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Implementing Inquiry Based Computational Modeling Curriculum in the Secondary Science Classroom

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Implementing Inquiry Based Computational Modeling Curriculum in the Secondary Science Classroom

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Abstract

Implementing Inquiry Based Computational Modeling Curriculum in the Secondary Science Classroom

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Abstract: Better visualization of micro-level structures and processes can greatly enhance student understanding of key biological functions such as the central dogma. Previous research has demonstrated a need of introducing novel methods to increase student understanding of these concepts. The intention of this report is to show how computational modeling programs (CMPs) can be successfully used as an innovative method of teaching biology concepts that occur at a molecular level. The use of computers and web-based lessons are not new topics in secondary education studies but there is not an abundance of research related to computational modeling alone. We began by researching the many studies that have already indicated the benefits of using computers in the classroom with an emphasis on CMPs and simulations. Of these, we focused mostly on the ones that showed increased student engagement and influenced understanding of core science concepts. Based on the literature reviewed, a framework for curriculum designed around CMPs is proposed. Lastly, a model lesson is discussed to provide an example of how these professional grade tools can be employed in the classroom. This report provides a basis for the continued development of constructivist curriculum built around the use of professional grade computational tools in secondary science classrooms.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

There is a wealth of research and discussion in education literature over the role of using computers to enhance student learning in secondary classrooms dating back to the early 1980's (Akpan, 2001; Bracy, 1982; Stratford 1997). The role of the computer in education is multifaceted. For example, computers add a break from traditional teaching methods as they easily engage students through the interactive and graphic properties of computers. Implementing computer based learning in the classroom provides an active learning experience for students by engaging students through multiple styles of learning including visual, kinesthetic, auditory styles. Additionally, computers offer students a chance to gain valuable experience with a tool that is commonplace in post secondary education and the modern workplace. However, in spite of these known benefits, there is a lack of literature showing quantitatively whether or not classroom computer use directly influences student learning as compared to traditional methods of teaching (Fouts 2000). Likewise, there is a deficiency of readily accessible curriculum built around the use of professional grade computation tools for the study of science, technology, engineering and math (STEM).

There are many professional grade computational modeling tools available for use in science and engineering applications. Most STEM curriculum objectives focus on specific science standard based objectives. This report narrows the subject matter focus to a specific field of research through design of a constructivist perspective of learning to connect the curriculum to application. The subject matter investigated is the high tech field of drug discovery and design. A bioengineering focus provides a topic that is relative to many secondary science subjects as it is a multi-practice field of study: researching and engineering pharmaceuticals involves subject matter from many fields of

science including biology, chemistry, physics, and engineering. This multi-practice basis provides relevance to core subject area secondary science curriculum. Also, drug discovery is a fast growing and sustainable field of research offering career potential for STEM minded students.

Central to the field of drug discovery is the study of biomolecular structure and function; and, more specifically, the study of proteins, protein synthesis, and protein interactions with themselves and other compounds. Previous studies have already discussed a lack of student knowledge of key concepts related to protein interaction and structure (Altiparmak and Nakiboglu Tezer 2009). The complex nature of the central dogma has challenged constructivist curriculum writers for years. There have been many attempts at improving instruction of this topic through various means including increased lab use, designing different manipulatives, and including kinesthetic activities. Recent studies show that three-dimensional modeling of molecules can enhance student understanding of complex molecular interactions by providing connections between visual and tactile perception (Bivall et al. 2011). Many of the three dimensional modeling programs that are used by scientists to investigate biomolecular structure are also available for educational use in the secondary science classroom. Although previous research suggests that computer visualization tools can lead to better learning outcomes for students, classroom implementation of these advanced instructional models has been slow. The purpose of this report is to provide secondary science educators and curriculum developers an informational overview of available professional grade molecular visualization tools and ideas for implementation into secondary science constructivist curriculum.

Chapter 2: Computers and Computational Modeling Programs (CMP's) in the Classroom

The application of computer based learning in the classroom has been a popular topic in educational research since as early as computers became widely available for public use in the 1980's. Early use of computers in the classroom fell in line with a behaviorist approach to teaching as the computers functioned mostly as a support tool for traditional teaching methods Student use of computers was mostly secondary to content learning in the form of word processing and data management applications used mainly for reporting information in addition to very basic drill and practice style programs for reinforcing content understanding (Fouts 2000). Today, the use of computers remains important in education; both as a processing toll for synthesizing and reporting knowledge and as an easily accessible way to practice the knowledge and skills necessary to perform adequately on standards based assessments. Through the rapid advancement of computer technology, classroom use of computers began to align much more with a constructivist learning model as software programs began to allow students access to "real world" applications (Fouts 2000). Modern classrooms benefit from the use of programs where students are able to learn by doing through the use advanced educational simulations and professional grade modeling environments. Interactive programs such as simulations have been found to help motivate student learning by providing visualizations of difficult to understand concepts as well as placing a greater emphasis on the use of problem solving skills (Lui 2011). Also, with a wealth of online databases students have instant access to the same information that is available to professionals. Coupling the use of these programs in secondary science classes with inquiry based, open

ended instructional modules helps to keep instruction aligned with post-modernist learning methods.

THE ROLE OF COMPUTERS IN SECONDARY SCIENCE CLASSROOMS

Computer based simulations and modeling programs can aid students in better understanding complex dynamic systems in addition to aiding in the development scientific reasoning skills (van Borkulo et al. 2011). Interactive CMP's allow students to make connections between the dynamic visual environment of the program and the physical models and pictures observed in other learning applications. Additionally, using CMP's in conjunction with inquiry based instruction or project based instruction better enables students to apply their knowledge of concepts. By encouraging student application of knowledge, curriculum becomes more student centered as students learn by doing, which is more favorable to the learning process than simply seeing, hearing and reading (Akpan, 2001). Constructivist teaching methods such as improved visualization encourage students to apply knowledge and make judgments in order to obtain a desired product or result that is directly related to a real world component, such as the testing or design of a drug to target a specific condition. Furthermore, students get to practice and problem solve with these tools in a situation that is less stressful than lab work (Rutten 2012). For students that are targeting careers in bioengineering or other related fields of study, the use of CMP's will better prepare them for college and the workforce by providing practice time with a professional grade tool.

Students often struggle with visualizing complex systems operating in a microscopic environment. Integrating computers into secondary science classrooms can have a positive impact on student learning at this level (Wu et al. 2000). Cellular processes and intracellular drug interactions occurring at the micro level are complex and

dynamic systems which may challenge early developmental visualization skills. Simulations and modeling programs provide an interactive visualization to simplify this complex process.

Classrooms now have ready access to the same equipment and programs as those used by professionals. Using this readily available technology will enhance classroom learning by providing a more meaningful, relevant and engaging approach to teaching central dogma concepts. In a 2000 study sponsored by the Gates foundation, Fouts points out the multiple benefits of including computer activities in lessons that go beyond just the improvement of teaching content; students gain experience using a tool that is commonplace in both academic and professional settings. Kozma et al. (2000, 136) take the concept of computational methods further by focusing on specific methods used by laboratory scientists that can be used in the process of scientific inquiry. Their findings indicate that the visualization skills used by experts in the field to "move flexibly between different types of representations and use them together to express their ideas and to understand their domain" would be equally beneficial to secondary science students. Wu et al. (2001) investigated the value of implementing a three dimensional computer based modeling program to improve student understanding of symbolic and molecular representations of organic molecules. The authors used pre and post test analysis to determine the effectiveness of student use of the eChem chemistry visualizing tool. The use of the program was valuable in engaging student interest and effective in aiding students in making transformations between 2-D and 3-D models. Statistical evidence supports the inclusion of computational modeling as well as traditional models, such as ball-and-stick models, in lessons to include different learning preferences. The authors also mention the value of eChem and other computational models in enhancing

cognitive development by providing multiple visualization methods for students to explore.

