3-D Molecular Designs
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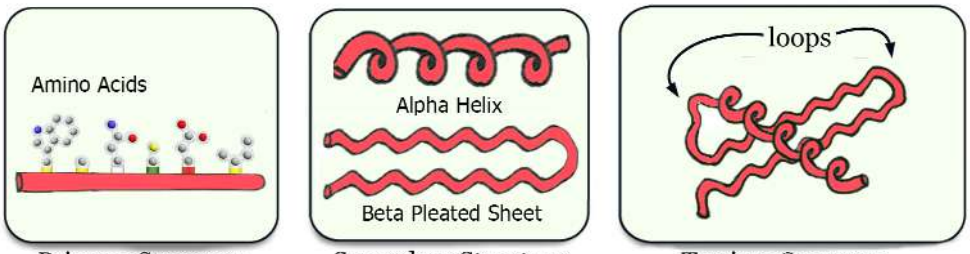
Student Handout 2 Key

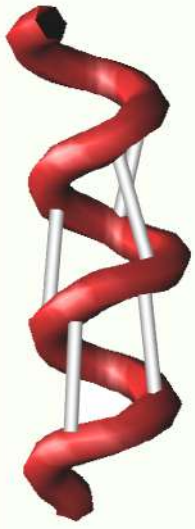
Secondary Structure

In the previous protein folding activity, you created a *generic* or *hypothetical* 15-amino acid protein and learned that basic principles of chemistry determine how each protein spontaneously folds into its characteristic 3-dimensional shape. You learned that the sequence of amino acids in a protein (from N-terminus to C-terminus) is called its ***Primary Structure***. The final folded, 3-dimensional shape of your protein is called its ***Tertiary Structure***.

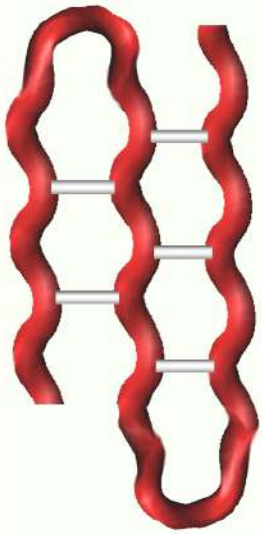
In this second protein folding activity, you will now learn about the ***Secondary Structure*** of proteins. This Secondary Structure consists of alpha helices and/or beta sheets. Proteins commonly contain a combination of alpha helices and beta sheets. In fact, proteins can be thought of as a series of alpha helices and beta sheets, joined by ***loops*** of less regular protein structure.



Primary Structure | Secondary Structure | Tertiary Structure



An ***alpha helix*** is a compact right-handed helix, with 3.6 amino acids per turn of the helix. The amino acid sidechains are bonded to the alpha carbon of each amino acid and radiate outward from the helix. The alpha helix is stabilized by hydrogen bonds – weak bonds between the amino nitrogen of one amino acid (x), and the carbonyl oxygen of another amino acid (x+4) located four residues further along the chain.



A ***beta sheet*** is an extended, zig-zag structure in which individual *strands* are positioned parallel or anti-parallel to each other to form flat sheets in proteins. Since the amino acid sidechains are bonded to the alpha carbons of each amino acid, they are alternately orientated above and below the plane of the sheet. The beta-sheet is stabilized by hydrogen bonds between the amino nitrogen of one amino acid and the carbonyl oxygen of another amino acid in an adjacent beta strand.

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Amino Acid Starter Kit

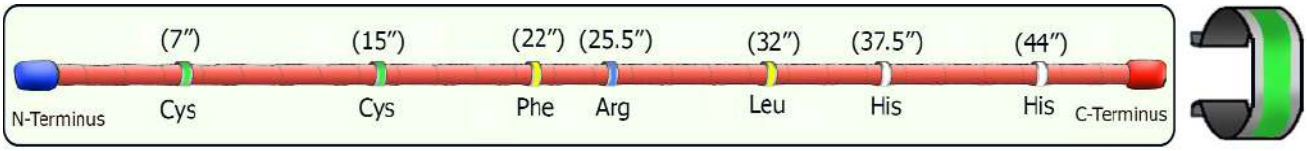
Folding a Toober Model of the Zinc Finger

