



NSF Engineering Research Center

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Title

Building and Modeling of molecular biomolecules & biosystems.

Overview

Using structure prediction, molecular building software, and molecular docking, we will explore the physical and functional capabilities of biomolecules. Students will explore nucleic acids, protein structures, and binding to demonstrate the intermolecular interactions that occur in the body and build environments. This will aid students in visualizing the development process and small scale interactions that occur experimentally.

Key Search Words

Biology, K10+, Genetics, Molecular Biology, Modeling, Polypeptide, Computational biology, Ligand, Receptor, Visualization, Microbe, Pathogen, Molecular Building, Molecular Docking, Nucleic, AntiMicrobial Peptide*

Learning Objectives

- [LS.Bio.1.1] Students will correctly identify and describe characteristics of molecular biomolecules with the use of technological resources and tools.

- [LS.Bio.1.5] Students will demonstrate mastery of central dogma processes within a biological system and use computational skills to build, manipulate, and illustrate molecular biomolecules & biosystems.
- [LS.Bio.1.2] Students will use computational skills to illustrate how antimicrobial peptides interact with other microbes during intermolecular processes.

Curriculum Alignment

From the North Carolina Standard Course of Study K12 Science, Biology (NCDPI, 2024):

- “LS.Bio.1.1 Construct an explanation to illustrate relationships between structure and function of major macromolecules essential for life.”
- “LS.Bio.1.5 Construct an explanation to summarize how DNA and RNA direct the synthesis of proteins.”
- “LS.Bio.1.2 Carry out investigations to illustrate how enzymes act as catalysts for biochemical reactions and how environmental factors affect enzyme activity”

Classroom time required

About 2-3 consecutive class periods. Below is designed for a block schedule; however, times allotted for each activity can be adjusted as needed.

First Block Period (1 hr 30 min)

- Activity 1: Identifying and Describing Characteristics of a Protein **[30 min]**
 - rcsb.org databank tools & resource overview [10-15 min]
 - Student practice [10-15 min]
- Activity 2: Protein Building using Computational Skills **[40 min]**
 - pymol.org website and tools overview [15-20 min]
 - Student practice [15-20 min]
- Assessment of Understanding **[20 min]**

Second Block Period (1 hr 30 min)

- Review of Assessment Activity **[15-20 min]**
- Enzyme/Substrate Review **[10 min]**
- Activity 3: Molecular Docking **[25 min]**
 - Teacher-led software overview [10-15 min]
 - Student practice [10 min]
- Assessment of Understanding **[35 min]**

Materials & Technology

- Laptop - one computer per student or one computer per small group of no more than 4 students
 - Rcsb website, cabsdock website, PyMOL software
- WiFi
- FlashDrive- one per student or one per small group
- HardDrive (teacher)
- Canvas access
- 3 button mouse

Safety

There are no safety issues to be aware of or consider when conducting this activity.

Teacher Preparation for Activity

Teacher should ensure that supplemental videos, exemplar pdb downloads, canvas uploads, pyMOL app installation, resources, and articles are in place for students to access prior to, during, or after activities that will aid in recalling computational skills and real-world biomolecule/peptide applications.

Student Preparation for Activity

Required: students should have the pyMOL app installed on their computer.

Not required, but recommended that students should use resources, canvas uploads, class notes, and videos provided by the teacher to have an understanding of what they will be asked to explore during lesson.

Procedure

Day 1

- Activity 1: Identifying and Describing Characteristics of a Protein
 - rcsb.org databank tools & resource overview
 - Teacher should instruct students to open the rcsb.org databank website on their laptops and to follow along features of the website (i.e. how to search a protein, how to view the structure, where to locate characteristics of the given protein, and how to download and save the protein structure to their computers & flash drive as a pdb)

****In the event that a student does not have a laptop or has not downloaded the app, pair them with another student and have them follow along.****

- Teacher should select one specific protein for students to search and model to students the features of the website– things such as how to search the protein, how to view the structure, where to locate characteristics of the given protein, how to highlight the DNA/Amino Acid sequence of the protein, and how to download the protein structure to their computers & flash drive as a pdb.
- Student practice
 - Teacher should place students in small groups (no more than 4)
 - Teacher should instruct students in their small groups to explore databank, selecting any protein of their choice, and engage in group discussion of characteristics and things they notice about the given protein (i.e. students should consider the structure, species, nomenclatures, etc.)
 - Teacher should assess students' understanding of computational skills and ability to correctly identify and describe given protein by asking students to download their chosen protein and upload as a canvas assignment; the submission should include not only the

protein download but also a 4-7 sentence description of the protein (can be in the format of a paragraph or bullet points)

