Comparative visualization of protein conformations using large high resolution displays with gestures and body tracking

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ABSTRACT

Automatically identifying protein conformations can yield multiple candidate structures. Potential candidates are examined further to cull false positives. Individual conformations and the collection are compared when seeking flaws. Desktop displays are ineffective due to limited size and resolution. Thus a user must sacrifice large scale content by viewing the micro level with high detail or view the macro level while forfeiting small details. We address this ultimatum by utilizing multiple, high resolution displays. Using 27, 50", high resolution displays with active, stereoscopic 3D, and modified virtual environment software, each display presents a protein users can manipulate. Such an environment enables users to gain extensive insight both at the micro and macro levels when performing structural comparisons among the candidate structures. Integrating stereoscopic 3D improves the user's ability to judge conformations spatial relationships. In order to facilitate intuitive interaction, gesture recognition as well as body tracking are used. The user is able to look at the protein of interest, select a modality via gesture, and the user's motions provide intuitive navigation functions such as panning, rotating, and zooming. Using this approach, users are able to perform protein structure comparison through intuitive controls without sacrificing important visual details at any scale.

Keywords: Molecular visualization, bioinformatics, multiple views, virtual environments, large high-res displays, stereo displays

1. INTRODUCTION

The significance of protein structure prediction is great in many fields including, but not limited to, bioinformatics. However, structure prediction methods are prone to inaccuracy, often offering multiple potential structural configurations instead of a single solution. As the provided structures are potentially invalid, experts must examine the conformations. Comparing, contrasting, and exploring the candidate structures is generally performed using standard desktop computers—, though such equipment provides a non-optimal environment for such a task.

Even with the increase in resolution and size that affordable, standard displays have experienced in recent years, many displays do not support high resolutions. As a result, these displays are ill-suited for high-resolution, detail-oriented data work. Desktop monitors that do support high resolutions still pose a substantial obstacle due to their small physical display size. When comparing multiple protein conformations, the user must have multiple viewers open at once.

If these viewers are displayed side-by- side, the resolution for exploring fine details in each conformation is limited by both resolution and display area. If the presented conformations are stacked, each view using the maximum resolution possible, only one may be examined at a time. By precluding multi-structure comparisons, the user loses inter-protein context as well as context within the collection of proteins. Such problems are a detriment to the workflows of researchers. The application research presented here provides a potential solution to these problems.

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The implemented solution involves utilizing large, high resolution displays to maintain detail clarity at all levels. Utilizing open source virtual environment software, Vrui VR Toolkit,[1] combined with 27 50" displays in a 3 wall configuration, a suitable application environment is established. Each display presents a single protein conformation to the user which may be manipulated independently of the other structures. Such a setup allows the user to view micro scale features on one conformation while comparing against another structure at the macro level without sacrificing the presented details. A user may also have the same conformation on multiple displays, using one display to show micro level details and another display showing a macro level visualization. These are but a few of the potential configurations for such an environment. More configurations are proposed as future tasks. However, when using such an environment the traditional mouse and keyboard control paradigm become insufficient and unintuitive.

Forgoing the standard mouse and keyboard control system, a body tracking and gesture based control system is utilized. Body tracking is performed using reflective spheres and a Natural Point IR camera tracking system.[2] Gesture recognition is performed using a data glove with 6 accelerometers, the AcceleGlove,[3] and a constructed library which collects hand position data from the glove and uses LibSVM[4] to perform gesture recognition.

Body tracking fulfills two functional needs: a selection mechanism and a modulation mechanism. Modality switches are performed using gestures. The user may look at a molecule they wish to manipulate and use the data glove to switch to a panning modality. The movements of the user translate the protein conformation to the desired orientation.

This manuscript presents implementation details as well as findings and potential future developments that are organized as follows. Section 2 presents related work in the area. Section 3 provides specific implementation details for the environment, visualizations, and control mechanisms. Details for use cases and the results of the implementation are presented in Section 4. Section 5 details potential future developments and leads into Section 6, the conclusion.

2. RELATED WORK

Molecular visualizations have been an area of interest for many years. Such interest is a reflection of both the visualizations' abilities to enhance understanding by communicating large amounts of data in a natural and interactive manner and the high interest in molecular fields such as bioinformatics. Exploratory environments targeting protein analysis, visualization environments enabling collaboration, and virtual reality environments for protein manipulation and design are a few examples of developments in the field. Each of which offers a different perspective into molecular science.

