Molecular Case Studies

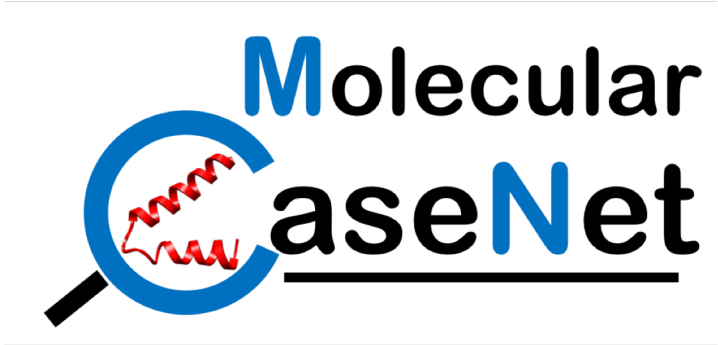
From Data to Data Science (QUBES Summer Workshop 2019)

William and Mary , Williamsburg VA

July 15 2019

Overview

- Introductions
- Case Studies
- Molecular Case Studies
- Nicholas' Story
- An Invitation



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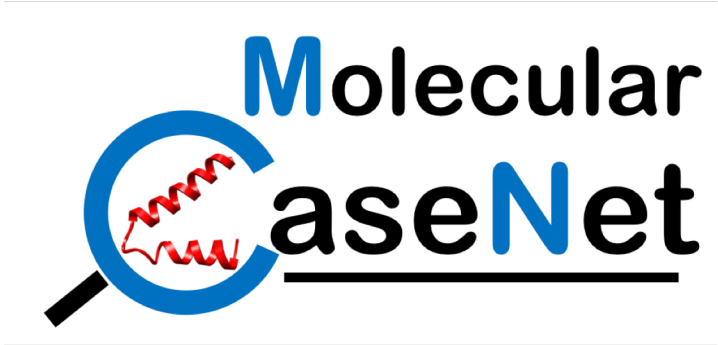

Getting to Know You

- Take a moment to think about your favorite protein molecule to teach about. (1 minute)
- Turn to your neighbor and introduce yourself (1 min each). Tell them about
  - what course (s) you teach or would like to teach and
  - and your favorite molecule!
- At the end of these three minutes you will introduce your neighbor and his/her favorite protein (1 min each)