CMP's programs are available that can be easily employed to relate the importance of the structure of proteins to their function within a particular context. Students can use the CMP's to analyze protein structure-function dynamics by observing the interactions of proteins with various ligands and by building their own proteins and ligands, along with structural and functional analysis applications. Most CMP's include a user interface that allows easy switching between different representations including sticks, spheres, cartoons, surfaces, and electron density allowing students to view multiple representations of the same molecule.

OVERVIEW OF COMPUTER MODELING PROGRAMS FOR USE IN SECONDARY SCIENCE CLASSROOMS

There are many computer simulations and modeling programs available for implementation secondary science education. Although there are many programs and simulations that have been proven to be effective in increasing learning outcomes in the classroom (Rutten 2012), to keep things in the scope of a drug discovery unit framed under a constructivist model, only programs that have professional application will be discussed in detail. This does not imply that popular simulation programs like Phet (2011), Molecular Workbench (2011) and Explore Learning (2012) are not valuable tools to support learning. These simulations offer dynamic visualization support, which can be used as a supplement to instruction as well as providing scaffolding prior to introducing students to professional grade modeling programs.

An on-line search of molecular modeling programs used in professional applications revealed more than 80 possible programs. Based on the number of times programs appeared during an online search, and throughout a literature review, for this

report, it was determined that most common professional molecular viewer programs, applicable to use in secondary education, are PyMOL (http://www.pymol.org), Jmol (http://jmol.sourceforge.net/), VMD (http://www.ks.uiuc.edu/Research/vmd/), UCSF Chimera (http://www.cgl.ucsf.edu/chimera/), Rasmol (http://rasmol.org/)and Swiss PDB Viewer (http://spdbv.vital-it.ch/). All but the PyMOL CMP can be downloaded freely from the hosting websites. The PyMOL software is available in a free downloadable format for educational purposes only with the limitation that the free downloadable version is not regularly updated. All programs offer three dimensional, dynamic visualizations of molecules as well as allowing multiple types of molecular coordinate files for input such as the popular pdb, and mol, xyz, cif formats. The selection of programs among professionals is a matter of personal choice and often relates back to early experience and familiarity. Professional grade CMP's have multiple applications for bioengineers including visualizations, animations, editing, and rendering of high quality imagery for publication.

Chapter 3. Secondary Science Curriculum and CMP

KEY PERSPECTIVES TO DESIGNING CURRICULUM AROUND COMPUTATIONAL MODELING PROGRAMS

Designing active inquiry based science curriculum around professional modeling environments can lead to enhanced learner problem solving skills as well as a broadened knowledge of science concepts (Fund 2007). However, sufficient support needs to be included to guide students through the process and encourage them to reflect on their learning as they go, especially when working with advanced tools like professional grade CMP's. Proper implementation of CMPs into science curriculum can support constructive learning and other progressive learning strategies. This includes designing curriculum around three key perspectives as suggested by Zhang et al: meaningful, systematic, and reflective (Zhang et al 2004).

Meaningful curriculum encourages learners to recall and apply prior knowledge by introducing subject matter that can be connected with previous experiences and interactions from outside of the classroom and be applicable to future work. Doing so helps make connections with the proposed problem in order to visualize, as well as formulate hypothesis and understandings, around "real world" problems. Designing curriculum around real world themes and including professional grade tools and materials can help keep curriculum meaningful as well as relevant.

To keep things systematic, curriculum built around professional grade tools should include a structure that helps students stay on track with specific learning goals of the unit. Constructivist learning emphasizes open-ended curriculum; however, the inclusion of professional grade tools, especially advanced CMP's, requires a structure that encourages students to employ scientific reasoning while working in the programming environment openly while providing guidance to maintain student focus on

specific objectives at particular points. The multiple features and presence of advanced features inherent to the programs can be both distracting and daunting to many secondary science instructors and students.

A reflective element can be maintained in science curriculum by including self monitoring prompts that keep students focused on the objectives as well as making connections between what their current goals and the overall objectives are. Reflection reminds students of learning goals during activities and encourages integration of new knowledge and skills. Also, prior knowledge needs to be reinforced to assist students with making connections between the tools, the specific objectives, and previously introduced related content.

INQUIRY BASED INSTRUCTION

True constructivist curriculum designed emphasizes inquiry based learning that is as open ended as possible. According to National Science Education Standards, inquiry is "a multifaceted activity that involves making observations; posing questions; examining books and other sources of information to see what is already known; planning investigations; reviewing what is already known in light of experimental evidence; using tools to gather, analyze, and interpret data; proposing answers, explanations, and predictions; and communicating the results" (National Science Education Standards 1996, 23). In other words inquiry is the general method that scientist go about in doing their work. This suggests a model that secondary science activities should be built around. Just as working scientists do not do everything exactly as the model suggests every time, science activities do not need to be built around a rigidly structured model of inquiry. For example, observations directly related to the objective, which lead in an alternate direction, can occur at multiple times throughout the

investigation, leading to new questions and requiring reevaluation of the plan. This less structured, "real world" application of inquiry leads to more open-ended learning. However, application in the classroom requires an element of structure to keep things in focused on specific objectives that are required to be met as is the case with assessment based instruction (Rutten 2012). Therefore, the application of professional grade tools in secondary science inquiry learning requires a measure of structure to allow students as much decision making freedom as possible while maintaining a focus on the outlined objectives.

SUPPORT FRAMEWORK FOR CMP CURRICULUM

Constructivist and postmodernist science curriculum is dependent on keeping inquiry as open ended as possible. However, some form of structure is always recommended and especially so in the case of CMP curriculum design. Fund (2007) provides evidence for four basic structural components that are aligned with Zhang's three key perspectives that can be included to support curriculum designed for computer learning environments. Designing curriculum that includes a structural, reflective, subject matter and enrichment element can provide the necessary support for including professional grade tools in secondary science curriculum. By including a structural component in curriculum design, the lessons will include a general framework that helps guide students through the cognitive learning processes. This is especially important in light of the complex nature of professional grade tools that can lead students feeling overwhelmed or easily distracted with all the advanced program features. A reflective component includes revisiting cognitive learning concepts as well as encouraging use of meta-cognitive skills. This component serves to provide self-monitoring and self-assessment as the student progresses through a lesson. In the case of group work, the

reflective component includes group self-reflection and assessments. The subject matter component focus on the specific knowledge and skills students are expected to understand for specific objectives. These are easily addressed through short guiding questions that serve to increase knowledge acquisition as well as help implicitly guide students through the problem solving process. The enrichment component includes questions that are designed to ensure student comprehension of the subject matter as well as activating higher order thinking skills. This is obtained through in-depth questions that ask students to do things such as compare or contrast, predict, apply to other conditions, find causes, make decisions, and locate additional information (McGregor 2007).

