Lecture 4 (9/14/20)

- Reading: Ch3, 75
  Ch1, 16-20
  Ch4, 115-116
  Ch3, 75-82
- Problems: Ch1 (text); 13,16
  Ch4 (text); 12
  Ch3 (text); 1,6
  Ch3 (study guide); 1,2,3

NEXT

- Reading: Ch3; 82–87, 92–94
- Problems: Ch3 (text); 2,3,4,7,11,12
  Ch3 (study guide); **4,5,6,8,9**
  Ch2 (text); 34

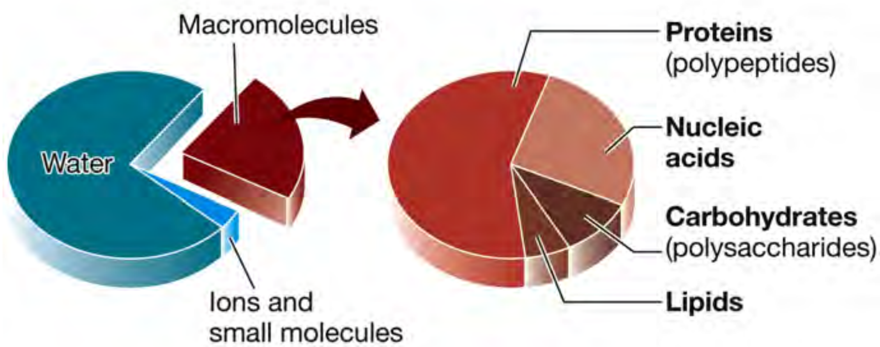
Lecture 4-1 (9/14/20)

OUTLINE

Components of Life

- Proteins
  - Definition
  - Size
  - Shape
  - Solubility
  - Stability
- Types
  - Familiar
  - Structural
  - Functional
- Ways of depicting Shape
- Configuration vs. Conformation

Review from Lecture 1: Components of Life



Going to talk about each of these and discover for each:

1. cellular functions
2. monomeric units
3. name of the bond that makes the polymer
4. characteristics of the macromolecule in terms of shape

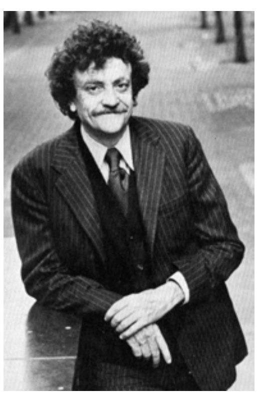
Macromolecules in living organisms: proteins, carbohydrates, nucleic acids, “lipids”; nearly all are polymers

Polymers are composed of smaller molecules called **monomers**, which are part of the **precursors** of the polymer

- *Proteins:* combinations of 20 kinds of amino acid precursors
- *Polysaccharides*: sugar monomers, called monosaccharides (many kinds), are combined. Both monomers and polymers are called *Carbohydrates*
- *Nucleic acids*: combinations of 8 kinds of nucleotide precursors/monomers
- [*Lipids*: non-covalent forces maintain interactions between lipid monomers]

Proteins

What is the secret of life?



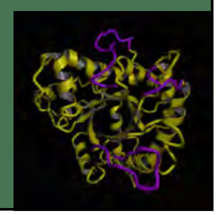
"He said he hoped a lot of us would have careers in science,' she said. She didn't see anything funny in that. She was remembering a lesson that had impressed her. She was repeating it, gropingly, dutifully. 'He said, the trouble with the world was...'

'The trouble with the world was,' she continued hesitatingly, 'that people were still superstitious instead of scientific. He said if everybody would study science more, there wouldn't be all the trouble there was.'

'He said science was going to discover the basic secret of life some day,' the bartender put in. He scratched his head and frowned. 'Didn't I read in the paper the other day where they'd finally found out what it was?'

