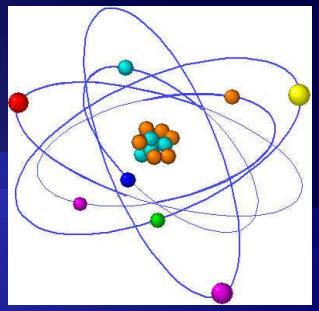
Session 2

BUILDING BLOCKS

Atoms



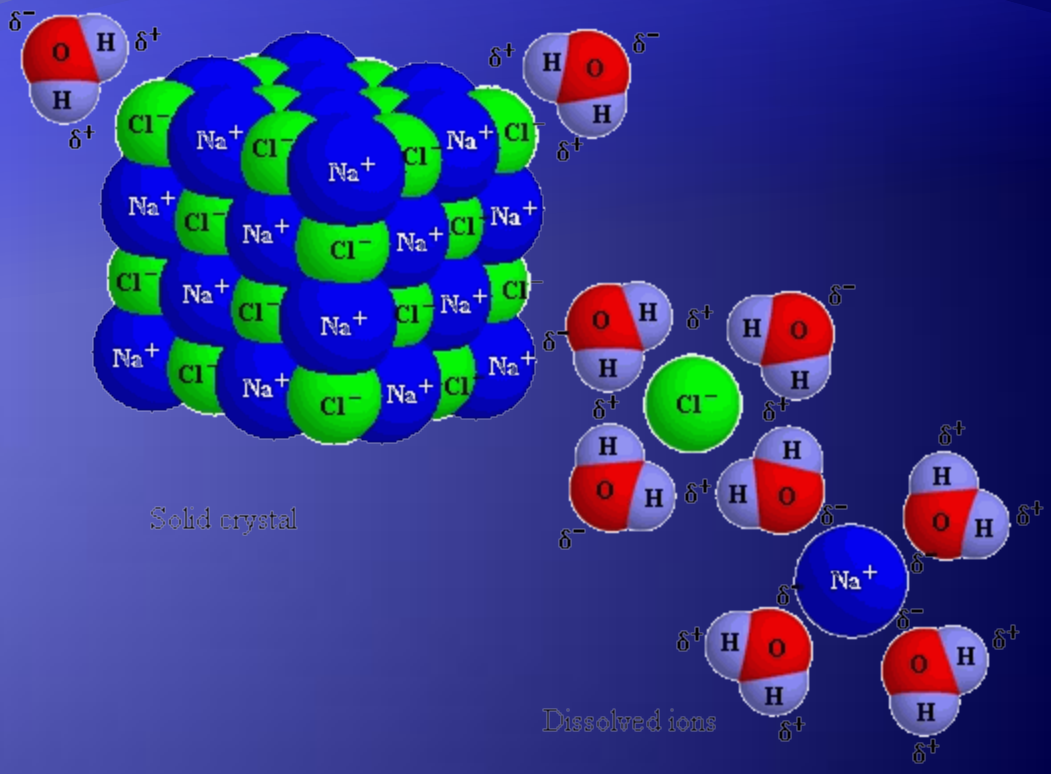
- Six basic elements
  - Hydrogen (H), Carbon (C), Nitrogen (N), Oxygen (O), Phosphorous (P), Sulfur (S)

Atoms	H	C	N	O	P	S
Valency	1	4	5	6	5	6
Electronegativity	2.1	2.5	3.0	3.5	2.1	2.5
H. Sapien (%)	9.3	19.4	0.8	62.8	0.6	0.6
Bacteria (%)	9.9	12.14	3.0	73.7	0.6	0.3
Earth (%)	0.9	0.2	0.9	50	0.12	0.12

- Valence electrons determine the bonding
- Electronegativity determines the polarity
- Composition is similar between living organisms

Molecular Bonds

- Ionic bonds
- Covalent bonds
- Hydrogen bonds
- Van der Waal bonds
- Hydrophobic interactions
- Catch bonds



Water is polar because of unequal e⁻ sharing:

O = 3.5 vs. H = 2.1 (e⁻ negativity)

Solvents and hydrocarbon chains are nonpolar:

