Augmented Tangible Interface for Molecular Biology Group 2, HCI Winter School

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ABSTRACT

Augmented Reality and Tangible Interfaces have multiple applications in molecular biology. Laboratories in the research and academia field make use of them to visualize complex molecular structures and more and more complex data sets, while other uses include the illustration and teaching to students of molecular biology. The opportunity not only for visualization of the structural models, but direct manipulation, offers a new method of developing a deeper understanding of complex models and relationships between molecules. Augmented Tangible Interfaces have seen a surge in development and research in recent years, and see a promising prospect of further development with improving technology. In this literature review, we go over papers that propose solutions to the introduction of a whole new way of interacting in a precise science domain.

1 INTRODUCTION

In the context of molecular biology, researchers have introduced new technologies that help representation, collaboration and manipulation of virtual molecules. This paper addresses the current state of the art in this approach, and leads to the future possibilities offered by a growing research subject.

The Covid pandemic has shone a light on the importance of understanding and manipulating the smallest elements, in order to react to and handle nature's unpredictability. In recent years, research has made strides in the development of virtually enhanced environments for macro/micro biology and virology. Those technologies offer a whole new range of possibilities in many completely different domains, and this paper addresses the state of the research regarding these technologies applied to the domain of molecular biology. Those applications are aimed either at teachers or students for an academic purpose, or researchers. The importance of the targeted user group goes to show what kind of impact the introduction of such technologies could bring to our world.

An opinion that is common to all the research teams who worked on the articles we reviewed, is that, when it comes to handling 3D objects, the more accurate the representation of the object, the more efficient the interaction. There already exist 3D models used in classes to represent molecules, but the physical limitations are quickly met. This is where virtual representations come in, removing the limits of the size of the molecule represented, whether the user has enough 3D models to represent the whole molecule, etc.

However, moving from physical to virtual also generally means removing the 3D representation, as the visualisation will be operated on a 2D screen. Which is exactly what VR and AR address, as they immerse the user in a virtual environment, giving them the possibility to apprehend a model rendered in 3D. The works presented in this literature review aim at creating a tool to overcome this lack of 3D manipulation on virtual representations of molecules.

2 RELATED WORK

Here we focused on three different approaches taken by the research teams : the *Application in Education* is about the solutions thought of to make the learning more fun and engaging by using new means of teaching. The *Application in Molecular Visualisation and Manipulation* can contain papers targeting both students and researchers, but is particularly about reproducing, visualising and manipulating specific molecules in a new kind of environment. The *Development and Adaptation* explains how some older papers, in which the applications of their discoveries remained blurry, can, and have, been applied to the field of molecular biology today.

2.1 Application in Education

The environment in which most people are introduced to molecular biology is school. If augmented interactions were to become widely spread in the domain of molecular biology, school would need to be considered as of the utmost importance. Research teams have been working on devices that more or less fit public school's budgets to bring a new kind of education to students.

As a good basis for what's to follow, it is important to cite Goddard et al. [7], who have investigated the question of whether virtual reality can be useful for visualizing and analysing molecular structures and three-dimensional (3D) microscopy. They explored the use of VR in studies of drug binding to proteins, effects of mutations, building accurate atomic models and other. They developed three VR applications: *ChimeraX* to analyse molecular structures and data, *AltPDB* for collaborative discussions, and *Molecular Zoo* for teaching young students the characteristics of biomolecules. The conclusions the researchers draw include the suggestion that the ability to perceive spatial relations is greatly enhanced in VR compared to conventional displays. VR advantages are described as immersive visualization. The researchers also elaborate on drawbacks of VR applications, namely the heavy and bulky physical properties of available headsets. Goddard et al. [7] conclude that current devices provide technological challenges that remain to be solved to prove their worth. Educational applications avoid most of the technical difficulties, and are suggested to have the greatest potential for making production-quality VR applications in the near term. These conclusions are shared by Safadel et al. [15], who explain that students tend to prefer using a novel way of receiving and using information. The results of their experiment clearly show that using virtual environments to visualize and manipulate molecules for instance, worked better than with a common desktop interface. It also showed that results were encouraging regarding the implication and seriousness of people with low spatial ability. In a domain that evolves around spatial recognition and uses spatial frameworks, including less inclined people is also an important step.