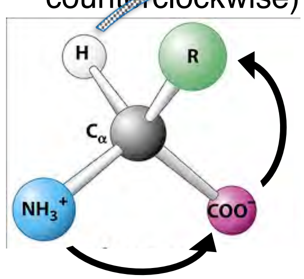
— Kurt Vonnegut Jr., Cat's Cradle

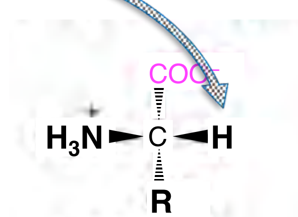
Proteins

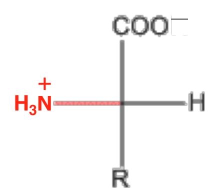


Definition: Proteins are a linear polymers of L-α-amino acids. (generally composed of 20 different types)

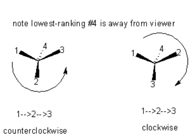
"L" refers to the old-style of configuration* nomenclature (S in R/S) comes from Greek for rotation to the left (levo-rotation; counterclockwise)







*counter clockwise rotation = S = L

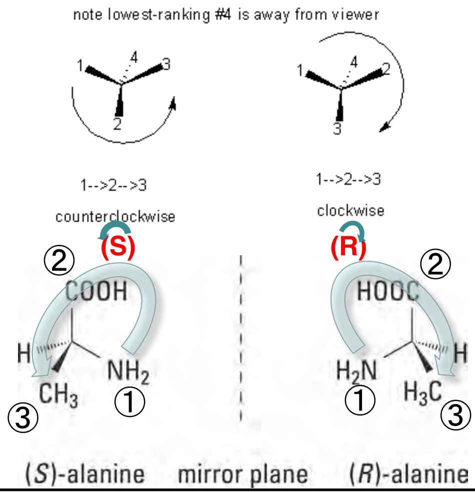


Fisher projections define a chiral carbon with carbons in chain up and down and substituents left and right. For amino acids, the higher MW substituent (amino group) is on the left, its "L".

*arrangement of bonds

Definition: Proteins are a linear polymers of L-α-amino acids. (generally composed of 20 different types)

"L" refers to the old-style of configuration* nomenclature (S in R/S) comes from Greek for rotation to the left (levo-rotation; counterclockwise)



Proteins

The 4 S's for Proteins:
- Size
- Shape
- Solubility
- Stability

Size of Proteins

The Size's for Proteins are variable due to the length of the polymers:

Protein polymers range from
~30-50 AA (insulin) to 50,000 AA (dystrophin)

Smaller than ~30 AA are usually called peptides

Protein diameters are much larger than Water:
10-20 Å in diameter to 1000 Å

Size of Proteins

TABLE 5-1 Compositions of Some Proteins

Protein	Amino Acid Residues	Subunits	Protein Molecular Mass (D)
Proteinase inhibitor III (bitter gourd)	30	1	3,427
Cytochrome *c* (human)	104	1	11,617
Myoglobin (horse)	153	1	16,951
Interferon-γ (rabbit)	288	2	33,842
Chorismate mutase (*Bacillus subtilis*)	381	3	43,551
Triose phosphate isomerase (*E. coli*)	510	2	53,944
Hemoglobin (human)	574	4	61,986
RNA polymerase (bacteriophage T7)	883	1	98,885
Nucleoside diphosphate kinase (*Dictyostelium discoideum*)	930	6	100,764
Pyruvate decarboxylase (yeast)	2,252	4	245,456
Glutamine synthetase (*E. coli*)	5,616	12	621,264
Titin (mouse)	35,213	1	3,906,488

