Course Introduction

CCP-SAS 2015

Atomistic Modeling for Small Angle Scattering: A Short Course

May 26-28, 2015

Institut Laue-Langevin, France

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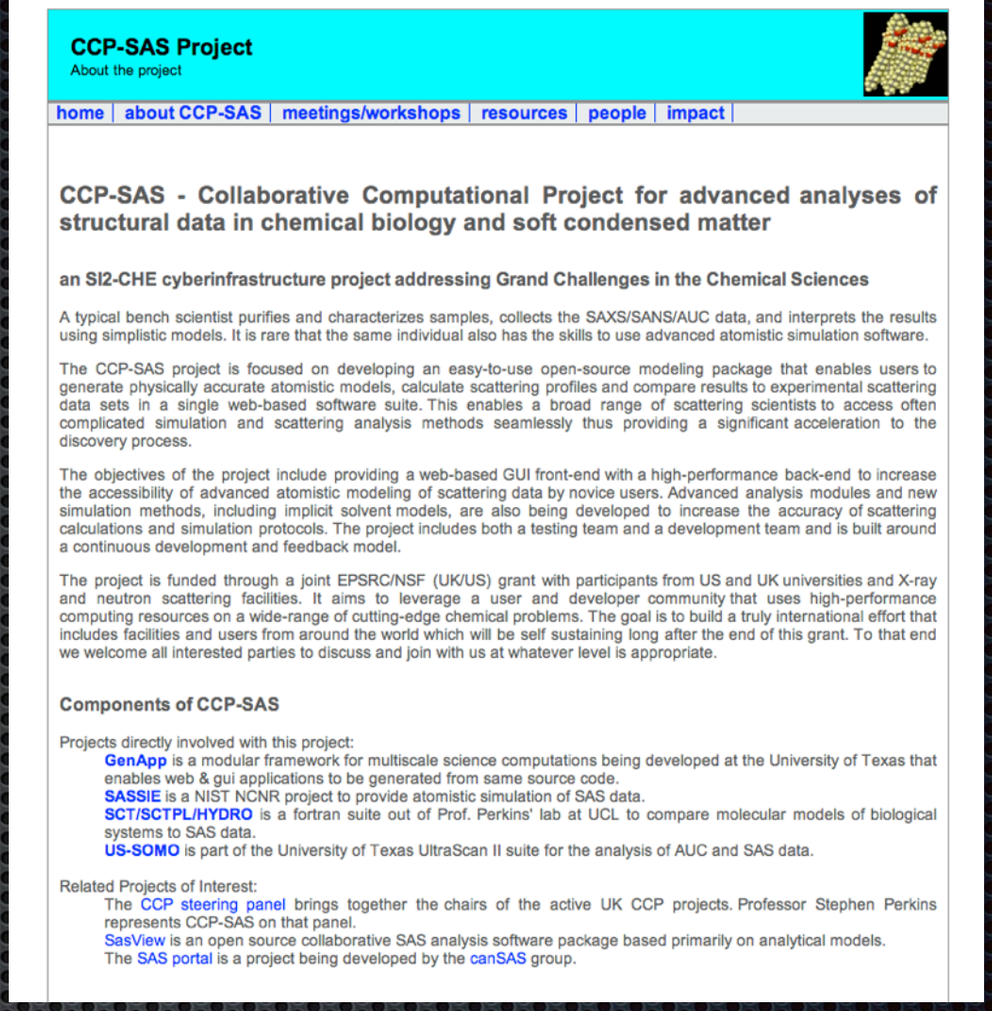
ccpsas.org

Scatters & Simulators

Develop a community of users and developers to advance atomistic modeling of soft-condensed matter

Open Source



lower barriers

diamond

Science & Technology Facilities Council ISIS

Argonne NATIONAL LABORATORY

NCNR

EPSRC Engineering and Physical Sciences Research Council

UCL

NIST National Institute of Standards and Technology Technology Administration, U.S. Department of Commerce

SCHOOL OF MEDICINE UT HEALTH SCIENCE CENTER DEPARTMENT OF BIOCHEMISTRY

THE UNIVERSITY OF TENNESSEE KNOXVILLE

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Goals

PRACTICAL introduction to atomistic methods to model biological systems

with respect to X-ray & neutron scattering

STRUCTURE

SAXS/SANS

NR

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Course Outline

Tuesday 5/26/2015

Time	Lead	Activity	File
9:00 - 9:15 AM	JEC	Course Introduction	lecture_0.pdf
9:15 - 10:30 AM	JEC	Lecture 1: Coordinates to Structure	lecture_1.pdf
10:30 - 10:45 AM		**Break**	
10:45 - Noon	DWW/JEC/EHB	Lab 0: Software Installation & SASSIE-web	lab_0.pdf
Noon - 1:00 PM		**Lunch**	
1:00 - 2:45 PM	DWW/HZ/EHB	Lab 1: VMD and PDB Scan	lab_I.pdf
2:45 - 3:00 PM		**Break**	
3:00 - 5:00 PM	DWW/HZ/EHB	Lab 2: PSFGEN/NAMD	lab_II.pdf

