CCPBioSim

HECBioSim

Biomolecular Simulation

Aspirations, Limitations and Prospects

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In pursuit of an accurate spatial and temporal model of biomolecules at the atomistic level: a perspective on computer simulation

as a biophysical tool

Alan Gray, Oliver G. Harlen, Sarah A. Harris, Syma Khalid, Yuk Ming Leung, Richard Lonsdale, Adrian J. Mulholland, Arwen R. Pearson, Daniel J. Read and Robin A. Richardson

Acta Cryst. (2015). D71, 162–172

Current State of the Art

Quantum mechanics

Atomistic MD

Coarse-grained MD

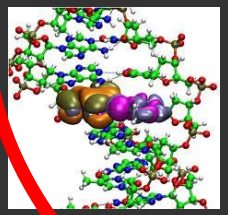
Dissipative particle dynamics, Lattice Boltzmann

Finite element analysis

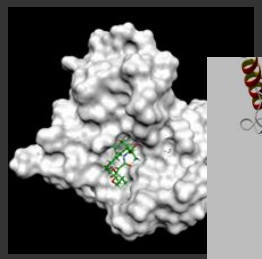
CCPBioSim

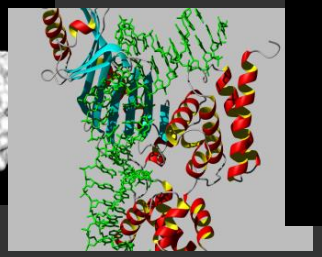
Accuracy ⟷ Size/ timescale

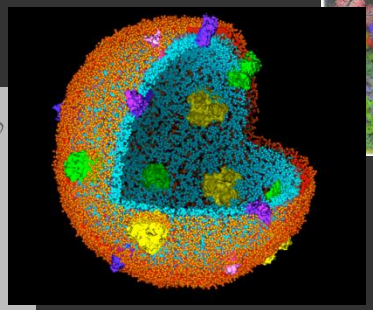
100 atoms

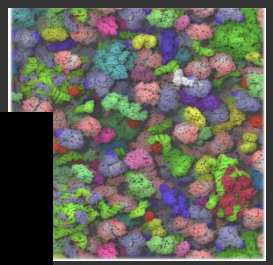


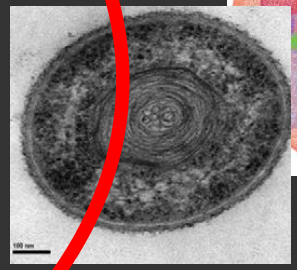
10,000 atoms/μs
1 million atoms/ns

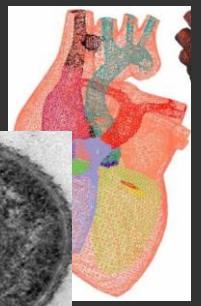












Photosynthesis
Enzyme catalysis

Molecular recognition

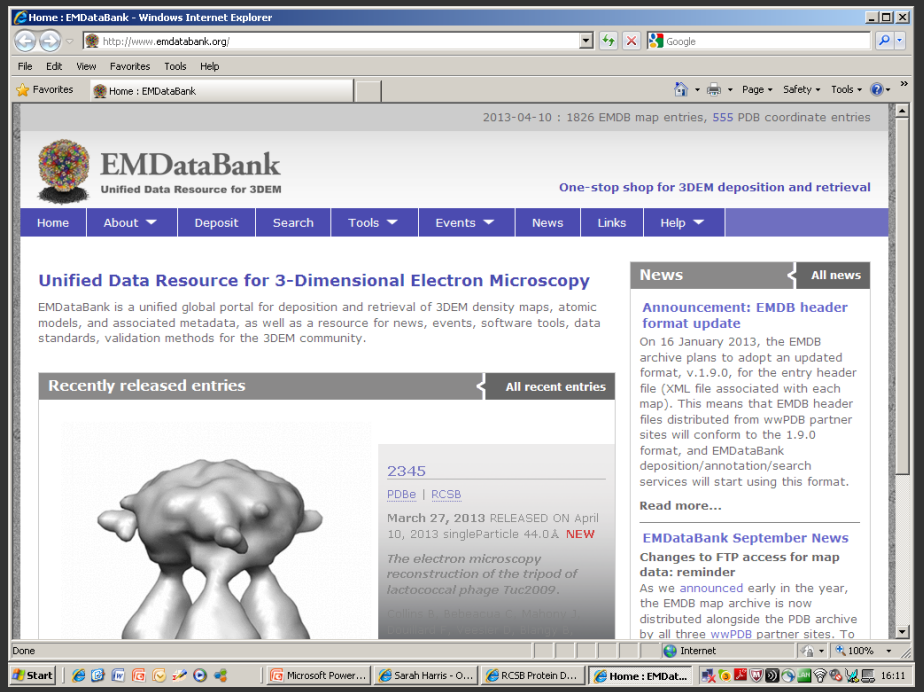
Cytoplasmic crowding, supermolecular structures

