

# Applications of visualization technology in the structural sciences

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## ABSTRACT

The structural sciences are undergoing a transformation driven by advancements in visualization technologies that aid researchers in understanding and communicating experimental data from complex molecular systems. New applications of integrative structural biological and biophysical approaches add a wide variety of complementary information from a broad range of scientific disciplines. These approaches extend structural biophysical methodologies to enable research by the incorporation of a variety of data streams and utilization of tools like molecular graphics, virtual reality, and machine learning. To redefine how structural data—particularly from cryo-electron microscopy and x-ray crystallography—are fed forward for scientific exploration and communication, the advances in tools for data visualization and interpretation have been critical. By bringing molecular systems into an interactive three-dimensional space, these novel technologies enhance research workflows, facilitate structure-based drug design, and create engaging educational experiences. Taken together, these visualization innovations are essential tools for advancing the field by making concepts more accessible and compelling.

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## INTRODUCTION: THE ROLE OF VISUALIZATION IN STRUCTURAL SCIENCE

The structural sciences have been making critical contributions to the study of life by providing structures of molecular machines. The biophysical technologies of x-ray crystallography, nuclear magnetic resonance (NMR), and cryogenic electron microscopy (cryoEM) rely on the effective visualization at the atomic level of molecular systems to uncover the complexities of biological mechanisms.<sup>1</sup> Traditional methods of data representation have been guided by three-dimensional (3D) modeling software to produce static images that have often constrained researchers' ability to explore intricate structures fully to understand their underlying biochemistry.<sup>2</sup> In addition, a common focus of structural biologists is to create a representation of a macromolecule in isolation. This reductionist approach is partially driven by the experimental workflow, where the target of study needs to be isolated or purified to a high degree of homogeneity to be able to yield high-resolution models. However, 3D model building is an act of interpretation with inadequate information because experimentally determined maps of targets of interest may not always be able to yield

full atomic coordinates with unambiguous elemental identities.<sup>3</sup> To gain greater insight, sometimes several experiments are combined that perturb the core target to give rise to heterogeneity that allows additional conformational or catalytic states to be determined.<sup>4,5</sup>

Software innovations have enhanced structural visualization and interpretation of experimental data. In particular, single particle analysis approaches in cryoEM yield a consensus map that can be further analyzed to highlight the heterogeneity of conformations in the sample. Heterogeneity analysis programs explore both discrete and continuous heterogeneity in datasets to highlight the ranges of motion macromolecular complexes undergo.<sup>6</sup> Crystallography approaches aid in determining defined conformational state models through the constraints of the crystal lattice. Molecular dynamics simulations can be applied to these models to propose potential molecular motions and pathways.<sup>7</sup> Solution approaches through NMR can add additional experimental information to highlight the kinetics and dynamics of biological macromolecules.<sup>5</sup> Each structural biology modality has tools that may be combined to provide a more comprehensive testable model of biological molecules in motion.<sup>8</sup> Advancements in

visualization technology have provided scientific communicators with new ways to combine and present information. In this Perspective, we summarize some of the visualization techniques that can be applied to experimental structural data, discuss the broader applications and impact of these techniques, and look toward future challenges and opportunities in this developing field.

### CURRENT DEVELOPMENTS IN VISUALIZATION TECHNOLOGY

One of the bottlenecks in data visualization is that refinement and reconstruction programs have limited visualization features. Model-building programs and structure refinement programs tend to be optimized to assist users with building a model that both agrees with the experimental data and the underlying physics of biological systems.<sup>9,10</sup> However, there are limitations when dealing with large macromolecular complexes and considering a systems-level approach incorporating all the components within a biochemical pathway. Rather than exporting static images from a structure refinement or model-building program, dedicated animation software can be used to bring biomolecular data to life with sophisticated 3D modeling and molecular movie-making tools.<sup>11,12</sup>

The Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) uses the molecular graphics tool *Mol\** to render structures within a browser window that are interactive and motif-searchable.<sup>13</sup> Similarly, the Cambridge Crystallographic Data Center Cambridge Structural Database (CCDC CSD) offers the paid software Mercury that renders structures using *POV-RAY*<sup>14</sup> and is more suitable for small molecule structures. The *CrystalMaker Suite*<sup>15</sup> is a powerful tool for diffraction simulation and model building. The polyhedral graphics option is particularly suited to display mineral structures and model void spaces.