Mixture of “Lectures” and hands-on “Lab” exercises

Student Projects or Advanced “Labs”

~10:30 AM & ~2:45 PM : Break

Noon: Lunch

WED @ 1 PM: Group Photo

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Course Outline

Tuesday -- Build Structures & Run MD

Wednesday -- Build Systems & Run MC, Calc. SAS

Thursday -- Advanced MD/MC & Student Projects

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“Student Projects”

Who?

Where?

Project(s)?

Expectations?

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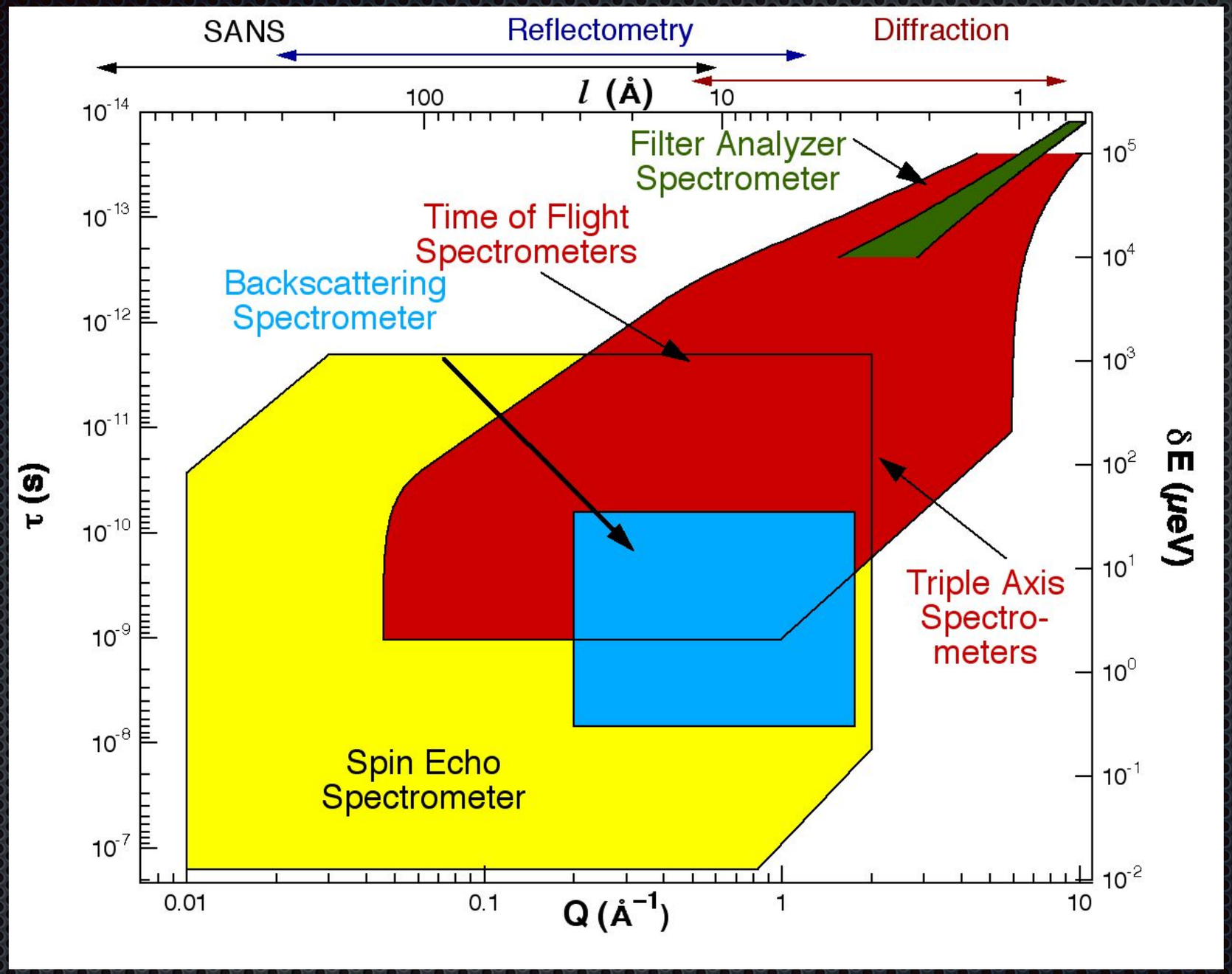
Time & Space @ NCNR



