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Technology Report

Real-Time Interactive Simulation and Visualization of Organic Molecules

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ABSTRACT: Three-dimensional visualization of molecular simulations in virtual reality (VR) is an emerging teaching tool in chemical education. This work describes a VR application which can generate a 3D molecular dynamics (MD) simulation from arbitrary molecular structures and renders that MD simulation trajectory on a VR headset in real-time. This system uses the ZeroMQ (ZMQ) message passing framework for multisimulation to multiclient VR visualization of MD simulation. All MD simulations are done in the HOOMD-blue simulation engine, and the graphics for the VR are rendered in Unity3D. The key feature that sets this software apart from previous 3D viewer programs is the real-time simulation and thus the ability to manipulate thermodynamic variables like temperature on the fly. This allows viewers to build an intuitive understanding of the effects of thermodynamics state variables in a hands-on way. This application was used as a pedagogical tool with high school students, and the curriculum used, along with outcomes of the activity, has been presented here. This application can provide an interactive tool for teaching thermodynamics and statistical mechanics, and even as a diagnostic tool for MD simulations for research purposes.

KEYWORDS: *First-Year Undergraduate/General, High School/Introductory Chemistry, Graduate Education/Research, Curriculum, Laboratory Instruction, Collaborative/Cooperative Learning, Hands-On Learning/Manipulatives, Computational Chemistry, Molecular Modeling*

INTRODUCTION

The role of laboratory work in chemistry education has been long-established with the aim of helping students develop critical thinking skills, a problem-solving ability, and interpretation skills, along with a conceptual understanding of scientific theory and models.[1−4] However, some fundamental concepts in chemistry like chirality, stereochemistry, molecular thermodynamics, etc. are inherently abstract and theoretical in nature and require students to develop visuospatial skills (the ability to explain physical phenomena using molecular representations) to fully understand these concepts.[5] A mental picture of atomic-scale phenomena is essential to develop this skill, but there is no microscope that can provide a movie of atomic-scale phenomena in general. This makes it difficult to design lab activities to teach molecular concepts and help students connect them to macroscopic phenomena.[6,7] Computer generated visualizations can serve this purpose and are regularly employed in chemistry courses to build students' intuition about atomic effects. Physically accurate molecular behavior can be generated with first-principles simulations, and visualizations of such simulations have been in regular use since the mid-1990s.[8−24] These visualizations can be instrumental in making abstract concepts accessible and building understanding of microscopic chemical phenomena in both students and researchers alike.[25−30]

Until recently, visualizations were inherently limited to 2D projections of 3D chemical systems, due largely to the constraints of available display technology. These 2D displays result in the loss of some spatial information on molecules. With the recent advent and popularization of virtual reality (VR) and augmented reality (AR) technology, it is now practical to achieve true 3D graphics at a practical cost. (Note: Here by "true" 3D graphics, we mean graphics that can be manipulated or interacted with by a user moving or manipulating an object in 3D space, rather than traditional point-and-click manipulation methods, like computer mice or touch screens.) AR/VR provides a perception of depth that may improve understanding of inherently 3D concepts like dihedral angles, chirality, and crystal structures. Due to it being a fully immersive environment, VR also allows students to interact with the simulated systems and get feedback based on their actions.[31] This facilitates spatial ability in students that enables them to draw a connection between chemical models and real-life phenomena, which they often struggle with.[32]

The AR/VR tool for visualization of concurrent molecular dynamics (MD) simulations described here is called SimView. SimView can be used as an AR or VR tool, depending on users' choice and resources available, since the graphics are rendered through Unity[33] which supports multiple AR/VR platforms, including Google Daydream and Cardboard, the HTC Vive, Oculus Rift, and Apple iPhone (ARKit). Here, SimView is described as a VR tool because Daydream VR headsets were used with Daydream-compatible smartphones for the educa-