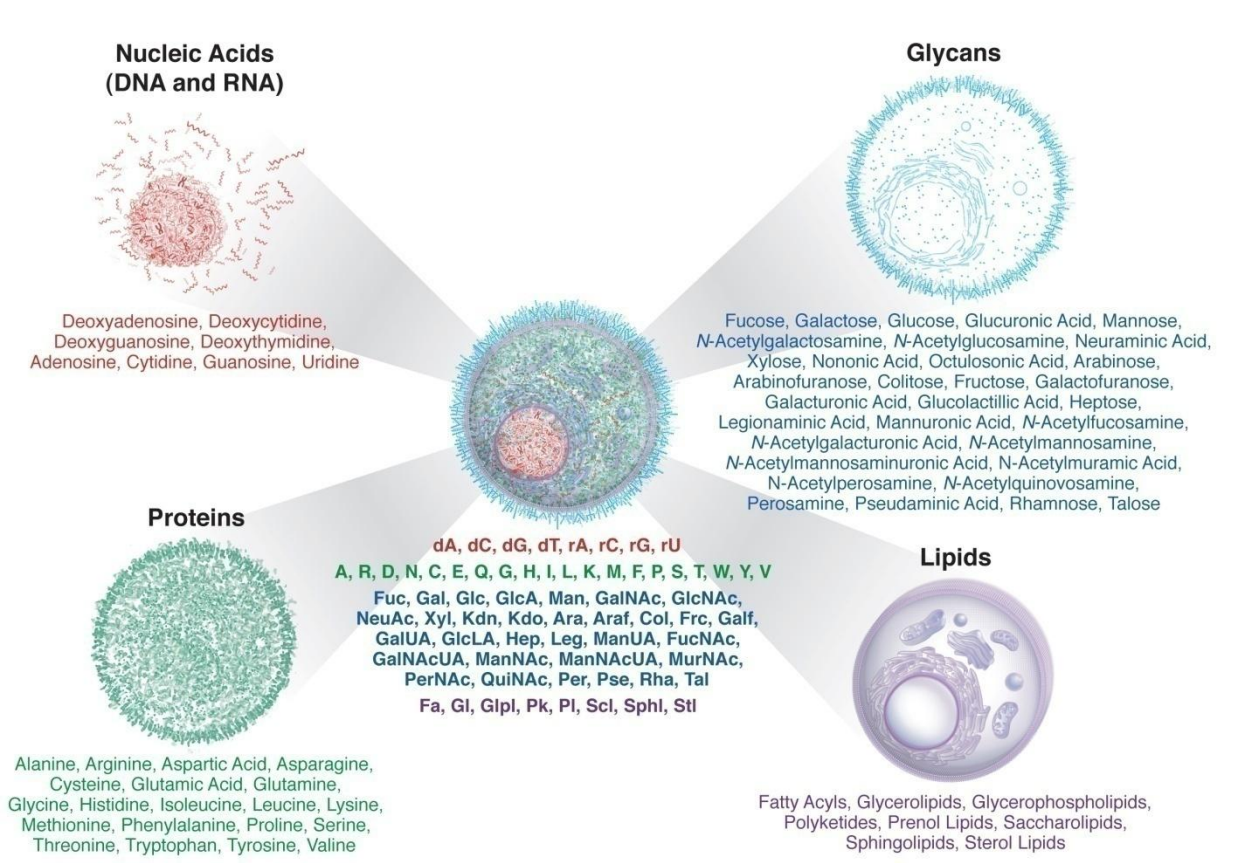
C = 2.5 vs. H = 2.1

Fundamental Units of Organisms

- All life is from 68 molecular building blocks

Nucleic Acids
8 nucleosides

Proteins
20 amino acids



Glycans
32+ sugars

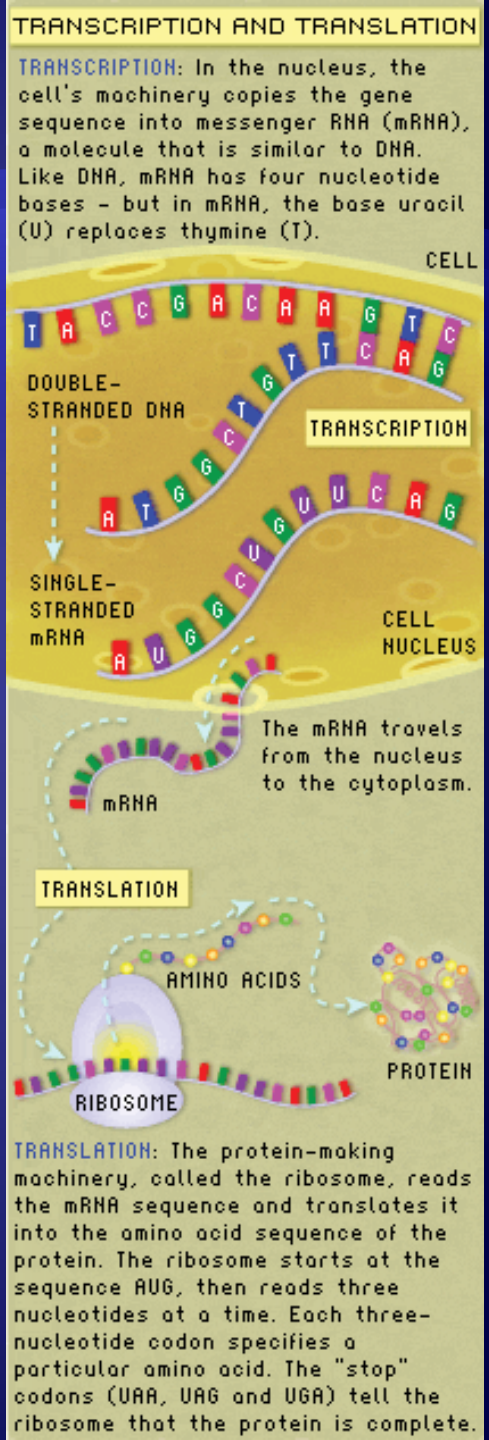
Lipids
8 types

"From the construction, modification, and interaction of these components, the cell develops and functions." –James Marth

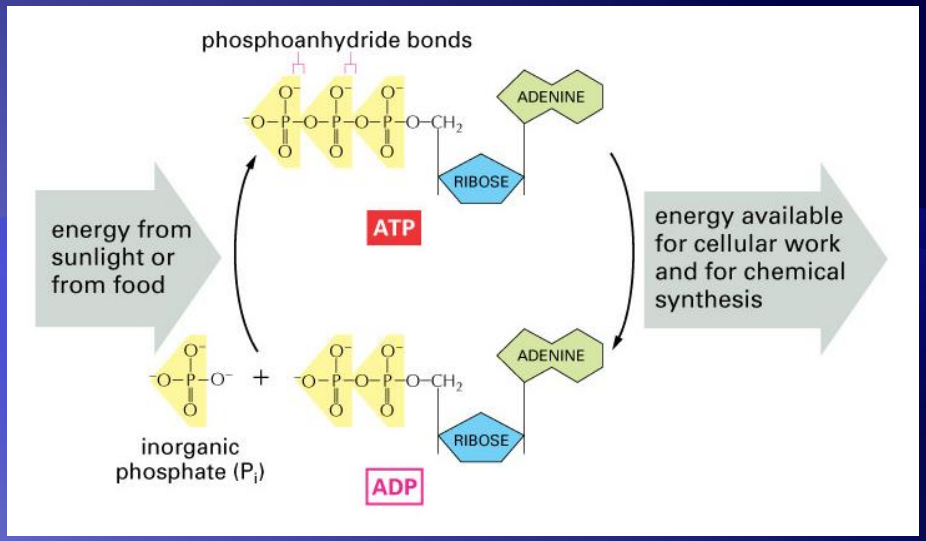
J. Marth "A Unified Vision of the Building Blocks of Life" *Nature Cell Biology*, 2008,10(9):1015-16

Nucleic Acids

- DNA – genetic code
  - Adenine, Guanine, Cytosine, Thymine
- RNA – translation into proteins
  - Adenine, Guanine, Cytosine, Uracil
  - Messenger RNA (mRNA)
  - Transfer RNA (tRNA)
- Others…
  - Ribosomal RNA (rNA)
  - Small interfering RNA (siRNA)
  - Micro RNA (microRNA)
  - Small nuclear RNA (snRNA)

