#### Session 2 BUILDING BLOCKS

#### Atoms

#### Six basic elements

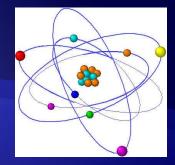
Hydrogen (H), Carbon (C), Nitrogen (N), Oxygen (O), Phosphorous (P), Sulfur (S)

Atoms	Н	C	Ν	0	Р	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

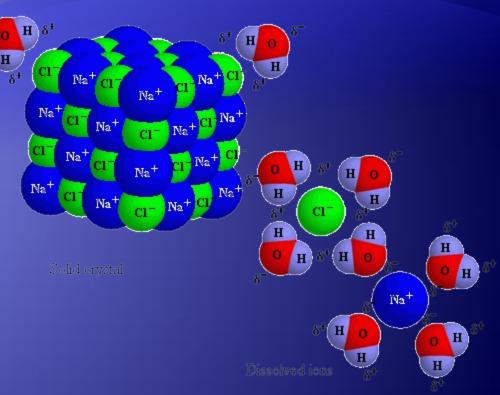
Electronegativity determines the polarity

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<sup>-</sup> sharing:

 $O = 3.5 \text{ vs. } H = 2.1 (e^{-} \text{ negativity})$ 

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



Threonine, Tryptophan, Tyrosine, Valine

#### **Nucleic Acids** Glycans (DNA and RNA) Deoxyadenosine, Deoxycytidine, Fucose, Galactose, Glucose, Glucuronic Acid, Mannose, Deoxyguanosine, Deoxythymidine, N-Acetylgalactosamine, N-Acetylglucosamine, Neuraminic Acid, Adenosine, Cytidine, Guanosine, Uridine Xylose, Nononic Acid, Octulosonic Acid, Arabinose, Arabinofuranose, Colitose, Fructose, Galactofuranose, Galacturonic Acid, Glucolactillic Acid, Heptose, Legionaminic Acid, Mannuronic Acid, N-Acetylfucosamine, N-Acetylgalacturonic Acid, N-Acetylmannosamine, N-Acetylmannosaminuronic Acid, N-Acetylmuramic Acid, N-Acetylperosamine, N-Acetylquinovosamine, Perosamine, Pseudaminic Acid, Rhamnose, Talose Proteins dA, dC, dG, dT, rA, rC, rG, rU Lipids A, R, D, N, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, V Fuc, Gal, Glc, GlcA, Man, GalNAc, GlcNAc, NeuAc, Xyl, Kdn, Kdo, Ara, Araf, Col, Frc, Galf, GalUA, GICLA, Hep, Leg, ManUA, FucNAc, GalNAcUA, ManNAc, ManNAcUA, MurNAc, PerNAc, QuiNAc, Per, Pse, Rha, Tal Fa, GI, GIpl, Pk, PI, Scl, Sphl, Stl Alanine, Arginine, Aspartic Acid, Asparagine, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Fatty Acyls, Glycerolipids, Glycerophospholipids, Polyketides, Prenol Lipids, Saccharolipids, Methionine, Phenylalanine, Proline, Serine,

Glycans

Lipids

8 types

32+ sugars

"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

Sphingolipids, Sterol Lipids

### **Nucleic Acids**

#### DNA – genetic code

Adenine, Guanine, Cytosine, Thymine

#### RNA – translation into proteins

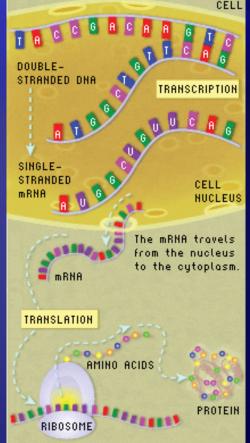
- Adenine, Guanine, Cytosine, Uracil
- Messenger RNA (mRNA)
- Transfer RNA (tRNA)

#### Others...

- Ribosomal RNA (rNA)
- Small interfering RNA (siRNA)
- Micro RNA (microRNA)
- Small nuclear RNA (snRNA)

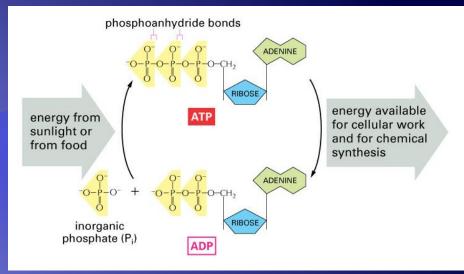


TRANSCRIPTION: In the nucleus, the cell's machinery copies the gene sequence into messenger RNA (mRNA), a molecule that is similar to DNA. Like DNA, mRNA has four nucleotide bases – but in mRNA, the base uracil (U) replaces thymine (T).



