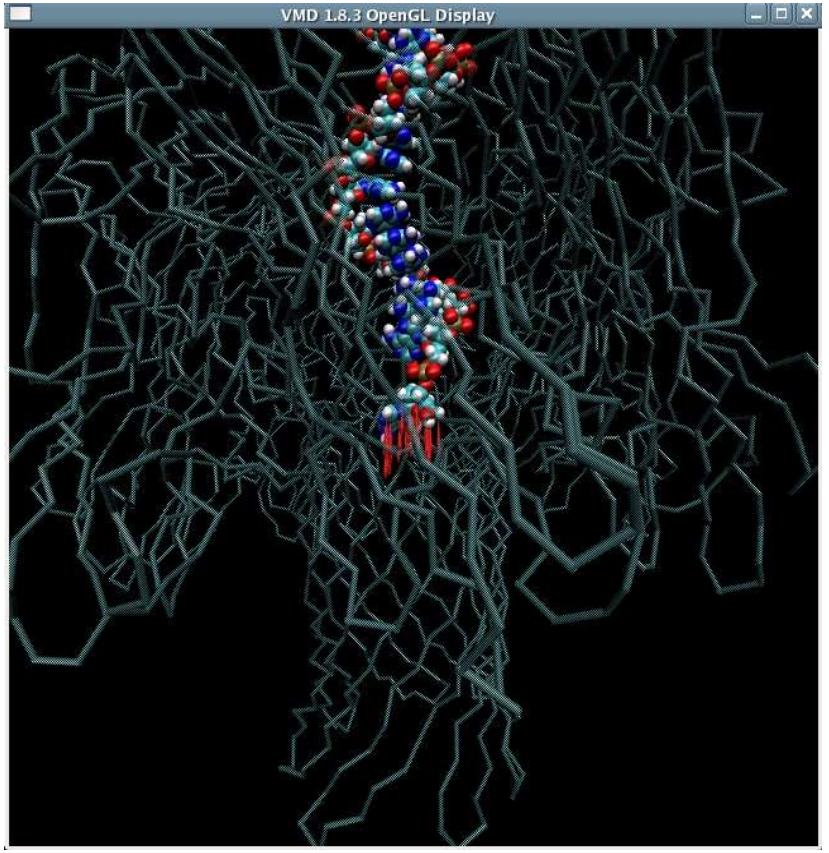
Simulated Pore Interactive Computing Environment: Using grid computing to understand DNA translocation across protein nanopores



RealityGrid

ESLEA
Exploitation of Switched Lightpaths for e-Science Applications

Jha, Harvey, Coveney, Pickles, Pinning, Pezzi & Clarke

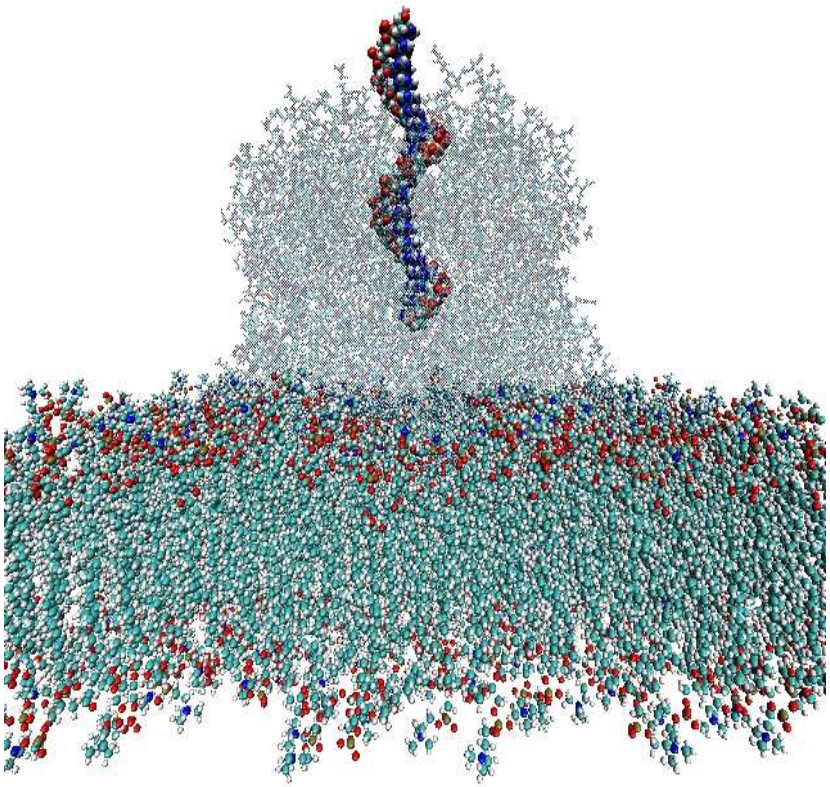
Simulated Pore Interactive Computing Environment