Cells, biological tissues, organs

Biological Structural Databases

The Protein Data Bank (PDB)

The EM Data Bank (EMDB)



Atomistic co-ordinates

Volumetric data

Data standardisation and validation

SAS-DataBank?

Successes

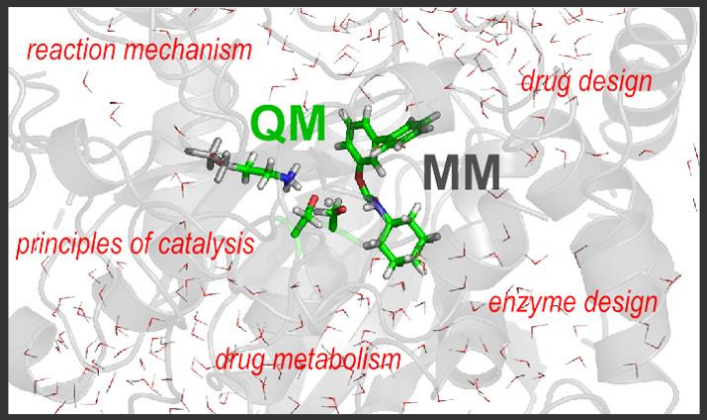
Well established software & visualisation tools
(GROMACS/AMBER/NAMD/DL_POLY)
(VMD/PYMOL/CHIMERA)

Ubiquitous in pharmaceutical industry (High throughput screening)

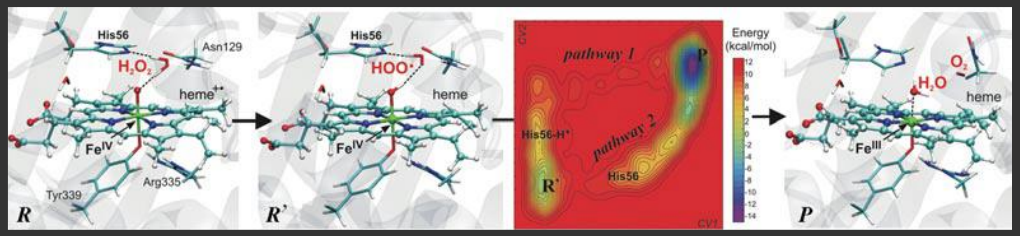
Reasonable parallelisation/ported to GPU

Nobel prizes in 2013

PDB: QM,QM-MM, MD, Coarse-grained

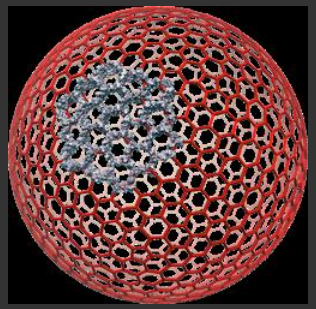


Van der Kamp & Mulholland, Biochemistry (2013)