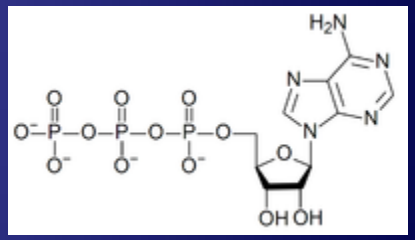


Nucleoside Triphosphates



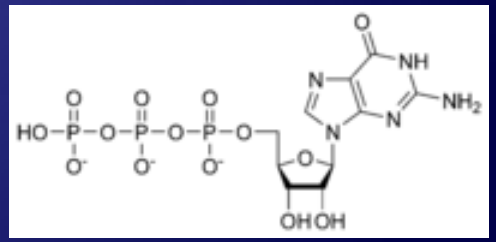
- ATP – energy currency
  - Adenosine triphosphate
  - ATP + H_2O → ADP + PO_4^{3-} + 7.3 kcal/mol
  - Actin & Myosin

ATP

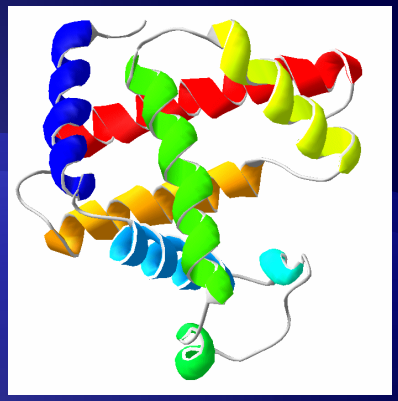


- GTP - regulatory
  - Guanosine triphosphate
  - G-protein Signal Transduction
  - Microtubules

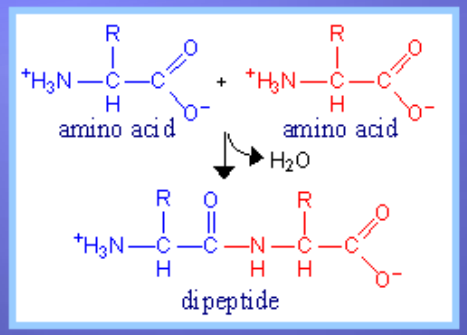
GTP

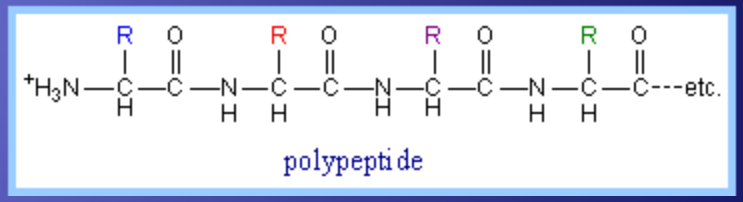


Proteins



- Individual amino acids are translated into long chains called polypeptides
- Peptide bond: carboxyl + amino → CO–NH + H_2O

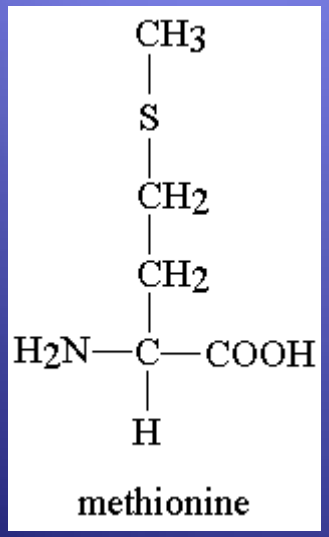




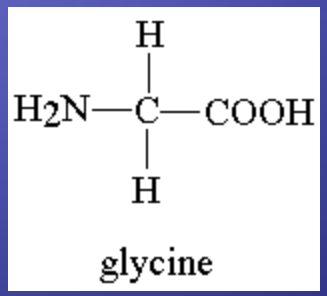
- Residue (R): each amino acid in a polypeptide
- Residue sequence read from N-terminal to C-terminal
- Final sequence will "fold up" into a 3-dimensional structure
- Substitution of just one residue can change a protein's structure-function relationship

Amino Acids

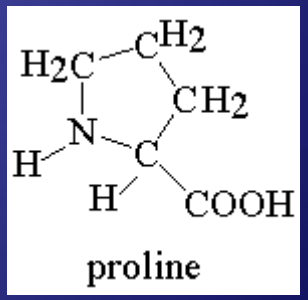
- Central carbon plus amino group ($-NH_2$), carboxyl group (-COOH), hydrogen atom (-H), and distinct side chain (20 in total)
- Side chains determine shape and function



Met, M
Start of all proteins

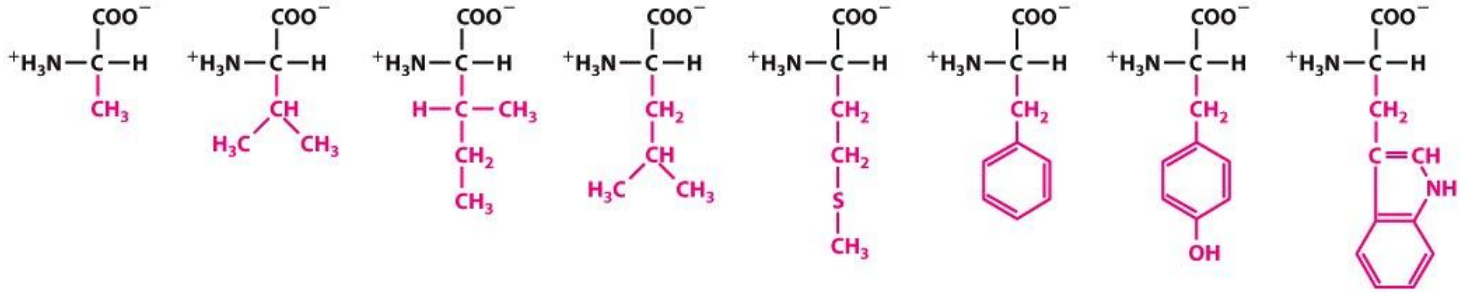


Gly, G
Simplest
Hydrophobic



Pro, P
Forms a rigid kink

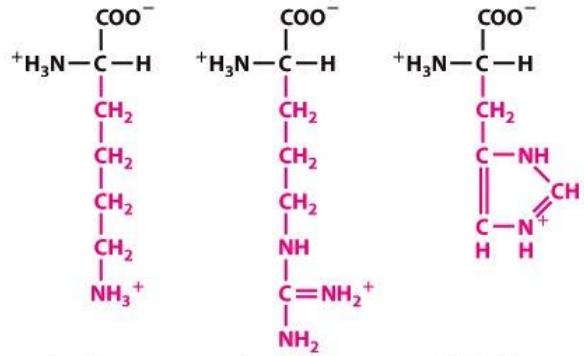
HYDROPHOBIC AMINO ACIDS



Alanine (Ala or A) | Valine (Val or V) | Isoleucine (Ile or I) | Leucine (Leu or L) | Methionine (Met or M) | Phenylalanine (Phe or F) | Tyrosine (Tyr or Y) | Tryptophan (Trp or W)

