Chapter 3

# Physical Models Support Active Learning as Effective Thinking Tools

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From the perspective of a novice student, the molecular biosciences are inherently invisible. A challenge facing bioscience educators is to help students create detailed mental models of the biomolecules that make up a living cell and how they all work together to support life. With the advancement of rapid-prototyping, also known as 3D (three dimensional)-printing, physical models of biomolecules are entering undergraduate classrooms as tools to aid in constructing mental models of biological phenomena at the molecular-level. This relatively new pedagogical tool requires evidence-based practices for optimal use in aiding student conceptual and visual development. This chapter presents current evidence for the use of physical models as learning tools, while also introducing case studies on how physical models of biomolecules are designed and assessed in undergraduate molecular bioscience settings.

## Introduction

In this chapter, we focus on development, use and assessment of biomolecular physical models in undergraduate molecular bioscience education. Here "molecular biosciences" encompasses any course utilizing concepts featuring biomolecules, ranging from monomers to macromolecules that support life on the molecular level (*e.g.* introductory biology; general, organic, and biochemistry (GOB); biochemistry, molecular biology, and cellular biology courses). At the undergraduate level, *Vision and Change* identifies modeling and simulation as core competency and disciplinary practices


Bussey et al.; Biochemistry Education: From Theory to Practice
ACS Symposium Series; American Chemical Society: Washington, DC, 2019.

(*1*). The Next Generation Science Standards (NGSS) Framework definition of models includes diagrams, physical replicas, mathematical representations, analogies, and computer simulations that are tools for the student to engage in "developing questions, making predictions and explanations, analyzing and identifying flaws in systems, and communicating ideas (*2*)."

Moreover, models provide an opportunity for the student to engage in an iterative process of "comparing their predictions with the real world and then adjusting them to gain insights into the phenomenon being modeled (*2*)." This is the vein in which the potential power of models lies, as many authors suggest that learning barriers, particularly those related to abstract concepts, arise from unchallenged incorrect ideas, flawed mental models and the inability to relate new concepts to other knowledge (*3*, *4*). Here, we predict using physical models will further the student's development of a robust mental model that is able to overcome misconceptions and further the student's learning progression in the molecular biosciences.

Since no model is identical to the concept it represents (else it would cease being a model), students need to be trained to be skeptical in analyzing any model (*5–7*). Students who can examine a model and explain how the model is both like and unlike the real thing it represents demonstrate a conceptual understanding of what the model represents. Furthermore, like the Hindu fable of the blind men and the elephant, each model only represents a part of the whole, and it is through transitioning among *multiple representations* that we gain a true sense of what models represent (*8*). As such, physical models offer an avenue to develop students' visual literacy skills, a recognized compounding variable in the abstract nature of the molecular biosciences wherein students are inundated with a variety of representations containing differing levels of abstraction (*1*, *9–11*). Several studies suggest that these representations can lead to student learning difficulties and propagate misconceptions (*4*, *12–16*). For example, spectacular animations of molecular processes help to convey difficult concepts, yet they often provide a "wow" factor to the expert, while moving through the information too quickly for a novice to process (*17*). Molecular visualization software allows educators and students alike to rotate and spin structures in virtual 3D space, but our assumption that students are able to "see" the objects in 3D may be a false one, especially if they have never experienced similar, tangible structures in the real world (*18*). One possible explanation for these difficulties is that current molecular bioscience curricula include little to no explicit instruction on interpreting, evaluating and moving through levels of representations (*4*, *9*, *19*, *20*). Physical models of abstract concepts can aid in developing visual literacy skills that also support the overall aim here – to develop robust learner mental models that enable students to think like scientists.

Until recently, students' primary exposure to physical models was limited to the use of small molecule modeling kits in a chemistry course. Advances in structural biology began to reveal the 3D structure of macromolecules, but it was impossible for students to construct physical models of these complex structures. During this same time, the development of molecular visualization software made it possible for students to experience virtual representations of macromolecules in a computer environment. Today, advances in an additive manufacturing process known as rapid prototyping – commonly referred to as 3D-printing – have made it possible to construct physical models of complex molecular structures (Figure 1) (*21*). As 3D-printing technology continues to evolve, it is becoming possible to create models with complex color schemes in a variety of materials from hard plaster to flexible plastic and rubber. The recent explosion of low-cost filament-based 3D printers now makes it possible for molecular bioscience educators to acquire this modeling technology for as little as several thousand dollars.