Beyond determining whether or not AR and VR can be useful in teacher's classes, Garcia-Bonete et al. [5] examined the possibilities that AR and VR application offer in an educational context. Their research yielded the conclusion that this kind of visualization extends the student's toolbox for interacting with content in structural biology and adds immersion. However, Garcia-Bonete et al. [5] also remark that technology must evolve and mature further to become more user-friendly in the field of pedagogy. AR and VR cannot always be completely interchanged, but participants rated them similarly relevant. Garcia-Bonete et al. [5] also issue a warning to be careful in implementing audio narrative during VR/AR exercise, and not overload the capacity of the wearer in an unfamiliar environment.

Taking into account some of the previous conclusions or even some earlier ones that do not appear here, applications of AR for education were created by research teams : one of those is presented by Vega Garzón et al. [19] in their research on using augmented reality to teach biochemistry to students. Their experiment shows the potential of their Augmented reality Application *Augmented Reality Metabolic Pathways (ARMET)* to improve the assimilation of biochemistry abstract concepts. Students are able to use AR to manipulate 3D molecules in real time. The results of the experiment show that ARMET helps students develop skills such as collaborative learning, peer review and visual literacy skills, which are essential characteristics for interpreting molecular models and metabolic maps. ARMET also allows teachers to systematize criteria and indicators, and track students' progress and performance in real time.

Another application is the proposition of Sung et al. [18], who remind us that using 2D support to represent 3D objects might not be the best way to learn. They created an app based on AR to help students apprehend in a more complete manner the intricacies of molecular models. The main limitation was the comparison to more advanced tools that have more options and fit professional users. However, they successfully implemented their design in a classroom for a few years and were able to confirm that overall, students enjoyed using it because of how easy it was to understand. And also because it helped them in a broader sense to improve their spatial recognition.

Increasing the understanding and ease the learning of chemistry for students as well as speeding up the process of designing new molecules for scientists, that is what the team of Maier et al. [10] tried to do by designing an AR application. By manipulating a tracker, the user can change the position and rotation of the molecule. It is also possible to use multiple trackers to create links between the molecules and create a new one. The molecules' rotation will adapt due to the forces between the molecules. This approach could be useful for teaching to help students to visualise the molecule in 3D and in science to help them speed up the process of developing and designing new molecules.

2.2 Application in Molecular Visualisation and Manipulation

Databases around Molecular Biology keep growing as the structure and process models become more complex, but accessing and manipulating digital information is a critical issue for research in molecular biology. That being said, the interactions used to study these models have been mostly limited to mouse and keyboard.

Gillet et al. [6] adapted an augmented reality system to allow 3D representations generated by the *Python Molecular Viewer* to be overlaid upon a tangible molecular model. Their system was prototyped in an inexpensive portable form, using off-the-shelf components and they affirm that the system can be integrated to classrooms for a reasonable cost. And cost is something that is recurrent in this field, to virtually reconstruct a physical molecular model, cheaper solutions using basic hardware are often preferred to specific and very expensive products.

Martinez et al. [11] present one of them. Basing their work off of a simple RGB camera, they presented a light device to scan a molecule by moving the device around it. This technology relies on 2D point extraction and association to form on the screen as much of the molecule as possible. They then fill in the remaining atoms that they couldn't find with the camera by using the biological knowledge of a database to infer on the nature of the physical molecule.

