1.1 - Amino Acids and Protein Structure

Gibbs Free Energy

- the energy of a chemical reaction that is available to do work
  - aka 'available energy'
- **ΔG = change in Gibbs free energy = G(products) - G(reactants)**
- Gibbs free energy takes into account enthalpy (heat) and entropy (disorder)
  - **ΔG = ΔH - TΔS**
    - ΔH - change in enthalpy
    - ΔS - change in entropy
    - T - temperature in Kelvin
- **-ΔG = exergonic reaction → free energy is released; favourable, spontaneous reaction**
  - free energy of the products is lower than free energy of the reactants
- **+ΔG = endergonic reaction → free energy is absorbed; unfavourable, non-spontaneous reaction**
  - free energy of reactants is lower than free energy of the products
- -ΔH → exothermic, heat released
- +ΔH → endothermic, heat absorbed
- +ΔS → more disorder
- -ΔS → less disorder

How do we get **-ΔG?**

- **ΔG = ΔH - TΔS**
- **so to get -ΔG, we need:**
  - **-ΔH**
  - **+ΔS**
  - or any combination that leaves **ΔG negative**

$$K_{eq} = \frac{[C]^c_{eq}[D]^d_{eq}}{[A]^a_{eq}[B]^b_{eq}}$$

K = the thermodynamic equilibrium constant for the reaction

- describes the position of the reaction at equilibrium (the relative concentrations of each component at equilibrium)
  - remember K>1 = more products than reactants; K<1 = more reactants than products, K=1 → same concentration of products and reactants

Free Energy and Equilibrium

$$aA + bB \rightleftharpoons cC + dD$$

$$\underset{\text{Free energy Change}}{\Delta G} = \underset{\text{Standard}}{\Delta G^o} + RT \ln \frac{[C]^c_i[D]^d_i}{[A]^a_i[B]^b_i}$$

- **ΔG - the actual free energy change for the reaction**
  - describes the amount of work that the reaction can do
  - ΔG is variable (depends on how far the reaction is from equilibrium)
    - if the reaction starts further away from equilibrium, more work is needed to be done before the reaction can reach equilibrium
- ΔG depends on:
  - the initial concentrations of the reactants and products **at the start of the reaction**
  - ΔG° - the free energy change under standard conditions (fixed)
    - a constant for the particular reaction, measured under standard conditions
    - the amount of energy that the reaction would absorb/release under standard conditions
- **so ΔG is variable, but ΔG° is fixed**

Standard conditions

- use of standard conditions allows free energy changes to be easily compared
- 298K (25 degrees celsius)
- gases at partial pressure of 1 atm
- reactants and products at 1M concentrations (except H+ in biochemistry standard conditions because that is pH 0, which will cause our enzymes to denature/be inactive)
- reactions in biochemistry standard conditions must occur in a well-buffered aqueous solution of pH 7 AND have 1mM of Magnesium (because many enzymes use Mg as a cofactor) → use **ΔG'°**
- so **ΔG = ΔG'° at standard conditions (ie the free energy change under standard conditions)**

ΔG is 0 at equilibrium

- the reaction can do no more work at equilibrium
- so **ΔG° is related to the equilibrium constant, making it a constant**

Free energy allows us to predict:

- what is the driving force of the reaction? - enthalpy or entropy changes or both?
- what is the position of the reaction at equilibrium
- is the reaction spontaneous?
- under what initial conditions will a reaction occur spontaneously?
- does the reaction need to be coupled with a favourable reaction?

Ways to make unfavourable reactions favourable:

1. keep the concentration of products much lower than reactants
   a. whether a reaction is spontaneous or not depends on **ΔG, NOT ΔG°**(ΔG° can still be positive)
   b. the ratio of products/reactants **MUST BE <1** for ln(products/reactants) to be negative
   c. so we keep the concentration of reactants HIGH, and the concentration of products LOW
   d. this can be done by:
      i. **removing one or more products at a much faster rate than it is produced**
         1. eg in reaction of glycolysis, aldolase (enzyme) converts F-1,6-bisP to DHAP and GA-3-P
         2. but GA-3-P is rapidly consumed by the next step, which keeps the product concentration low
      ii. **replenishing one reactant at a rate much faster than it is removed**