- Transport of biomolecules through protein pores not well understood. Semi-flexible polymer in confined geom.

- Fully atomistic simulations crucial to capture pore-protein interaction. Long timescale (~10s microseconds).

- Size, complexity & timescale make simulations computationally intensive.

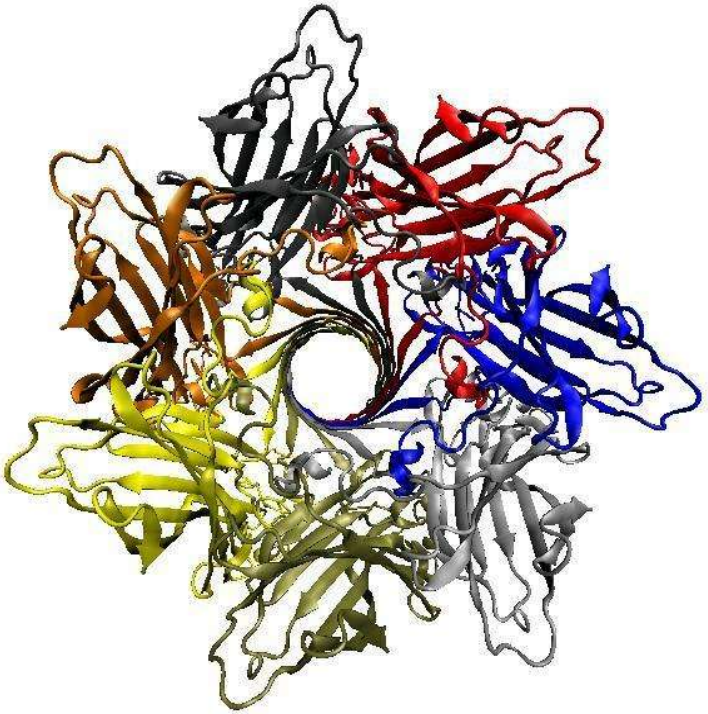
3X10^7 CPU (*tightly-coupled*) hours using “simple” MD. Need to do better...



DNA translocation through an alpha-hemolysin protein pore embedded in a lipid layer. ~275k atoms. Water not shown

SPICE: Grid Computing Using Novel Algorithms (1)

- Novel Algorithm: Steered Molecular Dynamics (SMD) to “pull DNA through the pore”. Jarzynksi's Equation (JE) to compute equilibrium free energy profile from the non-equilibrium pulling.
- Reduce computational cost by 50-100!
- Trivial – in theory, not in practise; Introduces two variable parameters. Determine “optimal” choice of parameters.
- Replace one long sim with multiple (~100) short(er) sims



A view into the pore from the top end. Note the seven fold symmetry of the system.