It is natural to visualize and interact with protein structures in 3D. In many cases, data sets are hard to locate, but protein data is readily accessible. Databases such as the Protein Data Bank[5] freely offer well-known model formats for proteins. The high level of accessibility is a boon for visualizations but it is also an indicator that it is high interest data. It is data that when properly visualized can aid many users in their work. Such databases and external applications also may offer browser-based visualization.[6]

Browser based visualizations offer portability while facilitating constant collaboration between users and interaction with users in different ways as they move throughout their daily routines. In this system however a browser based visualization will not be used. Browsers are flexible and offer similar graphical capabilities with the advent of WebGL but are not suited for this application. In order to establish a solid foundation for high performance visualizations, it is most appropriate to use a desktop application. The desktop allows applications to operate as needed outside of the many constraints of a browser such as lacking support for CUDA and restricted file IO facilities.

Many visualizations provide a single scene of a structure to the user which may be explored in familiar ways with common tools but also using custom tools, such as flashlights.[7] Bergman et al. focused on the interactive construction of molecular visualizations and heavily engaging the user. By creating useful, generic tools, Bergman et al. facilitated visualization development.[7] The platform we are creating has the primary function of visualization presentation versus the development of new visualizations. Because Bergman et al. made it clear that a flexible tool system was beneficial, our choice in toolkit supports such a tool system. Our

system allows for substantial additions to manipulation and interactions through menus presented to the user in the virtual environment.[1]

Kreylos et al. also delve into interactive protein manipulation through protein construction using inverse kinematics with assistive guides.[8] Similar to Bergman et al.[7] the system allows users to interactively construct protein conformations. The usage of visualization guides and inverse kinematics provides useful aids to assist users with proteins manipulation.[8] In the future, similar assistive features may be added to our system as it matures. The underlying platform supports these extensions. Kreylos et al. noted an issue of interest in the application: the existence of difficulty in the manipulation of 3D objects on a 2D desktop display. Our system offers facilities that allow this issue to be resolved in various ways including but not limited to stereoscopic 3D, IR tracking, and supporting the addition of new interaction devices.

Moritz et al. explore the visualization of protein data sets in stereo in a CAVE and noted that the manipulation methods common for a VR environment—head tracking and controllers—were effective and necessary to see details of interest for the users.[9] The authors also recognized that 3D added valuable insight and quality to the user's experience. The ability of the user to analyze proteins and recognize details and differences increased versus traditional 2D representations. Moritz et al. use common representations including ball and stick models and cartoon models. Related visualizations of molecular surfaces, such as Connolly surfaces, and interactive visualizations of molecular dynamics, also offer substantial aids to researchers. Our system was started with a single visualization paradigm but facilitates extension to all aforementioned visualizations as well as others.

A thorough exploration of the process of creating large wall display environments is detailed by Michel Beaudouin-Lafon.[10] The details of the process serve to show others the results of his approach. Wall-sized Interaction with Large Datasets (WILD) was created by Michel Beaudouin-Lafon through an integrateive process to serve "... small groups of users who need to interact with large amounts of complex data".[10] While the big picture goal of WILD is different than our focused application, there is substantial overlap in both findings and use cases. Michel Beaudouin-Lafon identifies that large displays are necessary for aiding users performing scientific discovery —his target demographic. Users require high-resolution wall displays to clarify details, to organize vast amounts of different data relevant to the same phenomena, and to identify differences in similar data.[10] Michel Beaudouin-Lafon also promotes the creation of custom solutions to afford the developers freedom to experiment. While it will be extended in the future to other applications, our initial system focuses on identifying small differences in protein conformations similar to the use case identified by Michel Beaudouin-Lafon.[10]

Endert et al. offer insight into the impacts of large display environment configuration on user perception and tasks.[11] In order to provide an effective working environment, considerations should be made to often overlooked details such as the arrangement of monitors and type of displays.[11] Endert et al. suggests that LCDs are optimal for powerwalls (large wall display environments) due to pixel density and minimizing physical space usage, amongst other reasons. It is also identified that LCDs have prominent bezels when compared to projectors. Powerwalls in general are critiqued because they are not suited for general purpose usage but limited instance usage such as experiments, instead.[11] Selecting proper tools, tool placement, display layout curvature, user stance, and providing adequate navigation space are design considerations that Endert et al. identify as being important to creating an effective work environment. While the target application of Endert et al. is the creation of a general purpose work environment suitable for daily work, a departure from the initial goal of our facility, the insights presented still apply.[11]