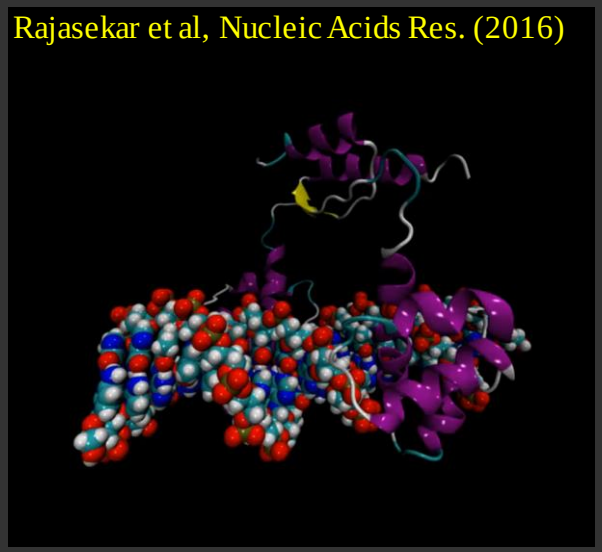
Molecular mechanisms of catalase reaction with metadynamics

Barducci et al WIRES 2011

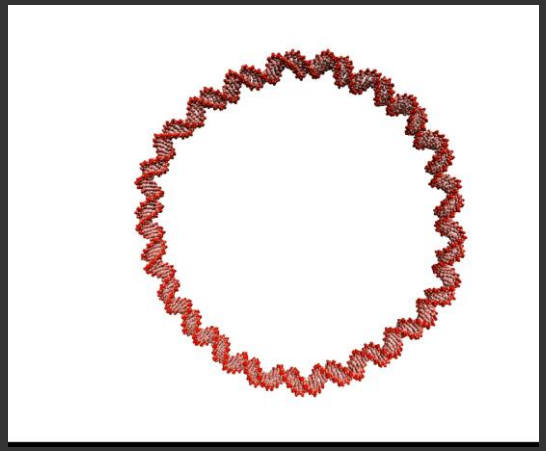


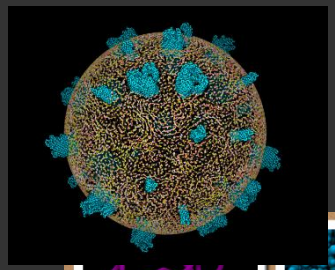
Paper Self-Assembling Cages from Coiled-Coil Peptide Modules (Science 2013)

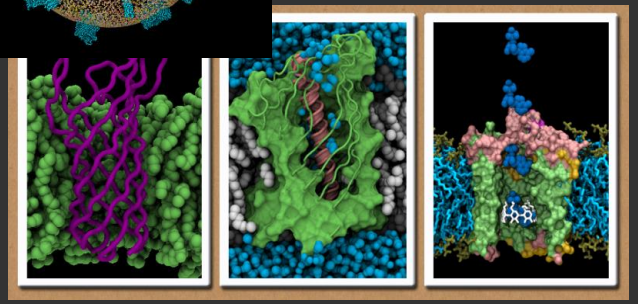
Rajasekar et al, Nucleic Acids Res. (2016)



Noy et al, Biophys J, 2017







https://symakhalidresearchgroup.wordpress.com/gallery/

Challenges

Connecting with experimental data (limitations in accessible length/time-scales)

