Drug Design Workshop

Engaging Context Data Integration

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Data source

Drug Design Workshop, retrieved from: http://www.drug-design-workshop.ch/

To specifically test potential drug candidates on COX1 and/or COX2:

http://www.drug-design-workshop.ch/cox.php

Binding modes that follow from running the drug through a protein databank (link is for COX1 and ibuprofen:

http://www.drug-design-workshop.ch/bindingmodes.php?target=COX1&ligand=Ibuprofen

Pharmacokinetic information (again for ibuprofen): http://www.swissadme.ch/index.php

Lesson Enhancement

A few weeks ago my STEAM students and I explored the topic of animal testing for medicinal and cosmetic purposes. It occurred to me that my students have little to no awareness of modern ways of drug design. I asked if they would be interested in exploring this in more detail and they all enthusiastically responded with a yes. I designed a series of lessons based on the Drug Design Workshop. The overall goal of the series is for students to obtain hands-on experience with modern drug design and learn about the data-driven, computational aspects of it.

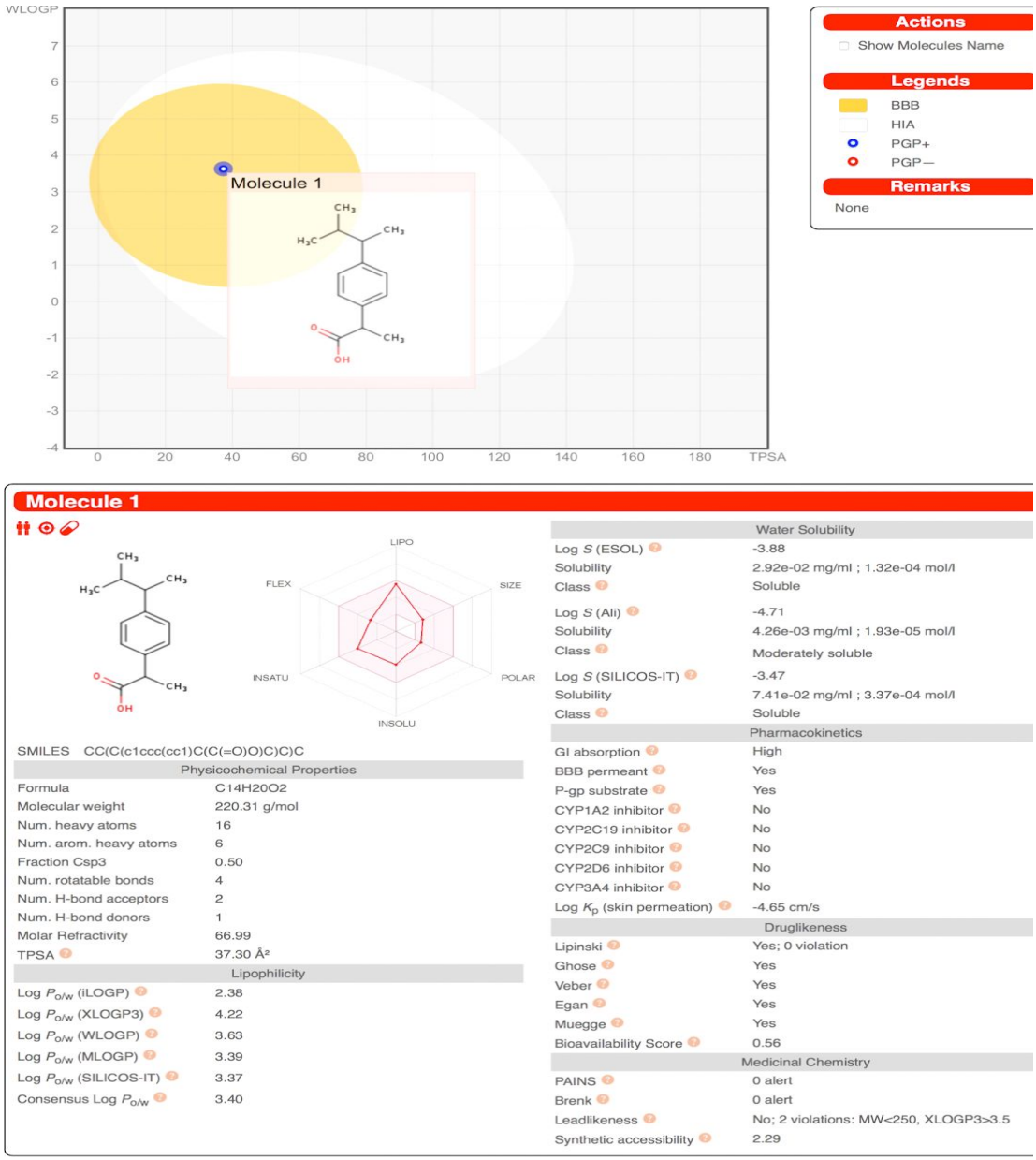
Concepts that I will address in the Drug Design Workshop are:

