Become an Inventor and Create the Medicine of the Future

Summary

Students experience the engineering design process applied to drug discovery. Students will learn quantum mechanics principles and how to design and modify molecules. They will be introduced to the potential for quantum mechanics in the field of biology to contribute to the development of futuristic sustainable photo-synthetic or other technologies. They will continue with learning how they can utilize cheminformatic methods to evaluate druglike nature and medicinal chemistry friendliness of one or multiple small molecules that they design in an effort to support drug discovery. They will be posed with real unsolved diseases and prompted to design a hypothetical drug that may potentially aid the condition. The objective is to experience problem solving through computational approaches. Students are guided by short directions. Students should work in teams, but each student should be responsible to make their own molecule and conclude their findings. As a team they should go through at least three design/test iterations, aiming to achieve a possible solution within the classroom time constraints.
This engineering curriculum aligns to Next Generation Science Standards (NGSS)
HS.Engineering Design.
https://www.nextgenscience.org/topic-arrangement/hsengineering-design

Engineering Connection

Engineers use cheminformatics and bioinformatics to study, understand and predict molecular and atomistic properties. Cheminformatics is a rapidly growing field that facilitates drug discovery. Students act as biomedical and chemical engineers following the steps of the engineering design process to design, test and improve drug development prototypes using computer based molecular representations, games and molecular calculations.

Learning Objectives

After this activity, students should be able to:

- Describe the basic principles behind Quantum Mechanics
- Able to use molecular modeling software to create 3D molecular representations
- Describe the steps of the engineering design process (*https://www.teachengineering.org/k12engineering/designprocess*) and the value of testing and redesign.
- Explain how cheminformatics aid engineers in discovery.
- Elaborate on the importance of design considerations for engineers.

Educational Standards

Next Generation Science Standards (NGSS)
(https://www.teachengineering.org/standards/ngss)
HS.Engineering Design
https://www.nextgenscience.org/topic-arrangement/hsengineering-design

Materials List

Computer and access to internet connection.

Worksheets and Attachments

No worksheets will be used. All work will be computer generated by students with their results, .jpg images of their molecules and computer simulations. Additionally, they could take notes from the videos. They will also provide you with a full report at the end of the lesson.

More Curricula Like This

Chemical Wonders: Materials and States of Matter
https://www.teachengineering.org/activities/view/nds-2224-bio-engineering-proteins-dna-modeling-testing

The Building Blocks of Matter
https://www.teachengineering.org/lessons/view/cub_mix_lesson1

Pre-Req Knowledge

A basic understanding of chemistry and how diseases, as presented in the associated lesson

Introduction/Motivation

(Introduce to the class the following scenario.)

Congratulations, you have invented a new miracle drug. Together, we have experienced the devastation that incurable virus diseases can have in our daily living.

Yet, the world has generated a tool that we all use. The tool is the computer. In addition, the connectivity that the internet offers allows us to collaborate all over the world in real time.
What if we could use these two tools to solve mysterious diseases? Or The viral infections of the future? Maybe cure cancer? And many other conditions that are unresolved in our current world.
Yes! You may discover the next miracle drug!
The field of Cheminformatics and Bioinformatics offers you the opportunity to be creative and to test your own prototype!
Before a company may purchase your drug design, you must prove to them that it works by demonstrating it with some potential data calculations. They want to see if your drug may meet the basic standards. demonstrate control over the drug's initial release time and duration time.

