



Supplemental Materials

for

Minds at Play: Using an Online Protein Folding Game, FoldIt, To Support Student Learning about Protein Folding, Structure, and the Scientific Process

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Appendix 1: In-class activity (key is available to instructors upon request)

Protein Folding Activity

Learning Objectives

1. Conceptualize the three-dimensional nature of proteins.
2. Discuss the role of hydrogen bond formation in secondary structure.
3. Discuss the role of amino acid side chains in protein folding.
4. Consider difficulties in predicting protein structure, and solutions to this problem.

Instructions

1. Turn on the laptop and open the “Foldit” program.
2. When it asks for your username and password, select “play offline” (bottom right). When it asks if you are sure, click “yes”.
3. The main menu gives you three options. Select “Intro Puzzles”.
4. Complete all Level 1 and Level 2 puzzles: “Sidechains” and “Backbone Packing”. These show you how the program works. Answer the following questions

Q1.) The Foldit program teaches players that side chains don’t like to be too close to each other or to the backbone. What is the chemical term for this?

Q2.) What does the “shake” feature do? Do you think that proteins have a built-in “shake” feature when they fold *in vivo*? If so, how do you think it might work?

Q3.) Several of the proteins for level 2 have short *alpha*-helices. If you mouse-click on the white background and move the mouse, you can rotate the whole protein. Which way do the side chains of the amino acids point on the *alpha*-helices?
(note: you can use the menu tab at the bottom left to return to any puzzle to view it again)

5. Complete **level 3-1**, in which you make a small *beta*-sheet, and answer the following questions:

Q4.) Are side chains involved in H-bond formation that creates *beta*-sheets?

Q5.) Describe the location of the side chains in *beta*-sheets. (hint: click on the background and rotate the structure.)

6. Continue with the puzzles in level three. When you have completed **level 3-4**, take a moment to rotate the structure and examine the pleated *beta*-sheet that you just created.

Q6.) Is a *beta*-sheet a flat (planar) structure?

Q7.) Does the *beta*-sheet have to form from amino acids that are close to each other in the primary structure of a protein? Explain your answer.

Q8.) The proteins you have been folding have which type(s) of structure: primary, secondary, tertiary, quaternary? Explain.

Optional: Finish level 5 of the tutorial puzzles, then go back to the main menu and select "science puzzles". You have completed the background to do the "easy mini freestyle" beginner puzzle. If you finish level 6 of the tutorial puzzles, you've done the background for the "mini Arabidopsis multi-start puzzle."

7. Go to the home page for Foldit and browse the site to learn more about what Foldit is and why it exists:

fold.it/portal/info/science

Q9.) Where does Foldit come from? (Who made it and why?)

Q10.) What retroviral protein had its structure solved by Foldit players?

Predicting protein structure based on amino acid sequence is notoriously difficult, and there are many approaches being tested in this field. From the FAQs section of the Foldit website, one of their current goals is as follows:

"The current series of Science Puzzles, the Grand Challenges, are meant to generate the evidence needed to prove that human protein folders can be more effective than computers at certain aspects of protein structure prediction."

Q11.) What do you think about this goal? What can humans "bring to the table" that would assist computer-modeling of protein structure?