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# Opportunities for Actuated Tangible Interfaces to Improve Protein Study

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## Abstract

We outline strategies for actuated tangible user interfaces (TUIs) to improve the study of proteins. Current protein study tools miss fundamental biology concepts because graphical and symbolic interfaces do not allow users to intuitively manipulate complex physical forms. Actuated, tangible tools may enhance understanding at all levels of protein study. To advance TUI awareness of protein study, we present an overview of protein concepts and current protein study tools. Thirty-six protein researchers, engineers, professors and students recommend design guidelines for tangible interfaces in protein study, and we outline research directions for TUIs to improve protein study at all educational levels.

## Keywords

Tangible User Interface, Education, Biology, Actuation

## ACM Classification Keywords

H.5.2: Information Interfaces and Presentation: User Interfaces. J.3 Life and Medical Sciences. K.3.1 Computer Uses in Education.

## ACM General Terms

Design, Human Factors

### Introduction

Shortly after their discovery, proteins were named after the Greek word *protas* meaning "of primary importance [1]." As protein study advances, this name proves increasingly accurate. Proteins mediate every process in the human body, from translating genetic information to digesting nutrients. Our understanding of the human body starts with the study of proteins. Yet, formal biology education lacks the tools to effectively introduce proteins to future doctors and researchers. Many tools have been developed to visualize and understand protein function, but none captures the fundamental mechanisms of proteins. This shortcoming stems, in part, from the difficulty to represent and manipulate complex 3d objects with traditional interfaces like GUI tools or symbolic (programming, mathematical) languages.

Readers of this paper are no doubt familiar with fundamental principles of TUIs: direct manipulation, graspability, and close coupling of representation and control [9]. To apply those principles to the study of proteins, it is necessary to understand the fundamental principles of protein interactions and the existing tools for their study. First, the underlying concepts of protein function are outlined. Then, the current tools are described and their ability to address those underlying concepts is discussed. We then discuss the results of interviews with 36 instructors, students and researchers who study proteins and discuss possible directions for TUIs at multiples levels of protein study.

### Protein Fundamentals: Forces and Actions

Each protein has a role. These roles are carried out through specific actions that occur due to specific forces.

Generally, the relevant forces at the molecular scale are *chemical* and *thermodynamic* forces. For example, the bonds between the atoms of a protein are held by chemical forces. Thermodynamic forces dictate the arrangement of those atoms through energy and entropy.

Chemical and thermodynamic forces cause two general types of protein action: *interaction* and *reconfiguration*. *Interaction* refers to the protein influencing or being influenced by other molecules. This interaction may be as simple as breaking ATP down to ADP, releasing energy in the process [19]. The interaction may be much more complicated, as when two separate proteins join to form a larger functional protein [16]. *Reconfiguration* refers to the shape of the protein changing. In one configuration, certain surfaces of the protein are exposed to the outside environment and others are protected. A reconfiguration exposes previously protected surfaces, and vice versa.

Interaction and reconfiguration are often intimately coupled, and are fundamental to the function of proteins. Current protein study tools do not adequately address these mechanisms because they do not give intuitive handles to interact with the complex 3d shape-changes that make proteins function.

### Context: current tools for protein study

Current protein study tools use crystallography-based structural information, first available in 1958 [11]. Three-dimensional structural information has been solved for almost 50,000 proteins and is freely available through the Worldwide Protein Data Bank [2]. Four classes of tools exist to utilize this information: molecular viewers, CGI animations, virtual molecular modeling and 3D-printed tangible models.

### Molecular Viewers

RasMol [18], and other programs like it, instantly provide impressive 3D representations

(Figure 1, top) from any crystallography file. The models are highly accurate and contain a wealth of valuable data. The combination of high accuracy and immediate, free access to protein models via the internet has made molecular viewers the most prominent visualization tool in research.

These viewers, however, *completely* neglect interaction and reconfiguration and the forces behind those movements. They provide a snapshot of the protein, with limited information about their form and only inferred information about their behavior. Researchers, armed with background knowledge and/or theories on the protein of interest, can make some use of the static portrait. Students, however, see a colorful, detailed image and not much else. Molecular viewers provided an accessible starting point for more advanced protein study tools: CGI animations and 3D-printed tangible models.

### CGI animations

CGI technology has been used to animate the static protein representations of the molecular viewers [13]. These animations add information about interactions and reconfigurations to the structural information (Figure 1, center).