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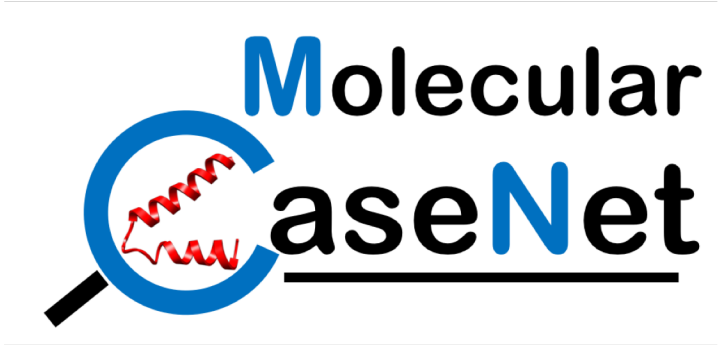
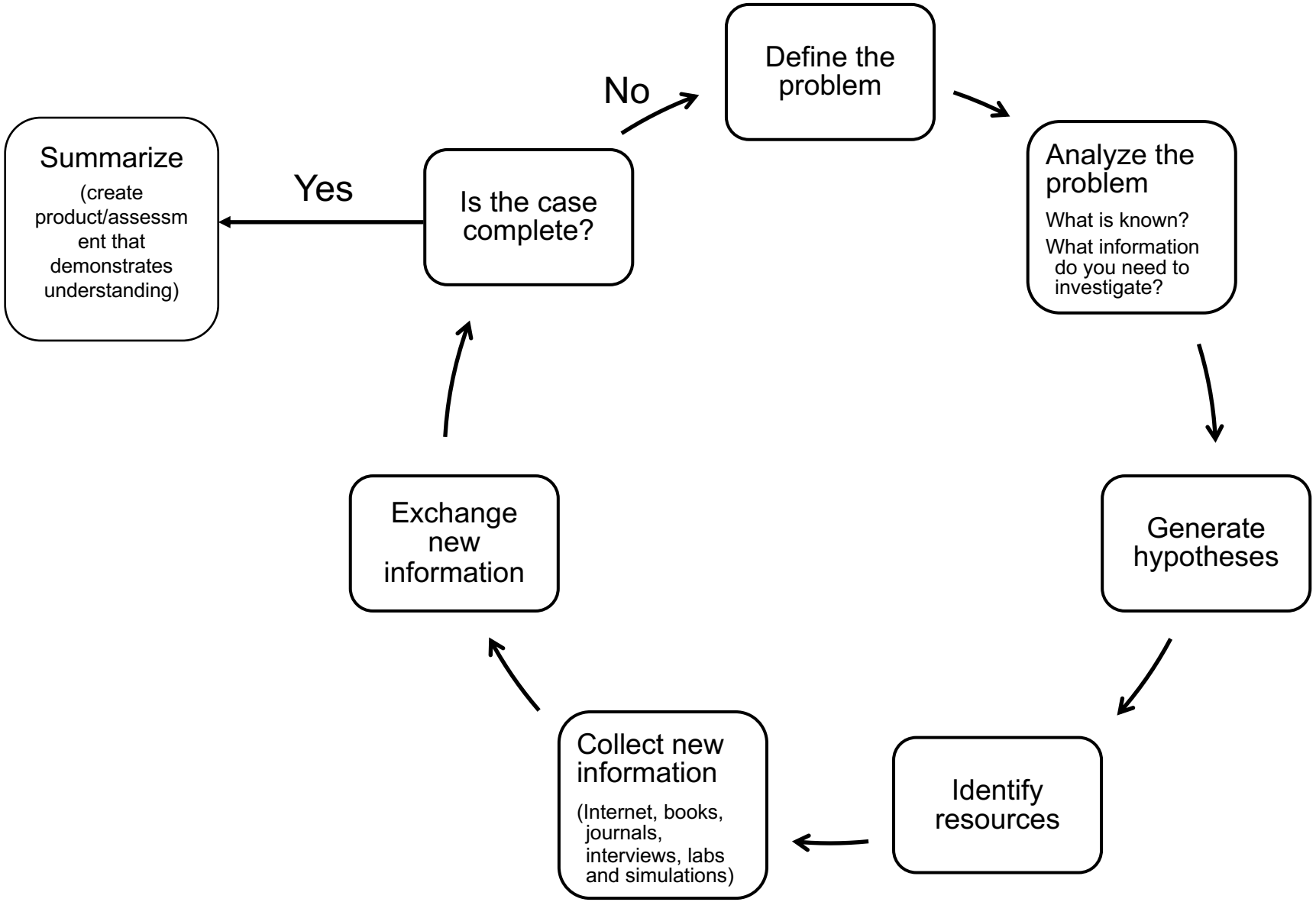


Learning with Case Studies

- It starts with a story….. based on complex, real-world situations

Students	**Instructors**	**Learning**	**Case Type**	**Benefits**
work in groups	act as facilitators	Instructor-directed	Launch new learning	• Motivate students • Deeper learning • Increases retention • Persistence in the disciplines
gain new information through self-directed learning	function as learning experiences designers	Self-directed, active, integrated, cumulative, and connected	Application of concepts learned	• Critical analysis • Observation • Computation • Written and oral communication • Logic • Decision-making


Define the problem
Analyze the problem
What is known?
What information do you need to investigate?
Generate hypotheses
Identify resources
Collect new information
(Internet, books, journals, interviews, labs and simulations)
Exchange new information
Is the case complete?
No
Yes
Summarize
(create product/assessment that demonstrates understanding)