With the same goal, which is to facilitate the creation of virtual 3D models on computers, Vincke and his team et al. [20] built a tangible system. They based it on the [Peppytide molecular model] and embedded sensors into 3D printed models of atoms. With these tools, the users can manipulate them to create a complex molecule by interacting with physical objects. The paper explains how they built their system and its components.

Another way to represent and study these molecules would be through physical models as 3D printing now allows for these molecules to be recreated physically. Chakraborty and Zuckermann [4] take this one step further by constructing and validating a flexible, scaled physical model of the polypeptide chain that accurately reproduces the physical behaviours of the chain. Their creation, *Peppytide*, accurately depicts bond length and bond angles, the short-range rotational barrier imposed the backbone dihedral angles and the long range stabilization which results from hydrogen bonds in the backbone. A particularity is that their model is foldable which therefore allows an easier understanding of the intricacies of bipolymer chain foldings and unfoldings.

Chakraborty and Zuckermann [4] note that *Peppytide* could play an important role in the teaching of these concepts since polymer chain folding is a fundamental of architectural concept in biology. Gillet et al. [6], on the other hand, explains how they plan to develop a spatially tracked data probe that is supposed to enable interaction with both physical and virtual models. The users would be able to point at the tangible model and receive visual feedback on the virtual one. They also plan on developing methods to allow markerless spatial tracking and thus reducing the prerequisites for the system while preserving the benefits of 3D visualisation.

To learn and understand spatial reasoning of molecules, students are using 2D models, 3D handhold models and computerized models. The research team of Behmke et al. [1] developed a AR application on smartphones to provide a new way of learning to students and enhance their experience. They carried out an experiment comparing students learning with the app and students learning with handhold models. The results obtained show that they were not a huge difference between the two methods. However, one of the most frequent feedback was that the application showed a lack of interaction.

Salvadori et al. [16] state that using 3D representation for objects is more efficient than using 2D, but they add that the transition from one to the other has to be as smooth as possible. This was the key motivation behind the design that the team proposed, and named *Caffeine*. This VR tool, besides being an immersive solution to visualize static molecules, also focuses on rendering and analyzing trajectories by implementing "key-frames". Hence being suitable for more than just representation and manipulation, which is what research teams and professionals might be more eager to use.

For these potential users especially, the context is as important as the molecule itself. To allow a large amount of information to be displayed without overwhelming the user, Kingsley et al. [9] created a Virtual Reality application, *Nanome*, in which they focused on the collaborative aspect of work, and on the manipulation of molecules. This application is based on an exhaustive database of the known molecules and is addressed to research teams.

The collaborative aspect is also sought out by International research facilities who chose to examine the application of Augmented reality devices available on the market in the context of molecular biology. Müller et al. [12] have investigated the AR headset *HoloLens*, distributed by Microsoft, and examined its opportunity for immersive analytics in molecular visualisation. An important factor for good performance and a comprehensive analysis of molecular data in AR is the rendering speed. Müller et al. [12] evaluated the capabilities of the *HoloLens* using publicly available protein data sets, and conclude that different methods give maximum performance, depending on data set size and image footprint of the final rendering. Regarding future application of AR, Müller et al. [12] suggest the extension of their prototype into a collaborative immersive analytics application for different areas of bioinformatics. They also suggest the implementation of a GUI into the current speech-based user interface, to create an environment in which collaboration on the same project is feasible.

2.3 Development and Adaptation

Collaboration is a subject that is increasingly interesting as it improves efficiency. That being said, the ways to reach this collaboration through computers are still being discovered. Billinghurst and Kato [2] noticed that Virtual Reality, while it appears as a natural medium for computer supported collaborative work, actually separates the user from the real world. Thus, the Mixed Reality approach, by overlaying virtual objects on the real world, the users can see each other, the real world and the virtual images at the same time. The authors go on to present multiple examples of collaborative body that were tested and that prove that these Mixed Reality interfaces improve collaboration in a natural manner. The reason being that gestures and non-verbal behaviours used in face to face collaboration could very easily be adapted into a Mixed Reality Collaboration. Billinghurst and Kato [2] also explain how well Mixed Reality interfaces allows users to interact with virtual objects through the use of real world objects, and thus enhancing the existing real world objects.

