NAMD
Features and Capabilities

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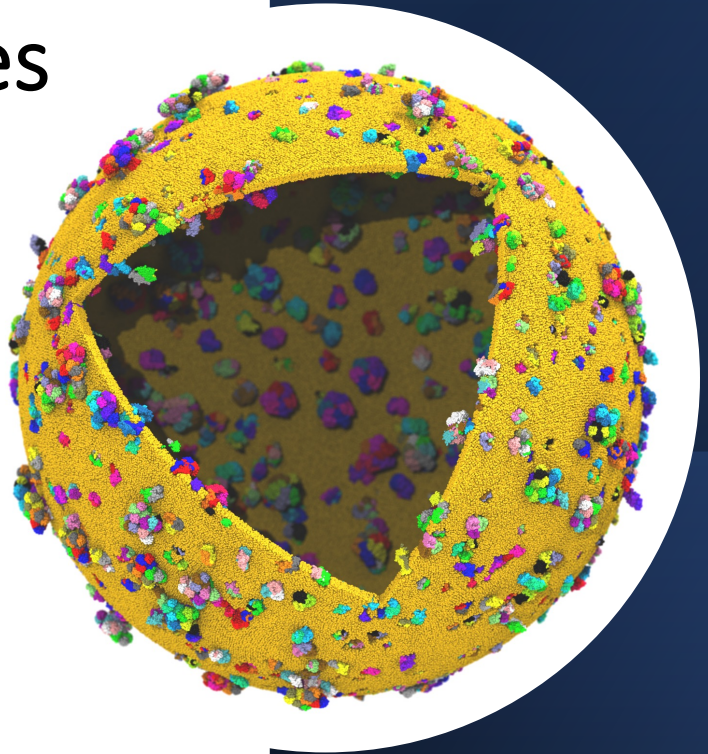
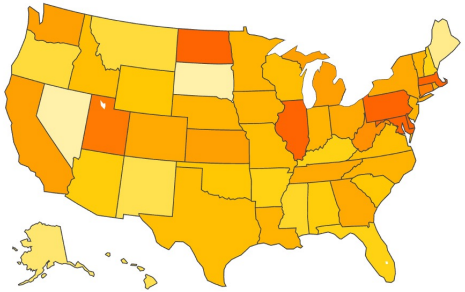


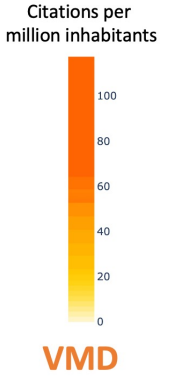
Computational Biophysics

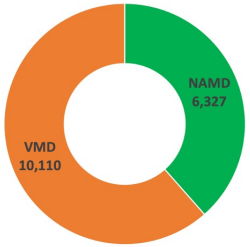
Virtual Workshop, 2021

NAMD: Not just Another Molecular Dynamics!

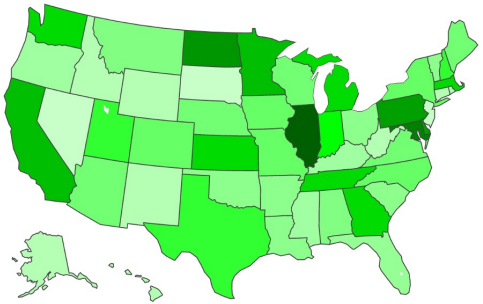
- From 1996 to 2021

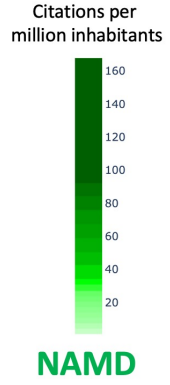




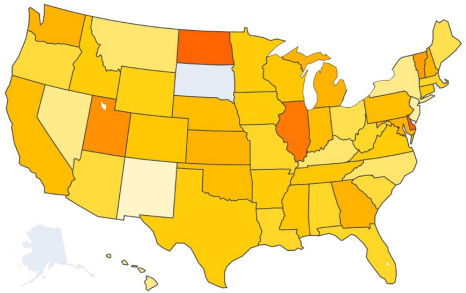


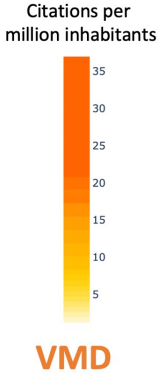
Citations by US researchers

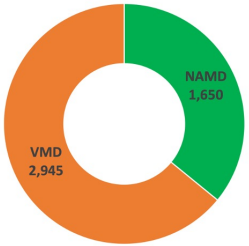




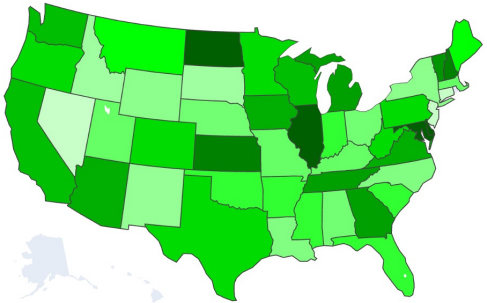
- From 2018 to 2021

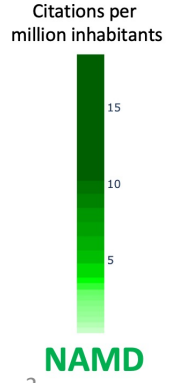






Citations by US researchers

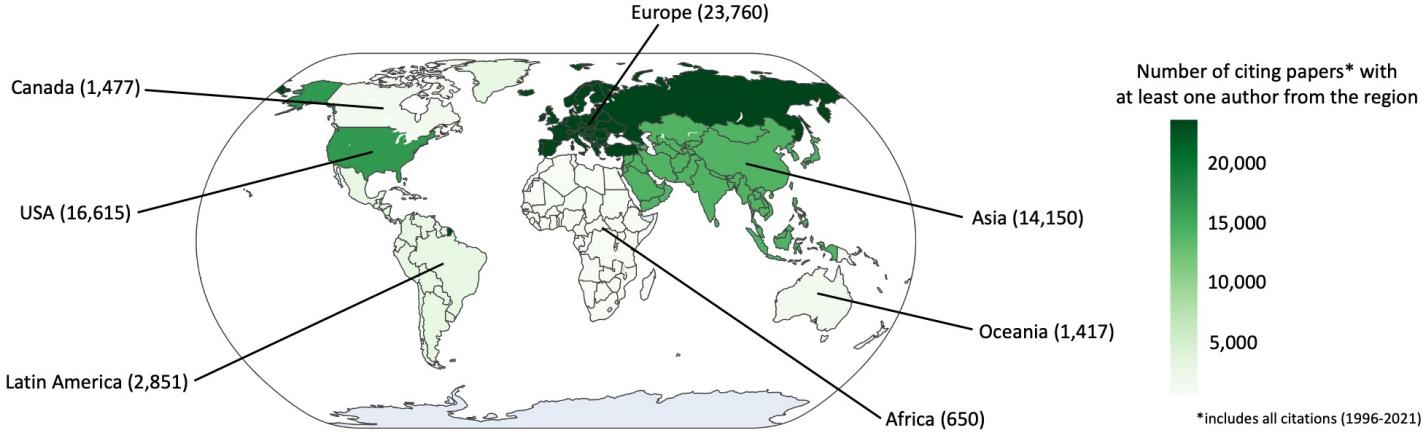




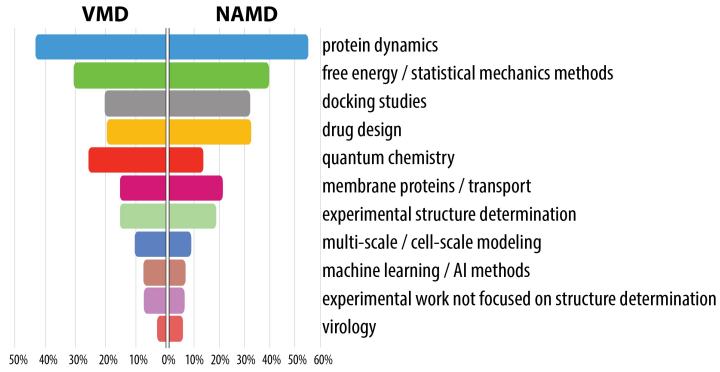
Distribution of VMD and NAMD citations across the US. Both software have been cited by authors in every single US state.

NAMD: Not just Another Molecular Dynamics!

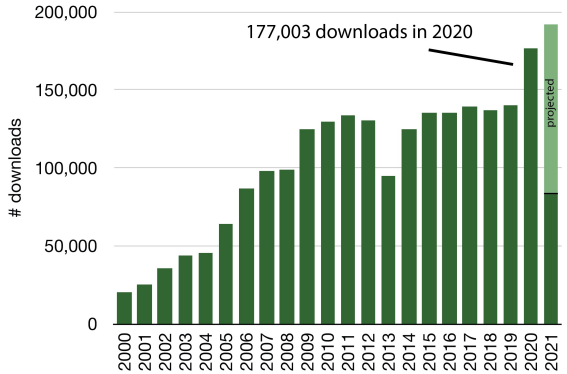
1996-2021: 37,000 papers published that have cited VMD and/or NAMD.



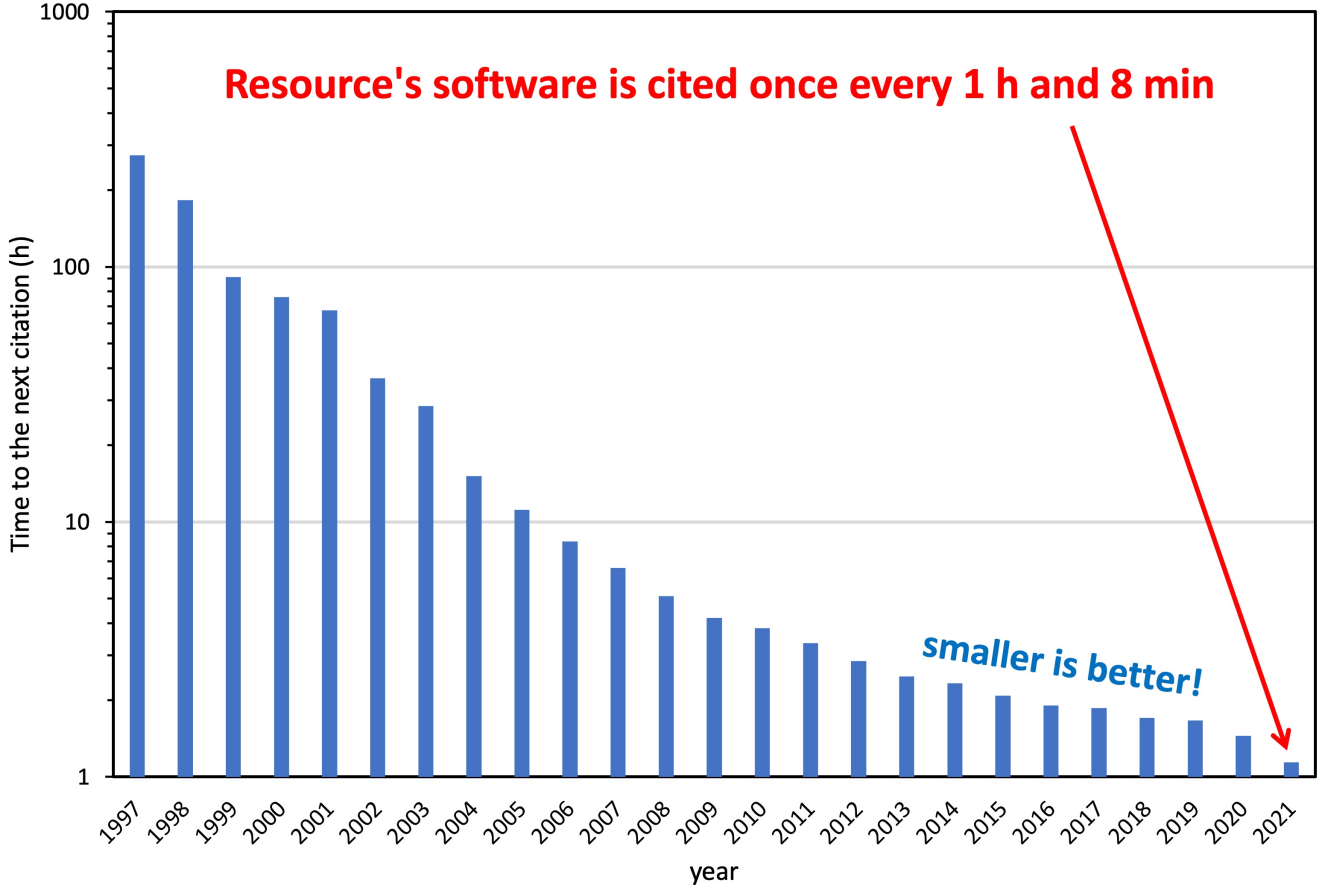
VMD and NAMD are used in a broad range of biological fields