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tional activity. Other AR/VR methods of visualizing chemical systems and simulations already exist,[34−37] but SimView differs from them in a few key ways. The primary purpose of all these tools is visualization, not necessarily interactivity or collaboration. The goal of this project was to create a tool that is collaborative and interactive to be used as a kind of VR laboratory activity. Interactivity requires an ongoing MD simulation, to allow for user input to be taken into account (e.g., changing the system pressure). Collaboration requires concurrent views of the same system. SimView uses Unity-based AR/VR software, along with a low-latency multiclient network model implemented with the ZeroMQ[38] (ZMQ) message passing library to visualize an ongoing simulation that can be viewed concurrently by multiple users in the AR/VR space. Thus, SimView has all of the aforementioned criteria for suitability for collaborative education. Table 1 shows a side-by-side comparison of SimView and other AR/VR visualization methods. Note that this messaging and simulation code can be combined with other visualization methods, and this work should not be taken solely as another competing method for visualization in AR/VR. As seen from Table 1, Narupa has functionality similar to that of SimView, the difference being that Narupa's technology targets VR headsets while SimView targets phone-based AR/VR.

After submission of this paper, Google announced the discontinuation of manufacture of their Daydream VR headsets, but the existing Google VR apps will still be supported on phones.[39] Since our initial activity was performed with Daydream headsets, we include pricing information in Table 1 to reflect this. However, since our software is built with Unity, it can still be used with other Unity-based VR or AR technologies, e.g., smartphones alone for AR viewing.

Table 1. Comparison of Available Molecular Dynamics Visualization Tools

System	VMD[8]	Ovito[9]	UnityMol[21]	Narupa[37]	SimView
Real-time	×	×	√	√	√
Manipulate simulation	×	×	√	√	√[a]
Concurrent viewing	×[b]	×[b]	×	√	√
Arbitrary SMILES	N/A[c]	N/A[c]	×	×	√
3D/2D	2D	2D	3D	3D	3D
VR user interface	N/A	N/A	√	√	×
Choice of representation	√	√	√	√	×

[a]SimView allows for on-the-fly adjustment of temperature, whereas Narupa and UnityMol allow manipulation of particle positions via VR controllers. [b]While multiple users can load the same trajectory, they will not view it at the exact same frame as other users. [c]This category only for real-time simulation visualization tools.

THE SOFTWARE

The SimView system is designed to use the HOOMD-blue[40,41] simulation engine to simulate desired molecules and the Unity3D[33] engine to render the graphics for VR. The user inputs a SMILES (Simplified Molecular-Input Line-Entry System) string[42−44] and the density to set up the simulation. Other optional inputs are simulation temperature, number of particles, and simulation duration. The SMILES string is then processed to obtain the corresponding molecular structure using RDKit,[45] an open-source cheminformatics toolkit for Python.[46] A simulation box is set up using mBuild,[47] a systematic molecule builder in Python, and a HOOMD-blue simulation is run for this system using the OPLSAA[48] force field in the NVT ensemble at the chosen temperature, for the number of timesteps specified. If the user does not specify any of the optional inputs, the default values are used. The default values for temperature, number of particles, and number of