In our facility, LCDs have now been replaced with LED displays in our environment but retain the same benefit profile. Our interaction mechanism and tooling has been chosen for our initial application appropriately. A glove is used to track gestures and IR cameras track body movements. There is substantial space in the area for the user to physically maneuver. The integration of body movements allows users to explore the space with wireless tools. Users are able to stand in our environment. Functionality while sitting is dependent upon the desired interactions and will be improved in the future. The arrangement of the monitors is such that a user is surrounded by the space and may use their periphery in virtual environments as opposed to recreating an environment in which document editing and e-mail are primary applications.

Similar to Endert et al.,[11] Muller et al. designed THE VVand tiled display environment but focused on stereoscopic 3D design. The target use case was the visualization of particle simulations such as molecular

dynamics, similar to those in Reda et al.[12] Muller et al. note that the bezels present an issue with LCDs but assure that the cost, power requirements, and difficulty in setup (calibration, seam alignment) of projectors offset their practicality. These reasons are precisely why our system utilizes LED displays instead of projectors; the cost of bulb replacement alone for high quality projectors is prohibitive.[13] Muller et al. constructed a two-tier cluster, using InfiniBand as the backing application network.[13] The two-tier design focuses on remote rendering, using one tier for displaying images and the secondary tier to perform the rendering.[13] By using InfiniBand Muller et al. are able to engage the rendering cluster and transfer the resulting framebuffers to the display cluster for presentation.[13] In our system there is a single tier. This is both from a budget perspective and because our intended virtual environment software communicates information about the scene, such as the user position, instead of transmitting rendered frames.

Reda et al. demonstrate that modern computational power enables the visualization of large molecular dyanmics simulations in high resolution while remaining interactive.[12] Interactivity was provided using head tracking and 6DOF devices, affording the user abilities such as exploring the simulation scene but also modifying transfer functions interactively.[12] It is common to use such tracking systems and devices in conjunction with visualizations and the benefits have been widely discussed. It is established by Reda et al. that the need for immersion in molecular visualizations is significant. The authors also present a hybrid visualization model combining volumes and glyphs into a singular visualization.[12] The union of the two visualizations allows users to identify and evaluate details presented by each visual simultaneously.

The tasks we are targeting with our system are similar in intent and nature to that of Reda et al., reinforcing the idea that immersive interaction is necessary.[12] The hybrid visualization for materials also provides a potential future use case if our system evolves to support other content areas. The hybrid visualization is used in such a way that it is a single space for the user to navigate. Our initial system exploration differs in that instead of using the common single space paradigm, it offers a basis for the separation for visualizations per screen.

Two other visualizations that deal specifically with the comparison of related data—ensemble visualizations—are presented by Phadke et al.[14] The visualizations presented are *pairwise sequential animation* and *screen door tinting*. Pairwise sequential animation utilizes spatial samples from each member of the ensemble while using attributes such as color and shape to represent desirable traits.[14] By varying each member's visibility over time, an animation is built, and it is possible to distinguish between overlapping members when played back.[14] Screen door tinting is a method where screen space samples of a reference member are tinted based on the difference between the reference sample and other member samples.[14] Phadke et al. demonstrated the need for such comparative visualizations in high energy physics, but their application is not limited to physics. Comparative ensemble visualizations are needed in many fields. Our base system presents a simple initial visualization but provides a foundation on which to integrate other useful visualizations such as those presented by Phadke et al. The ability of visualizations to highlight areas that differ between members is valuable when comparing complex conformations with minute differences.

In visualizations such as the large scale molecular dynamic simulations in,[12] viewing multiple simulations simultaneously while interacting with them intuitively could be a large boon. Users may need to have multiple simulations visualized with differing transfer functions while comparing the impacts simultaneously side-by-side. The utility of multiple displays and coordinated views is substantial, and though intuitive and natural, such layouts are not always integrated into visualizations or related facilities.

The importance of coordinated views is significant and substantial enough that Forelines and Lilien adapted a single display application to a multi-display environment with such views.[15] The work provided enhanced collaboration for visualization of large molecules. At some point, the user may become overwhelmed by the enormous amount of data and conformations presented. Likewise display configuration and other factors may influence the effectiveness of our approach, thus, user studies of these issues are the focus of future development.