1. **Analyzing and interpreting data -**
    a. the binding score between a potential drug candidate and its target protein as an indication for the strength of the bond between the drug candidate and its target protein

   b. basic pharmacokinetics of a potential drug candidate using the 'spiderweb' hexagon from SwissADME (SwissADME, p. 3) and the boiled egg model (SwissADME, p. 8)
   c. connecting these two indicators and use them to create a drug candidates that optimizes both binding score *and* pharmacokinetics

2. **Using computational thinking** - all data from SwissADME is based on available online information about protein structure and characteristics. Students will access this datasource with their potential drugs to calculate and interpret information regarding the drug.
3. **Developing possible solutions in an engineering design problem**. After the initial exploration phase, the students will design their own drug candidate in the Drug Design Workshop. The workshop uses a Marvin4JS sketcher for this. Initially they will focus on creating a potential drug with the highest possible binding score. This requires from them that they focus on small details inside the target molecule that allow for improved binding to the target protein and through a process of design, calculate the binding score, evaluate and redesign, they will eventually create their optimal candidate.
4. **Optimizing the design solution.** Once the students have developed the compound with the highest binding score, they will enter it into the SwissADME databank to obtain pharmacokinetic information. They will then have to redesign their drug candidate in order to create a compound whose characteristics most closely resemble the hexagon in the bioavailability 'spiderweb' as shown in the illustration below. For simplicity reasons

my lesson will only focus on the boiled egg and the ‘spiderweb’ hexagon (see illustration below).



Source: *J. Chem. Educ.* 2017, **94**, 335-344. DOI: 10.1021/acs.jchemed.6b00596

Both the Drug Design Workshop with its Marvin4JS molecule builder and the connected SwissADME database will greatly enhance my lesson because they allow students to design and

test drug candidates and then redesign and retest them based on feedback from the database. Direct instruction or watching videos don't even come close to students creating and building molecules by themselves and then testing them and having to interpret the feedback in order to redesign. I will gear my lessons less toward understanding the building process of small organic compounds as to understanding the multi-faceted aspects of drug design.

Using data in the classroom

I think using data in the classroom is extremely valuable. It makes science 'real' in that it gives it hands and feet. It makes students aware of the importance of being accurate in gathering data, thinking through the process of data collection and it enhances critical thinking skills when it comes to analyzing data. Gathering information and meaning from data is a skill that students will benefit from all their life and it goes way beyond science. Choosing a student loan with favorable interest rates and repayment schedules, investing money, selecting what to pack when going on a trip, knowing when to evacuate when a hurricane is forecasted - these are just a few examples of situations where we have to choose and decide based on data. In my experience students need practice and training in analyzing data and knowing what it means. The Drug Design Workshop is just one example of a series of activities that lends itself to this.

Besides all that, analyzing and interpreting data is a recurring skill in the NGSS philosophy (Science and Engineering Practices). In addition to that, an assignment like the Drug Design Workshop also addresses many Common Core Math Standards such as making sense of

problems, using mathematical tools (although 'hidden' in the programming), abstract and quantitative reasoning (Common Core Standards for Mathematical Practices).

Visual Presentation

I choose this data source based on my students' interest and because the lesson series is adapted for the 'general public' and high school students (Daina, A., et al.). The data sources itself provide clear visuals in which binding score and pharmacokinetics are immediately visible. With some background instruction, my students will be able to interpret the information to the level that is required for this assignment. The really neat thing is that the workshop lends itself for much more than just this fairly basic introduction to drug design. I can envision advanced Chemistry and Biology students being interested in this and they will come into the program with a much more detailed knowledge of proteins and chemistry. Another reason for me to choose the Drug Design Workshop materials is that it weaves together Chemistry, Biology, Technology and Math, therefore making it a great fit for the STEAM program at my school.

Interdisciplinary STEM

The data from the Drug Design Workshop integrates technology (using an existing, web-based database) to perform advanced mathematical calculations, resulting in information that allows students to learn more about the biology and the chemistry of drug-protein interactions and the biology and chemistry of drugs inside our bodies. I think this is a beautiful illustration of how real life science is multi-disciplinary and how it requires experts from different STEM fields to

communicate together in order to create a reliable database and to give meaning to the results of the database calculations.

Bibliograhpy

Daina, A., et al, (2017). Drug Design Workshop: A Web-Based Educational Tool to Introduce Computer-Aided Drug Design to the General Public. *Journal of Chemical Education, 94,* 335-344

Daina, A., Michielin, O., & Zoete, V., (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports.* 7:42717. DOI 10.1038/srep42717

Science and Engineering Practices, from https://ngss.nsta.org/PracticesFull.aspx (assessed on October 12, 2018)

Common Core Standards for Mathematical Practices, from http://www.insidemathematics.org/common-core-resources/mathematical-practice-standards (assessed on October 12, 2018)