Science Driver: Bio-Transport Computations

Computing of Transport Processes in Biological Systems

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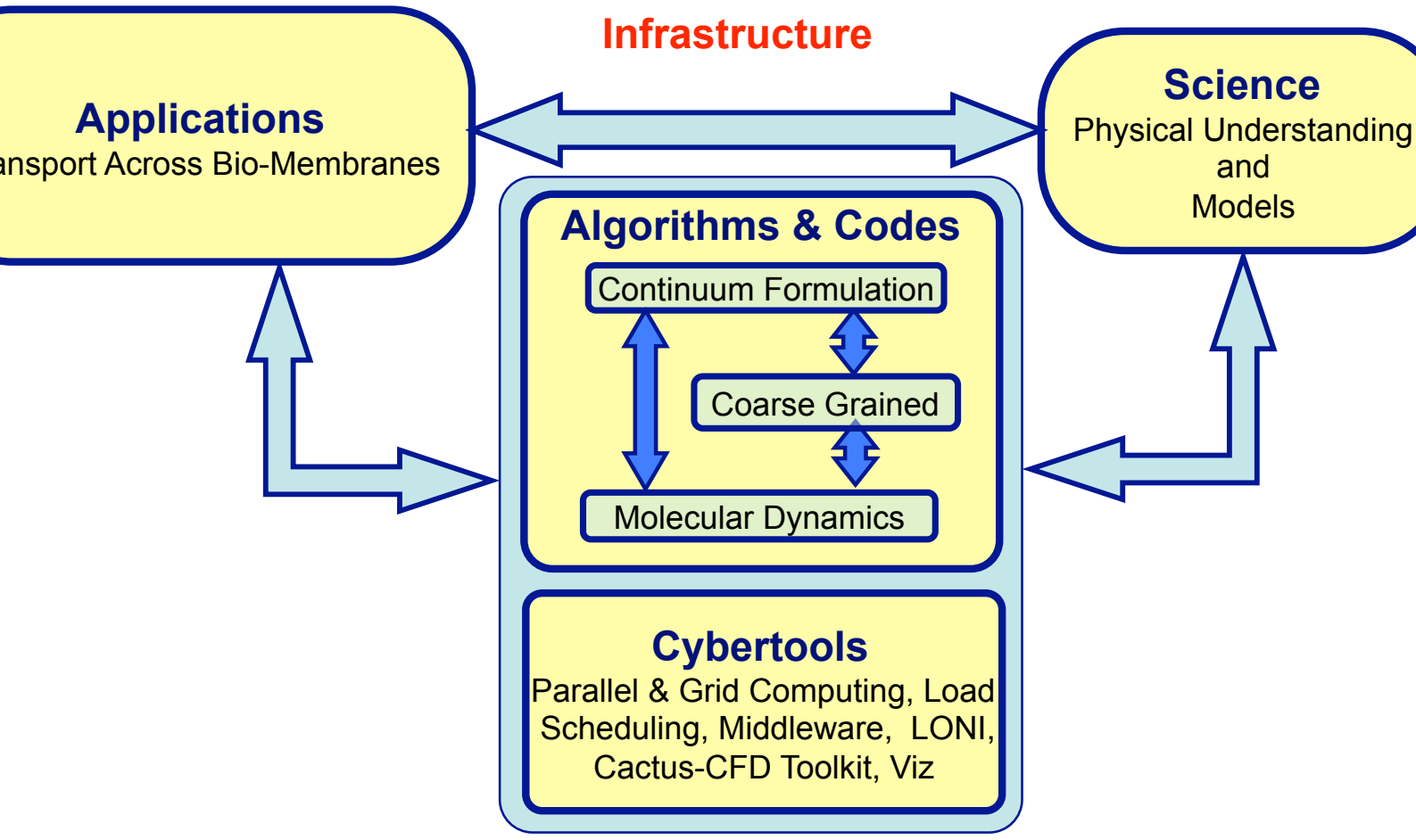
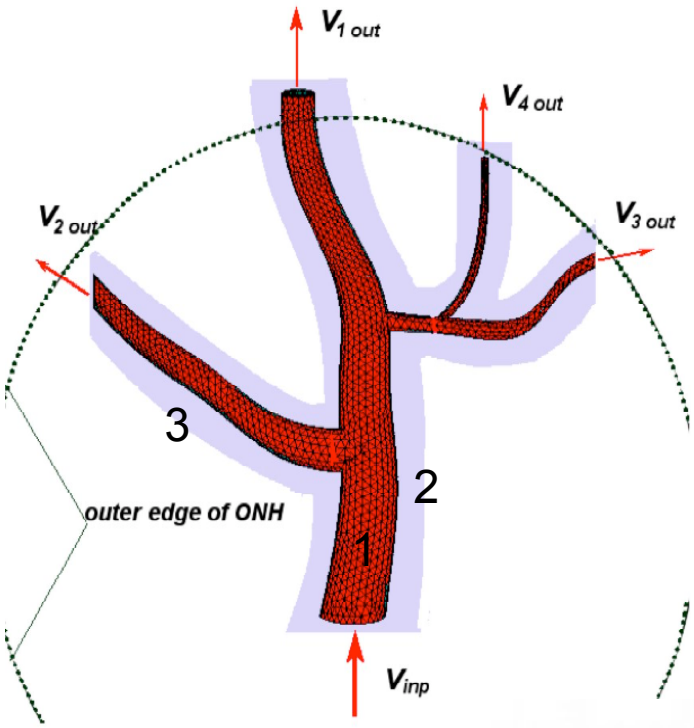
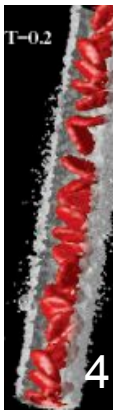
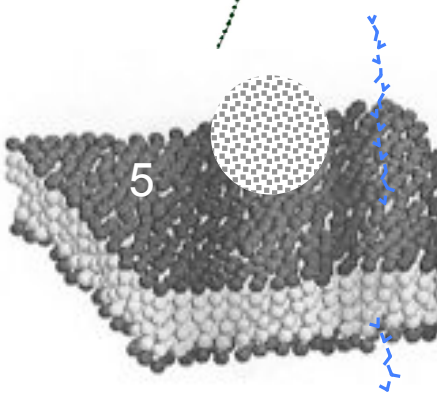

