















NanoVer Server: A Python Package for Serving Real-Time Multi-User Interactive Molecular Dynamics in Virtual Reality

Harry J. Stroud ¹✉, Mark D. Wonnacott ¹, Jonathan Barnoud ¹, Rhoslyn Roebuck Williams ¹, Mohamed Dhouioui ¹, Adam McSloy ², Ludovica Aisa ¹, Luis E. Toledo ¹, Phil Bates ², Adrian J. Mulholland ², and David R. Glowacki ¹

¹ Intangible Realities Laboratory, Centro Singular de Investigación en Tecnoloxías Intelixentes (CiTIUS), Universidade de Santiago de Compostela, Spain ² Centre for Computational Chemistry, School of Chemistry, University of Bristol, United Kingdom ✉ Corresponding author

DOI: [10.21105/joss.08118](https://doi.org/10.21105/joss.08118)

Software

- [Review](#) 
- [Repository](#) 
- [Archive](#) 

Editor: [Abhishek Tiwari](#) 

Reviewers:

- [@jkrajniak](#)
- [@samuelmurail](#)

Submitted: 13 February 2025

Published: 27 June 2025

License

Authors of papers retain copyright and release the work under a Creative Commons Attribution 4.0 International License ([CC BY 4.0](#)).

Summary

NanoVer Server is a Python package that facilitates real-time multi-user interactive molecular dynamics (iMD) simulations. It is part of the NanoVer software ecosystem, interfacing with standard molecular dynamics packages to run iMD simulations and serve them to local and remote clients over a network ([Figure 1](#)). This package includes a Python client that connects to the server, enabling researchers to incorporate iMD into their existing Python- and Jupyter-based workflows, and a suite of Jupyter notebook tutorials. Furthermore, NanoVer Server interfaces with the NanoVer iMD-VR package to facilitate its primary application: the exploration of molecular systems using interactive molecular dynamics in virtual reality (iMD-VR).

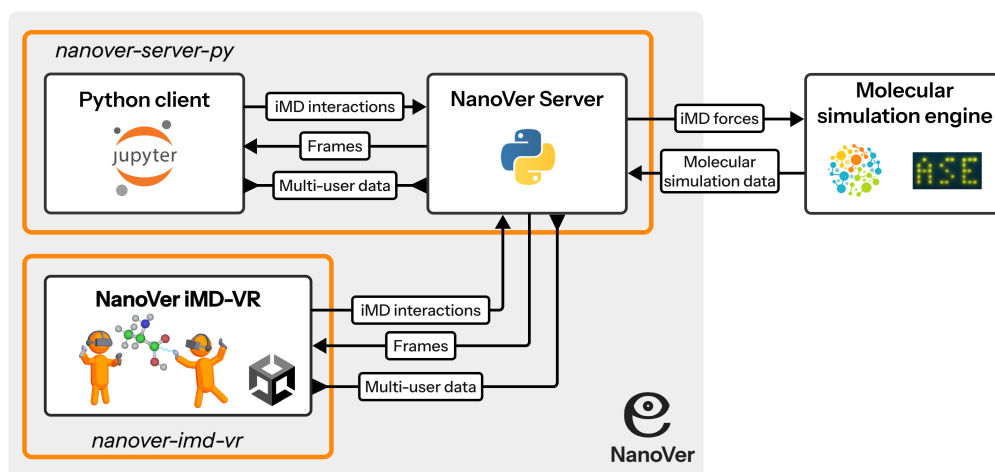


Figure 1: Systems diagram of the NanoVer ecosystem for iMD (displayed within the grey box) that illustrates how NanoVer Server communicates data between the molecular simulation engine and connected clients, and between clients themselves. The orange boxes indicate the contents of the GitHub repositories for NanoVer Server ([nanover-server-py](#)) and NanoVer iMD-VR ([nanover-imd-vr](#)).