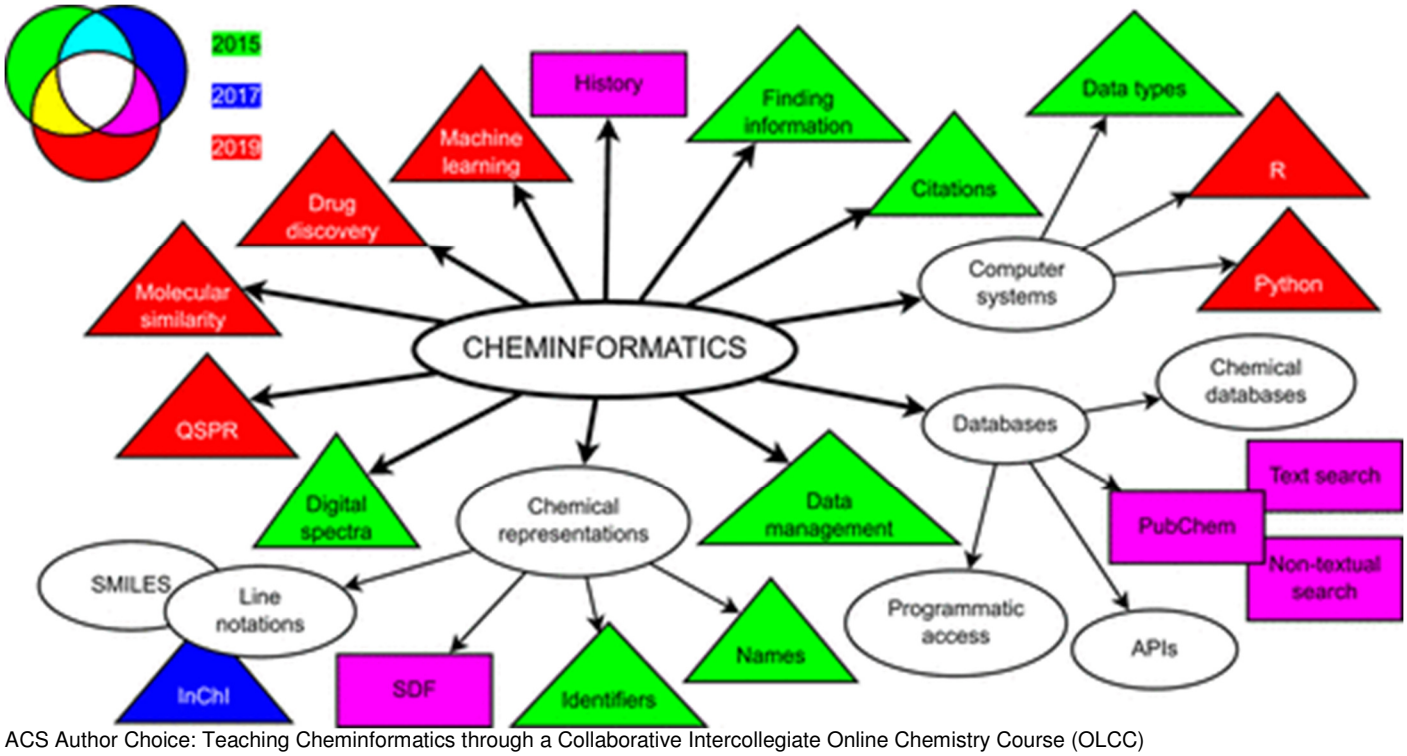
For this engineering challenge, you will use only simple use your computer and your collaboration with your team members to represent your new, miracle drug molecules.

Procedure

In today's world of discovery in science the process of drug discovery is one that requires the use of computers and informatic techniques to perform various tasks with vast amounts of chemical data such as data collection, storage, search, retrieval, transformation, analysis, visualization, and many others. In fact, currently, Computer and informatics skills in analyzing biological and chemical data are considered an important requisite that employers look for in job-seeking students.

Drug discovery is a highly interdisciplinary area where Biology, Chemistry, computer science, good reading and writing skills, along with scientific skills are necessary.

To give you an idea of the various areas that this new and exciting field of discovery brings you can look at the following image. The image shows in white the tools and knowledge that one may acquire and use to apply to gain access to the triangles in red. Similarly, the tools in white circles can produce information shown in the green triangles. Finally the result of an investigation may be stored in the purple boxes.



ACS Author Choice: Teaching Cheminformatics through a Collaborative Intercollegiate Online Chemistry Course (OLCC) Sunghwan Kim, Ehren C. Bucholtz, Kristin Briney, Andrew P. Cornell, Jordi Cuadros, Kristen D. Fulfer, Tanya Gupta, Evan Hepler-Smith, Dean H. Johnston, Andrew S.I.D. Lang, Delmar Larsen, Ye Li, Leah R. McEwen, Layne A. Morsch, Jennifer L. Muzyka, and Robert E. Belford Journal of Chemical Education 2021 *98* (2), 416-425
DOI: 10.1021/acs.jchemed.0c01035

Our purpose in this learning unit will be to use and apply in white circles: SMILES, Computer Systems, Databases and Chemical representations to the single red triangle of Drug discovery.