TRANSLATION: The protein-making machinery, called the ribosome, reads the mRNA sequence and translates it into the amino acid sequence of the protein. The ribosome starts at the sequence AUG, then reads three nucleotides at a time. Each threenucleotide codon specifies a particular amino acid. The "stop" codons (UAA, UAG and UGA) tell the ribosome that the protein is complete.

# Nucleoside Triphosphates

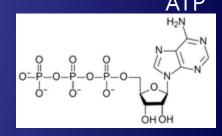


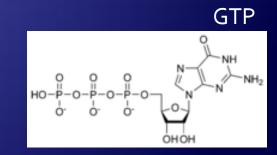
#### ATP – energy currency

- Adenosine triphosphate
- ATP +  $H_2O \rightarrow ADP + PO_4^{3-} + 7.3 \text{ kcal/mol}$
- Actin & Myosin

#### • GTP - regulatory

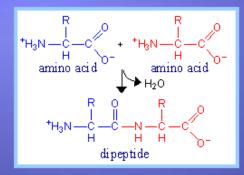
- Guanosine triphosphate
- G-protein Signal Transduction
- Microtubules

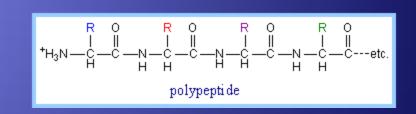




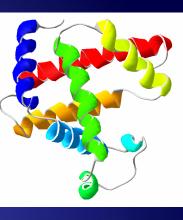
### Proteins

- Individual amino acids are translated into long chains called polypeptides
- <u>Peptide bond</u>: carboxyl + amino  $\rightarrow$  CO–NH + H<sub>2</sub>O





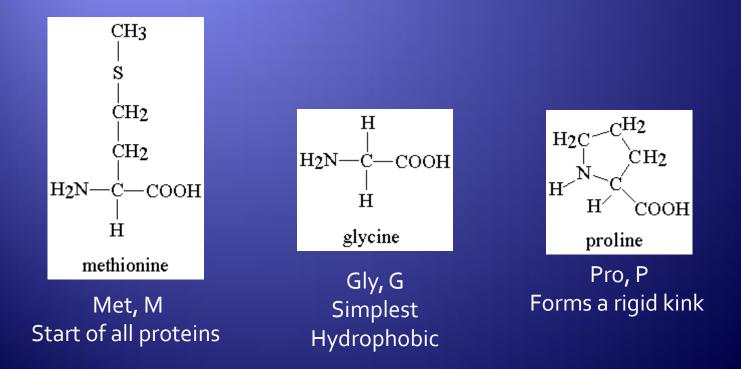
- <u>Residue (R)</u>: each amino acid in a polypeptide
- Residue sequence read from N-terminal to C-terminal
- Final sequence will "fold up" into a 3-dimensional structure
- Substitution of just one residue can change a protein's structure-function relationship