Statement of need

Background

The family of simulation methods encompassed by the term molecular dynamics (MD) are indispensable for exploring the temporal evolution and properties of atomic and molecular systems (Alder & Wainwright, 1958, 1957, 1959; McCammon et al., 1977; Rahman, 1964; Verlet, 1967). MD has been used to study a plethora of chemical and biological systems (van Gunsteren et al., 2018) in a broad range of applications, including the prediction of protein structures (Geng et al., 2019), simulation of drug docking in protein-ligand systems (De Vivo & Cavalli, 2017), and characterisation and nano-engineering of materials (Lau et al., 2018). One of the major challenges when using MD simulations to explore the dynamics of systems in atomic detail is the sampling of rare events; many significant molecular processes occur over timescales substantially longer than are computationally feasible to model for most researchers, even when harnessing the power of high-performance computing (Kamenik et al., 2022; Yang et al., 2019). This is particularly true for biological systems (Hollingsworth & Dror, 2018), which often comprise hundreds of thousands of atoms (Brooks et al., 2024), with state-of-the-art simulations capable of modelling $\mathcal{O}(10^9)$ atoms (Dommer et al., 2023). A wide variety of enhanced sampling techniques have been developed to tackle the issue of insufficient sampling by brute force MD simulations (Hénin et al., 2022; Kamenik et al., 2022; Yang et al., 2019). Families of such techniques include (though are by no means limited to) umbrella sampling (Kästner, 2011; Torrie & Valleau, 1977), metadynamics (Barducci et al., 2008; Laio & Parrinello, 2002; Valsson et al., 2016), steered molecular dynamics (Izrailev et al., 1999; Park et al., 2003), replica exchange approaches (Geyer, 1991; Sugita & Okamoto, 1999; Swendsen & Wang, 1986) and adaptive biasing force methods (Comer et al., 2015; Darve & Pohorille, 2001). Though effective, many of these techniques have certain limitations, such as (a) requiring a priori definition of a reaction coordinate, collective variable(s) and/or constraints or restraints on the system; (b) needing a large number of simulation steps and/or multiple parallel simulations; or (c) employing adaptive strategies that are not guaranteed to sample the desired behaviour.

Interactive molecular dynamics (iMD) is a nonequilibrium enhanced sampling method that allows researchers to adaptively bias molecular simulations on-the-fly in real time (O'Connor et al., 2018, 2019; Rapaport, 1997; Stone et al., 2001). In iMD, researchers can tailor biasing forces in real time in response to the evolving system dynamics, eliminating the need to pre-program perturbations. A number of programs have implementations of iMD, including for example TeraChem (Luehr et al., 2015), SCINE (Weymuth & Reiher, 2021), and NAMD/VMD (Stone et al., 2001), which enable researchers to interact via haptic interfaces with molecular systems visualised on 2-D screens. Fewer programs are available that enable researchers to interact with 3-D MD simulations in a natively 3-D environment, which is especially important for exploring complex molecular structural transformations (O'Connor et al., 2018). One example is ExaViz, where users can interact with molecules in a CAVE-like virtual environment (Dreher et al., 2014).

Virtual reality (VR) provides a natural interface for visualising molecular systems by mapping the 3-D simulation space of the molecular system to a 3-D virtual environment that the researcher can inhabit. While several programs already enable molecular visualisation in VR (Bennie et al., 2023; Cassidy et al., 2020; Cortés Rodríguez et al., 2025; Doutreligne et al., 2014; Ozvoldik et al., 2023; Pettersen et al., 2021), few support the combination of VR-enabled 3-D visualisation with real-time iMD, with notable examples including Narupa (O'Connor et al., 2019) and UnityMol (Delalande et al., 2009; Doutreligne et al., 2014). Performing iMD in VR (iMD-VR) allows users to interact directly with molecular simulations in their native 3-D environment, enabling researchers to reach out and 'touch' molecules as if they were tangible objects (Roebuck Williams et al., 2020, 2024). Many studies have demonstrated the utility of iMD-VR for research applications, in areas spanning protein-ligand binding, (Deeks, Walters, Hare, et al., 2020; Deeks, Walters, Barnoud, et al., 2020; Henry Chan et al.,

2021; Walters et al., 2022), protein conformational dynamics (Juárez-Jiménez et al., 2020), machine-learning potential energy surfaces (Amabilino et al., 2019, 2020), discovering reaction networks (Shannon et al., 2021), materials science and catalysis (Crossley-Lewis et al., 2023), and chemistry & biochemistry education (Bennie et al., 2019).

NanoVer Server

NanoVer is a software ecosystem that grew out of the Narupa project (O'Connor et al., 2019) and employs a server-client architecture to perform real-time multi-user iMD simulations, with an emphasis on iMD-VR (Figure 1). NanoVer builds upon the development efforts of Narupa, with a focus on quantitative accuracy and a unified approach to iMD across supported simulation engines. NanoVer Server facilitates iMD by providing an interface between a molecular simulation engine and connected clients, equipping researchers with tools to interact with the molecular system in real time. NanoVer Server interfaces with several packages that are used to perform, visualise and analyse molecular simulations (Eastman et al., 2024; Gowers et al., 2016; Larsen et al., 2017; Michaud-Agrawal et al., 2011; Nguyen et al., 2018), with particular support for OpenMM. As a Python package, NanoVer Server is well-suited to Python- and Jupyter-based workflows, and can therefore be easily integrated with many of the existing tools of the computational chemistry community and beyond. Furthermore, NanoVer Server is free, open-source, and designed to be customisable and extendable to interface with other molecular simulation engines.