In this activity, you will fold a model of the first of three zinc fingers of the Zif268 protein. The primary structure of this zinc finger is:

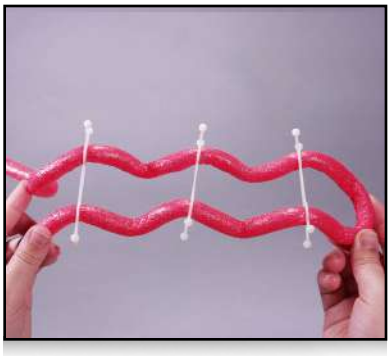
N-Terminus P Y A (C) P V E S (C) D R R (F) S (R) S D E (L) T R (H) I R I (H) T G C-Terminus

The sidechains of the seven amino acids circled in the above sequence will be included in the model you fold.

1. ***Primary Structure:*** Map the positions of the seven amino acids on the mini-toober. Since the toober is 48 inches long, and the zinc finger is 28 amino acids long, each amino acid occupies 1.7 inches of toober. Using a ruler, measure the distances shown below, and add a labeled metal clip to the toober at each position. Label the clip with an appropriately colored dot.



2. ***Secondary Structure:*** Fold the toober into its secondary structure. The first 13 amino acids (the first 22 inches from the N-terminus) should be folded into a 2-stranded beta sheet. This can be made by creating a zig-zag structure that is bent in the middle as shown in the photos below. You can also add the plastic ***hydrogen bonds*** to your model as shown in the far right photo.



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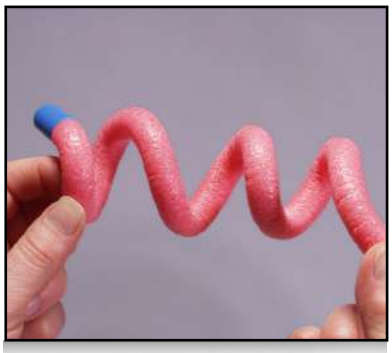
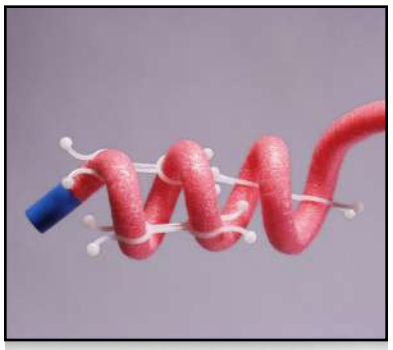
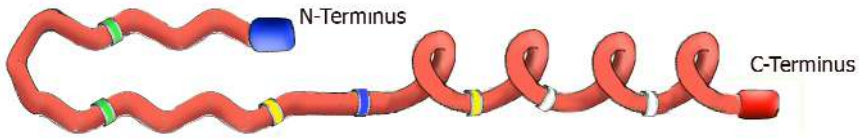
Folding a Toober Model of the Zinc Finger (continued)

The last 14 amino acids of the zinc finger exist as a compact, right-handed alpha helix. This can be made by wrapping the mini-toober around your finger to create four 360 degree turns as shown in the photos below. Add the hydrogen bond connectors as shown in the far right photo.

Your mini-toober should now look similar to the one shown below.



