Protein Structure: A Hands-on Activity

By George Malacinski and Donna Pattison

Goals:

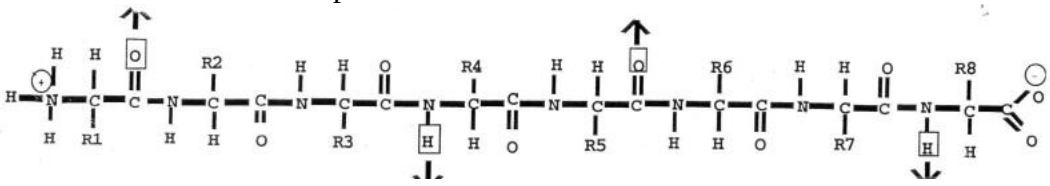
1) To examine the importance of hydrogen bonding in the stabilization of the alpha-helix.
2) To understand how the structure of the alpha-helix was determined.

Overview:

While the concept of primary, secondary, tertiary, and quaternary structure can be easily covered in a Powerpoint slide or two, memorization of the definitions and a firm understanding of what a protein is and how it is organized are not the same thing. Simply presenting definitions also fails to demonstrate to students the process of science or the "how we came to know" aspect. Generally, we present the basic overview of definitions on protein structure because students still need to master the vocabulary for the field. Next, we show students a video (link below) of an interview with Linus Pauling. It is an opportunity for students to hear how the structure of the alpha helix was discovered from the scientist himself. Finally, we have students create a paper alpha-helix using the provided template so that they move from primary structure to secondary structure while focusing on the role of hydrogen bonds in stabilizing the helix.

Activity:

1. Pass out the templates as students are entering the classroom or lecture hall. This generates some curiosity about what will be happening in class for the day.
2. Give a overview of protein structure and the definitions for primary, secondary, tertiary, and quaternary structure.
3. Have students look at their templates. Discussion can be clicker driven if desired.



1. What is this?

a. DNA
b. RNA
c. Protein
d. Carbohydrate

2. **In what form is this protein?**
    a. Primary
    b. Secondary
    c. Tertiary
    d. Quaternary

4. Show students the Linus Pauling interview about how he figured out the structure of the alpha-helix: http://scarc.library.oregonstate.edu/coll/pauling/proteins/video/1973v.3-alpha.html. The clip is from "The DNA Story" (1973); VSM Productions by Ronald Fouracre and Peter Shaw. In case the link no longer works the transcript is below:

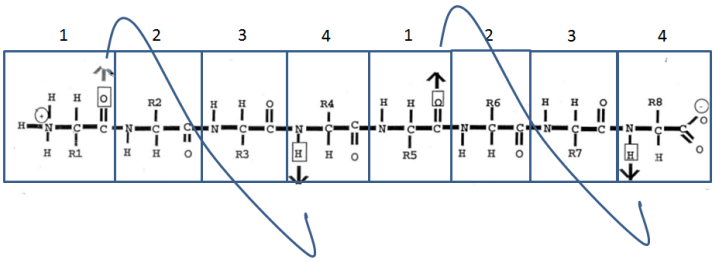
Transcript

Linus Pauling: *One day, when I was Eastman Professor at Oxford in the spring of 1948, I caught a cold. It was before the vitamin C days! I caught a cold and after a day or two in bed of reading science fiction and detective stories, I got tired of that, and thought, why don't I discover the alpha helix? Something like that - why don't I try to find how polypeptide chains are folded in a way compatible with all the knowledge we have of structural chemistry and such that they can form hydrogen bonds to hold the parts of the molecule together?*

I took a piece of paper, much like this piece, and drew on it a representation of an extended polypeptide chain, with the distances approximately right and the angles right. Except, one angle did not have the right value. I still have that original piece of paper, by the way. This is the bond angle of the alpha carbon that didn't have the right value. I folded the paper - actually, it took several trials - I folded it along several parallel lines through the successive alpha carbons.

Finally, I found a way by folding the paper to make this bond have an angle of 110 degrees. I finally found a way of folding such that when I fit it together, there was an N-H-C-O bond formed by each N-H group, and each C=O group. The hydrogen bond held the structure together and had just the right dimensions. I found that this structure, which turned out to be the structure of hair and horn and fingernail, and also present in myoglobin and hemoglobin and other globular proteins, a structure called the alpha-helix, had 3.6 residues per turn of the helix. A helical structure where there are 3.6 residues per turn.

5. Have students draw a box around each amino acid on their template. This process helps remind them of the basic units of a protein and the structure of an amino acid. Next, have the students make the helix using their templates. They need to match up the arrows on the template such that the hydrogen bonding pattern is correct. In this short template, the H on the N in residue 4 aligns with the O in residue 1 as shown below. This will create a coiled alpha helix pattern.



Extensions:

1. I generally talk about the fact Linus Pauling won not one, but two Nobel Prizes: one in Chemistry (1954) for the structure of the alpha helix and the Nobel Peace Prize in 1962 for his activism in limiting the testing and proliferation of nuclear weapons. The story of Linus Pauling's role in the race for the structure of DNA is also fun to include. Linus Pauling proposed a triple helix with the sugar-phosphate backbones in the center and the bases facing outward from the axis. The negative charge on the backbone would make such a structure highly unstable. It's a great example that sometimes the most brilliant minds can make a mistake. Even the world's most famous scientists are only human.

2. Once students have made their alpha helices, a general discussion of what it would take to create tertiary structure is useful. We ask the students to "show us quaternary structure" and they very quickly hold their helices next to their neighbors. Showing students the linear primary structure (template itself), secondary structure (coiled alpha helix), and quarternary (paired helices) structure provides a visual reinforcement to complement the definitions.