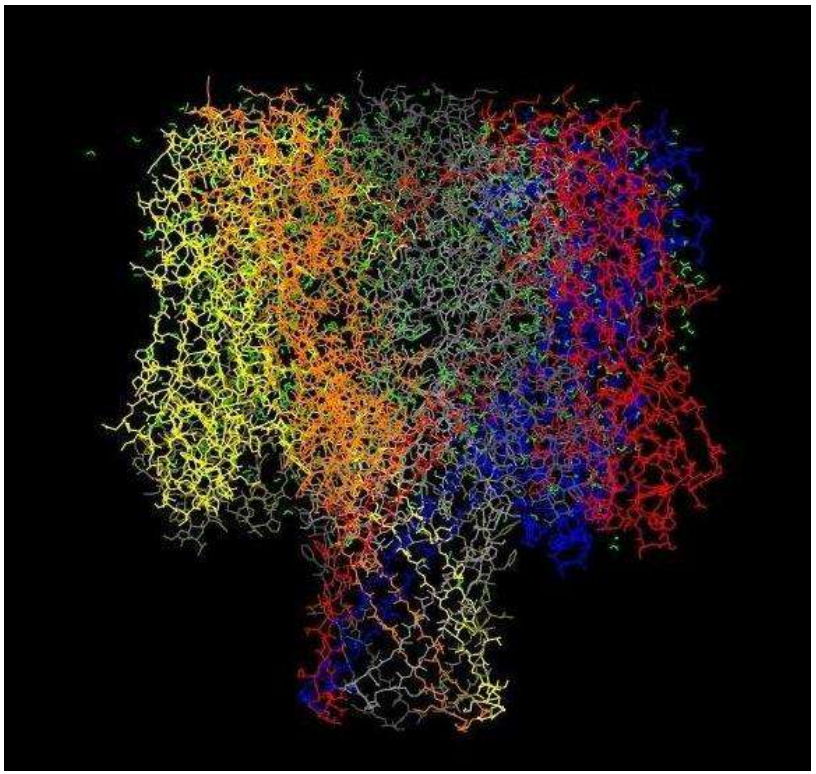
SPICE: Grid Computing Using Novel Algorithms (2)

- Distribute multiple large-scale sims
  Coupling delocalized sim and viz resources

  "Live coupling": Interactive simulations -- use viz to steer sim.

  Not just parameters...

- Grid facilitates greater resource utilization, novel analysis & uniform interface making ~100 simulations more manageable



Transform comp intractable problem using SMD+JE
Not just exploits grid infrastructure, but requires it...

SPICE: Computing the Free Energy Profile (FEP)

Step I: Understand structural features using static visualization

Step II: Interactive simulations for dynamic and energetic features
- Steered simulations: bidirectional communication.
  Qualitative + Quantitative (SMD+JE)
- Haptic interaction: Use haptic to feel feedback forces

Step III: Simulations to compute "optimal" parameters values
75 simulations on 128/256 processors each.

Step IV: Use computed "optimal" values to calculate full FEP along the cylindrical axis of the pore.