WILEY

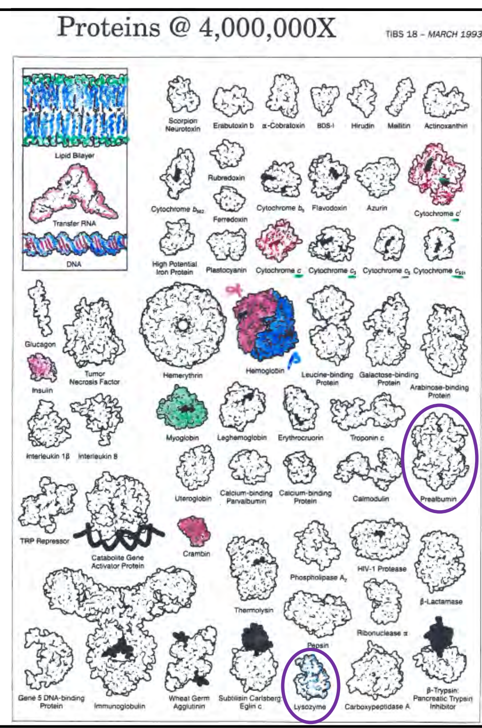
Shape of Proteins

The Shape's for Proteins are variable due to the size of the polymer as well, but much more due to the AA composition and sequence of the amino acids in the polymer.

HUGE variability!!

All these variable shapes are governed by those non-covalent bonds we just discussed: H-bonds, hydrophobic effect, van der Waals, and ionic interactions.

Shapes of Proteins: all same scale



Shape of Proteins

The **STRUCTURE** of proteins has been divided into **four** categories:

1) **primary structure –** sequence of amino acids

2) **secondary structure** – small units of repetitive structure

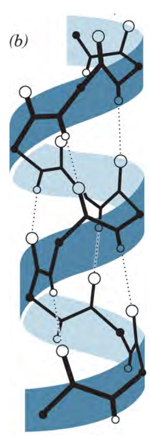
3) **tertiary structure** – overall 3D shape

4) **quaternary structure** – shape of ≥2 chains

Levels of Protein Structure

– Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly – Ala –

primary structure – (amino acid sequence in a polypeptide chain)

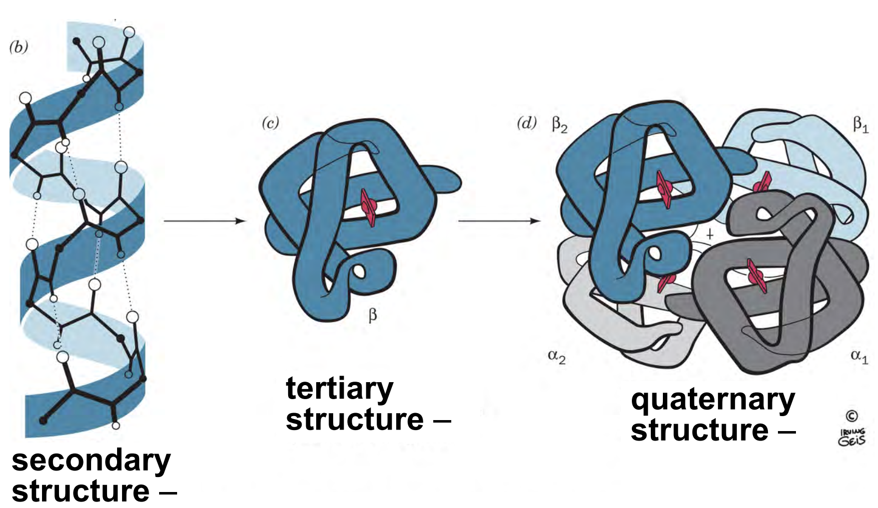


secondary structure –

Levels of Protein Structure

– Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly – Ala –

primary structure – (amino acid sequence in a polypeptide chain)



Solubility of Proteins

The Solubility's for Proteins are variable due to the size of the polymer and the composition and sequence of the amino acids in the polymer, but generally they are polar and thus soluble in water.

As we will see, the amino acids have "R" groups that differ by their solubility, hence also proteins.

