NAMD
Features and Capabilities

Mohammad Soroush Barhaghi

NIH Biotechnology Center for Macromolecular Modeling and Bioinformatics
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

Computational Biophysics
Virtual Workshop, 2021
NAMD: Not just Another Molecular Dynamics!

- From 1996 to 2021
- From 2018 to 2021

Distribution of VMD and NAMD citations across the US. Both software have been cited by authors in every single US state.
NAMD: Not just Another Molecular Dynamics!

1996-2021: 37,000 papers published that have cited VMD and/or NAMD.

VMD and NAMD are used in a broad range of biological fields:
- Protein dynamics
- Free energy / statistical mechanics methods
- Docking studies
- Drug design
- Quantum chemistry
- Membrane proteins / transport
- Experimental structure determination
- Multi-scale / cell-scale modeling
- Machine learning / AI methods
- Experimental work not focused on structure determination
- Virology

Over 2.2 million total downloads of Resource software

Number of citing papers* with at least one author from the region

*includes all citations (1996-2021)
NAMD: Not just Another Molecular Dynamics!

Resource's software is cited once every 1 h and 8 min

(smaller is better!)

(year)

(Time to the next citation (h))
NAMD: Not just Another Molecular Dynamics!

About 350 papers published in just over one year describe COVID-related research employing the Resource’s software

Over 30 NIH-funded publications

NIH-funded Research

US investigators

Other Countries
NAMD: Not just Another Molecular Dynamics!

Winner of 2020 ACM Gordon Bell Special Prize for HPC-Based COVID-19 Research.

Images rendered by VMD.

Developed in object-oriented C++ starting from the mid ‘90s
- Designed for parallel scaling of large biomolecular systems
- Uses Charm++ parallel messaging framework
- Supports: Unix/Linux, Windows, and MacOS
- Cloud computing: AWS and MS Azure

\[ F_i = -\frac{dV}{dr_i} \]
\[ a_i = \frac{F_i}{m} \]
\[ s_i = s_{0i} + v_i t + \frac{1}{2} a_i t^2 \]
NAMD Features

Numerical Integrators

- Verlet
- Stochastic dynamics (BBK)
- Multiple time stepping (r-RESPA)
- Constrained dynamics (SHAKE)

NAMD Features

Supported Force Fields:
- CHARMM
- AMBER
- OPLS-AA
- GROMOS
- CHARMM Drude Polarizability

Supported Force Fields:
- Implicit Solvent: Generalized Born implicit solvent (GBIS)
- Explicit Solvent:
  - 3-site: TIP3P
  - 4-site: TIP4P
  - 5-site: SWM4-NDP (Drude)
NAMD Features

Supported Ensembles

- NVE
- NVT
  - Langevin dynamics
  - Stochastic velocity rescaling
- NPT
  - Langevin piston
  - Berendsen barostat
- Constant-pH
NAMD Advanced Features (External Forces)

**Constant Forces**

\[ U(\vec{R}, t) = \frac{1}{2} k_1 \left[ vt - (\vec{R}(t) - \vec{R}(0)).\vec{n} \right]^2 \]

**Steered MD:**

\[ \frac{1}{2} k_2 \left[ (\vec{R}(t) - \vec{R}(0))^2 + ((\vec{R}(t) - \vec{R}(0)).\vec{n})^2 \right] \]

**Restraints:**

\[ U(\vec{R}, t) = \frac{1}{2} k \left[ (\vec{R}(t) - \vec{R}_{\text{ref}}).\vec{d} \right]^2, \vec{d} = \hat{i}, \hat{j}, \hat{k} \]

**Rotating Restraints**

**Symmetry Restraints**
NAMD Advanced Features (External Forces)

Interactive MD (IMD)

Tcl Forces

Tcl Boundary Forces: e.g. Spherical or cylindrical

Targeted MD (TMD):

\[ U(\vec{R}, t) = \frac{1}{2N} k \left[ \left( RMS(\vec{R}, t) - RMS^*(\vec{R}, t) \right) \right]^2 \]

Double-sided TMD:

\[ U(\vec{R}, t) = \frac{1}{2N} k \left[ \left( DRMS(\vec{R}, t) - DRMS^*(\vec{R}, t) \right) \right]^2 \]

\[ DRMS(\vec{R}, t) = RMS_1(\vec{R}, t) - RMS_2(\vec{R}, t) \]
NAMD Advanced Features (External Forces)

External Electric Field

Grid Forces → MDFF → Fit the structure to the cryo-EM density map

(A) Single DNA strand passing through an α-hemolysin nanopore
(B) Electrostatic potential contour map

(A) The X-ray structure of an adenylate kinase protein (PDB:1AKE).
(B) The protein structure rigid body docked to the density map.
(C) The protein structure inside the density map after running a MDFF simulation.
(D) The overall quality of fit (cross correlation) during a MDFF simulation.