OTHER FACTORS FOR GUIDING POSTMODERNIST CMP BASED CURRICULUM

To help keep curriculum in tune with a postmodernist format, a problem based learning (PBL) style of lesson design is encouraged. PBL is reflective of inquiry based instruction as it is an in-depth, focused investigation of a topic that begins with the proposal of a problem, a complex question, or a challenge. Also, both inquiry learning and PBL require students to use critical thinking skills. However, inquiry based learning can be taken on individually, while PBL requires a group approach where students are required to practice career skills, such as team collaboration, written and oral communication, and technology equipment usage. A challenge when combining PBL with CMPs is the inclusion of student guided learning. When combined, the presence of student directed planning and management, and the open ended nature of, PBL make it difficult to achieve a truly student centered instructional curriculum required to support student use of with professional grade CMPS. However, not all instruction must be in PBL form to maintain a postmodernists learning style. Some level of pre-teaching, practice and other expository learning styles are important to prepare students for the

challenges encountered in well designed, rigorous projects. In fact, differentiation within classrooms often requires expository instruction to be included during projects in the form of scaffolded instruction and workshops.

Scaffolding is an instructional method that limits the complexities of learning objectives based on students' zone of proximal development. "The zone of proximal development is the distance between what children can do by themselves and the next learning that they can be helped to achieve with competent assistance" (Raymond 2000, 176). Scaffolded instruction requires incremental steps that challenge the student to advance by building on and integrating ever increasing levels of prior knowledge. As the learner approaches the desired level of learning, support is sequentially withdrawn until learners can complete the target tasks on their own. In light of CMP based curriculum, scaffolded instruction can help reduce the overwhelming nature of the advanced commands embedded in the programs.

In addition to supportive structures being embedded in secondary science curriculum that focuses on all students, individual student needs will have to be addressed as well. All students will not come into new units with the same set of knowledge and skills. To aid in differentiating constructivist curriculum, individualized instruction will need to be put in place. Focused instructional units can be prepared ahead of time that will address knowledge and skill areas that will be particularly challenging. As the need arises, facilitators can bring select students into side groups, or "workshops," that focus on particular knowledge and skill requirements to bring these students back up to pace with the main group. Workshops can also be used to introduce new knowledge and skills during the course of a project to more advanced individuals and groups and subsequently allowing these advanced learners return the new information to the main group.

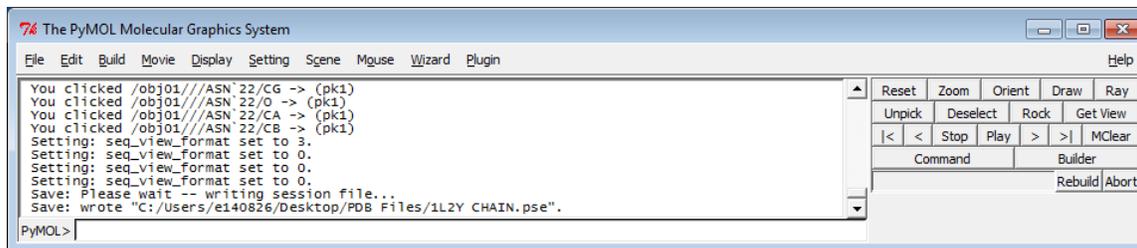# Chapter 4: The PyMOL CMP and the Protein Data Bank (PDB)

PʏMOL

The CMP used in the lesson detailed in this report is the PyMOl program. This modeling program was chosen due to its widespread use in professional applications, the quality of the graphic user interface, ease of importing and exporting data, and the quality of the graphics. The PyMOL CMP (www.pymol.org) is one of few open source molecular visualization tools available for use in structural biology. PyMOl is written mostly in Python programming language, a multi-paradigm language that permits several programming styles; object-oriented programming and structured programming are fully supported. PyMOL runs in all common operating systems and displays high-quality images of biomolecules that can be manipulated through mouse and command prompt control. The PyMOL program was designed for use by scientific professionals with emphasis placed on function and not the ease of use. PyMOL includes a built in help feature and there are many tutorials available on line as well as the PyMOLwiki (www.pymolwiki.org).

Although PyMOL has been set up for use by professional scientists and bioengineers, it has many features that make it a valuable tool for science classrooms as well. The advanced features of the program do not have to be used to gain the benefits of the program; basic functions and features of the program are easily useable and understandable with minimal training. The program supports multiple modes of representing biomolecules, including: wire bonds, ball-and-stick, dot surface, solid surface, wire mesh surfaces, and cartoon ribbons. These multiple visualizations provide various means of representing the various levels of protein structure. The program includes easy to use features that allow individual atoms, molecules, proteins, protein chains, and protein complexes to be visualized through various means including isolation,

color-coding and labeling. Additionally, Hydrogen bonding and other molecular interactions can be easily displayed and further analyzed.

Advanced functions include molecular editing features at multiple levels. Any molecule downloaded from databases can be visually edited by eliminating atoms or protein chains from view. This is a valuable feature in that areas of focus can be isolated for easier analysis. The user can also create objects using the builder feature included with the program. The builder feature allows for the virtual assembly of biomolecules by adding from a selection of atoms, atomic structures, or amino acids.

The user interface is divided into two separate displays. The external graphic user interface (Figure 1) includes most of the command features such as a command line prompt and the file and edit tabs common to many programs. The external GUI also provides a running script of each session and is the location of the builder window. The viewer window (Figure 2) displays the three-dimensional image of the downloaded file next to the Object Control Panel. Mouse control allows for full three-dimensional manipulation of the molecule as well as zoom and three button mouse control commands in the view display window. The control panel allows for multiple object controls including viewing modes, labeling, coloring, hiding, removing, and calculating.

Figure1:   The PyMOL External GUI (The PyMOL Molecular Graphics System, Version 1.5.0.4 Schrödinger, LLC).