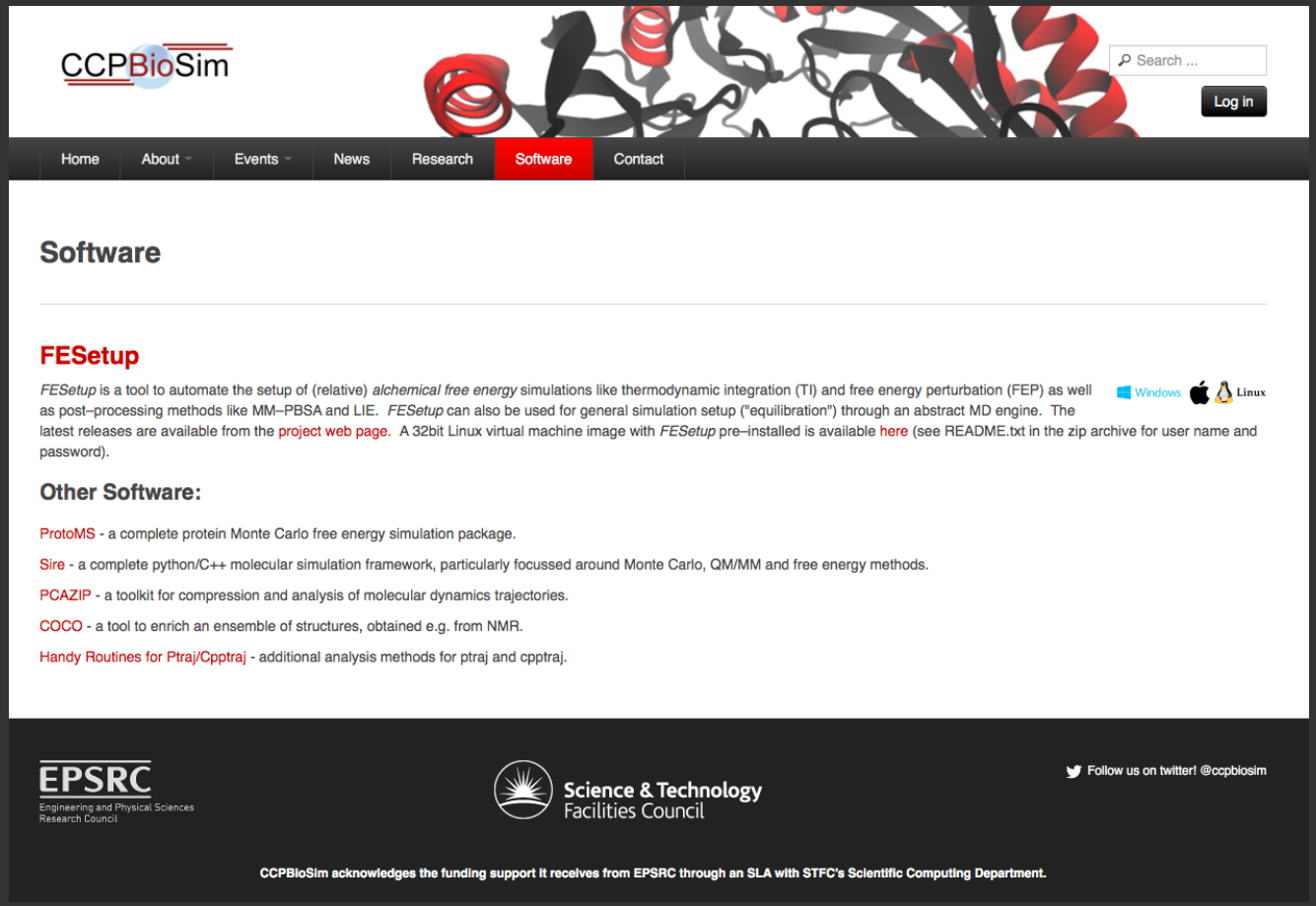
Method validation (eg forcefields)

Software usability/avoiding the “black box”

Exploiting hardware (e.g. GPUs/parallelisation)