Instead of a traditional single user, applications have focused on providing distributed groups interactive visualization environments for remote molecular research. Collaborative environments such as those developed by Chastine et al.[16] and Lee et al.[17] allow multiple users to explore the same space and molecules while sharing their findings and interacting with the models using data gloves, Chastine et al. recognized a multi-view system was necessary to allowed scientists different scopes of operation.[16] These collaborative environments give scientists the ability to work together despite being distributed geographically.

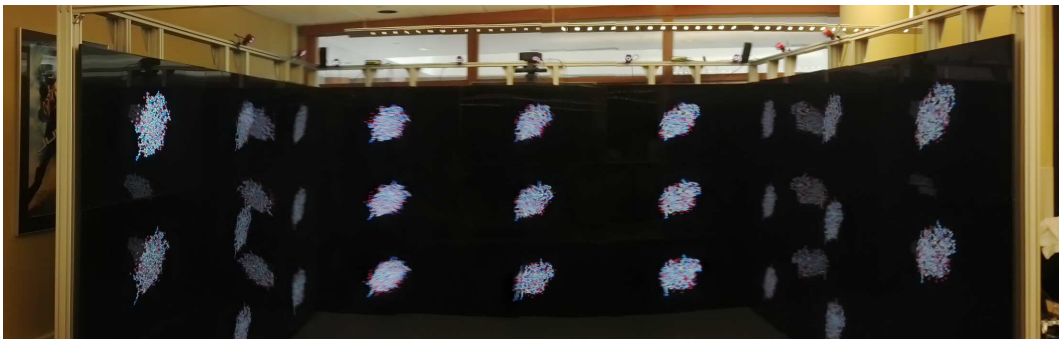

Figure 1. A full photo of the DIVE setup with the application displaying the virtual environment of proteins.

Collaborative visualizations are another area where seeing differences presented side by side, or viewing the activities of team members in one view has the potential to be a powerful tool. This is a goal of our initial exploration. The base system we have constructed does not explicitly support remote collaboration; however, it does not preclude it either. This is not a primary goal but in the future may be considered a feature if our client audience finds it necessary. Visualizations have also extended outside of the traditional desktop environment into extremely high resolution facilities and into the virtual reality arena.

In order to achieve high-resolution display technologies, the common solution trends toward using tiled arrangements of displays using different shape paradigms. For example, the Reality Deck introduced by Papadopoulos et al.[18 19] utilizes a rectangular room layout to achieve a display with a combined resolution of 1.5 billion pixels. Reda et al.[12] present a large-scale visualization of single molecular structures using a tiled, high-resolution display developed by Febretti et al.[20] Edmiston et al.[21] presented a touch-based interface for virtual environments using large-scale tiled display framework with a quadratic footprint.

Using virtual environments (VE) has proven to be extremely beneficial in many research areas outside computational sciences.[22] Targeting immersion, VEs have ushered in another level of interaction with proteins and the analysis process. The importance and benefits of improved navigation, visualization, and manipulation are well recognized in the protein domain[8].[9] Using the high interactivity of VEs, environments in which users may create proteins with real-world constraints such as collisions and using intuitive tools based on inverse kinematic algorithms have been established.[8]

Virtual reality environments have been leveraged to construct applications that enable the interactive design of drugs, citing virtual reality (VR) as offering substantial strides over standard visualization configurations.[23] Protein docking, the process of fitting together proteins, has been made interactive using a VE, taking advantage of humans' innate abilities to solve fittings tasks and even integrating haptic feedback[24].[25]

Many of these molecular visualizations are motivated by proteins in some regard. However, specifically targeting protein structure prediction comparative visualizations is uncommon for visualization environments though the field is an immediate candidate to experience exceptional benefits from such developments. A visualization often provides an aid by which the user may determine features and flaws identified through differences with known or correct structures.

Many research papers present differences by showing images side by side in a grid. This simple but effective mechanism, when combined with natural interfaces, presented on multiple, high-resolution, large displays and other virtual environment elements, becomes a significant tool. This manuscript provides the implementation details of such an application foundation. By creating a significant foundation with an initial visualization we have established a baseline which we can extend into other use cases. The use case in this application of the system is focused on assisting in protein structure comparisons.

3. METHODOLOGIES

The system is composed of multiple software parts and run on hardware which was already covered. For ease of understanding, an overview of the implementation is provided, followed by specifics for both the visualization elements and interaction mechanisms.