Some proteins are not soluble; e.g., α-keratin

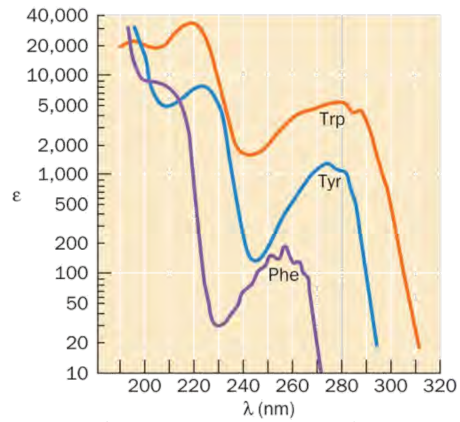
Stability of Proteins

The Stability's for Proteins are variable as well and the reasons are not completely known.

Measuring protein concentration: Lab

Most p… the degree of
color is … Beer's Law).

- F… thing that is "…
  endent on … it being a … t with the … he hydrogen … nplex that is … E changes … bonds.



After Wetlaufer, D.B., Adv. Prot. Chem. 7, 310 (1962).

- Take advantage of absorbance of amino acids in the ultraviolet region of the spectrum.

Measuring protein concentration: Lab

Most proteins are not colored. If so, then the degree of color is proportional to the concentration (Beer's Law).

- React with chemicals to create something that is "colored" (colorimetric)
  - Must be a product that is not dependent on different amino acids; specific to it being a polymer
    1) Copper ions in base will react with the amide nitrogen supplanting the hydrogen with the copper making a complex that is colored.
    2) Coomassie Brilliant blue DYE changes color when bound to peptide bonds.
- Take advantage of absorbance of amino acids in the ultraviolet region of the spectrum.

Types of Proteins

Familiar

Egg white (mostly ovalbumin and lysozyme)

α-keratin (hair, nails, feathers)

Casein (milk protein)

Zein (corn protein)

Myosin/actin (muscle proteins)

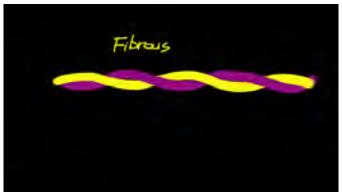
Collagen (tendons, cartilage, extra-cellular matrix, gelatin)

Schratin (insect exoskeleton)

Types of Proteins

Based on Structure

- Fibrous (α-keratin, myosin, F-actin, tubulin, collagen)
- Globular (hemoglobin, enzymes, antibodies)



Properties	Fibrous Protein	Globular Protein
Shape	Long and narrow	Rounded / spherical
Role	Structural (strength and support)	Functional (catalytic, transport, etc.)
Solubility	(Generally) insoluble in water	(Generally) soluble in water
Sequence	Repetitive amino acid sequence	Irregular amino acid sequence
Stability	Less sensitive to changes in heat, pH, etc.	More sensitive to changes in heat, pH, etc.
Examples	Collagen, myosin, fibrin, actin, keratin, elastin	Catalase, haemoglobin, insulin, immunoglobulin

Types of Proteins

Based on Function

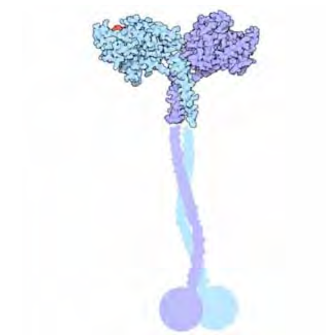
- *Enzymes*—catalytic proteins
- *Binding or Transport Proteins* (carry substances within the organism or membrane bound to transport in and out.)
  a. Globins (hemoglobin (Hb), Mb; carry di oxygen)
  b. Cytochromes (Fe in a porphorin ring; carry electrons)
  c. albumins (serum; carry fatty acids)
  d. immunoglobulins (antibodies, defense)
  e. receptor proteins (receive and respond to molecular signals)
  f. Genetic regulatory proteins regulate when, how, and to what extent a gene is expressed (transcription/translation factors)
- *Storage proteins* store amino acids (casein, zein).
- *Signal proteins; hormonal and regulatory proteins*—control physiological processes

Types of Proteins

Based on Function (cont.)