****Teacher should be monitoring student progression throughout the activity and providing assistance when needed.****

- Activity 2: Protein Building using Computational Skills
 - pymol.org website and tools overview
 - Teacher should instruct students to open the PyMOL app that they should have already downloaded on their laptops.
 - Teacher should instruct students to recall the protein we first identified and downloaded from activity 1 collectively as a class. Teacher will ask students to follow along and model to students how to open and upload the molecule in the pyMOL app.
 - Once the molecule is uploaded, teacher will guide students through mouse controls, tools, and features of the website– such features include different viewing of the structure, highlighting different parts of the structure in a variety of colors, building a protein by adding sequence bases/amino acids, highlighting parts of a sequence, using command line building tool, and how to modify and/or mutate a sequence.
 - Student practice
 - Teacher will place students back in small groups and instruct them to use the computational skills just learned to import the molecule they independently chose from Activity 1 and play around with the learned tools/features.

**** Students are not required to submit anything for this activity. However, if the teacher would like to assess their computational skills, students could be asked to submit this as an extra credit assignment on canvas. Submission should include a snapshot of the uploaded structure and a brief description of the features/tools used in their models.****

- Assessment of Understanding
 - Teacher should instruct students to take out a sheet of paper to show work and open the PyMOL app for this assessment.
 - Teacher will display a DNA sequence on the board, along with a codon chart, and instruct students to use the given DNA sequence to build the protein in the PyMOL software. Teacher should advise students to recall

their knowledge of the central dogma as they work through building the protein.

- Once protein is built, students should implement at least one feature/tool in the pyMOL software to their model. Students will need to explain what tool they decided to use and how it affected the view/structure of their molecule.
- Upon completion, students will take a snapshot of completed structure, including the associated DNA & amino acid sequence, and upload their models and explanations into canvas.

****For extra credit, students can also upload their work, detailing the central dogma process of converting the DNA into a protein****

Day 2

- Review of Assessment Activity
 - Teacher will review the “assessment of understanding” activity from the previous day with students by cold calling students to guide discussion on steps of the central dogma completion, then model how this could have been inputted into the software.
 - Teacher should allow students to follow along on their laptops and in their notes and address common mistakes or misconceptions he/she noticed.
- Enzyme/Substrate Review
 - Teacher should engage in “brain dump” activity with students, allowing them to dump information they remember regarding enzyme and substrate activity within small groups. Students will share responses with the class.
- Activity 3: Molecular Docking
 - Docking Overview
 - Teacher will instruct students to go to cabsdock website
 - Teacher will show students a short video describing the cabsdock process
 - https://youtu.be/EOqRF-JOTFg?si=y-BpvtMI_eBPpMoV
(Cabsdock, 2015)
 - Teacher will utilize a completed docking run to show examples of results.
 - Student practice
 - Teacher will place students back in small groups and instruct them to use the computational skills just learned to demonstrate and analyze binding activities of a ligand and substrate

- **Assessment of Understanding**
 - Teacher will place students in small groups (no more than 4) and assign a specific DNA sequence to each group (similar to activity 2). Within their groups, they will need to use their knowledge of the central dogma processes to help them identify and determine their assigned peptide.
 - Students should use the “rcsb” website and pyMOL software to visualize and demonstrate what this peptide should look like. Students will screen capture this model to upload later as a part of their submission.
 - Upon completion, students will then be tasked with using the cabsdock software to demonstrate ligand/receptor binding combinations of their assigned peptide, and determine the best combination using the “scoring” tool
 - Once determined, students will work together in small groups to create a 2-3 paragraph explaining their computational analysis processes and understanding.
 - Students will be asked to submit their work via canvas, including their explanation paper and screenshots of their models, sequences, and work throughout.

****OPTIONAL: Upon teacher discretion, he/she could require students to present work as a group for a “project” grade.****

Differentiation

- **Learning deficit accommodations:**
 - Day 1: as it pertains to day 1 assessment, depending on their level of deficiency, the teacher could accommodate students by providing the RNA OR amino acid sequence instead of the DNA for students to use in building their protein. By doing this, students are not required to perform the central dogma process from the very beginning; instead, they would be expected to convert the RNA to amino acids or simply use the given amino acid sequence to build the protein. Students could also be allowed to use notes to recall the steps of “protein synthesis.”
 - Day 2: as it pertains to day 2 docking assessment, students with learning deficits could be accommodated by requiring them to only show one possible binding combination and explain this in simple comparison of how enzymes bind with substrates.