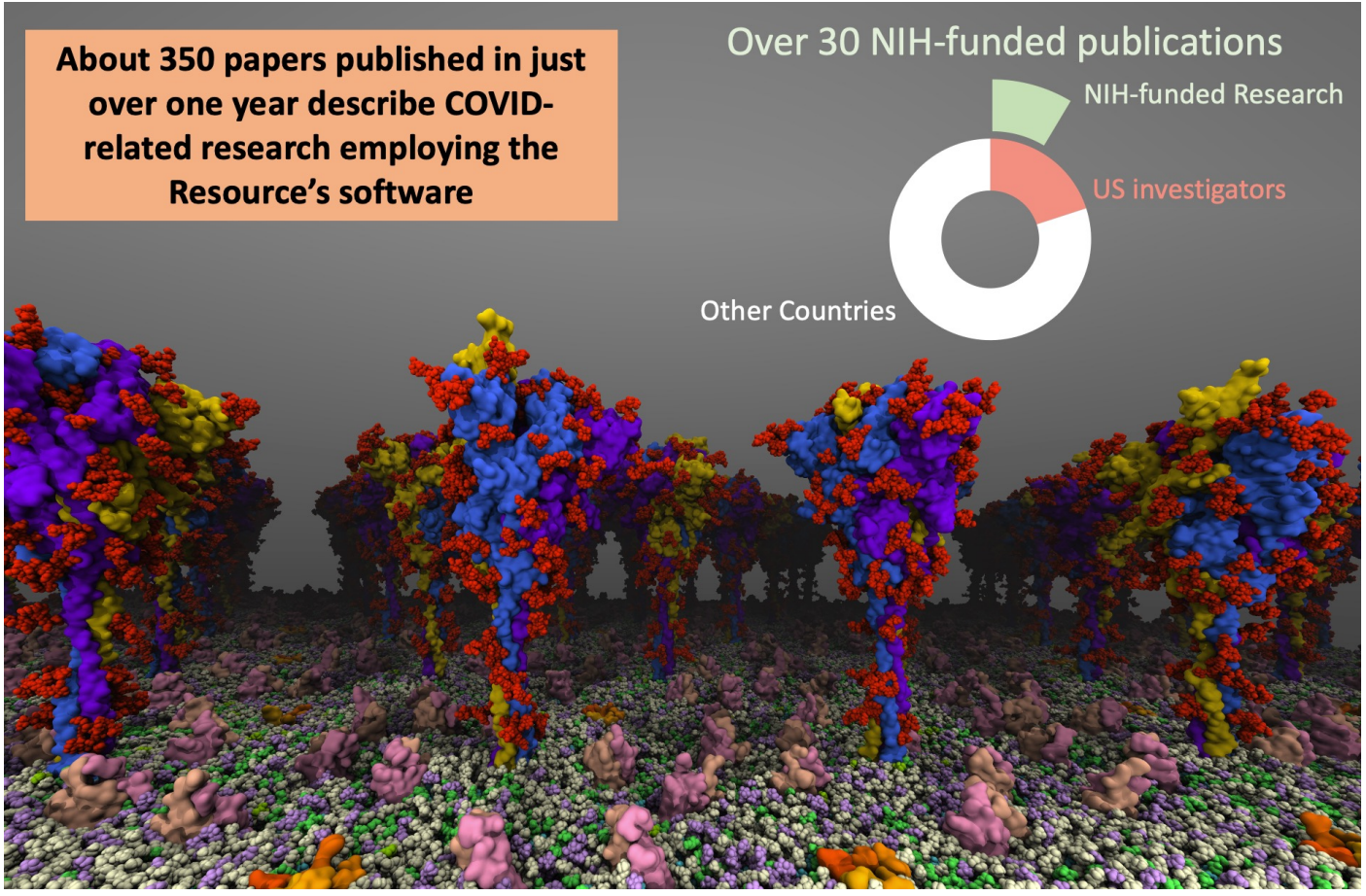
Over 2.2 million total downloads of Resource software



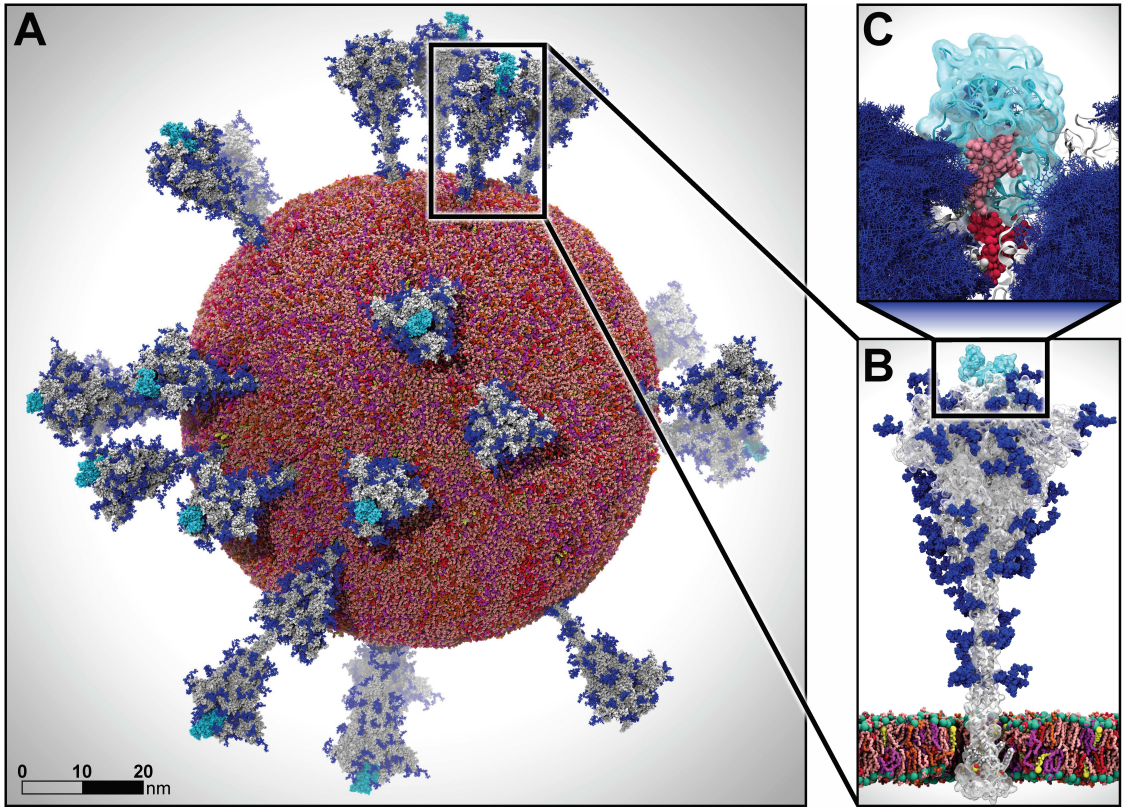
NAMD: Not just Another Molecular Dynamics!



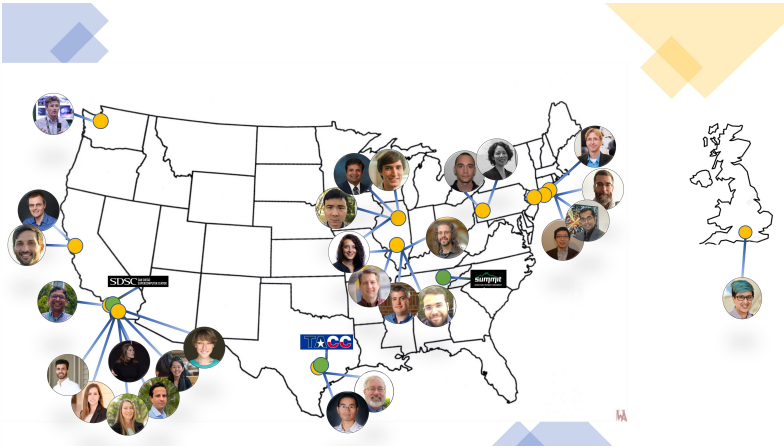
NAMD: Not just Another Molecular Dynamics!



NAMD: Not just Another Molecular Dynamics!



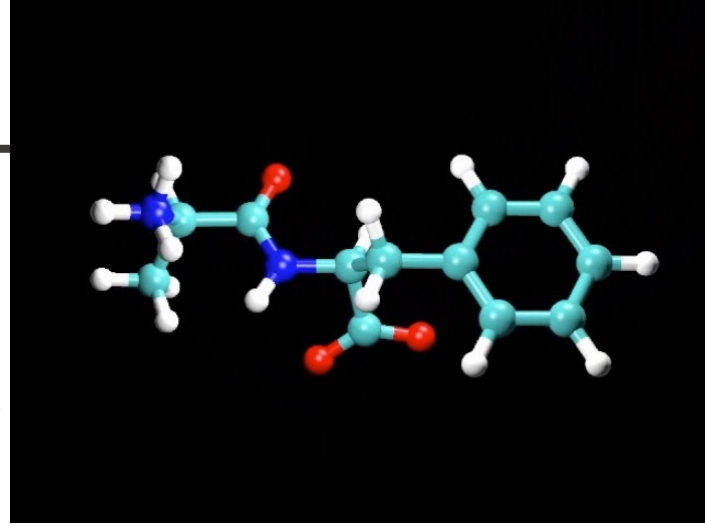
Winner of 2020 ACM Gordon Bell Special Prize for HPC-Based COVID-19 Research.



Images rendered by VMD.