- *Structural proteins* provide physical stability and movement (collagen, keratin, histones).
- *Motor proteins:* convert chemical into kinetic energy (kinesin, dyenin, flagellin, myosin)

Shapes of Enzymes: all same scale



kinesin

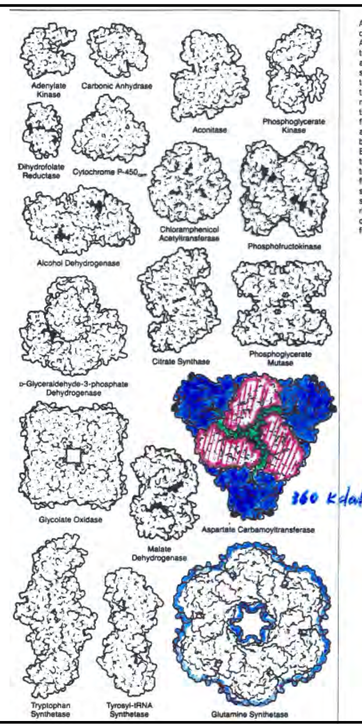
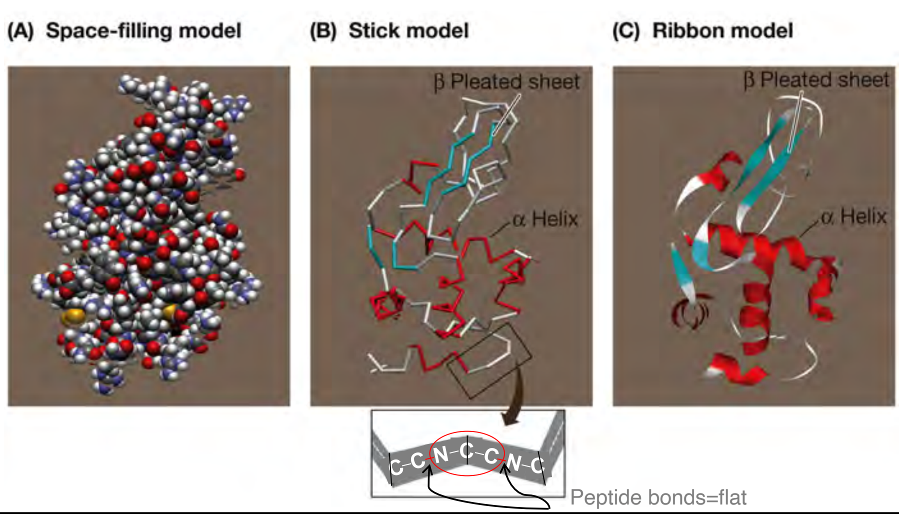


Figure 1

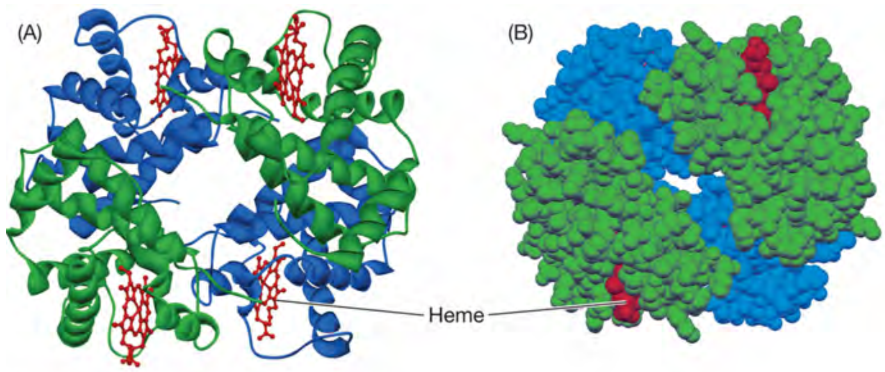
A sample of soluble proteins drawn at a consistent magnification of 4 000 000×. All heavy atoms are drawn in each structure; individual atoms are 1–2 mm diameter. Cofactors and substrates are shaded. The orientation of each is chosen to show the protein's maximal extent or to highlight some unusual feature. Three non-protein structures are included on the first page for size reference. On the first page, the proteins in the top row are toxins and those in the two rows below are electron transport proteins. Below the box are five 'hormones' and to their right are three rows of carrier proteins. In the bottom third of the page, the five proteins on the left have unusual shapes, tailored for binding to large substrates, and the small proteins to the right are various hydrolases. On the second page, enzymes are shown graded from small to large.