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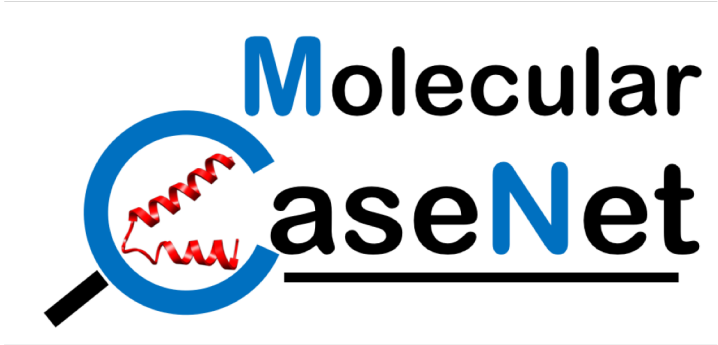


NSF DBI-1827011 Project Goal and Objectives

Goal: To assemble a new network (Molecular CaseNet); for developing case studies at the interface of biology and chemistry, discussed at a molecular level, and in atomic detail; and engaging educators in using them for biology, chemistry, and biochemistry education at the undergraduate level.

Proposed Objectives	RCN-UBE Proposal Focus
1. Determine case study topics and format	Active- and inquiry-based learning
2. Develop model case-studies, with input from diverse participants to ensure curricular relevance	Incorporating emerging sub-disciplines (e.g., bioinformatics, proteomics, and spatial reasoning) into biology curriculum
3. Share model cases to recruit new members to the network	Strategies for engaging biology (and chemistry) faculty in professional development activities

Invitation: To become a part of the next phase of the NSF project to develop and test molecular case studies