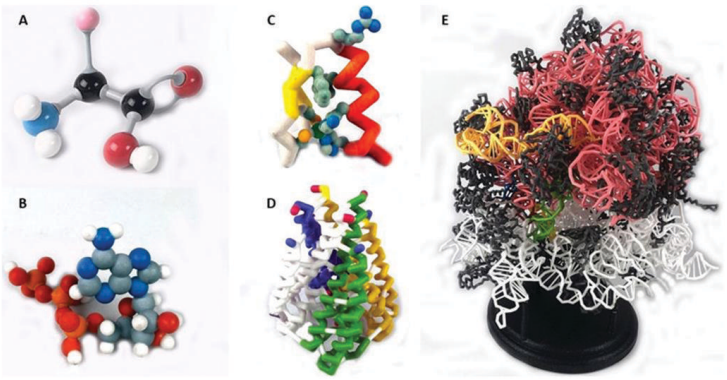


*Figure 1. Physical models of molecular structures.* ***A.*** *An amino acid – constructed by students using a small molecule kit. Models B-E are "assemblies of atoms," constructed by 3D printing.* ***B.*** *ATP with magnet-docked phosphate groups.* ***C.*** *A zinc finger (PDB ID: 1ZAA)* ***D.*** *A four-subunit potassium channel (PDB ID: 1J95).* ***E.*** *The 70S E. coli ribosome (PDB ID: 4V5D) with magnet-docked large and small subunits, three tRNAs and a short stretch of mRNA.*

A wide variety of models have been used in all scientific disciplines to represent complex, often abstract concepts. Most studies on physical models have been conducted in organic chemistry courses or K-12 education, with relatively few investigating student learning and behavior with biomolecular physical models at the undergraduate level. Among these studies, however, exists evidence for student learning gains in different molecular bioscience settings. In two related studies, Oliver-Hoyo and authors report not only increased student engagement but also integration of knowledge across biochemistry concepts after using a series of macromolecules with small molecules (*22*, *23*). Another investigation demonstrated better learning gains for students participating in a molecular dissection activity involving a 3D physical DNA model compared to the comparative building activity (*24*). In biology, higher learning gains for females are cited after using a physical protein model in one class session (*18*), while another retroactive study using several physical models related to the flow of genetic information demonstrates learning gains independent of gender (*25*). In fact, lower achieving students demonstrated the highest absolute gains (*25*). This last study is discussed in greater detail later in this chapter. A few studies have examined the impact of combining physical models with virtual activities, and, although there is some disagreement on the degree of impact, these studies do conclude with higher learning gains associated with the complementary use of these visual tools (*26–28*). Although these results are promising, more research is needed on best practices with physical models and on how and when students learn using these tools. Much of this, however, will hinge on increased educator and student access to, and training with, physical models.

Herein, we introduce three case studies involving physical models of biomolecules in an active learning undergraduate classroom setting. Particular consideration for the use of physical models for students requiring accessibility services is presented in the final case study. Each case study stems from and works closely with the Milwaukee School of Engineering's (MSOE) Center for BioMolecular Modeling (CBM), and as such we begin with an introductory case study on the CBM's history of engaging communities of students, educators and researchers in physical modeling.

## Case Study I: The CREST Project

### Modeling Projects

The CBM explores the use of tactile, physical models of macromolecules and their building blocks – created by 3D printing technology – as a novel way in which to introduce students to the invisible world of molecular bioscience. Initiated in 1999, the CBM was originally focused on the creation of accurate custom models of proteins for use by researchers. But in 2001, the development of new design software (RP-RasMol) made it possible for the first time to involve teachers and their students in the *design* of these physical models. As we began to incorporate model design into our professional development programs for high school science teachers, we quickly realized that not only were the models effective teaching tools, but that the *process of modeling* was an even more powerful experience. This realization led to the development of the student modeling projects, in which a small team of students and their teacher work closely with a research lab to create a physical model of a protein that is central to the work of the lab.

Although our initial insight into the power of modeling as a successful pedagogical approach involved high school teachers and their students in the SMART Team program (Students Modeling A Research Topic), we soon began exploring the use of this approach at the undergraduate level (*29*). We launched a series of CREST Projects (Connecting Researchers, Educators and STudents) resulting in additional insights into the power of modeling at the undergraduate level. A CREST modeling project combines (i) *a student-centered modeling project* involving an active research lab with (ii) *a collaborative instructional materials development project* in which collaborative teams create materials that engage classroom students in an inquiry-driven exploration of the research project (*30*).

The most recent iteration of CREST explores the value of engaging undergraduates in the community of science through meaningful conversations with researchers at a professional meeting (*31*). The program identifies an awardee whose research will be presented at the annual American Society for Biochemistry and Molecular Biology (ASBMB) meeting. Teams of undergraduates explore some aspect of the research topic and design and build a physical 3D model to tell the molecular story of the structure and function of one of the proteins involved in this research. Teams tell their molecular story at a poster session at the ASBMB meeting, attend the award lecture, then meet with the researcher and colleagues in a "CREST Conversation." These physical models become the shared mental model among researchers and students and allow students to engage in authentic scientific conversations with the researchers (*32*).