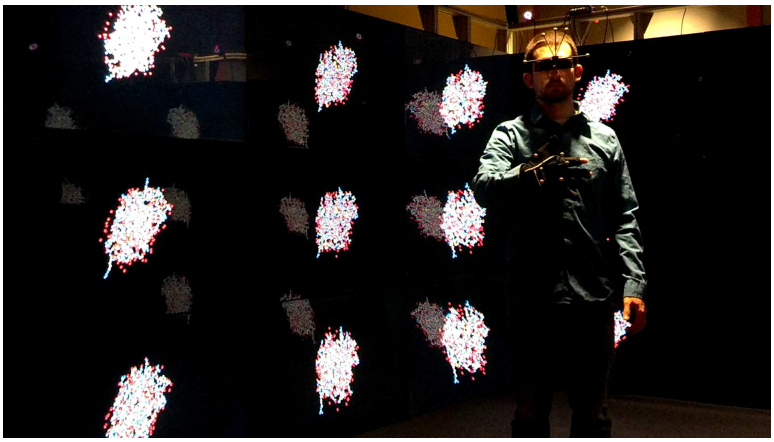

Figure 2. The reflector sphere setup during comparison. The spheres are used by the IR tracking system to track both the users head and hand movements.

3.1 Overview

The implementation uses open source virtual environment software, Vrui VR Toolkit,[1] in conjunction with OpenSceneGraph[26] to manage the visualizations, associated assets, and provide the backbone for the integration of input devices. Each display shows a single protein conformation as input by the user at initialization. The system also supports and uses active stereoscopic 3D rendering to increase user's awareness of spatial relations. Head tracking integration is also provided by the toolkit. Standard IR tracking via a Natural Point OptiTrack[2] system using reflective spheres on a set of 3D glasses determines the users view direction in order to select a protein conformation. An AcceleGlove[3] a data glove using accelerometers, is used to control the manipulation modality. An appropriate library was developed to interface with the glove that also performs static gesture recognition using LibSVM.[4] The users selection of an interaction modality—panning, rotation, or scaling—allows the users movements to modulate conformations' orientations through arm movements.

3.2 Multiple Views Visualization

The environment used for this application is made up of 27, 50" LED displays, operating at resolutions of 1920x1080, arranged in 3 adjacent walls. While the 3 wall layout provides users with a surrounding experience it also minimizes the amount of walking distance a user must go to look at different structures. When using a single wall or curved wall a user may need to back up or walk further and as a result their context for comparison may suffer. Each wall contains 9 displays arranged in 3 rows of three monitors. The displays support active stereoscopic 3D. The displays are used in 3D mode to enhance the users judgment of spatial relationships. This mode may be disabled. To control the displays, a cluster of computers is used with a master node and one computer driving a single wall of displays.

In order to support the entire wall with only a single computer, a setup of three ATI FirePro V7900 are used. Each graphics card has four DisplayPort outlets. Using an active DisplayPort to DVI adapter, the displays are connected to the graphics card. This allows one column of displays to be driven by a single graphics card, thus allowing one computer to control an entire wall of displays. Since the displays utilize active stereo glasses, all displays must be synchronized perfectly or otherwise increased ghosting will be apparent. Therefore, all graphics cards between the master and nodes driving the walls are synchronized using ATI's S400 sync card.

Since the active shutter glasses used by the displays are RF-based no syncronization or any special care has to be taken with the infrared-based tracking system unlike with some IR-based shutter glasses where interference can occur with tracking cameras. A configuration of eleven OptiTrack Flex 13 is used for tracking the head position and hand movements. These tracking cameras are mounted on the top perimeter of the aluminum framing that supports the displays.

The displays are part of an immersive virtual environment and are managed using the Vrui VR Toolkit.[1] Vrui VR Toolkit provides many useful facilities for virtual environments, especially in the areas of system

independent configurations and input device management. Using the toolkit, the physical environment enclosed by the displays is managed as a coordinate system and is transformed into world coordinates for visualizations. Access to such transformations makes arranging the protein conformations such that a single protein is centered on each display possible. Moreover, when environments are properly configured with the toolkit an application's portability to other VE facilities is greatly increased.