NanoVer Server performs quantitatively accurate iMD simulations, delivering on-the-fly metrics about the molecular simulation including energies, particle forces and velocities, and the perturbations induced by the user including the collective user forces, potential energy and cumulative work done. As the molecular simulation progresses, simulation data is delivered to connected clients in data structures called 'frames', which provide a snapshot of the state of the system at that point in time. The server allows users to tune the relationship between simulation time and real time during iMD simulations by specifying the number of simulation steps n performed by the molecular simulation engine between frame publishing events. This feature allows users to choose a small simulation time step—facilitating accurate integration of the equations of motion—without needing to visualise every simulation step.

To achieve quantitatively accurate iMD, the server adopts the following blueprint between the publishing of each frame:

- 1) Perform n simulation steps, applying the iMD forces calculated during the previous iteration
- 2) Calculate all current iMD forces applied to the system given its current configuration, passing this information to the simulation engine—these forces will be applied for the next n simulation steps
- 3) Compile the data describing the current state of the system (including the iMD forces calculated in step 2) into a frame and publish to the connected client(s)

The blueprint above yields a full description of the forces acting on the molecular system during each time step, enabling quantitative analysis of the evolution of the system during iMD interactions.

NanoVer Server interfaces with NanoVer iMD-VR, a VR client that enables researchers to visualise and interact with real-time iMD simulations in virtual reality and includes support for the latest generation of standalone Meta Quest head mounted displays. The server-client architecture of NanoVer facilitates multi-user iMD-VR by sharing live updates among all connected clients describing each user's current state (e.g. interactions, avatar position). With NanoVer, multiple VR clients can connect to a server to occupy the same virtual environment from the same physical space (colocated clients) and/or from different physical spaces (distributed clients), as illustrated in Figure 2. This flexible structure has great potential

for collaborative research: for example, previous iMD-VR frameworks have demonstrated that cloud computing can be used to facilitate real-time multi-user iMD-VR across large physical distances (Deeks, Walters, Barnoud, et al., 2020; Deeks et al., 2023; Glowacki et al., 2022; Jamieson-Binnie et al., 2020). Furthermore, the communication protocol on which NanoVer Server is built comprises general tools for constructing multi-user VR experiences, which has the potential to extend beyond application in computational chemistry.

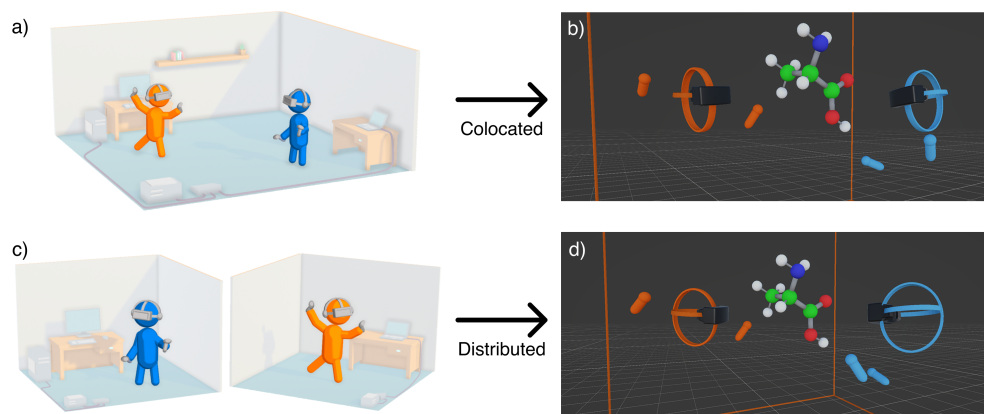


Figure 2: Illustration of colocated and distributed VR setups, and the relationship between the users' physical spaces (left) and virtual spaces (right). In colocated setups, there is a one-to-one mapping of the absolute positions of the users' bodies in physical space (a) to their avatar positions in the virtual space (b). In distributed setups, users occupy different physical spaces (c) and their virtual spaces are overlaid (d).

Availability

NanoVer Server can be installed as a [Conda package](#) and the source code is available on [GitHub](#). The [documentation](#) is available online, including instructions on [how to install NanoVer Server](#).

NanoVer Server also has a suite of [Jupyter notebook tutorials](#), many of which demonstrate how to use the server in conjunction with the [NanoVer iMD-VR client](#). Details of [compatible VR setups](#) can be found in our documentation. For new users, the [basics notebooks](#) are a good place to start, which provide hands-on tutorials that introduce many of the key features of NanoVer.