A simple MDFF example of fitting a protein structure into a density map.
NAMD Advanced Features: Colvars

These features are contributed to NAMD by Giacomo Fiorin (NIH) and Jérôme Hénin (CNRS, France)

Colvars

Collective variables module for molecular simulation programs

A software module for molecular simulation programs, which provides a flexible and high-performance platform for present and future algorithms. Reference online:

- LAMMPS version: PDF HTML
- NAMD version: PDF HTML
- VMD version: PDF HTML

Reference manual:

- LAMMPS version: PDF HTML
- NAMD version: PDF HTML
- VMD version: PDF HTML

https://colvars.github.io/
https://github.com/Colvars/colvars
https://www.ks.uiuc.edu/Research/namd/2.14/ug/node53.html

biases

colvars

components

colvar{
  name d
  distance {
    name d_1
    componentCoeff 1.0
    group1 {atomNumbers 1 2}
    group2 {atomNumbers 3 4 5}
  }
  distance {
    name d_2
    componentCoeff -1.0
    group1 {atomNumbers 7}
    group2 {atomNumbers 8 9 10}
  }
}
colvar{
  name c
  coordNum {
    name coord
cutoff 6.0
    group1 {atomNumbersRange 1-10}
    group2 {atomNumbersRange 11-20}
  }
}
## NAMD Advanced Features: Colvars

### Components

<table>
<thead>
<tr>
<th>Scalar</th>
<th></th>
<th>Non-scalar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. distance</td>
<td>18. Orientation projection</td>
<td>1. Distance vector</td>
</tr>
<tr>
<td>2. Distance z</td>
<td>19. tilt</td>
<td>2. Distance direction</td>
</tr>
<tr>
<td>3. Distance xy</td>
<td>20. Spin angle</td>
<td>3. cartesian</td>
</tr>
<tr>
<td>4. Polar theta</td>
<td>21. gyration</td>
<td>4. orientation</td>
</tr>
<tr>
<td>5. Polar phi</td>
<td>22. inertia</td>
<td></td>
</tr>
<tr>
<td>6. Distance inverse</td>
<td>23. Inertia z</td>
<td></td>
</tr>
<tr>
<td>7. Distance pairs</td>
<td>24. Eigen vector</td>
<td></td>
</tr>
<tr>
<td>8. Dipole magnitude</td>
<td>25. Alpha dihedrals</td>
<td></td>
</tr>
<tr>
<td>10. Dipole angle</td>
<td>27. Dihedral Principle Component</td>
<td></td>
</tr>
<tr>
<td>11. dihedral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Coordinate number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Self coordinate number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Group coordinate number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Hydrogen bond</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. RMSD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Orientation angle</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Biases

1. Thermodynamic Integration
2. Adaptive Biasing Force
3. Extended-system Adaptive Biasing Force
4. Metadynamics
   a. Ensemble-Biased Metadynamics
   b. Well-tempered metadynamics
   c. Multiple-walker metadynamics
5. Harmonic restraints
   a. Moving restraints: SMD
   b. Moving restraints: US
   c. Changing force constant
6. Harmonic wall restraints
7. Linear restraints
8. Adaptive Linear Bias
9. Multidimensional histograms
10. Probability distribution-restraints
NAMD Advanced Features: Colvars

(A) Boltzmann sampling favors low-energy regions.

(B) Depositing harmonic potentials in US.

(C) ABF, or its extended-Lagrangian (eABF).

(D) Depositing Gaussian potentials in MtD.

(E) Combination of MtD, eABF, and meta-eABF.

(F) Multiplewalker extension of MtD.

(G) Multiplewalker extension ABF or eABF.

(H) Multiplewalker extension meta-eABF.

