Communicating Research to the General Public

At the March 5, 2010 UW-Madison Chemistry Department Colloquium, the director of the Wisconsin Initiative for Science Literacy (WISL) encouraged all Ph.D. chemistry candidates to include a chapter in their Ph.D. thesis communicating their research to non-specialists. The goal is to explain the candidate's scholarly research and its significance to a wider audience that includes family members, friends, civic groups, newspaper reporters, state legislators, and members of the U.S. Congress.

Ten Ph.D. degree recipients have successfully completed their theses and included such a chapter, less than a year after the program was first announced; each was awarded $500.

WISL will continue to encourage Ph.D. chemistry students to share the joy of their discoveries with non-specialists and also will assist in the public dissemination of these scholarly contributions. WISL is now seeking funding for additional awards.

Wisconsin Initiative for Science Literacy

The dual mission of the Wisconsin Initiative for Science Literacy is to promote literacy in science, mathematics and technology among the general public and to attract future generations to careers in research, teaching and public service.

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Development of a β-Peptide Retroaldolase and Efforts Toward Other Catalytic Foldamers

by

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Chapter 6

Comparing a Slinky® to a Metal Spring: Foldamers and Their Applications

Our bodies are incredibly complex organisms. Each person is believed to have trillions of cells that make up our skin, bones, and everything in between. All of this complexity can be traced back to our DNA (Figure 1). DNA is what we inherit from our parents and is responsible for determining our physical characteristics, such as whether we are a man or a woman, how many fingers and toes we have, and the color of our eyes. It is the blueprint that makes us human.

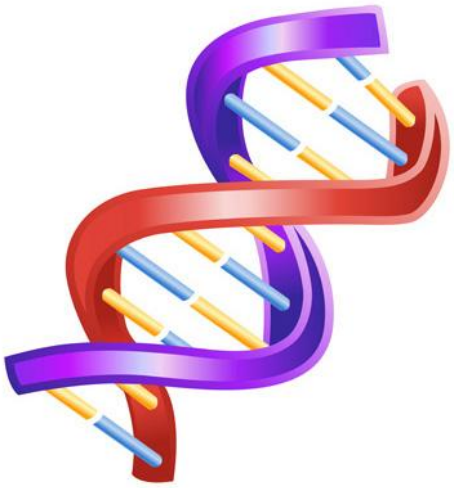

Figure 1: Cartoon of DNA in its familiar double-helix conformation.[1]

If DNA acts as the blueprint of a human being, then proteins are the machines that put us together and keep us alive. Our bodies translate the information in our DNA into proteins that perform very specific tasks. Which proteins are created is determined by which portion of our DNA our body translates. It is believed that human DNA carries the instructions to make ~23,000 different proteins, each with its own function in our body.

Proteins are often big molecules. When compared to a simple molecule, like sugar, proteins can be hundreds of times larger (Figure 2). Most proteins fold into a

unique shape that plays a direct role in the job they perform. These jobs fall into three general categories. The first involves providing structure to our cells and organs. These proteins act like the steel support beams inside most large buildings, around which everything else is built. The second category involves passing signals from one part of the body to another. Puberty, for example, occurs because our brain releases proteins (hormones), which cause other parts of the body to grow and mature. The final job category involves accelerating the rate at which one molecule is converted into another molecule. This process, known as catalysis, is responsible for (among other things) breaking down the food we eat and turning it into nutrients that the body can absorb. We'll come back to catalysis in more detail shortly.