Three Representations of Lysozyme

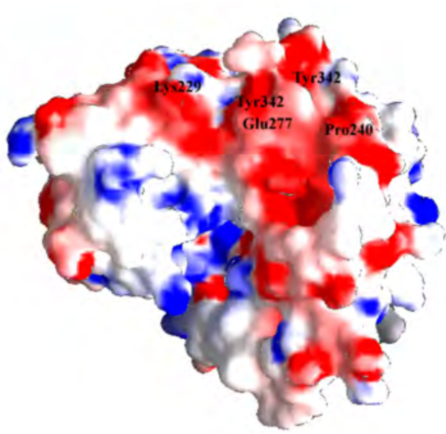
Complete descriptions of tertiary structure have been worked out for many proteins.

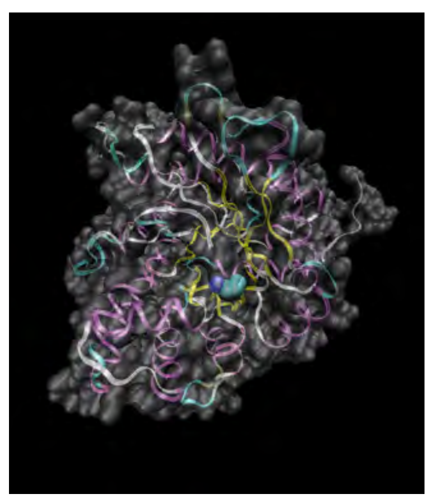


Hemoglobin

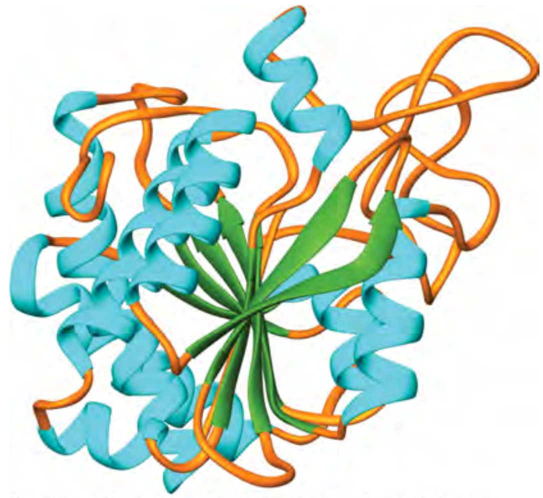


Aldolase





Bovine Carboxypeptidase A



Based on an X-ray structure by William Lipscomb, Harvard University.
PDBid 3CPA.

http://www.rcsb.org/pdb/explore/explore.do?structureId=3CPA

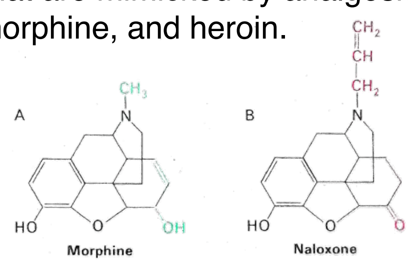
Carboxypeptidase A
PDBid 3CPA

Configuration *versus* Conformation

EXAMPLE:

In biology, peptides can have an amazing versatility in function.

One example are the endorphins–signal molecules produced by the brain that are mimicked by analgesic drugs such as codeine, morphine, and heroin.