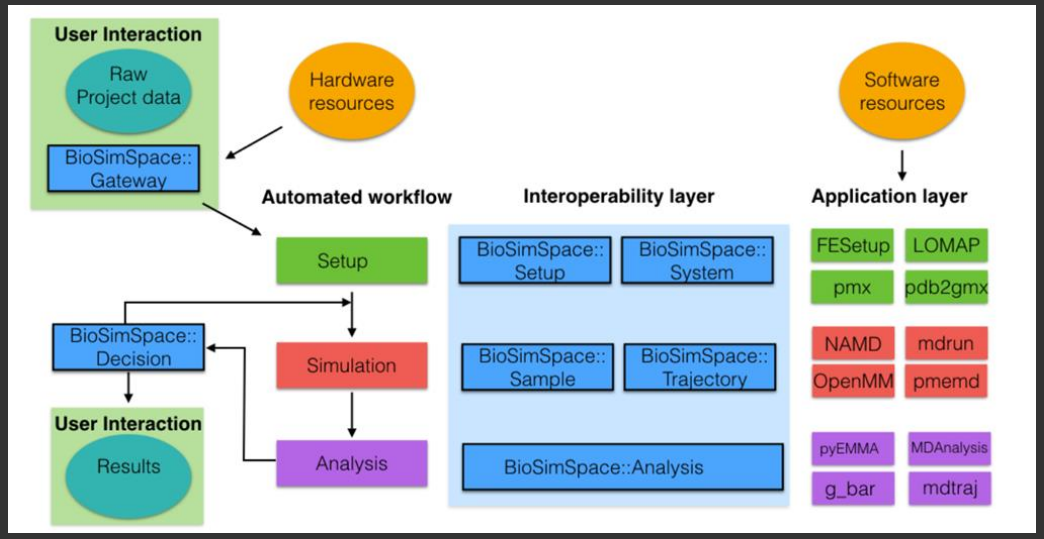
Enhanced sampling/multi-scale approaches are required ~ need for method development at all stages

Method and Software Development



New and old methods need to reach our community e.g. workshops/conferences/online tools

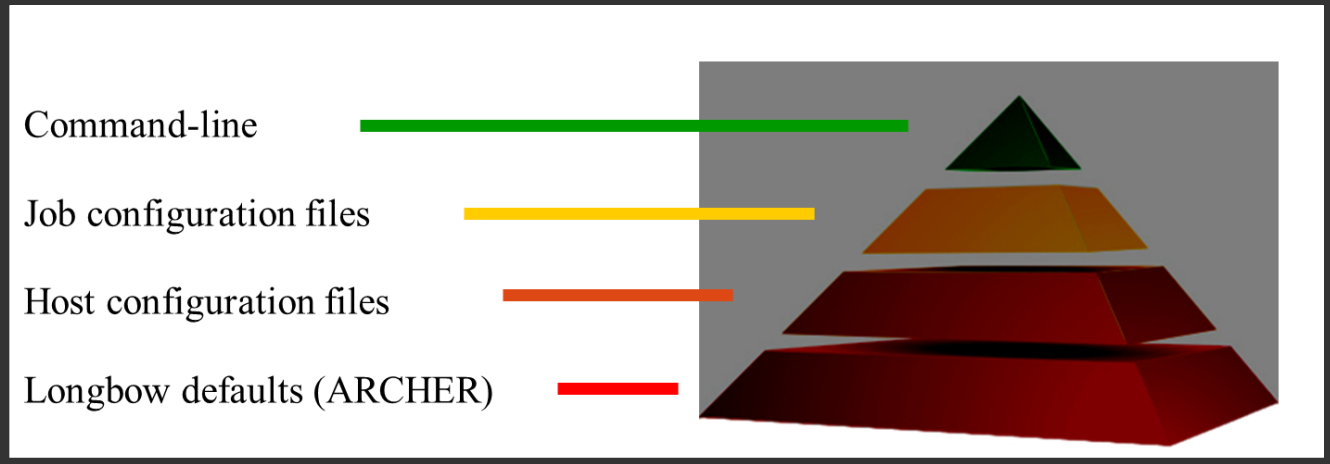
Software Flagship: **BioSimSpace**



Python translation layer to allow tools communicate

Easier to write robust and reusable workflow components

Longbow: Submission and retrieval of multiple HPC jobs



Training

http://www.ccpbiosim.ac.uk/events/workshop-course-material

Collaborations with other CCPs to understand scientific challenges and share resources and expertise

Collaborative Conferences

Two way street – Complementary Methods CCP4 2014

CCPN/CCPBioSim Joint Conference 2016

2nd Conference on Multiscale Modelling of Condensed Phase and Biological Systems - CCPBioSim & CCP5 2016

Multiscale Modelling of Condensed Phase and Biological Systems 2014

Collaborations with other CCPs to understand scientific challenges and share resources and expertise

Essential to avoid duplication of effort.