Molecular CaseNet Steering Committee



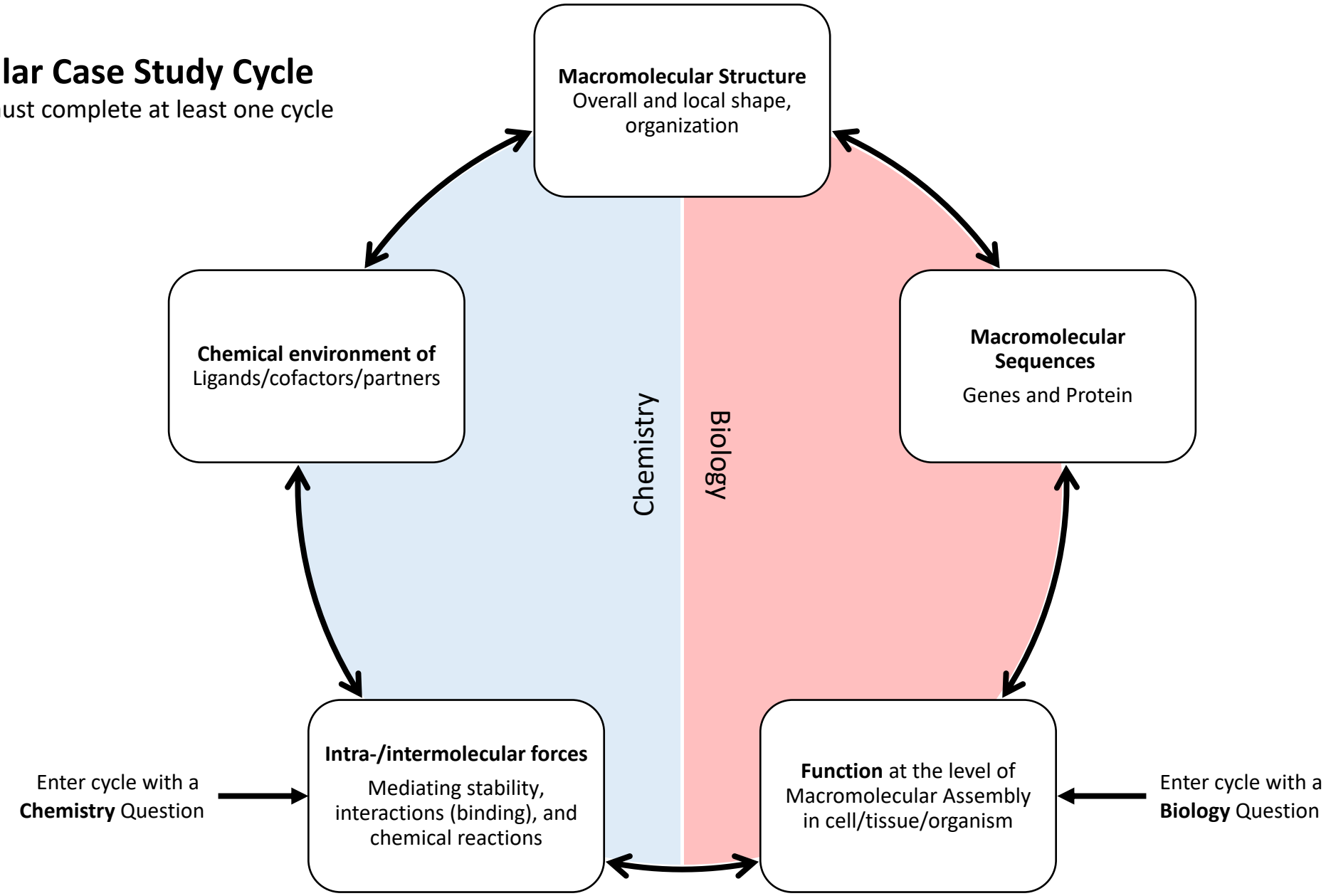




Name	Kimberly Cortes	Shuchismita Dutta	Henry Jakubowski	Melanie Lenahan	David Marcey	Patricia Marsteller	Cassidy R. Terrell
Affiliation	Kennesaw State University, GA	Rutgers University, NJ	College of Saint Benedict, St John's University, MN	Raritan Valley Community College, NJ	California Lutheran University, CA	Emory College of Arts and Sciences, GA	University of Minnesota, Rochester, MN
Expertise	Developing, incorporating, and assessing the impact of active learning modeling activities	Using PDB data/ tools/ resources to promote a structural view of biology in biology and chemistry education	Using molecular modeling and active learning in blended classes in chemistry & biochemistry	Biology, genetics, cell biology, and molecular biology education in a Community college	Creating web-based macromolecular visualization exhibits (using JSmol)	Developing case studies and case networks	Developing and assessing 3D virtual and physical modeling activities for biochemistry education

Molecular Case Study Cycle

All cases must complete at least one cycle



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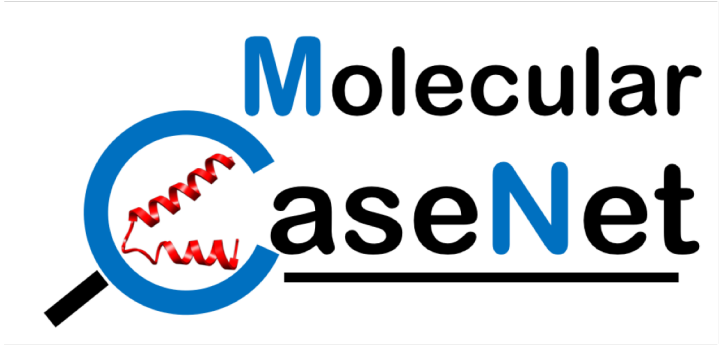


Caution! Immersion coming

- https://www.youtube.com/watch?v=iKQmQHh4E2w

Considerations in Case Development

Your Thoughts?

