

Forces Influencing Protein Structure

Josh Lees

- ## Forces Influencing Protein Structure
- Hydrophobicity/Hydrophilicity
 - H-bonding
 - Van der Waals/Dispersion Forces
 - Electrostatics
 - Disulfide Bridges

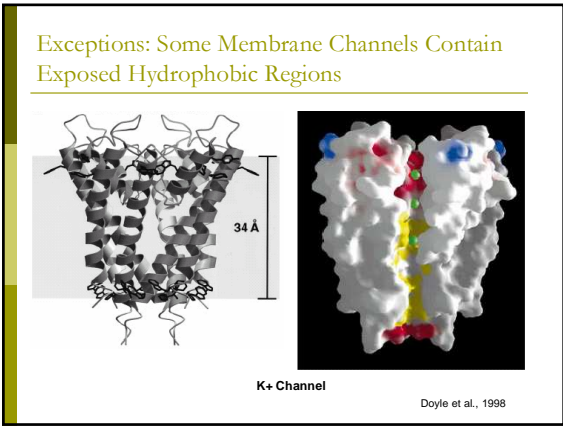
Side-Chain Hydrophobicity/Hydrophilicity is a Primary Determinant of Protein Structure

Polar / Charged (Hydrophilic) residues are generally found on the outside of proteins, in contact with the solvent

Nonpolar (Hydrophobic) residues generally pack toward the core, away from solvent

<p>Glutamine</p> <chem>NC(=O)CC(N)C(=O)O</chem>	<p>Tyrosine</p> <chem>NC(=O)C(Cc1ccc(O)cc1)C(=O)O</chem>	<p>Glutamate</p> <chem>NC(=O)CC(O)C(=O)O</chem>	<p>Histidine</p> <chem>NC(=O)C(Cc1c[nH]cn1)C(=O)O</chem>
<p>Asparagine</p> <chem>NC(=O)CC(N)C(=O)O</chem>	<p>Serine</p> <chem>NC(=O)CC(O)C(=O)O</chem>	<p>Threonine</p> <chem>NC(=O)C(C(C)O)C(=O)O</chem>	<p>Alanine</p> <chem>NC(C)C(=O)O</chem>
<p>Tryptophan</p> <chem>NC(=O)C(Cc1c[nH]c2ccccc12)C(=O)O</chem>	<p>Lysine</p> <chem>NC(=O)CCCC[NH3+]</chem>	<p>Arginine</p> <chem>NC(=O)CC[NH2+]</chem>	<p>Methionine</p> <chem>NC(C)C(S)C(=O)O</chem>
<p>Aspartate</p> <chem>NC(=O)C(O)C(=O)[O-]</chem>	<p>Proline</p> <chem>C1CC[NH2+]C1</chem>	<p>Isoleucine</p> <chem>CC(C)C(C)C(C)C(=O)O</chem>	<p>Leucine</p> <chem>CC(C)C(C)C(=O)O</chem>
		<p>Phenylalanine</p> <chem>NC(Cc1ccccc1)C(=O)O</chem>	<p>Valine</p> <chem>NC(C)C(C)C(=O)O</chem>

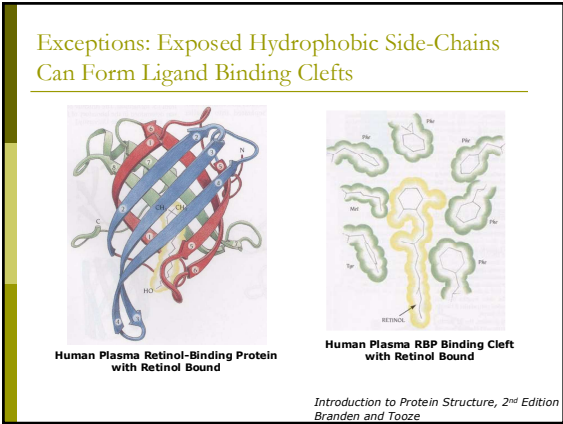
Introduction to Protein Structure, 2nd Edition Branden and Tooze



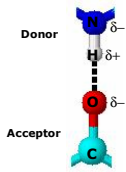
Exceptions: Surface Hydrophobic Residues May Serve Specific Functions

- Exposed surface hydrophobic side-chains often form surfaces for protein-protein interactions
- Long hydrophobic stretches can also form transmembrane structures

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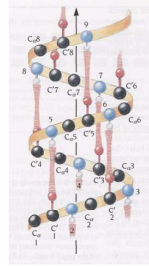


Hydrogen Bonding



- H-bonds form when a hydrogen is shared by two partially negatively charged atoms
 - In proteins, the participating atoms are always N/N, O/O, or N/O
- H-bonds are necessary both for secondary and tertiary structure

Hydrogen Bonding is Crucial for Secondary Structures

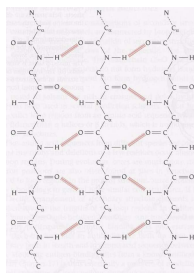


α-helix

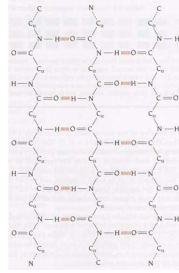
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- H-bonds between backbone amines and carbonyl oxygens allow the formation of α-helices and β-pleated sheets

Hydrogen Bonding in β-Pleated Sheets



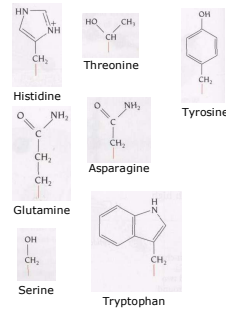
Parallel β-Sheet



Antiparallel β-Sheet

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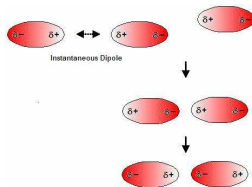
Hydrogen Bonding of Polar Side-Chains



- Polar side chains also participate in structure-stabilizing hydrogen bonds at the core of a protein

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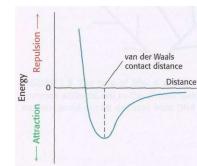
Van der Waals Interactions



- Caused by fluctuation in the positions of electrons on uncharged atoms
- Very weak individually (~10³ times weaker than covalent bonds), but can sum to a very significant effect on protein stability

Van der Waals Interactions

- Can be repulsive or attractive, depending on the proximity of interacting atoms
- Influence side-chain packing at the core and stabilize protein-protein interactions at the surface



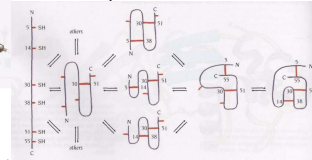
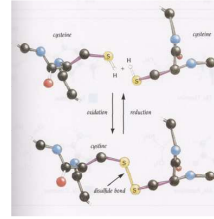
*Biochemistry, 5th Edition
Berg, Tymoczko, and Stryer*

Charge and Electrostatics

- Charged and polar side-chains frequently play an important role in ligand/substrate binding and protein-protein interactions, not to mention catalysis
- Charged side-chains stabilize the structure at a protein's core through H-bonds and salt bridges and at the surface through interactions with solvent and with binding partners

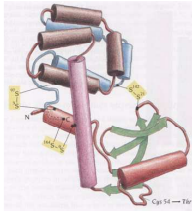
Disulfide Bridges

- Cysteines can be oxidized to form covalent S-S bonds between amino acids distant in primary sequence



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Disulfide Bonds Can Contribute to Tertiary and/or Quaternary Structure



T4 Lysozyme



Immunoglobulin

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