Online tools to easily build augmented reality models of biomolecules that run right on the web

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Running title: Swift building of augmented reality models of biomolecules for web display

Abstract. Several groups developed in the last years augmented and virtual reality (AR/VR) programs and apps to visualize 3D molecules, most rather static, limited in content, and requiring software installs, some even requiring specialized hardware. During the Covid-19 pandemic, our team launched moleculARweb (https://molecularweb.epfl.ch), a website that offers interactive content for chemistry and structural biology education through web-based AR that works on consumer devices like smartphones, tablets and laptops. The website quickly got thousands of student and teacher users, a substantial fraction of them accessing from their homes given the pandemic. Teachers have been increasingly requesting more biological macromolecules to be available in AR, a demand that we cannot satisfy individually. Therefore, to allow them to build their own material, and also to help us expedite development of activities, we built a web interface where any user can build any online AR experience in few steps starting from a PDB structure or from virtual objects/scenes exported from VMD. We here briefly describe the tool, that is accessible at https://molecularweb.epfl.ch/pages/pdb2ar.html.
Introduction

Incidentally with the Covid-19 pandemic, we launched during 2020 moleculARweb, a website for chemistry and structural biology education through augmented reality (AR) that works on consumer devices like smartphones, tablets and laptops.1 The website (https://molecularweb.epfl.ch/) provides several activities where students and educators can either handle virtual molecules and other chemistry-related entities like electronic orbitals with paper-printed markers to compare them in 3D and even to make them interact, or simply anchor virtual molecules to a flat surface such as a table to inspect them immersively by freely moving around them. Each activity is delivered as a regular webpage, so users do not need to install any programs to use them. They just need to access the web page of interest and enable the webcam. More details about moleculARweb are available in our recent publication1 (or its preprint), which focuses more on topics pertinent to chemistry and stresses AR achieved through printed markers, only barely introducing examples of biomolecular assemblies and markerless AR, which are the focus of this work.

moleculARweb quickly got thousands of users, students and teachers, many of them accessing from their homes due to the pandemic (constantly monitored at https://clustrmaps.com/site/1ar2f). Online and in-person surveys showed positive effects on learning, strong engagement by students, and high success rates in making the AR activities work, the latter likely due to the entirely web-based nature of the tools, which facilitates deployment as noticed by multiple works.2,3

Since the release of moleculARweb, teachers have been increasingly requesting more AR material, especially for biological macromolecules. As this demand is very hard to satisfy, we built a tool that teachers can use to build their own material, also helping us to expedite the development of new activities. This new tool consists in a web interface where users can easily build any online AR experience in few steps and without any knowledge about AR, VR nor programming, starting either from a PDB structure or from virtual objects/scene exported from the VMD4 molecular graphics program. Figure 1 shows a summary of the pipeline from input to output. The input can be either a PDB file of a system prepared by the educator or fetched right from the Protein Data Bank, to be converted by moleculARweb into AR objects, or a ready-to-
use VR object or scene exported from VMD. The output consists of two AR view modes, one where the object is attached to a cubic marker printed and folded from paper, just like the cube marker of moleculARweb’s Virtual Modeling Kit, and another where the object is displayed in the space of the user just lying over any flat surface. The educator gets a link to the resulting web-AR visualizations by email, that can then be shared with students. In this short article we describe this tool, accessible at https://molecularweb.epfl.ch/pages/pdb2ar.html, with examples covering the two possible kinds of inputs, which we call input modes 1 (from PDB) and 2 (from premade 3D objects).

Figure 1. Pipeline for creating customized webAR experiences on molecular systems, starting from coordinates (illustrated in Figure 2) or from premade VMD objects or scenes (illustrated in Figure 3). The direct link to the tool is https://molecularweb.epfl.ch/pages/pdb2ar.html. The cube marker can be printed and folded from https://molecularweb.epfl.ch/assets/markers/allmarkers.pdf. AR with markers works in all modern browsers and operative systems on smartphones, tablets and desktop computers (user needs to enable webcam use when prompted for the first time); while markerless AR works only in Chrome (best if version 92 or higher) on WebXR-enabled smartphones.
Input mode 1: Atomic coordinates in PDB format

The first and simplest way to use this new tool is to copy-paste a PDB file of a system prepared by the educator or fetch it directly from the Protein Data Bank using its PDB code, as illustrated in Figure 2 for the protein myoglobin from PDB ID 1MBN. Once the PDB file is ready (Figure 2A) the user clicks “Detect molecules” to which the app responds with two lists: one of all protein and nucleic acid molecules detected, and one with all additional special small molecules or “ligands” (Figure 2B). For each entry of these two tables, the user can indicate whether to display it or not, how to display it, and what colors to use (protein and nucleic acid chains are repeated twice in the list to allow multiple representations, such that for example a given protein chain can be displayed as cartoons and also as sticks). Users acquainted with the VMD molecular graphics program will find familiar the terms used in the lists. For example, for 1MBN one can choose to show protein chain A as “New cartoon” colored in “Yellow” and then choose to display the HEM group as “Licorice” colored by “Atom name” but highlighting the central iron atom as a sphere (“VDW”) colored “Tan”.