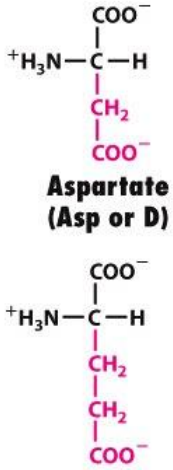
HYDROPHILIC AMINO ACIDS

Basic amino acids



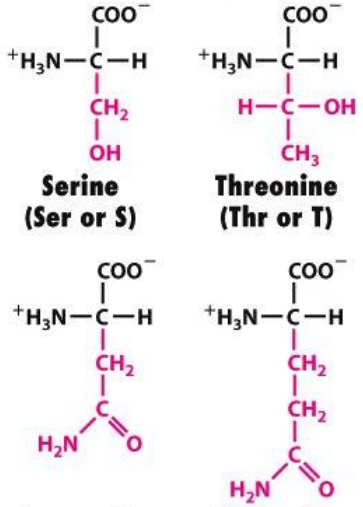
Lysine (Lys or K) | Arginine (Arg or R) | Histidine (His or H)

Acidic amino acids



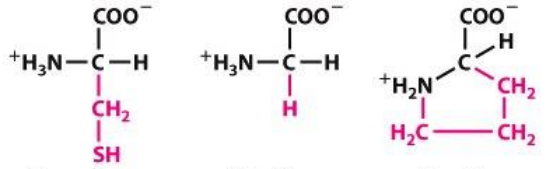
Aspartate (Asp or D) | Glutamate (Glu or E)

Polar amino acids with uncharged R groups



Serine (Ser or S) | Threonine (Thr or T) | Asparagine (Asn or N) | Glutamine (Gln or Q)

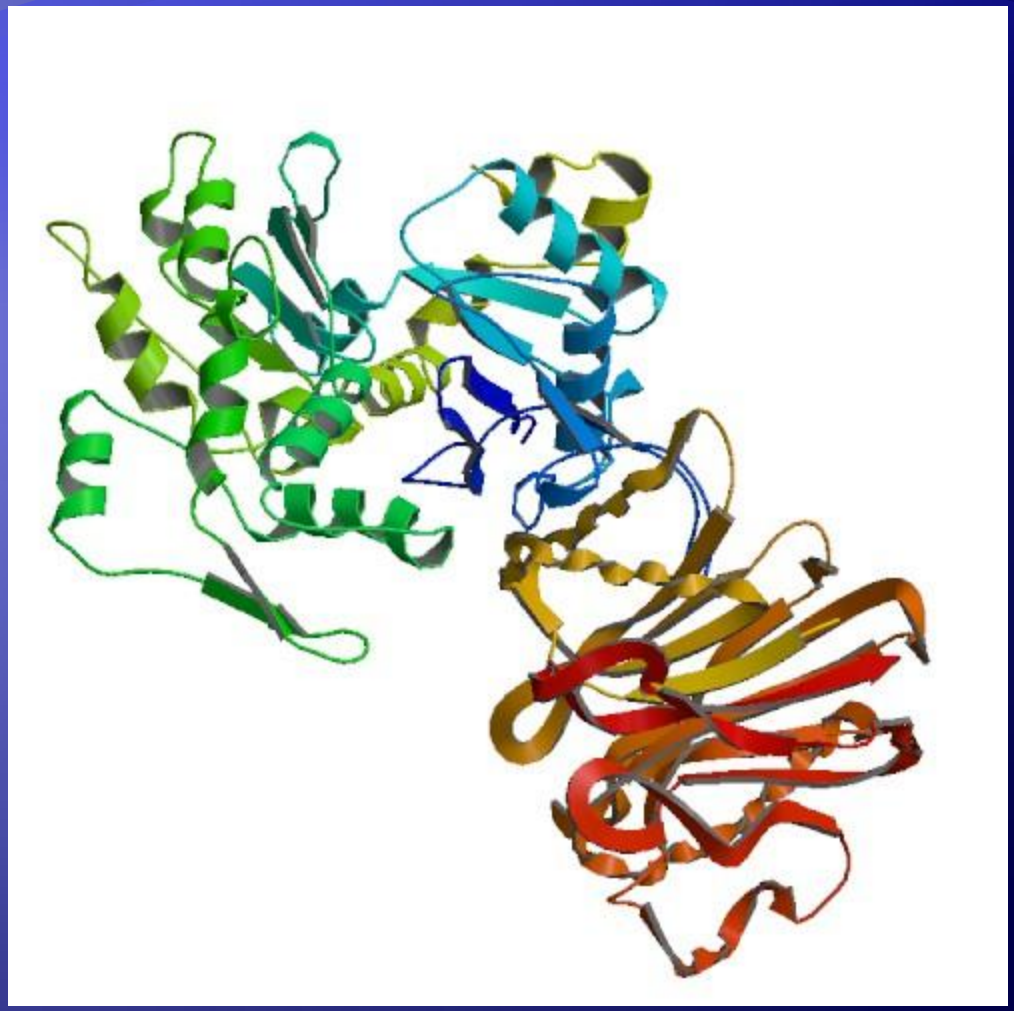
SPECIAL AMINO ACIDS



Cysteine (Cys or C) | Glycine (Gly or G) | Proline (Pro or P)

