



Marine Biotechnology and Bioinformatics

for Teachers

CN3D – Human Hemoglobin vs. Sickle Cell Hemoglobin



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Introduction/Background/Context

Students will be introduced to the bioinformatics tool CN3D. CN3D is a software program that allows researchers to visualize biomolecular structures, sequences and alignments. It is often used to view and compare protein structures.

We currently know the amino acid sequences of approximately 875,000 proteins and the three-dimensional structure of only about 7,000 proteins (Campbell & Reece, 2005). After introducing students to protein structure and function, transcription, translation, and genetics (including discussion of proteins involved in genetic disorders), the opportunity to view proteins, and dysfunctional proteins will enable students to connect structure with function by visualizing changes in the three-dimensional structure of the protein.

This bioinformatics activity is designed for use by 9-14 biology students.

This bioinformatics activity fulfills the following California State Standards:

- Cell Biology**
- 3.A. Students know the overall design of molecular biology involves the flow of information from transcription of chromosomal DNA to the synthesis of translation of proteins in the cytoplasm.
- Genetics**
- 4A. Students know how mutations in the DNA sequence of a gene may or may not affect the expression of the gene or the sequence of amino acids in an encoded protein.
 - 4a. Students know spatial location of cells in and outside organisms is usually due to differential patterns of gene expression rather than to differences of the gene itself.
 - 4a. Students know proteins are different from one another in the number and sequence of amino acids.
- Investigation & Experimentation**
- 4.a. Select and use appropriate tools and technology, such as computer-linked probes, spreadsheets, and modeling software) to perform tests, collect data, analyze relationships, and display data.
 - 5.a. Investigate a science-based societal issue by searching the literature, analyzing data, and communicating the findings. Examples of issues include evaluation of food, cloning of animals by somatic cell nuclear transfer, choice of energy sources, and land and water use decisions in California.

STEM Connection
Bioinformatics researchers, crystallographers, and biomedical engineers would use this technology.

Instructional Goals

- The goals of this lesson are:
1. For students to become aware of the wealth of biological information available on-line that can be studied and researched.
 2. For students to see the structural differences in proteins that can lead to disease states as well as being able to manipulate the proteins themselves.
 3. For students to become excited about the possibilities for future study.
 4. For students to make observations and draw their own conclusions.

Learning Objectives

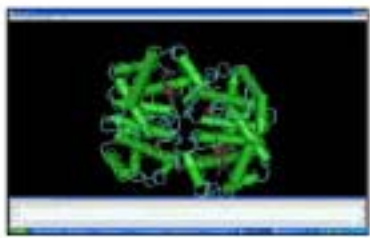
- Upon completion of this lesson, students will be able to:
1. Compare protein sequences to determine amino acid changes that cause disease states.
 2. Use the CN3D program at a basic level.

Method

- Materials/Resources**
- In order to complete this lesson, the following materials are needed:
- A computer with internet connection for every student or pair of students
 - CN3D software preloaded from the following website: <http://www.ncbi.nlm.nih.gov/Structure/cn3d/cn3d.html>
 - CN3D activity worksheet



Students log onto website for downloading the CN3D software. A double-click icon for CN3D will start firing up the software.



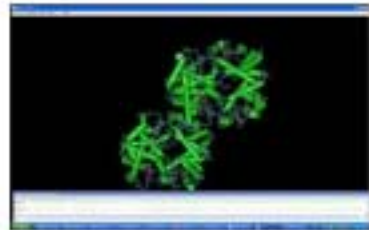
The protein structure and sequence for the deoxygenated form of normal human hemoglobin.

Method cont.

- Procedure for Lesson**
1. Students will log on to www.ncbi.nlm.nih.gov and search the database for normal human hemoglobin. They will view the hemoglobin structure.
 2. While viewing the structure they will change menu options in Style. Rendering shortcuts. Changes in these styles will allow students to view the protein structures in various styles, some emphasizing overall structure, others emphasizing individual atoms, and still others emphasizing conserved domains.
 3. Next, students will load and view the human sickle cell hemoglobin protein.
 4. Students will compare the amino acid sequences of the two hemoglobin proteins, using this information to find these differences in the proteins and relate these to the two different protein structures they are viewing.
 5. Finally students will view additional disease-causing proteins that they have previously researched.



Elizabeth, Leah, Matthew, Jonathan, and Art Thompson viewing the hemoglobin proteins using CN3D software.



The protein structure and sequence for the deoxygenated form of sickle cell hemoglobin.

Results/Learning Outcomes

- Student comments on what they learned:
- "I was interested in seeing the four different molecules under the color. It is interesting how each hemoglobin is made of two of one polypeptide and two of another. The three dimensional image is so complex!"
Elizabeth, 12th grade
 - "I think that this website is amazing and it makes me want to learn more about proteins so I can have a better understanding and be able to use this website to a fuller extent."
Kelsey, 12th grade
 - "Seeing the aligned domains where oxygen actually attaches to the hemoglobin is pretty cool."
Matt, 12th grade
 - "One little change in the amino acid sequence can distort the whole protein."
Melissa, 12th grade

Conclusion/Lessons Learned

Students were excited about what they learned in this lesson. I was interested in the different responses. Although all students in this class are highly motivated, some of the students who tend to have lower test scores made the most significant observations concerning changes in protein structure from normal hemoglobin to sickle cell hemoglobin.

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