Using a single structure candidate per display is an intuitive way to separate each candidate for the user. Such a distribution also reduces the impact of the displays bezels by using them as visual boundaries instead of interference. This way, the user may instead utilize such boundaries as opposed to being forced to ignore them, mentally correcting visualizations spread across the boundaries. Each display provides a perspective projection window into the visualized space, allowing a more natural and visually correct presentation of the structures. The protein configurations reside within the same space as well, meaning that if it is desirable the user may move the molecules closer together, onto the same screen, or scale a molecule across multiple screens. The management of the candidate conformations data is performed using OpenSceneGraph.

In this case, OpenSceneGraph provides a scene graph implementation for managing virtual environment visualization assets. This enables easy programmatic interaction with models, textures, physics, shadows, and other desirable elements. In this implementation OpenSceneGraph is used to ingest various conformation model file formats, position each model accordingly to fit within a respective displays' boundaries, and for managing the user's transformations of each structure. The integration of the two allows more file formats to be used and with further integration of the physical environment parameters will enable extensive flexibility when switching between visualization facilities.

Figure 3. The AnthroTronix AcceleGlove used for collecting gesture data.

3.3 Interaction

The physical environment used for display information in the VR toolkit is also the space that is monitored for IR tracking. Using the integrated head tracking facilities Vrui VR Toolkit offers, body tracking is utilized for user inputs. The user wears glasses that have reflective tracking spheres mounted on them and any movements are subsequently accessible by the visualization. The user is able to look at a protein structure, a virtual ray is generated based on the users viewing direction, and a point of intersection with the structures bounding spheres is calculated. Using that point of intersection, the protein conformation is selected for manipulation and has the actions of the user applied to it as transformations.

Protein structures are manipulated by gestures and body movements *in lieu* of a mouse and keyboard as the latter is not well suited for virtual environments. The user has their view tracked using IR sensors, and when looking at a molecule, the user may control that specific molecule using gestures and arm motions. This view is tracked by a NaturalPoint OptiTrack[2] system consisting of 11 cameras.

The cameras are mounted above each of the display walls and provide heavy coverage of the area between the walls. Reflective spheres mounted on a pair of active 3D glasses enable the tracking of the user's head,

Figure 4. The NaturalPoint[2] OptiTrack Flex 13 camera used for body tracking.

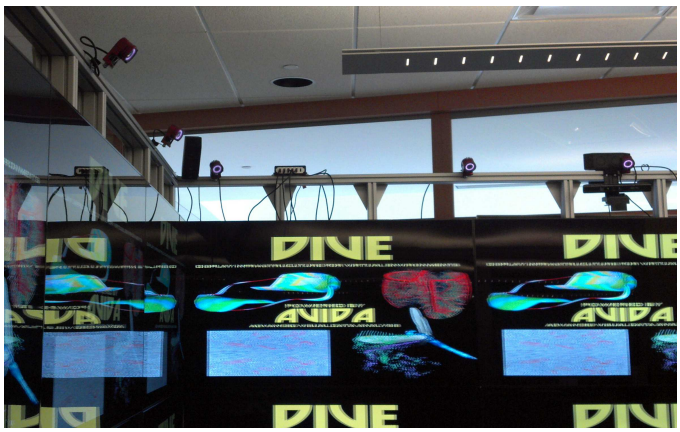

Figure 5. Multiple NaturalPoint OptiTrack Flex 13 cameras mounted on the DIVE.

specifically position and view direction. Spheres are also attached to the data glove in order to track the user's arm movement. In addition to tracking the arm movement, the user's hand gestures are monitored.

The user chooses a manipulation modality, rotation, panning, or scaling, by making the respective gesture for each modality. The software developed for the AcceleGlove, using libSVM, identifies the user's static gesture. A switch to the manipulation modality in the visualization takes place based on the gesture. While making this gesture, the user may move their arm to rotate the molecular structure they are viewing. The gestures used in this implementation were as follows: an open hand with fingers fully extended for translation, a thumbs up gesture for rotation, and a closed fist to avoid any manipulations from taking place.

The data glove software was constructed to communicate with a wired or wireless version of the data glove and extract data from it while offering access to its data reporting options. The AcceleGlove ships with Java software. The software performed static gesture recognition. The software contains a developer API which allowed users to interact with the gloves from their own software. The majority of visualization software in our lab utilizes C++. Instead of needing to write a wrapper or some other mechanism to interact with our applications and integrate into build processes, in a previous effort we constructed a C++ API to interact with the AcceleGlove. This was possible because the AcceleGlove also supports a serial API.

