Module 1 Overview

Amino Acids

- Nonpolar: P. GAVLI MWF (*Gly uncharged not nonpolar*)
- Polar (ST NYCQ) and charged (REKDH)
- Rare:
    - Selenocysteine: like cys but Se (no S); deprot @ physio pH
    - Pyrrolysine: like lys but heteroatom (no amide); syn from 2 lys atoms
    - Hydroxylysine/ Hydroxyproline: post-trans modified; found in connective tissue (collagen)
    - Carboxyglutamic acid: post-trans modified; Glu that undergoes carbox; found in clot factors
    - Pyroglutamic acid: free AA of Glu or Gln becomes lactam; found in bacteriorhodopsin
- Essential (can't be biosyn): VHMILKWTF (Very Heavy Milk is essential, WTF)
- Condit essential (req at times): RPCGYQ (conditionally, Real People Can Get Your Questions)
- Dispensable (can be biosyn): DEANS (Deans meets demands)

Protein

1. Structure

- Conformation: atom rot; no bond break in tertiary/ quaternary
- Configuration: atom placement; bond break in tertiary/ quaternary
- Rama plot: stat distr of combos of backbone dihedral angles ϕ and ψ to shoe allowed conforms
- Stabil arises from many intermolec H bonds and reduc in SA to solvent during folding
- Secondary
    - A-helix: H bonds, dipoles btw N/C, helix cap since no H bond at end
    - Other helices:
        - Alpha: 3.6 residues/turn, 1.5Å rise/residue, 5.4 rise/turn (pitch), φ =-60, ψ = -45
        - 3 sub10: 3.0 peptides/ turn, 6.0Å pitch
        - Pi: 4.4 peptides/ turn, 5.2Å pitch
        - Left handed: 3.3 peptides/ turn, 9.8Å pitch
    - B sheet: b turn type 1 (Pro at pos 3) and type 2 (Pro at pos 2 and Gly at pos 3)
        - Rise per residue: 3.47Å for antiparallel & 3.25Å for parallel strands
- Tertiary
    - Globular
        - Noncovalent, somewhat stable (spreadout prot→ more E)
        - *Max internal bonds and min solvent contact*
        - Mediate cell fxn (many formations can be created = diversity for cell)
        - Types: a, B, a/B, a+B
    - Fibrous:
        - Covalent, max intermolec bonds and molec contact,
        - Keratin: 2 right-handed α-helices → elongated left-handed superhelix
        - β-Keratin: Gly-Ala/Ser-Gly-Ala/Ser....
        - Collagen: Gly – X – Y (X = Proline, Y = Hydroxyproline)
        - 3 left-handed helices → elongated right-handed superhelix
        - Ramachandran/ Kartha published 1st triple helical conformation via fiber diffraction

- Quaternary
    - H bond, ionic on prot surface, weak forces stabil, hpo drive prot fold
    - Advan: RACES → Reg of PPI, Assemble catalytic sites, Coop, Efficiency, Stabil
    - Isologous (1 line of rot ***sym***) and heterologous (2 lines) btw prot subunits
    - Cell ex: flagella tail (prot act as motor)
    - Disease ex: CJD, CF, ADm, emphysema, familial amyloid polyneuropathy cancer

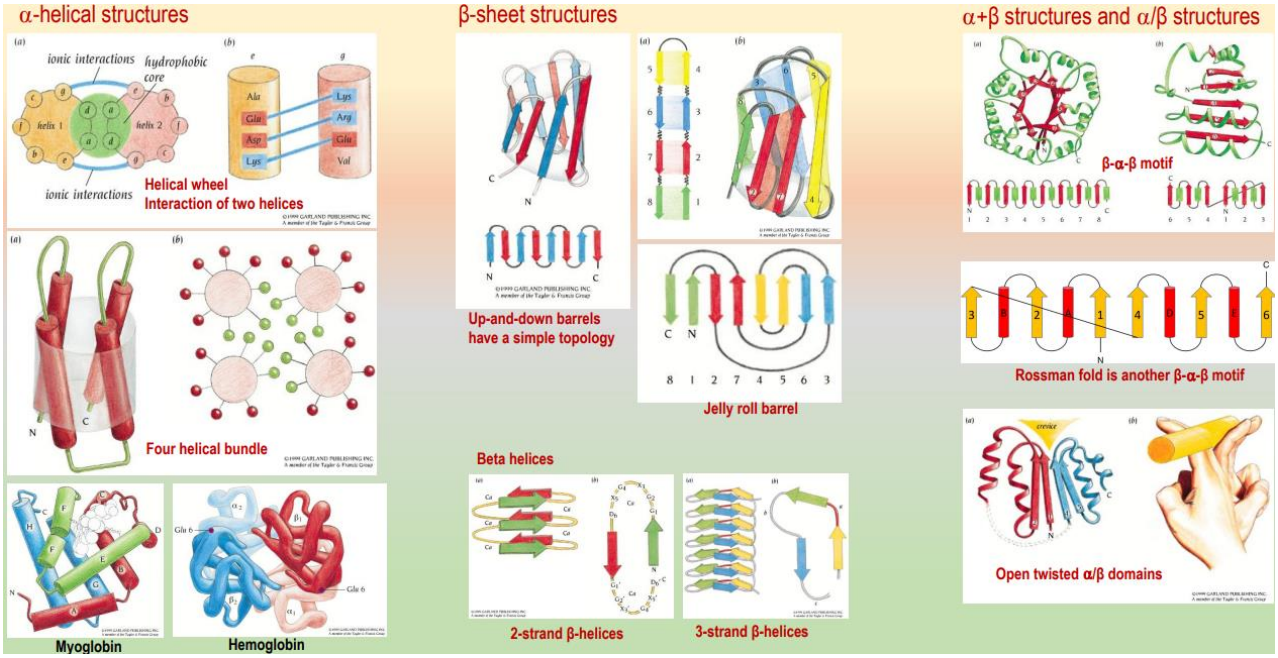
2. Purification

- Ion exchange chrom: acidic molec attracted to cation media; basic to anion
- Size exclusion chrom: large molec elute last (small trapped in pores)
- Immunoaffinity chrom most effective w/ specific activ (enz activ per mg of prot)
- Prot conc det via UV @280nm and dep on arom AA (T/Y absorbs ~280)

