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Multi-resolution modelling of biological systems in LAMMPS

ARCHER Virtual Tutorial, 19th Oct 2016
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Outline

• ARCHER eCSE programme

• Implementation of Dual Resolution Simulation Methodology in LAMMPS
  • ELBA force-field
  • Implementation in LAMMPS
  • Performance testing
  • Summary
ARCHER eCSE programme

- Funding for the ARCHER user community to develop software
  - Implementation of algorithmic improvements within an existing code
  - Improving the scalability of software on higher core counts
  - Improvements to code which allows new science to be carried out
  - Porting and optimising a code to run efficiently on ARCHER
  - Adding new functionalities to existing codes
  - Code development to take a code from a Tier-2 (Regional) or local university cluster to Tier-1 (National) level bringing New Communities onto ARCHER
- Projects typically 3 months – 1 year
- Next call closes 31st Jan 2017
ARChER eCSE programme

• More information on the ARChER website:
  • https://www.archer.ac.uk/community/eCSE/
  • Project Reports
  • How To Apply
  • List of funded projects

• Webinar from last month:
  • https://youtu.be/WRGsNKWrNIc
Implementation of Dual Resolution Simulation Methodology in LAMMPS

- eCSE04-7 (January 2015)
- PI: Prof. Jonathan Essex, Southampton
- 6 person-months funded: August 2015 – August 2016

- **Objective:** enable fast and reliable calculations with the ELBA force-field in LAMMPS
  - New integrators
  - Parallel load balancing
ELBA Force-field

• **ELBA** = **ELectrostatics-BA**sed coarse grained forcefield

• Originally for studying lipids
  - Also applied to other biomolecules

• Explicit solvent
  - One dipolar bead per water molecule

• Allows for atomistic detail e.g.
  - Using CHARMM parameters

138 atoms -> 15 CG beads
ELBA Force-field

- Implemented in BRAHMS-MD (Biomembrane Reduced-Approach Multiresolution Simulator for Molecular Dynamics):
  - [https://code.google.com/archive/p/brahms-md/](https://code.google.com/archive/p/brahms-md/)
  - Limited user base, single developer -> not sustainable
  - No parallelisation -> small systems

- Why LAMMPS?
  - Main interaction types already implemented
  - Support for spherical particles
  - r-RESPA multiple timestepping
  - Flexible, scalable, large user base
Implementation in LAMMPS

- LAMMPS fix nve/sphere integrator does not conserve energy well
- Better scheme to integrate rotational d.o.f. - DLM
  Dullweber, Leimkuhler and McLachlan, JCP 107(15) 1997

1. Construct rotation matrix $Q$ from dipole (taken as the body-fixed z-axis)
2. In body-space, apply rotations around each local axis:

   \[
   \begin{align*}
   \omega_b &= Q \omega_s \\
   R_1 &= R_x(\frac{\delta t}{2} \omega_1), \quad \omega = R_1 \omega, \quad Q = R_1^T Q \\
   R_2 &= R_y(\frac{\delta t}{2} \omega_2), \quad \omega = R_2 \omega, \quad Q = R_2^T Q \\
   R_3 &= R_z(\delta t \omega_3), \quad \omega = R_3 \omega, \quad Q = R_3^T Q
   \end{align*}
   \]

3. Finally, compute the new dipole:

   \[
   \mathbf{\mu}_s = Q^T [001] \cdot ||\mu||
   \]
Implementation in LAMMPS

- 4000 ELBA water beads, 10fs timestep, 20ps NVT, 20ps NVE

fix thermostat all langevin 303 303 200 48279 omega yes
Implementation in LAMMPS

- 128 DPMC molecules in water, 75ps NVT, 100ps NVE
Implementation in LAMMPS

- DLM integrator enabled by an optional argument:
  - fix nve/sphere … update dipole/dlm

- Also for other ensembles:
  - Constant temperature / NVT (Nosé-Hoover)
    - fix nvt/sphere … update dipole/dlm
  
  - Isothermal-isobaric (Nosé-Hoover / Parrinello-Rahman)
    - fix npt/sphere … update dipole/dlm

  - Isenthalpic (Parrinello-Rahman)
    - fix nph/sphere … update dipole/dlm
Implementation in LAMMPS

- Load balancing schemes:
  - None
  - Shift
  - RCB

- Problem for dual-resolution simulations!
  - 90% of computational cost is force evaluation
  - Not all particles are the same
  - r-RESPA – some forces are computed more frequently than others

Implementation in LAMMPS

- New load balancing metrics:
  - Weighting by particle groups
    - Uses LAMMPS existing `group` command e.g.
      ```
      group solute type > 1
      group water type 1
      ```
    - `balance 1.1 shift xyz 50 1.1 weight group 1 solute 2.5`
Implementation in LAMMPS

- New load balancing metrics (subsequently added by LAMMPS developers):
  - Weighting by number of neighbors – weight neigh
  - Weighting by compute time – weight time
    - Doesn’t account for the different particles types contributing to different parts of the computation (pair, bond, kspace, neigh)
  - Weighting by arbitrary user-defined variables – weight var
Performance testing

- Bovine Pancreatic Trypsin Inhibitor (BPTI) dual-resolution model:
  - 882 atoms, CHARMM force-field
  - 6136 water molecules, ELBA beads

- No r-RESPA
- 1fs timestep
- Up to 10% speedup over non-weighted balance
Performance testing

- 1:4 r-RESPA ratio
- Water pair forces + dihedral forces computed every fourth step
- Larger weightings better (2.5-3.0)
- Up to 36% speedup over non-weighted balance
Performance testing