Infrastructure
Applications
ansport Across Bio-Membranes
Science
Physical Understanding
and
Models
Algorithms & Codes
Continuum Formulation
Coarse Grained
Molecular Dynamics
Cybertools
Parallel & Grid Computing, Load
Scheduling, Middleware, LONI,
Cactus-CFD Toolkit, Viz

Prediction and understanding of oxygen transport in biological systems

1. Continuum flow in larger vessels-Navier Stokes
2. Porous media transport across vessel walls & tissues-Brinkmann
3. Structural deformation of vessels/tissues-
4. Particle flow in capillaries-Lattice-Boltzmann
5. Atomistic transport across cellular interfaces-Molecular Dynamics
6. Upscaling from atomistic to continuum







Development of computationally efficient numerical methods or algorithms needed for biological transport calculations

- ✓ Structural calculation using a meshless particle method
- ✓ Flow-Structure Interaction (FSI) methodology using Immersed Boundary Method (IBM)

Yea

Contributing to improved science-understanding of small molecule flow/transport physics under asymmetric concentrations and applied stresses

- ✓ Asymmetric calculations of molecule/particle transport across lipid bilayers

Yea

Contributing to improved computational infrastructure- collaborating with the cybertools group responsible for developing the CFD toolkit

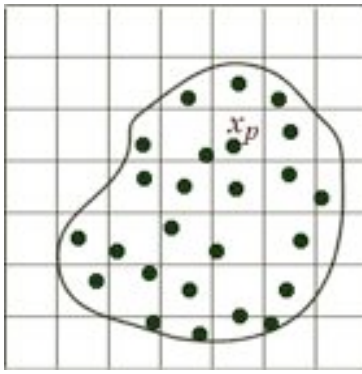
- ✓ Development of cactus-compatible routines for transport and flow calculations
- ✓ Validation Studies

Yea

Contributing to improved science-understanding of oxygen flow/ transport physics under elevated pressures

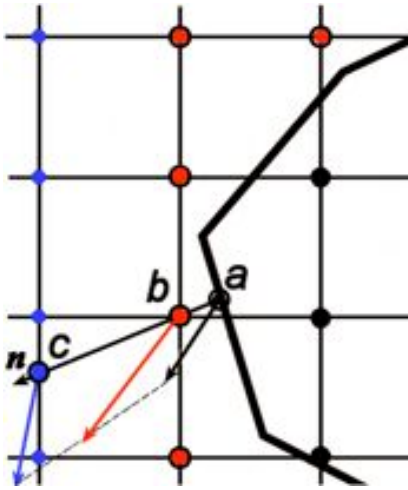
ontinuum flow and transport calculations