Where do we start?

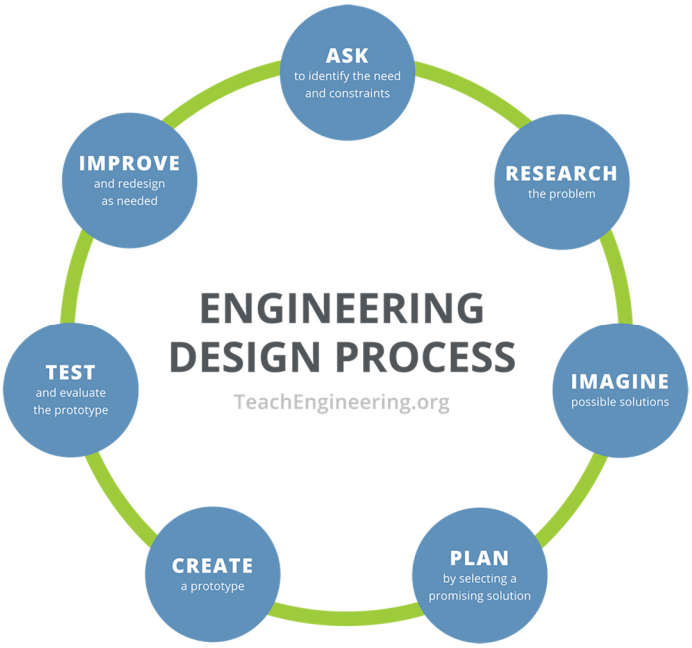
Watch the following videos to generate questions about the possibilities.

Video: Illuminating the secret world of your glycans
https://www.youtube.com/watch?v=sT1qghJZdW8&t=183s

Video: Bioinformatics
https://www.youtube.com/watch?v=182AzhLiwxc&t=1s

YOUR TASK
Can you design a new medicine that may provide a better performance to a health condition like a disease or infection ?

To reach your goal you are asked to utilize the Engineering Design Thinking Process.



Empathize: **Explore, Research and Learn**

In order to better understand the job, the principles behind it and the process to be utilized we must gain knowledge through research, collaboration and by testing our knowledge and abilities.