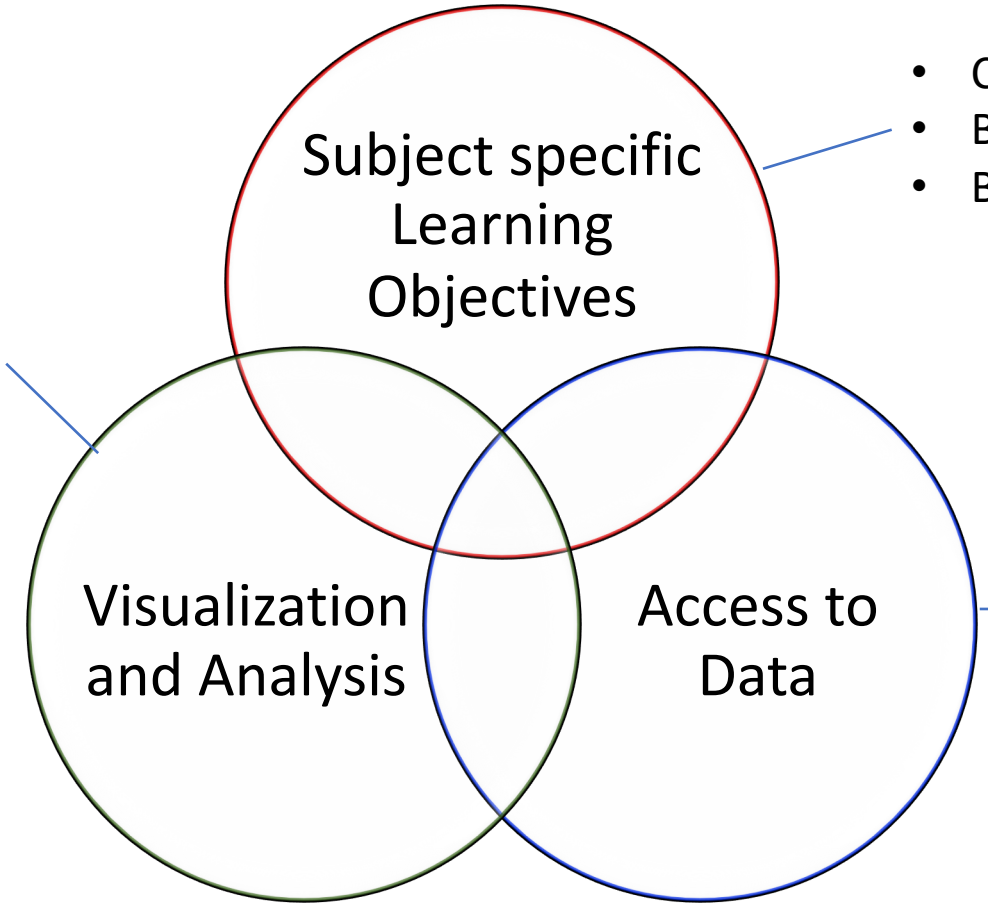
- What do you think this case is about?
- What do you already know that relates to this case?
- What do you need to know to understand the case?
- How do you think this case could be used in your class?

Our Thoughts

- Subject specific Learning Objectives
- Access to Data: bioinformatics, scientific literature
- Visualization/Analysis: prior exposure
- Molecular Case Study Cycle

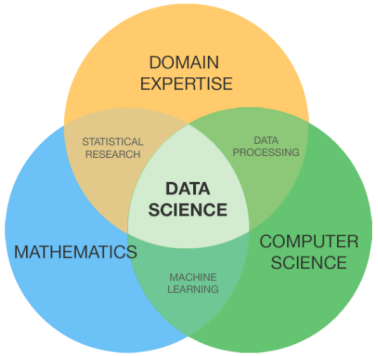
Molecular Case Study Design Considerations

- Limited/no prior exposure: OMM
- Some prior exposure: iCn3D
- Extensive prior exposure: PyMol, UCSF Chimera



- Chemistry
- Biology
- Biochemistry

- Class size: Large vs Small
- Interaction: Group vs Individual
- Level: Intro vs Advanced
- Control: Open ended vs Guided
- Assignment: Worksheet, Presentation, etc.