- Other useful accommodations would be to allow these students to work in small groups, providing paragraph frames and/or sentence starters to aid their explanations, providing a graphic organizer or other visual that lists and describes vocabulary associated with the content that may be difficult for students to recall, and to make it optional for them to use at least one software tool in their model.

- **English Language learner accommodations:**
 - Day 1: as it pertains to day 1 assessment, to accommodate these students, the teacher could provide them with a visual of the RNA sequence already divided into codon sets OR a visual of the amino acid sequence to use when building the protein instead of requiring them to start from DNA. Another consideration could be to require them to use color-coding within their models (i.e. making the Adenine in the structure green, Thymine blue, color-coding the ligand from the receptor, etc.)
 - Day 2: as it pertains to day 2 docking assessment, students could be required to show only one binding combination using specific colors, such as making the ligand blue and the receptor pink, using these references within their explanations.
 - Other useful accommodations would be to allow them to work in small groups, use of notes, providing paragraph frames and/or sentence starters to aid their explanations, and providing a graphic organizer or other visuals that lists and describes vocabulary associated with the content that may be difficult for students to recall.

- **Advanced learners:**
 - Day 1: as it pertains to the day 1 assessment, to challenge these students, teacher could require them to not only build their molecule using the provided DNA sequence, but to also use specific tools such as selecting/highlighting the last 10 amino acids within the protein sequence or requiring them to perform a specific mutation within the sequence at a certain point and highlight the changes in the structure to include with their submissions. Students could also be challenged to create an explanation as to how this change in sequence or structure of the molecule could potentially affect an organism.

- Day 2: as it pertains to the day 2 docking assessment, the teacher could require students to consider and explain how their assigned peptide can be applied medically.

Assessment/Check for Understanding

- Activity 1 Submission: This submission would allow the teacher to assess student's computational skills of using a databank and allows the teacher to assess student ability to correctly identify and describe biomolecules, specifically proteins. The teacher should look for correct nomenclature of molecule, detailed description of structure, and any other things they notice regarding the molecule.
- Activity 2 Submission (optional): This submission would allow the teacher to assess the student's computational skills of importing, viewing, and manipulating molecules.
- Assessment Activity (day 1 & 2): These submissions (and possible presentation) will allow the teacher to not only assess student's overall computational skills of the software being used, but also assess student mastery of NC standards pertaining to the central dogma and intermolecular processes. Successful completion of this assessment requires students to recall and practice learned information of DNA, RNA, the intermolecular processes involved with protein expression, and enzymatic activity.
- The accommodation in place for advanced learners takes the assessment a step further as the teacher is also able to assess student mastery of other NC standards as it pertains to mutations, genetics, and intermolecular interactions such as enzyme/substrate binding.

Required resources

- Protein Data Bank
 - www.rcsb.org
 - This is the website that students will use to explore, identify, and describe proteins, DNA, and microbial structures.
- Molecular Visualization App

- www.pymol.org
- This is the software that students will use to visualize, build, and manipulate proteins, DNA, and microbial structures.
- Cabsdock
 - <https://biocomp.chem.uw.edu.pl/CABSdock/>
 - This is the software that students will use to visualize and analyze possible binding combinations between peptides and substrates.

Supplemental resources

See attachments for articles and guide.

- Practical Pymol for Beginners
- Cabsdock video embedded in lecture
 - https://youtu.be/EOqRF-JOTFg?si=y-BpvtMI_eBPpMoV

Sources

- Kurcinski, M.; Jamroz, M.; Blaszczyk, M.; Kolinski, A.; Kmiecik, S., “CABS-dock web server for the flexible docking of peptides to proteins without prior knowledge of the binding site.” *Nucleic Acids Res* 2015, 43, (W1), W419-24.
https://youtu.be/EOqRF-JOTFg?si=y-BpvtMI_eBPpMoV
- NC State Board of Education “NC Standard course of study K12 Science, Biology” (2024) Department of Public Instruction, chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/<https://www.dpi.nc.gov/documents/cte/curriculum/science/biology-standards/open>

Appendices

See attachments for articles.

- Antimicrobial Peptides: An Emerging Category of Therapeutic Agents
- Antimicrobial Peptides: Classification, Design, Application and Research Progress in Multiple Fields
- Molecular Docking: Approaches, Types, Applications and Basic Challenges
- Modeling peptide–protein complexes: docking, simulations and machine learning

