BLUE WATERS

SUSTAINED PETASCALE COMPUTING

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The Use of Petaflop Simulations in Optimization of Amber Force Field

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GREAT LAKES CONSORTIUM
FOR PETASCALE COMPUTATION

I use Blue Waters to:

- **Initiate multidisciplinary cross team collaboration of 4 labs**
  - *Bernholc, Cheatham, NCSA, Poltev*
- **Run large-scale (1K-4K nodes) electronic structure simulations**
  - *CCSD(T) and DFT MD*
- **Create experimental and theoretical dataset for validation of approximate computational methods**
  - *Experimental Cluster Geometries (Dimer, Trimer, Tetramer)*
  - *Computed Interaction Energies*
- **Optimize electrostatic model of Amber force field**
  - *Fit Charges to Condensed Phase*
- **Run Lennard-Jones Parameter Sweep**
  - *Grid Search*

Project Motivation

- MD simulations based on classical force fields are the major consumers of supercomputing cycles
- The quality of underlying parameters determines the accuracy of bio-molecular force fields
- Well-optimized parameters can save tons of compute time and human resources
- Force Field optimization is challenging
  - Need to reproduce condensed-phase experimental data

Real-space Multi-Grid method (RMG)

- **Density functional equations solved directly on the grid**
- **Multigrid techniques remove instabilities by working on one length scale at a time**
- **Non-periodic boundary conditions are as easy as periodic**
- **Short-range discretizations**
- **Allows for efficient massively parallel implementation**

See E. L. Briggs, D. J. Sullivan and J. Bernholc Phys. Rev. B 54, 14362 (1996).

Ultrasoft pseudopotentials:

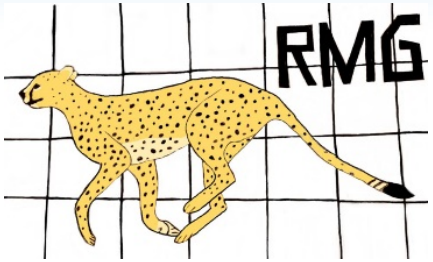
M. Hodak, S. Wang, W. Lu and J. Bernholc, PRB 76, 085108 (2007)

Kohn-Sham DFT/Orbital-free DFT for embedding biomolecules:

M. Hodak, W. Lu, J. Bernholc, JCP 128, 014101 (2008)

Performance on 3,872 Cray XK7 (K20x GPU)
Blue Water nodes: 1.14 PFLOPS

RMG Main Features



- Gamma and k-point calculations, spin polarization
- Runs on Linux/Unix, Windows and Mac
- Scalable to hundreds of thousands of CPU cores
- Supports thousands of GPU-nodes with multiple GPUs per node
- OpenBabel support for importing atomic structures
- Supports both ultrasoft and norm-conserving pseudopotentials
- Wide choice of DFT functionals including van der Waals via vdW-DF
- Hellman-Feynman forces, structure optimization and molecular dynamics
- To be released: optimally localized orbitals, quantum transport via self-consistent non-equilibrium Green's function (NEGF) formalism
- Upcoming capabilities: DFT+U, hybrid functionals, semi-local pseudopotentials