Amino Acid Sequence

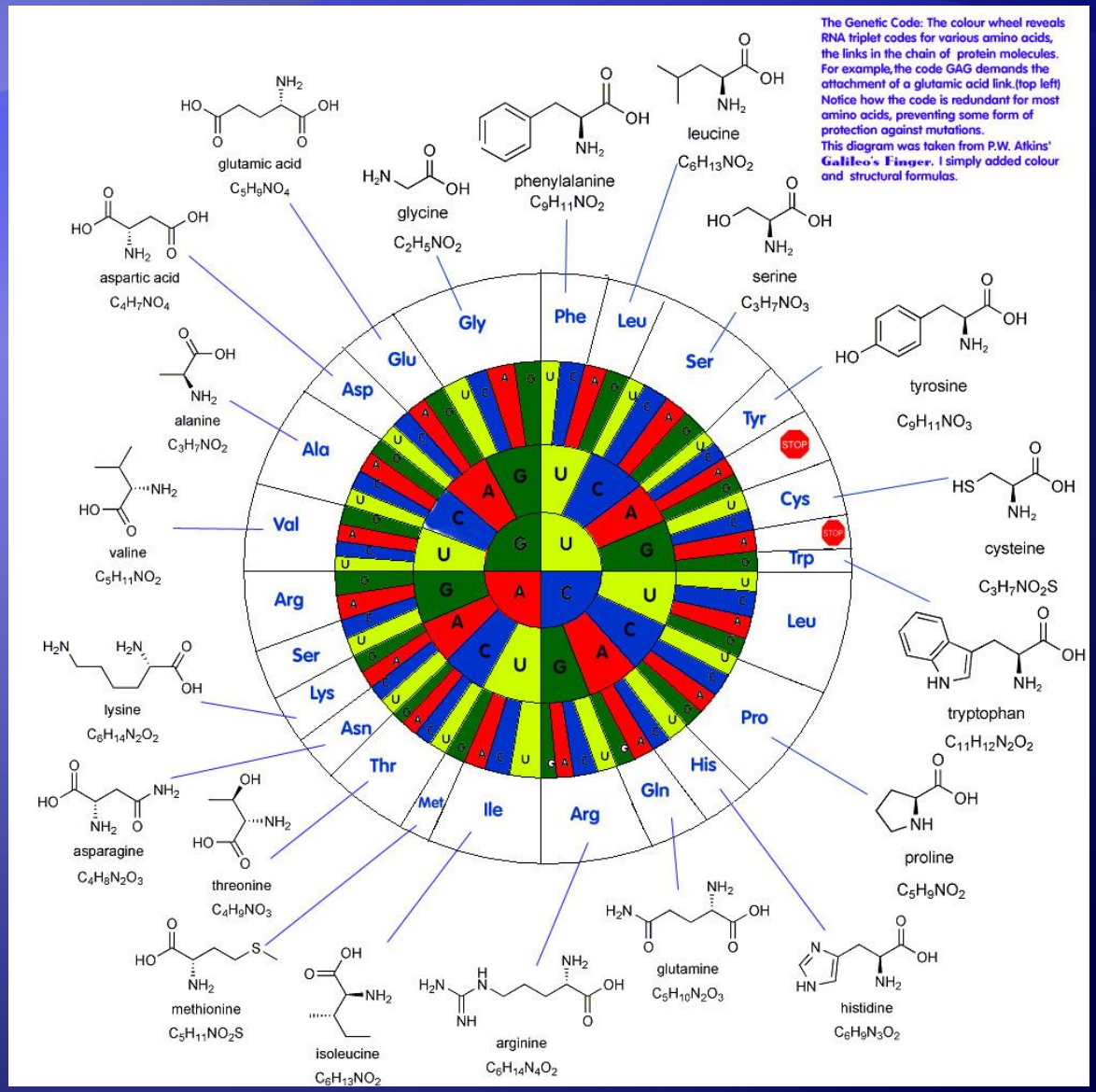
MCEEETTALVCDNGSGLCKAG
FAGDDAPRAVFPSIVGRPRHQ
GVMVGMGQDSYVGDEAQSK
RGILTLKYPIEHGIITNWDDME
KIWHHSFYNELRVAPEEHPTLL
TEAPINPKANREKMTQIMFET
FNVPAMYVAIQAVLSLYASGRT
TGIVLDSGDGVTHNVPIYEGYA
LPHAIMRLDLAGRDLTDYLMKI
LTERGYSFVTTAEREIVRDIKEK
LCYVALDFENEMATAASSSSL
EKSYELPDGQVITIGNERFRCP
ETLFQPSFIGMESAGIHETTYN
SIMKCDIDIRKDLYANNVLSGG
TTMYPGIADRMQKEITALAPS
TMKIKIIAPPERKYSVWIGGSIL
ASLSTFQQMWISKPEYDEAGP
SIVHRKCF



SMOOTH MUSCLE ACTIN (ACTG2)