- 1:8 r-RESPA ratio
- Larger weightings better (3.0-4.0)
- Up to 65% speedup over non-weighted balance
Summary

• DLM integrator for NVE/NVT/NPT/NPH dynamics
  • Stable for water up to 16fs timestep
  • Included in LAMMPS stable release 30 Jul 2016

• New load balancing metrics
  • Better performance for r-REPSA and hybrid pair force
  • Include in LAMMPS patch release 27 Sep 2016

• More information
  • Tutorials, references, discussion: https://sgenheden.github.io/Elba/

Installed on ARCHER
module load lammps/elba
ARCHER eCSE05-10 Project

• **Adding Multiscale Models of DNA to LAMMPS** (09/2015 – 08/2016)
  • Dr Oliver Henrich (PI, UoE), Prof Davide Marenduzzo (Co-I, UoE), Dr Thomas Ouldridge (Co-I, Imperial College London)
  • Overview:
    o Implemented **oxDNA coarse-grained DNA model** for single- and double- stranded DNA into LAMMPS code
    o Implemented new **Langevin-type rigid-body integrators**
    o Software available from **CCPForge** ([https://ccpforge.cse.rl.ac.uk/gf/project/cgdna](https://ccpforge.cse.rl.ac.uk/gf/project/cgdna)) soon as **LAMMPS USER-package**
    o Currently adapting utility software of oxDNA standalone version
From DNA to Chromosomes

- Haploid human genome contains 3.2 billion base pairs organised in 23 chromosomes
  - Diameter of DNA strand = $2 \times 10^{-9}$ m
  - Total length of DNA in human cell = 2 m
  - Diameter of spherical ‘blob’ of DNA in human cell = $2 \times 10^{-6}$ m

- Hierarchical organisation
  - Histone octamer
  - Nucleosome core particles 200 bps
  - 10 nm beads-on-a-string
  - 30 nm chromatin fibre
  - Smallest loop in chromatin fibre 50,000 bps
Atomistic Simulation of DNA

- Good for capturing fast conformational fluctuations and protein-DNA binding
- Usually limited to a few 1000 base pairs
- Phenomena on large time and length scales, e.g. DNA supercoiling or nucleosome positioning are permanently out of reach
Coarse-grained simulation with oxDNA

• Must deliver correct longitudinal and torsional persistence length, electrostatics, if sequence-specific correct melting temperature, elastic constants …

• oxDNA: top-down approach of a CG model, nucleotides modelled as rigid bodies (DOF are COM & quaternion)

• Parameterize interaction between nucleotides with 6 independent interactions (7 for implicit electrostatics)

1 nucleotide
**oxDNA Force Field**

- **Backbone**: FENE (finite extensible nonlinear elastic) springs
- **Excluded volume**: Lennard-Jones potential
- **Stacking**: harmonic angle $\times$ Morse potential
- **Cross-stacking**: harmonic angle $\times$ harmonic distance potential
- **Coaxial stacking**: harmonic angle $\times$ harmonic distance potential
- **Hydrogen bonding**: harmonic angle $\times$ Morse potential
oxDNA Force Field

- Smoothed, truncated and modulated forms of the above
- 1 bonded interaction (backbone), 5 pair interactions (excluded volume, stacking, hydrogen bonding, cross-stacking, coaxial stacking)

For full details see Thomas Ouldridge, Coarse-grained modelling of DNA and DNA self-assembly, DPhil, University of Oxford, 2011.
Parallel Performance

Benchmarks:

- Low density: array of 100 DNA duplexes with 600 base pairs long (see above) = 60 kbp
- High density: array of 1600 duplexes = 960 kbp
60 kbp benchmark

- Single node
  - Nlocal 5000
  - Nghost 1300
  - MPI < 5% (LMP)
  - compute 86% (LMP)
  - acos 12%
  - q_to_exyz 11%

- 2048 MPI-tasks
  - Nlocal 60
  - Nghost 225
  - MPI > 50%
  - compute 43% (LMP)
Craypat Performance Analysis

960 kbp benchmark

- Single node
  - Nlocal 80000
  - Nghost 8300
  - MPI < 3%
  - compute 88% (LMP)
  - acos 12%
  - q_to_exyz 12%

- 2048 MPI-tasks
  - Nlocal 940
  - Nghost 480
  - MPI < 13%
  - compute 82% (LMP)

Single node (24 MPI-tasks) 2048 MPI-tasks
Applications

DNA gel

Stand displacement

Liquid-crystalline states of DNA

DNA tiles

DNA nanostructures

DNA tetrahedra
Code Distribution

- LAMMPS version via CCPForge
  - [https://ccpforge.cse.rl.ac.uk/gf](https://ccpforge.cse.rl.ac.uk/gf)
  - Project: **Coarse-Grained DNA Simulation** (cgdna)
  - Anonymous subversion access
    - svn checkout [https://ccpforge.cse.rl.ac.uk/svn/cgdna](https://ccpforge.cse.rl.ac.uk/svn/cgdna)
- In the near future also as **LAMMPS USER-package** with extended documentation
- Standalone version from [https://dna.physics.ox.ac.uk](https://dna.physics.ox.ac.uk)
http://www.archer.ac.uk/training/

- Face-to-face courses
  - timetable, information and registration
  - material from all past courses

- Virtual tutorials & webinars
  - https://www.archer.ac.uk/training/virtual/
  - timetable plus slides and recordings
  - please leave feedback on previous tutorials after viewing material
Goodbye!

Thanks for attending

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