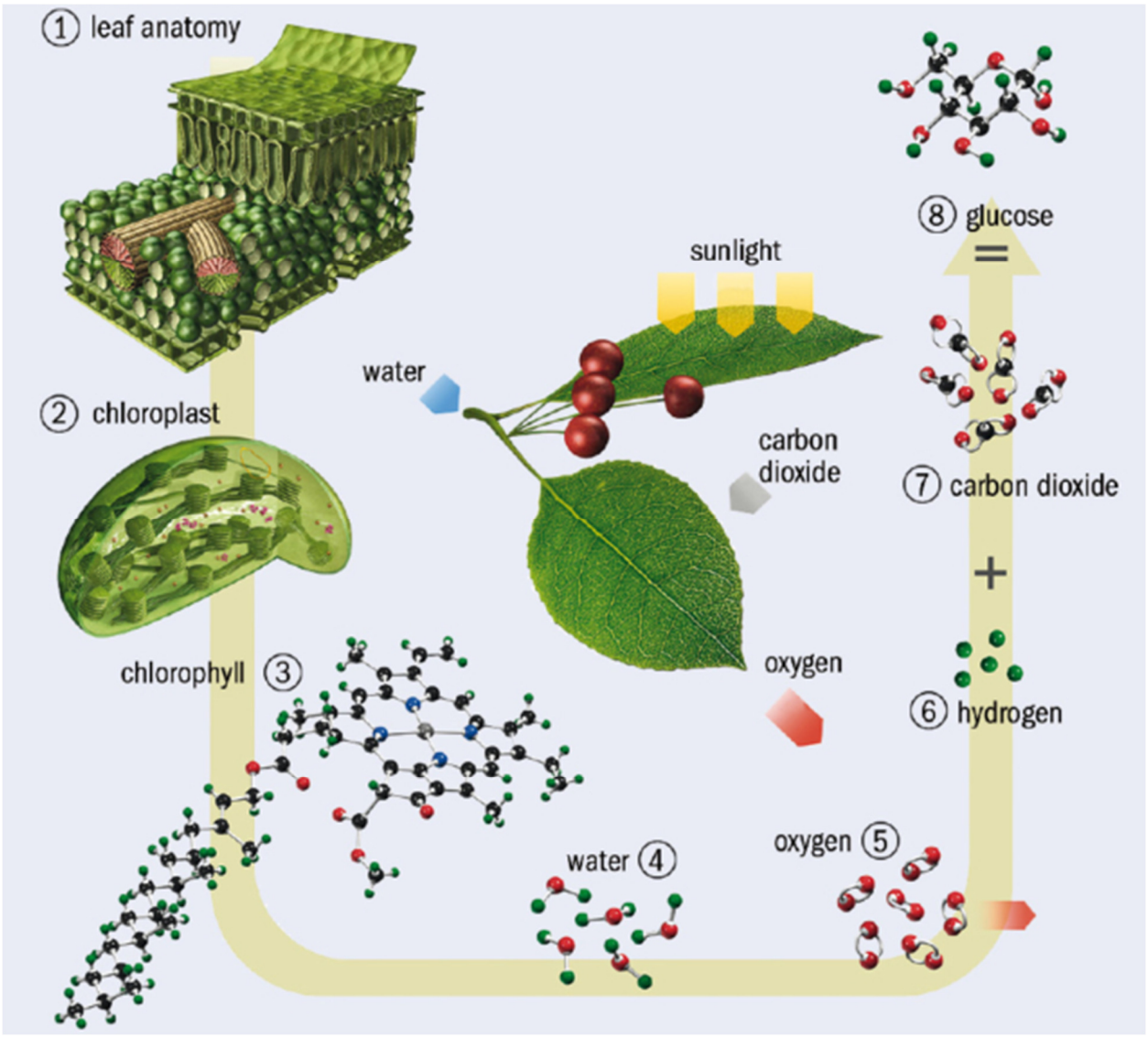
First research task

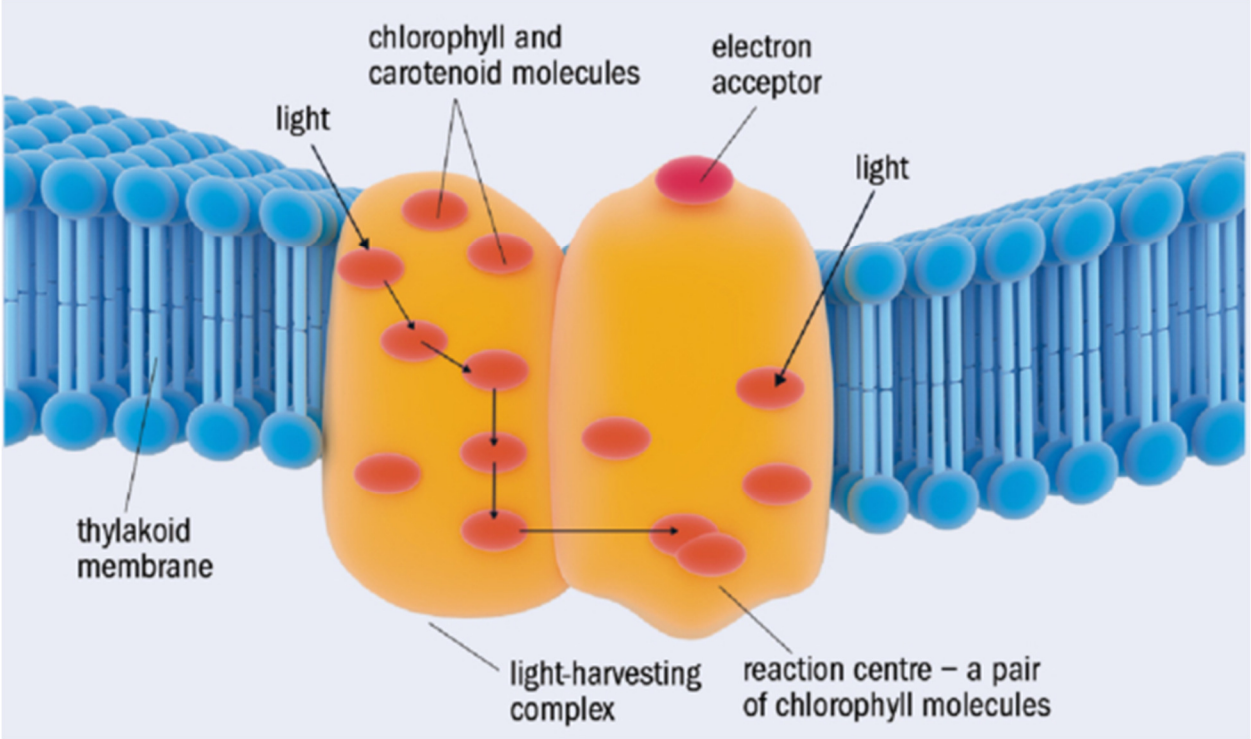
Show that quantum theory could contribute to scientific understanding of living systems and to new approaches leading to invention.