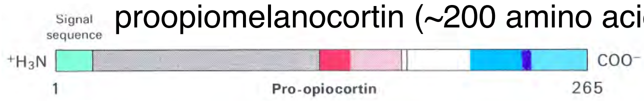


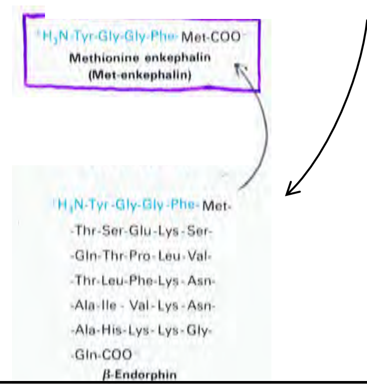
The smallest endorphin is called Met-enkephalin which is an active penta-peptide sequence of Tyr-Gly-Gly-Phe-Met.

Somehow the SHAPE of these drugs and this peptide must be similar to bind to the same pain receptors

Configuration *versus* Conformation

Met-enkephalin is biosynthesized from a larger protein called proopiomelanocortin (~200 amino acids).

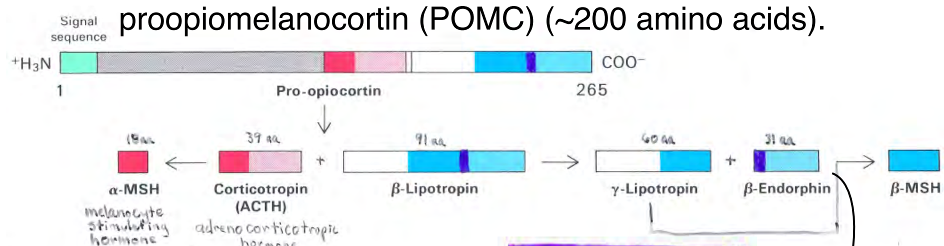


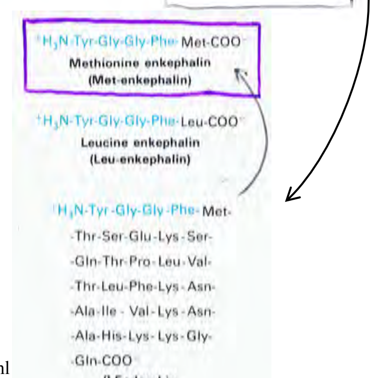


Can this peptide have the same shape as morphine?

Configuration *versus* Conformation

Met-enkephalin is biosynthesized from a larger protein called proopiomelanocortin (POMC) (~200 amino acids).



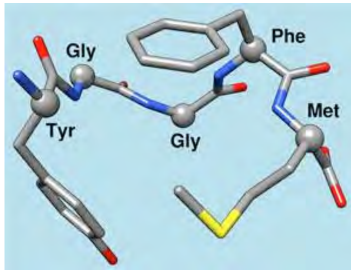


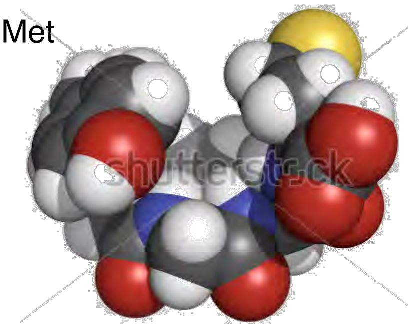
Can this peptide have the same shape as morphine?

https://melanocytestimulatinghormone.weebly.com/structure.html

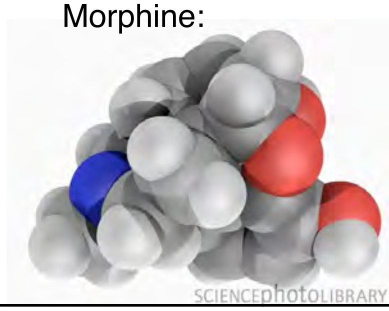
Configuration *versus* Conformation

Met-enkephalin: Tyr-Gly-Gly-Phe-Met





Morphine:



Configuration *versus* Conformation

CONFORMATION is the spatial arrangement of substituent groups that are free to assume different positions in space WITHOUT breaking any covalent bonds due to free rotations.

CONFIGURATION is the spatial arrangement by which substituent groups or atoms are covalently linked in a molecule. Different configurations REQUIRE breaking covalent bonds.