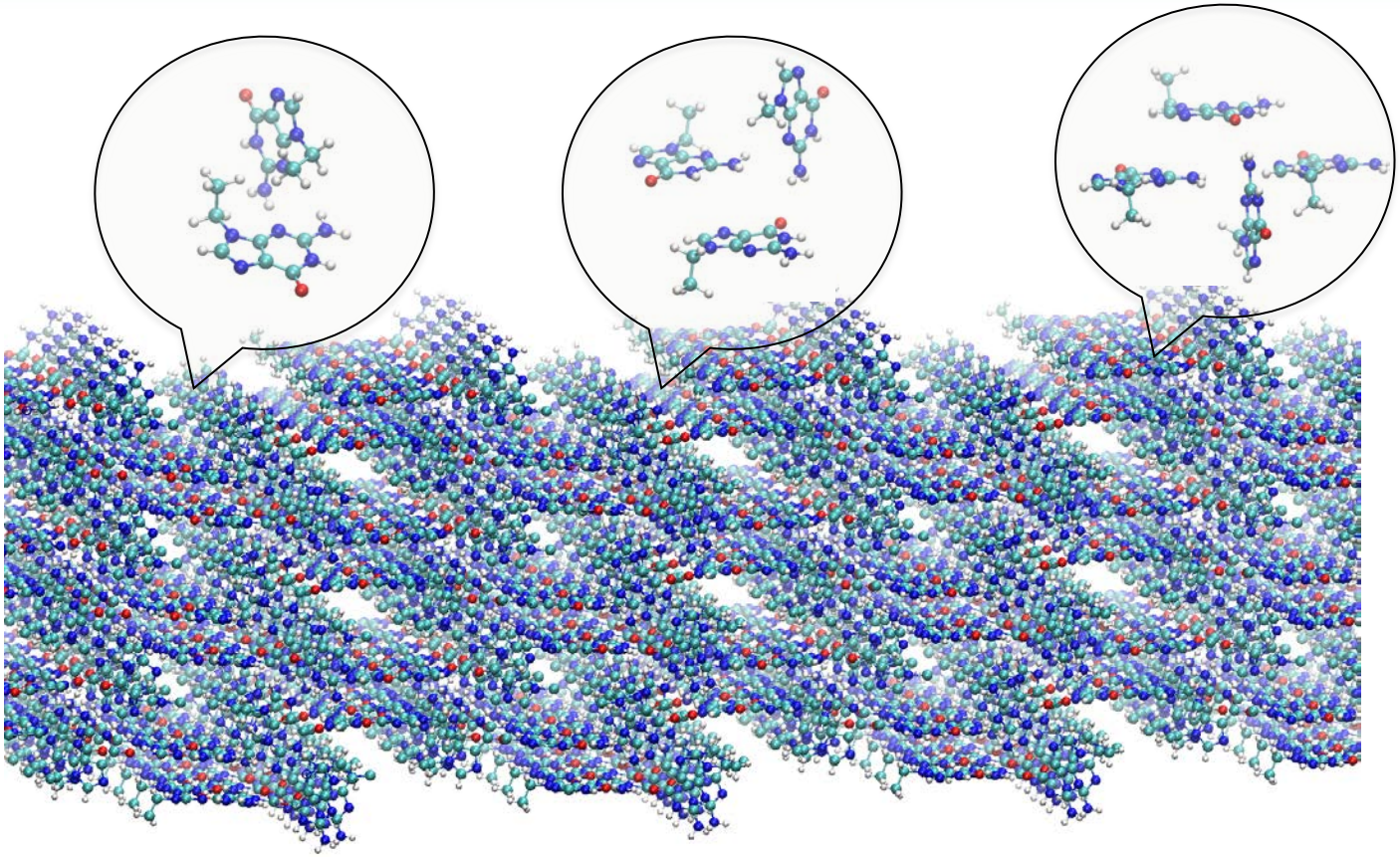
RMG Code Release

- Code & binaries (for Linux distr., Mac, Win)
- Blue Waters portal for Cray XE6/XK7