Due to the natural tendency of researchers wanting to interact with experimental data and create accurate, validated models, there have been continual developments in software packages and suites that assist with not only visualization but also model-building and annotation (Table I). ChimeraX is an advanced molecular visualization tool widely used by the cryoEM community and researchers across various fields to analyze molecular structures, density maps, and other complex datasets.<sup>16</sup> As this program has been adopted by researchers, it expanded to meet the community needs by including a wide array of features, such as integration into databases like RCSB PDB and AlphaFoldDB, VR support, and Python scripting, making it a powerful tool for scientific discovery and educational applications. The implementation of Python scripting in these programs also allows researchers to optimize structural analysis tools, such as PyMOL,<sup>12</sup> toward specific applications. With these scripts, researchers may extend data interpretation by enabling molecular docking and other analysis features within these programs and create visualization sessions that can be shared allowing researchers a more collaborative environment by means of highlighting particular views and arrangements of structural models. Moreover, advanced rendering tools and real-time animation techniques are now capable of depicting molecular motion, offering deeper insights into protein–ligand interactions, conformational changes, and allosteric regulation.<sup>17</sup>

Digitized animation tools are being used to create information-rich and visually compelling molecular animations that capture current hypotheses on diverse molecular and cellular processes.<sup>18</sup> These visualizations have broad applications in scientific research,

communication, education, and outreach. New tools and workflows in this space are enabling researchers to more readily create dynamic visualizations of the processes they study. In orthogonal scientific fields, the development of new technologies has aided scientists to move beyond static representations and step inside molecular landscapes, interactively manipulating atomic structures in real time.<sup>19–21</sup>

An essential aspect of scientific discovery is sharing findings and making complex concepts accessible to a broad audience. Artistic renderings and animations have proven to be powerful tools for science communication, bridging the gap between technical research and public understanding. Artists who are also scientists have masterfully combined art and biological sciences to create detailed works that depict cellular landscapes with scientific accuracy.<sup>22</sup> Similarly, animation and hand-drawn illustrations are used to translate intricate molecular processes into visually engaging narratives, making them easier to grasp for both scientists and non-experts.<sup>23,24</sup> By integrating art with science, these creators enhance engagement, inspire curiosity, and improve education, demonstrating the critical role of visual storytelling in modern scientific communication.

Machine learning (ML) and artificial intelligence (AI)-driven approaches continue to refine structural predictions and analysis, enabling researchers to bridge experimental and computational models more effectively.<sup>25,26</sup> ML/AI is revolutionizing data processing by automating complex structure analysis and generating predictive models of molecular and ligand interactions.<sup>27</sup> As scientific studies look into the cell, visualizing these intricate structures in their native context remains computationally challenging. To address this, researchers are leveraging video game physics engines, such as *Unreal Engine*,<sup>28</sup> to render massive biological macromolecules at the atomic level in real time, facilitating interactive navigation within cells. ML/AI-driven techniques further optimize this process by automating molecular segmentation, enhancing volumetric rendering, and improving predictive modeling of macromolecular interactions.