14
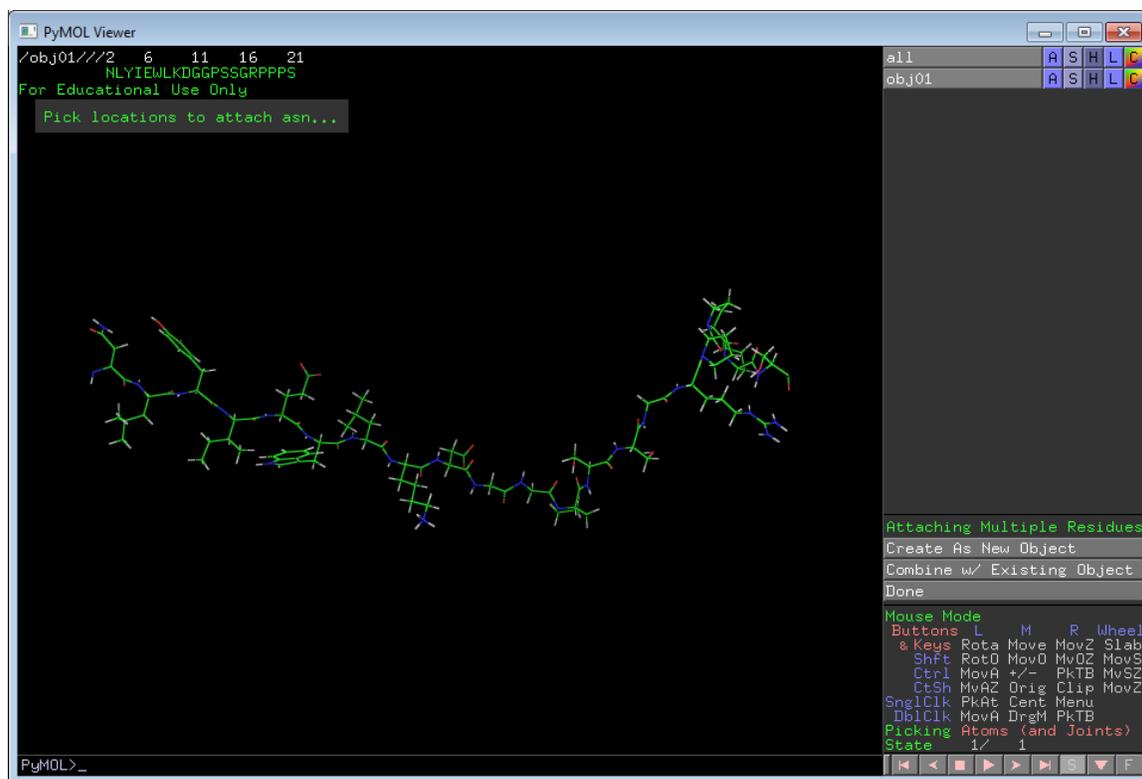
Figure 2:   The PyMOL Viewer Window (The PyMOL Molecular Graphics System, Version 1.5.0.4 Schrödinger, LLC.).

PDB

There are many online sites that store the structural information of biomolecules including proteins, DNA, RNA, and ligands. The structural information for these molecules is determined from x-ray crystallography and nuclear magnetic resonance experiments that define the three dimensional structure of the molecules while in a crystal formation or while in solution. The three dimensional (x, y, z) atomic coordinates are then stored in a unique file in the database and can be downloaded directly into CMP's or stored for later use. In addition to allowing quick and easy access to thousands of protein

structural codes one on line protein database, RCSB PDB (www.pdb.org Bermen et.al),
includes other information on proteins that can be used in science classrooms.

The Protein Data Bank (PDB) offers detailed information on all proteins that have
documented structural information. In addition to the detailed structural information, the
site provides links to the research article(s) that the information comes from. The home
page provides a protein search initiator as well as additional features that can be valuable
to educators such as latest news and research associated with protein structure research,
featured molecules and molecules of the month, and educational resources. The
educational resources page provides lesson plans, tutorials, and activities related to
biomolecules, viruses, and current topics in bioengineering.

Chapter 5: Lesson Discussion

STANDARDS ASSESSED AND OBJECTIVES

By the end of this instructional unit the student will be able to explain how and why cells synthesize new molecules through the process of transcription and translation and how these new molecules relate to other key cellular processes. Student will investigate the structure function relationship of proteins and ligands through a drug discovery project. The final product of this three lesson unit is a presentation of their findings in a scientific article format that will be presented in a power point format. The presentation must include images of the subject molecules captured from directly from student generated images using the PyMOL CMP. The instructional unit is designed with an emphasis on two of the Texas Essential Knowledge and Skills (TEKS) but also ties indirectly into many of the TEKS (Table 1, TEKS addressed provided in Appendix A). The two core TEKS addressed involve the synthesis of polypeptides and the central dogma. Due to the presence of so many concepts, placement of this instructional unit early in the sequence of secondary biology curriculum related to physiology due to the interrelatedness of these concepts with the central dogma of molecular biology. Also, there are many TEKS not directly related to the central dogma that are best studied if students have background knowledge of the DNA-RNA relationship and the process of protein synthesis. The lessons covered in this unit also provide information relevant to other biology knowledge and skills where prior knowledge can be integrated into the new concepts.

17

TEKS		Core	Concepts Related to Central Dogma	Best studied with prior knowledge of Central Dogma	Relevant to other biology concepts
Sciences Concepts	Student Expectations				
4			X		
	B	X			
	C				X
5			X		
	A				X
	C			X	
6			X		
	A				X
	B			X	
	C	X			
	D			X	
	E			X	
7			X		
	A				X
	G				X
9			X		
	A				X
	C				X
	D				X

Table 1:   Texas Essential Knowledge and Skills Addressed in the Unit

SUPPORT MODEL

During the design of the included lessons, emphasis was placed on providing incremental levels of support for student use of the professional grade CMP, PyMOL. Curriculum was designed around the support framework guidelines outlined in the curriculum design section of this report. The first two scaffolding lessons focus on introducing and familiarizing students to the PyMOL operating environment while investigating topics in protein structure, function, and synthesis. These introductory

lessons are highly structured in an effort to keep the objectives in focus. In addition to specific instructions to guide students through the use of the program, questions are scattered throughout the lesson. The questions are intended to provide all levels of support as students advance through the lessons. The questions have been labeled with a two letter code to show what area of support the question is targeting as follows:

Guiding Questions	**GQ**		Reflection Questions	**RQ**
Discussion Questions	**DQ**		Enrichment Questions	**ER**

Structural support questions are labeled as guiding questions. These questions appear the most as they are intended to maintain a systematic structure by having students address key points in the lesson. The responses can usually be short, concise statements that answer a specific question such as making an observation or prediction, or drawing conclusions from observations. Reflective questions appear throughout the lesson to ensure that students take the time to synthesize what they have learned so far in the lesson. This helps students to make connections with prior knowledge and thus reinforces understanding of the objectives. Discussion questions appear when there is a need for subject matter support. These questions aid students in understanding specific content related concepts as they answer guiding questions through explanations. Discussion questions can have students answer questions to aid in retaining newly acquired knowledge and to ensure improved understanding of key concepts. Enrichment questions involve high order reasoning skills and often ask students to apply their new knowledge to other concepts. Enrichment can involve content that is not obviously related to the lessons objective but instead are intended to aid in the development of meta-cognitive skills.

LESSON ONE

The visualizing proteins lesson provides a structured introduction to the PyMOL CMP while the students are introduced to the structure-function relationship of proteins. The basic intention of this lesson is to provide the first level of scaffolding to enable students to be familiar with the modeling environment during the final, less guided, lesson. The content related subject matter addressees the structure of amino acids and their physical characteristics. Students begin by following a step by step procedure found on the PyMOL Wiki that introduces the basic control features of PyMOL while exploring a bacterial potassium channel protein. Two questions follow this first activity. Question one is a guiding question; students draw conclusions from the visualization of the protein complex. The second question is a discovery question asking the student to describe the structure of this protein in a different context. Part two of the first lesson continues the tutorial as the students respond to a series of guiding questions about the naming of amino acids and their physical properties. Students will be introduced to both the amino acid codon chart and the amino acids and groupings chart during these questions. Section three guides the students through more basic functions as well as the process of imaging proteins by having students save a specific view of the channel protein. Section four is a series of guiding questions that leads students through a discovery of the secondary structures of the protein by observing and comparing data from PDB.org and the PyMOL viewer. The lesson finishes with an enrichment question that has students focus on the application of both PyMOL and PDB to the field of drug discovery.