The next step, after having chosen the wanted representations, is to click “Build VMD script” which will result in a portion of code to be executed at our servers to produce the AR scene (Figure 2C). The point of showing this script is that users familiar with VMD can edit it to fine-tune the final scene.

The “Submit” button at the end runs only if the user provided a title for the activity and an email where to receive the results. A few seconds after clicking this button the user will receive an email with a link to the prepared visualization (Figure 2D). If the view is not as intended the user can make changes right there in the web tool to immediately get further emails with the changes applied.

As exemplified in Figure 2E-G for the input based on PDB structure 1MBN, the link delivered by email opens first an AR experience that works with molculARweb’s cube marker (Figure 2E). At the bottom right of this view a button labeled “3D” opens up a view with a white background (Figure 2F) from which a subsequent button launches a markerless AR view where the virtual object lies on a flat surface detected by the device (Figure 2G). The first two modes work in all devices, i.e. smartphones, tablets and computers, while the markerless mode works only on WebXR-enabled smartphones and tablets as it requires the device’s pose
estimation capabilities. This is also valid for inputs prepared from premade VMD scenes, described in the next section.

Figure 2. Creating a model from PDB 1MBN (myoglobin) to show its overall fold as cartoons, heme group as sticks and iron ion as a sphere. In (A) the user fetches of copy-pastes the PDB file and clicks “Detect molecules”; in (B) it choses what representations and colors to use and clicks “Build VMD script” to get the VMD script shown in (C). Users familiar with VMD can optionally edit this script. After providing a title and email address the user clicks “Submit” and after a few seconds will receive an email with a unique link to display the AR experience (D). Opening the link in the email leads first to visualization with a cube marker (https://molecularweb.epfl.ch/assets/markers/allmarkers.pdf) that works in phones,
laptops or computers (E). Clicking on the 3D button opens the white background view (F), that also works on all devices and where users move the object with the finger or mouse. Then clicking on the last button leads to the immersive AR mode where the object sits on flat surfaces, without any markers, on smartphones and tablets (G). We leave this specific example on myoglobin ready to view at https://molecularweb.epfl.ch/pdb2ar/myoglobinfrompdb1mbn/. Notice that AR with markers works in all modern browsers and operative systems on smartphones, tablets and desktop computers (user needs to enable webcam use when prompted for the first time); while AR without markers works only in Chrome (best if version 92 or higher) on WebXR-enabled smartphones.

Input mode 2: VMD-generated Wavefront objects

If the user is familiar enough with VMD to prepare its own models as Wavefront objects (pairs of OBJ-MTL files), these can be submitted directly together with a title and an email address to let the system build the AR displays. The user then receives an email with a link to the AR views much like with the normal PDB-based input mode (Figure 3A).

This input mode has two advantages. For PDB files, it allows finer control than what input mode 1 offers (although mode 1 is already quite complete and can be extended by editing the VMD script before submitting to the website, at the stage shown in Figure 2C). But most importantly, input mode 2 extends the range of applications as it allows users to build in their local computers 3D scenes from molecules other than proteins or nucleic acids, and even from objects other than atomic coordinates such as isosurfaces or meshes representing orbitals or electron densities. As examples, Figure 3B shows a membrane with its lipids represented as sticks; Figure 3C shows a T4 bacteriophage rendered as an isosurface from an experimental Cryo-electron tomography map; Figure 3D shows a composition for a membrane-embedded dopamine receptor bound to a transmembrane G protein and with a ligand bound; Figure 3E shows an aerolysin molecule inserted inside a membrane, acting as a ion-conducting nanopore; Figure 3F shows a cryotomography-based 3D reconstruction of the SARS-Cov2 viral particle, with even Spike and ribonucleoproteins resolved; Figure 3G shows the active site of carbonic anhydrase with a ligand bound where only selected residues are displayed as sticks; and Figure 3H shows a liposome patch rendered from a coarse-grained model using a combination of Quick Surface and VDW representations.
Build your own webAR views

Upload 3D structures in PDB and make small changes to the model to a custom marker on the user without extra steps. This tool is especially useful for easy comparison with other QC methods. Small changes to PDB do not change structure, for example scenarios do not include substitution of crystallography or total calculation.