Virtual and augmented reality (VR/AR) technologies are playing an increasingly significant role in molecular visualization by allowing researchers to engage with complex structural datasets in immersive, interactive environments. VR platforms provide the ability to examine macromolecular assemblies from all angles, simulate molecular docking interactions, and navigate through intricate structural landscapes in ways that traditional two-dimensional (2D) representations cannot offer. Emerging tools allow scientists to collaborate remotely on 3D and, by adding a time element, four-dimensional (4D) molecular data, fostering a more interactive approach to structural analysis and drug design.<sup>21,29</sup> In addition, educational programs are incorporating VR-based molecular visualization to train the next generation of structural biologists, providing students with hands-on experiences in molecular modeling and spatial reasoning.<sup>30,31</sup> AR applets allow students to visualize structures on their cell phones without the need for specialized equipment.<sup>32</sup>

In parallel with digital advancements, 3D printing has emerged as a valuable tool for representing molecular structures in a tangible format, facilitating both research collaboration and educational outreach. By translating structural data into physical models, scientists can better conceptualize the spatial organization of proteins, nucleic acids, and macromolecular complexes.<sup>33</sup> These models are particularly useful in discussing structure–function relationships, as they allow for direct manipulation of features that are otherwise difficult to interpret in

**TABLE I.** Molecular visualization, model-building, and annotation software for structural biology.

Category	Software	Key features	Applications	References	Online content
Databases	RCSB	Experimentally determined 3D structures from the Protein Data Bank (PDB) archive and Computed Structure Models (CSM) from AlphaFold DB and ModelArchive	Public database	13	@RCSBProteinDataBank on YouTube <i>Guides</i> <i>PDB-101</i> <a href="https://www.rcsb.org/#Category-learn">https://www.rcsb.org/#Category-learn</a>
	CCDC	Fully curated organic and metal-organic structures	Licensed database with free services	14	@CCDCCambridge on YouTube <i>Training and Learning</i> <a href="https://www.ccdc.cam.ac.uk/community/training-and-learning/">https://www.ccdc.cam.ac.uk/community/training-and-learning/</a> <i>On-demand Training</i> <a href="https://www.ebi.ac.uk/training/on-demand">https://www.ebi.ac.uk/training/on-demand</a>
	EMDB	Public archive of three-dimensional electron microscopy (3DEM) maps	Public database	48	<i>PyMOL wiki</i> <a href="https://pymolwiki.org/index.php/Main_Page">https://pymolwiki.org/index.php/Main_Page</a>
Molecular visualization and rendering	PyMOL	High-quality molecular rendering, scripting, and animation	Structural analysis, molecular docking, publication-quality images	12	• Paywalled tutorial documentation • Individual contributors on YouTube • Online certification course through Schrödinger (paid) @ucsfchimerax8387 on YouTube <i>Tutorials</i> <a href="https://www.cgl.ucsf.edu/chimerax/tutorials.html">https://www.cgl.ucsf.edu/chimerax/tutorials.html</a> <i>Videos</i> <a href="https://www.cgl.ucsf.edu/chimerax/docs/videos/">https://www.cgl.ucsf.edu/chimerax/docs/videos/</a> <i>Tutorials</i> <a href="https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials">https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials</a>
	ChimeraX	Advanced visualization, VR support, integrative modeling	Cryo-EM map analysis, multi-scale modeling, interactive molecular exploration	16	<i>Tutorials</i> <a href="https://www.cgl.ucsf.edu/chimerax/tutorials.html">https://www.cgl.ucsf.edu/chimerax/tutorials.html</a> <i>Videos</i> <a href="https://www.cgl.ucsf.edu/chimerax/docs/videos/">https://www.cgl.ucsf.edu/chimerax/docs/videos/</a> <i>Tutorials</i> <a href="https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials">https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials</a>
	VMD (Visual Molecular Dynamics)	GPU-accelerated rendering, molecular dynamics analysis, interactive trajectory visualization	Structural biology simulations, molecular docking, drug discovery	49	<i>Tutorials</i> <a href="https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials">https://www.ks.uiuc.edu/Research/vmd/current/docs.html#tutorials</a>
	Mol* (MolStar)	Web-based visualization for large molecular complexes	Cryo-EM, protein structures from PDB, interactive web integration	50	@RCSBProteinDataBank on YouTube
	Jmol	Lightweight, web-based molecular visualization	Interactive teaching, small molecule visualization, NMR analysis	51	<i>Jmol wiki</i> <a href="http://wiki.jmol.org/index.php/Main_Page">http://wiki.jmol.org/index.php/Main_Page</a>
Immersive and interactive visualization	Nanome	VR-enabled molecular modeling, collaborative drug discovery	Structural drug design, protein-ligand interaction studies, real-time collaboration	52	@Nanome on YouTube <i>Webinars</i> <a href="https://meet.nanome.ai/webinars">https://meet.nanome.ai/webinars</a> <i>Advanced Tutorials</i> <a href="https://docs.nanome.ai/">https://docs.nanome.ai/</a>
	syglass	Immersive VR visualization of molecular and cellular structures	Education, structural biology training, interactive exploration	29	@syglass253 on YouTube <i>Tutorial Videos</i> <a href="https://www.syglass.io/academy">https://www.syglass.io/academy</a>