The data glove library is required to perform gesture recognition, and the chosen method is to use Support Vector Machines (SVM), specifically the implementation provided by libSVM.[4] Using scaled input data from the glove acceleromters as features, a SVM model is built using libSVM. The model and scaling information is then exported to a set of files. The model files are read in by the AcceleGlove library at application initialization and recognition of static gestures. Based on the position of the glove's accelerometers, static gestures, such as the

hand with fingers fully extended, are then recognized and reported in real time.

The library is integrated into the visualization environment as a tool for the Vrui VR Toolkit. By using a tool implementation, the user may choose to enable or disable the gesture based input using the menu system. The user may also choose to use another method, another tool, to use to explore the virtual environment. This also enables multiple gesture sets to be presented as differing tools, enabling the user to choose which set of gestures and which manipulations are desirable at the moment.

4. RESULTS AND DISCUSSION

The implementation outlined resulted in a fully functional visualization environment system. Users are able to provide the paths of models to the application via the command line. Upon launch, the models are automatically distributed, centered on each display. The user may then navigate the space using traditional virtual environment controls or gesture-based controls to continue exploring the models. The advantage of this layout becomes extremely apparent versus other designs and is quite intuitive. Application experts tested the system and provided valuable feedback, a process that will not only be continued but extended as our project progresses. Users noted these benefits and were able to readily manipulate the different conformations once informed of the predetermined gestures and their bindings. Users reported that the environment was quite suitable for the target application. However, some desirable modifications were readily identified.

Changes such as providing a mode in which the molecules are completely separated and do not visually exists within the same scene would be of great use to the user. Likewise, adding visual cues as to which molecule or monitor was being utilized and allowing users to resize visualized structures assigned space to more or fewer screens were found to be desirable. Another small nuance that was detected was the users need to wear the IR trackers and glove, being able to perform tracking and recognition effectively without physical accessories would be a great stride for natural usability. IR tracking of the gloves movements suffered on occasion from the user rotating their hand in a natural manner but blocking some of the reflective spheres. It was found that while the user was navigating, more intuitive gestures would also be useful, which is an existing feature of the data glove library and already readily available to users.

Gestures are flexible and able to be rebound by the user without changing the application. The library created to interface with the data glove and perform gesture recognition applies a mapping from the gestures to text values. These text values are entered by the user during recording and may be later edited through a text file. When recording new gestures if the same text mappings are entered, the application will use these new gestures at runtime for manipulation operations. This feature adds to the flexibility already present from the Vrui VR Toolkit.

The Vrui VR Toolkit enables users to establish virtual environments in many different configurations. More importantly, once the configuration is complete, applications based on the toolkit are able to utilize the available configuration parameters and leverage the automatic environment initialization to create portable virtual environment applications. In this manner an application utilizes the values available in the toolkit configuration files may be moved to other environments while remaining effective without modification. An application written to function in a multi-projector environment may then be moved to a desktop and remain functional identical—especially if the input devices in the two environments are identical.

The environment is not only useful for molecular visualizations but other visualizations as well. Any type of work that requires multiple contextual tiers to be visible at once, especially those requiring comparison, may be well suited to this type of environment. The comparison of medical imagery such as CT or MRI data from patients at different time frames is one example. A physician may examine scans taken over time and explore the data sets visually for differences that may have been missed by automated algorithms. The visible details in a high resolution, large display environment that small change may engender further examination. While scanning resolutions also impact visible details both screen and scanning resolutions undergo constant advancements that may increase available resolutions. One example is the recent emergence of more cost effective "4K" monitors that use a 3840 x 2160 resolution.

While the environment is useful for many applications in its current state, instead of presenting an end product this is the potential beginning of a virtual environment toolset for protein analysis. We specifically

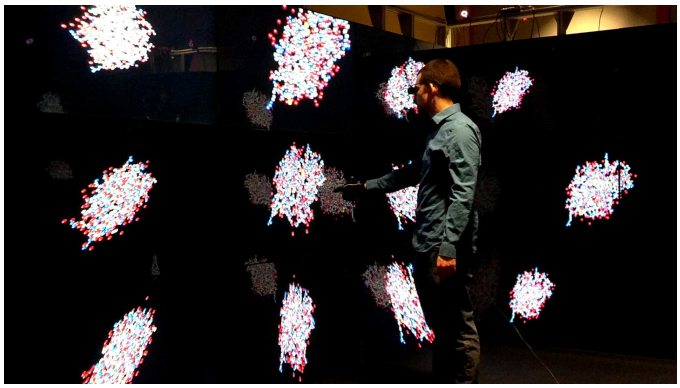

Figure 6. A student using the implemented system to identify a difference in presented conformations.

focused on conformation comparison as it is a useful segment of a larger project and provides a relevant use case. This is however just the beginning of the system, a basis on which we can build the rest of our system. The exploratoration has resulted in a base system that is a good foundation on which to base further development. Regarding further development, there are further features and development that may be of use in different applications.