While existing CGI animations provide valuable information about interactions and reconfigurations, *information about the forces causing these actions remains hidden*. In an animation, proteins seem to move as independent actors and the chemical and thermodynamic forces causing those actions are

neglected. Additionally, the information provided is limited by the animation medium: a 2D screen. In current animations, the author must force a particular viewpoint on the viewers, which can obscure important interaction details. Finally, animations can only be made for proteins with *well-known* mechanisms, making them useless for novel research.

### Virtual Molecular Modeling

Digital molecular structure and interaction information has been paired with the virtual reality environment to create a virtual interaction between scientist and molecule. Some, such as Stalk [12] and VIBE [5], use the CAVE virtual reality environment. Molecular information is used to project a three-dimensional molecular model that can be pushed and pulled by the user.

Virtual Molecular Modeling adds interaction and reconfiguration information, as well as information about the forces behind those movements. However, the virtual reality environment is not an intuitive physical space. There is no force feedback to the user and the projected three-dimensional image remains an illusion rather than a tangible physical object.

### 3D-printed Tangible Models

3D-printing technology has been used to create physical versions of the molecular viewer protein representations [8]. These tangible models bring highly detailed structural information into our intuitive physical space. UI's include one-piece, rigid representations of specific proteins; passive articulated models that introduce flexibility to the UI by breaking the protein into multiple, interconnecting units; articulated models further enhanced by the addition of magnets simulating bonds between molecules; and

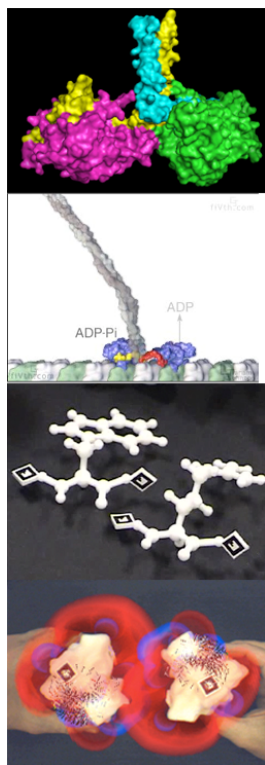


Figure 1. Current Protein Study Tools: (top to bottom) Molecular viewers, CGI Animations, Virtual Molecular Modeling and Augmented Articulated Models.

finally, articulated models paired with digital information in an augmented reality environment [7].

Augmented reality (AR) markers on the model are used to superimpose additional information onto the tangible models. This enables scientists to virtually change the amino acids in the structure quickly and cheaply. The physical model, with AR markers, held by the scientist corresponds to an image on the scientist's computer that replaces the AR markers with digital representations of the desired amino acids (Figure 1, bottom).

The tangible models can be used to illustrate interactions and reconfigurations, sometimes even representing forces (e.g. the articulated model equipped with magnets). For either students or researchers, passive tangible models can approximate some forces through magnets and other mechanisms. However, to truly recreate the forces causing protein interaction and reconfiguration, actuated models are needed. These actuated models are our essential opportunity for TUI contributions to protein study.

### **Findings: design guidelines from students, instructors and researchers**

Thirty-six leading specialists and graduate students in four distinct fields of study—macro-molecular dynamics, molecular motors, crystallography and educational tool design for biology—evaluate the concept of actuated models for biology education and research. We outline our interview methodology, discuss problems with existing tools, and summarize interviewees' design recommendations.

#### *Interview Methodology*

Demographics were split roughly equal among the fields (8-10 each), with some interviewees involved in

two or more fields. Over half the interviewees were current students (20); many having a minimum of three years' advanced teaching and research experience as well. Our interview methodology included passive observations of interviewees in their daily work as well as focused interviews about a number of topics:

- *Educational background and philosophy:* The educational perspectives and experiences of the interviewees give context to their feedback, including preferred learning styles of both instructors and students.
- *Critique of existing biology curriculum:* An open discussion of the failures and successes of the current educational tools and methods, such as addressing if students are well prepared for careers in biology and related fields.
- *Suggestions for new tools:* Motivated by their own learning/teaching styles, interviewees provided ideas and clarification for the type of tool needed, addressing what would help them better understand protein function and interactions?
- *Review of conceptual prototypes:* Interviewees were given conceptual UI models at the end of the interview and gave feedback and design suggestions for new approaches to UI designs.