Casalino, *et al.* (2020). **AI-Driven Multiscale Simulations Illuminate Mechanisms of SARS-CoV-2 Spike Dynamics**. https://doi.org/10.1101/2020.11.19.390187

NAMD:



$$\vec{F}_i = -dV / d\vec{r}_i$$

$$\vec{a}_i = \vec{F}_i / m$$

$$\vec{s}_i = \vec{s}_{0i} + \vec{v}_i t + \frac{1}{2}\vec{a}_i t^2$$

- 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

$$V = V_{str} + V_{bend} + V_{tors} + V_{oop} + V_{vdW} + V_{es}$$

$$V_{es,ij} = Q_i Q_j / \varepsilon_r R_{ij}$$

$$V_{vdW,ij} = \varepsilon_{IJ}\left[\left(\frac{R_{IJ}}{R_{ij}}\right)^{12} - 2\left(\frac{R_{IJ}}{R_{ij}}\right)^{6}\right]$$

$$V_{oop} = \frac{1}{2} k_{oop} \omega_{oop}^2$$

$$V_{tors,ijkl} = \frac{1}{2}\left[V_1(1+\cos\varphi) + V_2(1-\cos 2\varphi) + V_3(1+\cos 3\varphi) + \ldots\right]$$

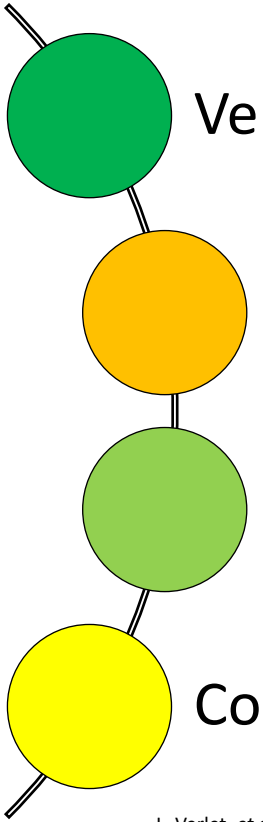
$$V_{bend,ijk} = \frac{1}{2} k_{IJK}\left(\theta_{ij} - \theta^0_{IJK}\right)^2$$

$$V_{str,ij} = \frac{1}{2} k_{IJ}\left(l_{ij} - l^0_{IJ}\right)^2$$

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 Features

Numerical Integrators



Verlet

Stochastic dynamics (BBK)

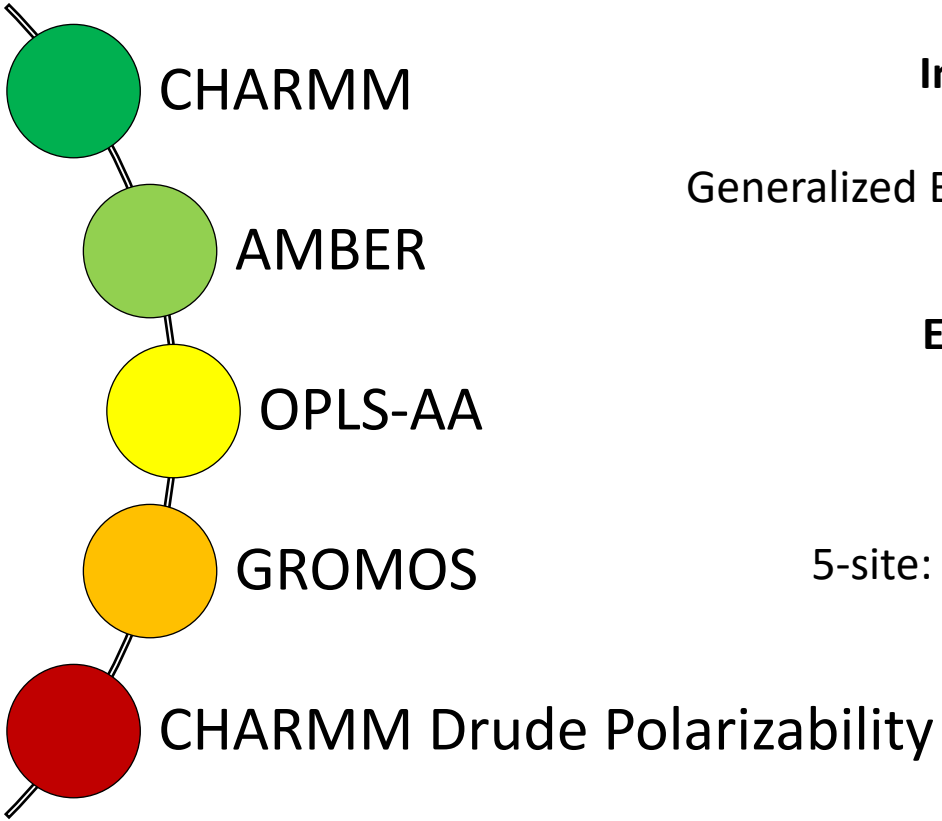
Multiple time stepping (r-RESPA)

Constrained dynamics (SHAKE)

L. Verlet, *et al.* Phys. Rev. 159, 98–103 (1967).
J. Ryckaert, *et al.* J. Comput. Phys. 23, 327–341 (1977).
M. Tuckerman, *et al.* J. Chem. Phys 97, 1990–2001 (1992).
A. Brünger, *et al.* J. Chem. Phys 105, 495–500 (1984)

NAMD Features

Supported Force Fields



Implicit Solvent

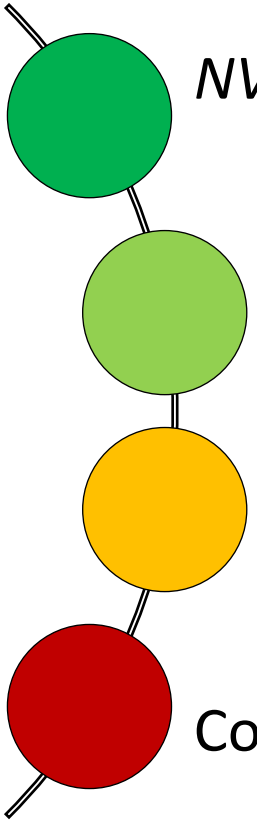
Generalized Born implicit solvent (GBIS)

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

Steered MD:

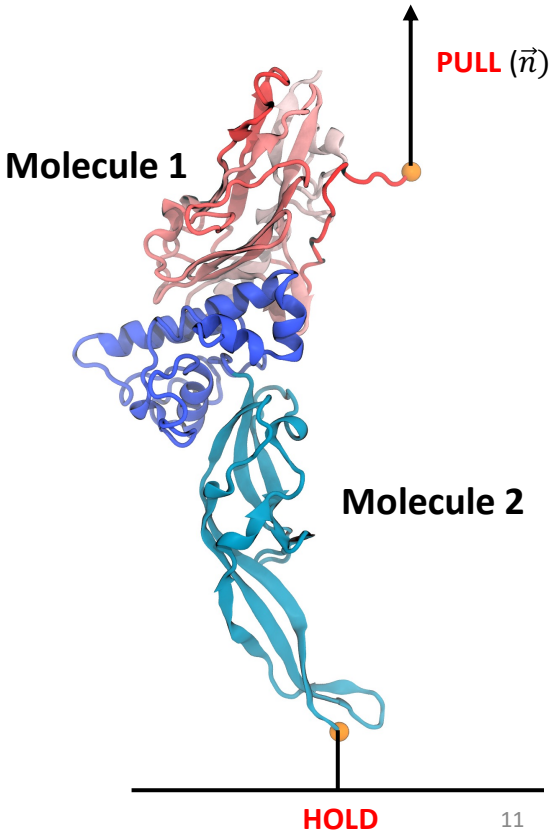
$$U(\vec{R},t) = \frac{1}{2}k_1\left[vt - \left(\vec{R}(t) - \vec{R}(0)\right).\vec{n}\right]^2 + \frac{1}{2}k_2\left[\left(\vec{R}(t) - \vec{R}(0)\right)^2 + \left(\left(\vec{R}(t) - \vec{R}(0)\right).\vec{n}\right)^2\right]$$

Restraints:

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

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:

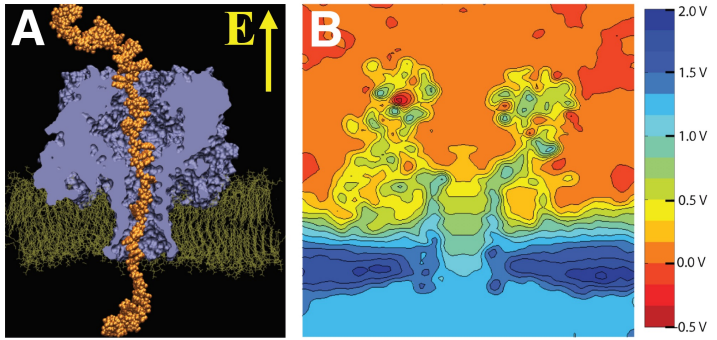
$$U(\vec{R},t) = \frac{1}{2N}k\left[\left(DRMS(\vec{R},t) - DRMS^{*}(\vec{R},t)\right)\right]^{2}$$

$$DRMS(\vec{R},t) = RMS_{1}(\vec{R},t) - RMS_{2}(\vec{R},t)$$

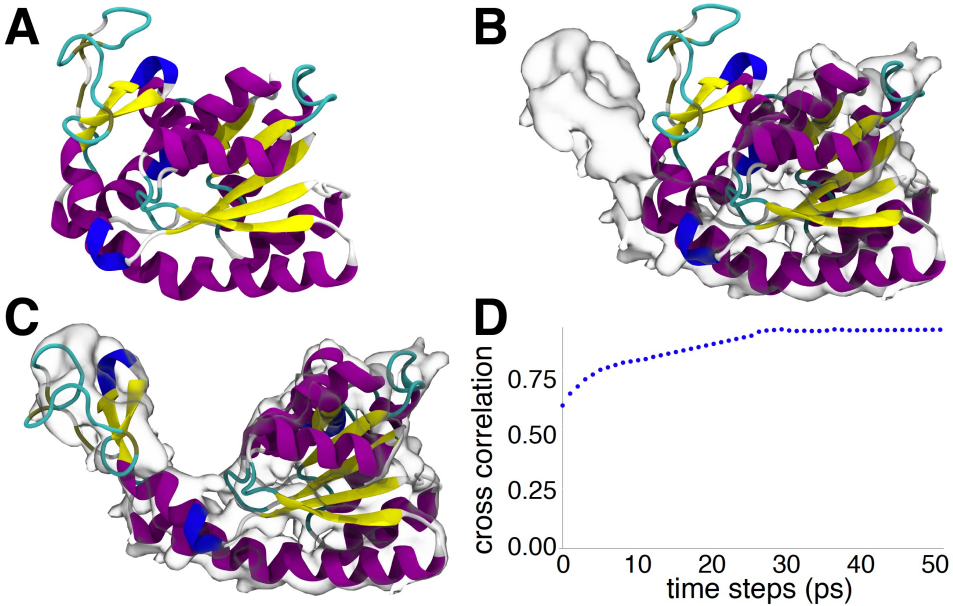
NAMD Advanced Features (External Forces)

External Electric Field

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

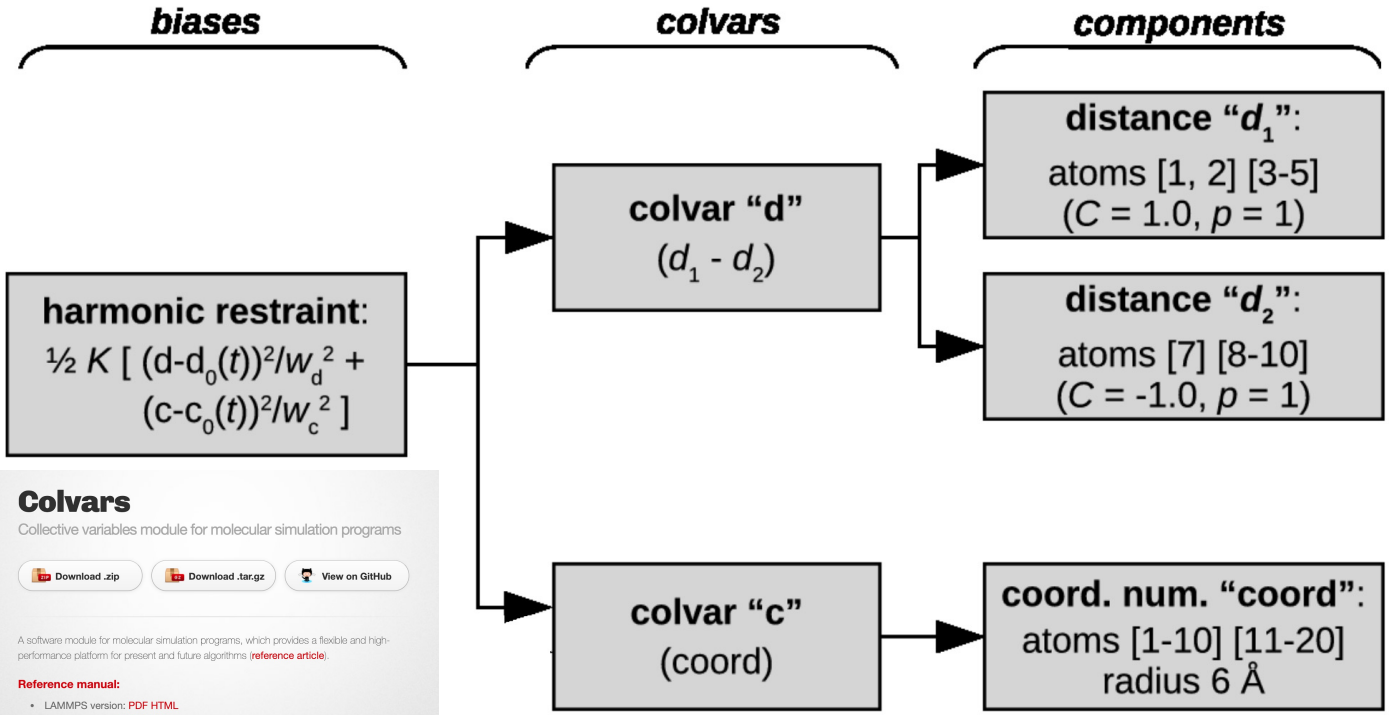


(A) Single DNA strand passing through an α-hemolysin nanopore
(B) Electrostatic potential contour map



A simple MDFF example of fitting a protein structure into a density 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.

