QUICK FIX

Modeling Protein Structure & Function: Pencil Transferase

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Key Words: *Protein; structure; function; model; mutation; enzyme; 3-D.*

The interrelationship of structure and function is a key theme of biology. One important example of this relationship involves how the three-dimensional shapes of proteins are related to the roles they play at the cellular level. The treatment of protein structure in many introductory textbooks, however, is cursory and focuses on the relationships among primary, secondary, tertiary, and quaternary structure without a clear link to how these levels of organization contribute to functional aspects of the protein. This short and engaging hands-on activity helps reinforce the connection between the ultimate spatial conformation of a specific protein and its "job." By exploring the structure and function of a hypothetical protein, students develop a conceptual understanding of how these important elements connect in real life (e.g., the roles of actin and myosin in muscle contraction, of proton pumps in cellular energy conversions, or of immunoglobulin proteins in helping an immune system fight off foreign invaders). Although this activity was designed for secondary-level students, it could also be modified for undergraduates. With the advent of free and readily accessible programs for viewing protein structures, as well as an increasing number of structure files and curated collections of proteins, biology instructors have at their disposal an array of examples of the striking beauty and diversity of proteins. A brief glossary and selected resources are listed at the end of this article.

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Pipe cleaners (a.k.a. chenille stems) are often used to represent protein structure. This activity adds the important dimension of how structure is related to protein function, and presents optional extensions that explore the potential impacts of mutations. Students are presented with a pipe cleaner and asked to solve the following problem: they must use the pipe cleaner to transfer a pencil from one desk to another. Students may bend the pipe cleaner as needed but may not touch the pencil with their hands when they are moving the pencil across desks. After the pencil has been successfully moved, students should retain the shape of the pipe cleaner that successfully moved the pencil. Lastly, students hold their creations aloft so that class comparisons are possible.

Students will have made a protein called "pencil transferase" – an enzyme whose "job" it is to transfer a pencil. The various solutions to the problem of how to transfer a pencil will reveal some functional constants. For example, students will notice that each protein has a region (often one or more loops) that will "bind" to the pencil. This observation can be used to introduce the concept of a "domain": *protein domains* are identified by their folding properties, compact structure, evolutionary origin, and/or function. In this activity, the emphasis is on the functional definition of a domain. Therefore, the loop region can be referred to as a "pencil binding domain," and the region(s) of the pipe cleaner held by the students (by which the protein "binds" to the hands) can be referred to as the "handle domain(s)." Students can quantify the number of proteins with 0, 1, or 2 or more pencil binding or handle domains observed in all the proteins developed by the class.

The model offers many opportunities to discuss specific aspects of protein structure, such as the way in which nonadjacent portions of a linear amino acid sequence or *primary structure* (represented by the straightened pipe cleaner) may interact with one another to form important functional domains of the protein. Some students might create pencil-binding domains with multiple loops – these could be considered similar to an alpha helix *secondary structure*. The entire pipe cleaner model (containing both pencil binding and handle domains) can be considered analogous to a *tertiary structure*. In order to model *quaternary structure*, several pencil transferase pipe cleaner models can be bundled together to represent a type of protein composed of several polypeptide chains whose job is to bind and transport multiple pencils.