Acknowledgements

This work is supported by the European Research Council under the European Union's Horizon 2020 research and innovation programme through consolidator Grant NANOVR 866559. D.R.G. recognises the Axencia Galega de Innovación for funding as an Investigador Distinguido through the Oportunius Program, and the Xunta de Galicia (Centro de investigación de Galicia accreditation 2019–2022, ED431G-2019/04). A.J.M. recognises funding from the European Research Council under the European Horizon 2020 research and innovation program (PREDACTED Advanced Grant Agreement no. 101021207). A.J.M. and A.M. were funded by BBSRC grant number BB/T017066/1. P.B. is funded by the Royal Society Entrepreneur in Residence Scheme.

Author contributions: H.J.S. software development and documentation, figure creation, paper writing and submission; M.D.W. software development and documentation, paper editing; J.B. software development and documentation; R.R.W. software development and documentation,

paper editing, figure creation; M.D. software development and documentation, paper editing; A.M. software development; L.A. software development and documentation, paper editing; L.E.T. software development, figure creation, paper editing; P.B. project coordination; A.J.M. project coordination, principal investigator; D.R.G. project coordination, principal investigator. All authors reviewed and approved this paper for submission.

We would like to thank all previous contributors to NanoVer. A full list of contributors to NanoVer can be found in the [CONTRIBUTORS file](#) in the public repository.

Finally, we would like to thank the developers of the Python packages used by NanoVer Server, and the Python community as a whole for providing a great ecosystem that facilitates development of free and open source scientific software.

References

- Alder, B. J., & Wainwright, T. E. (1958). Molecular dynamics by electronic computers. In I. Prigogine (Ed.), *Proceedings of the International Symposium on the Statistical Mechanical Theory of Transport Processes (Brussels, 1956)* (pp. 97–131). John Wiley Interscience.
- Alder, B. J., & Wainwright, T. E. (1957). Phase Transition for a Hard Sphere System. *The Journal of Chemical Physics*, 27(5), 1208–1209. <https://doi.org/10.1063/1.1743957>
- Alder, B. J., & Wainwright, T. E. (1959). Studies in Molecular Dynamics. I. General Method. *The Journal of Chemical Physics*, 31(2), 459–466. <https://doi.org/10.1063/1.1730376>
- Amabilino, S., Bratholm, L. A., Bennie, S. J., O'Connor, M. B., & Glowacki, D. R. (2020). Training atomic neural networks using fragment-based data generated in virtual reality. *The Journal of Chemical Physics*, 153(15), 154105. <https://doi.org/10.1063/5.0015950>
- Amabilino, S., Bratholm, L. A., Bennie, S. J., Vaucher, A. C., Reiher, M., & Glowacki, D. R. (2019). Training Neural Nets To Learn Reactive Potential Energy Surfaces Using Interactive Quantum Chemistry in Virtual Reality. *The Journal of Physical Chemistry A*, 123(20), 4486–4499. <https://doi.org/10.1021/acs.jpca.9b01006>
- Barducci, A., Bussi, G., & Parrinello, M. (2008). Well-Tempered Metadynamics: A Smoothly Converging and Tunable Free-Energy Method. *Physical Review Letters*, 100(2), 020603. <https://doi.org/10.1103/PhysRevLett.100.020603>
- Bennie, S. J., Maritan, M., Gast, J., Loschen, M., Gruffat, D., Bartolotta, R., Hessenauer, S., Leija, E., & McCloskey, S. (2023). A virtual and mixed reality platform for molecular design & drug discovery-Nanome version 1.24. *Workshop on Molecular Graphics and Visual Analysis of Molecular Data*. <https://doi.org/10.2312/molva.20231114>
- Bennie, S. J., Ranaghan, K. E., Deeks, H., Goldsmith, H. E., O'Connor, M. B., Mulholland, A. J., & Glowacki, D. R. (2019). Teaching Enzyme Catalysis Using Interactive Molecular Dynamics in Virtual Reality. *Journal of Chemical Education*, 96(11), 2488–2496. <https://doi.org/10.1021/acs.jchemed.9b00181>
- Brooks, C. L., MacKerell, A. D., Post, C. B., & Nilsson, L. (2024). Biomolecular dynamics in the 21st century. *Biochimica Et Biophysica Acta (BBA) - General Subjects*, 1868(2), 130534. <https://doi.org/10.1016/j.bbagen.2023.130534>
- Cassidy, K. C., Šefčík, J., Raghav, Y., Chang, A., & Durrant, J. D. (2020). ProteinVR: Web-based molecular visualization in virtual reality. *PLOS Computational Biology*, 16(3), e1007747. <https://doi.org/10.1371/journal.pcbi.1007747>
- Comer, J., Gumbart, J. C., Hénin, J., Lelièvre, T., Pohorille, A., & Chipot, C. (2015). The Adaptive Biasing Force Method: Everything You Always Wanted To Know but Were Afraid To Ask. *The Journal of Physical Chemistry B*, 119(3), 1129–1151. <https://doi.org/10.1021/jp506633n>