#### *Recommendations of students*

*"Proteins are three dimensional and textbooks and chalkboards have two dimensions. We're missing a third of the information."*

—College-level biology student

Students unanimously stated that they arrived at college unprepared to tackle advanced protein

concepts. Almost half of students (~40%) were uncomfortable applying protein knowledge even after taking several courses in the Massachusetts Institute of Technology Biology Department curriculum, because they never fully understood basic protein concepts. One student summed up her difficulty, saying, "proteins move due to forces that we can't see or experience; it's hard to visualize that movement." Analysis of student interviews suggested the need for actuated tangibles.

- Tangible Models — Protein shape and spatial interaction determine function. Giving students a tangible model to manipulate in physical space supports a spatial understanding lacking in current tools.
- Kinetic automation — provide real-time, intuitive kinetic information about protein conformations.

#### *Recommendations of Instructors*

Instructors supported students' claim that actuated, tangible models are needed, and named cost as the number one obstacle to incorporating tangible models in the classroom. A tool must provide enough value in student learning to justify the investment. Instructors added design criteria that address economy:

- Durability – Passing models out in lecture often results in damage. A robust model that withstands student wear will improve the experience of more students.
- Integrate with common curriculum – A model must fit into a typical protein lesson plan to provide strong ties to course material. A stand-alone example will not draw connections between major concepts.

#### *Recommendations of Protein Researchers*

Researchers were enthusiastic about the possibilities of tangible, actuated models, but their demands are more difficult to achieve:

- Universal Application – A useful research model must be able to take the form of *any* protein. Researchers often study multiple proteins at one time; the cost and time of developing a separate model for each protein would render the models useless.
- Force Replication – The chemical and thermodynamic forces at work in protein interaction and reconfiguration must be accurately represented to provide a tool for groundbreaking research. An inaccurate tool would lead to unreliable discoveries of unknown mechanisms.

However, a research model does not necessarily have to fit these requirements perfectly to be useful. One professor we interviewed recalled a useful model in her recent research:

*It was just a piece of wire bent in the approximate shape of our protein of interest. [Our collaborator] brought it in to lab and we were amazed by what we could observe in such a crude model. After studying this protein for years with state-of-the-art digital modeling software, we gained several insights from a couple of minutes holding a bent piece of wire.*

Even simple tangible models make extensive information accessible to the human learner. A small improvement to a bent wire model could provide additional insight.

#### **Results: technologies and trends for protein study**

By applying current trends in TUI to protein study, very useful educational and research tools may be

developed. Our aim is not to solve this problem in this paper or to present draft interfaces; rather, we hope to outline ways in which this new domain may be fruitful for applying TUIs without representing those ways as explicit 'implications for design' [6]. After highlighting promising technologies to apply to this domain, we will illustrate how TUIs could be applied to the protein study at multiple levels.

#### *Technologies*

The potential for TUI contribution to biology is illustrated by five technologies: PHANToM, modular robots, Topobo, Senspectra, and Posey.

The PHANToM haptic interface allows the user to interact with digital force information in the physical environment [17]. The device has been used and improved for applications requiring very high accuracy and precision [3]. The interaction PHANToM enables is very similar to the interaction needed to connect scientists with the forces affecting proteins. Visual Molecular Dynamics [8] was developed to use haptic devices like PHANToM to probe molecular data. A wealth of digital information is available on such forces in proteins [4, 20], but PHANToM provides limited intuitive interaction. The next step is incorporating the force information of PHANToM into the form of a molecule.

Modular robots have been constructed from simplified building blocks, much like proteins are constructed from amino acid building blocks. Using the technology of modular robots, actuated protein models could be constructed for any protein. In addition, algorithms exist for automatically detecting the configuration of a modular robot [14], a feature that would be incredibly useful in matching a modular protein tool to computer analysis. A major challenge, however, is that proteins

consist of hundreds or thousands of amino acids, far more building blocks than the typical modular robot.

Topobo is a constructive assembly system with kinetic memory, the ability to record and playback physical motion [16]. Like the modular robots, the building block assembly of Topobo lends itself to the amino acid construction of proteins. The kinetic memory of Topobo may facilitate greater interaction between scientist and protein. As a researcher or student explores the possible actions of a protein, they could record their discoveries for further review.

Senspectra, another system assembled of smaller building blocks, provides real-time visual information about structural strain in the construction [11]. The nodes and sensor joints of Senspectra bear a remarkable similarity to the atoms and bonds within an amino acid. The bonds between atoms are arranged to provide the lowest energetic configuration of the molecule, which is analogous to attempting to minimize the strain in a Senspectra construction. The visualization of strain in the bonds of a model could facilitate an interaction between scientists and the thermodynamic forces of a protein.