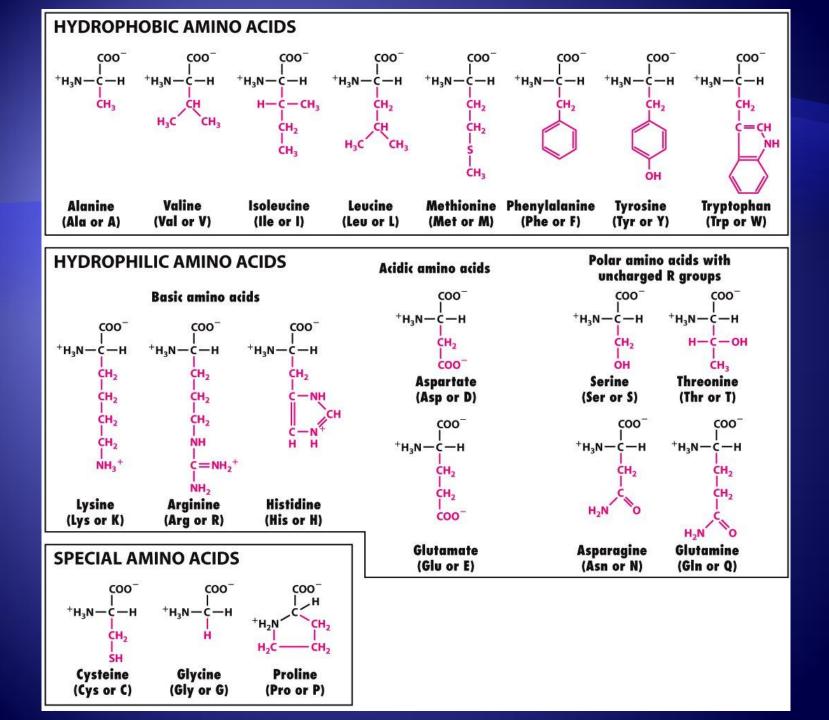


#### **Amino Acids**

 Central carbon plus amino group (-NH<sub>2</sub>), carboxyl group (-COOH), hydrogen atom (-H), and distinct side chain (20 in total)

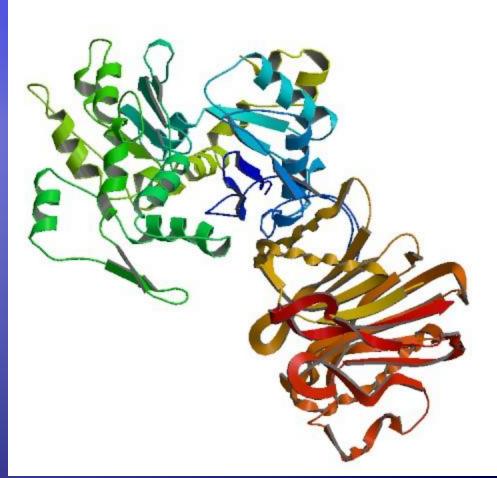
Side chains determine shape and function





### **Amino Acid Sequence**

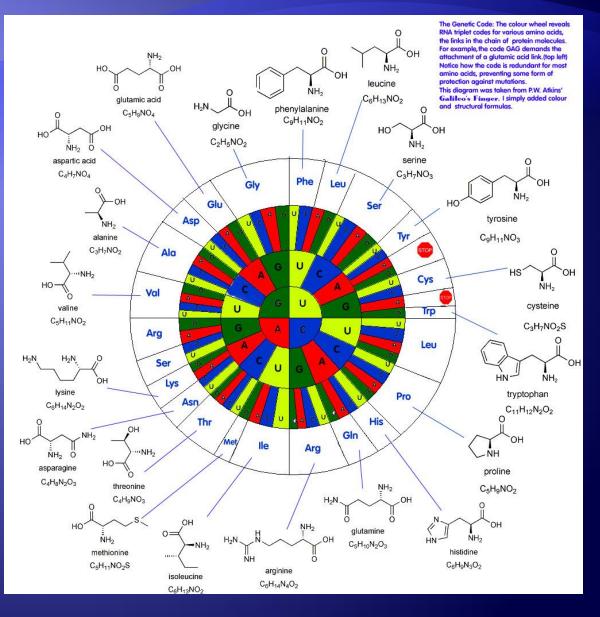
MCEEETTALVCDNGSGLCKAG FAGDDAPRAVFPSIVGRPRHQ GVMVGMGQDSYVGDEAQSK RGILTLKYPIEHGIITNWDDME KIWHHSFYNELRVAPEEHPTLL TEAPINPKANREKMTQIMFET FNVPAMYVAIQAVLSLYASGRT TGIVLDSGDGVTHNVPIYEGYA LPHAIMRLDLAGRDLTDYLMKI LTERGYSFVTTAEREIVRDIKEK LCYVALDFENEMATAASSSSL EKSYELPDGOVITIGNERFRCP ETLFOPSFIGMESAGIHETTYN SIMKCDIDIRKDLYANNVLSGG TTMYPGIADRMQKEITALAPS TMKIKIIAPPERKYSVWIGGSIL ASLSTFOOMWISKPEYDEAGP SIVHRKCF



