Modeling Protein Folding

Instructional Goals

1. Protein Function and Primary Structure

describe purpose and definition of proteins
identify components of proteins (amino acids) and their chemical characteristics
explain how peptide bonds form to build chains of amino acids
describe how proteins are synthesized in the ribosomes using information from RNA

2. Secondary Protein Structure

explain how characteristics of amino acids cause new bonds to form within the protein
predict possible shapes or configurations of protein as it moves in solution
illustrate the two basic secondary structures (α-helix, β sheet)

3. Protein Folding (Tertiary Structure)

analyze proteins' secondary structure for rigid and non-rigid areas
decide how rigid and non-rigid areas, combined with amino acid chemical characteristics, determine the protein's final structure
form a conclusion about the reasons for, and effects of, the final "tangled" configuration of the protein
formulate a hypothesis concerning the energy of the final configuration with respect to the linear protein initially produced by the cell

Note: While there are no serious safety issues in this unit, students should be cautioned when working with tinkertoys, sticks, and paperclips that this is a serious lab activity and appropriate behavior is expected. Teachers may wish to require wearing of safety glasses during the activities.

Note: Specific timetables have been avoided in this document, since school schedules vary and each class/teacher combination will explore the concepts in the activities and discussions at different paces. It is intended that the discovery process will be driven by the students' interest and curiosity.

Overview

In this unit students come to recognize that living organisms consist of many differentiated proteins. These proteins are comprised of amino acids, and it is their sequence and resulting three dimensional structure that make them both stable and active. The mechanisms that determine the final structure consist of basic physical forces at the atomic and molecular level.

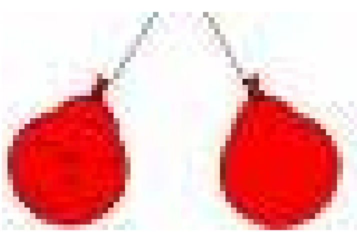
Students will come to understand that amino acids form protein chains with covalent bonds and that remaining side groups will bond with a combination of hydrogen bonds, Van der Waals forces, disulfide bonds, and hydrophobic bonds. Final configuration will also depend on relative flexibility of regions on the protein. As in all physical and chemical systems, the most stable configuration will have the lowest possible energy level. The intention is that this will be a short (approximately one week) unit.

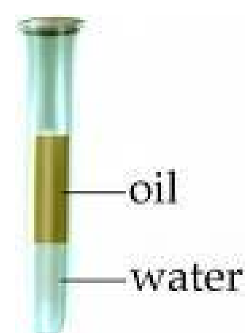
Instructional Notes

Instead of beginning with a paradigm lab, the first activities review basic properties of proteins. Instructional materials have been placed in a PowerPoint presentation to accompany this short unit.

PowerPoint Presentation (or instruction)

- Complete presentation and discussion of general information on proteins and primary structure
- Demonstration of intermolecular forces (charged balloons, oil and water) – student discussion relating these forces to amino acids – four total types of bonds:
    - hydrogen bonds
    - disulfide bonds
    - Van der Waals forces
    - electrostatic interaction





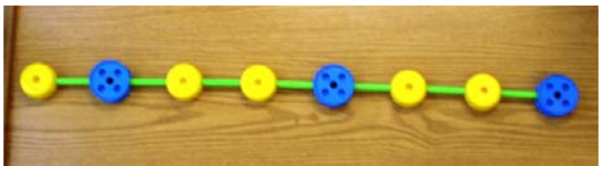
Activity 1

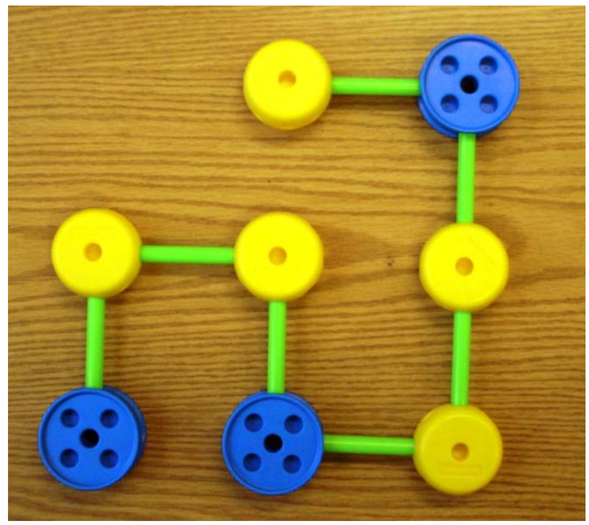
Apparatus

Tinkertoys – assorted (the newer, plastic ones offer some colors)