Although a number of scientific professional societies encourage undergraduate participation, both in attending meetings and in presenting posters, unless there is a specific lecture that pertains directly to students' research, undergraduates can feel overwhelmed and inadequate as scientists when attending scientific sessions. The CREST Program allows teams of students to design a physical model to tell a molecular story, attend a scientific session on that specific topic, then meet with their peers and researchers to discuss the topic in depth within the context of a professional meeting. We hypothesize that this meaningful engagement will help students identify as scientists, one of the key affective traits required for retention in STEM fields, especially for groups underrepresented in the sciences (*33*, *34*). Indeed, undergraduates who participated in extracurricular CREST projects expressed greater confidence and identity as scientists and viewed their faculty advisor as a collaborator more than a mentor as a result of participation in CREST (*30*). The greatest gains in

these affective domains was seen in undergraduates from primarily undergraduate institutions (PUI) which lacked research opportunities for undergraduates (*30*).

**Instructional Materials Development**

Recent calls for reform in delivering science instruction emphasize the need to shift from lecturing to student-centered learning (*1*). Yet educators are slow to adopt better learning strategies (*35*, *36*). There are numerous obstacles to overcome to adopt new methods. Change is difficult (*37*). Educators need to be dissatisfied with the current methods, and there needs to be a viable alternative that is clearly advantageous (*38*, *39*). Even the best methods, when executed poorly, yield less than ideal results. Furthermore, few things are done perfectly the first time they are tried. Therefore, educators need appropriate training in using new innovations and a management of expectations on their first attempt at implementation (*40*). Perhaps of the greatest significance is the need for time – time to reflect, time to fail, time to analyze progress, time to revise, and time to share successes and challenges with others. Educators benefit from a community of peer support, as well as ongoing professional development support and administrative backing to encourage persistence to success (*40–42*).

In answer to these challenges to implementation of best practices, a second aspect of the CREST Project engages collaborative groups (researchers, educators, students) in creating student-centered instructional materials that make current research accessible to early career trainees. The CBM offers a summer faculty workgroup meeting that allows educators to get away from their routines and focus on developing innovative materials for their classrooms. These "micro-sabbaticals" provide focused time for educators to collaborate in developing new ideas, and ongoing interactions during implementation provide the peer support needed to work through obstacles to adoption. Since most teaching is done in isolation, educators value cross-disciplinary collaboration and recognition from peers that their ideas are valuable (*30*). Participants also reported that having a set time dedicated to working on projects, as well as collaborators with whom to work, allowed them to dedicate the time needed to develop materials and implement new teaching strategies in their classes (*30*).

The three case studies below were seeded by CREST collaborations and highlight a progression from the design or choice of physical model to the learning assessment for molecular bioscience courses. In all, these case studies provide molecular bioscience educators with information on the design/choice of physical models, design of correlating assessment of student learning, and types of evidence from assessment analysis.

## Case Study II: Carbohydrate Models

Of the four major macromolecules (proteins, lipids, nucleic acids), the structure-function relationship of carbohydrates is relatively unexplored in molecular bioscience education, with greater instruction time devoted to metabolism and laboratory exercises focused on chemical reactivity differences (*43*, *44*). As such little to no evidence exists on student learning with these biomolecules - even though they possess a range of structure-function properties and offer an excellent opportunity to engage students in several threshold concepts in biochemistry.

Carbohydrate curriculum typically begins by introducing vocabulary related to the structures of monosaccharides; this foundational scaffolding is then used to introduce structure-function concepts related to disaccharides and finally ending with structure-function comparison among various polysaccharides. Even at the start, students have a hard time understanding and visualizing

the small differences in structures of monosaccharides which then impedes understanding di- and polysaccharides. The conceptual and visualization skills needed to understand chirality may be a significant learning barrier in understanding carbohydrates' structure-function relationships. For example, a simple hexose like glucose has four chiral centers and an additional chiral center on the anomeric carbon upon ring formation. Upper level students who have completed the organic chemistry curriculum can successfully build correct ring structures using organic model kits, such as Prentice-Hall, Darling or Maruzen sets, due to the familiarity with cyclohexane. However, forming α- and β-linkages from those glucose models is often beyond their skill set, and, even when they manage to do it, they cannot make the connections between the linkages and resultant polysaccharide properties. The linkages as shown in most line representations (e.g. Haworth projections or chair conformations) are meant to focus attention on identifying the linkages.

The line representations, however, do not convey how α- and β-linkages impose the steric restrictions in three dimensions that lead to the different structural properties of amylose and cellulose, respectively. The 3D structure of amylose (PDB ID: 1C58) shows the helical nature of amylose as well as hydrogen bonding possibilities. While the structure of cellulose straight chain polymer is not available directly on the RCSB Protein Data Bank site, structures of enzymes bound to different cellodextrins containing three to nine β-D-glucose units are available (PDB IDs: 4C4C, 3QXQ, 4TF4, etc.). Instructors may utilize virtual visualization tools, such as Jmol, to show students the end results of repeated α- and β-linkages for amylose and cellodextrins, or skilled students may even manipulate the virtual structures themselves. However, the path from linkage to final structure still remains muddy for most students. Physical models where students can make different linkages and manipulate structures to ''see'' steric restrictions for themselves would be useful.