There is a new approach to understand and explain how our world works. This approach aims to look at matter, cells, and biological processes from the extremely small world of atoms. This atomistic approach aims to understand how electrons work inside atoms. To gain access to this diminutive world scientists are utilizing **Quantum mechanics (QM).** The fundamental theory that describes the properties of subatomic particles, atoms, molecules, molecular assemblies and their properties. QM allows us to describe energy transfer and electron transfer in a framework based on electronic surface hopping. One of the best biological examples of this is Photosynthesis. During the acquisition of light by plants,molecules and pigments inside the plant are associated with the transfer of energy and charge, the latter of which involves electrons, protons and ions. Exciting electrons result in energy transfer and the charge transfer in photosynthesis results in the liberation of our much needed Oxygen molecules.

Therefore, your first research task will be to learn and understand the basic principles of QM. This will involve the superpositions of electronic quantum states, the process by which green plants and some bacteria turn sunlight into chemical energy – gains light-harvesting efficiency by exploiting the phenomenon of "quantum coherence".
Also, you will be introduced to the theory of the quantization of energy. The QM concepts have been extended to molecules, where absorption of quanta of energy—photons—occurs at particular energy levels and gives rise to molecules that then possess very different properties.

Images https://physicsworld.com/a/is-photosynthesis-quantum-ish/


① leaf anatomy
② chloroplast
chlorophyll ③
water
sunlight
carbon dioxide
oxygen
water ④
oxygen ⑤
⑥ hydrogen
⑦ carbon dioxide
⑧ glucose



Now you are ready to Explore, Research and Learn
Introduce students to Photosynthesis with two short videos
Watch:
Photosystem I
https://www.youtube.com/watch?v=hj_WKgnL6MI

Photosystem **II**
https://www.youtube.com/watch?v=3UfV060N27g&t=174s

Research and find more information about the molecules involved in photosynthesis (resource 9, 10)
Learn about Photosynthetic pigments (11)
Identify various photosynthetic pigments (10-13)
Learn about SMILES (4, 15,16)
Read The true color of Chlorophyll
https://www.mpsd.mpg.de/17628/2015-04-chlorophyll-rubio
PLAY the game Particle in a Box
http://learnqm.gatech.edu/WebGLtest/index.html

Play the game Quantum Moves 2 (Psi and Delta (learn Probability, energy levels, Potential profiles)
https://www.scienceathome.org/games/quantum-moves-2/

As you may now begin to realize, molecules are everywhere and QM rules their world. Therefore, now you will learn about how computer software is utilized to build and represent visualizations of molecules. These 3D visualizations help us picture in our mind what molecules look like and what they might be able to do. Also, you will be asked to utilize two types of molecules one will be pigments, so you can associate them with Photosynthesis and with your everyday fruits and vegetables. The other set will be glycans, those presented in the first video and associated with cells, disease and treatments. Those two will eventually lead you to new ideas about possible drugs for medical conditions.

Build a simple molecule
https://phet.colorado.edu/sims/html/build-a-molecule/latest/build-a-molecule_en.html
Molecular Modeling (18,19)
Students will then explore various options to pigments
Using
Windows: IQmol 2.15
Avogadro
MOlview
https://molview.org/?cid=12085802
Introducing pigments to plants that would help them capture ultraviolet or infrared light could change that equation.
Molecular Modeling (18,19
Students will then explore various options to pigments
Using:
PubChem Drawer
https://pubchem.ncbi.nlm.nih.gov/edit3/index.html
Edit molecular data and analyze the resulting structures. Generate various surfaces based on the input information, check the current orbitals and densities, view and adjust animations by switching and correcting vibrational modes and reaction pathways.