The model also helps explains the differential impact of mutations in areas of the protein crucial to its function (binding domains) versus other regions. For example, a *substitution mutation* (in which one amino acid is substituted for another) may not have a harmful effect if it does not result in a change in amino acid sequence, if it
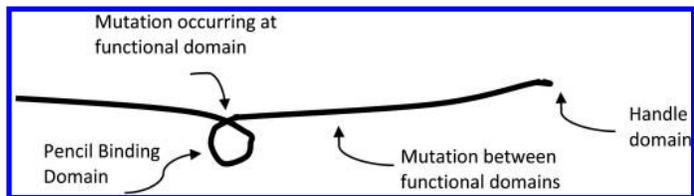
Figure 1. Pencil transferase model used to illustrate impacts of mutations on protein structure.
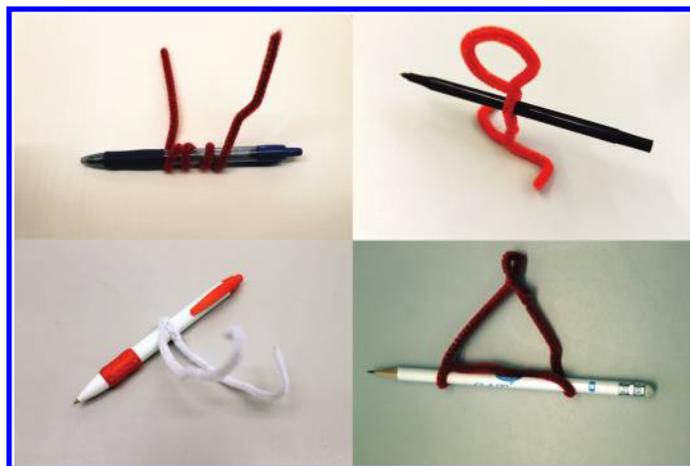

Figure 2. Sample "pencil transferase" models.

Figure 3. Science teacher Brian Gabert (Kent-Meridian High School, Kent, Washington) models his "pencil transferase" at an NWABR professional development workshop.

substitutes an amino acid with similar chemical properties, or if it happens between functional domains (Figure 1).

A substitution mutation at a crucial point in a functional domain, such as where the amino acids link together to make a loop, may destroy the shape of the protein altogether, thus destroying its function. A *deletion* or *insertion* mutation could also have drastic consequences, even if it occurred at a point distant to the functional domain, particularly if the insertion or deletion results in a change in the translation reading frame, which can destroy the protein.

Most importantly, the model reinforces that the shape of the protein is integral to its cellular role. Ask students, "Why do so many of the pipe cleaners have such similar shapes?" They should recognize that the shape of a protein corresponds to the functions it performs (Figure 2).

The short classroom activity described above is adapted from curricular materials focused on how bioinformatics tools and resources are transforming biology (Figure 3). *Understanding Bioinformatics: Genetic Testing* uses the context of testing for mutations in the *BRCA1* gene (breast cancer 1, early onset) to introduce bioinformatics while reinforcing basic concepts related to DNA, transcription, translation, and protein structure and function. Because our organization, the Northwest Association for Biomedical Research, is committed to promoting an understanding of biomedical research and its ethical conduct, the curriculum also addresses some of the ethical implications of acquiring and using genetic information. In our materials, this activity precedes a discussion of the BRCA1 protein, its binding sites, and how mutations in the protein could lead to an increased risk of breast cancer. The curriculum is funded through *Bio-ITEST: New frontiers in bioinformatics and computational biology*, a National

Science Foundation Innovative Technology Experiences for Students and Teachers grant (DRL 0833779) and is freely available online.

○ Selected Resources

NWABR Introductory Bioinformatics Curriculum (Understanding Bioinformatics: Genetic Testing):
http://www.nwabr.org/curriculum/introductory-bioinformatics-genetic-testing

Molecular viewing software:
Cn3D from the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/Structure/CN3D/cn3d.shtml) and Jmol (http://jmol.sourceforge.net/)

Curated collection of proteins: http://www.pdb.org/pdb/motm.do

○ Glossary

Functional domain: A region of the protein defined by its role.
Handle domain: Protein functional region that binds to the hand(s).
Pencil binding domain: Protein functional region that binds to the pencil.
Primary protein structure: Linear sequence of amino acids (polypeptide chain).
Protein domain: Region of a protein or polypeptide chain identified by the folding properties, compact structure, evolutionary origin, and/or function.
Quaternary protein structure: Several protein molecules organized into a multi-subunit complex.
Secondary protein structure: Local interactions between amino acids, often mediated by hydrogen bonds. The most common secondary structures are alpha helices and beta sheets.
Tertiary protein structure: Overall three-dimensional structure of a protein.

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