However, sometimes the real world objects can be enhanced without the help of Mixed Reality. Boncheva et al. [3] describe a way of creating a spontaneous folding of flat elastomeric sheets into free-standing 3D objects. They explore a new way to form 3D objects that combine the advantages of planar microfabrication with the advantages of 3D self-assembly. The pecularity of these 2D sheets is that they have integrated electrical circuits printed onto them, creating a closed circuit as soon as the sheet has self-folded into its 3D shape thanks to magnetic dipoles. Boncheva et al. [3] do note that more research is needed to clearly define the shape of the 2D cut, the placement of the magnetic dipoles and the mechanical characteristics of the membrane to allow a stable 3D structure.

This notion of self assembly was later put to the test. In their research on viral capsid assembly, Olson et al. [14] examine the self-assembly of the viral structures. The study shows that the structures assemble themselves within time in optimal conditions, even when more than one type of assembly unit is present. The researchers develop a physical model, as well as a digital model to replicate self-assembly of viral capsids on molecular scale.

Instead of using keyboards, mouse and tactile surfaces which are 2D interfaces to animate 3D character articulation, Jacobson et al. [8] designed a tangible input device composed of interchangeable, hot-pluggable parts . The user can quickly assemble a custom combination of joints to recreate the skeleton of a 3D articulated model. Different sensors are located in the parts of the model to detect rotations. The paper showed that by using this tool, users have less work to do. We can think about using this technology to apply it to molecule manipulation.

Furthermore, when talking about manipulation, one of the most frequent and important problems encountered in tracking systems is the occlusion. Smith et al. [17] designed a system that is able to track, with high precision, complex hand movements despite occlusion . This work could be applied to the physical representations of 3D molecules. During manipulation of atoms on a tracking system, the scientist could rotate the molecules without facing a problem of occlusion because of their hand, also the precision of hand tracking can be used to add interaction in the system.

Olson et al. [13] describe the development of structural molecular biology visualization from past to present. He names three functions that the process of visualization itself can aid in: Synthesis, Analysis, and Communication. His view of visualization implies its ultimate impact to be insight and understanding of complex models. He describes the development of technological advances over the years, and how it has shaped the visualization in molecular biology. While in the earliest days, physical models were used most commonly to demonstrate interactive three dimensional models, in the 1980s more and more structural biology and molecular graphics applications and innovations were developed. Currently, with over 130,000 protein structures freely accessible in the Protein Data Bank, and high definition colour displays accessible more than ever, we are able to utilize this technological advancement in the process of visualization. He further concludes that techniques today are being developed by multiple communities from different and diverse backgrounds. While a challenge for the field is how to best take advantage of all possibilities, the approaches available continue to evolve and become more complex. He sees Artificial Intelligence as a field of great prospect especially in regards to pattern discovery and image interpretation.

3 CONCLUSION

We proposed an overview of the current research on the use of tangible interfaces for molecular biology. Given the relatively recent development in the domain, the solutions offered all have some drawbacks and only have a limited interest. Even though they could very well be used in specific research labs for instance, it seems unlikely that one of them becomes a norm in this domain. The main reasons why were mentioned by some of the papers and are the guidelines for future research teams. The most frequent ones are the following : the cost of the device, the portability and the other discomforts brought by wearing a head-mounted display for instance. The ability to collaborate is at the heart of research, and still needs to be enhanced, especially in times where people can hardly meet and teams could use an "off-site" device such as the VR ones proposed in these papers.

However, as the development of this kind of solutions relies on the improvement of AR and VR tools, which is a growing field quickly evolving, we can expect many new propositions in the coming years. Hence addressing the limitations current solutions have and solving problems they may have risen in the meantime.

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