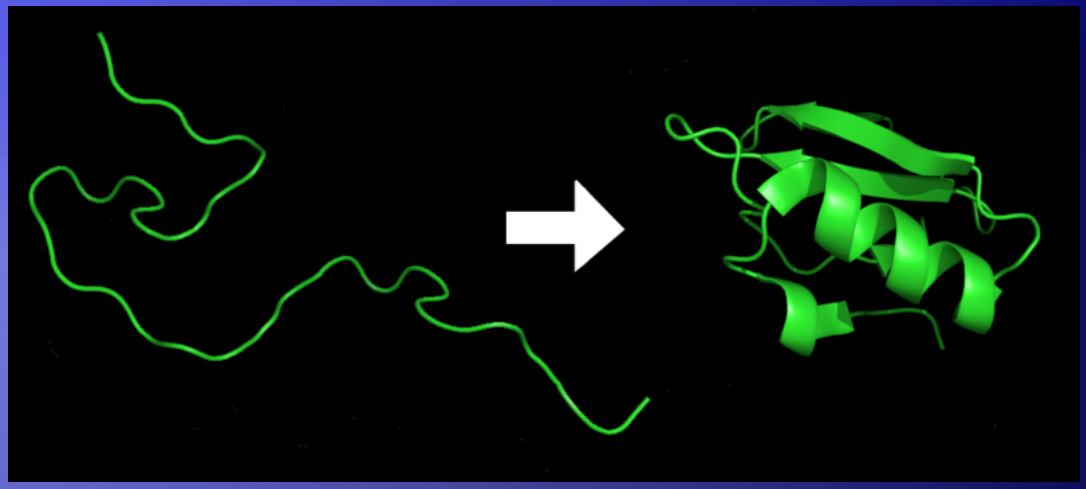
Translation

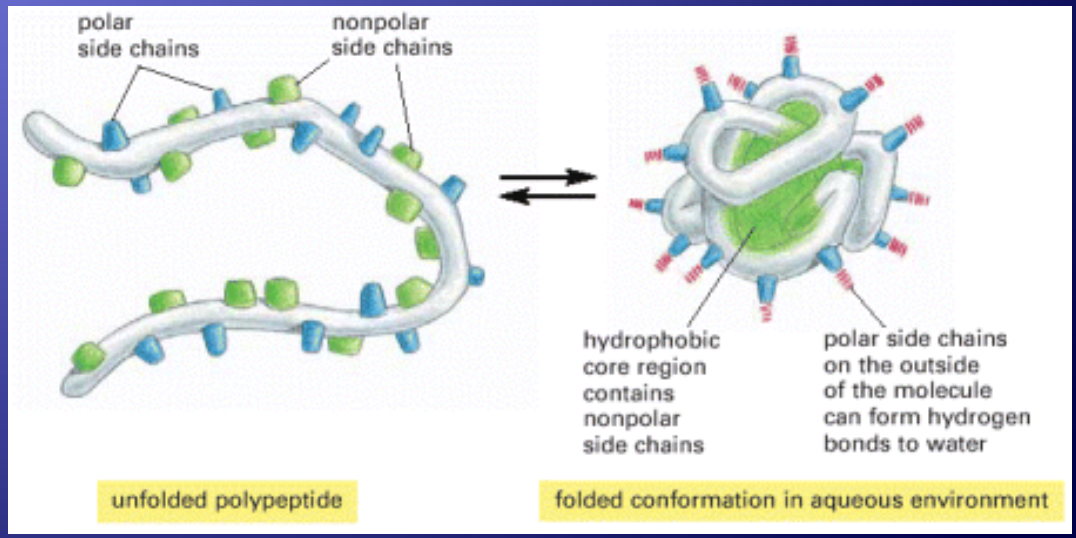
- Start with Methionine (AUG)
- Build codon by codon
- End with UAA, UAG, UGA



Protein Folding

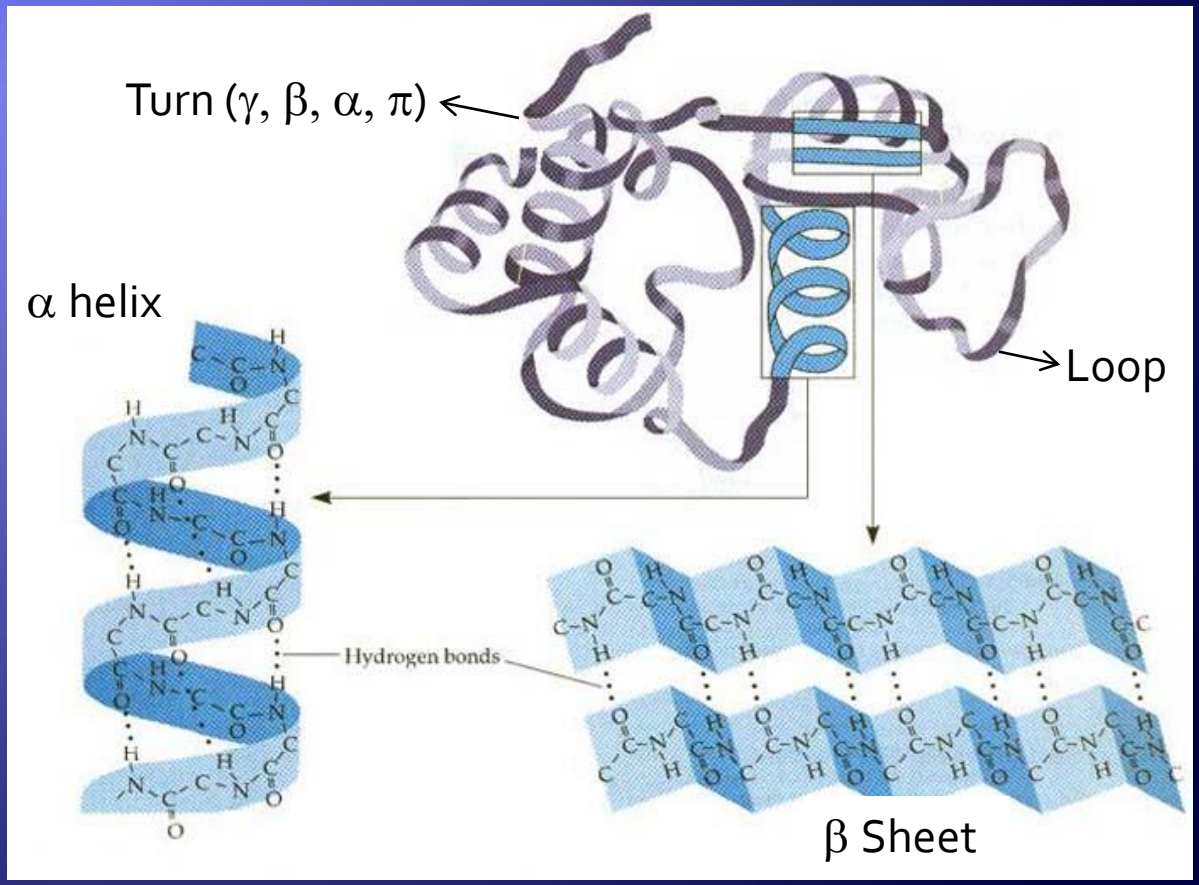
- Hydrophobic residues form inner core of protein
- Denaturing is loss of protein structure
- Post-translational modifications can change protein folding (…and change function)