Chromebook: Avogadro download
https://www.bestchromebookapps.com/avogadro-for-chromebook/

Now that you have acquired a better understanding and have empathized with scientists it is time now for you to define the problem you are about to challenge.

Vocabulary/Definitions

state: A state is a complete description of the observable properties of a physical system.
system: A sufficiently isolated part in the universe for investigation.
energy spectrum: The energy spectrum refers to the possible energy of a system.
atom: The basic unit of matter; the smallest unit of an element, having all the characteristics of that element; consists of negatively-charged electrons and a positively-charged center called a nucleus.

atomic theory: The theory that all matter is made up of fundamental particles called atoms; the concept of an atom as being composed of subatomic particles.

electron: Particle orbiting the nucleus of an atom with a negative charge.

molecule: The smallest unit of a substance that retains the chemical and physical properties of the substance; two or more atoms held together by chemical bonds.

neutron: Particle in the nucleus of an atom with no charge.

nucleus: Dense, central core of an atom (made of protons and neutrons).

proton: Particle in the nucleus of an atom with a positive charge.

Define the Problem:

Video: Mysterious brain disease emerges in New Brunswick: What doctors know so far
https://www.youtube.com/watch?v=GcE7GnUXkIc
Video Center for Bioinformatics and Computational Biology
https://www.youtube.com/watch?v=We_DLAJY1yE
Video Top 5 Incurable Diseases
https://www.youtube.com/watch?v=_dQ42Zytu-0
Video Rare and mysterious disease causes skin to fall off | 60 Minutes Australia
https://www.youtube.com/watch?v=bF5eOxwwihM
Video The pharmacy of the future? Personalized pills, 3D printed at home | Daniel Kraft
https://www.youtube.com/watch?v=-RkhAP0_ms4
Video Quantum AI and Machine Learning
https://www.youtube.com/watch?v=hWx2Rws3L-A
Video Learn CADD - Computer-Aided Drug Designing The Easier Way With Biotecnika
https://www.youtube.com/watch?v=NOyJPi7r18U

Ideate
The Swiss institute of Bioinformatics allows you to create and test ideas for new drugs. You can use a molecular SMILE modified and see how likely it is that it can be made. You may also see the biological effects and how your drug compares to others in the market.

Use swissadme (*http://www.swissadme.ch/index.php*) to verify if it is more or less likely for you to synthesize your molecule.
Find a similar molecule Use swissadme (*http://www.swissadme.ch/index.php*)
Also verify the other medicinal values.
Running a SwissSimilarity will determine if your molecule is unique!!
Test and develop: Use Machine Learning environments

Use the Engineering Design Drawing Rubric to guide your development
Use Machine Learning environments
Use swissadme (*http://www.swissadme.ch/index.php*) to verify if it is more or less likely for you to synthesize your molecule.

Use this video to guide you how to use Swissadame CADD session instructions (*https://www.youtube.com/watch?v=Xr66u2qagVI*). The SwissSimilarity will allow you to know if your molecule is unique!
Find a similar molecule. Use swissadme (*http://www.swissadme.ch/index.php*). Also verify the other medicinal values.

Assessment

Pre-Activity Assessment

Concept Review Discussion: Hold a class discussion to review concepts from the associated lesson. Ask students to ask questions about the main methods of drug discovery, including pros and cons for each, and list design considerations that engineers and doctors may have to take into account for designing the new medications.

Activity Embedded Assessment

Have students create a report based on the results from their interpretation of the swissadame results. Ask them to draw conclusions and to write what could be the next potential development to improve their design. Make sure to guide them through three design/build/test iterations; if they have time for more testing and improvement, provide them with extra time. Check their initial designs before they start to model their molecules. Have them hand in their completed results along with a team report which included all of the analysis and the group interpretations. Review their answers, models and testing results to gauge their depth of comprehension and engagement with the process.

Post-Activity Assessment

Summary Diagram of Designs and Improvements have students compile diagrams that show how their groups' designs evolved through testing and redesign, explaining what improvements they implemented along with the initial release times and release duration times for each design. Have students use computers and applications like PowerPoint® or something similar. Hold a group discussion on the process of drug discovery. Review their diagrams to gauge their understanding of the lesson and activity concepts.