Sampling of a rugged free-energy landscape.
NAMD Advanced Features: Colvars

Graphical representation of a Colvars configuration
NAMD: Accelerated Molecular Dynamics

\[ V^*(\vec{R}, t) = V(\vec{R}, t) + V_{\text{boost}}(\vec{R}, t) \]

\[ V_{\text{boost}}(\vec{R}, t) = \begin{cases} f(\vec{R}, t), & V(\vec{R}, t) < E_{\text{threshold}} \\ 0, & V(\vec{R}, t) \geq E_{\text{threshold}} \end{cases} \]

**Options:** \( V_{\text{dihedral}}, V_{\text{total}} - V_{\text{dihedral}}, \) or both

**Accelerated MD (aMD):**

\[ f(\vec{R}, t) = \frac{[E_{\text{threshold}} - V(\vec{R}, t)]^2}{\alpha + E_{\text{threshold}} - V(\vec{R}, t)} \]

**Gaussian Accelerated MD (GaMD):**

\[ f(\vec{R}, t) = \frac{1}{2} k [E_{\text{threshold}} - V(\vec{R}, t)]^2 \]
NAMD: Multiple Copy/Replica Algorithms

- Temperature replica exchange (T-REMD)
- Hamiltonian replica exchange ($\mathcal{H}$-REMD)
- FEP with $\lambda$ replica exchange (FEP/$\lambda$, $\mathcal{H}$-REMD)
- Umbrella Sampling with Hamiltonian replica exchange (US/$\mathcal{H}$-REMD)
- String method with swarms of trajectories (SMwST)

An illustration of the replica exchange molecular dynamic method.

Generic implementation of Multiple copy algorithm in the Charm++ RTS.

NAMD: Alchemical Free Energy

**FEP:** \[ \Delta F(A \rightarrow B) = -\frac{1}{\beta} \sum_{i=0}^{N-1} \ln[\exp[-\beta(U(\lambda_{i+1}) - U(\lambda_i))]]_i \]

**TI:** \[ \Delta F(A \rightarrow B) = \int_{\lambda=0}^{\lambda=1} \left( \frac{dU}{d\lambda} \right)_\lambda d\lambda \]

\[ U(\lambda) = \lambda U_B + (1 - \lambda) U_A \]

NAMD: Alchemical Free Energy

\[ \lambda U(r_{ij}, \lambda) = \lambda_{LJ} \varepsilon_{ij} \left[ \left( \frac{R_{\text{min}}^2}{r_{ij}^2 + \alpha(1 - \lambda_{LJ})} \right)^6 - \left( \frac{R_{\text{min}}^2}{r_{ij}^2 + \alpha(1 - \lambda_{LJ})} \right)^3 \right] + \lambda_{\text{Elect}} \frac{q_i q_j}{\varepsilon r_{ij}} \]

forward & backward

\[ \langle \exp[-\beta(U(\lambda_{i+1}) - U(\lambda_i))] \rangle_i \]

\[ \langle \exp[-\beta(U(\lambda_{i-1}) - U(\lambda_i))] \rangle_i \]

double-wide sampling

\[ \langle \exp[-\beta(U(\lambda_{i+1}) - U(\lambda_i))] \rangle_i \]

\[ \langle \exp[-\beta(U(\lambda_{i+1}) - U(\lambda_i))] \rangle_i \]

\[ P(\lambda_i \rightarrow \lambda_j) = \min \left\{ \exp\left[-\beta (U_j(\lambda_j) - U_i(\lambda_j) + U_i(\lambda_i) - U_j(\lambda_i))\right], 1 \right\} \]
MOPAC
- Semi-Empirical

ORCA
- Semi-Empirical
- Hartree-Fock
- Density Functional Theory
- Møller-Plesset (MP2)
- and more...

"Custom":
- Scripted Interface to wrap nearly any software
- Python scripts available for Gaussian, qChem, and TeraChem

NAMD: QM/MM

NAMD/ORCA input:
NAMD QM/MM configuration file
PSF (topology)
PDB (structure with identified QM atoms)

Link Atom
\( C_{\alpha} - H - C \)

QM Region
MM Region

Charge Redistribution Scheme
(Carbon “C” charge is distributed to preserve local polarization)

NAMD

QM (Partial Charges + Gradients)

PME

Atoms and Topology

QM atoms: Gradients & Partial Charges
MM atoms: Gradients due to Coulomb Interactions

MM atoms: Coordinates & Elements
MM atoms: Coordinates & Point Charges

ORCA

\( r_{\text{max}} \)

Point Charges (MM Partial Charges)
NAMD: Neural Network Potential (NNP)