TABLE I. (Continued.)

Category	Software	Key features	Applications	References	Online content
Model building and structure refinement	CraftCells	Minecraft-based 3D visualization of cellular structures	Structural biology education, whole-cell modeling, outreach	53	@QCB-NSF-STC on YouTube <i>Tutorial Videos</i> <a href="https://github.com/Luthey-Schulten-Lab/CraftCells">https://github.com/Luthey-Schulten-Lab/CraftCells</a>
	CellPAINT	Artistic molecular visualization, assembly of biological environments	Visualizing molecular structures in biological contexts, scientific illustration	54	@cellpaint3991 on YouTube <i>Documentation</i> <a href="https://ccsb.scripps.edu/cellpaint/cellpaint2-documentation/">https://ccsb.scripps.edu/cellpaint/cellpaint2-documentation/</a>
	Blender	General-purpose 3D modeling and rendering software	Molecular animation, structural biology visualization, educational content	55	@BlenderOfficial on YouTube <i>Blender Studio</i> subscription platform <a href="https://studio.blender.org/welcome/">https://studio.blender.org/welcome/</a>
	Coot	Interactive model building, real-space refinement	Protein structure refinement, crystallographic model correction	56	@PaulEmsley on YouTube <i>Tutorials</i> <a href="https://www2.mrc-lmb.cam.ac.uk/personal/pemsley/coot/web/tutorial/tutorial.html">https://www2.mrc-lmb.cam.ac.uk/personal/pemsley/coot/web/tutorial/tutorial.html</a>
	Phenix	Automated structure refinement, validation tools	Macromolecular crystallography, Cryo-EM model building, structure determination	57	@PhenixTutorials on YouTube <i>Past User Workshops</i> <a href="https://phenix-online.org/workshops_tutorials">https://phenix-online.org/workshops_tutorials</a>
	Rosetta	Computational protein modeling, flexible backbone docking	Protein structure prediction, de novo protein design, molecular docking	58	@RosettaCommons on YouTube <i>In-Person Bootcamps</i> <a href="https://rosettacommons.org/education/workshops/">https://rosettacommons.org/education/workshops/</a>
Annotation, segmentation and 3D reconstruction	Refmac	Maximum likelihood refinement, TLS refinement	Protein crystallography, structure determination, model validation	59	@ccp4579 on YouTube
	CrystalMaker Suite	Model-building, high-resolution vector graphics, stereographic projection, diffraction simulation	Publication-quality images, animation, 3D printing export	60	@CrystalMakerSoftware on YouTube <i>Video Tutorials</i> <a href="https://crystallmaker.com/crystal-maker/video-tutorials/index.html">https://crystallmaker.com/crystal-maker/video-tutorials/index.html</a>
	IMOD	3D reconstruction, image segmentation, and annotation tools	Electron tomography, cryo-ET structure analysis, cell and tissue modeling	61	<i>Guides</i> <a href="https://bio3d.colorado.edu/imod/#Guides">https://bio3d.colorado.edu/imod/#Guides</a>
	Amira	Multi-modal image processing, segmentation, 3D visualization	Structural biology annotation, cryo-ET analysis, medical imaging	62	@ThermoSciEMSpec on YouTube <i>Demos</i> <a href="https://www.thermofisher.com/software-em-3d-vis/xtra-library/how-@dragonfly_software_on_YouTube">https://www.thermofisher.com/software-em-3d-vis/xtra-library/how-</a>
	Dragonfly	AI-powered image segmentation, 3D rendering, and annotation	Cryo-EM/cryo-ET image analysis, tomography segmentation, data annotation	63	@dragonfly_software on YouTube <i>Tutorials</i> <a href="https://dragonfly.comet.tech/en/resources/user-tutorials">https://dragonfly.comet.tech/en/resources/user-tutorials</a> <i>Online/On-Site Trainings</i> <a href="https://dragonfly.comet.tech/en/support-and-training/training">https://dragonfly.comet.tech/en/support-and-training/training</a>