- Multiblock structured grid with continuous grid lines across block interfaces
- Fractional step algorithm with staggered grid locations for the velocity (stored at cell faces)
- Pressure-poisson equation for pressure
- Consistent second order differencing for diffusion and pressure terms and upwind biased differencing for the convective terms
- Explicit and implicit second order temporal differencing



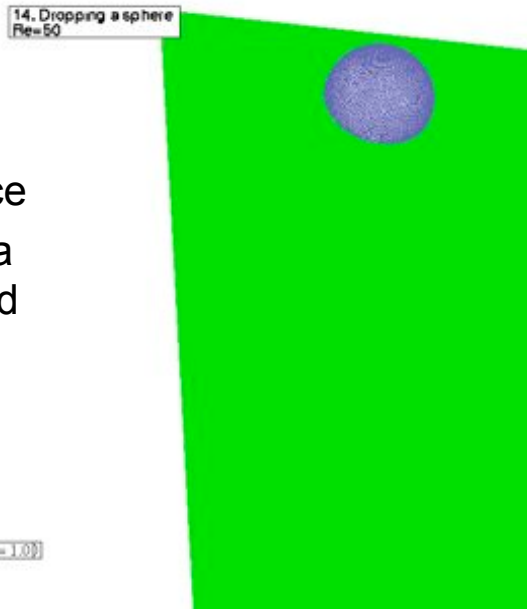
Background grid for soluti
momentum equations

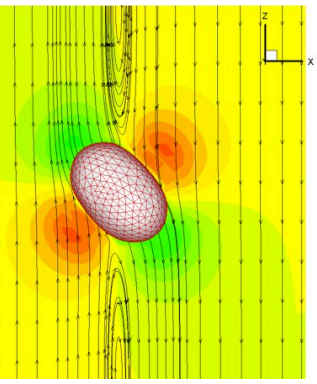
- Flow-structure interaction
  - Particle-based meshless calculations for structural deformations (called material point method-MPM)
- Immersed Boundary Methodology (IBM) for resolving boundary conditions along moving interfacial surfaces
- Flow-Structure Interaction for Biosystems

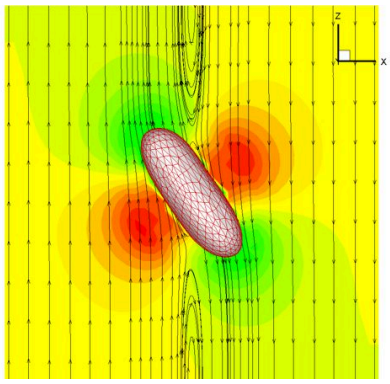


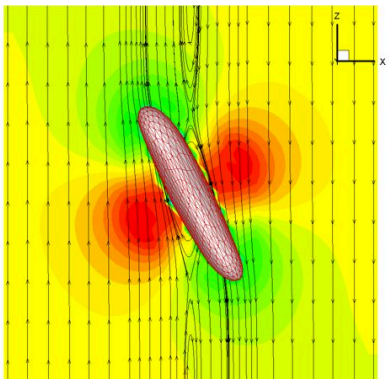
Material-Point Method (MPM) for structural deformations

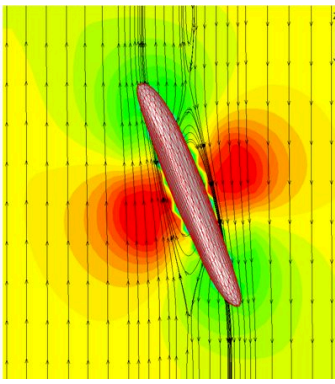
- Arbitrary distribution of points on the solid body/surface
- Material points are solved (deformation & stress) on a background grid that is independent from the fluid grid
- Flow-structure coupling through boundary/interface conditions
- Flow around deforming surface handled through IBM











- Collaborating with the WP4 group for the development of a CFD Toolkit;
- Finite volume, multi block;
- Data array structure consistent with current structure in Cactus;
- Multi-block grid from commercial grid generators;
- Baseline code developed for laminar flow; several benchmarks being run to provide WP4 input-output files for Toolkit verification and validation;
- Long term plans are to transition to the Toolkit for the biosystems transport simulation;

- Implemented suggestions for improved performance of paralle code—seen improvements
- Discussions ongoing with Viz groups to get better access to better visualization codes (WP3)
- Discussions ongoing on use o a Lattice Boltzmann code for particle simulations
- Discussions ongoing on most effective ways of doing CFD-MD coupling