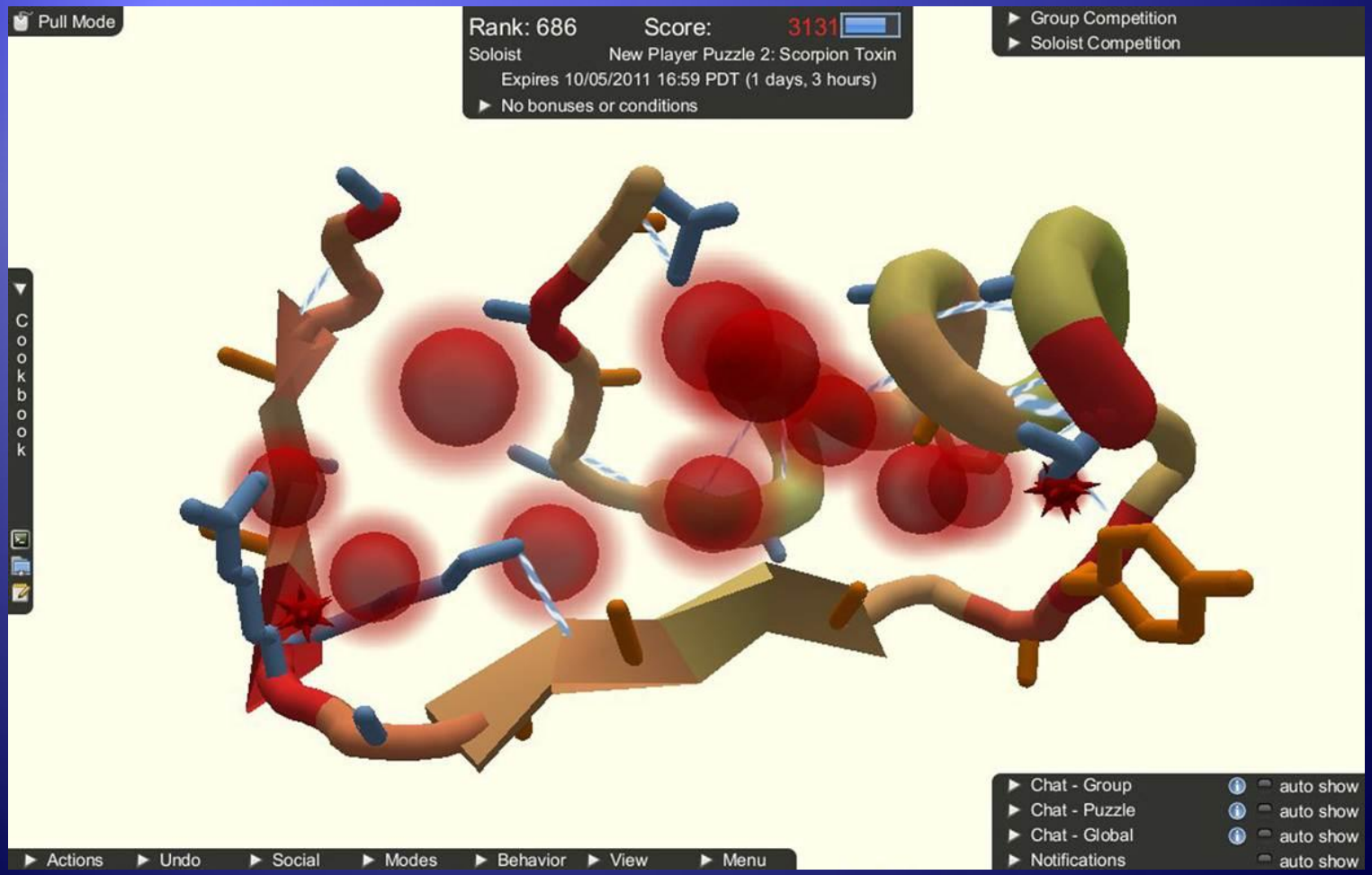
Protein Structure

- Primary – amino acid sequence
- Secondary – sub-structures through hydrogen bonds
  - Alpha helix
  - Beta sheet
- Tertiary – overall shape of a single protein unit
- Quaternary – union of more than one protein units



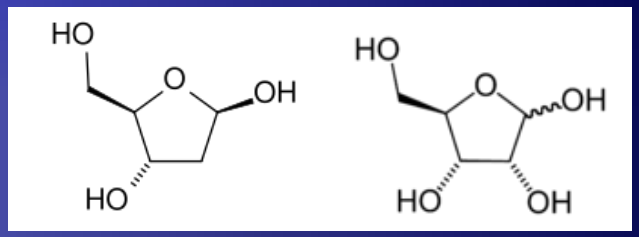
FoldIt (Hw1)

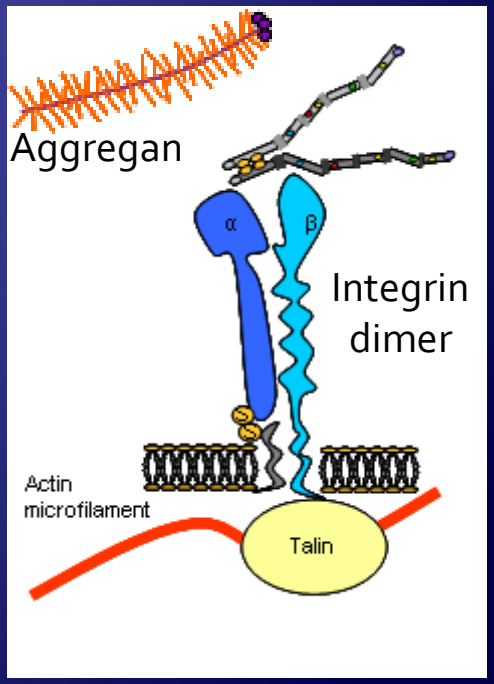
- Developed at UW by Seth Cooper from David Baker's Rosetta program



Glycans

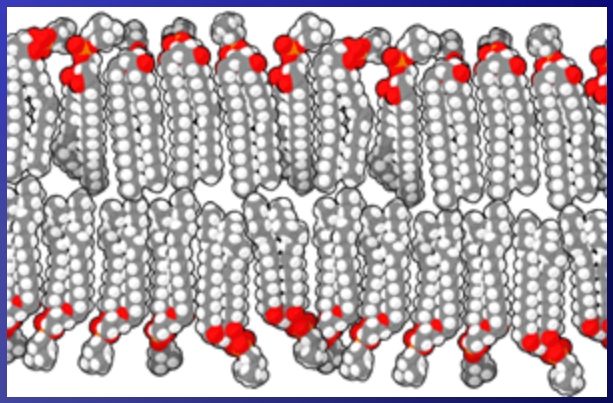
- "Carbohydrates" – hydrated carbons, (C, H, O)
- Combinatorial:
  - Glycoproteins – transmembrane proteins, e.g. integrins
  - Proteoglycans – protein core with polysaccharide chains, e.g. ECM's aggregan
  - Glycolipids – located in extracellular layer of the cell membrane