traditional visualizations. The ability to output stereolithography files, a common format for 3D printers, from molecular modeling software has lowered the barriers for researchers to print complex biomolecular structures<sup>33,34</sup> and small molecules,<sup>35</sup> supporting both experimental design and classroom instruction. Significant efforts have been made to create 3D models of symmetry and crystallography concepts for use in the classroom. These models are often created with *Blender*<sup>36</sup> and *SolidWorks*<sup>37</sup> and can be viewed on a cell phone or 3D printed.

As more researchers adopt these technologies, the structural sciences are becoming increasingly interactive, making molecular research more accessible to both specialists and broader audiences. Looking ahead, the continued convergence of structural biology techniques with machine learning-driven modeling, real-time visualization, and physical modeling technologies is poised to transform the field. These innovations are not only improving research methodologies but also revolutionizing science communication by making complex biological structures more intuitive and engaging. By leveraging these emerging visualization technologies, structural biologists are expanding the frontiers of molecular exploration, facilitating new discoveries, and broadening the impact of structural science across disciplines.

### BROADER APPLICATIONS AND IMPACT

As visualization technologies continue to evolve, their applications in structural biology are extending beyond fundamental research and education into translational science, clinical applications, and biotechnology. These advancements are driving a paradigm shift in biomedical research, where visualization is not just a tool for understanding but also a crucial component of decision-making in healthcare and biotechnology.<sup>38,39</sup>

One emerging application is the use of AR and VR platforms in clinical and translational research works. Physicians and biomedical researchers are increasingly adopting these technologies to explore anatomical and molecular structures in 3D, improving diagnostic accuracy and surgical planning.<sup>40</sup> AR overlays onto a patient who can assist with preoperative planning and provide real-time insights into patient's status,<sup>41</sup> while VR environments allow for interactive training in complex medical procedures.<sup>42</sup> These cross-disciplinary integrations underscore the broad impact of visualization technologies in advancing both fundamental and applied sciences.

Educational and outreach efforts are also benefiting from these innovations and continue to redefine how complex structural information is communicated. As more educators adopt VR game-based<sup>43</sup> learning approaches, they are lowering barriers to scientific literacy making molecular and cellular science more accessible to students, educators, and the general public. A wide variety of free resources are available for the classroom.<sup>44</sup> This democratization of scientific exploration ensures that future generations of scientists are equipped with intuitive and powerful tools to advance structural science and its applications.

Beyond education, immersive environments offer a unique way to engage with experimental data and refine research approaches. By stepping inside molecular structures, scientists can better visualize molecular interactions, identify structural features that may not be apparent in static models, and explore biological complexity in new ways. This direct engagement with data can inspire innovative approaches in structure-based drug design, synthetic biology, and bioengineering. Researchers can use these environments to test structural hypotheses, refine computational models, and develop new methodologies that push the boundaries of structural biology.

### CHALLENGES AND OPPORTUNITIES

Despite the transformative impact of visualization technologies in the structural sciences, several challenges must be addressed to ensure their widespread adoption. One of the main obstacles is the accessibility and affordability of hardware and software. While immersive environments offer powerful ways to explore biological structures, the cost of high-quality headsets and computing systems remains a limiting factor, particularly for smaller research labs and educational institutions. Expanding access to these tools through cost-effective solutions and institutional support will be essential for broadening participation in immersive scientific exploration.