Annual grand CCP meeting? Grand CCP science challenge?

The Future….

Computation for Biomolecular Cryo-Electron Microscopy and Tomography

Thursday 13 July 2017 - Workshops
- on Wednesday 13 September 2017 - Conferences

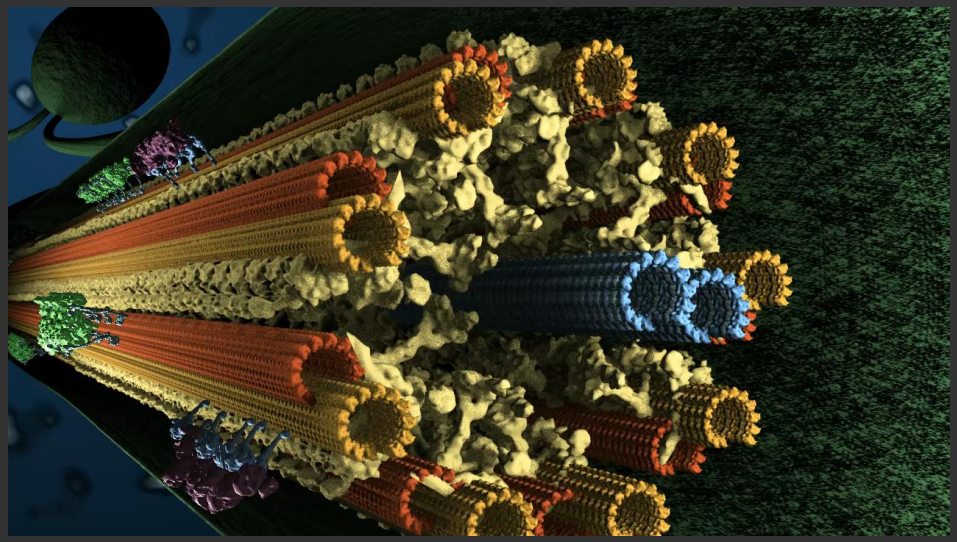
5th Annual CCP-BioSim Conference: Frontiers of Biomolecular Simulation

Wednesday 13 September 2017 - Conferences

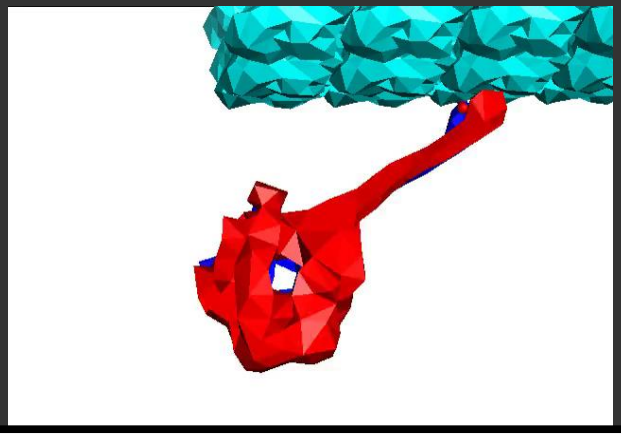
All Welcome!