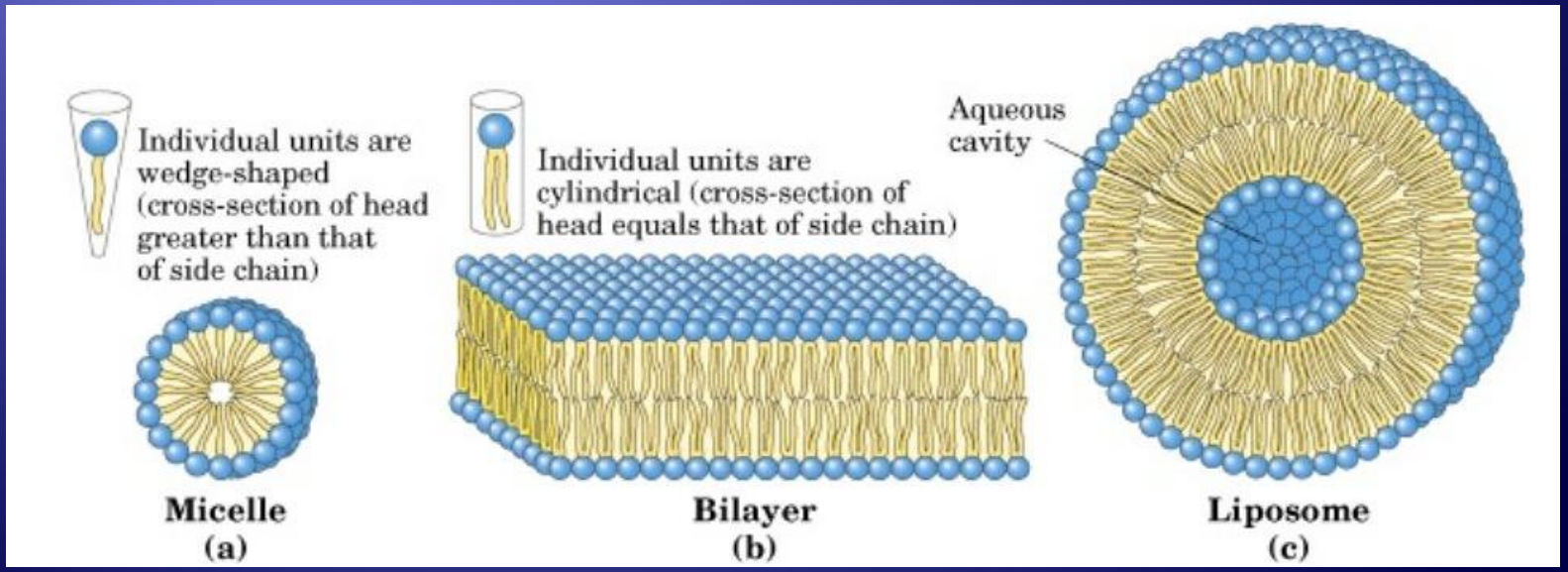




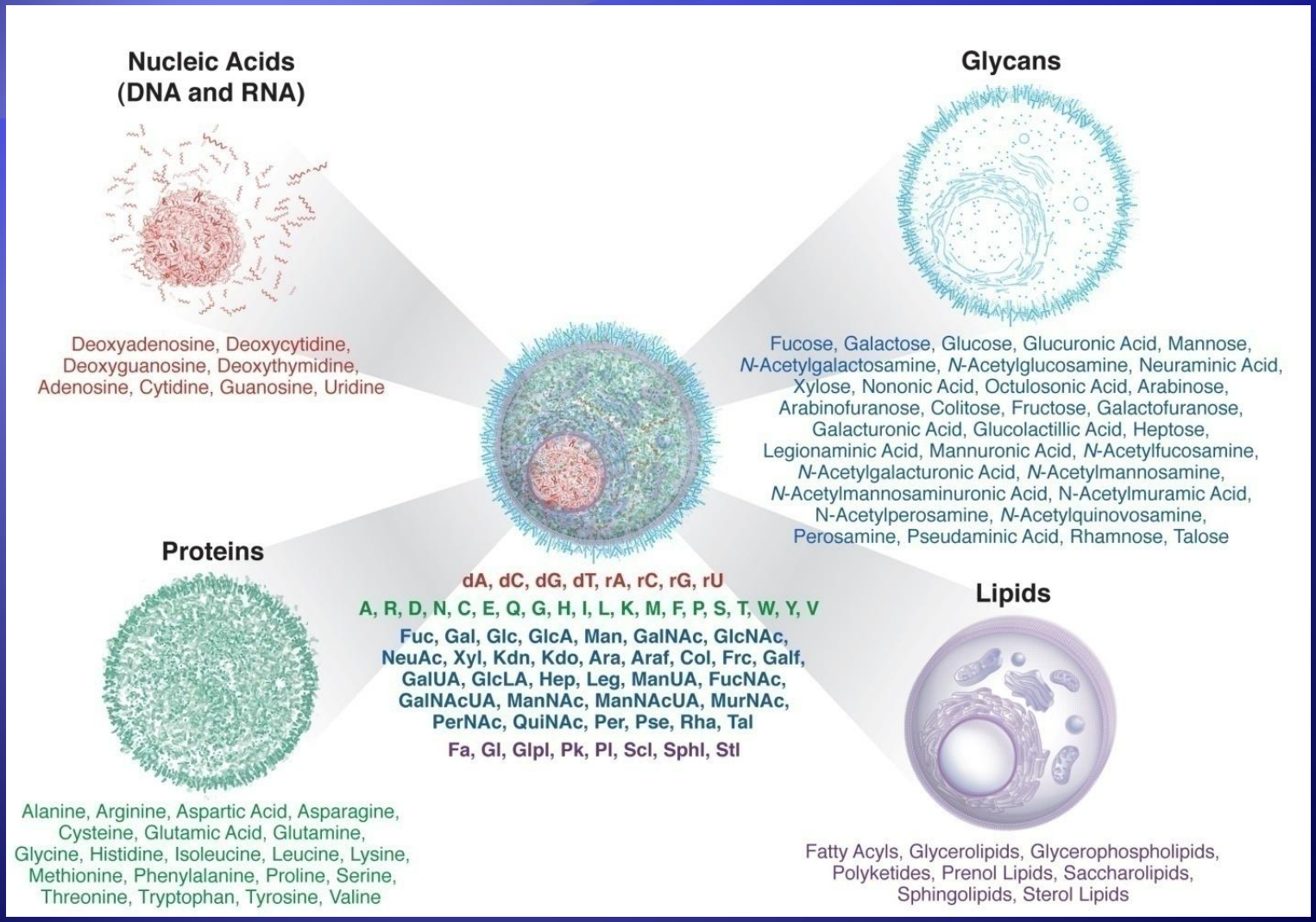
Lipids

- Phospholipids have nonpolar hydrocarbon tails and negatively charged phosphate heads
- In water. phospholipids cluster together to form bilayers
- At air-water interface, tails point out and you have soap bubbles





All Together Now…



Questions?