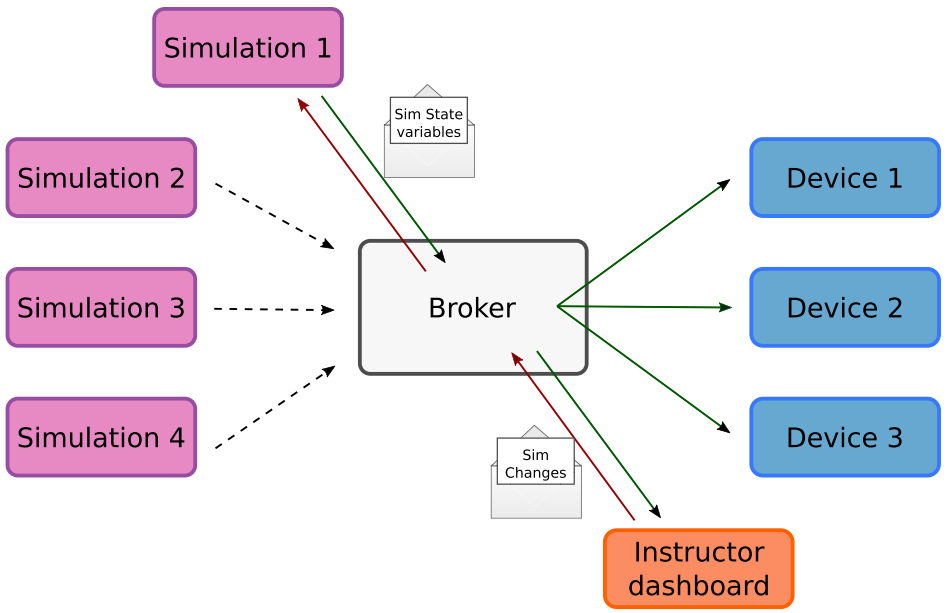

Figure 1. Communication scheme for visualizing HOOMD simulations on the VR headsets using Unity3D. In this example, "simulation 1" is the active simulation which sends simulation state messages to the broker. The broker sends this information to all devices (or clients), each of which filters the message received and then renders the graphics. The instructor dashboard is a special client that can receive as well as send messages. A message is sent to the broker from the instructor to make changes to the active simulation or to switch to an inactive simulation. The green and red solid lines indicate downstream and upstream communication, respectively. The dotted black lines indicate that simulations 2−4 are inactive but can be activated.

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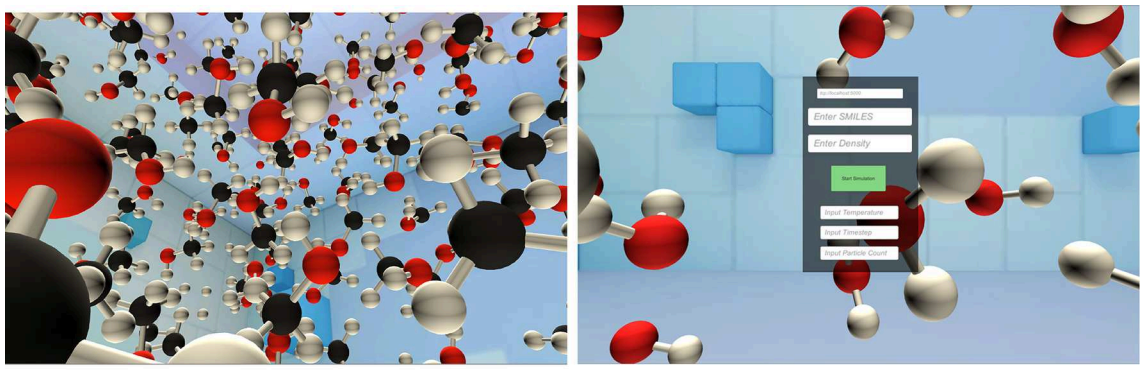

Figure 2. (a) Screenshot of rendered 3D graphics for a box of methanol molecules in VR. The atoms are colored according to the standard CPK drawing scheme. (b) Screenshot of the instructor view when launching a simulation.

timesteps are set to 298 K, 10,000 particles, and 10^6 steps, respectively. Currently, a limitation of SimView is that the chemical space that can be visualized is limited to small- or medium-sized organic molecules by the choice of force field used to simulate the systems.