Posey is a computationally-enhanced hub-and-strut construction kit [19]. The physical construction of Posey is visually enhanced onscreen, much like the augmented reality models of proteins [7]. Molecule Explorer is a software companion that turns Posey into a basic chemistry ball-and-stick model and pairs it with enhanced digital information. A similar software companion designed especially for protein study may serve as an excellent starting place for actuated tangible protein study tools.

Trends in TUIs are providing the technology necessary to enable actuated tangible models for protein study. Current protein study tools leave ample opportunity for TUI contributions to the field. An actuated tangible model may facilitate the next scientific breakthrough.

#### *Protein tools for three levels of study*

To highlight the vast possibilities of TUI contribution to biology and the study of proteins in particular, we propose directions for new tool development at three levels of study: high school biology education, college biology education, and professional research. Each level illustrates distinct educational and UI opportunities and needs.

#### HIGH SCHOOL BIOLOGY: KINETIC TANGIBLE MODELS

Though most children learn the word *protein* early in life, through advertising or parental urges to eat well, high school biology is usually their first introduction to the meaning of that word. Unfortunately, they have rather poor tools to help them through this first encounter with a very complex concept. In many schools, students have only a textbook and one or two educational videos to rely upon. Textbook illustrations are incapable of showing movement and educational videos are usually played once in a dark room of sleepy students. Most importantly, protein concepts are primarily spatial lessons, but none of their common tools take up space in the physical world.

#### Kinetic protein model

A kinetic model of a single protein (figure 2) can demonstrate the main high school level protein concepts: function, conformation, and energy. For example, kinesin, a simple molecular motor that transports other proteins from the inner cell to the cell periphery, is both important and could particularly benefit from TUIs due to its dynamic nature.

Restricting the view to one molecule allows the designer to hide many advanced principles within the model that will affect function. The pieces of Topobo could be modified to represent the quaternary structure of each amino acid chain in kinesin; the kinetic memory could be used to record kinesin's movement. Because details are hidden in the model, students can focus on general concepts. For students with no biological intuition, a physical model can reference a familiar situation to build intuition. Comparing the feel of gears in the moving model to structural changes in the actual protein allows students to understand how proteins change shape. Adding a stationary microtubule base for Topobo-based kinesin to walk along, as shown in Figure 2, completes the molecular story.

#### COLLEGE BIOLOGY

College students currently have access to very limited visualization tools: freeware protein viewers, textbook illustrations, and occasional classroom models. None of these tools address movement or the mechanisms of folding, some of the main concepts introduced at this level. It is very important for college students to see proteins moving in physical space. A kinetic tangible that illustrates *structure* and the *connections* between structure and movement is needed for adequate understanding.

#### Amino acid constructive assembly

Inspired by a familiar physical chemical modeling kit, an amino acid constructive assembly system (Figure 3) may allow students to connect a series of amino acid pieces together and then fold them manually. Amino acids are the smallest and most basic level of protein structure, so any kind of structure can be made. The folding is guided by mechanical and digital restraints built into every piece. Once folded, it is easy to understand the flexibility inherent in proteins and

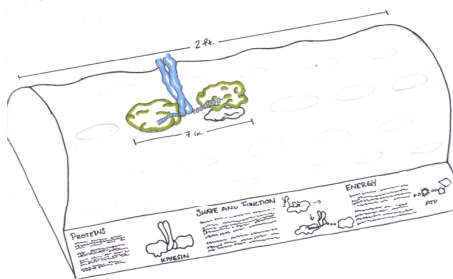


Figure 2. Kinetic Tangible Model of Kinesin.

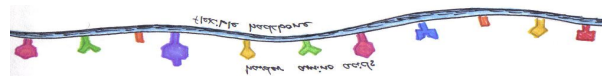


Figure 3. Amino Acid Constructive Assembly System.

conformation changes that must occur before interacting with other proteins.