Based on these observations, a simplified glucose model was designed with –OH groups on C2 and C3 fixed to the ring. Oxygen (-O-, red color) and hydrogen (-H, white color) atoms were designed as in most model kits with holes and linkers. The hydroxyl groups could be attached to C4 (below ring), C6 (above ring, away from C1) and either in the α- and β-positions on the anomeric C1. The anomeric C1 was colored grey while all other atoms including the fixed hydroxyl groups were tan colored. Clearly visible numbers were printed for each carbon, which is proposed to aid students in proper orientation of the model during instruction. The dihedral angles were chosen by comparison with available coordinates for amylose and cellodextrins and the model built using Spartan 14 modeling software. The choice not to use CPK coloring throughout was explicitly made to focus attention on those hydroxyl groups forming linkages; as students using glucose molecules built with organic kits often struggled with finding the correct –OH groups for linkages.

The models were used in an upper level Biochemistry course (6-8 students) and a lower level introductory GOB (General, Organic and Biochemistry) course for pre-nursing students (20-25 students) over two class periods. Each student had at least one glucose model to work with and first understood the α- and β-positions on C1. They then worked with partners to build maltose and cellobiose models. One unexpected benefit of working with physical models was the explicit connection between condensation and removal of water, since they physically had to remove water to make the glycosidic linkage. Students then worked in larger groups to extend maltose to amylose and cellobiose to cellulose. Numbered carbons helped with building 1,4 linkages. Even with five glucose residues linked together, the differences between the polysaccharide structures becomes unmistakable. The α-linkages result in a flexible chain that naturally curved and showed the beginnings of a helix. The β-linkages result in a rigid and linear fibril. (Figure 2)

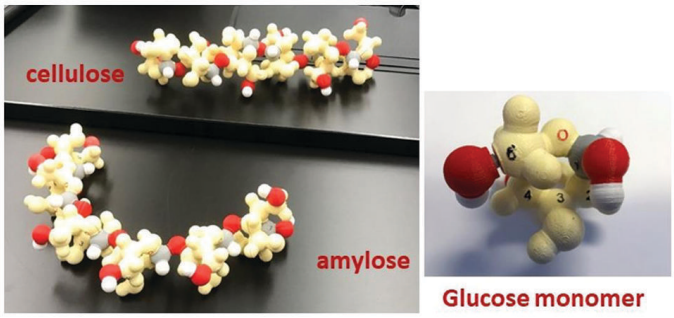


*Figure 2. Amylose and cellulose models (on the left) formed from repeated α- and β- linkages with glucose monomers. A single glucose monomer (on the right) shows the number and color scheme selected for the 3D printed models.*

Students were then instructed to locate and compare the linkages within the polymer, and with the model in-hand the differences were obvious. The α-linkages were exposed and readily seen while the β-linkages were harder to find even with numbered carbons. Students were directed to make the connection between availability of linkages and function of polysaccharides. Glucose in storage polysaccharides like amylose should be readily cleavable, and a helix exposes the linkages easily. Cellulose "hides" its linkages and prevents easy access and thus is a good structural polysaccharide. Different groups could come together to form longer chains or in the case of amylose, make 1,6 linkages to make amylopectin or glycogen. Additionally, the presence of a single free anomeric carbon with multiple branches illustrates how reducing ends are "used up" in storage polysaccharides.

The glucose models were simple enough to be used with lower and upper level students in different capacities. Pre-nursing students appreciated having their own glucose model to study before they started forming linkages. Some students were a little confused by tan coloring for most atoms, however this became a teachable moment about the limited nature of any given model. Biochemistry students were more used to working with multiple models representing a single structure and had no such difficulty.

After working with both GOB and biochemistry students, the models were simplified. The –OH group on C6 was fixed to the ring and colored tan. Only a few glucose models needed the –OH group on C6 to create branching and this focused the use of models solely on 1,4 linkages. The absence of CPK coloring does prevent students from visualizing hydrogen bonds between residues. The potential for using flexible linkers to simulate H-bonds is currently being investigated. In all, this set of physical models is designed to engage students in building mental models that integrate the unique and varied structure-function concepts of carbohydrate chemistry.

## Case Study III: Serine Protease Active Site Models

Educators allot a significant portion of molecular bioscience curriculum to proteins, compared to lipids, nucleic acids or carbohydrates. Protein status in these curricula is not surprising considering that this biomolecule offers an avenue to cover and integrate four of the five biochemistry threshold concepts: "physical basis of interactions, thermodynamics of macromolecular structure formation, free energy, and biochemical pathway dynamics and regulation (*45*)." As such, a plethora of intervention activities, from POGIL to virtual based tools, with corresponding learning outcomes and gains, are reported in the literature. Even with this, little research has explicitly identified student misconceptions related to this biomolecule. Compounding on the extensive time spent covering topics related to proteins are the vast array of representations students are exposed to throughout

the course of protein education. At the outset of this study we wanted to develop a series of physical modeling activities with accurate features to target student understanding of protein structure-function concepts while concurrently building students' visual literacy skills. We also sought to use a validated instrument for assessment to test the impact of these models. Here we describe the design of serine protease physical models that intentionally address the three primary misconceptions identified through the Enzyme Substrate Interactions Concept Inventory (ESICI): electronics, stereochemistry and geometric complementary (*46–48*).

