by kinases, phosphatases

Le Chatelier's Principle

Definition
Chemical reaction's position of equilibrium will shift towards favouring the production of either the products or the reactants in order to counteract changes in conditions, e.g. concentrations of compounds, temperature/pressure/volume of system
- Reactions near equilibrium are reversible
- Concentration changes have major impact on ΔG

Example:

$$\underbrace{N_2 + 3\,H_2}_{4\text{ moles}} \rightleftharpoons \underbrace{2\,NH_3}_{2\text{ moles}} \quad \Delta H = -92\text{kJ mol}^{-1}$$

- if you double the volume of the system → pressure will drop to 1/2 → reaction will shift left to produce more reactants since the left side has more moles of gas = more pressure exerted → increase pressure of system → counteract the change
- if you increase the temperature of the system → reaction will shift right to "consume" the additional heat → counteract the change
  - note: heat here can be seen as a reactant since enthalpy is negative
- if you decrease concentration of NH_3, reaction will shift right to produce more NH_3 → counteract the change

Metabolism

Sum of the chemical reactions occurring in a living organism
- **Catabolism** = break down → provide energy, e^-
- **Anabolism** = building up → take energy, e^-

Metabolic Pathway = Coordinated series of reactions that result in specific products
- Catalyzed by enzymes
- Occur in specific cells, locations (certain organs, tissues)

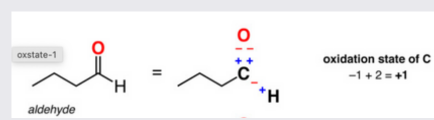
Flux = Rate at which molecules flow through each metabolic pathway
- Cell must change flux of molecules in each pathway to function
- Alter enzymatic activity
- Influenced by the concentration of metabolites
- The first reaction in a metabolic pathway after a branch point is often irreversible → target for control
- Some reactions ΔG<0, but most ΔG=0

Oxidation and Reduction

Overview
- **Reduction** = gain of electrons
- **Oxidation** = loss of electrons
- *Reduction of one molecule requires oxidation of another*
- ↑ **oxidation state** = the atom is more oxidized

Oxidation state of carbon
- For every bond to an electronegative atom, carbon's oxidation state increases by 1
- For every bond to hydrogen, carbon's oxidation state decreases by 1
- For every bond to carbon, the oxidation state does not change

Example:



Sourced from: https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Fundamentals/Oxidation_States_of_Organic_Molecules

Key electron carriers
- **NADH:** used in ATP synthesis
- **NADPH:** used in anabolic pathways (biomolecule synthesis)
- Carry electrons on the **nicotinamide** moiety
- Reducing agents

Oxidized form:
- Nicotinamide carries a positive charge
- NAD^+ or NADP+

Reduced Form:
- Net addition of a hydride ion (H-, one proton and two electrons) to nicotinamide neutralizes the charge
- NADH or NADPH

Ubiquinone/Coenzyme Q
- Used in generating ATP
- Electrons added to a quinone ring system
- Quinone group acquires two electrons and two protons to go from its oxidized form to its reduced form.
- Abbreviated QH_2
- Long hydrophobic polyisoprene tail embedded in inner mitochondrial membrane

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Note: Marvin was used for drawing, displaying and characterizing chemical structures, substructures and reactions, Marvin 24.4.1, Chemaxon (https://www.chemaxon.com)

biochem 2280.

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a handmade guide

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