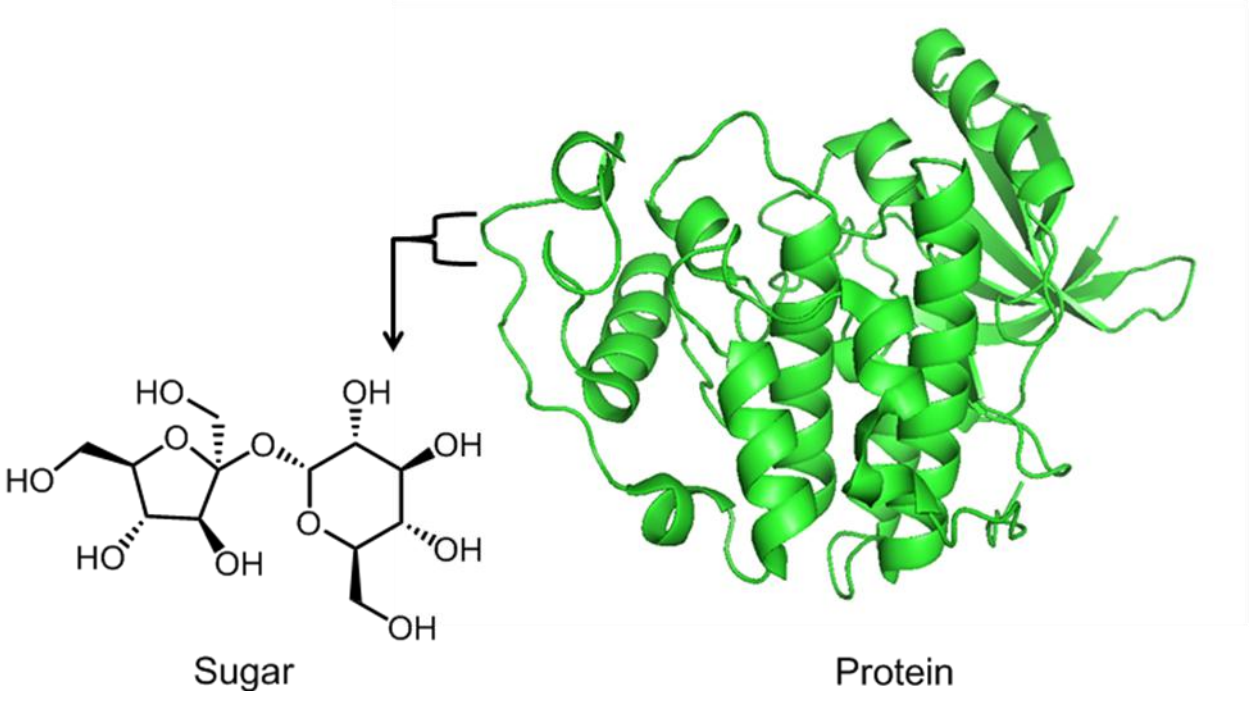

Figure 2: Chemical structure of sugar (left) and cartoon of a protein (right). The bracket near the upper left corner of the protein highlights the size of a single sugar molecule in comparison to the protein.[2]

Scientists have long been interested in building their own proteins that could perform a given task. Unfortunately, designing these large, complex proteins is a significant challenge. One way to get around this challenge is to create molecules with a simpler and smaller structure than proteins. While simple structures are easier to make, they often are not as efficient in doing the job of the protein they are intended to mimic. My graduate work has focused on designing and synthesizing a class of simplified protein mimics known as “foldamers” and figuring out what tasks they can perform in place of proteins.

Foldamers are rigid molecules that, as the name implies, “fold” into very specific shapes. In contrast, proteins can fold into thousands of different shapes. A good way to compare proteins and foldamers is to compare a Slinky® to a metal spring. Both a Slinky®, representing a protein, and a metal spring, representing a foldamer, are similar in that they are linear coils. A Slinky® normally has many more coils (making it longer than a metal spring) and can “fold” into any number of shapes (often tangles, Figure 3). On the other hand, a metal spring is so rigid that it can only slightly bend, stretch, or compress itself. While a metal spring (foldamer) can’t do as much as a Slinky® (protein), its limited size and flexibility means we have a much easier time studying the spring. This tradeoff is stacked in our favor because foldamers are simpler to synthesize (up to a given length) and alter than proteins.

Figure 3: One of the many "folds" a Slinky can adopt (left). A metal spring (right) has very little flexibility in comparison.[3]

With the strong understanding of what shape a foldamer adopts, my co-workers and I have been exploring what functions foldamers can perform. During the five years of my graduate work, co-workers have discovered foldamers that can act as antibacterial, antifungal, and antiviral agents. Other foldamers have been found to form liquid crystals, much like the materials used in Liquid Crystal Display (LCD) televisions. Some foldamers have even been shown to mimic proteins involved in some types of cancer and HIV infection, with the hope that they could one day act as treatments for these medical conditions. My work has focused on designing foldamers to act as catalysts.

A catalyst is a compound that increases the speed of a reaction without being consumed by the reaction. In other words, a catalyst can help a reaction to occur thousands of times in the same amount of time it may take the same reaction to happen once without the catalyst present. A fun experiment to do to show just how fast catalysts can speed up a reaction is to take a cracker or pretzel and chew it to a pulp. Instead of swallowing, leave the pulp in your mouth for a minute. Eventually, the

cracker or pretzel begins to taste sweet, like sugar. This is because there is a catalyst (also called an enzyme) in your saliva that breaks down the carbohydrate molecules in the cracker/pretzel into its smaller, sugar-like components. Now think about the fact that crackers and pretzels are left in their packaging for months but are still good to eat. This is because without a catalyst, carbohydrates break down very slowly. Without the enzymes in our saliva, stomach and intestines, food would not be converted to nutrients as fast as we need to survive.

Enzymes are much better at catalysis than many man-made catalysts, and are often employed by scientists and engineers in synthesizing pharmaceuticals and chemicals. An important example highlighting the use of enzymes to generate a product of interest is biodiesel production. Biodiesel is diesel fuel generated from materials like vegetable oil, animal fat, or plant matter instead of fossil fuel. Enzymes are currently the most efficient way to convert the animal or plant starting material to biodiesel. However, enzymes need to be grown in bacterial cells and purified, which is a very time consuming process. It could be more efficient if we could build our own catalysts using chemistry, as opposed to relying on bacteria to build our catalysts for us.

Foldamers that act as catalysts could be one way to quickly and efficiently generate products of interest, such as biodiesel, without having to rely on living organisms. The work described in my thesis describes how we discovered the first foldamer catalyst and subsequent efforts in designing additional catalysts. While the reaction that was catalyzed is simple, and the foldamer is not appropriate for complex reactions like biodiesel production, my efforts could serve as part of the foundation on which future foldamer researchers base their efforts.

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