- Cortés Rodríguez, F. J., Frattini, G., Phloi-Montri, S., Pinto Meireles, F. T., Terrien, D. A., Cruz-León, S., Dal Peraro, M., Schier, E., Lindorff-Larsen, K., Limpanuparb, T., Moreno, D. M., & Abriata, L. A. (2025). MolecularWebXR: Multiuser discussions in chemistry and biology through immersive and inclusive augmented and virtual reality. *Journal of Molecular Graphics and Modelling*, 135, 108932. <https://doi.org/10.1016/j.jmgm.2024.108932>
- Crossley-Lewis, J., Dunn, J., Buda, C., Sunley, G. J., Elena, A. M., Todorov, I. T., Yong, C. W., Glowacki, D. R., Mulholland, A. J., & Allan, N. L. (2023). Interactive molecular dynamics in virtual reality for modelling materials and catalysts. *Journal of Molecular Graphics and Modelling*, 125, 108606. <https://doi.org/10.1016/j.jmgm.2023.108606>
- Darve, E., & Pohorille, A. (2001). Calculating free energies using average force. *The Journal of Chemical Physics*, 115(20), 9169–9183. <https://doi.org/10.1063/1.1410978>
- De Vivo, M., & Cavalli, A. (2017). Recent advances in dynamic docking for drug discovery. *WIREs Computational Molecular Science*, 7(6), e1320. <https://doi.org/10.1002/wcms.1320>
- Deeks, H. M., Walters, R. K., Barnoud, J., Glowacki, D. R., & Mulholland, A. J. (2020). Interactive Molecular Dynamics in Virtual Reality Is an Effective Tool for Flexible Substrate and Inhibitor Docking to the SARS-CoV-2 Main Protease. *Journal of Chemical Information and Modeling*, 60(12), 5803–5814. <https://doi.org/10.1021/acs.jcim.0c01030>
- Deeks, H. M., Walters, R. K., Hare, S. R., O'Connor, M. B., Mulholland, A. J., & Glowacki, D. R. (2020). Interactive molecular dynamics in virtual reality for accurate flexible protein-ligand docking. *PLOS ONE*, 15(3), e0228461. <https://doi.org/10.1371/journal.pone.0228461>
- Deeks, H. M., Zinovjev, K., Barnoud, J., Mulholland, A. J., van der Kamp, M. W., & Glowacki, D. R. (2023). Free energy along drug-protein binding pathways interactively sampled in virtual reality. *Scientific Reports*, 13(1), 16665. <https://doi.org/10.1038/s41598-023-43523-x>
- Delalande, O., Férey, N., Grasseau, G., & Baaden, M. (2009). Complex molecular assemblies at hand via interactive simulations. *Journal of Computational Chemistry*, 30(15), 2375–2387. <https://doi.org/10.1002/jcc.21235>
- Dommer, A., Casalino, L., Kearns, F., Rosenfeld, M., Wauer, N., Ahn, S.-H., Russo, J., Oliveira, S., Morris, C., Bogetti, A., Trifan, A., Brace, A., Sztain, T., Clyde, A., Ma, H., Chennubhotla, C., Lee, H., Turilli, M., Khalid, S., ... Amaro, R. E. (2023). #COVIDisAirborne: AI-enabled multiscale computational microscopy of delta SARS-CoV-2 in a respiratory aerosol. *The International Journal of High Performance Computing Applications*, 37(1), 28–44. <https://doi.org/10.1177/10943420221128233>
- Doutreligne, S., Cragolini, T., Pasquali, S., Derreumaux, P., & Baaden, M. (2014). UnityMol: Interactive scientific visualization for integrative biology. *IEEE Symposium on Large Data Analysis and Visualization 2014, LDAV 2014 - Proceedings*, 109–110. <https://doi.org/10.1109/LDAV.2014.7013213>
- Dreher, M., Prevotau-Jonquet, J., Trellet, M., Piuze, M., Baaden, M., Raffin, B., Férey, N., Robert, S., & Limet, S. (2014). ExaViz: A Flexible Framework to Analyse, Steer and Interact with Molecular Dynamics Simulations. *Faraday Discussions*, 169, 119. <https://doi.org/10.1039/C3FD00142C>
- Eastman, P., Galvelis, R., Peláez, R. P., Abreu, C. R. A., Farr, S. E., Gallicchio, E., Gorenko, A., Henry, M. M., Hu, F., Huang, J., Krämer, A., Michel, J., Mitchell, J. A., Pande, V. S., Rodrigues, J. P., Rodriguez-Guerra, J., Simmonett, A. C., Singh, S., Swails, J., ... Markland, T. E. (2024). OpenMM 8: Molecular Dynamics Simulation with Machine Learning Potentials. *The Journal of Physical Chemistry B*, 128(1), 109–116. <https://doi.org/10.1021/acs.jpcb.3c06662>
- Geng, H., Chen, F., Ye, J., & Jiang, F. (2019). Applications of Molecular Dynamics Simu-