LESSON TWO

Lesson two is built around the same premise as lesson one: it serves as both a tutorial for using the PyMOL program as well as a content lesson. Lesson two includes some of the more advanced features of PyMOL while guiding students through the

central dogma. Students are given a 22 codon DNA section for a very small but complete protein, the TRP-cage. Before use of the CMP takes place, students go through the steps of transcription and translation using the appropriate charts. Afterwards, an enrichment question asks the students to complete an analogy of the process before moving on to the modeling portion of the lesson. In the modeling primary structure activity, students use the builder feature of PyMOL to assemble the amino acids into a chain. The PyMOL builder automatically links the amino acids into a chain as students "drag and drop" them into the viewer window. Following assembly, students are asked to use their knowledge of amino acid structure learned in lesson one to make predictions about the reaction occurring during peptide bond formation. Students finish this section by submitting an image of their labeled polypeptide on a white background. The next section of lesson one moves from transcription and translation to an investigation of protein secondary, tertiary and quaternary structure. For this, students are provided the PDB code for TRP-cage to allow them to visualize the structures. Students are then asked a series of questions to promote understanding of the concept before finishing with an enrichment question that has them synthesize the central dogma concept and protein folding through a labeled illustration.

The goal of the two scaffolding lessons was to guide students through an initial tutorial on using the program, with the inclusion of some content knowledge being gained along the way. If students already possess some knowledge and skills around the use of CMP's and where to find protein sequence codes, the lesson could easily be adapted to an inquiry base. While lesson one and two are not truly open ended, they do have some element of inquiry. Students are using a science tool to investigate a protein in a way a biomolecular scientist might in their efforts to identify potential drugs for further study.

Both the Protein Data Bank and PymOL are often used elements in research and design of drugs. By using CMP's to predict ligand affinity with active sites bioengineers are saving valuable lab time. Also, throughout the lessons students are making observations and either explaining or predicting from these observation. The lesson could be modified to have students use the PyMOL program and PDB to answer a student generated hypothesis regarding the function of the channel protein related to its structure.

LESSON THREE

Lesson three is a project based lesson that synthesizes the knowledge introduced in the previous two lessons with a real world application. Students are given a ligand that interacts with HIV-1 protease and are asked to provide a report on how the ligand interferes with the HIV life cycle. This lesson is designed to be more student centered than the previous lessons but still has a high level of structured support. However, in this project based lesson, support is provided mostly in the form of project milestones. Students are required to submit specific artifacts to allow the instructor to monitor progress. The milestones also provide students with a reflective component of support as they are able to self monitor their progress. Milestones are indicated in bold in the project roadmap (Appendix D) and the artifact for each is designated in the road map as well. To aid in student self monitoring and assessment, the final presentation rubrics are organized around the milestones. The organization of the lesson around the milestones provides a built in mode of structural support as students can easily relate milestones to project artifacts and to assessment.

The lesson begins with an entry document (Appendix D) that places them in a real world type scenario. They are asked to provide a professional report using professional grade tools. As students progress through the unit they will have to rely on knowledge

and skills gained in the previous two lessons. Students will also have to use online sources to research current topics in bioengineering and drug discovery to supplement their work. Each successive milestone accomplished is an element that will be included in the final product. A template is provided for the power point presentation final product. All project documents should be maintained in an electronic folder that students have open access to.

Chapter 6: Conclusion

Although previous research suggests that computer visualization tools can lead to better learning outcomes for students, classroom implementation of these advanced instructional models has been limited. A major problem is the availability of hardware itself: not all classrooms have the hardware required for classroom implementation of advanced CMP's. Availability issues include computers that are not present at all, or are in insufficient numbers, or the computers do not include hardware and software capable of handling the large amount of processing involved in computational modeling. Most professional grade modeling programs, like PyMOL, require sufficient RAM and high-quality graphics cards for optimal performance. Another challenge to implementing visualization tools in the classroom is training and practice time required for operating the advanced programs. Teachers may not have sufficient time for training or they themselves may not have the technology to allow practice in using the programs. Also, in order to write curriculum based on these programs, educators would have to have knowledge and experience using the programs. The risk of going in the direction of novel, untested methods of teaching fundamental concepts to students is a risk many educators do not want to take in a standards-based environment.

In spite of the difficulties of implementing professional grade CMP's in secondary science curriculum, STEM educators need to increase the presence of these valuable tools in science classrooms. Doing so can improve student understanding of key biological structures and processes such as protein structure and interactions. Used in conjunction with other modernistic instructional methods, use of computational modeling can replace less effective means of modeling biological processes related to proteins. The

use of CMP's could easily be extended into other secondary science subjects, especially chemistry, and other biology related subjects. Not only does increased use of technology help in increasing student learning, it is also serves to enhance the technology skills required to succeed in modern industry and research. By emphasizing the use of professional grade modeling tools in secondary classrooms, educators can better guide students into and prepare them for careers in science and engineering.

Appendix A: Texas Essential Knowledge and Skills for the Included Instructional Unit

Science concept 4: The student knows that cells are the basic structures of all living things with specialized parts that perform specific functions and that viruses are different from cells. The student is expected to:

B. investigate and explain cellular processes, including homeostasis, energy conversions, transport of molecules, and synthesis of new molecules; and

C. compare the structures of viruses to cells, describe viral reproduction, and describe the role of viruses in causing diseases such as human immunodeficiency virus (HIV) and influenza

Science concept 5: The student knows how an organism grows and the importance of cell differentiation. The student is expected to:

A. describe the stages of the cell cycle, including deoxyribonucleic acid (DNA) replication and mitosis, and the importance of the cell cycle to the growth of organisms;

C. describe the roles of DNA, ribonucleic acid (RNA), and environmental factors in cell differentiation;

Science concept 6: The student knows the mechanisms of genetics, including the role of nucleic acids and the principles of Mendelian Genetics. The student is expected to:

A. identify components of DNA, and describe how information for specifying the traits of an organism is carried in the DNA;

B. recognize that components that make up the genetic code are common to all organisms;

C. explain the purpose and process of transcription and translation using models of DNA and RNA;

D. recognize that gene expression is a regulated process;

E. identify and illustrate changes in DNA and evaluate the significance of these changes;

Science concept 7: The student knows evolutionary theory is a scientific explanation for the unity and diversity of life. The student is expected to:

A. analyze and evaluate how evidence of common ancestry among groups is provided by the fossil record, biogeography, and homologies, including anatomical, molecular, and developmental;

G. analyze and evaluate scientific explanations concerning the complexity of the cell.

Science concept 9: The student knows the significance of various molecules involved in metabolic processes and energy conversions that occur in living organisms. The student is expected to:

A. compare the structures and functions of different types of biomolecules, including carbohydrates, lipids, proteins, and nucleic acids;

C. identify and investigate the role of enzymes;

Appendix B: Lesson One Student Activity Guide

Lesson One
Visualizing Proteins

In this lesson you will be using the PyMOL program located on your computer desktop. PyMOL is a computational modeling program that is used by practicing scientist to study the structure and function of proteins.

Answer the Guiding Questions (**GQ**), Discussion Questions (**DQ**), Reflection Questions (**RQ**), and Enrichment Questions (**ER**) in your science notebook as you move through this activity to help you with the following learning objectives:

- Understand what proteins are and describe some of their physiological functions
- Explain how proteins are comprised of smaller units and describe these monomers

I. PYMOL BASICS

Let's begin by looking at a protein structure using the PyMOL software.