#### SMOOTH MUSCLE ACTIN (ACTG<sub>2</sub>)

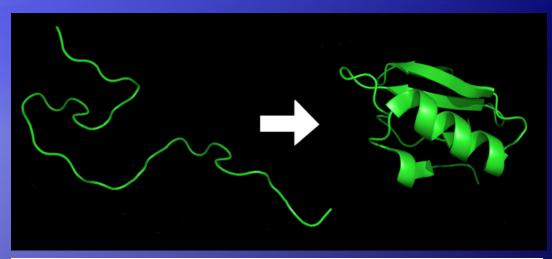
### **Translation**

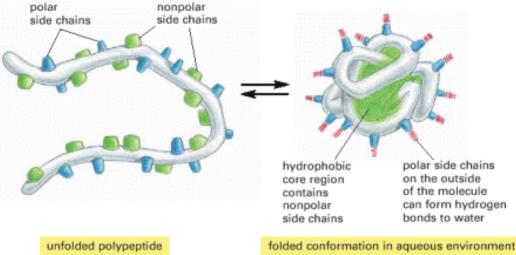
 Start with Methionine (AUG)
 Build codon by codon
 End with UAA, UAG, UGA



# **Protein Folding**

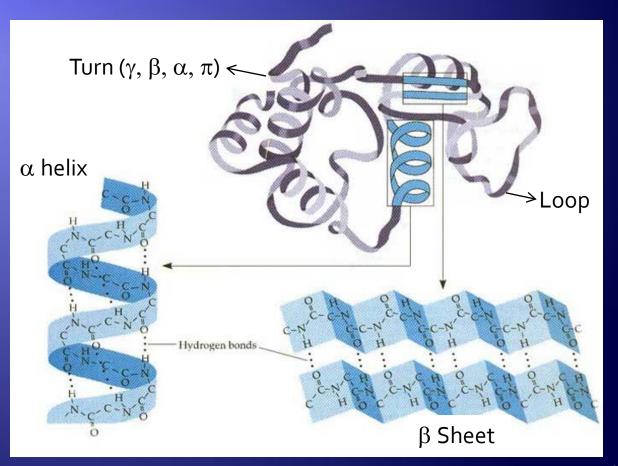
- Hydrophobic residues form inner core of protein
- Denaturing is loss of protein structure
- Post-translational modifications can change protein folding (...and change function)





### **Protein Structure**

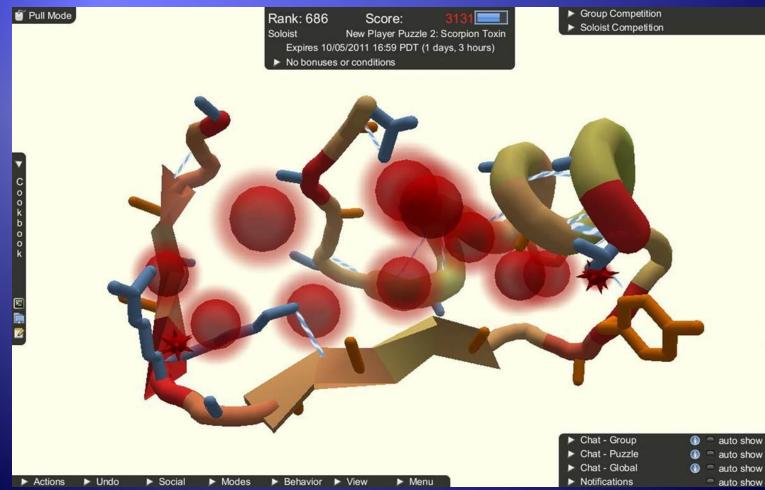
- Primary amino acid sequence
- Secondary sub-structures through hydrogen bonds
  - Alpha helix
  - Beta sheet
- Tertiary –
   overall shape of a single protein unit
- Quaternary union of more than one protein units