We chose to create a set of serine protease models for chymotrypsin, trypsin and elastase as these enzymes, their substrates and inhibitors are not only common examples in biochemistry textbooks but also because these enzymes are exceptional examples of: substrate specificity, transition state stabilization, acid-base and covalent catalysis, geographical differences between catalytic and binding residues, alteration of pKa values of active site residues to facilitate catalysis, and integration with enzyme kinetics and inhibitor concepts. Current instruction with the proteases usually focuses on one, primarily chymotrypsin, and then mentions others (typically elastase and trypsin) for comparison of binding pockets that highlight enzyme specificity. The visual representations of these enzymes in textbooks usually highlight either electronics or geometric complementary. Additionally, with 3D virtual modeling students are likely only analyzing one protease at a time. Here a set of proteases enables students to make direct comparison among all three enzymes. In particular after years of teaching with proteases we note that students struggle to build a mental model for geometric complementary, therefore we propose a set of physical models with several different renderings will best target this misconception.

While students demonstrate misconceptions related to each phenomenon separately, a complete understanding of how enzymes interact with substrates requires synthesis of all three concepts. The set of serine protease models was designed with respect to each targeted misconception. These models were developed with a team of undergraduates in conjunction with the CBM. As a team we decided on three major components for each protease as described in Table 1, an example of which is shown in Figure 3.

These physical models are used in an undergraduate biochemistry course taught with an explicit focus on increasing visual literacy skills through the use of models and modeling. The course follows a flipped classroom design in which students watch a concept-based video prior to class and complete a pre-class assignment. During the 50 minute course time students engage in active learning activities in groups of two or three students. The protease physical models are used across two course days. During these days a physical model set is shared between two groups, with each group completing their own activity. During the first day students are given an exploratory activity designed to have students identify and compare the enzymes, then identify and compare the substrate based on electronic, geometric complementary and stereochemical interactions among the pieces. During the second day with the protease model set, each group works through a problem-based learning (PBL) activity while having the models available for reference.

To measure whether these models impact student learning and the targeted misconceptions, several assessments were used in control and intervention semesters. In the control semesters students worked through the PBL activity without the use of models. In both the control and intervention semesters students completed the ESICI at the start and end of the semester; this instrument is used as a pre/post measure of student learning and misconceptions. Additionally responses to student answers on the in-class activities were rubric-scored with each item tagged with a corresponding misconception (electronics, stereochemistry, geometric complementary or some

combination). The same analysis was performed on correlating questions for students on individual exams on this material. Analysis of these data is forthcoming.

More recently the serine protease kit is employed in the NSF-funded Modeling for the Enhancement of Learning Chemistry (ModEL-C) longitudinal study aiming to define how models impact the learning process and cognitive load for students. In this study, biometric data is collected using electroencephalographic (EEG) and eye tracking tools and voice recordings from simulated learning environments where biochemistry students complete the serine protease activity described above. In addition, observational and rubric analyses of student responses to activities from the simulated learning environment and real classroom sessions provide further data for assessing student learning. From these findings, an iterative process for model and assessment design will be proposed for educators interested in designing 3D physical models with corresponding active learning assessments that optimize the cognitive load and target student misconceptions.

**Table 1. Serine Protease Model Design Features**

| | *Features of the physical model* | *Coloring and rendering* | *Proposed misconception targeted by the physical model* |
|---|---|---|---|
| Active site backbone model | Each backbone model shows the catalytic triad side chains and one - two key binding pocket side chains. | The key side chains are rendered in spheres with CPK coloring. The rest of the protein is rendered as alpha carbon backbone. | Electronics |
| Active site surface | Each surface plate model shows the surface topology of the active site. | The first iteration rendering used CPK coloring. In a second iteration, the surface plates were constructed of clear plastic so students could see the underlying atoms. | Electronics and geometric complementary |
| Substrates and inhibitors | Each designed substrate was docked using AutoDock in Chimera. One small molecules is a chymotrypsin inhibitor, Tosyl phenylalyl chloromethyl ketone (TPCK). | All substrate and inhibitor molecules are rendered in spheres with CPK coloring. | Electronics, stereochemistry, geometric complementary |

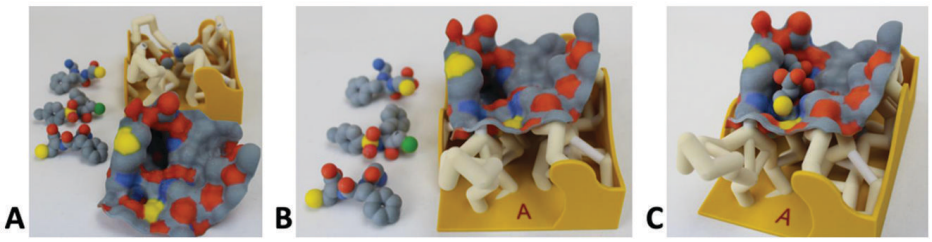


*Figure 3. Serine protease physical model.* ***A.*** *Backbone, surface place, substrate epimers, and inhibitor for chymotrypsin.* ***B.*** *Surface plate snapped on top of backbone with the substrate epimers and inhibitor on the left side.* ***C.*** *Substrate bound in the active site. Photos courtesy of Cassidy Terrell.*

In all, this set of physical models is designed to engage students in building mental models that decrease student misconceptions while also increasing student visual literacy and conceptual understanding. Additionally, we propose an avenue for using physical models to investigate cognitive load and engagement to better understand how students learn with this pedagogical tool.