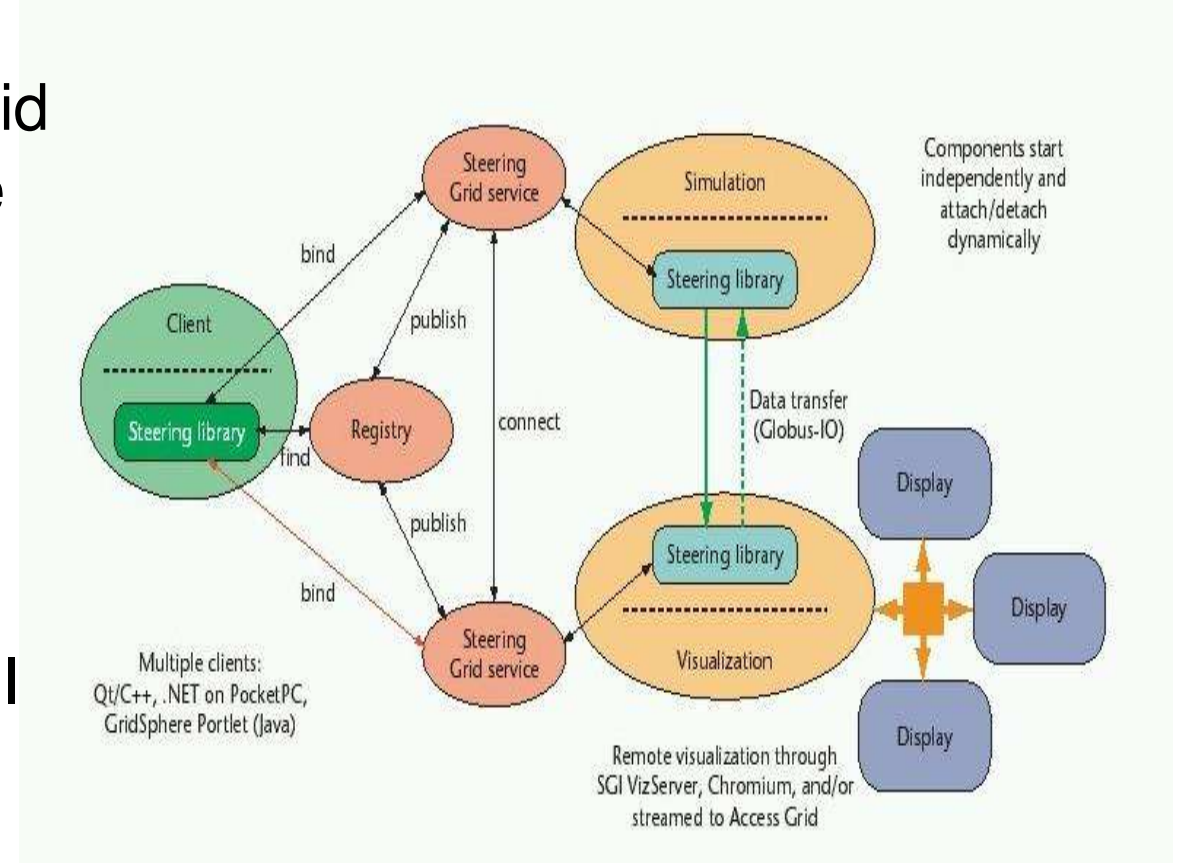
Requires ~250,000 CPU hours (100 simulations of 2500 CPU hours)!

SPICE: Grid Infrastructure (1)

RealityGrid Steering Infrastructure + NAMD (parallel MD engine)