Open the program

Notice the two screens. One is the viewer itself, this is where the pictures will be displayed once we load them, and the other is the external graphic user interface which supports command prompt input. The first activity is a tutorial on the basics of the program; be sure to connect the tasks in this activity with the overall use of the program: we will be using this program extensively during this learning unit.

Go to PyMolwiki.org > Tutorials (in the quick links window) > Practical Pymol for Beginners (http://www.pymolwiki.org/index.php/Practical_Pymol_for_Beginners) Read "The PyMol Interface" and then go through the steps of "Getting Started: explore a protein." (Hint: its "1BL8," not "1B18").

1 DQ. Rotate the protein till you get a view directly down its channel. Based on the symmetry of this protein, and the color coded chains, how many subunits, aka chains, make up this protein? Explain how you determined this from the illustration.

2 DQ. Imaging you had to describe the structure of this protein to someone over the phone; record your description below.

II. ADVANCED FEATURES OF PYMOL

Let's practice a little more with the user interface using 1bl8.

In the external GUI window, open Display and select "sequence." Note the change in the viewer window. This shows the one letter code for the sequence of the protein. You can change it from one letter code to amino acid abbreviation by selecting 'residues' in the sequence mode tab under Display control.

Return to the view of the protein down its channel make sure show surface or cartoon is off using the **H**ide button and you can see either lines, sticks, or both. Select one of the four Y shaped residues that are sticking out by themselves by clicking on it. You will notice a line appears in the selection slider display area indicating where in the sequence the residue is.

3 GQ. What is the name of this amino acid? (note: not the residue *code* but its *name*, you will have to use the Amino Acid Properties Chart in the project share folder to get the name from the three letter code).

4 GQ. What kind of amino acid is this? (polar, nonpolar, hydrophobic…)

5 DQ. Using the chart, what structural component do all the amino acids have in common? What physical properties provide variability in amino acid function?

Deselect the residues using the right side interface by selecting the **A**ction button next to (sele) and then *delete selection*.

6 GQ. There is one water molecule (HOH) shown in this protein structure, use the sequence tab to locate it and then explain its location.

III. CREATING AND SAVING IMAGES IN PYMOL

Now we will make a picture showing only one subunit of the 1bl8 protein and then save the image for export into another program.

Select the 1bl8 **A**ction button > *duplicate object*. Now you have another copy of the protein called obj01. Now go to Display > Sequence Mode > Chains and you will see the sequence as chains A, B, C, D for each individual protein unit. Click on one of the chains in the 1BL8 sequence to select that chain. Then go to the **A**ction button for the chain you just selected (sele) and select *remove atoms*. Now select the B,C,D chains for the obj01 protein unit and remove those atoms. Use a different **S**how mode for both the three chained 1BL8 and the one chain of obj01 to highlight the single protein chain.

Once you have the objects properly illustrated and lined up for a good view, add a white background by going to the Display > Background menu in the GUI. Then have the program render a higher quality illustration by clicking the Ray button in the External GUI. Once you get a good image, save the image through the File menu so it can be included in the portfolio for this unit.

IV. Protein Structure and Function

Lastly, let's see what the function of this protein is.

Go to the PDB.org website to help answer the following questions about "1bl8"

> **7 DQ**. In your own words, what is the general function of this protein?
>
> **8 GQ**. How many residues make up each chain? The total protein?
>
> **9 GQ**. What is the name of the secondary protein structure between residues 27 and 51?
>
> **10 GQ**. Confirm the structure is the same in the PyMOL viewer. By sure to have Show cartoon selected. Draw the way the structure looks in the PyMOL viewer. What would you call this shape?
>
> **11 GQ**. What is the name of the secondary protein structure between residues 113 and 115?

12 DQ. Confirm the same structural feature can be seen in the PyMOL viewer. Remember there are four chains, select the structure on all four chains and then describe the location of the active sight as related to its location on the protein. Provide an illustration to back up your description.

13 GQ. What is the name of the secondary protein structure between residues 75and 79?

14 RQ . What are the steps you would take to view a protein's structure on a modeling program like PyMOL If the only information you had to start with was the proteins name?

15 ER. How do you think professional scientists use bimolecular modeling programs like PyMOL to aid them in their work?

Appendix C: Lesson Two Student Activity Guide

Lesson Two

Building a protein: Visualizing Protein Synthesis Using a Computational Modeling Program

Answer the Guiding Questions (**GQ**), Discussion Questions (**DQ**), Reflection Questions (**RQ**), and Enrichment Questions (**ER**) in your science notebook as you move through this activity to help you with the following learning objective:

Explain the purpose and process of transcription and translation using models of DNA and RNA

I. BUILD A PROTEIN

We are going to build a protein using the PyMOL program. The program has a Builder feature that allows the user to drag and drop Amino Acids into the Viewer. The viewer automatically links the Amino Acids with the correct chemical bond. The information we need to build our protein is coded in DNA. Proteins can only be built in the cytoplasm (the environment outside the nucleus) and DNA never leaves the nucleus. We need to first make a copy of the DNA, called an RNA which can leave the nucleus, so we can get the code for making proteins to the ribosome (site of protein synthesis) in the cytoplasm to build our protein.

Protein Primary Structure: from DNA to Protein

---

1 RQ. Define the primary structure of a protein in your own words.

2 GQ. Define transcription; include an analogy of your own.

Transcription: from DNA to RNA code for our protein

On the attached document "Genetic and Structural Characteristics of HIV-1 Protease" you will find the DNA sequence for the 'TRP-cage' protein. Transcribe the DNA sequence to the mRNA sequence in the space provided.

Translation: from RNA to Poly peptide

> **3 GQ**. Define translation; include an analogy of your own.
>
> In the space provided, use the Amino Acid Code Chart in the share folder to translate the mRNA sequence into an amino acid chain, a polypeptide, using single letter code. Afterwards name the amino acids in the chain.
>
> **4 RQ.** Combine your analogies to include the entire process of protein synthesis from DNA to polypeptide.

Protein Primary Structure: Modeling Primary Structure

Tip: save your work often during this activity!

Open the PyMol Program. Click the builder tab in the far right of the External GUI. You are now in builder mode which will allow you to assemble models of biomolecules. Click the Protein tab in the Builder GUI. Now you can drag and drop the amino acids to illustrate the protein chain for TRP-cage.

Click the first amino acid in our chain, Asn. Then in the right viewer panel select 'create as new object' and Asparagine appears in the viewer with the normal attachment location highlighted by the spherical curser. Click the next amino acid in the builder GUI to add it to the sequence. Continue for all 20 amino acids. By right clicking in the open in the viewer window and selecting 'orient (vis)' will reorient the view of the molecule so you can see it in entirety. If you mess up in builder mode, it is usually easiest to just start over or reopen your saved work.

5 EQ. PyMOL automatically links the amino acids for use. During protein synthesis in cells, the same chemical reaction occurs for every combination of amino acid. What does this imply about where the reaction is occurring based on what you learned about amino acids in lesson one. If you need help, check out this interactive video: http://www.wisc-online.com/objects/ViewObject.aspx?ID=BIC007. Include a labeled illustration of the reaction.

Once you have assembled your polypeptide, go back to Command Mode (click command in the right panel of the External GUI) and display the sequence of the residues (refer to 1st tutorial if you need help with this). Use the sequence to double check your chain has the correct 20 amino acids in the correct order. Use **L**abel > residues to add labels to your polypeptide chain, change the background to white, then clean up and save the image as in the last lesson and submit it along with the other deliverables from this activity.