## Case Study IV: Flow of Genetic Information Models

The "Central Dogma of Molecular Biology" describes information flow in a cell, from storage in molecules of DNA through expression as functional products (proteins) (*49*). A thorough conceptual understanding of the purposes and underlying processes of genetic information flow is a crucial foundation on which numerous molecular biology topics are built. Hence, genetic information flow is one of five Core Concepts of *Vision and Change*, which has been further articulated in the Biocore Guide for interpreting the Core Concepts (2a) (*1*, *50*). Genetic information flow is also one of the four "Big Ideas" in the Advanced Placement Biology Curriculum Framework, and is described in the first objective in the Next Generation Science Standards for life sciences in high school (HS-LS1-1) (*2*, *51*). Typical undergraduate students, however, struggle with many ideas associated with genetic information flow and focus on superficial terms and representations such as "transcription" and "Punnett squares" but cannot visualize or articulate the underlying molecular processes behind the terminology (*52*–*59*).

Many undergraduate biology instructors have recognized the learning struggles and are interested in finding ways to improve student learning on topics related to genetic information flow. And while active-engagement pedagogies, when compared to lecture-only strategies, result in higher learning gains in STEM disciplines, our recent work has highlighted that physical models are better active-learning tools for helping students grasp certain topics related to genetic information flow (*25*, *60*–*63*).

We studied the use of physical models in a sophomore-level Cell and Molecular Biology course at a large, private university in the northeastern U.S. Many of the models used in this course were different from the 3D-printed, atomic-level models described above, but instead were based on more stylized, manipulable pieces made of craft foam, presenting a molecular level view of interaction of the macromolecules. For example, the Flow of Genetic Information Kit (FGIK) uses foam pieces to demonstrate how DNA is built by DNA polymerases in the process of replication, how RNA is built by RNA polymerases in the process of transcription, and how proteins are built by ribosomes in the process of translation (see Figure 4).

Through a retrospective analysis of student data on the validated Central Dogma Concept Inventory (CDCI) tool (*55*), the authors demonstrated significantly higher learning gains on CDCI questions that were associated with a physical model-based in-class activity compared with questions that were associated with clicker questions or peer discussion problems (*25*). The CDCI tool employs a multiple-select format, which helped the authors unearth interesting and useful patterns of student responses. While all students learned from engaging with the model-based activities, the researchers found that higher performing students improved their overall score by refining their almost-fully-correct responses. For example, if a correct question response was ABD, the higher pattern of responses from the higher performing students went from AB (pre) to ABD (post). Lower performing students entered the course with less content knowledge, overall. The authors found that lower performing students improved by recognizing more correct vs incorrect responses after engaging with the model-based activities. For example, if a correct question response with ABD, lower performing students went from choosing (ACE) to (AB). Lower performing students may

not have left the course with complete expert-like mental models, but this group made some of the greatest learning gains, strongly suggesting they had created new (and correct) knowledge.

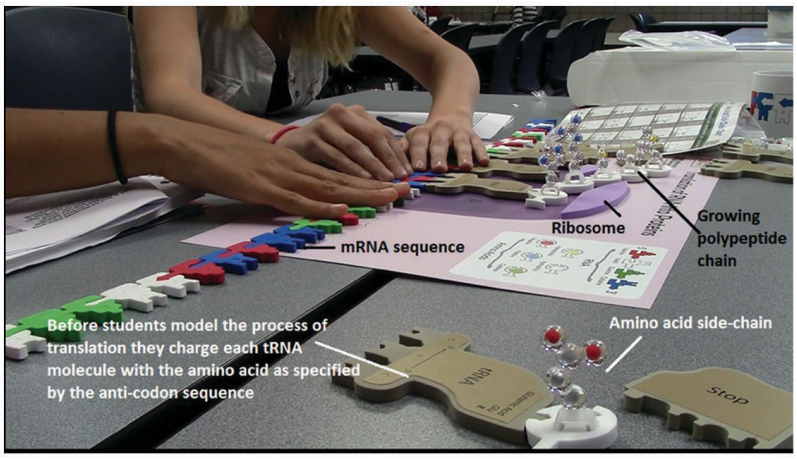


*Figure 4.* ***The Flow of Genetic Information Kit (3DMD).*** *Students explore the process of protein translation using a model-based activity. Photo courtesy of Leslie Kate Wright.*