https://www.kdnuggets.com/2018/04/data-science-interview-guide.html

Learning Objectives

Chemistry	Biology	Biochemistry	Modeling and Presentation
1. Identify different kinds of intermolecular forces (IMFs), stabilizing the structures of biomacromolecules (protein, nucleic acid, etc., in this case hemoglobin) 2. Identify and differentiate covalent and noncovalent interactions of a bound ligand to a biomacromolecule (in this case, heme and oxygen binding to hemoglobin) 3. Visually explore, analyze, and explain how mutation in a protein can lead to altered protein structure/ function/ properties. In this case, describe the physiological impact of structural changes resulting from the mutation at Glutamate 6 to Valine in the hemoglobin beta chain of sickle cell hemoglobin (HbS) leading to sickling of cells.	1. Protein Structure: a. Identify amino acids (backbone and side chains) within a protein molecule b. Name, depict, and predict potential of chemical groups in small and biomacromolecules for noncovalent and covalent interactions c. Describe the different levels of protein structure – i.e., identify primary (1°), secondary (2°), tertiary (3°), and quaternary (4°) structures within proteins d. Identify covalent (coordinate) interactions between small molecule (O_2, CO) and metal ions in the Heme group 2. Protein Function: a. Explain the structure of native adult hemoglobin (HbA), including tetrameric structure, and the role of hemes in binding oxygen b. Describe weak bonds (salt bridges) that stabilize the deoxy conformation of HbA c. Describe how the structure and binding properties of hemoglobin (Hb) allows oxygen binding in different tissues and physiological states 3. Cells and Molecules: a. Explain the structural difference between native adult hemoglobin (HbA) and sickle cell (HbS) beta globin proteins and the genetic cause (molecular basis) of this difference b. Describe how the sickle cell mutation affects different levels of protein structure and shape of cells. 4. Explain how red blood cell sickling can lead to pain	1. Protein building blocks: a. Identify amino acids (backbone and side chains) within a protein molecule b. Identify functional groups and their properties (hydrophobic/hydrophilic, acid/base, nucleophile/electrophile, H-bond donors/acceptors, relative solubility, redox state) within biomolecules and their constituent monomers; c. Name, depict, and predict potential of chemical groups in small and biomacromolecules for noncovalent and covalent interactions. d. Identify covalent (coordinate) interactions between small molecule (O_2, CO, NO) and metal ions in the Heme group 2. Protein Structure: a. Describe the different levels of protein structure – i.e., identify primary (1°), secondary (2°), tertiary (3°), and quaternary (4°) structures within proteins b. Describe properties of and identify/ differentiate among specific types of secondary structures in protein - including α helices, β sheets (parallel and antiparallel), π helices, and other β structure (reverse turns); 3. Protein Function: a. Describe and compare the structure and features of T and R states of Hemoglobin (Hb) and their binding properties for reversible binding ligands b. Describe how the structure and binding properties of hemoglobin allows oxygen and CO_2 binding in different tissues and physiological states (cooperative binding) c. Use the binding properties of different forms of Hb for O_2 and CO_2 to explain graphs of fractional saturation vs pO_2 (Bohr effect) d. Describe and compare binding of other gases (e.g., CO and NO) to hemoglobin. 4. Cells and Molecules: a. Explain the structural difference between native adult hemoglobin (HbA) and sickle cell (HbS) beta globin proteins and the genetic cause (molecular basis) of this difference b. Describe and compare deoxy states of normal and sickle cell hemoglobin. c. Describe how the sickle cell mutation affects different levels of protein structure and shape of cells. d. Explain how red blood cell sickling can lead to pain	1. Use of public Bioinformatics data resources and scientific literature to learn about specific topics in biology 2. Use online interactive web tutorials to display and understand structural features of biomacromolecules, ligands, and their interactions 3. Display different renderings of molecules and proteins using web-based molecular modeling programs, given instructions for their use 4. Optimally orient molecules in interactive web tutorials or display key feature of structure and function using web-based modeling programs 5. Use screen capture to create images and inclusion of information from public biological data resources to create an educational presentation explaining the molecular bases of a biological function or process.

Nicholas' Story

Molecular Exploration

Getting to Structure

Introduction

Macromolecular Structure
Overall and local shape, organization

Chemical environment of
Ligands/cofactors/partners

Macromolecular Sequences
Genes and Protein

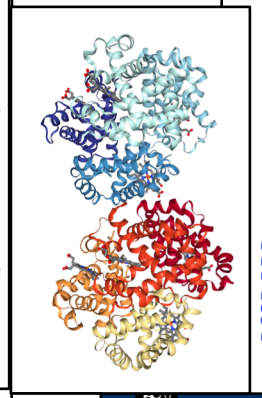
Intra-/intermolecular forces
Mediating stability, interactions (binding), and chemical reactions