Such a constructive assembly should focus on levels of structure. Amino acid subunits must be pared down to their simplest form. Simple subunits will not be comparable to molecular models seen in chemistry classes, as the scale is vastly different. Like chemical modeling kits, accuracy is critical: if the bond length, strength, and shape are designed well, higher levels of structure will fall together accurately. The strain detection and visualization of Senspectra could be combined with the force interaction of PHANToM to create a highly accurate and intuitive constructive assembly system. The system shown in Figure 3 would consist of amino acid building blocks joined by bond connectors. The Senspectra-based connectors would provide a visual guide for protein folding, based on strain. Connection to a PHANToM-like system could provide a physical force guide for folding, based on the arrangement of amino acid building blocks and the resulting chemical interactions.

College students have a wide variety of backgrounds. Some will have taken several biology classes and have a reasonable bit of intuition. Others will have only taken one introductory high school class, and have no more intuition than the average high school student. It is important for a tool at this level to address each individual's needs, and construction kits have been

shown to meet users at multiple levels [16]. The basic fundamentals of folding should be well illustrated, and more experienced students can explore nuances of protein folding and "lock-and-key" fitting.

#### PROFESSIONAL RESEARCH

Science demands high levels of accuracy, which limits the types of tools available to researchers. In the study of any protein, there are two major questions: what does it do and how does it do that? To answer these, scientists now rely heavily on protein viewers and articulated models. As discussed in the introduction, these tools are mostly static, and as such, provide limited scope. We believe the next step in this area is an advanced augmented reality environment that incorporates haptic information in the tangible model.

#### Haptic Augmented Reality Environment

The haptic augmented reality environment (Figure 4) includes a crude actuated constructive assembly system, imagined as a modular PHANToM. This system would essentially be an advanced version of Posey, with the major upgrade of the PHANToM force feedback. Each piece will contain mechanical and digital properties and the pieces fit together in a rough approximation of any protein. The model connects to a computer and a protein-viewing program. As the researcher twists and bends the model, the computer sends information about resistance to bending and bond strength to the model. With each new conformation, the researcher can feel the relative ease with which a protein can be molded, helping researchers understand possible conformations a protein may assume. Since discovering conformations is critical to understanding function, such a tool may accelerate discoveries in fields such as drug design.

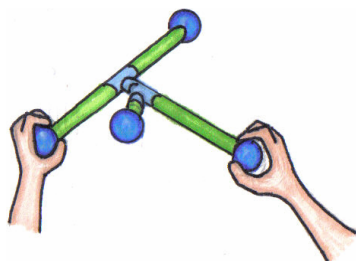
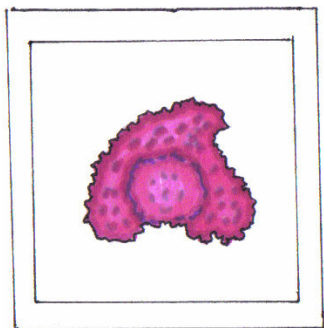


Figure 4. Haptic Augmented Reality Environment with digital representation and haptic constructive assembly system.

While a crude controller for a complex protein allows a unique opportunity to oversimplify, a professional can fill in conceptual gaps in the model. In this tool, we take advantage of oversimplification by using structural motif subunits in the constructive assembly system. Several motifs appear repeatedly in proteins, so a wide number of proteins could be roughly approximated from a series of motif subunits. Motif subunits keep the model small and manageable, since proteins usually contain on the order of 10 motifs.

A main priority for scientific professionals, accuracy is the primary concern in this tool. The computer handles most of the details, but the physical-digital interaction must be designed very carefully. Some accuracy was forfeited in the physical model with the motif subunits, to keep the tool adequately simple, so the computer must recognize the physical model's failings and compensate for them. The model will be a rough approximation of the protein of interest and the computer must map the inaccurate physical model to the digital information very accurately. The model must respond quickly and strongly to physical input so that the intuitive sense of pulling and pushing is not lost.

### Conclusion

Actuated tangible interfaces can improve protein study by providing physical handles to manipulate and understand the complex 3d shapes and movements that determine protein function. A survey of the current protein study tools reveals significant limitations, and a survey of recent TUI research highlights the advantages of tangible interfaces in addressing those limitations. Exploratory interviews with 36 experts and students strongly reiterate both limitations and opportunities. We have discussed directions for at every level of protein study.

At one time, mechanical tools like the microscope contributed to milestone advances in biology and public understanding. Now, as we delve deeper into more complex issues, the immense computing power of the digital world is necessary for study. The TUI community has a unique opportunity to significantly improve the field of biology. Its particular area of expertise – developing the interface between the physical and digital worlds – is exactly where the challenge of new tools lies. We encourage TUI developers to look closely at protein study tools and contribute to the understanding of our world.

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