NAMD Advanced Features: Colvars




```
colvar{
  name d

  distance {
    name d1
    componentCoeff 1.0
    group1 {atomNumbers 1 2}
    group2 {atomNumbers 3 4 5}
  }
  distance {
    name d2
    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}
  }
}
```


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

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

NAMD Advanced Features: Colvars

Components

Scalar

1. distance
2. Distance z
3. Distance xy
4. Polar theta
5. Polar phi
6. Distance inverse
7. Distance pairs
8. Dipole magnitude
9. Angle
10. Dipole angle
11. dihedral
12. Coordinate number
13. Self coordinate number
14. Group coordinate number
15. Hydrogen bond
16. RMSD
17. Orientation angle
18. Orientation projection
19. tilt
20. Spin angle
21. gyration
22. inertia
23. Inertia z
24. Eigen vector
25. Alpha dihedrals
26. Alpha angles
27. Dihedral Principle Component

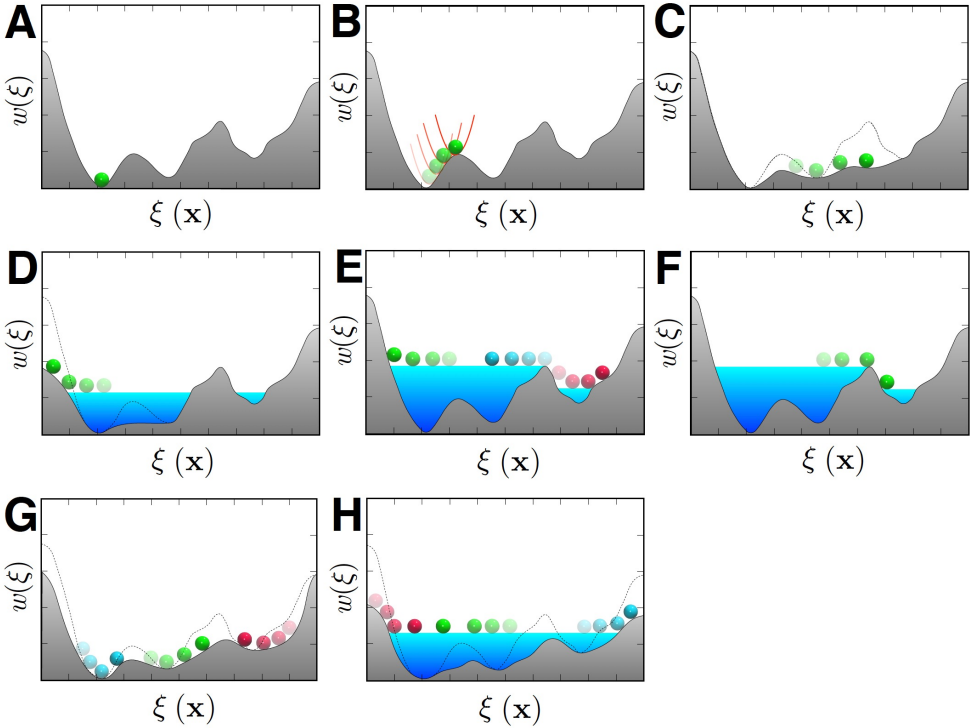
Non-scalar

1. Distance vector
2. Distance direction
3. cartesian
4. orientation

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



Sampling of a rugged free-energy landscape.

(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.

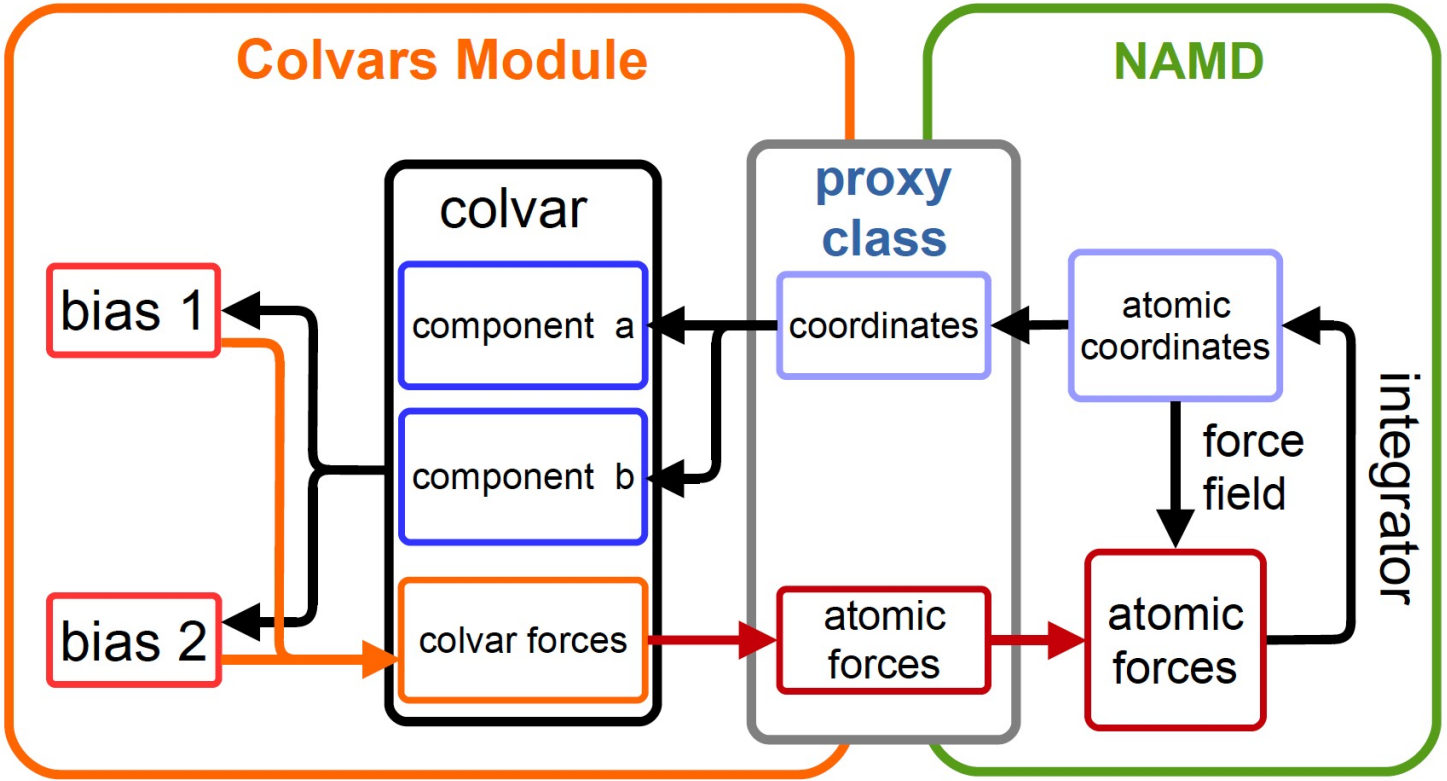
(E) Combination of MtD, eABF, and meta-eABF.

(F) Multiplewalker extension of MtD.

(G) Multiplewalker extension ABF or eABF.

(H) Multiplewalker extension meta-eABF.

NAMD Advanced Features: Colvars



Graphical representation of a Colvars configuration

NAMD: Accelerated Molecular Dynamics

$$V^*(\vec{R},t) = V(\vec{R},t) + V_{\text{boost}}(\vec{R},t) \quad V_{\text{boost}}(\vec{R},t) = \begin{cases} f(\vec{R},t), & V(\vec{R},t) < E_{\text{threshold}} \\ 0, & V(\vec{R},t) \geq E_{\text{threshold}} \end{cases}$$

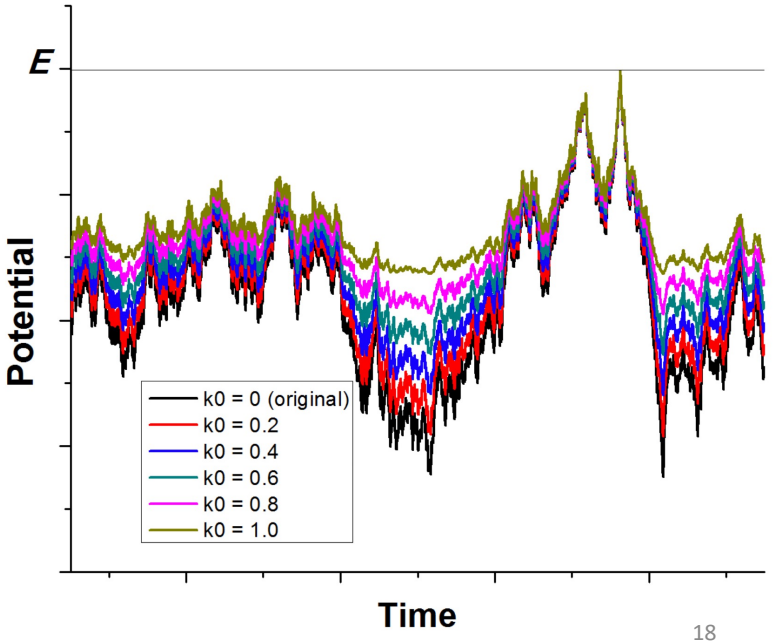
Options: V_{dihedral}, V_{total} - V_{dihedral} , or both

Accelerated MD (aMD):

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

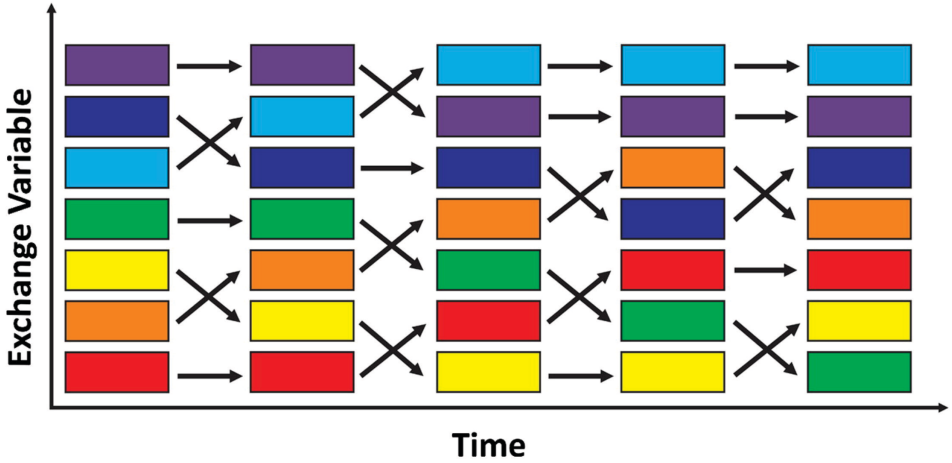
Gaussian Accelerated MD (GaMD)

$$f(\vec{R},t) = \frac{1}{2}k\left[E_{\text{threshold}} - V(\vec{R},t)\right]^2$$

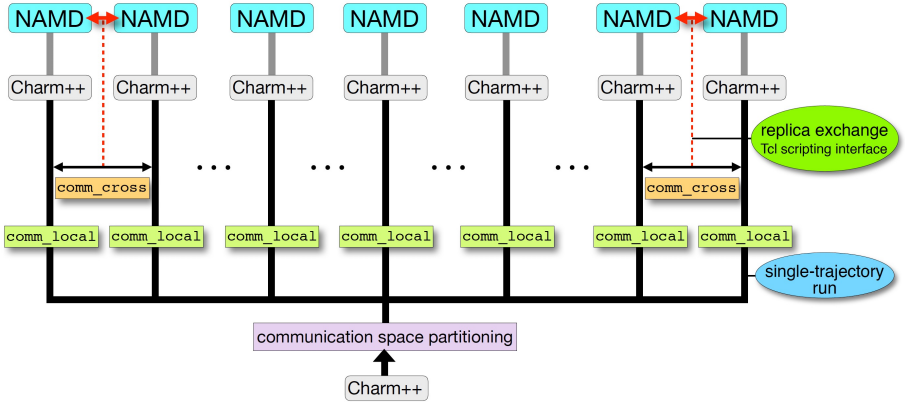


NAMD: Multiple Copy/Replica Algorithms

- Temperature replica exchange (T-REMD)
- Hamiltonian replica exchange ($\mathcal{H}$-REMD)
- FEP with λ replica exchange (FEP/(λ, $\mathcal{H}$)-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.