5. FUTURE DEVELOPMENTS

There are many enhancements that could prove useful for the presented software, covering visualizations, input files, window management, and interaction. A select few are mentioned in this section and some further applications are noted.

The Vrui VR Toolkit offers substantial information about the configuration of the physical environment, translating the information to generate appropriate visualization space. This information may be integrated and leveraged further to provide more autonomous initialization of a comparison environment. Optimally a user would only need to configure the virtual environment—a condition that is already mandatory. The application can then access the existing configuration and automatically perform the arranging of the protein conformations. This development is being actively pursued as it is such a natural and beneficial extension in all use cases, as is the display of the currently active manipulation modality.

A few potential visualization improvements were revealed while performing this study. A visual cue reflecting which gesture is currently being recognized or which manipulation mode is currently active would prove useful. Due to the inaccuracies associated with gesture recognition, for effective use it is important to maintain a sense of the manipulation modality that is enabled. Without this context the user may feel as though they are making a specific gesture but the recognition system may disagree and without visual confirmation, the user must determine the enabled mode by direct testing, changing the current orientation of the conformation.

The perspective projection of the molecules provides a realistic visualization of the modeled conformation. However, the distortion present from the projection may be undesirable in some cases and instead a orthogonal projection preferred. Adding the ability to switch between these two projections would be useful, as would the ability to switch between a single unified conformation space and separate spaces per structure.

Another useful visualization modification would be the ability to dynamically adjust the area, whether by screen or physical units, that a visualization takes up. A user may then explore a single molecule using the full resolution of a wall, or the entire environment, and once done switch back to comparing multiple conformations. Alternative rendering modalities would also be another improvement, specific to molecular visualization, such as enabling a view of secondary or tertiary structure, or Van der Waals surfaces. Adding other visualizations is also being actively pursued in order to further this base exploration.

As with many VR systems that require the user to move around, fatigue is of potential concern. In our system we have multiple potential points of fatigue. The user currently stands during conformation comparison. Allowing the user to sit down may be necessary to avoid fatigue, in which case body tracking may then need to

be toggled on or off. Similarly, the user points and uses hand gestures. At some point this may result in hand, wrist, arm, and shoulder fatigue. There may be other fatigue factors as well. A formal user study is necessary to evaluate the impacts of fatigue.

While this manuscript targets the application use case of molecular conformation visualization, it is not the only use of this software. Any set of models may be explored in the manner described once the data has been converted to the correct modeling format. By utilizing OpenSceneGraph the number of formats supported by the system is non-trivial and includes common formats, such as Collada (.dae) and Wavefront (.obj). Therefore a user may import architectural models and perhaps visualize changes over time or an animator may view animation frames in series, with a frame per display. There are many other potential applications which could be explored and due to the abundant usage of side-by-side comparisons, benefit greatly from such software.

6. CONCLUSION

Effective, manual, protein structure validation via comparison of multiple candidate protein conformations requires both proper visualization and manipulation. Desktop systems are often improperly equipped to offer the necessary high-resolution, highly detailed views of many protein conformations at once. Virtual reality environments, such as a CAVE, offer high enough data resolutions to provide. Generally, multiple display facilities are utilized as an immersive single view into a scene. With some careful manipulation of the visualized scene, such visualization paradigms lend themselves to an interactive comparison of multiple protein structures. In such an environment, alternative interface methods such as gestures and body tracking prove to be intuitive, natural, and are arguably necessary for effective interaction. We have constructed a system that combines all of these elements to provide a foundation for further visualization development.

We detailed the base system developed with a focus on assisting conformation analysis. We highlighted the interaction mechanisms used, as well as the visualization paradigms accessed, in this initial, foundational application. Areas in which the system could be improved and potential future research areas are identified. Applying such a system to bioinformatics research could provide users performing protein conformation identification with a decisive advantage over traditional desktop methods.

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