A communication system between HOOMD-blue and the Unity3D engine enables the real-time visualization of these simulations. In order to provide a low-cost education tool, SimView was designed to be compatible with AR/VR devices as low in computational power as the average Daydream-ready smartphone. To accomplish this, the simulations are run remotely on a server. The light-weight messaging library ZMQ[38] is used to bridge the remote server and the users' devices. ZMQ is fast and distributed which minimizes the communication overhead, and ZMQ also has multiple language APIs which make cross-language development easier. Figure 1 shows the communication scheme between simulations and users' devices (referred to as "clients"). The centerpiece of the downstream communication (simulation to clients) is a broker-centered publisher−subscriber model,[49] while any necessary upstream communication (clients to simulation) is handled by a router/dealer pattern through the same broker. The router/dealer pattern is ZeroMQ's asynchronous version of the normal send/receive pattern. This asynchronous nature is important for SimView because it is crucial for the user experience that the VR scene not be blocked from running due to the messaging.

The publisher (or simulation) sends simulation state messages to the broker which sends a copy of this message to each of the subscribers (or clients). The subscribers perform the necessary message filtering locally so that the broker does not need to keep track of each individual client's state. An advantage to using the broker is that the broker allows the simulation server to be ignorant to the number or nature of the connected clients, which makes it possible to connect many clients simultaneously. This feature was tested by connecting 12 VR headsets to a simulation at once, which produced no lag in the rendered graphics. There are no connectivity issues predicted for a higher number of connected client devices; 12 headsets were used to test based on the availability of resources. Another advantage is that the broker acts as a switch, allowing the user to alternate between a number of simulations. The broker performs the dual function of keeping track of the current active simulation and routing the state variable updates and particle positions that it receives from the active simulation. This allows the user to switch between simulations through the instructor dashboard, if they launch multiple simulations on the server. This results in easy, convenient comparisons between different ongoing simulations. Apart from switching between simulations, the user can interact with simulations by modifying thermodynamic state variables. The temperature, density, and pressure can be adjusted in this view using the keyboard or by connecting external dials. When used as an educational tool, comparing between simulations can help students recognize how a given change in thermodynamic variables affects various simulated systems and, in turn, help them understand underlying microscopic concepts associated with these changes. Figure 2 shows a screenshot of the graphics rendered in Unity3D for a box of methanol molecules along with the instructor view when launching a simulation.

EDUCATIONAL USE

SimView can be used to supplement classroom teaching for a chemistry curriculum on how thermodynamic principles arise from molecular motion. SimView is intended to provide a new type of laboratory experience, allowing students to have a hands-on activity with concepts that are normally impossible as a laboratory activity. Specifically, see curriculum topics proposed in Table 2. SimView is similar to a laboratory activity because it is interactive and collaborative. The interactivity comes from the ability to modify the simulation parameters with a dial, switch between simulations, and change view by moving your head. SimView, as described in our activity below, can be collaborative because all students share the same simulation. This means discussion can occur, for example, about how a density change affected the molecular motion.

The authors conducted a workshop using SimView as a part of the Upward Bound (UB) Math/Science Program at the University of Rochester.[50] The Rochester City School District (RCSD) consists of 90% Hispanic, Latino, and black students with a 63% graduation rate and produces fewer college bound students than most other schools.[51] The said populations are also underrepresented minorities in chemistry. The UB program is designed to help these RCSD minority students gain exposure to college-like experiences and motivate them to pursue a college degree.

SimView was used as an interactive in-class activity for this workshop to teach a class of 10 high school students about

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Table 2. Example Curriculum and Assessment Questions to Teach High School Students about Phase Diagrams Using SimView

Topic	Assessment Questions
Temperature, pressure, density	1. You want to boil water at 50 °C. How would you do it?
	2. True or false: When you squeeze a water balloon, the pressure increases and the density of water remains the same.
	3. We know that pressure decreases when we go up a mountain. Will the water still boil at 100 °C?
	4. In what state do water particles move fastest?
Molecules and intermolecular forces	1. What are molecules made of?
	2. How many atoms does water have?
	3. How many bonds can nitrogen form?
	4. Is water a polar or nonpolar molecule?
Introduction to phase diagrams	1. What are the states of matter?
	2. True or false: Gases are the most compact at the molecular level
	3. Water is liquid at room temperature. Why is that? (a) Water is polar, (b) water is nonpolar, (c) water is hydrophobic
	4. A map of how temperature and pressure relate to phase is called a (a) TP-map, (b) valency, (c) phase diagram
Mixtures	1. What three quantities are most important for knowing the phase of a molecule?
	2. Do liquids mix more easily at low or high temperatures?
	3. What drives the mixing of the molecules? (a) Valency, (b) energy, (c) entropy