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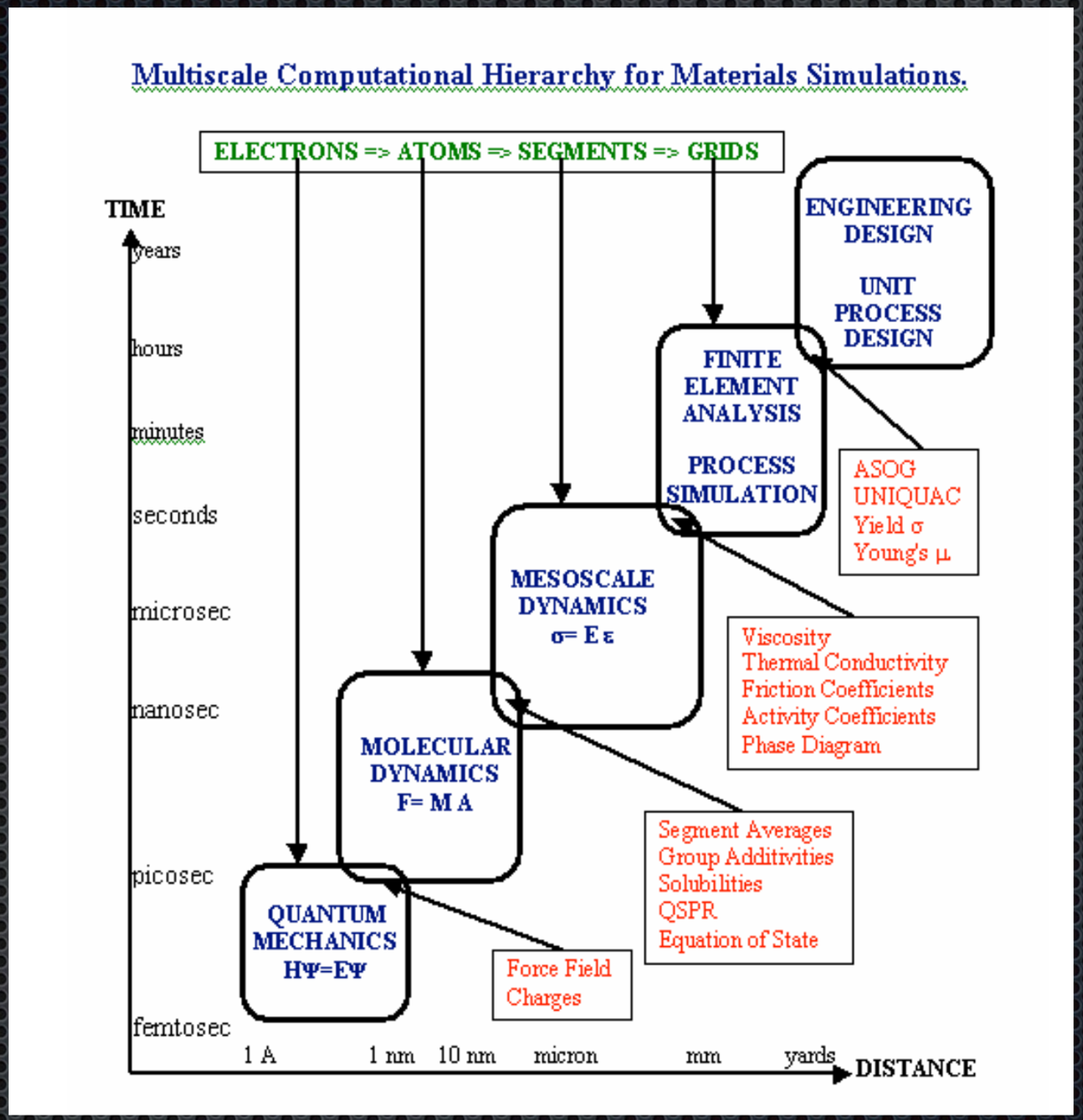
Size, Motions, & Theory