- lation in Structure Prediction of Peptides and Proteins. *Computational and Structural Biotechnology Journal*, 17, 1162–1170. <https://doi.org/10.1016/j.csbj.2019.07.010>
- Geyer, C. J. (1991). Markov chain Monte Carlo maximum likelihood. *Computing Science and Statistics: Proceedings of the 23rd Symposium on the Interface*, 156–163.
- Glowacki, D. R., Roebuck Williams, R., Wonnacott, M. D., Maynard, O. M., Freire, R., Pike, J. E., & Chatziapostolou, M. (2022). Group VR experiences can produce ego attenuation and connectedness comparable to psychedelics. *Scientific Reports*, 12(1), 8995. <https://doi.org/10.1038/s41598-022-12637-z>
- Gowers, R. J., Linke, M., Barnoud, J., Reddy, T. J. E., Melo, M. N., Seyler, S. L., Domański, J., Dotson, D. L., Buchoux, S., Kenney, I. M., & Beckstein, O. (2016). MDAAnalysis: A Python Package for the Rapid Analysis of Molecular Dynamics Simulations. In S. Benthall & S. Rostrup (Eds.), *Proceedings of the 15th Python in Science Conference* (pp. 98–105). <https://doi.org/10.25080/Majora-629e541a-00e>
- Hénin, J., Lelièvre, T., Shirts, M. R., Valsson, O., & Delemotte, L. (2022). Enhanced Sampling Methods for Molecular Dynamics Simulations [Article v1.0]. *Living Journal of Computational Molecular Science*, 4(1), 1583. <https://doi.org/10.33011/livecoms.4.1.1583>
- Henry Chan, H. T., Moesser, M. A., Walters, R. K., Malla, T. R., Twidale, R. M., John, T., Deeks, H. M., Johnston-Wood, T., Mikhailov, V., Sessions, R. B., Dawson, W., Salah, E., Lukacik, P., Strain-Damerell, C., David Owen, C., Nakajima, T., Świderek, K., Lodola, A., Moliner, V., ... Morris, G. M. (2021). Discovery of SARS-CoV-2 M pro peptide inhibitors from modelling substrate and ligand binding. *Chemical Science*, 12(41), 13686–13703. <https://doi.org/10.1039/D1SC03628A>
- Hollingsworth, S. A., & Dror, R. O. (2018). Molecular Dynamics Simulation for All. *Neuron*, 99(6), 1129–1143. <https://doi.org/10.1016/j.neuron.2018.08.011>
- Izrailev, S., Stepaniants, S., Isralewitz, B., Kosztin, D., Lu, H., Molnar, F., Wriggers, W., & Schulten, K. (1999). Steered molecular dynamics. In P. Deuffhard, J. Hermans, B. Leimkuhler, A. E. Mark, S. Reich, & R. D. Skeel (Eds.), *Computational Molecular Dynamics: Challenges, Methods, Ideas* (pp. 39–65). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-58360-5_2
- Jamieson-Binnie, A. D., O'Connor, M. B., Barnoud, J., Wonnacott, M. D., Bennie, S. J., & Glowacki, D. R. (2020). Narupa iMD: A VR-Enabled Multiplayer Framework for Streaming Interactive Molecular Simulations. *ACM SIGGRAPH 2020 Immersive Pavilion*. <https://doi.org/10.1145/3388536.3407891>
- Juárez-Jiménez, J., Tew, P., O Connor, M., Llabrés, S., Sage, R., Glowacki, D., & Michel, J. (2020). Combining Virtual Reality Visualization with Ensemble Molecular Dynamics to Study Complex Protein Conformational Changes. *Journal of Chemical Information and Modeling*, 60(12), 6344–6354. <https://doi.org/10.1021/acs.jcim.0c00221>
- Kamenik, A. S., Linker, S. M., & Riniker, S. (2022). Enhanced sampling without borders: On global biasing functions and how to reweight them. *Physical Chemistry Chemical Physics*, 24(3), 1225–1236. <https://doi.org/10.1039/D1CP04809K>
- Kästner, J. (2011). Umbrella sampling. *WIREs Computational Molecular Science*, 1(6), 932–942. <https://doi.org/10.1002/wcms.66>
- Laio, A., & Parrinello, M. (2002). Escaping free-energy minima. *Proceedings of the National Academy of Sciences*, 99(20), 12562–12566. <https://doi.org/10.1073/pnas.202427399>
- Larsen, A. H., Mortensen, J. J., Blomqvist, J., Castelli, I. E., Christensen, R., Duřak, M., Friis, J., Groves, M. N., Hammer, B., Hargus, C., Hermes, E. D., Jennings, P. C., Jensen, P. B., Kermode, J., Kitchin, J. R., Kolsbjerg, E. L., Kubal, J., Kaasbjerg, K., Lysgaard, S., ... Jacobsen, K. W. (2017). The atomic simulation environment—a Python