Function at the level of Macromolecular Assembly in cell/tissue/organism

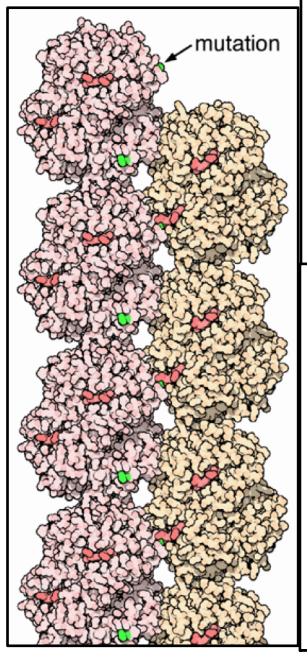
Chemistry

Biology

OMM

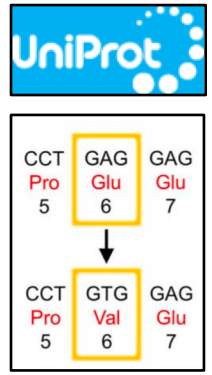


RCSB PDB



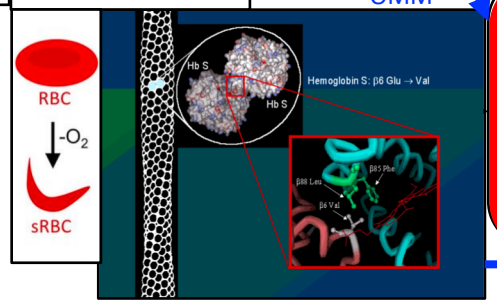
PDB-101

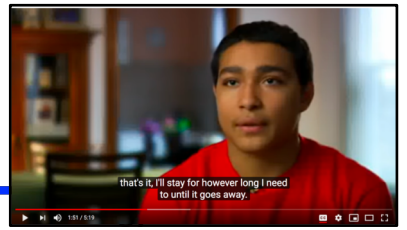
Deoxy HbS structure (PDB ID 2hbs)



Mutation of Glu6Val in HbS

OMM

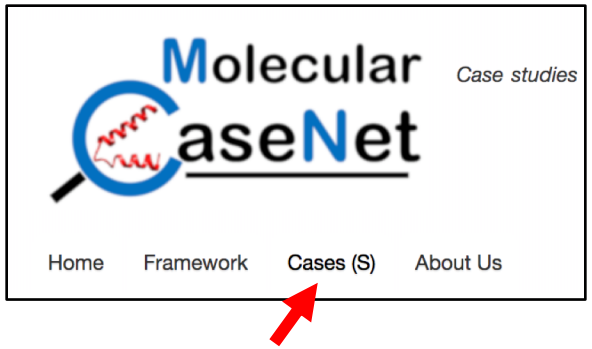




Q1. What is the molecular basis for Nicholas' condition (sickle cell disease)? What causes his pain crises?

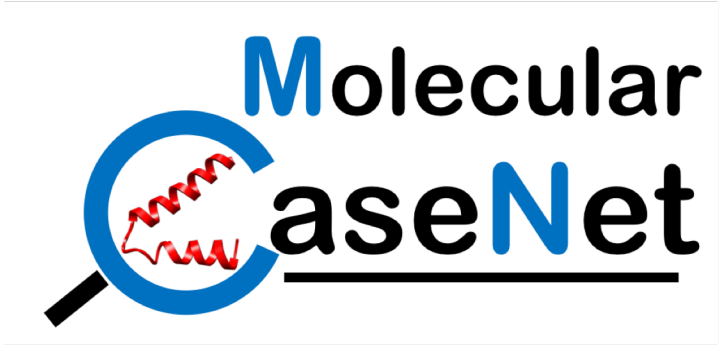
Molecular CaseNet Website

- Go to https://molecular-casenet.rcsb.org/
- Open the Cases tab
- Working through the case
  1. *Introduction*: Watch video. Read the overview and suggestions for running the case at your convenience
  2. *Getting to Structure*: Start exploring the case question(s) and identify relevant molecules to explore.
  3. *Molecular Exploration*: Explore molecular interactions to understand and explain the molecular mechanism of the question at hand
  4. *Assessment:* Apply **knowledge** and **skill** to solve a new problem/challenge



Exploring Nicholas's Story

- Go to https://molecular-casenet.rcsb.org/



Nicholas' Story – Discussion, Notes and more

- What was your initial impression? Share a few unexpected ones only now. We can discuss this further during the rest of the week

- Log into the website
  - U: teacher
  - P: Teachscience7!