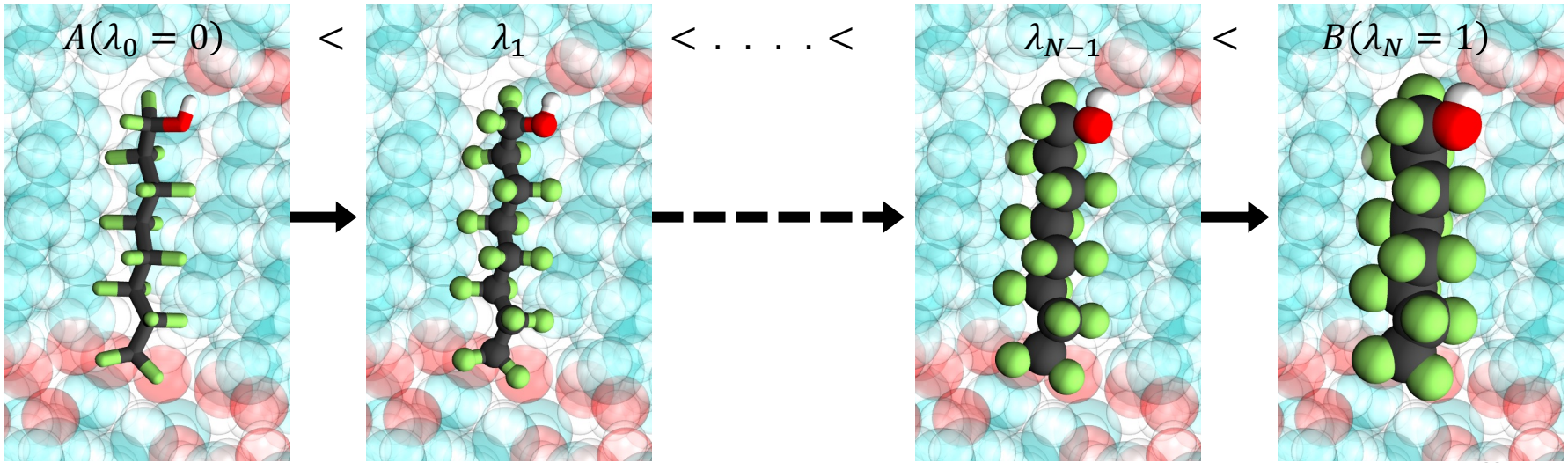
JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al. JCP, 2020
RC Bernardi, et al. Biochimica et Biophysica Acta, 2015

NAMD: Alchemical Free Energy

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

TI: $$\Delta F(A \longrightarrow B) = \int_{\lambda=0}^{\lambda=1} \langle \frac{dU}{d\lambda}\rangle_\lambda \, d\lambda$$

$$U(\lambda) = \lambda U_B + (1-\lambda)U_A$$

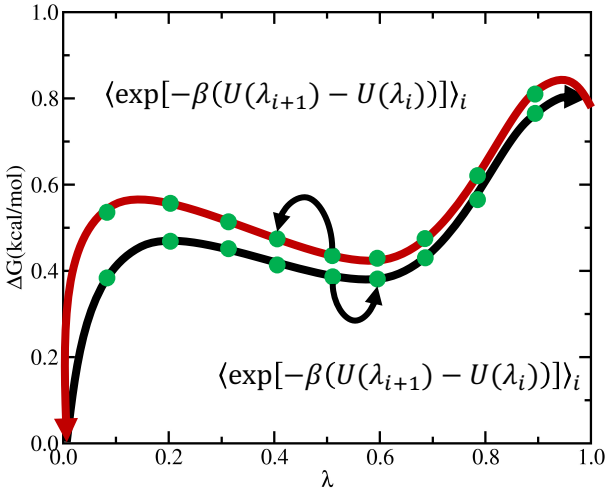


M Soroush Barhaghi, C Luyet, JJ Potoff. Mol. Phys 117 (23-24), 3827-3839

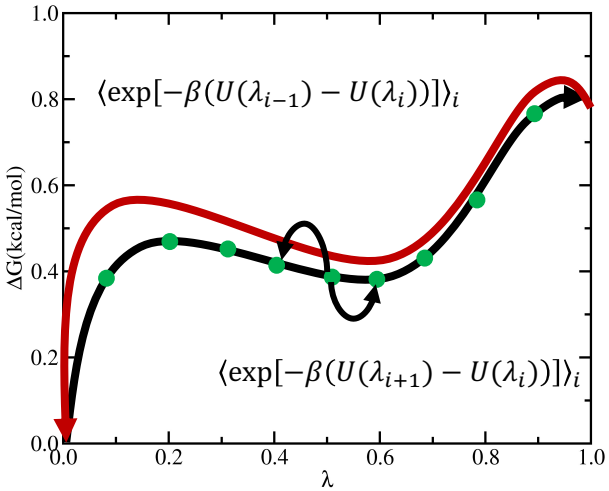
NAMD: Alchemical Free Energy

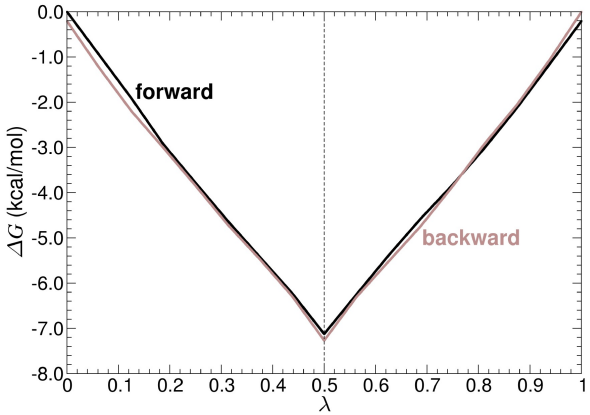
$$\lambda U(r_{ij},\lambda) = \lambda_{LJ}\epsilon_{ij}\left[\left(\frac{R_{\min}^2}{r_{ij}^2+\alpha(1-\lambda_{LJ})}\right)^6 - \left(\frac{R_{\min}^2}{r_{ij}^2+\alpha(1-\lambda_{LJ})}\right)^3\right] + \lambda_{Elect}\frac{q_i q_j}{\epsilon r_{ij}}$$

forward & backward



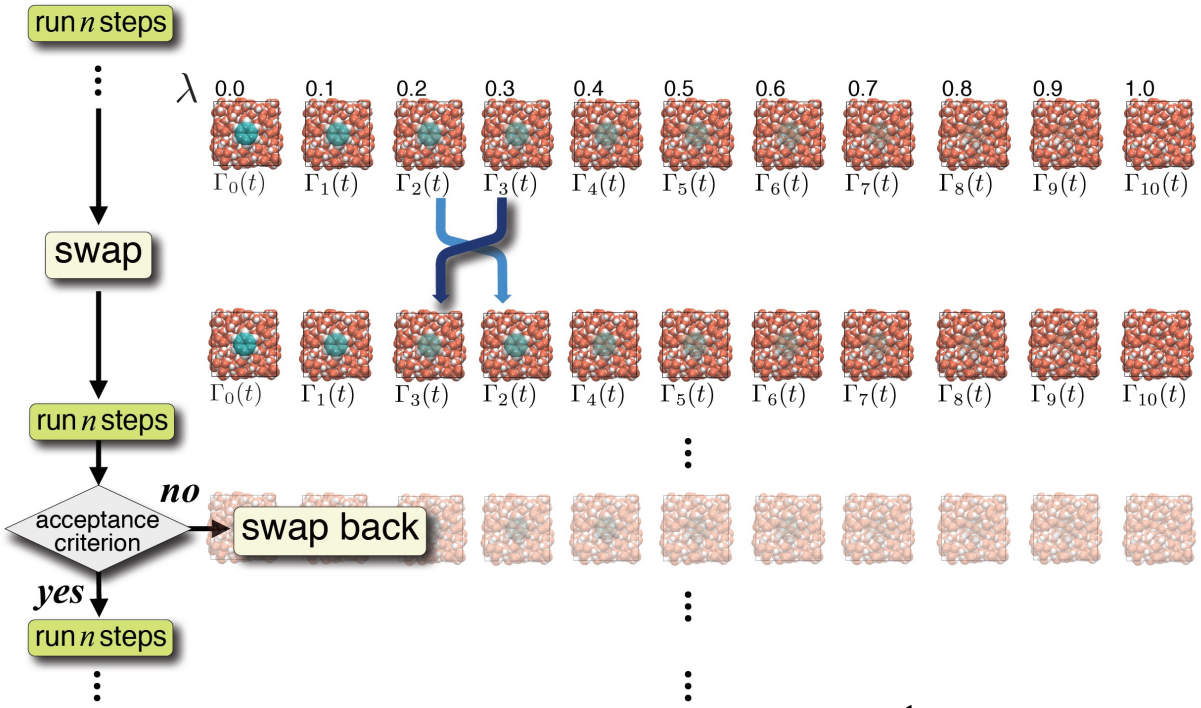
double-wide sampling





Jorgensen, W. L.; Ravimohan, C. J. Chem. Phys. 1985, 83, 3050-3054
Pearlman, D. A.; Kollman, P. A. J. Chem. Phys. 1989, 91, 7831-7839
Berendsen, H. J. C. in Renugopalakrishnan, V.; et al. Eds. Proteins, Structure, Dynamics and Design ESCOM, 1991, 384-392

NAMD: Hamiltonian-exchange FEP



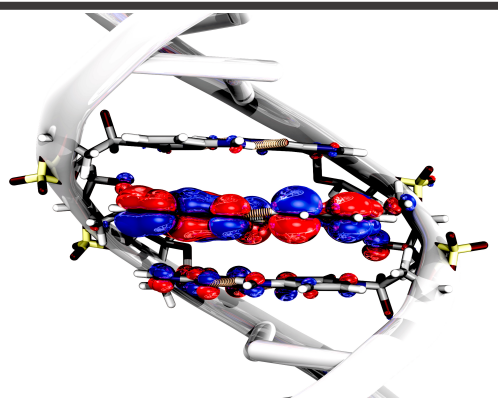
$$P(\lambda_i \rightarrow \lambda_j) = \min\left\{1, \exp\left[-\beta\left(U_j(\lambda_j) - U_i(\lambda_j) + U_i(\lambda_i) - U_j(\lambda_i)\right)\right]\right\}$$