3. Sequencing

- Purpose: find prot fxn, domain struc, primary struc, predict 3/4 strc, eval prot relat
- Types: Sanger method (common, analyze AA one by one) and mass spec (cleave prot frag & analyze their masses)
- Steps: CDIFR (Can DIFRentiate prot)
    1. Chain sep
    2. Disulfide cleavage
    3. Identify N/C terminals
    4. Fragment chain (to make shorter)
        a. Enzyme fragmentation: chymo/trypsin cuts at Arg or Lys
        b. Chemical fragmentation: cyanogen bromide cuts at Met
    5. Reconstruct seq: Edman degrad prod peptides in seq and seq det by seeing which parts overlap

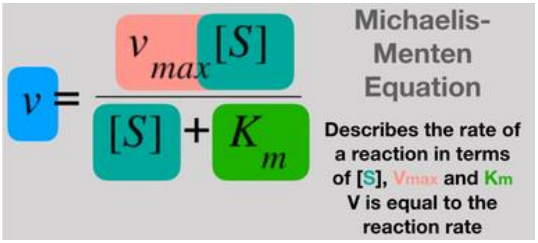
4. Folding



Enzymes

- Kinetic (faster made prod) favored over thermo (more stable prod)
- Reg to ensures metab rxn rate is approp for cell req
- Coenz: haloenz (coenz on enz) and apoenz (coenz not on enz)

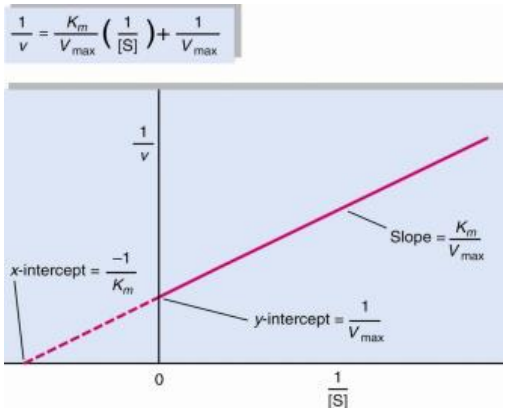
1. **Michaelis-Menton**

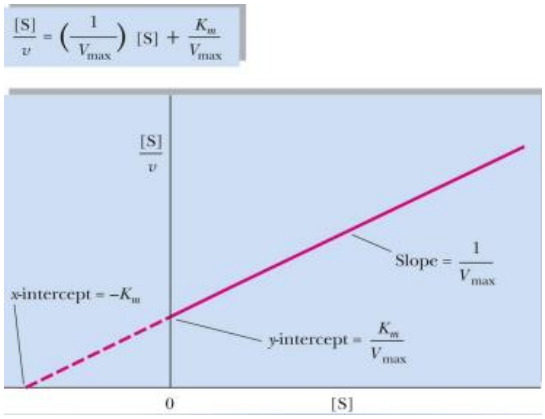


- Catalytic power: cat rxn rate to uncat rxn rate ratio
- Catalytic effic: how well enz turns over prod (kcat/ Km)
- Kcat = turnover #, kcat = vmax/ E total
- Km = substrate amt at half of vmax (high = weak bind, low = tight bind)

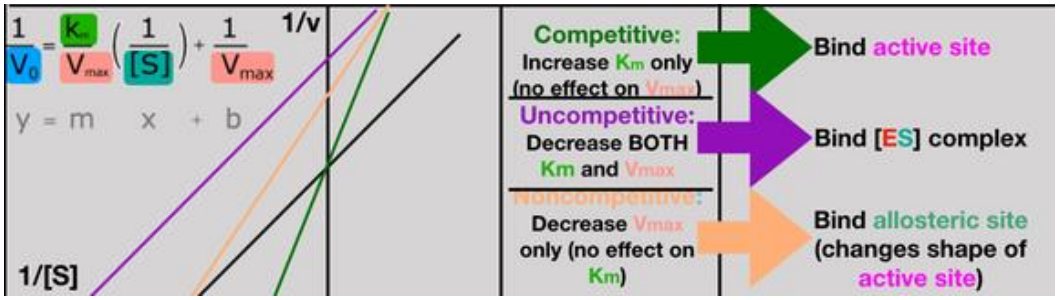
2. **Biomolecular Rxns**: ordered (lead substrate binds 1st) or random (either substrate binds 1st)
3. **Lineweaver-Burk** (left) **& Hanes-Woolf** (right)

- Best bc less errors in plot





4. **Competition**



Thermodynamics

- Sys: isolated (no E/matter exchange), closed (E exchange), open (E/matter exchange)
- 1st Law: not create/ destroy → E = q+w (q is heat and w is work)
- Work assumes const pressure sys (most bio sys are)
- Pos ΔH° means bond breaking → unfolding → exposed hpo → E raised → thermo unstable
- 3rd Law: entropy approaches 0 as T reaches 0K (decr T = decr S)
- *1st law = enthalpy (H), 2nd = entropy (S), 3rd = heat capacity (Cp)*