Introduction

Protein Virtual Reality (VR) is an important educational tool for visualizing the form and function of various proteins. Proteins are exceedingly complex biological macromolecules and visualizing them in a way that adequately reflects their complexity is quite difficult. Textbooks can only display proteins in two dimensions. They are therefore forced to forgo the elements of a protein’s shape that are essential to its functionality. Online visualizations offer a way to look at proteins in 3D space. They can be used to look at the protein from different angles, and are a more accurate visual of the secondary, tertiary, and quaternary structures of the protein. They also allow the user to look at different kinds of visualizations of the protein and place ligands for the protein in their appropriate binding pockets.

While being able to visualize pockets in 3D is more impactful than a 2D textbook, it is still limited in that it does not allow one to be completely immersed within the image of the protein. However, virtual reality protein software would allow one to be completely immersed within the image of the protein. It could elucidate areas of the protein that are deeply hidden and difficult to visualize using a 3D visualization software.

Virtual Reality is currently at the forefront of technology. While many of its uses are in the area of entertainment, it is also being used as an important tool by the scientific community. Surgeons have been starting to look at virtual reality scans before surgery to study what a particular organ looks like before they attempt to repair it (Matthews). Using virtual reality for protein modeling would help not only with education on protein shape and structure but also potentially with drug discovery. Currently, virtual screening methods are being used to deduce promising starting molecules. Virtual reality would enhance these capabilities because it would give an immersive view of the potential binding pocket for a drug. It would allow researchers to get a more detailed idea about how a potential molecule might be positioned in the binding pocket and the kinds of interactions it might have (Ratamero).

Our project would greatly help with looking at those specific interactions. Having the ability to enclose specific amino acids in spheres that the user can single out would help the user identify specific interactions. These interactions could be with a potential new drug or they could be between different amino acids in the protein itself. Our project will improve the functionality of Protein Virtual Reality because it will elucidate the identity of the specific interactions that the user is already viewing in the program.

Visualization of biomolecular systems began with the display of 3D forms on a 2D platform. Two of the most commonly used software applications for this are Visual Molecular Dynamics (VMD) and PyMol. VMD allows the user to display and analyze molecules in MacOS X, Unix, or Windows. This program is free and has source code readily available. It is widely used for its different styles and coloring methods, as well as its ability to run simulations (Humphrey). PyMol is a similar stand-alone application that is used for 2D visualization of 3D molecular structures on operating systems such as MacOS and Windows. Proteins can be visualized in color-customizable representations such as Cartoon, Ribbon, or Sticks, which allows the user to personalize their biomolecular structure for better understanding of the figure itself (The PyMOL Molecular Graphics System). Both of their softwares also allow individuals to upload their personal Python scripts and molecular models for viewing structures and dynamic interactions.

These two applications, however, require local installation by the user and can prove to be not only memory-consuming, but also difficult to navigate for beginners. Jmol, Web3DMol, iCn3D, and other similar web-based applications can be run in a browser window without the need for downloading additional software or learning command line interactions, but are still only capable of displaying a 2D representation of 3D structures on a screen.

Although the ability to view biomolecular systems has increased structural discoveries, bioinformatic feats, and worldwide awareness of molecular models, researchers are still debating which interface is the most accurate and user-friendly. Overall, existing methods have yet to provide an immersive experience of being inside the protein for the viewer, and it can be difficult to comprehend the 3D structure and orientation of the molecule by just looking at it on a screen. It is easy to miss important characteristics, such as intermolecular interactions, when visualizing on a flat screen. In an attempt to solve these issues, there has been the recent development of software to visualize a molecule using gaming tools in a VR environment. This ensures that the user can not only display a molecule, but also step inside the system itself and manipulate the environment to their desired orientation. ProteinVR seeks to provide the best of both worlds, pairing the 3D visualization of molecules of heavy local software applications with the easy and accessible appeal of current open source 2D visualization programs.

To tackle the issue of accessibility, ProteinVR is a free and open source browser-based application. These features will allow users to dodge licensing fees, as well as the hardware requirements needed to run memory consuming software. ChimeraX, for example, can cost up to $20,000 depending on the number of users. The free use extends only to non-commercial use, while ProteinVR provides a free platform for both commercial and non-commercial uses (The PyMOL Molecular Graphics System). PyMOL, another open source protein viewing software, does not guarantee long term free usage. ProteinVR will be freely available to any users rather than only those in academic institutions, and will not have change the licensing agreement for the duration of the program’s use (UCSF ChimeraX). ProteinVR’s usability directly from the web browser will also allow cross platform use. Differences in operating system will not have an effect on the usability of the program, and it is even able to run on mobile devices. In addition, the simple and intuitive UI will allow new users to easily learn and operate the application.