phase diagrams from a molecular perspective. The curriculum presented in Table 2 was used to conduct this workshop consisting of four 90 min sessions. Each of the four topics in the Table 2 was taught as a 90 min session, and each session was split into three parts: (1) 30 min traditional lecture to lay out background and concepts for the activity, (2) 40 min VR activity time which also included discussion of concepts, and (3) 20 min discussion to recap and summarize what students had learned. This format was chosen because previous studies have shown that prelab preparation and postlab discussion help students gain a better understanding of chemical phenomena.[52−54]

Once the students were introduced to the concepts, two groups of 5 students each took turns using the VR headsets for 20 min each. For the VR activity, students were asked to view certain preselected systems in VR. The systems were selected on the basis of the topic being discussed to best illustrate the concepts covered in the lecture, and to help them think about the assessment questions. The simulations were loaded beforehand by the instructor through the instructor dashboard so that the students needed minimal instruction on how to use SimView. Students were only required to put on the headsets to view the simulations. During the activity, the instructor view of the simulation was connected to a mixed reality table-top (Figure 3) that was previously developed by the authors.[55] Two dials were connected to the table-top which controlled the temperature and density variable inputs. The table-top made it easier for the instructor to see what the students were looking at and guide the discussion. The students were able to interact with the system and change the temperature and density of the simulation using the respective dials while viewing the systems. Use of the dials was demonstrated to students before they began the activity. The students were free to explore the system in VR independently first. Since all students were viewing the same system and the temperature and density dials are only connected to the instructor view, students had to collaborate by discussing the system and come to a consensus to explore a different temperature or density state. After that, the instructor guided discussion to help them connect the curriculum concepts with what they were viewing