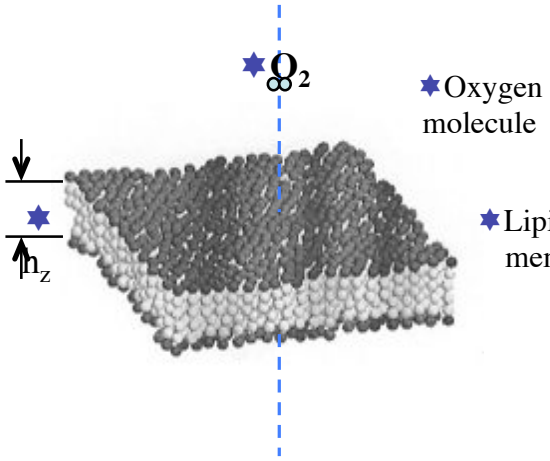
sion rate and permeability coefficients across el walls and tissues for different conditions are rally not known reliably (difficulty in in situ urements)

cifically designed MD simulations under ent conditions can provide:

tomistic insight and molecular mechanism nderlying the transport of O_2 across a lipid ayer membrane in order to determine which etails are important for the permeation process.

erive the oxygen diffusivities, D_{O2}, inside the nomogeneous region of a lipid bilayer.

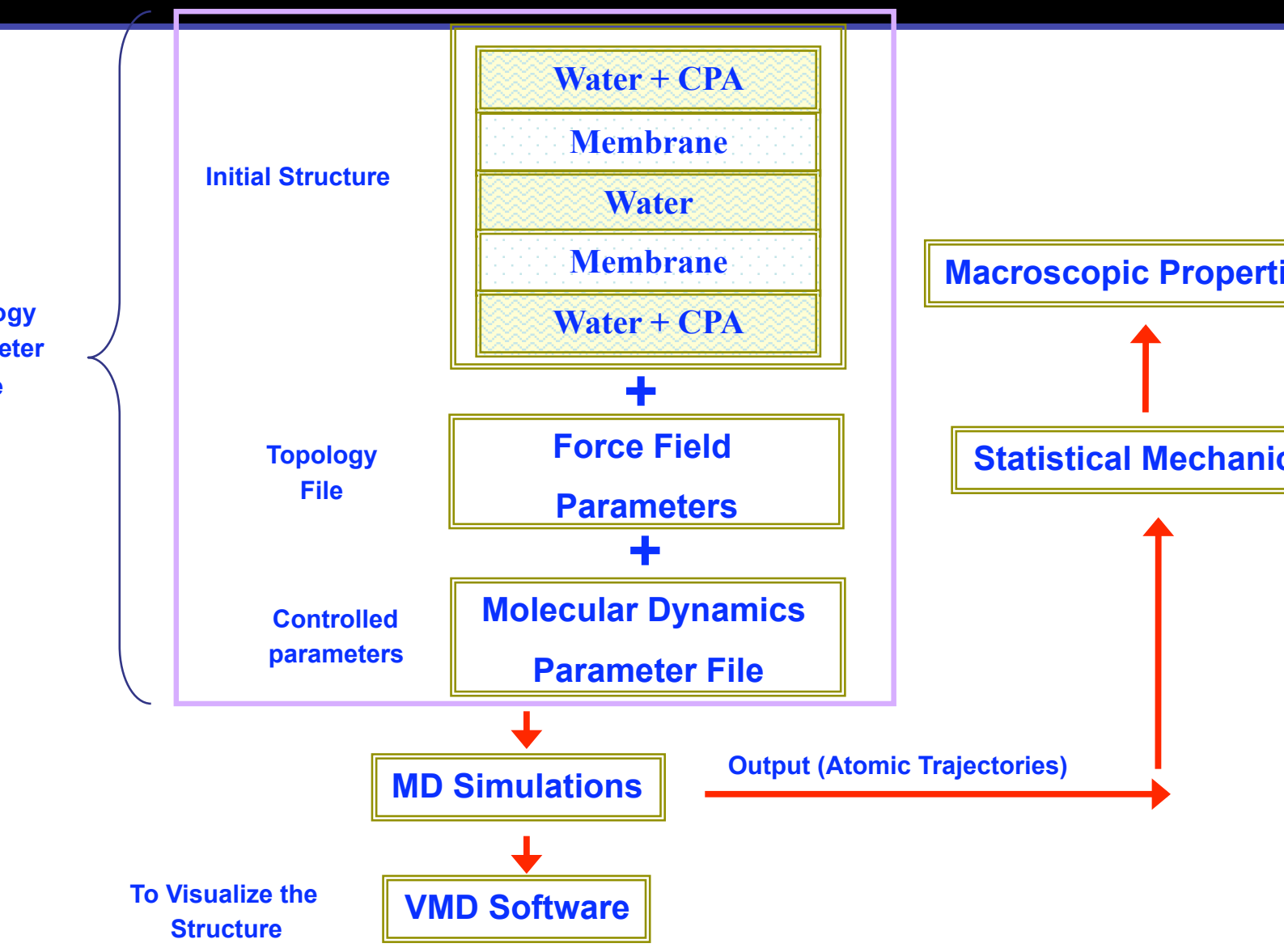
erive permeation rates, P_{O2}, indirectly via mputation of the free energy and diffusion rate ofiles of a O_2 molecule across the lipid bilayer.