ProteinVR also addresses the restrictiveness of the 2D modeling that exists in other web-based protein viewers. ProteinVR offers both a 2D and 3D view of any protein, while still being operable within a web browser. ProteinVR can be synced with virtual reality tools to allow the user a 3D visualization.

When addressing protein visualization in virtual reality a variety of issues can be discovered with two major issues the group would like to address. These issues relate to generating optimized 3D sphere structures in virtual reality based on the provided set of data points in the x, y, and z direction planes. This needs to be completed for not only individual atoms, but also for entire chains or residues depending on user input. This input will also come in the form of JSON files which are specifically designed for access from web server to browser. The first issue arises with generating this sphere structure while minimizing or completely avoiding overlap with other atom’s 3D space. This involves creating a system that makes the smallest sphere possible for the user to interact with and see but also covers every point of the molecule. Enveloping every point with reduced overlap in a spherical space gets very difficult as file size increases. The second issue relates to providing labels for these spheres in the same shared space. Currently no ideal method exists to use the provided data points to generate an optimized label in the virtual space. This label needs to be easily readable for the user while not overlapping with any other atoms in the shared region. Our goal is to successfully create and optimize free web-based use to advance the future of research.

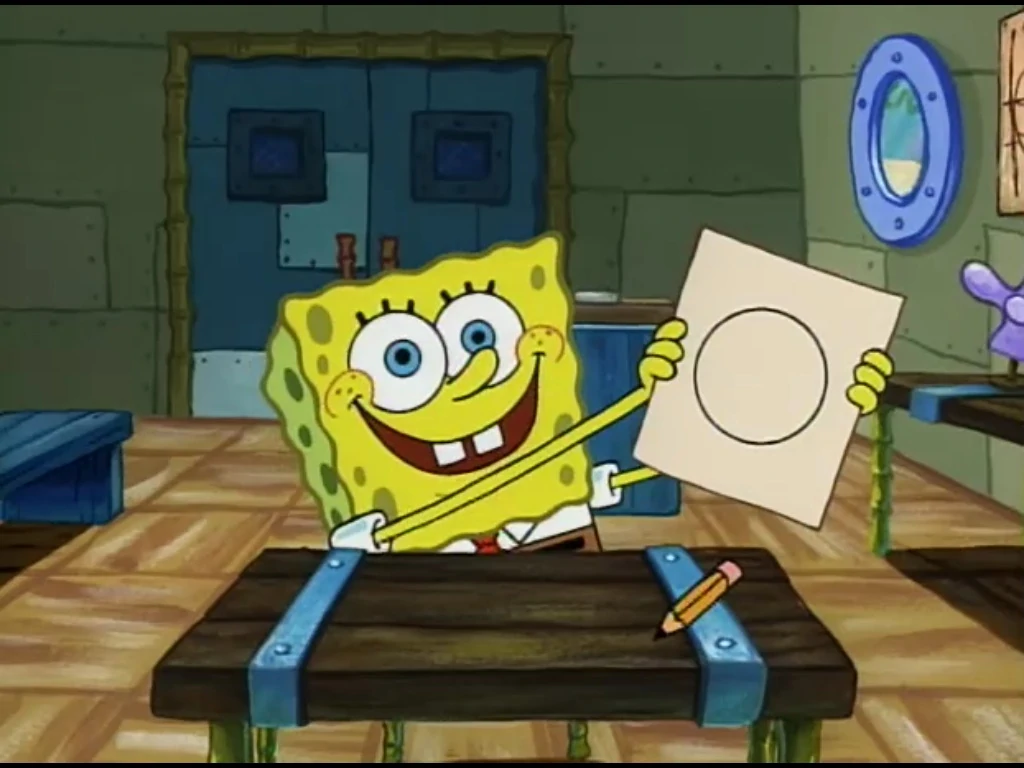
Citations

Ratamero, Erick Martins et al. “Touching proteins with virtual bare hands : Visualizing protein-drug complexes and their dynamics in self-made virtual reality using gaming hardware.” *Journal of computer-aided molecular design* vol. 32,6 (2018): 703-709. doi:10.1007/s10822-018-0123-0

Humphrey W, Dalke A, Schulten K. VMD: visual molecular dynamics. *J Mol Graph*. 1996;14(1):33–28. doi:10.1016/0263-7855(96)00018-5

The PyMOL Molecular Graphics System, Version 1.2r3pre, Schrödinger, LLC.

Contributions:



For the introduction section the various research and discussion was divided between the seven members of the group as evenly as possible. Devin wrote about the biological question at hand. Elizabeth and Jake addressed why the question is important. Shivani and Amy wrote the section on the existing methods to solve this problem and why they are inadequate. Finally, Jesse and Andrew wrote about our group’s proposed solution and how it is better than existing tools. Each member contributed in writing their section with citations and proofreading the other sections of the introduction.

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