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

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Software

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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).

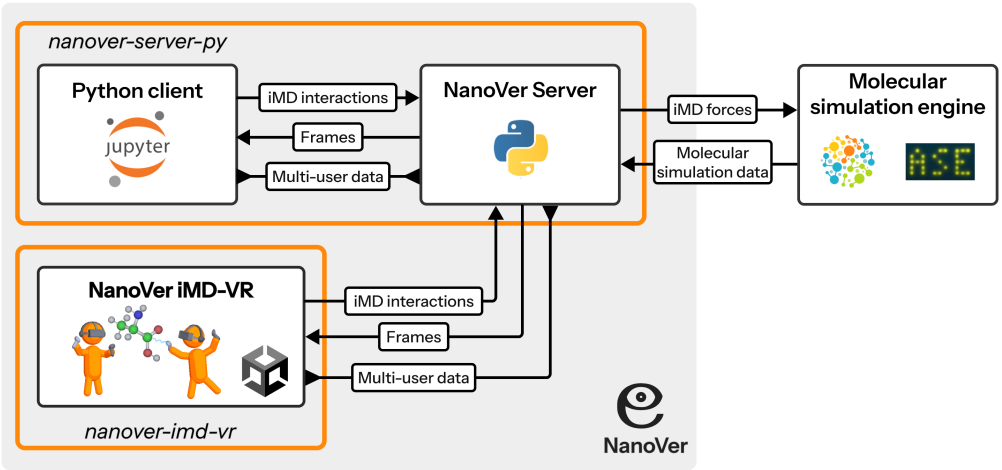

Figure 1: Systems diagram of the NanoVer ecosystem for iMD (displayed within the grey box) that illustrates how NanoVer Server communicates data between the molecular simulation engine and connected clients, and between clients themselves. The orange boxes indicate the contents of the GitHub repositories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

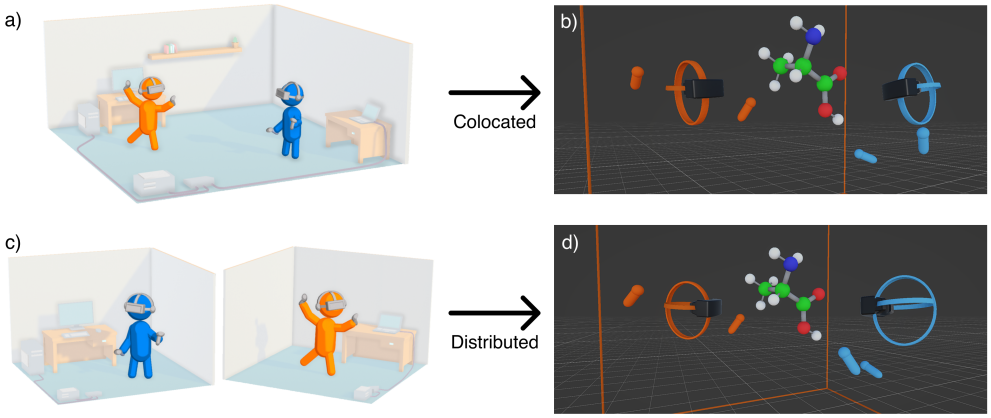

Figure 2: Illustration of colocated and distributed VR setups, and the relationship between the users' physical spaces (left) and virtual spaces (right). In colocated setups, there is a one-to-one mapping of the absolute positions of the users' bodies in physical space (a) to their avatar positions in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

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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.

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