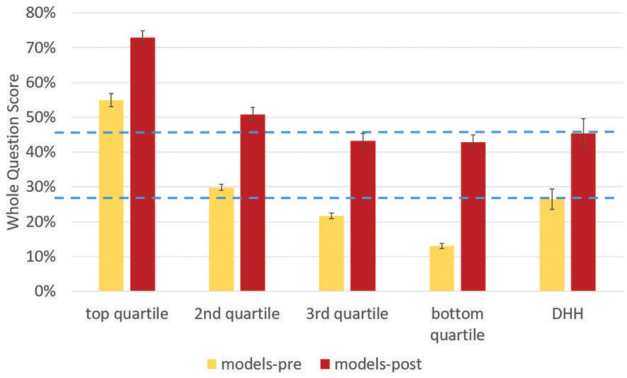


*Figure 5. Model based activities showed dramatic learning gains for all students, including low performers (bottom quartile) and deaf/hard of hearing (D/HH). In this analysis, each multiple-select question was scored as right or wrong (no partial credit). Students were ranked in quartiles by their scores on the entire CDCI at the beginning of the semester, although their performance is shown only for questions related to model-taught concepts. Dotted lines show that on average, D/HH students fell between the 2nd and 3rd quartile, both pre and post instruction. Error bars are SEM, n=426 with 34 D/HH.*

Out of the 426 students included in the study, 34 of the students identified as Deaf or Hard-of-Hearing (D/HH), a population that faces significant challenges in post-secondary settings and lags behind hearing peers in B.S. college degree attainment (*64*). D/HH students, who are also underrepresented in STEM, may experience communication barriers in undergraduate classes and may not be able to fully participate in and learn from typical lectures and discussions (*65*). Research also shows that D/HH students may overestimate their own understanding of the material which may contribute to the overall gap in B.S. degree achievement compared to undergraduate hearing peers (*64*, *66*). For example, in 2015 33% of all hearing individuals (ages 25-64) had completed a B.S. degree compared to only 18% of D/HH individuals of the same age range. Similar to English Language Learners (ELLs), D/HH students may face additional challenges when trying to understand a spoken lecture (or spoken discussion) while also trying to take notes during class (*65*).

Thus, strategies that activate information channels, other than spoken language, such as manipulation of models and model-based activities, may be especially useful for learners who are D/HH or have diverse communication styles (Figure 5) (*65*, *66*). Dissecting out the D/HH students from the above analysis showed that D/HH made the same dramatic learning gains as hearing students on model-based questions.

While future work is needed to probe more deeply into why models are such effective learning tools, several cognitive theories such as constructivism, zone of proximal development, reduction of cognitive load and shared mental models, support the notion that models and model-based activities are effective tools for deep learning. Here we briefly describe each of these theories and suggest why they may be particularly important in the context of D/HH, English Language Learners (ELL), or other special populations.

**Constructivism**

This theory postulates that students learn best when they construct their own explanations through guided activities (*67*). The dynamic, physical model-based activities allow learners to explore and build (through manipulation of the actual models) but also allow for refinement and reorganization of students' mental models of molecular processes. A constructivist approach may be especially beneficial for D/HH learners because these students may be supported during classes by sign language interpreters or real-time captionists. In a traditional lecture-based course D/HH may not be able to write things down or take notes for themselves because they have to split their attention between the board (or PowerPoint slide) and watching the interpreter or captioning screen. Using a model-based activity is very hands-on with D/HH students working directly with the model, and not relying on interpreters or captionists as the conduit for information.

**Zone of Proximal Development**

Learners often require scaffolding to learn new things; in other words, it is difficult to incorporate ideas that are too far away from their prior knowledge (*68*). Physical models may offer a "bridge" to learners with a shaky/incomplete mental model of transcription, when they are trying to learn about gene expression. Offering this bridge is beneficial to all students but may be especially helpful for deaf students because, compared to hearing peers, they enter post-secondary institutions with greater differences in academic preparation and educational experiences (*69*).

**Reduction of Cognitive Load**

Learners can be expected to hold only 5-9 pieces of information in their working memory at a time (*70*). Thus, the cognitive structure of humans restricts the types of environments that are ideal for deep learning (*71*, *72*). A lecture that incorporates 15 new vocabulary or technical terms probably is not ideal for deep learning! Physical models serve as an extension of cognitive space for learners; instead of having to remember details and terms of a process, learners can look at, point to and manipulate a physical 3D structure. As with hearing peers, D/HH students often must balance cognitive load with new learning opportunities. Unlike hearing students, D/HH students who communicate using American Sign Language (ASL) may have another challenge; when interpreters encounter an unfamiliar term or a word that is not connected with a standard ASL sign (or a sign they are aware of), they may invent a brand new sign on the fly to communicate a term or idea (*73*). This phenomenon may increase cognitive load in D/HH learners as they may have to

keep track of another ASL sign during a class. Physical models may alleviate some of the cognitive load faced by D/HH learners since they will have to rely less on ASL interpreters and can handle the model themselves.