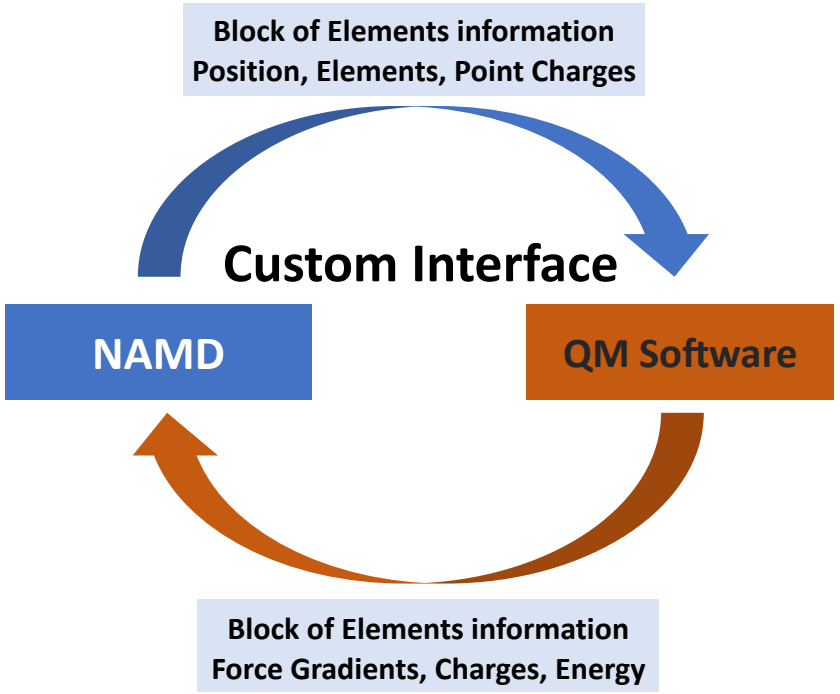
W. Jiang and B. Roux. J. Chem. Theory Comput. 6, 2559–2565 (2010).
JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al. JCP, 2020

NAMD: QM/MM

MOPAC
- Semi-Empirical

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

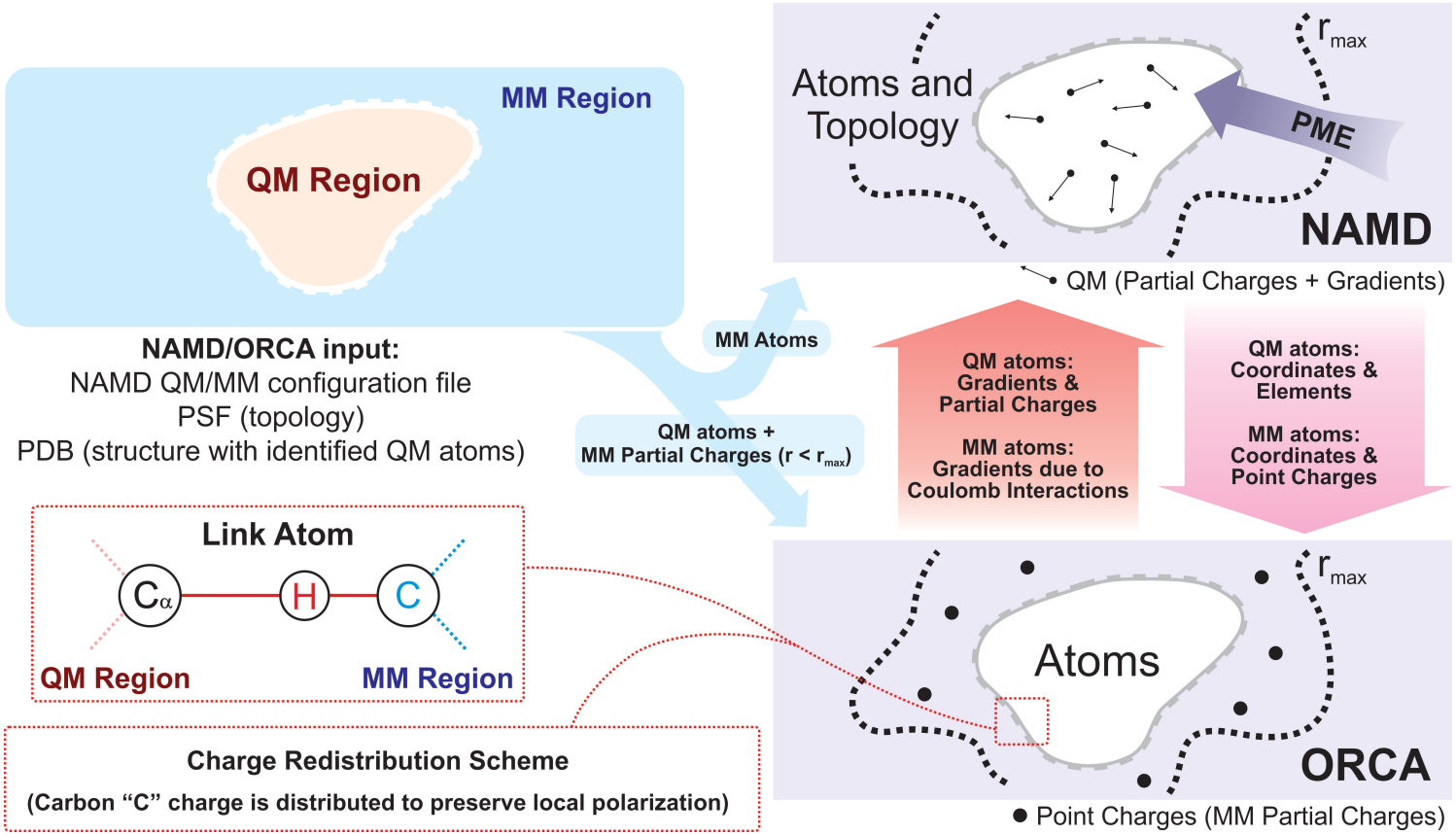




***"Custom"*:**
- Scripted Interface to wrap nearly any software
- Python scripts available for Gaussian, qChem, and TeraChem

Melo*, M. C. R.; Bernardi* et al. Nat. Methods 15, 351–354 (2018).

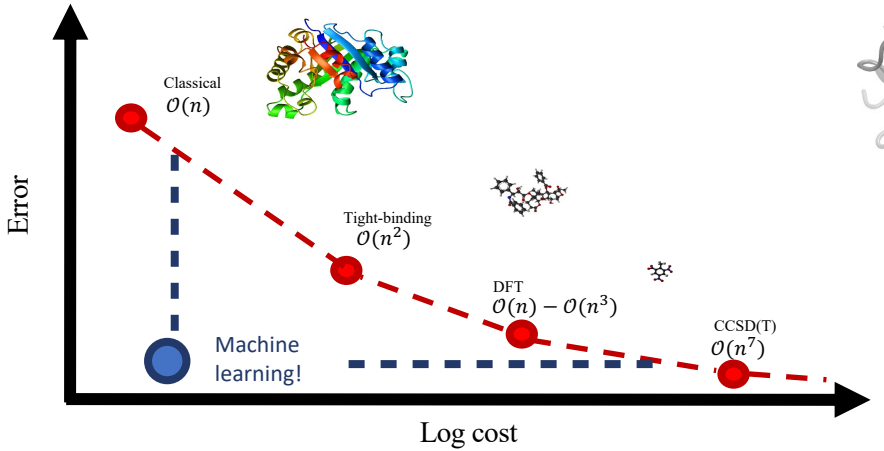
NAMD: QM/MM

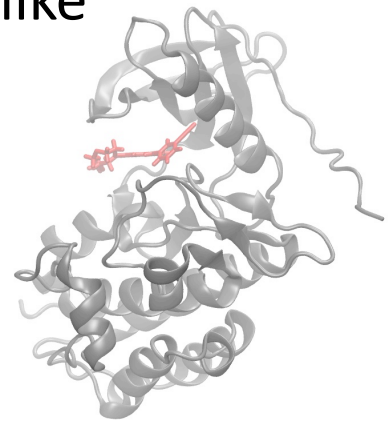


Melo*, M. C. R.; Bernardi* et al. Nat. Methods 15, 351–354 (2018).

NAMD: Neural Network Potential (NNP)

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





4HJO
EGFR
erlotinib

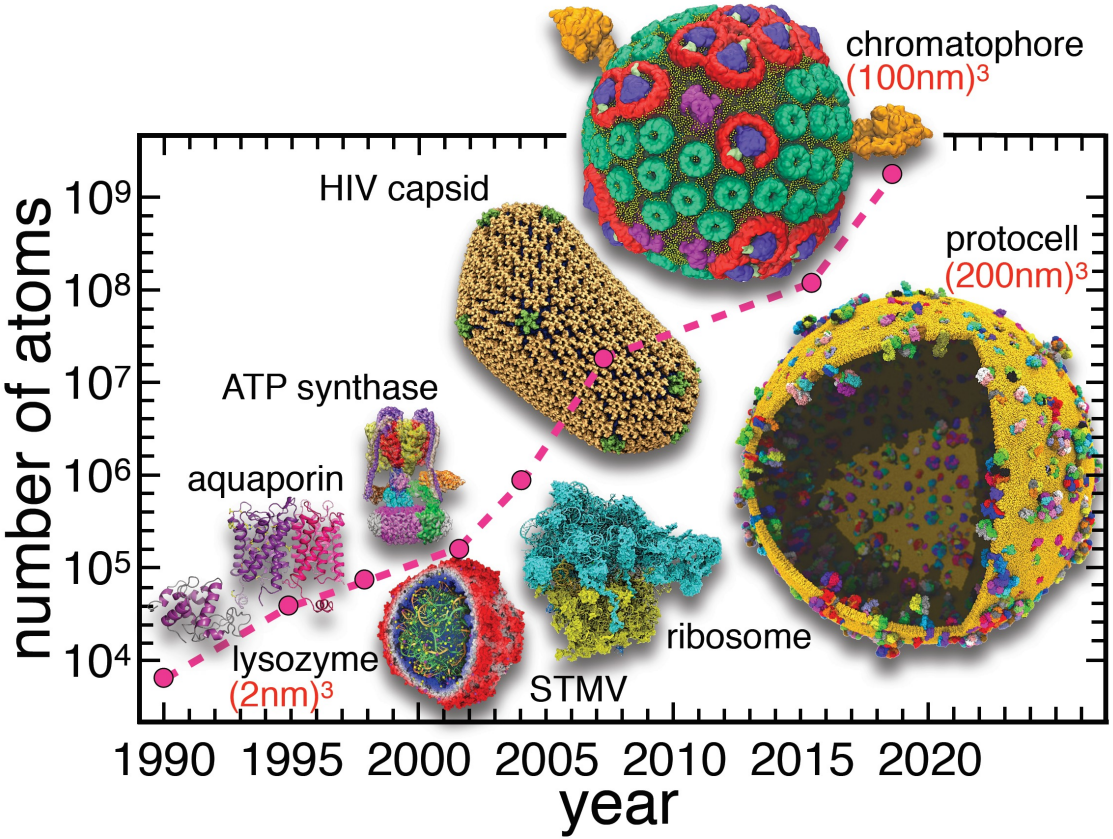
QM/MM Method	ps/day
TeraChem DFT	3.1
NNP/MM Method	
ANI-1x (PyTorch)	120
ANI-1x (C++)	200
ANI-1ccx (C++)	200