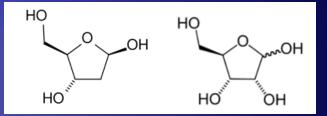
# FoldIt (Hw1)

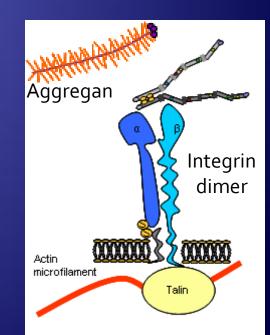
 Developed at UW by Seth Cooper from David Baker's Rosetta program



# Glycans

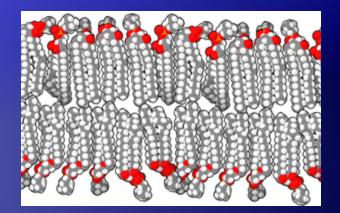
- "Carbohydrates" hydrated carbons, (C, H, O)
- Combinatorial:
  - Glycoproteins transmembrane proteins, e.g. integrins
  - Proteoglycans protein core with polysaccharide chains, e.g. ECM's aggregan
  - Glycolipids located in extracellular layer of the cell membrane

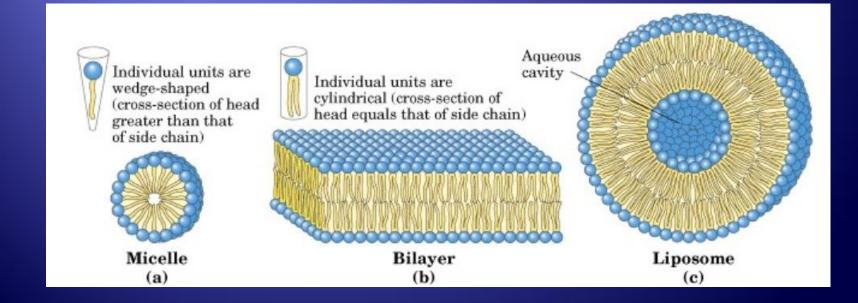




# Lipids

- 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



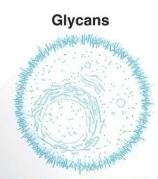


### All Together Now...

#### **Nucleic Acids** (DNA and RNA)



Deoxyadenosine, Deoxycytidine, Deoxyguanosine, Deoxythymidine, Adenosine, Cvtidine, Guanosine, Uridine



Fucose, Galactose, Glucose, Glucuronic Acid, Mannose, N-Acetylgalactosamine, N-Acetylglucosamine, Neuraminic Acid, Xylose, Nononic Acid, Octulosonic Acid, Arabinose, Arabinofuranose, Colitose, Fructose, Galactofuranose, Galacturonic Acid, Glucolactillic Acid, Heptose, Legionaminic Acid, Mannuronic Acid, N-Acetvlfucosamine, N-Acetylgalacturonic Acid, N-Acetylmannosamine, N-Acetylmannosaminuronic Acid, N-Acetylmuramic Acid, N-Acetylperosamine, N-Acetylquinovosamine, Perosamine, Pseudaminic Acid, Rhamnose, Talose

#### **Proteins**



Alanine, Arginine, Aspartic Acid, Asparagine, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, Valine

#### dA, dC, dG, dT, rA, rC, rG, rU A, R, D, N, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, V

Fuc, Gal, Glc, GlcA, Man, GalNAc, GlcNAc, NeuAc, Xyl, Kdn, Kdo, Ara, Araf, Col, Frc, Galf, GalUA, GlcLA, Hep, Leg, ManUA, FucNAc, GalNAcUA, ManNAc, ManNAcUA, MurNAc, PerNAc, QuiNAc, Per, Pse, Rha, Tal

Fa, Gl, Glpl, Pk, Pl, Scl, Sphl, Stl

#### Lipids



Fatty Acyls, Glycerolipids, Glycerophospholipids, Polyketides, Prenol Lipids, Saccharolipids, Sphingolipids, Sterol Lipids

# **Questions?**