### Shared Mental Model

As learners manipulate the physical model they alter their existing mental models to align more closely with the physical model. Students working in a group have a structure to which to refer as they share ideas and engage in discussion. Thus, physical models become the embodiment of a shared group mental model, improving the learning experience for all. There is a correlation with students' sense of belonging to a STEM community and college persistence, but deaf college students, among others, may struggle to achieve that sense of belonging. Including model-based activities during class may help D/HH students form connections with their peers (*74*, *75*).

Active learning classrooms that incorporate physical models of molecular biological processes improve learning for all students, but particularly for low performers and individuals with communication difficulties. We suggest that models are helpful beyond simply encouraging active engagement because they 1) make the abstract more concrete, 2) provide a shared mental model for discussion, 3) do not depend on jargon or vocabulary, and 4) promote dynamic rather than static conceptions.

## Conclusions and Future Directions

Although each of the case studies detailed above has unique features, they demonstrate that physical models can be employed in a variety of ways to create shared mental models among researchers, educators and students. There are several common threads shared by two or more of these cases:

- The first two cases engage undergraduates in designing models. Making decisions about which structures to depict to tell a molecular story, or to best compare similar structures, or how to resolve two conflicting pieces of data in the literature, requires students to think like scientists (*76*).
- Cases II and III employ backward design by first identifying learning objectives, then targeting student misconceptions in the design of instructional materials (*77*). The physical models serve as mental models and thinking tools, optimizing cognitive load so that students can develop a deeper conceptual understanding.
- Cases I-III utilize accurate physical models to explore molecular interactions and connectivity. Case IV, on the other hand, employs schematic models that focus on a molecular process (DNA replication, transcription, translation). There is value in using *both* types of models, as well as in transitioning among multiple models of the same structure (*78–84*).
- The first time students use a new tool (ie models), they need to learn HOW to use the tool. Students experience frustration when they are expected to simultaneously learn how to use a new tool and master the concepts. Students need time to explore models before they are expected to master the concepts the model conveys. Educators can bridge the gap by orienting students to the models, discussing the use of color and renderings of the models as well as limitations of models. Just as in observing fine art, novices must be guided to an

understanding of what they are viewing by an expert in order to appreciate the nuances of models they explore.

- To be the most effective, students should be exposed to models throughout a course/curriculum. Multiple representations of the same molecular story allow students to layer details for greater complexity. Models of similar structures allow students to compare and contrast, growing their conceptual understanding. Multiple *types* of models (physical vs. virtual, schematic vs. accurate) allow students to develop skills in transitioning among models.

As discussed in Case IV, incorporating physical models in the molecular biosciences classroom may be especially beneficial for D/HH students. The goal of universal design for learning is to optimize learning experiences for *all* students, recognizing that all students learn differently (*85*). Indeed, each of the cognitive theories discussed in Case IV as applying to D/HH students is applicable to *all* students.

Careful design of physical models as instructional tools will make molecular visualization accessible to a wide variety of learning differences. Physical models serve as a tactile embodiment of mental models, eliminating the need for cumbersome vocabulary in developing a conceptual understanding. This is valuable for both D/HH students and those for whom English is a second language. Careful color selection and the addition of tactile distinctions make the molecular world accessible to color blind and visually impaired students, respectively.

Along these lines, other limitations and challenges exist for educators using physical models in the classroom and/or laboratory environment. Monetary costs of acquiring the models remain a barrier for use. Even if some models are purchased there may not be enough models for every student, and sharing may impede the models' intended use. The models also often require the educator to provide information on orientation, color and proper use.

However, there are several options for educators who are interested in incorporating physical models in the classroom. The Milwaukee School of Engineering has a Model Lending Library with a variety of models (*86*). Borrowers schedule online for a three week loan period (one week for shipping out, one week for classroom use, and a third week for return shipping) and pay only return shipping costs. Educators interested in building their own models can take advantage of a free designs available online (*87*, *88*). Guidance is available for those wishing to build models using their own tabletop extrusion printers, or purchased inexpensively through 3D printing services (*89–91*).

As physical models become increasingly utilized as a pedagogical tool, educators and researchers may consider avenues for investigating student learning and optimal design elements to both the model and assessment. Such studies could investigate the impact of color, size and scale, types of renderings to use together, relevance/impact of spatial reasoning and visual literacy skills, and best practices for classroom use. Additionally, comparative studies using 3D printed models and traditional organic kits from Prentice-Hall, Darling or Maruzen could offer insights into which approach best supports student learning. Along these lines no evidence on student learning exists to determine the impact of students creating 3D physical models compared with using pre-made physical models.

## Acknowledgments

The CREST Project is supported by the National Science Foundation under award numbers DUE-1022793, DUE-1323414 and DUE-1725940.

The serine proteases kit, data collection and analysis is supported by the National Science Foundation under the ModEL-C project with award numbers: IUSE 1711402 and 1711425.

Any opinions, findings, and conclusions or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the National Science Foundation.

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