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Size, Motions, & Theory

Time scales and amplitudes of protein motions

Presently accessible

Type of Motion	Timescale (s)	Amplitude (Å)	Functionality
Local: • Atomic fluctuations • Side chain motions	$10^{-15} – 10^{-12}$	< 1	• Ligand docking flexibility • Ligand diffusion pathways
Medium scale: • Loop motion • Rigid body motion (e.g. helices)	$10^{-9} – 10^{-6}$	1 – 5	• Active site conformation adaptation • Binding specificity
Large scale: • Domain motion • Subunit motion	$10^{-6} – 10^{-3}$	5 – 10	• Hinge bending motion • Allosteric transitions
Global: • Helix-coil transition • Folding/unfolding • Subunit association	$10^{-3} – 10^{4}$	> 5	• Hormone activation • Protein functionality

Neutron spectroscopy is unique because it enables the simultaneous measurement of both the time and length scale dependence of dynamics

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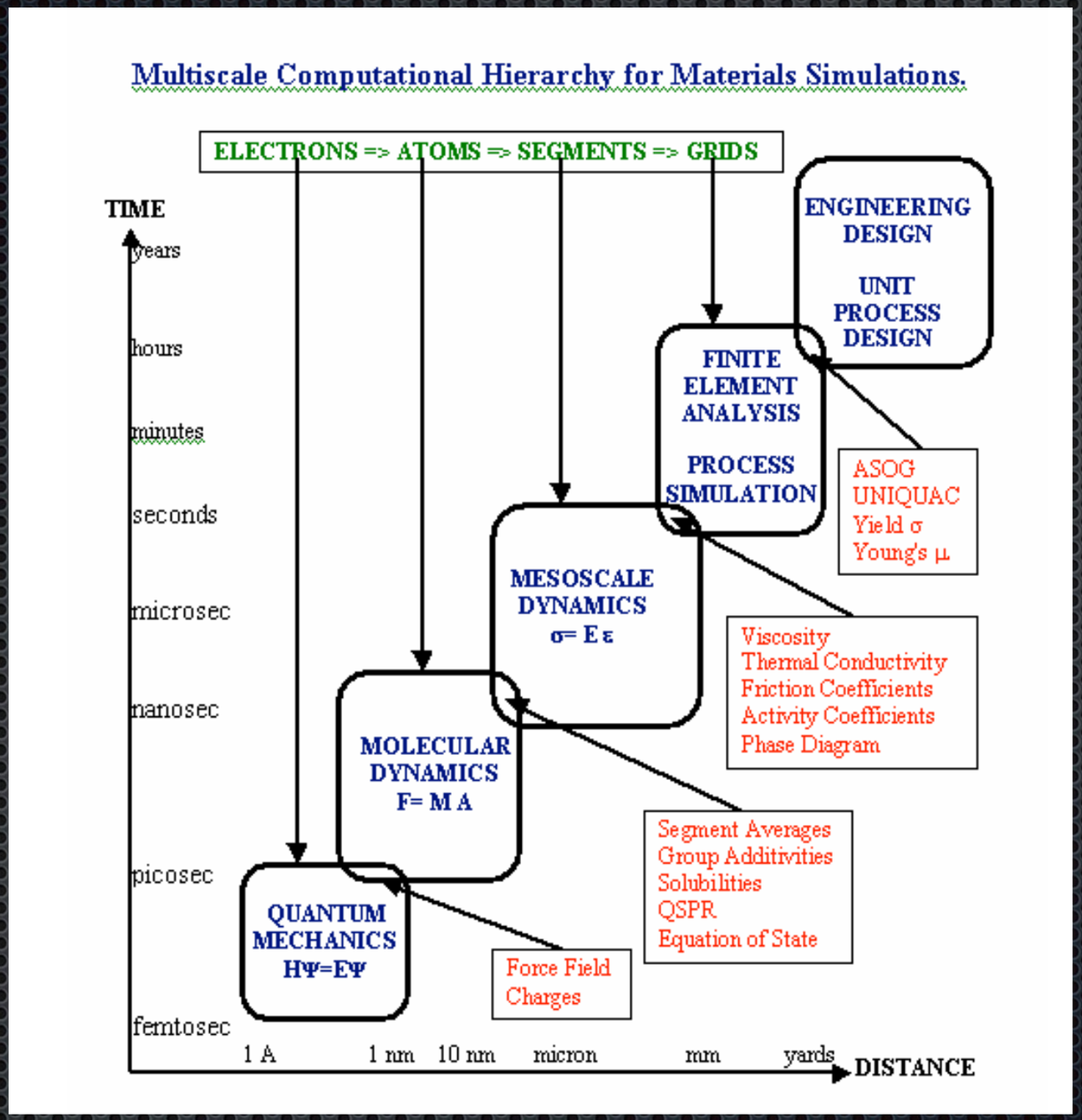
Size, Motions, & Theory