II. PROTEIN SECONDARY, TERTIARY, AND QUATERNARY STRUCTURES

Immediately following translation, proteins fold up on themselves into what is called their secondary and tertiary structures. Watch this video before moving on:
http://www.dnatube.com/video/2127/Structure-of-protein
To see secondary and tertiary structures of our TRP-cage, use PDB code 1L2Y in the PyMOL viewer.

6 GQ. Describe the secondary structures found in the TRP-cage protein

7 GQ. Describe the tertiary structure of TRP-cage protein.

8 RQ. Define what is meant by primary, secondary, tertiary, and quaternary structure of proteins and provide references to TRP-cage as examples.

9 DQ. Look closely at the structure of TRP-cage, why do you think it is named like this?

10 RQ. Use PDB to find a protein we have not looked at yet and describe its structural characteristics.

11 ER. Create a labeled illustration that explains the processes occurring during protein synthesis; include the following elements: transcription, translation, primary, secondary, tertiary and quaternary structures, nucleus, cytoplasm, ribosome, DNA, tRNA, rRNA, mRNA, amino acid, codon, polypeptide, primary-secondary-tertiary-quaternary structure.

Attachment: Genetic and Structural Characteristics of HIV-1 Protease

TRANSCRIPTION

DNA Sequence:

GTAAACCTGTATATTCAGTGGTTGGAACAGGGGGGTACCTGACGACGGGGAACCCCCACCACTAAT

mRNA Sequence:

_____

_____

TRANSLATION

Amino Acids Reside Code (single Letter Code):

___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

___ ___

Amino Acid Name:

_____ _____ _____ _____

_____ _____ _____ _____

_____ _____ _____ _____

_____ _____ _____ _____

_____ _____ _____ _____

_____ _____

Appendix D: Project Resources

This appendices contains the following documents, in this order, to aid in the implementation of the project based instructional unit discussed in this report:

1. Teacher Notes and Resources
2. Project Roadmap
3. Entry Document
4. Ligand Codes
5. Active Site and Ligand Workshop
6. Scientific Content Rubric
7. Project Presentation Rubric

1. LESSON THREE TEACHER NOTES AND RESOURCES

Introduction: Video addressing HIV/Drug Discovery

Introduce project. Go over unit objectives and standards. Play video followed by class discussion on HIV/AIDS and the role of proteins.

http://www.youtube.com/watch?v=RO8MP3wMvqg

Assign groups, have students get into groups and hand out entry document

Entry Document

Read in groups and annotate

Document Highlights:

- Provide info for lab: RNA Code for protein
- Identify ligands and interaction sites
- Identify and describe/illustrate drug that can interact with HIV-1 Protease
- Product Facts: explanation of final product – Provide a report that includes the following

37

- A summary the role HIV-1 Protease plays in AIDS, this includes:
  - A discussion of how HIV replicates itself
  - The role of Proteases in HIV life cycle
  - How HIV enters human cells
- The RNA sequence for one of the proteins in the HIV-1 Protease dimmer
- PyMOL Image(s) of your ligand in the active site
- Written description of the interactions at the binding site
- Discussion of how your ligand can interfere with HIV replication

Knows and Need to Knows

Have groups write down everything they know about the project from the document. Afterwards, combine all the knows in a list during a class discussion; combined list should be projected or written for entire class to see. Repeat for the need to knows. Discuss responsibilities of need to knows. Instructor should address need to knows that fall outside of students realm of acquiring. Some students will have more knows than the group and will have additional goals. Save completed form to use as a guide throughout the project.

Assignment of ligands and function of HIV-1 Protease

Assign each group a ligand from the Ligand Code list. Groups will research their assigned ligand and how it interferes with the viral life cycle. Completion and

submission of a report that meets the scientific content rubric's Function of HIV-1 Protease servers as the milestone for this section. Students should also submit a diagram of the HIV replication cycle.

Genetics/ Structural Information for HIV-1 Protease

Students will have to obtain the DNA sequence from the primary structure of HIV-1 protease obtainable from protein databases. Encourage groups to divide the sequence up between group members. Have students enter the correct sequence on the "official" DNA submission form. Completion of the submission form is the milestone for this section.

Active Site and Ligand

Interactions

Students use the PyMOL program to analyze their ligands interaction at the active site of HIV-1 Protease. Inform students of the Active Site and Ligand Workshop available in the share folder. Completion of this unit is marked by submission of the required image.

Drug Action

Students research further into the role of protein-ligand interactions associated with HIV/AIDS drug discovery. Students should cite current research in their discussion of the role of their assigned ligand in blocking viral replication. Students should also be encouraged to make inferences based on available information to predict drug action where applicable.

Final Product

A pwerpoint presentation serves as the final product for this unit. Students should be encouraged to synthesize all knowledge gained in this unit into the final product. A template for the ppt presentation is included in the share folder along with both a content and presentation rubric.

Resources

Proteins:

Protein Data Base (PDB): http://www.rcsb.org/pdb/home/home.do

HIV-PR with semiopen conformation of flaps (PDB ID *code* 1HHP).

Genes and Chromosomes:

Genetics Home Reference: http://ghr.nlm.nih.gov/

OMIN: http://omim.org/search?index=geneMap&search=107741

NCBI (DNA Sequence): http://www.ncbi.nlm.nih.gov/nuccore/NM_000041.2

2. COMPUTATIONAL MODELING OF PROTEINS PROJECT ROADMAP

Scaffolding Lessons
- Lesson One: Visualizing Proteins

- Lesson Two: Building Proteins

Project start
- Entry Document

- Entry Video

- Knows and Need to Knows

- Business   grouping, assignment of ligands, calendar, rubrics

Function of HIV-1 Protease
- Research assigned ligands and how they interfere with the viral life cycle

- Research current topics AIDS

- Product: Protein Structure – Function Summary (written explanation)

  Include secondary and tertiary structure
- Product: HIV replication diagrams

Genetics
- Determine the DNA sequence of HIV-1 Protease

- Product: DNA sequence submission form

Active Site and Ligand
- Identify and analyze ligand and active site of protein

- Product: Submission of image from active site and ligand walk through

Interactions
- Analyze and explain the interactions occurring at the active site

- Product: discussion questions from active site and ligand walk through

Drug Action

- Research how ligand actually works to interfere with HIV replication or apply knowledge of interactions at the binding site to infer the method of interference.

- Product: Peer and instructor evaluated writing

Final Product

- Peer and professional evaluated presentation; use presentation and scientific content rubrics for evaluation

3. ENTRY DOCUMENT

September 20, 2012

[Class Name]
Research Scientists
[School]
[**Street Address**]
[**City, ST ZIP Code**]

Dear Research Scientists:

Your group has been contracted to aid in the design of a new drug for the treatment of Human Immunodeficiency Virus (HIV). HIV destroys specific blood cells, called CD4+ T cells, which are a part of our immune system. Continued infection of the disease without treatment often leads to Acquired Immune Deficiency Syndrome (AIDS), a condition where the host's immune system is severely weakened. After many years and millions of dollars in research, there is still no cure for HIV/AIDS, only treatment. Approximately 50,000 Americans become infected with HIV each year and more than 619,000 people with AIDS in the U.S. have died since the epidemic began[1].

