A collaborative molecular graphics tool for knowledge dissemination with augmented reality and 3D printing

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Abstract

We propose in this article a concept called "augmented 3D printing with molecular modeling" as an application framework. Visualization is an essential means to represent complex biochemical and biological objects in order to understand their structures as functions. By pairing augmented reality systems and 3D printing, we propose to design a new collaborative molecular graphics tool (under implementation) for scientific visualization and visual analytics. The printed object is then used as a support for the visual augmentation by allowing the superimposition of different visualizations. Thus, still aware of his environment, the user can easily communicate with his collaborators while moving around the object. This user-friendly tool, dedicated to non-initiated scientists, will facilitate the dissemination of knowledge and collaboration between interdisciplinary researchers. Here, we present a first prototype and we focus on the main molecule tracking component. Initial feedback from our users suggests that our proposal is valid, and shows a real interest in this type of tool, with an intuitive interface.

CCS Concepts

• Computing methodologies → Modeling methodologies; Mixed / augmented reality; Scientific visualization; • Human-centered computing → Graphical user interfaces;

1. Introduction

In the field of molecular modeling, the practice of augmented and/or virtual reality is increasingly common even if, for non-initiated people, such technologies can still appear difficult to handle. Molecular modelers use these technologies to present their results on molecular modeling and numerical simulations of isolated molecules to all researchers from various disciplines (biology, medicine, chemistry, physics, etc.). However, they are often challenged by a lack of suitable tools that exploit these technologies and offer simple application for non-initiated scientists.

To address this lack, we propose to develop the "augmented 3D printing" concept for molecular modeling. It can be summarized by pairing Augmented Reality (AR) systems and 3D printing. Our purpose is to facilitate a greater and deeper understanding of the data and the mechanisms involved in the considered biological processes. To gain this objective, we design a new collaborative molecular graphics tools (under implementation) for scientific visualization and visual analytics. Here, we present a first prototype and we focus on the main molecule tracking component. The printed object is the support of the augmentation to overlay different visualizations and to make annotations. In AR, the user is still aware of his surrounding and can carry on a natural communication with his co-workers while turning around the object. This user-friendly tool will facilitate the knowledge dissemination and collaboration between interdisciplinary researchers.

In the following, a state of the art of recent advances in the AR, VR and 3D printing related to molecular field is given in section 2. Section 3 gives an overview of our pipeline with a focus on the preprocessing, live detection and augmentation steps, as well as the features of our interface. Finally before concluding, we discuss our first results and users feedback in section 4.

2. Related works

Stereoscopic rendering has long been used to visualise biological structures [MCB20]. Virtual Reality (VR) has recently gained a lot of attention again, thanks to the success of new, affordable and modern Head-Mounted Displays (HMD). VR is used for both data visualization [LBO*20, MHS*20] and data interaction [ODD*18] with or without collaboration. However, the main barriers inherent to this kind of device are the lack of self-perception, isolation from the environment and an interaction with controllers not always intuitive, as well as an eyestrain limiting the duration of work sessions. In addition, collaboration is difficult and requires the use of avatars to enhance the immersive user's sense of presence, which not replace the real physical presence.

Therefore, 3D printing is so appealing to biologists as they re-

turn to more traditional methods to communicate with others, in handling and appropriating the physical objects. However, 3D color printing remains quite expensive and limits the capabilities in terms of the diversity of information [BAU15, BATU18]. In fact, in both wet and *in silico* biochemistry, many representation modes are needed, which implies multiple printings for a same molecule.

AR systems can be used to display different information at the same place and to allow collaborative experiences [LBAK15], where co-located users can see and interact with shared 3D virtual objects. One of the most AR widespread HMD is the stand-alone (wireless) Microsoft's HoloLens™. Its limits in the molecular representation context are presented in [MKH*18]. Finally, a combination of 3D printing and AR has been tried [GSSO05] in using 2D markers in experiments reducing free manipulations of physical molecules. Rendering was carried out on a remote 2D screen, thus the user could not manipulate and visualize in direct the objects in natural and intuitive ways. An another similar tool [BB14], intended for educational use, augments a 2D marker, with an optical see-through in a live-captured video and renders different molecular models at this location. However, the handling of the 2D marker limits the rotation options and it is not so natural as the handling of a 3D object itself. In 2019 within a VR/AR context, an approach without the use of markers but with a color detection has been proposed by [MFVB19]. Their objective is different from ours, since they build a molecular virtual representation from a modular physical model. As well, commercial solutions, as vuforia [ptc21] and wikitude [wik21], not dedicated to the field exist but they are also based on color and shape characteristics that fail on our objects.