$$P = \frac{1}{\int_{z_1}^{z_2} \frac{\exp(\Delta G(z)/RT)}{D(z)} dz}$$

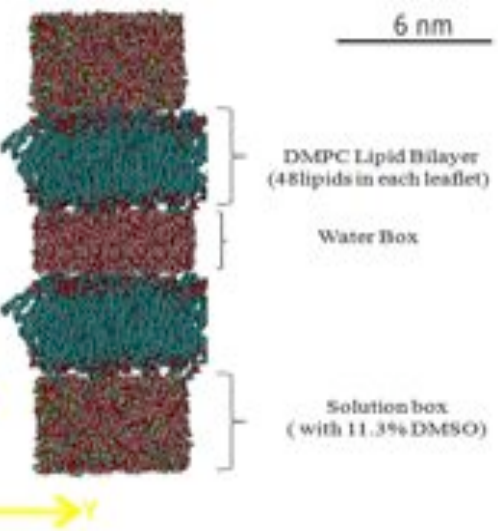
$$D = \frac{1}{3}\int_0^\infty \langle v(0)\cdot v(t)\rangle dt$$

MD Simulation Using "GROMACS"

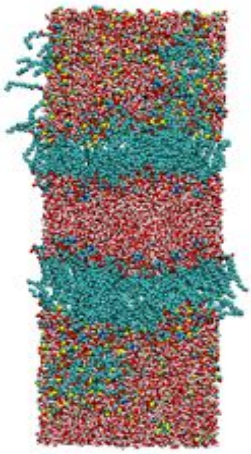


Structural changes in Lipid Bilayers

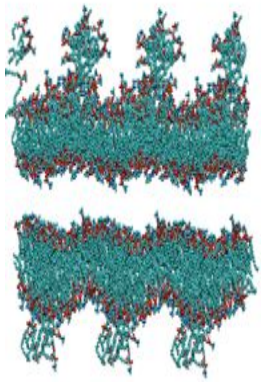
Initial system



(a) Whole system

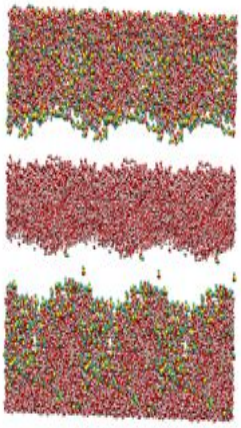


(b) Lipids only



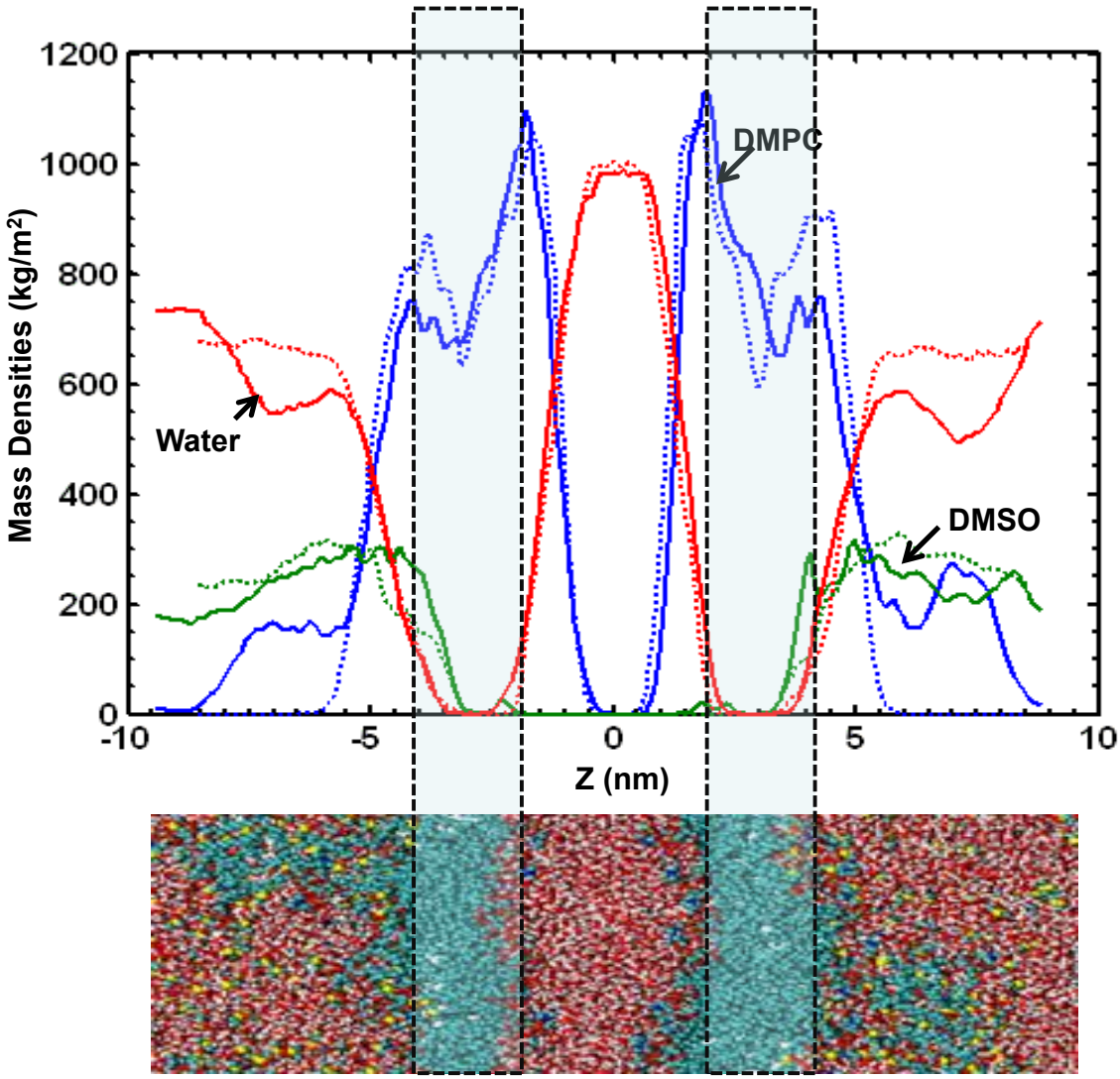
t=50ns

(c) Solution



- **No penetration of water molecules**
- **Data analyzed for mass density profiles, radial distribution functions, tail order parameters, and water orientation profile**

ass density profiles of : DMPC, DMSO, and wa



0ns profiles: dotted line ,50ns profiles: solid line

CFD

- ✓Improvements to the IBM (pressure interpolation)
- ✓Working on the MPM for greater robustness (implicit, parallel)
- ✓Simulation of transport in flexible tubes