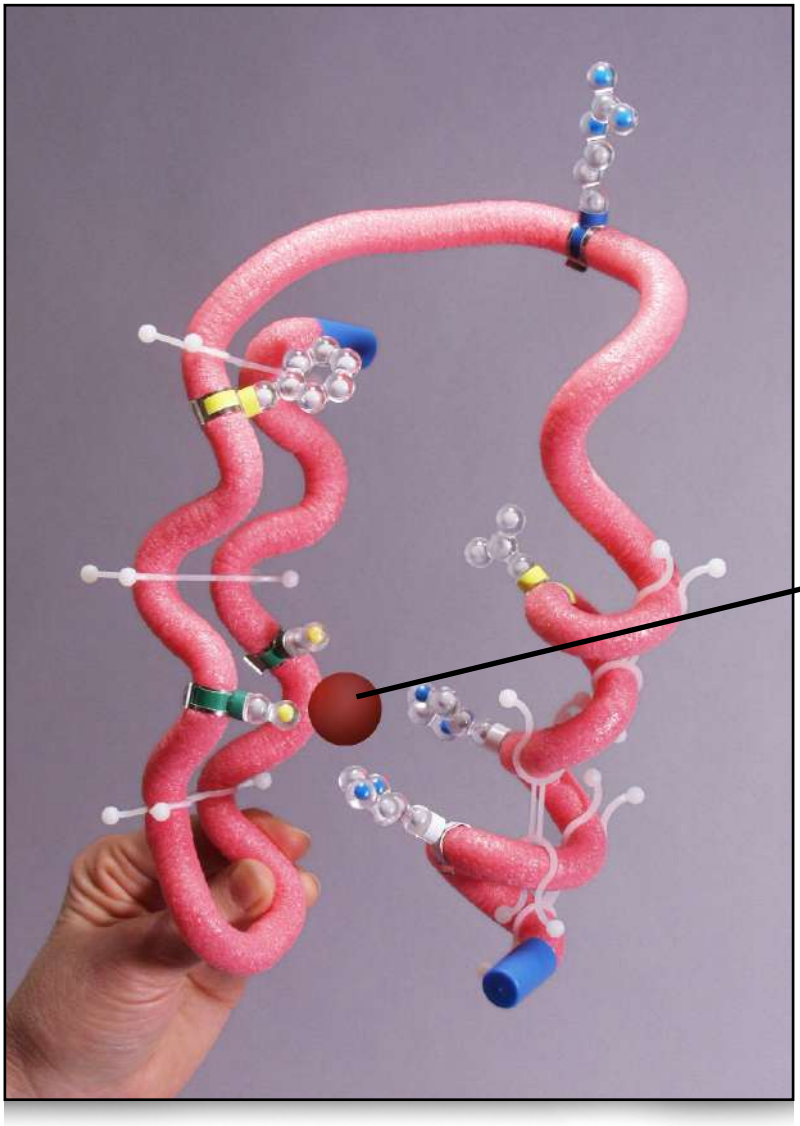
3. ***Tertiary Structure:*** Fold the beta-sheet and alpha-helix into the final tertiary structure of the zinc finger.

   Add the seven amino acid sidechains to the clips on the toober. In its final tertiary structure, these seven sidechains will be positioned such that:
   - The two cysteine and two histidine sidechains will be oriented so that they can simultaneously bind to a single zinc atom (not included in this kit) in the center of the structure.
   - The two hydrophobic amino acid sidechains phenylalanine (Phe, F) and leucine (Leu, L) will be orientated toward the inside of the structure.
   - The positively-charged arginine sidechain will be exposed at the top of the alpha helix, where it is available to bind to the negatively-charged phosphate backbone of DNA.

Folding a Toober Model of the Zinc Finger (continued)

As a folding guide, you can either use the photo shown below or the interactive Jmol image of a zinc finger on the CD included in the Amino Acid Starter Kit.

Note: As you fold your toober, you may need to rotate the sidechains around the mini-toober to make them adopt the desired final shape.



The zinc (not included with the kit) binds simultaneously to the two histidines and two cysteines.

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Folding a Toober Model of the Zinc Finger (Questions)

1. Both alpha helices and beta sheets are stabilized by hydrogen bonds.
   - Which atoms share the hydrogen in these weak bonds?

The nitrogen of an amino group and the oxygen of a carbonyl group.

   - Are these ***backbone atoms*** or ***sidechain atoms***?

Backbone atoms.

2. Describe the secondary structural elements that comprise a zinc finger:

A 2-stranded beta sheet and a short alpha helix.

3. How is a zinc atom involved in the stabilization of the zinc finger motif?

The zinc atom is simultaneously bound by the 2 cysteine and the 2 histidine sidechains.

4. Zinc fingers often bind to DNA. How might the arginine sidechain (positively-charged) shown on your model be involved in DNA binding?

DNA has a negatively-charged phosphate backbone. Therefore, the positively-charged arginine of the zinc finger can bind to DNA via an electrostatic interaction.

- Optional Activity - Zinc Finger Jmol

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