3. Implementation

Our tool is based on a pipeline (Fig. 1), which can be easily used by users (initiated or not) on their own data. It consists of two steps: preprocessing and live. Its input is data usual in the field of modeling: a .pdb file (Protein Data Bank [BWF*00]) and representations of results from different simulations.

3.1. Pipeline / Use case

The input data comes from existing molecular modeling simulation. These data can be obtained from popular desktop tools for molecular visualization such as VMD [HDS96], PyMOL [JZPP16] or UnityMol [LTDS*13] which allow the export of textured 3D polygonal objects in common formats such as obj. Each representation will be stored in a different obj file expressed in the same coordinate system. They will be imported into the interface.

In the preprocessing of the Fig. 1, the main representation (surface) is printed in 3D to allow a more physical user-friendly interaction during the live experience. It is also used to generate different views. These views from reference orientation and position are processed to create a database. It will be used to find the position and orientation of the printed object during the experiment.

In the live stage, the HoloLens wearer look at the printed molecule posed. It can be augmented as soon as its position and orientation are detected. This detection, based on the same processing as in step 1, is possible with the use of depth sensors and the 3D

spatial awareness of the device and our database. So the user can revolve around the augmented object, analyze the complementary and interaction of the different data and exchange with colleagues.

3.2. Preprocessing

The fundamental step of this tool is the detection of the object that needs to be augmented. This detection can be made easier by adding 2D markers or colorimetric marks on the object. These solutions have been discarded to avoid disturbing the user experience. Therefore, we chose to print the main representation of our object in a white neutral color both to optimize the augmentation process and to lower the printed costs. In addition, the object must be matte to avoid specular reflections when capturing the scene and to facilitate the detection process. As molecular objects have a very characteristic shape (invariant to rotations), we use to set up a detection by comparison of reference positions and orientations. Obtained by n views regularly distributed around the object [Des04], they are stored along with the image I_r in a database. In order to accelerate the comparison process and to minimize the size of the database stored on the HoloLens, these views will undergo the same processing as the live detection and a summary file with the ratio ($W \times H$) of each image is compiled. This file will be also stored in the database and used in the detection process. At the end of step, the database and the input data are uploaded once in the HoloLens.

3.3. Live detection

To facilitate the detection of the molecule, especially during the initialization step, we will place the molecule on a dark matte background. Thus, the effects of specular light, which would result in noise, will be limited. The global process is composed in three steps: cleaning, cropping and detection.

Cleaning Binarize the captured image $I \to I_b$
An Otsu adaptative thresholding with a binarization is applied on I (Fig. 2). Then the last light effects are denoized with morphological operation: an opening with a squared kernel of size 9.

Cropping Crop I_b to its region of interest $\to I_c$
I_b is cropped to its region of interest defined by the oriented bounding box of the largest white component and the size ratio of I_c is registered.

Detection Find the nearest reference orientation and position.
For each image I_r of the database, having a close size ratio ($< \beta$), the XOR operation is performed with I_c (Fig. 2). The number of pixels different is counted and give the error rate. The position and orientation of I_r with the lowest error rate is selected.

At the end of this step, as the additional data are all expressed in the same coordinated system, we are able to orient them in the same way as the printed molecule.