Discussion

- Show how Tinkertoys can be interconnected to form a chain of “molecules”
- Students should discuss what each part of the Tinkertoy model represents in the protein molecule
- Students discuss how to represent differences in the amino acids – write on the board
- Ask students to recall the environment surrounding the linear protein and to predict how the protein will evolve





Activity Performance

- Students assemble Tinkertoys into chains of “amino acids”, mixing hydrophobic, hydrophilic, polar, and non-polar parts (each group, try chains of length 8)
- Students predict a series of folds based on inter-molecular forces

Post-Activity Discussion

- Have student groups present their models and discuss the logic of their folds
- Ask about potential energy
- Connect multiple groups’ proteins and form more complex folds

PowerPoint Presentation (or instruction)

- Continue presentation with secondary structure
- Discussion of basic shapes (helix, sheet), stable due to bonding

Activity 2 – Rigid/Flexible Structure

Apparatus

- Popsicle sticks, drilled on each end with small holes (1/32 inch, enough for the wire of a small paperclip to fit through easily (50 per group)
- small paperclips (25 per group)*see end of document

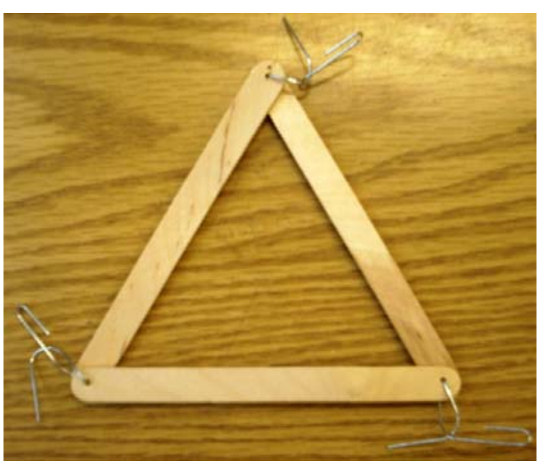
Discussion

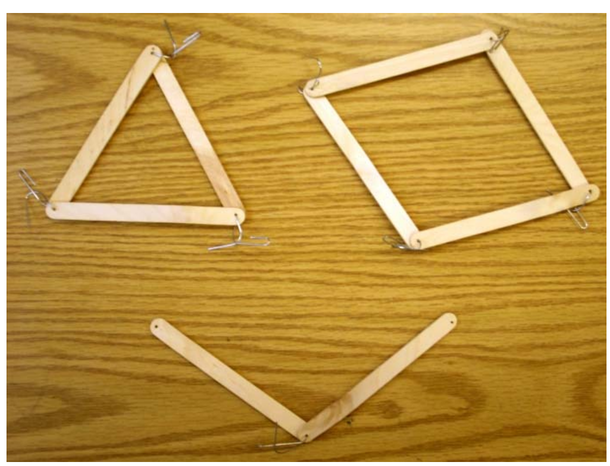
- Students discuss and define rigid versus flexible structures
- Why would this matter with folded proteins? What would the effects be?
- Are proteins completely rigid, partially rigid, or completely flexible?

Activity Performance

- First have students combine sticks into "simplest rigid structure"
- Next: Can you combine two rigid structures and still be rigid?
- Next: Make the simplest flexible structure
- Next: Make a closed flexible structure (2D)
- If you combine a flexible and a rigid structure, will it be flexible or rigid or both?
- Combine your pieces to make a larger structure with both rigid and flexible (hinge) areas.
- Challenge: Divide class in half, each half connects their assemblies, in the most compacted area and demonstrates rigid and flexible areas

(Note: As this is the first iteration of the popsicle stick/paper clip model, further inventiveness may significantly improve the quality of the joint connections at each vertex.)





PowerPoint Presentation (or instruction)

- Tertiary structure – have students discuss and identify rigid/flexible areas
- Online simulations, visualizing software, protein data banks
- RCSB data bank – search on protein name or type, use viewers below picture
- Have students work in groups if you have some computers, go to computer lab if you can, otherwise, do it with the teacher's computer and project the images
- Show web site from Center for Biological Physics

Assessment

At this point, student assessment will depend on the class (9th grade biology? 12th grade physics?) and instructor. Additionally, if a connection has been made with the university community, students will have the background necessary to understand and appreciate a contact experience with researchers.

*7/19/2007 – A field trip to Harbor Freight Tools found a cotter pin assortment (item # 41875-4VGA, $5.99 regular price – we got it on sale for $3.77) that included 150 1/8" x 1" and 150 3/32" x 1" cotter pins that are superior to the paper clips and, if students are reasonably careful, can be reused.