Amino acid folding basics

How do the chemical properties of amino acids affect the structure of a protein?

The sequence of amino acids determines the structure of a protein. Amino acids have a variety of chemical properties that determine how they will fold from their linear primary structure into their secondary and tertiary structures. This activity helps students determine how these chemical properties affect the structure of the final protein.

Ohio standards

- 6.LS.1: Cells are the fundamental unit of life
- 6.LS.3: Cells carry on specific functions that sustain life

Biology

- B.C.1: Cell structure and function
- B.C.2: Cellular processes
- B.H.1: Cellular genetics
- B.H.2: Structure and function of DNA in cells
- B.H.4: Mutations

Chemistry

- C.PM.3: Chemical bonding
- C.PM.6: Intermolecular forces of attraction

Student prior knowledge

Students should know that the order of amino acids in a protein are determined by the sequence of DNA bases that are carried from the nucleus by mRNA to the ribosome, where the tRNA anticodon brings the amino acid to be assembled into a protein.

Suggested timeline

One or two class periods

Materials

- 3D Molecular Design Amino Acid Starter Kit®
  shop.3dmoleculardesigns.com/products/amino-acid-starter-kit
- Alternative materials:
  - Sculpting bendable wire (1m per group)
  - Craft pipe leaners (20 different colors)
  - Key for which color pipe cleaner represents which amino acid
  - Information to describe chemical properties of amino acids

Teacher preparation

1. If using alternative materials, prepare bendable wire by cutting into 1m lengths.
2. Determine which color pipe cleaners will match with which amino acids.
3. Create an *amino acid sheet* to describe chemical properties of each amino acid: hydrophobic (nonpolar) or hydrophilic (polar), acidic or basic pH, positive or negative charge.

Procedure

1. Discuss the following with students before beginning. (See amino acid characteristics chart.)
    - Each protein is made of a specific sequence of **amino acids.**
      There are **20** amino acids found in proteins.
    - Each amino acid consists of two parts: a backbone and a side chain. **The backbone** is the same in all 20 amino acids while **the side chain** is different in each one.
    - Each side chain consists of a unique combination of atoms which determines its 3D shape and its chemical properties.
    - Based on the atoms in each amino acid side chain, it could be **hydrophobic**, **hydrophilic**, **acidic** (negatively charged), or **basic** (positively charged). When different amino acids join to make a protein, *the unique properties of each amino acid determine how the protein folds* into its final 3D shape. The shape of the protein makes it possible to perform a specific function in our cells.
2. Choose 15 "side chains." *Be sure to include two cysteine side chains!*
3. Attach amino acids to your wire (which represents the "backbone" of the amino acid).
4. Refer to the Amino Acid chart to see properties.
    a. Fold the hydrophobic to the inside of your protein.
    b. Fold the acids and bases so they are towards the outside, and then fold the chains so they are very close together.
    c. Bend the tuber so that the cysteine side chains are close together.
    d. Continue to fold your protein making sure that your hydrophilic (polar) side chains are also on the outside surface of your protein where they can hydrogen bond with water.
    e. Were you able to satisfy all properties? Congratulations! You just made a tertiary protein structure!

Suggested wrap-up

Have student groups share their protein structures with one another. Are there recognizable 3D shapes (i.e. alpha helices or beta sheets)? Ask students to complete the reflection questions on the student sheet.

Differentiation

Give students who are struggling with the procedure smaller numbers of amino acids to fold. Match students who have less knowledge with those who can help them to better understand the reasons for the folding.

Extensions

Give students who have a strong grasp of the concepts predict protein structures of longer amino acid chains. Show students the structures of well-known proteins: insulin, interferon, etc.

Support information

- Proteins serve major functions within an organism. One different amino acid can change the structure and function of the protein. Research is making new strides in how to impact the replication of proteins, particularly where they impact human health.
- Cystic fibrosis is a genetic disease where mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene cause the CFTR protein to become dysfunctional. When the protein is not working correctly, it's unable to help move chloride — a component of salt — to the cell surface. Without the chloride to attract water to the cell surface, the mucus in various organs becomes thick and sticky.

- Duchenne muscular dystrophy is another genetic disorder characterized by progressive muscle degeneration and weakness due to the alterations of a protein called dystrophin that helps keep muscle cells intact.
- Ohio Life Sciences companies such as Andelyn Biosciences has addressed Duchenne muscular dystrophy through gene therapy.
- CLARMETYX biosciences has developed a novel immune-enabling anti-biofilm antibody technology, which is designed to destroy the scaffold-like structure of a bacterial biofilm to allow the immune system with natural antibodies (immunoglobulins/glycoproteins) and/or antibiotics to more effectively eliminate bacteria.

Career connections

- **Protein engineers** analyze amino acid interactions and predict how proteins will fold, then use that information to design new proteins.
- **Biochemists and molecular biologists** study chemical processes and chemical transformations in living organisms, including DNA, proteins, and cell parts.