3.4. Augmentation

To reach an overlay of quality, the additional data must be positioned at the proper distance to respect the right scale. Therefore, we first need to know the distance at which the printed molecule is located. The HoloLens includes two depth cameras, one with a short focal length and one to the long range. As described in [HCL*20], the correspondence of one point on the color
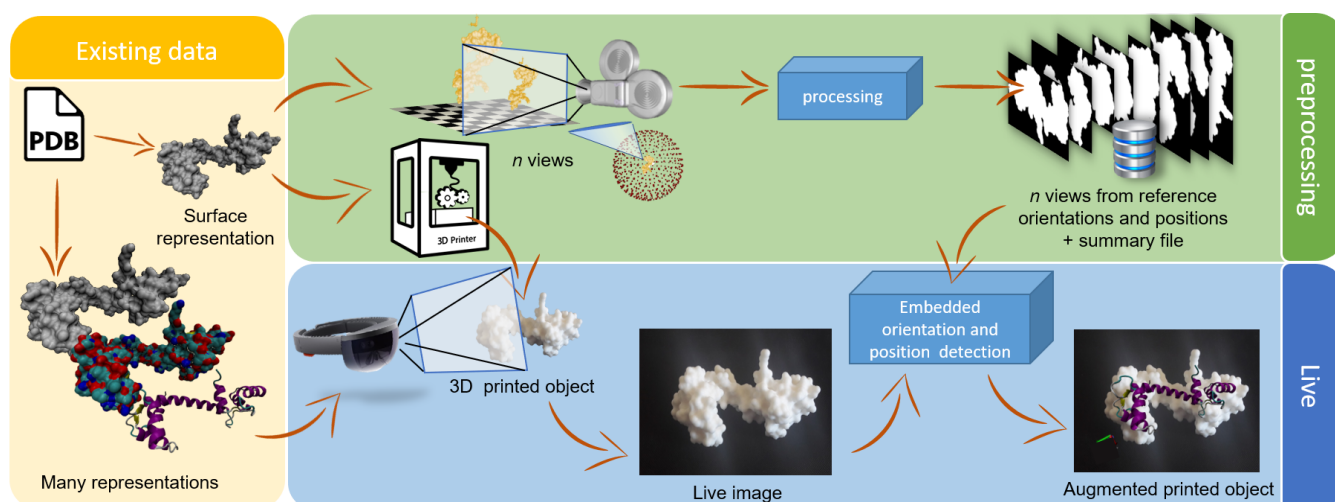
Figure 1: *Overall visualization pipeline. The input is existing data from simulation results in different visual representations. A first pre-processing step consists to print the main representation (solvent area surface) and to generate n views from the reference orientations and positions. A processing is applied on these views before storing them in a database. During the experience, the position and orientation of the printed object are found from the search of the live image in the database. Then, the augmentation is performed with the user chosen additional data. When the user moves the printed object, these steps must be repeated.*
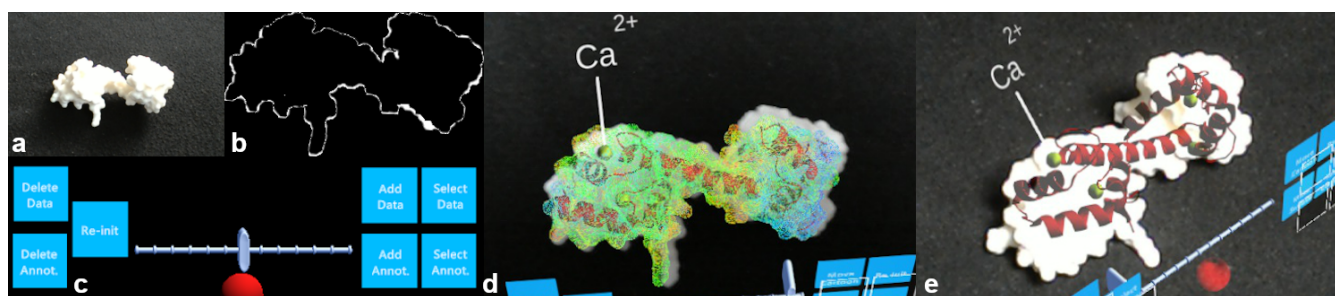

Figure 2: *Different steps of processing with a database of 4000 molecules, a difference in size ratio at 0.1 and a scaling factor at 2. The image I (a) is captured by HoloLens. To find the position and orientation of the printed molecule, the comparison (I_c XOR I_r (b)) between this processed image and each image in the database is performed, the one with the lowest error rate is selected. Then the result of the overlay (d, e) with the representations, selected by the user in the interface (c), is displayed: a wireframe surface colored according to the B-factor, a secondary structure representation (cartoon in red) and the 4 calcium representation (van der Waals in yellow). Note that the noticeable shift of the surface in d (id. e) is due to the monocular capture of HoloLens from a stereo view and not to incorrect positioning of the augmentation.*

map to the depth map can be computed. With it, we get the distance d_P of the point P in the depth map, where P is the projection on the surface of the origin point O of the object coordinate system. If O is not located inside the object, it is substituted by a point chosen by the user. In the preprocessing step, the position P and the distance d_O of O on the image plane were computed for each image I_r of the database and saved in the summary file. With P, d_P and d_O, we set up the augmentation on the printed object as illustrated in Fig. 2.

3.5. Interface

When the tool is launched, the summary file is loaded in memory with the different additional data of the printed object. Then the initialization step starts. During it, the user needs to look at the printed

molecule placed on the dark matte background for a few seconds. This step is necessary to detect a first time the printed molecule. During the experience, the user may choose one or more additional data to be displayed on the main representation. By default, these data are displayed at the same place as the printed molecule as illustrated in the Fig. 2. Moreover, to highlight one representation in relation to another, the user can adjust on the transparency of each one. This possibility will facilitate the dissemination of the relevant information to be communicated between the interdisciplinary researchers. In addition, the user can use the HoloLens' interactive gestures (hold, drag, tap) to move and zoom additional data and he can also annotated the printed molecule with predefined labels to locate and show particular interesting areas.