https://bluewaters.ncsa.illinois.edu/rmg

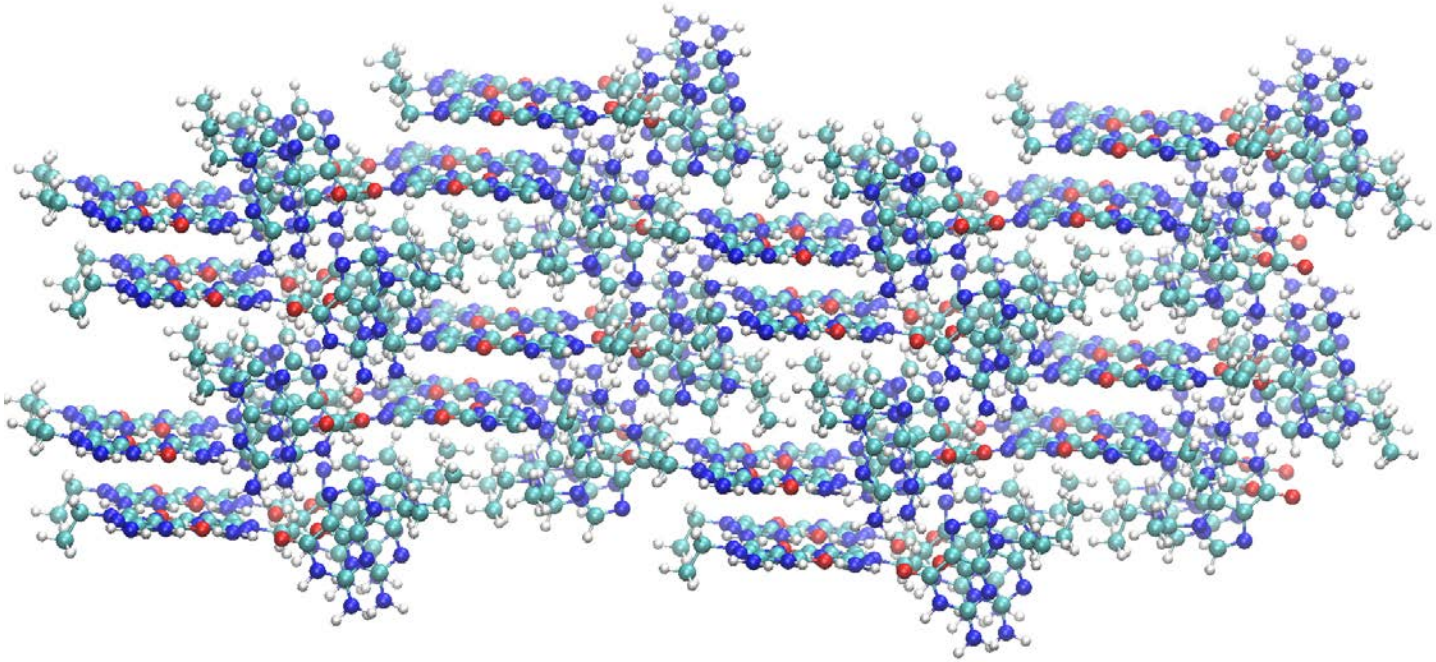
- Part of NSF's Sustained Petascale Performance benchmarks
  https://bluewaters.ncsa.illinois.edu/benchmarks
- Funded by Exascale Computing Project
- Graphical User Interface (GUI) for input & output
- Examples, documentation & discussion forum on sourceforge

Cluster Extraction from Crystals



- Processed 12 crystals of 5 nucleic acid bases
- Extracted 147 X-ray dimers, 1618 trimers, 11355 tetramers

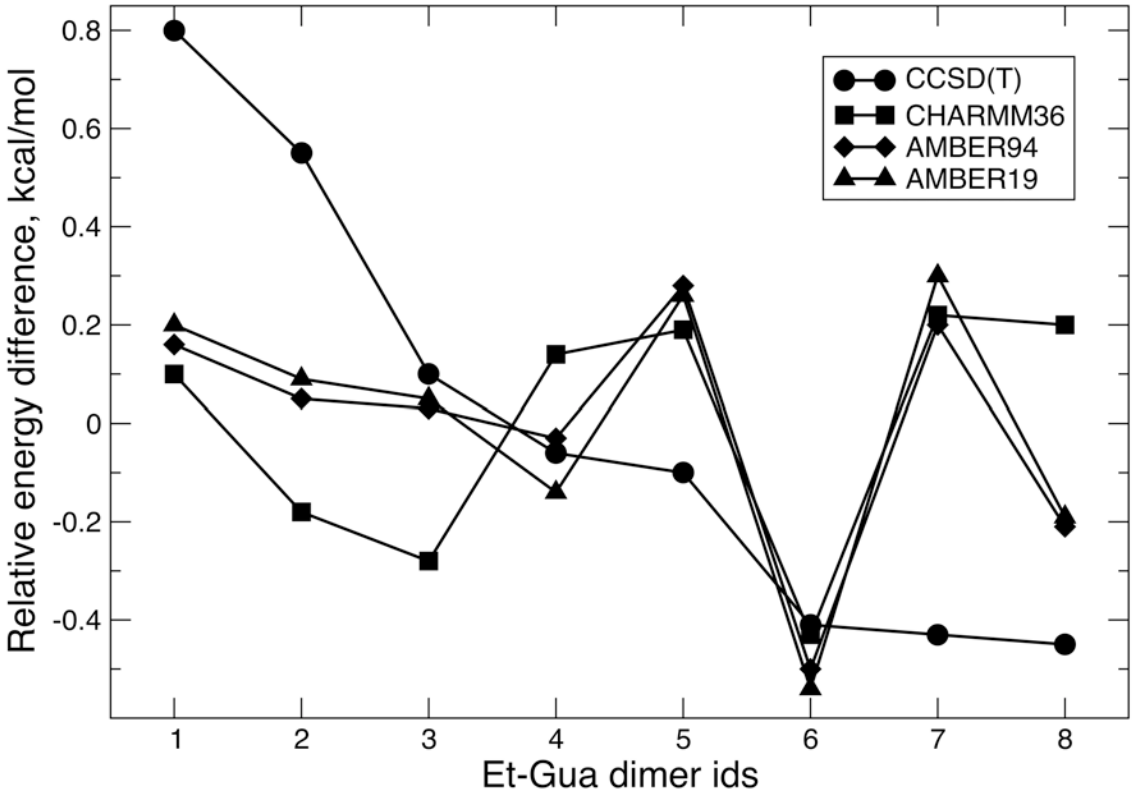
QM MD: Unit Cell of Et-Gua Crystal, 950 fs