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

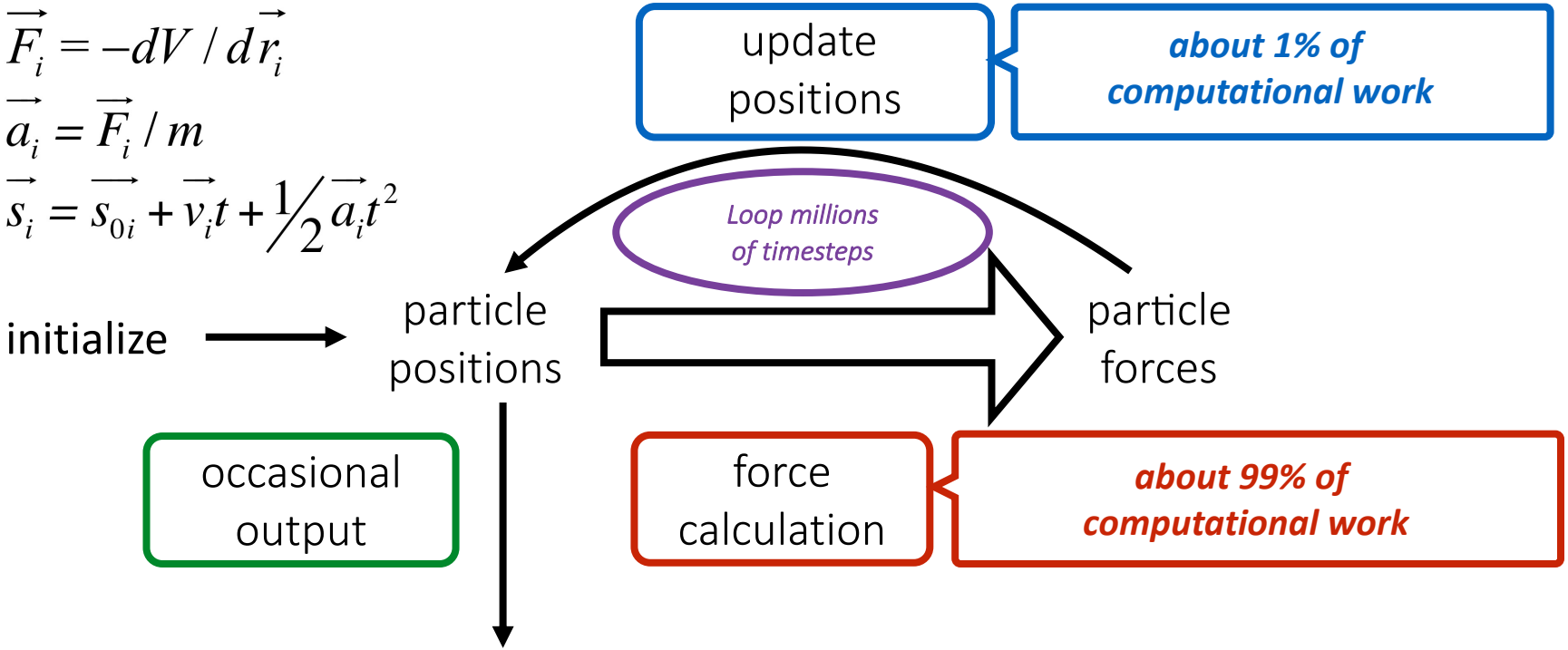
Lahey, S-L. J. and Rowley C. N. Chemical Science, 2020.
Ufimtsev I. S. and Martinez T. J., J. Chem. Theo. Comp., 2009, 5, 2619

NAMD Performance



NAMD: Computational Workflow

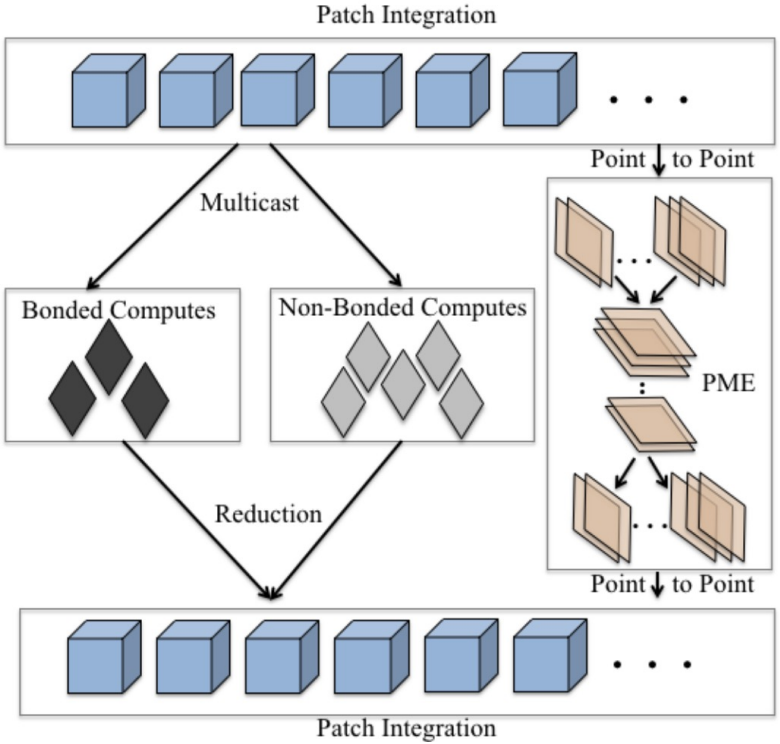
$$\vec{F}_i = -dV / d\vec{r}_i$$
$$\vec{a}_i = \vec{F}_i / m$$
$$\vec{s}_i = \vec{s}_{0i} + \vec{v}_i t + \frac{1}{2}\vec{a}_i t^2$$



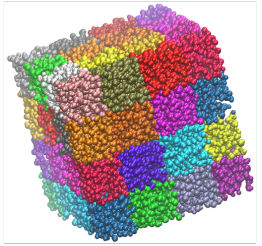
NAMD 2.1X: Parallelization

James Phillips

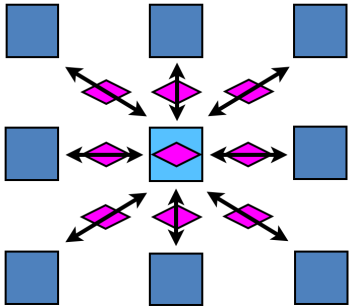
Antti-Pekka Hynninen



Spatial decomposition of atoms into patches



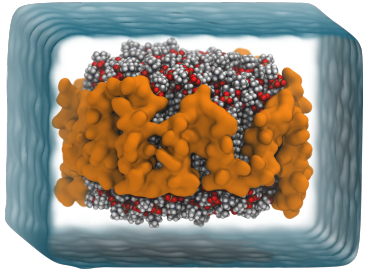
Work decomposition of patch interactions



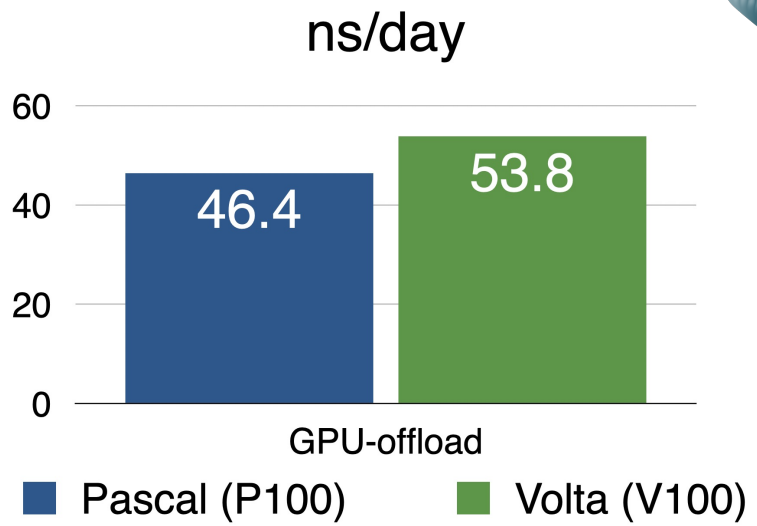
JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; **Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD**. JCP, 2020

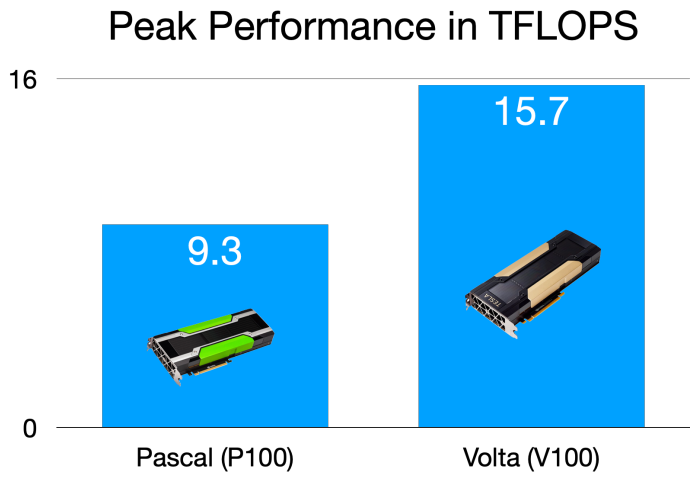
NAMD 2.1X: Performance

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





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

Hardware has ~70% perf. improvement!

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 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**!

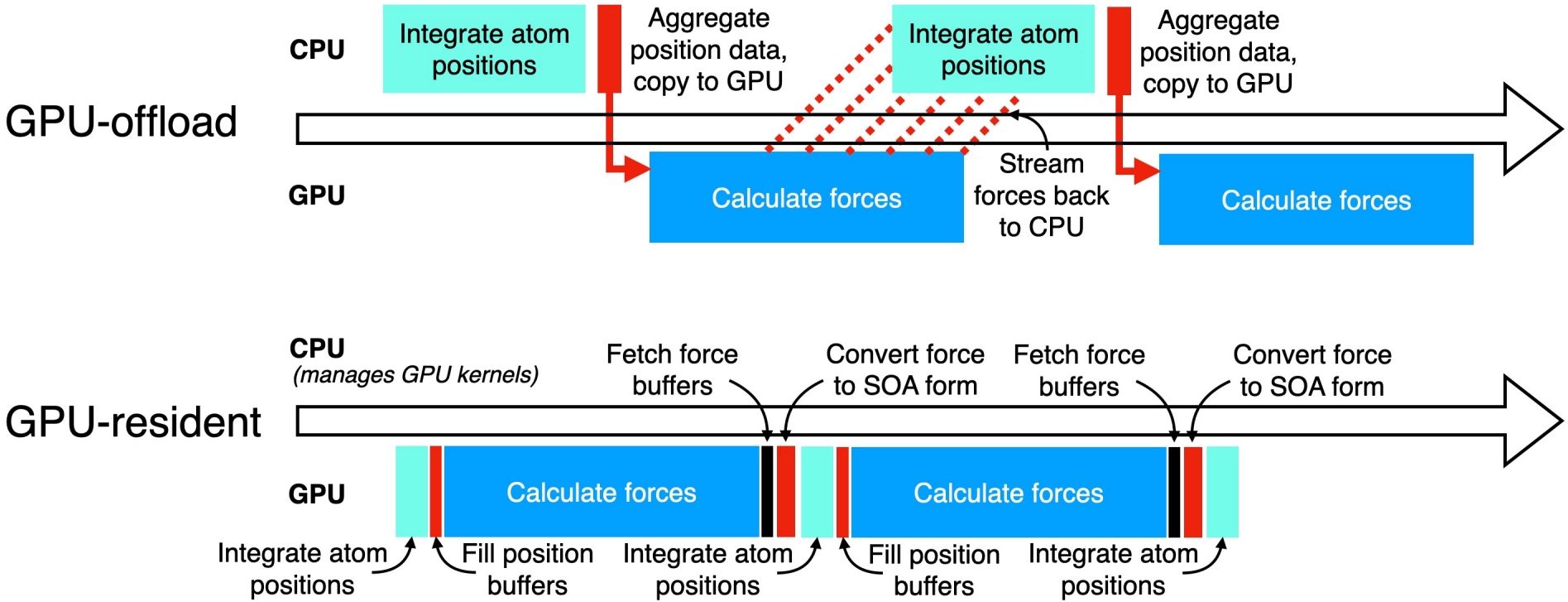
The DGX-2 has 16 V100 GPUs but only 48 CPU cores: We need to do more GPU work with less CPU Power