4. Results

4.1. Quantification of results

n images	1000	2000	4000	8000
Error rate	0.0841	0.0834	0.0818	0.0815

Table 1: *Average error rate evaluation (computed at the detection step) for the 10 sample images with the different database sizes under consideration.*

β ratio	0.05	0.1	0.2
Error rate	0.0833	0.0818	0.0818
Run time	39.75	55.87	60.07

Table 2: *Evaluation of the β size ratio considered, for the 10 sample images and a database size of 4000, with the comparison of the average error rate (computed at the detection stage) and the run time.*

s scaling factor	1	2	4
Error rate	0.0818	0.0818	0.1289
Run time *(in s.)*	55.87	35.76	31.75

Table 3: *Evaluation of the scale factors s considered, for the 10 sample images, a database size of 4000 and a β size ratio of 0.1 with the comparison of the average error rate (computed in the detection step) and the run time.*

In order to evaluate the global process and the database size, we captured 10 sample images from the HoloLens by varying the printed object orientation and the luminosity. For each captured image, we have study different database sizes *n* of 1000, 2000, 4000 and 8000 images and we have compared the average error rate obtained in the detection step as illustrated in Tab. 1. As the difference of this rate between the 4000 and 8000 databases is very small for a doubled number of images, we set *n* at 4000 for the continuation of these tests.

For a successful experience, we need smooth, latency-free interaction and augmentation. Since the bottleneck in global run time is the number of loaded images for comparison, it is essential to lower this loading number as much as possible. Therefore, different values for the β ratio using in detection step were tested (0.05, 0.1, 0.2) (Tab. 2). At 0.05, we note a degradation in the error rates, so we set β at 0.1.

In order to further speed up run time, we are considering changing the I_r image scaling factor *s* from 1 to 2 or 4 (Tab. 3) which would be applied on I_b. When the original resolution (1408,798) is divided by 4, the object's shape in the scaled image gets too coarse, increasing the error rates (Tab. 3). In contrast, for the 1 and 2 factor the two found reference images are identical. After taking into account the run time, the scaling factor *s* is set to 2. Thanks to these three parameters (*n*, β and *s*) the run time switches respectively from 60.07 to 55.87 and then 35.76 seconds. It should be noted that this initial work is a proof of concept and that none of the processes have been optimized.

4.2. User feedback

The preliminary tests were performed using the Calmodulin (CaM) protein. CaM (Calmodulin Modulated Protein) is ubiquitous in all eukaryotic cells and has numerous key roles in normal and pathological functions, as for instance a role for a long-set Qt in cardiovascular diseases. The known 3D structures of CaM present to both its N- and C- terms two equivalent symmetrical globular domains separated by a specific flexible linker region. We use the chain A of the 1UP5 [RMP96] crystallographic structure. This structure presents a specific shape due to a specific position of one helix in the C-Term part that allows to differentiate the global orientation of the protein. This structure facilitates the detection step for a better improvement of our protocol. We used Pymol to generate the .obj files of the different representations used in our tool: surface colored according to the B-factor (temperature factor in crystallographic data), cartoons in red and the 4 calcium in yellow (Fig. 2). Our main representation is the MSMS surface [SOS96], used for the 3D printing. The chosen size of the printing volume is $10 \times 10 \times 10$ *cm*, to guarantee that the user handled molecule does not exit out of his augmentable field of view, dictated by the technical specifications of the HoloLens. In our tool, the printed object is static and only the user is mobile: move towards, away from and around the object. He can also change the object's position and orientation if he relaunches the detection.

Our user panel, consisting of biochemists, biologists and molecular modelers, expressed a great interest. In particular, they appreciated the intuitive interface with the 3D visualization, coupled with the augmentation on the printed molecule. The tangible aspect of the molecule makes it easier to handle. The other interest is the collaboration ability around the object. Unlike a VR helmet the users appreciate to see each other and to be able to communicate freely with their usual gestures.

5. Conclusions and Future works

We proposed a first prototype of a molecular graphics tool for knowledge dissemination with AR and 3D printing dedicated to the HoloLens. In this paper, we focused on the main molecule tracking component. The implementation of this proof of concept has a relatively long run time for the initial step. It must be optimised in using the four CPU cores of the device. In addition, our tests have been limited to very specific shapes. Our next step is to relax this constraint. These first works have been validated by a panel of biologists and biochemists. Their feedback shows a true interest for this kind of tools. However, they require a more intuitive handling with the printed molecule, thus confirming our future work to transform the molecule into a fully tangible interface. This evolution will require a robust occlusion detection to address the presence of the user's hands and implementation of different collaboration modes (on-site and remote).

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