- library for working with atoms. *Journal of Physics: Condensed Matter*, 29(27), 273002. <https://doi.org/10.1088/1361-648X/aa680e>
- Lau, D., Jian, W., Yu, Z., & Hui, D. (2018). Nano-engineering of construction materials using molecular dynamics simulations: Prospects and challenges. *Composites Part B: Engineering*, 143, 282–291. <https://doi.org/10.1016/j.compositesb.2018.01.014>
- Luehr, N., Jin, A. G. B., & Martínez, T. J. (2015). Ab Initio Interactive Molecular Dynamics on Graphical Processing Units (GPUs). *Journal of Chemical Theory and Computation*, 11(10), 4536–4544. <https://doi.org/10.1021/acs.jctc.5b00419>
- McCammon, J. A., Gelin, B. R., & Karplus, M. (1977). Dynamics of folded proteins. *Nature*, 267(5612), 585–590. <https://doi.org/10.1038/267585a0>
- Michaud-Agrawal, N., Denning, E. J., Woolf, T. B., & Beckstein, O. (2011). MDAAnalysis: A toolkit for the analysis of molecular dynamics simulations. *Journal of Computational Chemistry*, 32(10), 2319–2327. <https://doi.org/10.1002/jcc.21787>
- Nguyen, H., Case, D. A., & Rose, A. S. (2018). NGLview–interactive molecular graphics for Jupyter notebooks. *Bioinformatics*, 34(7), 1241–1242. <https://doi.org/10.1093/bioinformatics/btx789>
- O'Connor, M. B., Bennie, S. J., Deeks, H. M., Jamieson-Binnie, A., Jones, A. J., Shannon, R. J., Walters, R., Mitchell, T. J., Mulholland, A. J., & Glowacki, D. R. (2019). Interactive molecular dynamics in virtual reality from quantum chemistry to drug binding: An open-source multi-person framework. *Journal of Chemical Physics*, 150(22), 220901. <https://doi.org/10.1063/1.5092590>
- O'Connor, M. B., Deeks, H. M., Dawn, E., Metatla, O., Roudaut, A., Sutton, M., Thomas, L. M., Glowacki, B. R., Sage, R., Tew, P., Wonnacott, M., Bates, P., Mulholland, A. J., & Glowacki, D. R. (2018). Sampling molecular conformations and dynamics in a multiuser virtual reality framework. *Science Advances*, 4(6). <https://doi.org/10.1126/sciadv.aat2731>
- Ozvodik, K., Stockner, T., & Krieger, E. (2023). YASARA Model–Interactive Molecular Modeling from Two Dimensions to Virtual Realities. *Journal of Chemical Information and Modeling*, 63(20), 6177–6182. <https://doi.org/10.1021/acs.jcim.3c01136>
- Park, S., Khalili-Araghi, F., Tajkhorshid, E., & Schulten, K. (2003). Free energy calculation from steered molecular dynamics simulations using Jarzynski's equality. *J. Chem. Phys.*, 119(6), 3559–3566. <https://doi.org/10.1063/1.1590311>
- Pettersen, E. F., Goddard, T. D., Huang, C. C., Meng, E. C., Couch, G. S., Croll, T. I., Morris, J. H., & Ferrin, T. E. (2021). UCSF ChimeraX: Structure visualization for researchers, educators, and developers. *Protein Science*, 30(1), 70–82. <https://doi.org/10.1002/PRO.3943>
- Rahman, A. (1964). Correlations in the Motion of Atoms in Liquid Argon. *Physical Review*, 136(2A), A405–A411. <https://doi.org/10.1103/PhysRev.136.A405>
- Rapaport, D. C. (1997). Interactive molecular dynamics. *Physica A: Statistical Mechanics and Its Applications*, 240(1), 246–254. [https://doi.org/10.1016/S0378-4371\(97\)00148-9](https://doi.org/10.1016/S0378-4371(97)00148-9)
- Roebuck Williams, R., Barnoud, J., Toledo, L., Holzapfel, T., & Glowacki, D. R. (2024). Measuring the Limit of Perception of Bond Stiffness of Interactive Molecules in VR via a Gamified Psychophysics Experiment. In L. T. De Paolis, P. Arpaia, & M. Sacco (Eds.), *Extended Reality* (pp. 190–198). Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-71707-9_13
- Roebuck Williams, R., Varcoe, X., Glowacki, B. R., Gale, E. M., Jamieson-Binnie, A., & Glowacki, D. R. (2020). Subtle Sensing: Detecting Differences in the Flexibility of Virtually Simulated Molecular Objects. *Extended Abstracts of the 2020 CHI Conference on Human Factors in Computing Systems*, 1–8. <https://doi.org/10.1145/3334480.3383026>