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

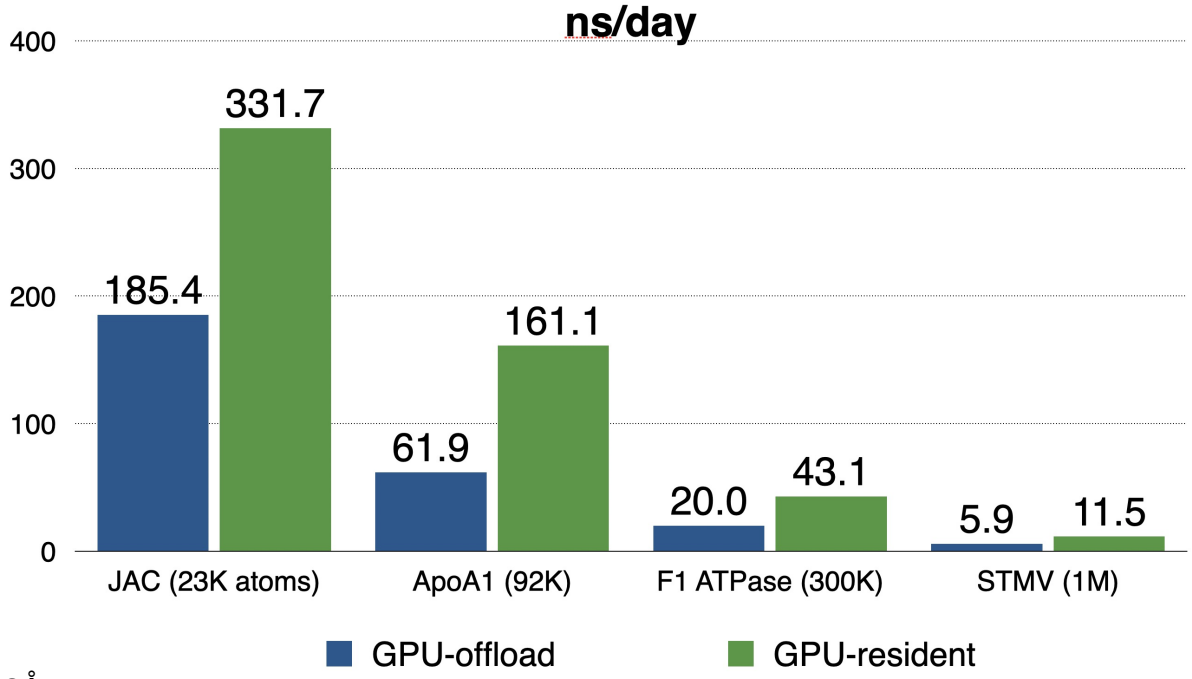


JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; **Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD**. JCP, 2020

NAMD 3: Single-node Single-GPU Performance

NVIDIA A100-PCIe

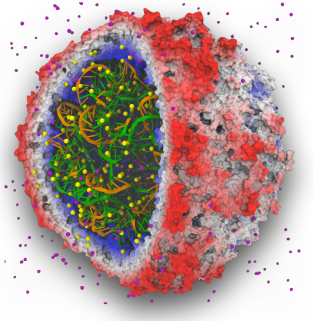
Intel Xeon Gold
6134 @ 3.2 GHz

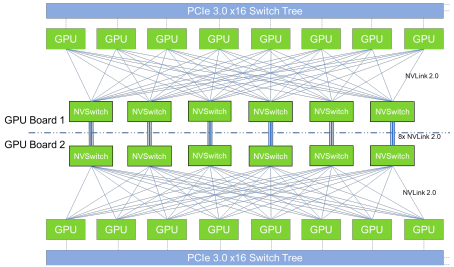


Simulation details:
NVE, CHARMM force field, cutoff distance 12Å,
MTS with 2fs time step and 4fs PME, rigid bond constraints.
Performance tuning parameter “margin” set to 4Å.
https://www.ks.uiuc.edu/Research/namd/benchmarks/

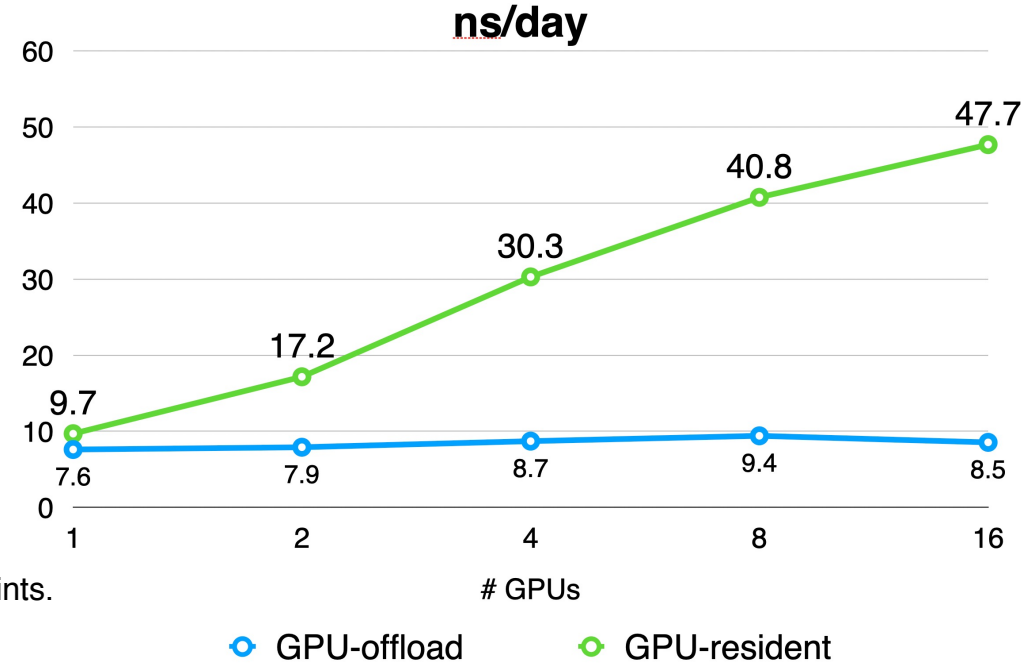
JC Phillips, D Hardy, JDC Maia, JE Stone, JV Ribeiro, RC Bernardi, et al.; **Scalable Molecular Dynamics on CPU and GPU Architectures with NAMD**. JCP, 2020

NAMD 3: Single-node Multi-GPU Performance





Satellite Tobacco Mosaic Virus (STMV)
1.06 M atoms



Simulation details:
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Performance tuning parameter “margin” set to 4Å.
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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

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) Pl

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

Version 2.15 ALPHA Release (2020-11-03) Platforms:

- **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-netlrts** (Multi-copy algorithms, single host or ethernet)
- **Linux-x86_64-netlrts-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-x86_64-verbs-smp-CUDA** (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-netlrts** (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

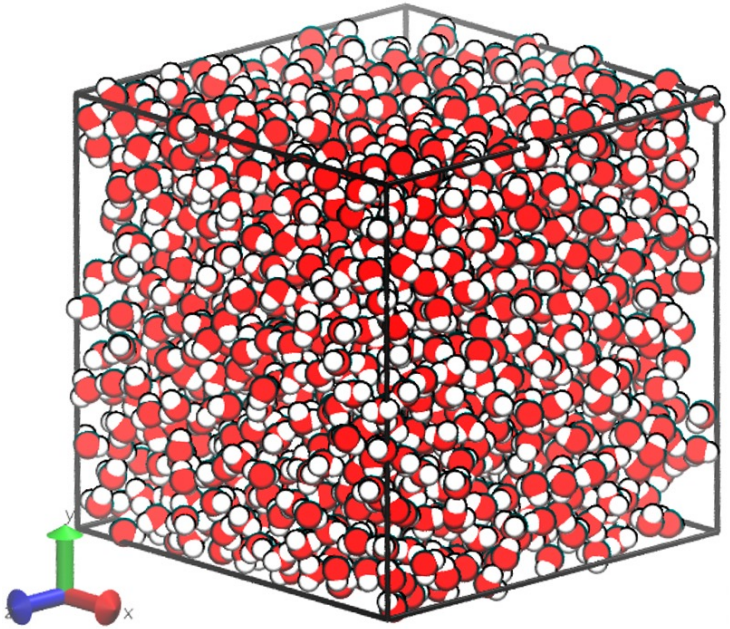
Advanced Features:

- ✓ 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

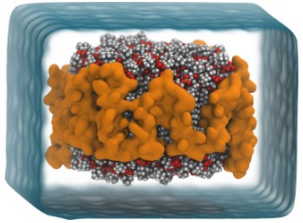
NAMD 3: Monte Carlo Barostat

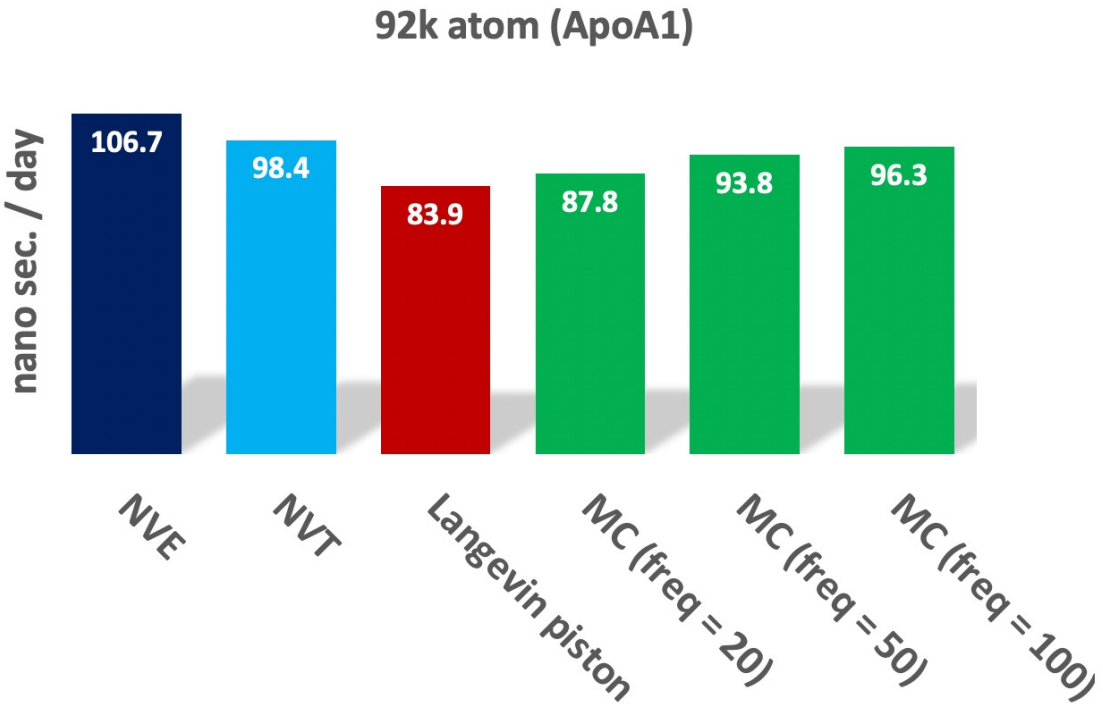
$$P_{acc} = \left[1, \left(\frac{V_{new}}{V_{old}}\right)^{N} e^{-\beta(U_{new}-U_{old})-\beta P(V_{new}-V_{old})}\right]$$



```
MonteCarloPressure          on
MonteCarloPressureFreq      50
MonteCarloPressureTarget    1.0
MonteCarloTemp              $temperature
MonteCarloAcceptanceRate    0.5
MonteCarloMaxVolume         640
MonteCarloAdjustmentFreq    10
```

NAMD 3: Monte Carlo Barostat Performance





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

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University of Illinois

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Centre National de la Recherche Scientifique Research Director
University of Illinois

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Physics Department
Auburn University

John Stone
Senior Research Programmer
University of Illinois

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Senior Research Programmer
University of Illinois

Julio Maia
MTS Software System Design Engineer
AMD

Jim Phillips
NCSA
University of Illinois

Mariano Spivak
Research Programmer
University of Illinois

Ronak Buch
Ph.D. Candidate
University of Illinois

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