App interfaces grid infrastructure through the ReG steering library

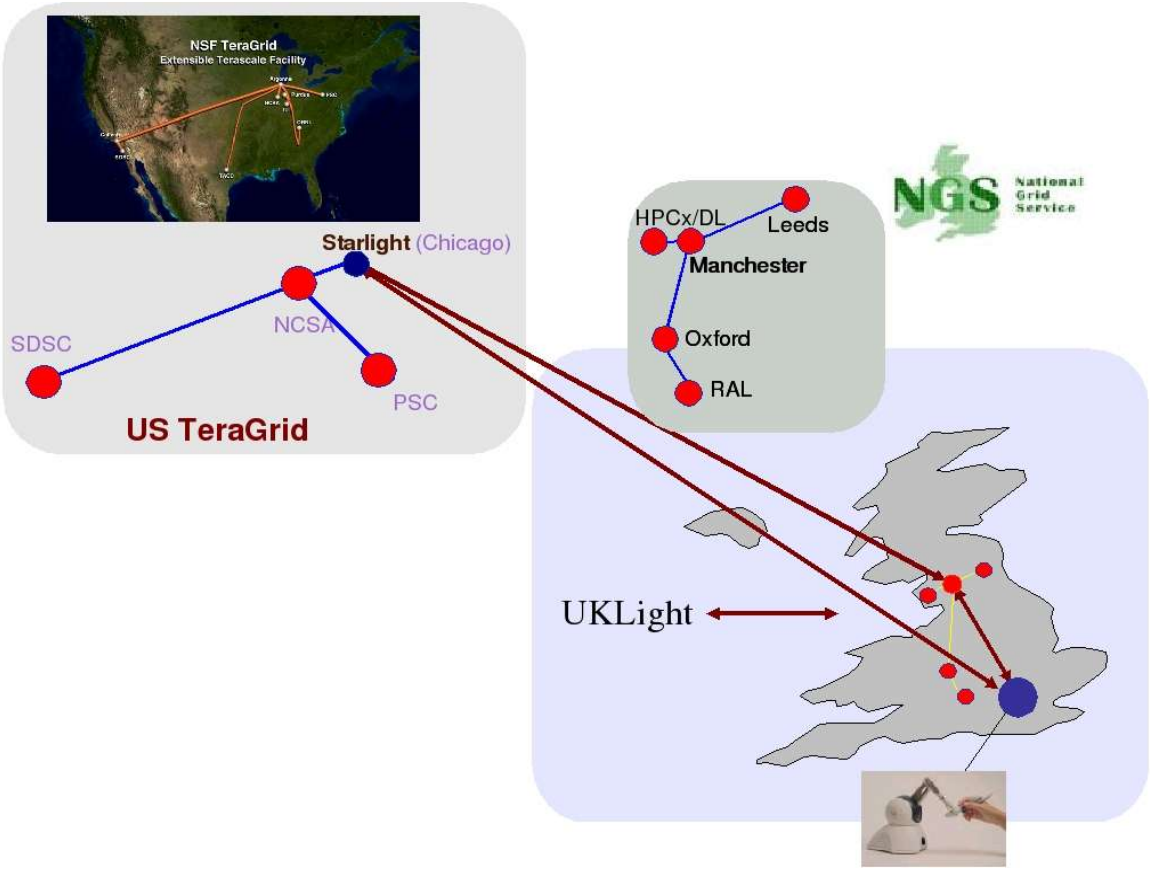
ReG Steering API:
-- launcher, steerer use server side API
-- App uses client side API



(WSRF::Lite based infrastructure for launching, steering, comm and notification soon)

SPICE: Grid Infrastructure (2)

Simulation: (II, III, IV)
NGS + TeraGrid
Visualization: (I,II)
Prism (UCL)
Sim–Viz connection:
UKLight/GLIF



Batch simulations post optimal parameter. N*ot batch sim to explore phase space*

Resources more *R-U-M* since TeraGyroid...
Middleware better? Or our trouble-shooting?

SPICE -- UKLight

+ Interactive simulations

  Qualitative (general) + Quantitative (specific)