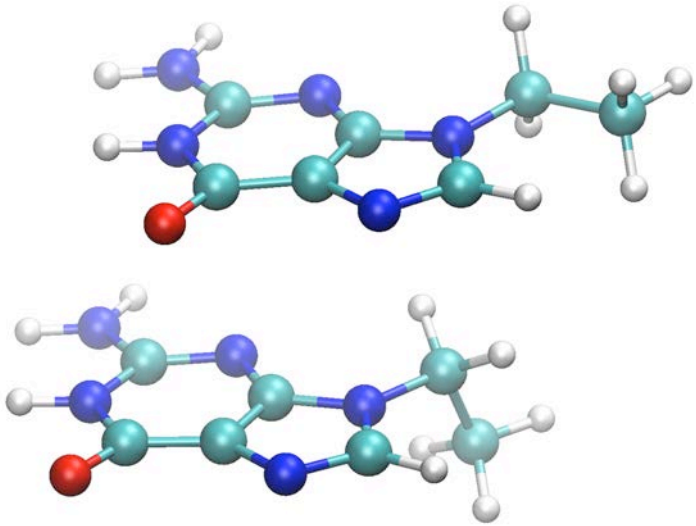


Molecular Dynamics simulation of Guanine crystal performed at the Density Functional Theory level to sample the conformational space of base-base interacting pairs in vicinity of the experimental thermodynamic energy minimum. Computed on 1024 BW nodes.

Extracted 216 dimer clusters from QM MD: 0.1 Å < RMSR < 0.2 Å

Relative Base-Base Interaction Energy





- Relative interaction energy difference vs. the average value
- Dimer id 3 corresponds to the crystal structure
- The remaining seven structures carry perturbed geometries obtained from QM MD

Resource Required for CCSD(T) Computations

- NWChem CCSD that includes previous NCSA contribution
- CCSD(T)/6-311++G** level of theory
- Singles and doubles for Et-Gua dimer (44 atoms including hydrogen) take 5651 seconds on 1024 XE6 nodes
- The portion of perturbative triples requires 5392 seconds on 4096 XE6 nodes
- Conducted 154 such computations

Intermolecular Interaction Energy in Clusters

Method	#records	AverErr	RMSD	MaxErr	Cluster ID
CH36	147	2.09 ± 1.95	2.85	8.34	018-dimer-guah-guah-01-06
AM94	147	2.09 ± 1.71	2.70	7.66	059-dimer-cytm-cytm-01-14
AM19	147	1.93 ± 1.57	2.48	7.14	018-dimer-guah-guah-01-06

Interaction energy is in kcal/mol

Amber19: Optimized force field

Amber19 has the lowest error

Conclusions:

- Optimization of bio-molecular force fields requires petascale resources
- Project produced the largest dataset of 147 dimer, 1618 trimer, and 11355 tetramer clusters of five nucleic acid bases extracted from 12 high-resolution crystals of nucleobases
- Cluster extraction from crystals produces the most important points on the potential energy profile of base-base interactions
- QM MD of crystals samples the energy profile near the experimental minima
- Fitting charges to X-ray clusters improves agreement with CCSD(T)
- New force field, Amber19 outperforms both Amber94 and CHARMM36

Acknowledgements

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