Using **NAMD** Hybrid QM/MM interface with **ANI** potential for the **drug** like molecules

<table>
<thead>
<tr>
<th>QM/MM Method</th>
<th>ps/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>TeraChem DFT</td>
<td>3.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NNP/MM Method</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ANI-1x (PyTorch)</td>
<td>120</td>
</tr>
<tr>
<td>ANI-1x (C++)</td>
<td>200</td>
</tr>
<tr>
<td>ANI-1ccx (C++)</td>
<td>200</td>
</tr>
</tbody>
</table>

8 Intel Xeon W3550 @ 3GHz + 1 NVIDIA Titan RTX
0.5 fs/step
DFT: wB97x/6-31G*

---

Smith et al. *Nature Comm.*, 2019, 10, 2903
Smith, logoa, Isayev., Roitberg *Chem. Sci.*, 2017, 8, 3192
NAMD Performance
NAMD: Computational Workflow

\[ \vec{F}_i = -\frac{dV}{dr_i} \]
\[ \vec{a}_i = \frac{\vec{F}_i}{m} \]
\[ \vec{s}_i = \vec{s}_{0i} + \vec{v}_i t + \frac{1}{2} \vec{a}_i t^2 \]

initialize

particle positions

force calculation

about 1% of computational work

about 99% of computational work

occasional output

reduced quantities (energy, temperature, pressure)

position coordinates (trajectory snapshot)

particle forces

update positions

Loop millions of timesteps
NAMD 2.1X: Parallelization

Spatial decomposition of atoms into patches

Work decomposition of patch interactions

NAMD 2.1X: Performance

Simulation details:
NVE, CHARMM force field, cutoff distance 12Å, MTS with 2fs time step and 4fs PME, rigid bond constraints. 
https://www.ks.uiuc.edu/Research/namd/benchmarks/

ApoA1: 92k atoms

Simulation details:
NVE, CHARMM force field, cutoff distance 12Å, MTS with 2fs time step and 4fs PME, rigid bond constraints.
https://www.ks.uiuc.edu/Research/namd/benchmarks/

NAMD 2.13 (2018) has ~20% perf. improvement from P100 to V100

Hardware has ~70% perf. improvement!
NAMD 2.1X: Limited Performance

• Offloading force calculation is not enough!
• Overall utilization of modern GPUs is limited
• We want better single GPU performance
  Majority of MD users run system sizes < 1M atoms on a single GPU
• Must transition from GPU-offload to GPU-resident!

The DGX-2 has 16 V100 GPUs but only 48 CPU cores: We need to do more GPU work with less CPU Power

David Hardy
Julio Maia

JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD. JCP, 2020
NAMD 3: Parallelization

GPU-offload

CPU
- Integrate atom positions

GPU
- Aggregate position data, copy to GPU
- Calculate forces
- Stream forces back to CPU
- Calculate forces

GPU-resident

CPU (manages GPU kernels)
- Fetch force buffers
- Convert force to SOA form
- Fetch force buffers
- Convert force to SOA form

GPU
- Integrate atom positions
- Fill position buffers
- Integrate atom positions
- Fill position buffers
- Integrate atom positions

JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD. JCP, 2020
Simulation details:
NVE, CHARMM force field, cutoff distance 12Å,
MTS with 2fs time step and 4fs PME, rigid bond constraints.
Performance tuning parameter “margin” set to 4Å.
https://www.ks.uiuc.edu/Research/namd/benchmarks/
Satellite Tobacco Mosaic Virus (STMV)
1.06 M atoms

Simulation details:
NVE, CHARMM force field, cutoff distance 12Å,
MTS with 2fs time step and 4fs PME, rigid bond constraints.
Performance tuning parameter “margin” set to 4Å.
https://www.ks.uiuc.edu/Research/namd/benchmarks/
Latest NAMD versions

- **Current stable release** is version 2.14 (Aug 2020)
- **Current development releases** are:
  - Version 3.0 alpha 9 (devel branch): Fast single- and multi-GPU
  - Version 2.15 alpha 1 (nightly build from master branch) - explicit AVX-512 support for good scaling on TACC Frontera

**Version Nightly Build (2021-06-29) Platforms:**

- Linux-x86_64-multicore (64-bit Intel/AMD single node)
- Linux-x86_64-multicore-CUDA (NVIDIA CUDA acceleration)
- Source Code