  Require 128/256px of HPC to compute fast enough for interactivity

  Steady-state data stream (up & down) -- few MB/sec

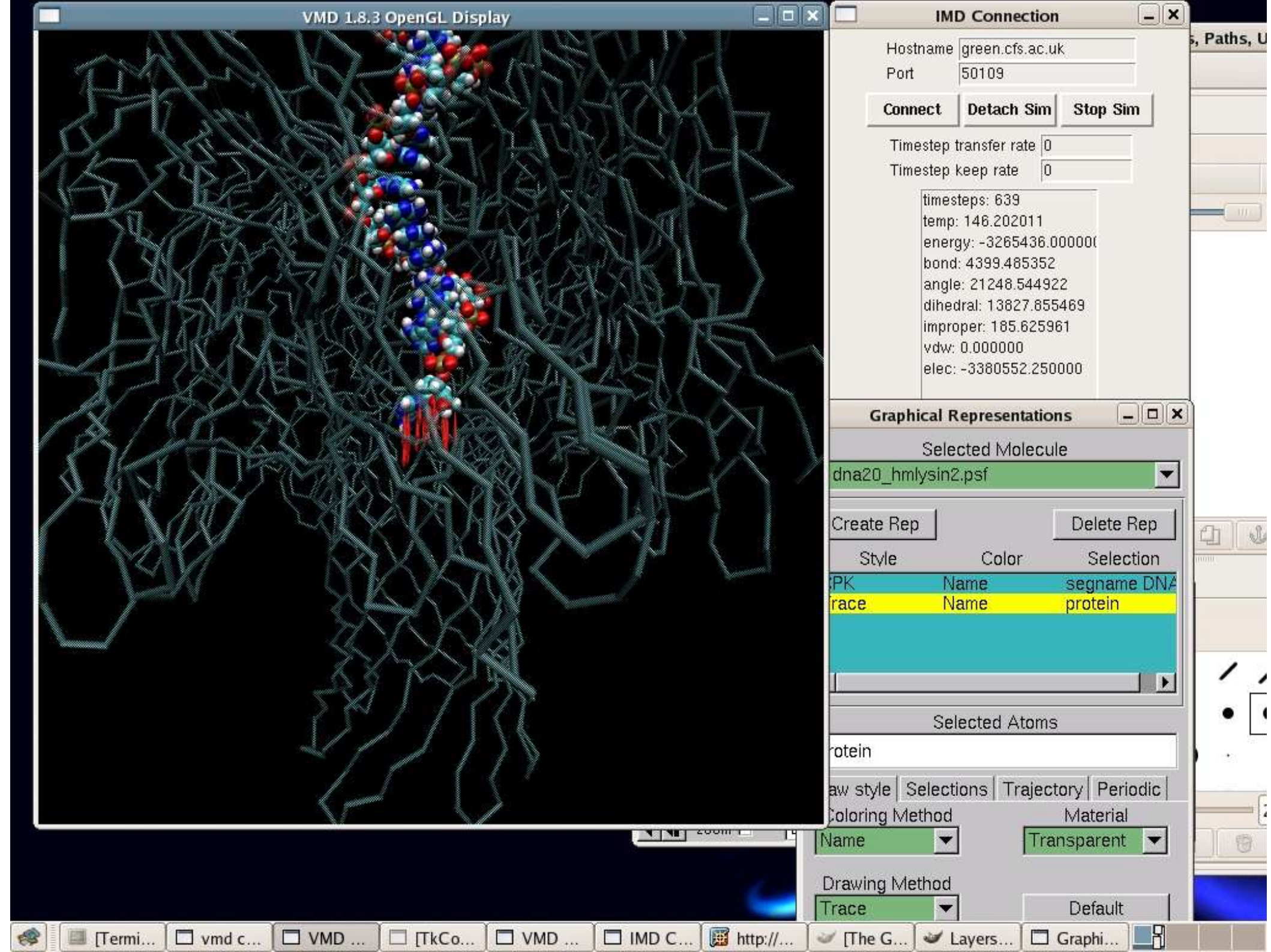
  Simple? "Unreliable" sim-vis commn simulation slowdown.?

  Interactive simulations perform better when using UKLight for communication between simulation and visualization!

  Advanced networks provide high QoS in terms of *packet loss, jitter* and *latency*.

  e.g ~20 vs 5 intermediate routers en route to NCSA from UCL-Prism

+ Total data generated in TeraBytes; replicated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Thoughts...

- Getting infrastructure to work needs to be made easier (e.g. dual homing of systems -- adminstrative nightmare)
- Develop better theoretical underpinnings:
  Experiments to understand effect of network (latency, jitter) & RTT with simulation configuration (px's, IMD frequency)
- Testing protocols for low latency?
- User interaction with CPS? (e.g. dynamic app driven reservation of lightpaths)
  Co-scheduling with other resources? Via ReG API?
  GLIF - Global Plane & Grid Integration Middleware WG

SPICE @ AHM05

- Tue 13:00 - 14:00 UCL
- Wed 09:00 - 13:00 EPSRC
- Wed 14:30 - 15:00 ESNW
- Thu 12:00 - 15:00 EPSRC

SPICE a finalist at the SC05 HPC Analytics Challenge
(also at SC Global and numerous booths at SC05)

http://www.realitygrid.org/SPICE