- Shannon, R. J., Deeks, H. M., Burfoot, E., Clark, E., Jones, A. J., Mulholland, A. J., & Glowacki, D. R. (2021). Exploring human-guided strategies for reaction network exploration: Interactive molecular dynamics in virtual reality as a tool for citizen scientists. *The Journal of Chemical Physics*, 155(15), 154106. <https://doi.org/10.1063/5.0062517>
- Stone, J. E., Gullingsrud, J., & Schulten, K. (2001). A system for interactive molecular dynamics simulation. *Proceedings of the 2001 Symposium on Interactive 3D Graphics*, 191–194. <https://doi.org/10.1145/364338.364398>
- Sugita, Y., & Okamoto, Y. (1999). Replica-exchange molecular dynamics method for protein folding. *Chemical Physics Letters*, 314(1), 141–151. [https://doi.org/10.1016/S0009-2614\(99\)01123-9](https://doi.org/10.1016/S0009-2614(99)01123-9)
- Swendsen, R. H., & Wang, J.-S. (1986). Replica Monte Carlo simulation of spin-glasses. *Physical Review Letters*, 57(21), 2607–2609. <https://doi.org/10.1103/PhysRevLett.57.2607>
- Torrie, G. M., & Valleau, J. P. (1977). Nonphysical sampling distributions in Monte Carlo free-energy estimation: Umbrella sampling. *Journal of Computational Physics*, 23(2), 187–199. [https://doi.org/10.1016/0021-9991\(77\)90121-8](https://doi.org/10.1016/0021-9991(77)90121-8)
- Valsson, O., Tiwary, P., & Parrinello, M. (2016). Enhancing Important Fluctuations: Rare Events and Metadynamics from a Conceptual Viewpoint. *Annual Review of Physical Chemistry*, 67, 159–184. <https://doi.org/10.1146/annurev-physchem-040215-112229>
- van Gunsteren, W. F., Daura, X., Hansen, N., Mark, A. E., Oostenbrink, C., Riniker, S., & Smith, L. J. (2018). Validation of Molecular Simulation: An Overview of Issues. *Angewandte Chemie International Edition*, 57(4), 884–902. <https://doi.org/10.1002/anie.201702945>
- Verlet, L. (1967). Computer "Experiments" on Classical Fluids. I. Thermodynamical Properties of Lennard-Jones Molecules. *Physical Review*, 159(1), 98–103. <https://doi.org/10.1103/PhysRev.159.98>
- Walters, R. K., Gale, E. M., Barnoud, J., Glowacki, D. R., & Mulholland, A. J. (2022). The emerging potential of interactive virtual reality in drug discovery. *Expert Opinion on Drug Discovery*, 17(7), 685–698. <https://doi.org/10.1080/17460441.2022.2079632>
- Weymuth, T., & Reiher, M. (2021). Immersive Interactive Quantum Mechanics for Teaching and Learning Chemistry. *CHIMIA*, 75(1–2), 45–49. <https://doi.org/10.2533/chimia.2021.45>
- Yang, Y. I., Shao, Q., Zhang, J., Yang, L., & Gao, Y. Q. (2019). Enhanced sampling in molecular dynamics. *The Journal of Chemical Physics*, 151(7), 070902. <https://doi.org/10.1063/1.5109531>