MD

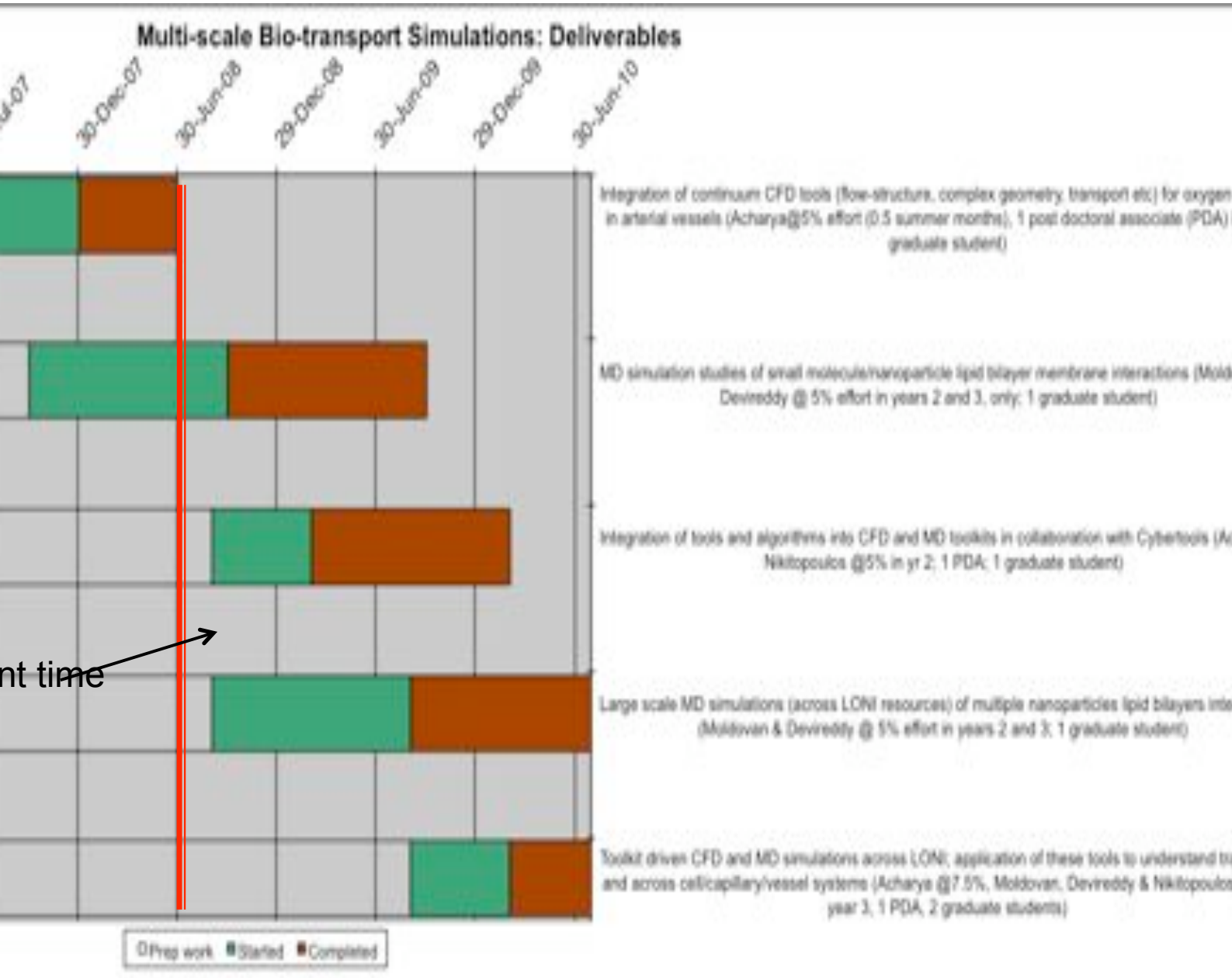
- ✓ Simulation of small molecules across lipid bi-layers