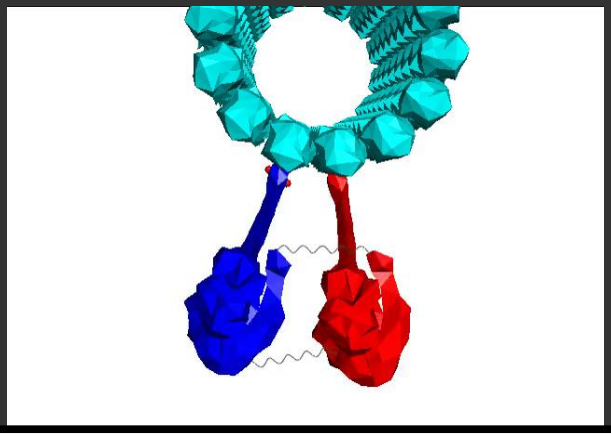
EMDB:Towards Ultra-structure ~ FFEA

Animation by Bara Malkova for Pagino group



What is the effect of the strength of the interaction between the monomers?

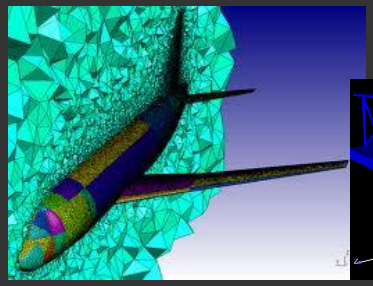




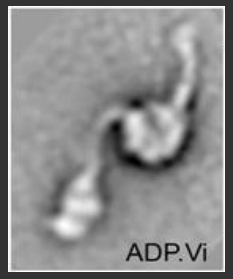
Fluctuating Finite Element Analysis (FFEA)

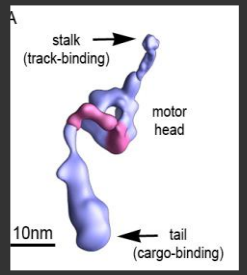
Fluctuating Finite Element Analysis (FFEA)

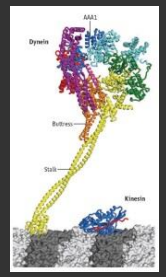
Finite element analysis describes the shape of a complex object using a 3D mesh.



EMDB/PDB file







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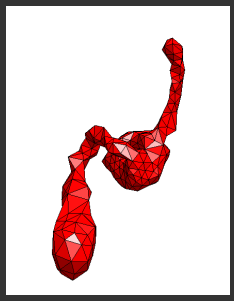
Generate mesh



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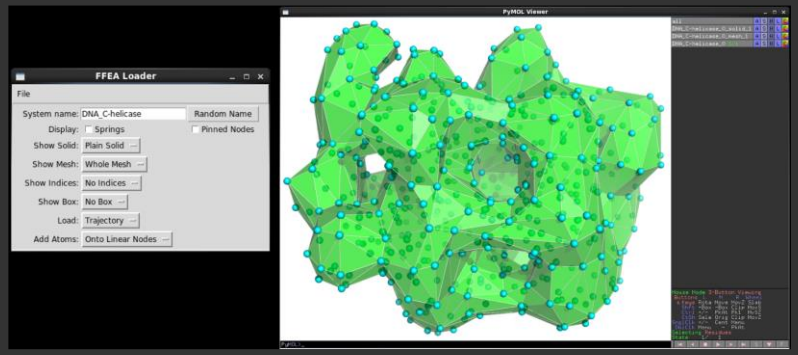
Assign material parameters



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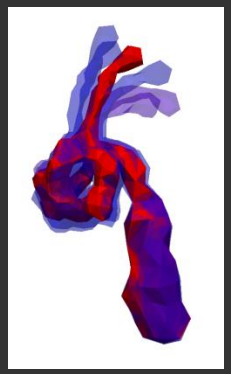
FFEA



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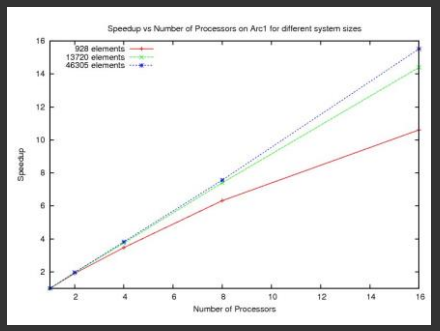
Analyse trajectory



Code uses shared memory parallelisation