(16 Jan 2017)

Molecular Biology Through Discovery
Problem Set 1: Strategies of Life, Protein

Part I: Strategies of Life

1.1. Which of the following are hydrophobic? Hydrophilic? Amphipathic?

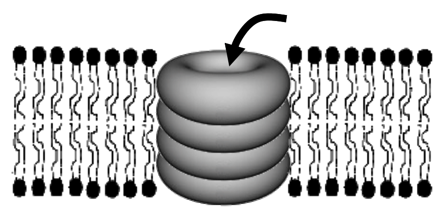
A. vinegar	D. sugar
B. skin	E. wax
C. tooth paste	F. rabid dogs

(The following problems require drawing. You might use Paint, PowerPoint or similar, or you can draw something and scan it somehow. Establish your own graphical conventions or – why not? – use those that appear in the Notes.).

1.2. Consider that at an air-water interface, amphipathic molecules expose their hydrophobic surface to air. Draw a picture of what a soap bubble might look like at the molecular level, using a long-sticked popsicle to represent a molecule of soap.

1.3. Phospholipase A2 is an enzyme commonly found in snake venom that acts by cutting off one of the two fatty acids on phospholipids. Draw a picture that shows how extensive action of the enzyme might detrimentally affect the structure of a cell membrane (including its overall shape). At the scale of your model, how big would a cell be?

Part II: Proteins



1.4. Some antibiotics form rings that stack and create a pore through the membrane. Consider a cyclic polypeptide antibiotic in which each ring is composed one instance of each of the four amino acids: serine, glycine, threonine, and alanine. If the atoms of the backbone are approximated by touching spheres of about 0.2 nanometers in diameter,† estimate the circumference of the pore (presume it to be a circle) and the diameter of the largest molecule that could fit through it. Approximate the circumference ($\pi \cdot$diameter) to be $3 \cdot$diameter. (Show work)

1.5. Before you cook an egg, the egg "white" is not at all white: it's clear. After you cook the egg, the "white" <u>is</u> white, because the large amount of globular protein has denatured (i.e., unfolded), and as a consequence, the protein has precipitated. Why should unfolding globular protein that are normally soluble in water cause them to stick to each other (which is what "precipitate" means)?

1.6. Lactate dehydrogenase (the last enzyme in human anaerobic glycolysis) is a soluble, multimeric protein. If you were to try to fold a single linear polypeptide chain of lactate dehydrogenase, you would find it impossible to do so without leaving a large number of hydrophobic amino acids exposed to water. Explain.

1.7. Use only the results of Sanger and Tuppy (1951) [Biochem J 49:463-481] to deduce as much of the structure of insulin you can. Do this (as a group effort) as if it were a geometric proof, appealing to lines within the tables (axioms) and truths you derive from them (theorems). For example:

	Assertion	Justification
A.	Thr-Pro*	Table 6, Line 8
B.	Thr-(Ala,Lys,Pro)¶	Table 9, Line 6
C.	Only one Pro	Table 14
D.	Thr-Pro-(Ala,Lys)	**A+B+C**†

*Meaning "The dipeptide N-Thr-Pro-C lies somewhere in the insulin polypeptide chain". The form N-XxxYyy-C means that the amino acids are read from amino end to carboxyl end.

¶ Meaning "A tetrapeptide somewhere in insulin begins N-Thr and is immediately followed by Ala, Lys, and Pro in some unknown order"

† Meaning "The assertion on this line follows from the assertions on lines A, B, and C"

1.8. Suppose that Sanger and Tuppy tried used their methods to deduce the structure of a protein that was not a linear array of amino acid but rather had branch points:

$$aa_a – aa_b – aa_c \begin{cases} aa_g – aa_h \text{ -- } \ldots \\ aa_p – aa_q \text{ -- } \ldots \end{cases}$$

What experimental results would they have obtained that would have allowed them to detect this structure?

Extra – in case you have the time and inclination

1.9. Make a set of 20 different graphical symbols representing the 20 amino acids. You may use colors, shapes, fill style, etc, but no letters or numbers. The symbols should be organized so that they are ***easy to write*** and ***easy to remember*** and that if two amino acids share some important characteristics then their symbols also are similar in some respect (but not identical).