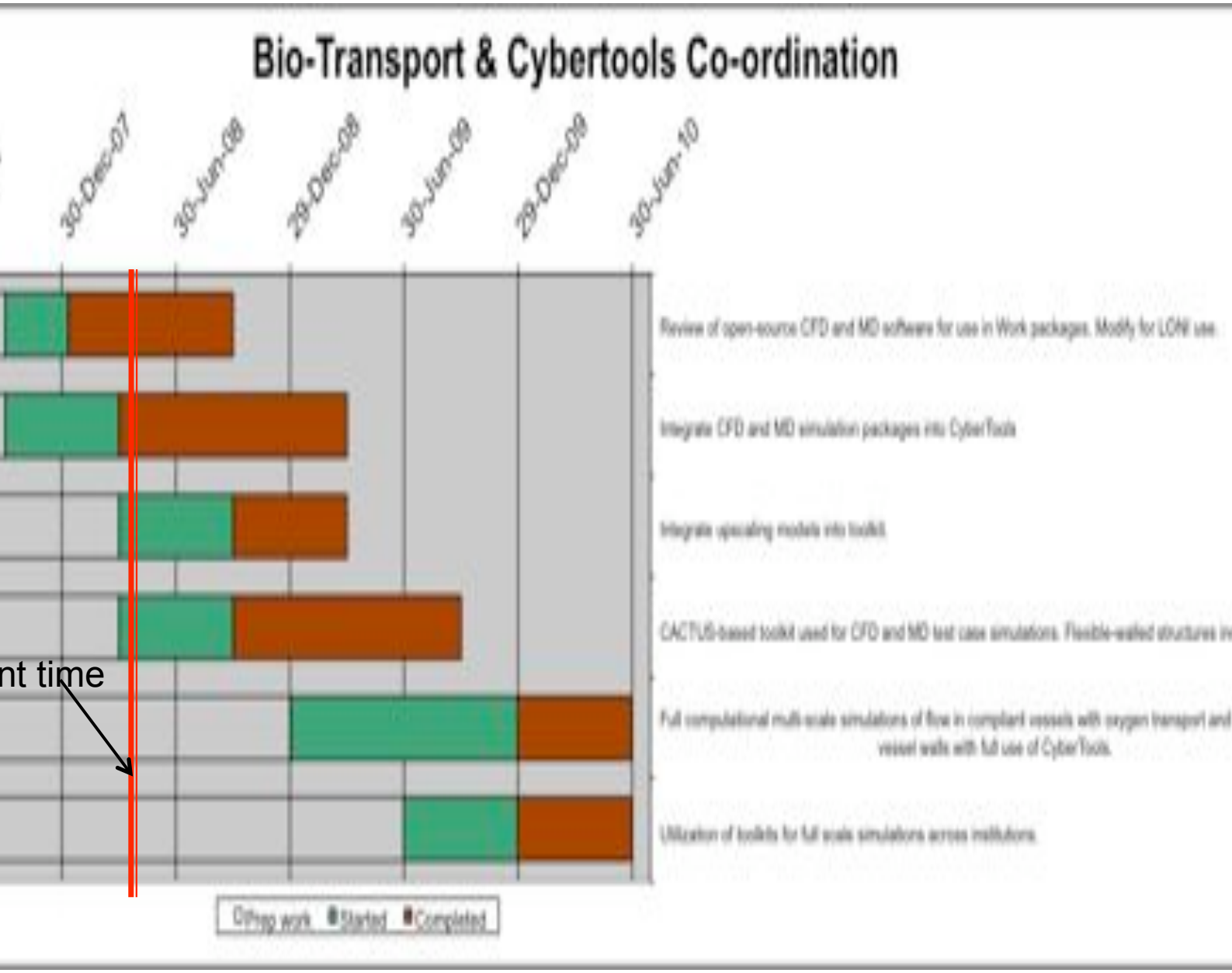
Collaboration with WP4

- ✓ Regular meetings with the WP4 team
- ✓Development of a simplified CFD code with data array structure consistent with Cactus for implementation as part of the CFD Toolkit

CFD-MD Coupling

- ✓Discussion on coupling strategy and approaches


Multi-scale Bio-transport Simulations: Deliverables
30-Dec-07
30-Jun-08
29-Dec-08
30-Jun-09
29-Dec-09
30-Jun-10
Integration of continuum CFD tools (flow-structure, complex geometry, transport etc) for oxygen
in arterial vessels (Acharya@5% effort (0.5 summer months), 1 post doctoral associate (PDA)
graduate student)
MD simulation studies of small molecule/nanoparticle lipid bilayer membrane interactions (Mold
Devireddy @ 5% effort in years 2 and 3, only; 1 graduate student)
Integration of tools and algorithms into CFD and MD toolkits in collaboration with Cybertools (A
Nikitopoulos @5% in yr 2; 1 PDA; 1 graduate student)
nt time
Large scale MD simulations (across LONI resources) of multiple nanoparticles lipid bilayers inte
(Moldovan & Devireddy @ 5% effort in years 2 and 3; 1 graduate student)
Toolkit driven CFD and MD simulations across LONI; application of these tools to understand tr
and across cell/capillary/vessel systems (Acharya @7.5%, Moldovan, Devireddy & Nikitopoulos
year 3, 1 PDA, 2 graduate students)
Prep work
Started
Completed


Bio-Transport & Cybertools Co-ordination
30-Dec-07
30-Jun-08
29-Dec-08
30-Jun-09
29-Dec-09
30-Jun-10
Review of open-source CFD and MD software for use in Work packages. Modify for LONI use.
Integrate CFD and MD simulation packages into CyberTools
Integrate upscaling models into toolkit.
CACTUS-based toolkit used for CFD and MD test case simulations. Flexible-walled structures in
Full computational multi-scale simulations of flow in compliant vessels with oxygen transport and
vessel walls with full use of CyberTools.
Utilization of toolkits for full scale simulations across institutions.
nt time
Started
Completed

Development of improved CFD methodologies for biological systems (complex
ometries, moving boundaries, multi-scale phenomena)

Utilization of CFD and MD methodologies for improved understanding of trans
cesses in biological systems

Supporting the development of Toolkit infrastructure for open source, scalable
community usage

FD-MD integration for resolving/integrating atomistic effects

uture interactions will also include the visualization groups and the portals gro