        1. eg in gluconeogenesis, glucose-6-phosphate is transported from the cytosol into the lumen of the ER to feed glucose-6-phosphatase
    e. these reactions are now 'kinetically driven'
2. **couple the unfavourable reaction (+ΔG'°) with a favourable reaction (very -ΔG'°)** in the active site of an enzyme
    a. by coupling reactions that share reactants and products, we can add the ΔG'° of the reactions together to give us a negative ΔG'°
        i. it is a very good start to have a negative ΔG'°
    b. this reaction is now thermodynamically driven
    c. this describes favourability under standard condition, we must always consider how actual conditions affect free energy change

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ATP

- adenosine triphosphate
- ATP is a nucleotide
    - a nucleotide has a base (adenine), a sugar (ribose) and phosphate groups (3 phosphate groups)
- ADP - adenine + ribose + 2 phosphate groups
- nucleoside → base + sugar
- there is a lot of energy released when the phosphoanhydride bonds undergoes hydrolysis

Bond energy

- energy is required to break bonds
- energy is released when any bond forms
- energy required to break bonds in the reactants is different to the energy released from bonds being formed in the products
- a favourable reaction is one where we get more energy out than energy put in to break the bond

ATP Hydrolysis

- ATP + H2O ←→ ADP + Pi (ΔG'° = -30.5 kJ/mol)
- so -30.5 kJ/mol of energy is released for this reaction
    - but the overall ΔG depends on [ATP], [ADP] and [Pi]
    - ΔG'° is also pH dependent (H+reactant/product) and [Mg2+] dependent
- nevertheless, **this reaction is highly exergonic**
- in order for a reaction to be favourable and spontaneous, **the energy of the reactants must be higher** than the energy of the products (the **reactants must be less stable than the products**)
    - **ATP is less stable than ADP** there are 4 negative charges adjacent to one another in ATP, but only 3 negative charges adjacent to each other in ADP
        - so the phosphoanhydride bonds between the phosphate groups in ATP experience more repulsion and strain, making them **weaker**
        - the phosphoanhydride bonds between phosphate groups in ADP experience less repulsion and strain, making them **stronger**
    - Pi produced from hydrolysis of ATP is also **very stable** because multiple **resonance states** exist
- so OVERALL, the products are more stable than the reactants
- therefore, the hydrolysis of ATP releases energy because:
    - ATP has a higher negative charge density than ADP → 4 negative charges next to each other compared to 3 (so ATP is less stable)
    - Pi is very stable because it has multiple resonance states
    - ATP phosphoanhydride bonds are relatively weak

- ADP phosphoanhydride bonds and Pi bonds are relatively strong
- ATP is not an energy-rich molecule, rather the hydrolysis of ATP releases a lot of energy

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Proteins

- main agents of biological functions involved in:
  - catalysis - enzymes eg enolase in the glycolytic pathway and DNA polymerase in DNA replication
  - transport - eg haemoglobin to transport O2 and GLUT 1 to transport glucose across cell membranes
  - structure - collagen and keratin
  - motion - myosin and actin
  - signalling (transduction) - receptors eg insulin and glucagon receptors that detect hormones in blood
- proteins are linear heteropolymers of **alpha-amino acids**
  - alpha amino acids have 4 substituents connected to the alpha carbon and is tetrahedral
- amino acids have properties that make them suitable to carry out biological functions:
  - capacity to polymerise
  - useful acid-base properties
  - varied physical properties
  - varied chemical functionality

Functional groups of amino acids

- all alpha amino acids (except proline) have common features
  - an acidic carboxyl group connected to the alpha carbon
    - carboxyl can be COO- or COOH
  - a basic amino group connected to the alpha carbon
    - amino can be NH2 or NH3+
  - an alpha hydrogen connected to the alpha carbon
- the 4th substituent is a unique feature of each amino acid (R group)

Chirality

- because amino acids have a carbon attached to 4 different substituents in a tetrahedral shape, they are **chiral (they can either be D- or L-)** → except glycine
- **naturally occurring proteins ONLY consist of L-amino acids**
- D- and L- describe the optical properties of the amino acids based on rotation of plane of polarised light when viewed from the light source
  - Dextrotatory (+): right or clockwise rotation
  - Levorotatory (-): left or anticlockwise rotation
- however, D-amino acids do not all rotate light clockwise and L-amino acids do not all rotate light anticlockwise
- in biochemistry, D- and L- refer to an empirical naming system based on what molecule synthesises them:
  - D-amino acids made by starting synthesis from D-glyceraldehyde
  - L-amino acids are made by starting synthesis from L-glyceraldehyde
- to determine the chirality of the alpha-carbon, look down the alpha hydrogen bond:
  - if you can read CORN clockwise, then it is a L-amino acid
  - if CORN is read anticlockwise, then it is a D-amino acid