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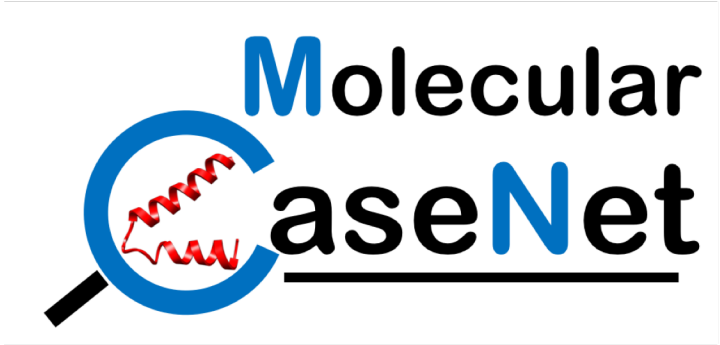
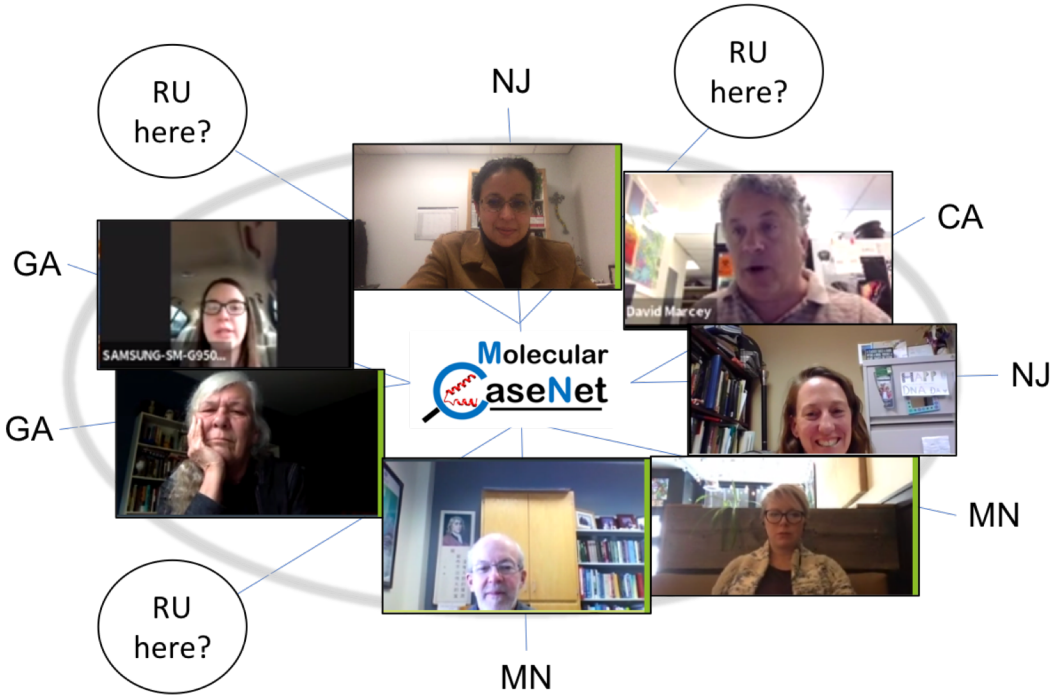


An Invitation … Join us to

- Collaborate with us on writing molecular cases
- Write your own molecular case
- Pilot molecular case(s) in your classroom and provide feedback

- Become a part of the next phase of the NSF project to develop and test molecular case studies



Interested? write to Shuchi at sdutta@rcsb.rutgers.edu

Summary

- Introductions
  - You and your favorite proteins
- Case Studies
  - Value of learning with case studies
- Molecular Case Studies
  - Framework and considerations
- Nicholas' Story
  - Your first impressions
- An Invitation
  - Join us …