Getting in a twist – Protein folding

Keywords: Proteins, biochemistry, molecular biology

Intro: The way in which polypeptide chains fold to form the 3D structures of proteins is key to generating the different physical and chemical properties that allow proteins to carry out a wide range of tasks in the body. This activity is aimed at getting audiences to understand the importance of 3D polypeptide folding with a tactile, involving activity.

Protein Folding Activity

Equipment: One 4ft length of 18-gauge insulated wire per participant

Method:

1. Have each participant produce an 8 amino acid polypeptide, using the instructions on the attached worksheet (see appendix).
2. Describe to your audience that hydrophobic side chains would cluster together, away from the outside, and positively and negatively charged side chains will try to pair up with one another.
3. Have the participants fold the wire into a compact 3D structure, with the hydrophobic side groups on the inside and in contact with each other.
4. Describe to your audience what forces are holding their 3D structures in shape, the importance of this (different protein properties), and why their shape is different from their neighbour's (different amino acid composition)
5. Have the participants stimulate thermal denaturation by shaking the 3D wire structures until they lose their shape.
6. Have the participants fold their wire with a neighbour, ensuring their hydrophobic side chains are in contact with their partners.

Results + Science: The length of wire represents an unfolded polypeptide chain, with every wire loop representing the side chain of an amino acid. By clustering the hydrophobic loops together at the centre of the 3D wire shape, you mimic the "hydrophobic effect" that partially governs how 3D structures are formed from polypeptide chains, where hydrophobic side groups move as far away from their water-containing surroundings as possible.

The shaking of the folded chain to disrupt its 3D structure mimics the effects of heat denaturing a protein. Heat increases the energy of a molecule, causing it to vibrate more. This can disrupt the weaker non-polar interactions holding the internal hydrophobic side chains of the amino acids together. The hydrophobic side chains become exposed to their watery exterior environment then interact with the hydrophobic side groups of adjacent denatured proteins, forming an aggregate – similar to what happens when you cook an egg.

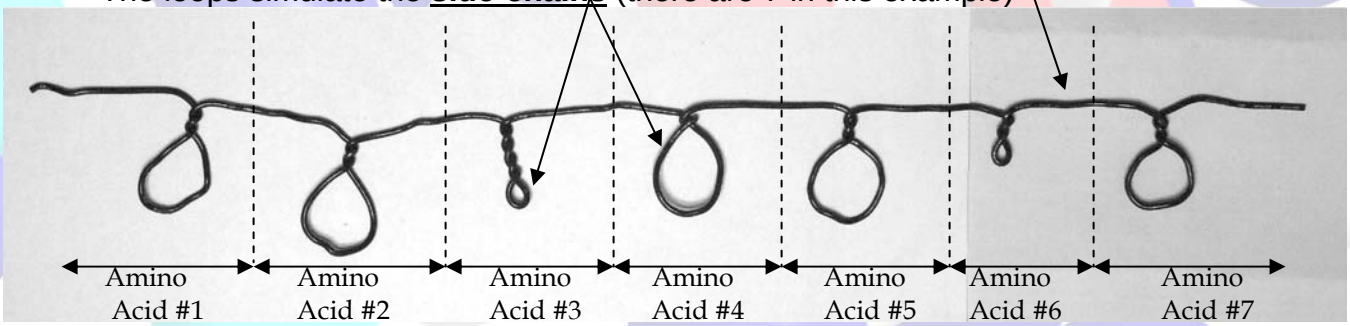
See also: White, B. (2006). *A simple and effective protein folding activity suitable for large lectures.* CBE Life Sciences Education *5(3),* 264-269.

Appendix: Handout for participants

Today, you will twist a piece of wire so that it simulates the behavior of a chain of amino acids (also known as a protein). We will then use this to explore protein folding.

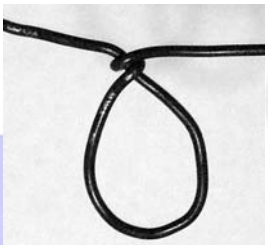
A simulated 7-amino acid protein is shown below; your protein will be similar although it may have a different pattern of loops.

- The more-or-less straight part of the wire simulates the **backbone**
- The loops simulate the **side-chains** (there are 7 in this example)



Side-chains

In the simplified world of this demonstration, there are three kinds of amino acids, each of which is represented by a different type of loop:

Hydrophobic	**Positively-charged**	**Negatively-charged**
		
A large open loop. Make it two finger-widths wide.	A long closed loop. Make it four twists long.	A short closed loop. Make it two twists long.

How to do it

Now you will twist your wire to make a protein of seven or eight amino acids. The sequence of amino acids is up to you, but it works best if your protein contains:

- More hydrophobic amino acids than charged ones.
- At least one positively-charged and one negatively-charged amino acid.

The measurements in this demonstration need not be precise; you will use the width of your fingers as a ruler.

- Leave two finger-widths of space un-twisted at the starting end.
- Leave three finger-widths of space between each amino acid.