To satisfy your contract, your group will research how specific ligands interact with a component of the HIV infection system, HIV-1 Protease, and then present your findings to a review panel. The requirements for the presentation are listed below and we have included a video on the basics of HIV infection.

> A summary the role HIV-1 Protease plays in AIDS
>
> Structural descriptions of HIV-1 Protease
>
> Computer generated image(s) of your ligand in the active site
>
> Written description of the interactions at the binding site
>
> Discussion of how your ligand can interfere with HIV replication

More information will be presented to you as it becomes available. Please work diligently, discovery of a cure for HIV/AIDS will alleviate pain and suffering from millions of lives worldwide.

Bigbo Diddly
Director of Empire Pharmaceuticals

1. AIDS.Gov. Last modified June 6, 2012. Accessed July 7, 2012. http://aids.gov/ hiv-aids-basics/hiv-aids-101/statistics/.

4. LIGAND CODES

	PDB Code	Ligand Type	Ligand Code	Role	Atom Count
0	1ODW	NONE (Native HIV-1 Protease)			
1	1OHR	VIRACEPT (R) (NELFINAVIR MESYLATE	1UN	Inhibitor	44
2	3AID	AMINIMIDE PEPTIDE ISOSTERE	ARQ	Inhibitor	42
3	2AID	NON-PEPTIDE INHIBITOR	THK		29
4	1HXW	A-84538	RIT	Inhibitor	50
5	1WBM	SYMMETRIC INHIBITOR	BLL	Inhibitor	48
6	1WBK	ASYMMETRIC INHIBITOR	568	Inhibitor	45
7	1HSG	L-735,524,	MK1	Inhibitor	45
8	2BQV	AHA455	A1A	Inhibitor	43
9	1IIQ	HYDROXYETHYLAMINE PEPTIDOMIMETIC	0ZR	Inhibitor	51
10	3OXC	Saquinavir	ROC	Antiviral Drug	98
11	3NWX	KVS-1	KVS	Inhibitor	56
12	3NYG	MVT-101	2NC	Inhibitor	54
13	7HVP	HYDROXYETHYLAMINE	JG3	Inhibitor	28+
14	3S45	amprenavir	478	Antiviral Drug	35+

5. ACTIVE SITE AND LIGAND WORKSHOP

Active site and Ligand Interactions

HIV-Protease, like other proteases, binds specific proteins and cuts them into smaller pieces. The proteins have sequences that allow them to chemically "fit" into the active site of the protein. If a different molecule has similar characteristics to the one meant for that protein it can also fit into the active sight, we call molecules that exhibit interactions like this ligands. A ligand in an active site usually causes the protein to do something different than what it was meant to do. In the case of HIV-1Protease, a ligand in the binding sight will prevent viral proteins from being able to bind in the active sight and therefore no viral proteins can be cut and readied for new virus assembly.

In this activity you will use your PDB file to identify, illustrate and label a ligand bound in the active site of HIV-1 Protease.

Open PyMOL and in the command line of the External GUI type: fetch <your 4 digit PDB code here>

Then bring up the sequence code by going to Display > sequence
Remove the waters from the view by clicking **H**ide > waters.
Now go to **A**ction > preset > ligands.

The viewer now shows the protein chains in cartoon line form and the ligand in stick form. Notice it is in the center of the protein as we anticipated. Zoom into the active site by holding down the right mouse button and moving the mouse back and forth.

Zoom in until you can see the yellow dotted lines. These represent the bonds between the ligand atoms and the amino acid atoms in the protease.

Before going any further, create a duplicate of the protein-ligand complex by clicking **A**ction > duplicate object.

Find the ligand in the sequence display by left clicking on the ligand molecule in the image. Notice the ligand is now highlighted in the sequence display and a locater tab shows up in the slider bar line. Scroll to it using the slider bar.

De-select the ligand by left clicking on the number highlighted number in the sequence display. Select all the amino acids in the protein by left clicking on the last amino acid residue code next to the ligand code and then move the slider all the way back to first amino acid in the sequence and SHIFT left click.

Now zoom into the ligand and de-select all of the amino acids that are interacting with the ligand in the active site. When you have these de-selected, go to (sele) > **H**ide > everything. Now only the ligand and associated amino acids are displayed.

Remember to save your project frequently. Now you can clean up the image and add labels. One you are satisfied, save the image and turn it in along with the discussion questions below.

6. SCIENTIFIC CONTENT RUBRIC

SCIENTIFIC CONTENT RUBRIC

	Beginning 1	Developing 2	Accomplished 3	Exemplary 4	Score
Function of HIV-1 Protease	Does not explain the function of the protein or relate it to AIDS	Does not completely explain the function of the protein or attempt to relate it to AIDS	Explains the function of the protein in the viral replication cycle but does not relate to AIDS	Explains the function of the protein in the viral replication cycle and relates how HIV infection leads to AIDS	
Structural	Does not provide DNA or structural information for HIV-1 Protease	Missing either the DNA sequence or the 2° and 3° structure for HIV-1 Proteas	Provides incorrect DNA sequence or structural information for HIV-1 Protease	Provides the correct DNA sequence for HIV-1 And description of 2° and 3° structure	
Active Site and Ligand	No Image Provided of assigned ligand in the binding site	Provides only one image of assigned ligand in the active site that lacks any add-ons	Provides quality PyMOL generated image of relevant molecules and includes at least one of the following add-ons: labels, different structural representations and/or color schemes	Provides more than one quality PyMOL generated image of relevant molecules that includes labels, different structural representations and color schemes	

47

Interactions	Provides no information on relevant interactions occurring at the binding site	Provides only the image or written explanation of the interactions occurring at the binding site	Provides both an image and an explanation of the interactions occurring at the binding site	Provides both a labeled image and a written summary that thoroughly explain the interactions occurring at the binding site	
Drug Action	Does not explain how the ligand can interfere with HIV replication	Attempts to explain how ligand interferes with HIV replication but is incorrect or poorly presented	Adequately relates how the ligand interferes with viral replication	Provides a well thought out argument of how the ligand can interfere with HIV replication	

7. PROJECT PRESENTATION RUBRIC

SCIENTIFIC PRESENTATION RUBRIC

Title of Presentation _____   Authors' names:

_____

_____

_____

_____

	Beginning 1	Developing 2	Accomplished 3	Exemplary 4	Score
Opening	Does not give any information about what to expect in the report.	Lacking a Title Page or Abstract. Title/Abstract provides little information.	Complete Title Page and Abstract	Complete Title Page and Abstract that is expertly written.	
Introduction	Does not provide a complete summary and/or problem statement	Provides some idea of the author's work but lacks structure/enough information. Problem statement not easily recognizable and/or poorly worded	Provides a summary of the author's work and includes an applicable problem statement	Thoroughly summarizes the author's work and includes a well written problem statement.	
Methodology	Poorly structured and/or does not adequately relate	Provides only some idea of how the author's went about obtaining their information	Organized explanation of how the author's went about obtaining their	Professional and well organized methodology	

	procedures used	and/or lacks structure	information		
Results And Discussion	Missing a majority of the information required to complete contract	Includes most, but not all information required in the contract	Includes all relevant information in the contract	Includes well designed discussion of all relevant information in the contract. Includes use of both graphical and written information	

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