**Version 3.0 GPU-Resident Single-Node-Per-Replicate ALPHA Release (2020-11-16) Platform:**

- Linux-x86_64-multicore-CUDA-SingleNode (NVIDIA CUDA acceleration (single-node))
- Linux-x86_64-netlirts-smp-CUDA-SingleNode (NVIDIA CUDA acceleration, multi-copy algorithms)

**Version 2.15 ALPHA Release (2020-11-03) Platform:**

- Linux-x86_64-multicore-AMDHIP (AMD HIP/ROCm acceleration)
- Linux-x86_64-multicore-AVX512 (x86_64 AVX-512)

**Version 2.14 (2020-08-05) Platforms:**

- Linux-x86_64-multicore (64-bit Intel/AMD single node)
- Linux-x86_64-multicore-CUDA (NVIDIA CUDA acceleration)
- Linux-x86_64-netlirts (Multi-copy algorithms, single host or ethernet)
- Linux-x86_64-netlirts-smp-CUDA (Multi-copy algorithms, single process per copy)
- Linux-x86_64-verbs (InfiniBand, no MPI needed, supports multi-copy algorithms)
- Linux-x86_64-verbs-smp (InfiniBand, no MPI needed, supports multi-copy algorithms)
- Linux-KNL-multicore (Intel Xeon Phi KNL processor single node)
- MacOSX-x86_64 (Mac OS X for 64-bit Intel processors)
- MacOSX-x86_64-CUDA (NVIDIA CUDA acceleration)
- MacOSX-x86_64-netlirts (Multi-copy algorithms)
- Win64 (Windows 7, 8, 10, etc.)
- Win64-CUDA (NVIDIA CUDA acceleration)
- Win64-MPI (Windows HPC Server, multi-copy algorithms)
- Win64-MPI-smp-CUDA (HPC Server with CUDA)
- Source Code
## NAMD 3: Supported features (ongoing development ...)

### Basic Features:
- **NVE**
- **NVT**
  - Langevin Dynamics
  - Stochastics Velocity Rescaling
- **NPT**
  - Langevin Piston
  - Berendsen Barostat
  - Monte Carlo Barostat
- Rigid Bond
- Harmonic Restraints
- Multiple Time Stepping
- PME

### Advanced Features:
- Free Energy Calculation (FEP/TI)
- Multi-copy simulations (e.g. T-REMD)
- External Electric Field
- Steered MD
- Grid Forces
- Targeted MD

JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD. JCP, 2020
NAMD 3: Monte Carlo Barostat

\[ P_{\text{acc}} = \left[ 1, \left( \frac{V_{\text{new}}}{V_{\text{old}}} \right)^{N} e^{-\beta (U_{\text{new}} - U_{\text{old}}) - \beta P (V_{\text{new}} - V_{\text{old}})} \right] \]

- **MonteCarloPressure** on
- **MonteCarloPressureFreq** 50
- **MonteCarloPressureTarget** 1.0
- **MonteCarloTemp** $temperature
- **MonteCarloAcceptanceRate** 0.5
- **MonteCarloMaxVolume** 640
- **MonteCarloAdjustmentFreq** 10
NAMD 3: Monte Carlo Barostat Performance

92k atom (ApoA1)

NVE  |  106.7
NVT  |  98.4
Langevin piston |  83.9
MC (freq = 20) |  87.8
MC (freq = 50) |  93.8
MC (freq = 100) |  96.3

1 core Intel Xeon E5-2650 v2 @ 2.60GHz
1 TITAN V GPU

cutoff 12
pairlistdist 13.5
margin 8
pairlistspercycle 100
nonbondedfreq 1
fullElectFrequency 2
MonteCarloAcceptanceRate 0.5
MonteCarloPressureFreq xxx
numsteps 50,000
timestep 2
Acknowledgement

Prof. Emad Tajkhorshid
NIH Center for Macromolecular Modeling and Bioinformatics Director
University of Illinois

John Stone
Senior Research Programmer
University of Illinois

Jim Phillips
NCSA
University of Illinois

Prof. Chris Chipot
Centre National de la Recherche Scientifique Research Director
University of Illinois

David Hardy
Senior Research Programmer
University of Illinois

Mariano Spivak
Research Programmer
University of Illinois

Prof. Rafael Bernardi
Physics Department
Auburn University

Julio Maia
MTS Software System Design Engineer
AMD

Ronak Buch
Ph.D. Candidate
University of Illinois

NIH Grant P41-GM104601