Investigating Questions

How can you improve your ability to create and interpret the design of new molecules?

How could a potential new drug development be initiated and how would one test its efficacy?

Troubleshooting Tips

There is no one single correct answer to this project.
If molecules are too large the processing may be complicated.
Recommendation is to stay with small molecules no more that 20-30 atoms.

Activity Extensions

You could easily engage students in DFT analysis with GAMMESS and other links which offer true analysis with atomistic calculations. One of the best resources for free cloud base DFT analysis or any other kind is Chemcompute (*https://chemcompute.org/*). Teachers will make a free account and they can submit the running jobs for their students.

Activity Scaling

You could potentially see this lesson as three separate goals:

a) Photosynthesis
b) Molecular modeling
c) Quantum Mechanics

Additional Multimedia Support

1) Open Source Molecular Modeling software
   https://opensourcemolecularmodeling.github.io/
2) Quantum Chemistry software -many free
   http://www.biomolecular-modeling.com/Software_Quantum_Chemistry.html
3) Avogadro: An advanced molecule editor and visualizer
   https://avogadro.cc/
4) Utilizing Smiles (with and without_python)-video introduction
   http://molecularmodelingbasics.blogspot.com/2016/05/a-brief-introduction-to-smiles-and-inchi.html
5) Computational Chemistry for Educators
   http://www.computationalscience.org/ccce/about/labs/labs.php
6) Article: Using Computational Chemistry Activities To Promote Learning and Retention in a Secondary School General Chemistry Setting
   https://pubs.acs.org/doi/abs/10.1021/ed300039y
7) List of resources: MoleCVUE
   https://sites.google.com/view/molecvue/activities
8) Artificial Photosynthesis Group at the Brookhaven National Laboratory
   https://www.bnl.gov/chemistry/ap/
9) Computational Chemistry Harvard University lecture and video
   https://sitn.hms.harvard.edu/flash/2013/computational-chemistry-shines-light-on-solar-energy-storage-in-plants/
10) Photosynthetic Cells
    https://www.nature.com/scitable/topicpage/photosynthetic-cells-14025371/
11) PubChem source of the molecular models used by students
    https://www.ncbi.nlm.nih.gov/
12) Photosynthetic Pigments
    https://ucmp.berkeley.edu/glossary/gloss3/pigments.html
13) Light and Photosynthetic pigments
    https://www.khanacademy.org/science/biology/photosynthesis-in-plants/the-light-dependent-reactions-of-photosynthesis/a/light-and-photosynthetic-pigments

14) Photosynthetic Pigments
https://www.biosciencenotes.com/photosynthetic-pigments/
15) Quantum Biology
https://royalsocietypublishing.org/doi/10.1098/rsif.2018.0640
16) SMILES and InChi
https://chem.libretexts.org/Courses/Fordham_University/Chem1102%3A_Drug_Discovery_-_From_the_Laboratory_to_the_Clinic/05%3A_Organic_Molecules/5.08%3A_Line_Notation_(SMILES_and_InChI)
17) SMILES Tutorial
https://archive.epa.gov/med/med_archive_03/web/html/smiles.html
18) Featured Chemistry Program Software
https://chemistry-program.software.informer.com/pages/4/
19) ChemCompute
https://chemcompute.org/
20) Avogadro for Chromebook
https://www.bestchromebookapps.com/avogadro-for-chromebook/
21) Human mind excels at quantum-physics computer game
https://www.nature.com/articles/532160a
22) Resources on Computational Chemistry
http://www.zyvex.com/nanotech/compChemLinks.html
23) Software used in Cheminformatics
https://www.researchgate.net/post/Has-anyone-compiled-a-list-of-software-processes-used-in-CADD
24) photodynamics simulations
https://pubs.acs.org/doi/abs/10.1021/acs.jpclett.0c00527
25) Deep learning for UV absorption spectra with SchNarc
https://aip.scitation.org/doi/10.1063/5.0021915
26) OPEN EDUCATIONAL RESOURCES: SIMULATIONS AND VIRTUAL LABS
https://libguides.mines.edu/oer/simulationslabs
27) Swissadame CADD session instructions
https://www.youtube.com/watch?v=Xr66u2qagVI
28) Chromebook: Avogadro download
https://www.bestchromebookapps.com/avogadro-for-chromebook/

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