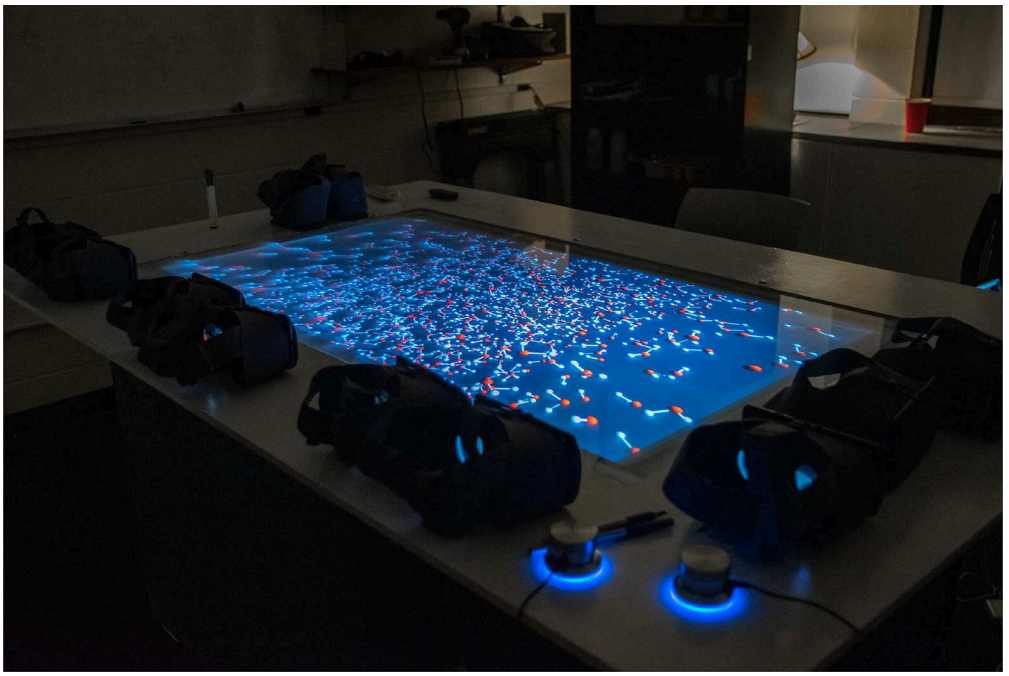

Figure 3. Activity setup for the workshop conducted with high school students. The instructor view was connected to the mixed reality table, and the dials (operated by students) were used to change temperature and density.

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on the headsets. For instance, to talk about phases, a simulation of water molecules was used. After a few minutes of student exploration, the instructor hinted to students to observe how molecular movement changed when they decreased or increased the temperature using the temperature dial. Students observed that the water molecules came close together and formed a lattice when they decreased the temperature to below 0 °C. This enabled students to connect a daily life phenomenon of ice formation to the microscopic concept of lattice formation during crystallization. Occasionally, while viewing simulations, students were surprised to see the resulting molecular structure since they expected something different. Since most of the participating students were not familiar with molecular simulations prior to this experience, the idea of molecules moving so rapidly was new to them.

The group-in-waiting was taken to a separate room, was paired with a group of undergraduate and graduate students in chemistry or chemical engineering, and got a chance to interact and talk about their college experiences, while the instructor led the VR activity. Once the first group was done with their VR activity, they had the same kind of interactions with college students and graduate students. This was in line with the UB program's aim of providing high school students with an exposure to science education in college and beyond to encourage them to pursue a career in STEM.

After the VR activity was completed, the students were asked to work on the assessment questions individually for a few minutes, and then the class discussed the questions as a group. Most students were able to answer close to 80% of questions correctly. Students answered with less hesitation during this discussion as compared with their participation during the lecture before the VR activity, though this was not a quantitative assessment.

Student Feedback

Students who had attended the SimView workshop were asked to provide feedback on their experiences of the workshop. Note that the feedback was not specifically targeted at the use of the software. Students stated that having VR to learn chemistry made it interesting: "It was interesting because it mixed chemistry and VR", "VR helped me take a peek inside of objects." The students were able to remember some concepts taught, when asked what they learned from the workshop: "Molecules have 3 important phases and also learned about solid, liquid, gas and plasma." The students were also asked about any improvements that should be made to the workshop, and none noted need for improvement.

DISCUSSION AND CONCLUSIONS

SimView is a AR/VR application that can teach molecular concepts via interactive molecular simulations. It helps students connect chemical perspectives between real-life occurences and microscopic, atomic-scale concepts. The use of SimView to supplement teaching in a classroom setting was demonstrated. For bigger class sizes, however, Simview with VR may be better suited as a lab activity. The ability to take SMILES strings as input allows the visualization of arbitrary molecules. This gives flexibility to instructors to use SimView for various chemistry topics. The chemical space that can be observed accurately in SimView is currently limited by the OPLSAA force field, although other force fields, including coarse-grained force fields, are implemented in the underlying simulation engine HOOMD-blue. SimView is developed in Unity and can be integrated with most AR/VR platforms. Manipulating simulation variables like temperature and density on the fly enables interactivity. SimView also incorporates collaboration since the students are viewing the same system and are able to talk to each other before changing the thermodynamic variables. One feature that SimView lacks is a VR UI for the students (or individual AR/VR devices). Overall, SimView can create new opportunities for hands-on learning of molecular-level concepts through interactive VR simulation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at https://pubs.acs.org/doi/10.1021/acs.jchemed.9b01161.

List of affiliated source code links (PDF)

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Notes

The authors declare no competing financial interest.

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