Another challenge lies in integrating these visualization tools with existing experimental and computational workflows. Structural science relies on a combination of techniques, from x-ray crystallography to single-molecule imaging, and ensuring that immersive environments can effectively complement these methods requires well-developed frameworks. By incorporating experimental data directly into interactive 3D spaces, researchers can better analyze complex molecular behaviors, refine structural models, and generate new hypotheses. Also, programs may not be as broadly applied and a certain amount of customization may be needed to extend these tools toward novel systems. Developing standardized approaches for merging visualization with experimental techniques will enhance the ability to extract meaningful insights from structural data.

Looking ahead, the continued integration of AI/ML will greatly enhance our ability to model, predict, and investigate biological structures, but their outputs must be experimentally validated to ensure accuracy and reliability. ML-driven simulations can propose structural hypotheses, automate predictions, and refine molecular models, but these computational insights remain dependent on experimental validation through biophysical assays. As visualization tools become more sophisticated, the synergy between AI-driven predictions and empirical validation will be essential to advancing discoveries.

Training and adoption remain critical areas for growth. As visualization technologies become more advanced, researchers and educators must learn how to effectively use them to enhance both scientific inquiry and instruction. Hands-on training programs, workshops, and virtual laboratories provide opportunities for students and scientists to explore molecular structures dynamically, offering perspectives that traditional 2D representations cannot. By allowing users to interact with structures at multiple scales, from single molecules to packed crystal structures, to whole cells, these tools foster a deeper understanding of structural principles and molecular mechanisms. With the rapid development of in-house apps and software, educators may find themselves with an abundance of resources, each one with its own user experience.

To complement these in-person learning opportunities, the development of accessible online resources—including walk-through tutorials and recorded demonstrations—is equally important. These educational materials would provide individuals who prefer self-paced learning a more accessible entry point for adoption. However, as expected with a large range of software options, the quality of documentation varies. This unevenness can create a barrier for some individuals and laboratories to adopt an otherwise powerful software. It is oftentimes not enough to write software and provide documentation for the end user to discover and navigate. Continuous development of accompanying resources including updates to the software documentation, user manuals, web tutorials, video tutorials, webinars, user

forums, mailing lists, and in-person training is necessary to build a large user base. For instance, Brian Toby's work teaching users how to navigate General Structure Analysis System (GSAS),<sup>45</sup> now GSAS-II,<sup>46</sup> is a particularly tenacious example of adjusting resources based on community needs.

Video tutorials are an especially helpful resource for introduction to software techniques, as they can be paused and replayed at the user's speed. The Dragonfly Daily YouTube playlist is a model example of combining video tutorials with example data on which to practice.<sup>47</sup> Software tutorial videos work well as a continuously updated resource. Blender, for example, not only offers professional training through the subscription service Blender Studio, but also promotes a specific hashtag on YouTube (#b3d) to aggregate free user-generated instructional content. The hashtag concept is a free and convenient way to collect user content, if officially promoted. Resources are linked in Table I to assist new users in getting started with the software mentioned in this article.

Moving forward, the continued development and refinement of immersive visualization tools will play a key role in driving scientific progress. By making these environments more accessible, integrating them seamlessly with experimental workflows, and expanding training opportunities, the scientific community can maximize their potential. These efforts will not only improve structural biology research but also transform education, outreach, and interdisciplinary collaboration, ensuring that immersive visualization remains a valuable tool for discovery and innovation.

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## AUTHOR DECLARATIONS

### Conflict of Interest

The authors have no conflicts to disclose.

## Author Contributions

**Edward T. Eng:** Conceptualization (equal); Writing – original draft (equal). **Nichole R. Valdez:** Conceptualization (equal); Writing – original draft (equal).

## DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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