Build-a-Polypeptide: A Hands-On Worksheet to Enhance Student Learning in an Introductory Biology Course †

Kristi Hall1, Jackson Dunitz2, and Patricia Shields2*

1College of Behavioral and Social Sciences, University of Maryland, College Park, MD 20742,
2Department of Cell Biology and Molecular Genetics, University of Maryland, College Park, MD 20742

INTRODUCTION

At our university, several biology classes serve both life science majors and non-majors. These groups contain students who have a weak (or nonexistent) chemistry background. Due to this apparent knowledge gap, many students struggle to understand the process of polypeptide formation via dehydration synthesis as well as the interactions between individual polypeptide chains. This inability to reason about how individual amino acids interact with one another prevents students from making the cognitive leap from primary to secondary structure. In turn, students do not fully understand how even higher levels of organizations (i.e. tertiary and quaternary interactions) form the final three-dimensional configurations of proteins. We designed Build-a-Polypeptide in an attempt to help fill that part of the knowledge gap. In this activity, students physically represent the process of polypeptide synthesis and R group interactions using a paper model. Essentially, this is a simple cut and paste project that allows students to build a beginner (i.e. highly truncated and simplified) model of protein folding. Previous research has shown that physical modeling can aid student understanding of complex topics (1, 2). With that in mind, we developed this interactive worksheet-based activity to improve student understanding of protein synthesis and structure formation. Our activity was created with two main objectives: a) to demonstrate how a dehydration synthesis reaction forms the carbon-nitrogen backbone of a protein and b) to show how different R groups of amino acids interact to develop tertiary structure. The activity was designed to give students a simplified model to demonstrate how polypeptides interact and form. This activity requires no laboratory equipment and can be completed within one (50-minute) class. Our worksheets were designed for use in introductory college-level biology courses, but could easily be adapted for high school or AP biology classes.

PROCEDURE

Preparing the activity

Build-a-Polypeptide was designed for an introductory-level biology course that typically enrolls over 300 majors and nonmajors each semester. We introduced this activity in a recitation-style discussion of 20 to 22 students led by two undergraduate learning assistants (ULAs); however, this activity is also suitable for the larger lecture classes broken into smaller groups. In this activity, students demonstrate an understanding of how amino acids are synthesized as well as how they achieve their tertiary structure by building a paper model.

The activity is completed in two parts. In the first part, the students “synthesize” a peptide chain that is five amino acids long. Using scissors and tape, the students perform a “dehydration synthesis reaction” to form peptide bonds (see Fig. 1). Once they have made their generic peptide backbone, they can move to step two. In step two, they select appropriate R groups to attach to their newly synthesized peptide based upon the potential interactions with a sample peptide they are given (see Running the activity, below, and Appendix 3).

Running the activity

Pairs or small groups allow students to think critically about what type of reactions and interactions between R groups will occur. For part one, each group is provided with five generic amino acids (see Appendix 1). Once they have completed step one, they are given a bank of R groups and a sample peptide that consists of five amino acids linked together (see Appendices 2 and 3).

Part 1: Building the five-amino acid peptide. Each group is provided with five generic amino acids and asked to undertake the following steps.

1. Perform a model dehydration reaction by removing the OH from the carboxyl end and the H from the amino end of the amino acid (Fig. 1).
2. Bond the amino acids together with tape connecting the nitrogen of the second amino acid to the

*Corresponding author. Mailing address: 3108 Bioscience Research Building, University of Maryland, College Park, MD 20742. Phone: 301-314-2595. Fax: 301-314-9489. E-mail: pshields@umd.edu.
†Supplemental materials available at http://jmbe.asm.org
carbon of the first amino acid. The first peptide bond is formed and a water molecule is generated (see Fig. 1).

3. Repeat steps 1 and 2 until the carbon-nitrogen backbone is five amino acids long.

**Part 2: R group interactions.** Each group is provided with a completed five-peptide-long sample with different R group combinations as well as a bank of R groups. The instructions are as follows.

1. Look at the sample peptide. Select R groups that will allow you to interact with the five amino acids on the sample.
2. Attach your R groups to the appropriate place on your synthesized peptide so that interactions can occur between the two peptides (see Fig. 2).
3. Indicate what types of interactions are occurring (e.g. ionic bonds).

**Post-activity discussion**

Once all of the groups have completed the activity, each group should present their finished products to the class and demonstrate or explain the type of interactions they encountered. Since four different sample amino acids are included in the activity (see Appendix 3), classroom discussion allows the entire class to be exposed to all five interactions demonstrated in the activity. Instructors should take this opportunity to reiterate the difference between interactions found in student models and actual proteins, pointing out why the models have no distinct shape.

**CONCLUSION**

Introductory biology students have difficulty with the chemical attributes of biology courses because many of them do not have the requisite chemistry background necessary to understand it. Through a hands-on modeling approach, Build-a-Polypeptide was designed to reinforce the basic concepts of a) polypeptide synthesis, b) R group interaction, and c) protein structure. First, the students model the process of dehydration synthesis. Second, students model R-group interactions. These activities enable students to better conceptualize how three-dimensional protein structures are dictated by amino acid order and R group interaction.

As we described earlier, our model is not (and was never intended to be) an accurate representation of all the levels of amino acid structure. We are very aware that the three-dimensional structure is much more complicated than our model suggests, and it is highly unlikely that a real peptide would contain this level of variance in R groups within a single five-amino acid span. When we designed the activity, we made the conscious pedagogical choice to model more types of interactions over representing strict realism. This is clearly explained to the students. We approached these problems as a “teachable moment”—explaining the difference between a model and reality is important for all students, and Build-a-Polypeptide is no exception. This activity was designed to show how lots of similar individual interactions ultimately lead to three-dimensional configurations.

Once students have built their peptide chain and determined the possible interactions between their strand and the sample peptide, they are asked to discuss their models and answer questions about the activity, further reinforcing the concepts.

Build-a-Polypeptide can be easily adapted for high-school or AP Biology courses. For example, students could reverse translate and reverse transcribe the polypeptide they constructed. In this way, the students can see the relationship between DNA sequences and proteins.
we initially designed this activity to demonstrate peptide synthesis, we found that the activity provided the added benefit of helping students truly understand dehydration synthesis reactions. Dehydration synthesis is a foundational reaction for macromolecule formation (not just peptides) and, in our experience, students often have trouble visualizing where the water originates from this reaction. This activity provided the added benefit of helping them to see that the process was both unidirectional (in terms of the orientation of the molecules) and reversible (in terms of macromolecule anabolism and catabolism). In addition, this activity helped to illustrate the significance of polarity and visually demonstrate the importance of the concept as it relates to R-group interactions in proteins. The Undergraduate Learning Assistants (ULAs) who led the activity reported that the activity appeared to be helpful for the students by reinforcing polypeptide synthesis and R-group interaction for students. Some ULAs even found that Build-a-Polypeptide reinforced their own understanding of polypeptide synthesis and R-group interactions as well.

SUPPLEMENTAL MATERIALS

Appendix 1: Generic amino acid
Appendix 2: Amino acid R groups
Appendix 3: Sample peptides

ACKNOWLEDGMENTS

We would like to thank the Howard Hughes Medical Institute and the University of Maryland, College Park, for supporting this project. The authors declare that there are no conflicts of interest.

REFERENCES