Your AR project is ready!
MolecularAR [noreply@molecularweb.epfl.ch]
https://molecularweb.epfl.ch/pdb2ar/membranepatch
Figure 3. Creating WebAR views from VMD scenes. (A) Pipeline: the user uploads Wavefront files (one .OBJ and one .MTL file) generated in VMD and provides a title and an email address. From this point onwards, the procedure is the same as for Input mode 1 detailed in Figures 1 and 2: the user receives an email with a link to a first activity where the object is displayed on the cube marker, and clicking on the “3D” button switches to the markerless modes. We show three example systems. (B) A patch of eukaryotic cell membrane modeled with CHARMM-GUI\textsuperscript{10} with phospholipids in grey and cholesterol in cyan, here seen on a cube marker in a smartphone (example accessible at https://molecularweb.epfl.ch/pdb2ar/membranepatch/). (C) T4 bacteriophage rendered as isosurface from Cryo-electron tomography map (EMDB 6082\textsuperscript{6}), accessible at https://molecularweb.epfl.ch/pdb2ar/t4bacteriophage/. (D) A dopamine receptor bound to a G protein and a ligand, seen without markers, from PDB ID 6VMS.\textsuperscript{7} In the inset the user moved into the ligand binding site. Example available at https://molecularweb.epfl.ch/pdb2ar/gpcr/. (E) An aerolysin molecule inserted in a membrane, snapshot from a simulation of ion conductance across the protein used as a nanopore\textsuperscript{8} (blue spheres are K\textsuperscript{+} ions and red spheres are Cl\textsuperscript{-} ions). Example accessible at https://molecularweb.epfl.ch/pdb2ar/aerolysinwithions/. (F) 3D shape of the SARS-Cov2 virus assembled from cryo-electron tomography and subtomogram averaging (EMDB 30430\textsuperscript{9}). Notice the ribonucleoparticles inside the virus and the Spike proteins exposed on its surface. Example accessible at https://molecularweb.epfl.ch/pdb2ar/sarscov2experimental/. (G) Crystal structure of a sulfonamide-bound human carbonic anhydrase (PDB 1AZM, hydrogens added\textsuperscript{11}) where only the drug and the protein residues of its binding pocket are shown as sticks, and the enzyme’s zinc ion as a sphere. This screenshot was taken on a smartphone in landscape orientation, with the system on a cube marker. See at https://molecularweb.epfl.ch/pdb2ar/sulfonamidewithhumancarbonicanhydrase/. (H) A liposome patch generated with CHARMM-GUI\textsuperscript{10} with its coarse-grained MARTINI builder. The polar heads are represented as smooth surfaces in tan color and the hydrophobic portion of the bilayer is completed as cyan coarse-grained spheres. This view is in a laptop computer using the cube marker. Example at https://molecularweb.epfl.ch/pdb2ar/liposomepatch/. Notice that AR with markers works in all modern browsers and operating systems on smartphones, tablets and desktop computers (the user needs to enable webcam use when prompted for the first time); while AR without markers works only in Chrome (best if version 92 or higher) on WebXR-enabled smartphones.

Virtually any scene created with solid objects in VMD can be exported as a Wavefront object (File \(\rightarrow\) Render, choose Wavefront, path and click “Start Rendering”) and then seen in AR through this tool. By “solid objects” we mean that line objects are not exported by VMD, at least as of version 1.9.4.

Final remarks

We have presented here a new tool to help users create their own AR views from plain PDB files containing atomic coordinates or from virtual objects or scenes exported from the VMD program. The tool is intended for educators and science communicators, but is actually open for free use without registration. Importantly, AR with markers works in all modern browsers and operating systems on smartphones, tablets and desktop computers (the user needs to allow webcam use when prompted for the first time); while AR without markers works only in Chrome (best if version 92 or higher) on WebXR-enabled smartphones and tablets.
We intend to keep the user-created content available for at least one month, but we reserve the right to shorten this time if required. When starting from PDB files, users can anyway always download the created OBJ+MTL files for local use and future use in the server by going directly through input mode 2.

We also reserve the right to select user-uploaded VR scenes of especial interest to use them as activities in the main moleculARweb website and for website promotion.

We conclude by reminding educators and students to please fill the surveys at https://molecularweb.epfl.ch/pages/feedback.html after having worked with the activities presented here or with any other activities of the moleculARweb site. This information is crucial to keep the website growing, to learn about how educators use the AR activities, and to learn to what extent AR actually helps students to learn.

Methods

The tools presented here rely on the same technologies used for our MoleculARweb\(^1\) site. Briefly, AR views are rendered entirely in the user’s device through content written entirely in HTML5, CSS and JavaScript\(^{12,13}\), exploiting several free, open-source libraries especially Three.js, AR.js, jsartoolkit, and ModelViewer\(^14\). The backend is built using node.js, express.js, nodemailer and multer to handle file upload, run VMD scripts, generate the output web pages, and inform users by e-mail. All the code behind these tools is available at GitHub: https://github.com/fcor/molecular-mirror-app (client) and https://github.com/fcor/molecular-mirror-backend (backend).

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