Goddard: Materials and Process Simulation Center (MSC)

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Typical systems

~19.2 atoms / AA
~136-18 ~ 118 Da / AA
~30 A**3 / water

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Typical systems

protein: 1745 atoms

protein in solution: 8417 atoms

protein powder:

polycrystalline: 2 proteins

+ 817 waters = 6171 atoms

protein in carbohydrate glass:

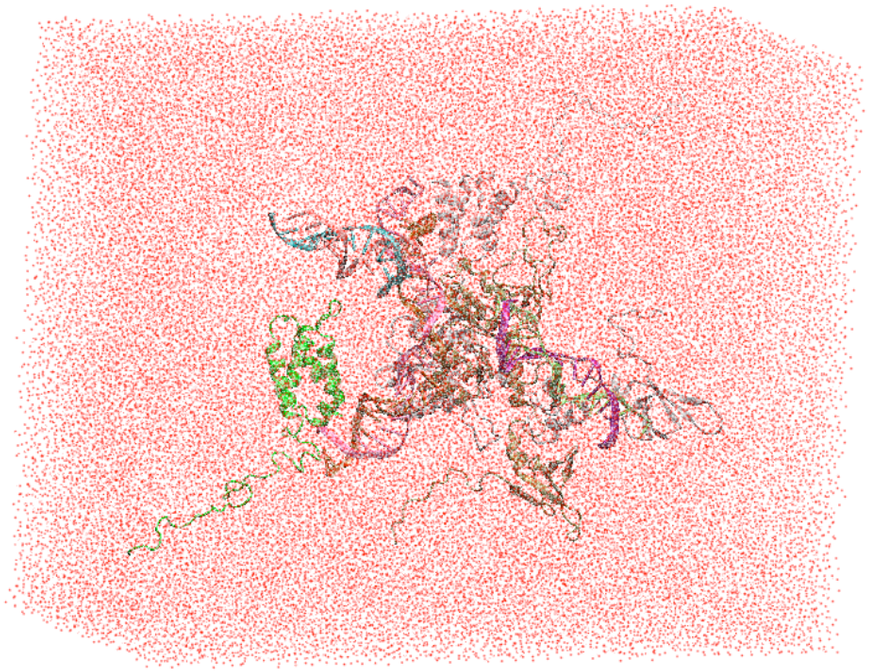
~30,068 atoms

protein/dna complex:

25874 atoms

protein/dna complex in solution:

397028 atoms



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Typical systems

~19.2 atoms / AA
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~30 A**3 / water

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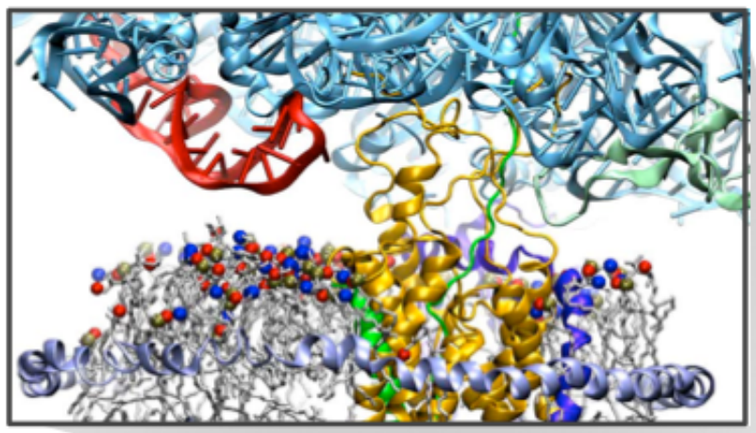
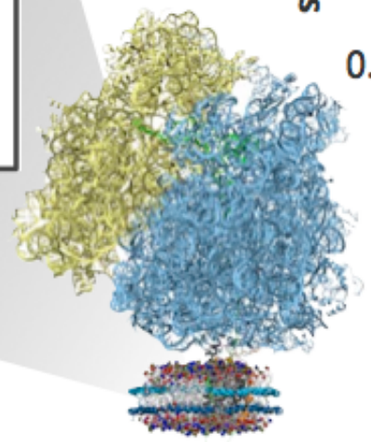
Pushing the limit

2006: STMV (NAMD) 10^6 atoms, 50 ns: “desktop ~ 35 years”, 48 2.4 GHz CPUs, 0.7 ns / day : Structure **14**, 437-449 (2006).

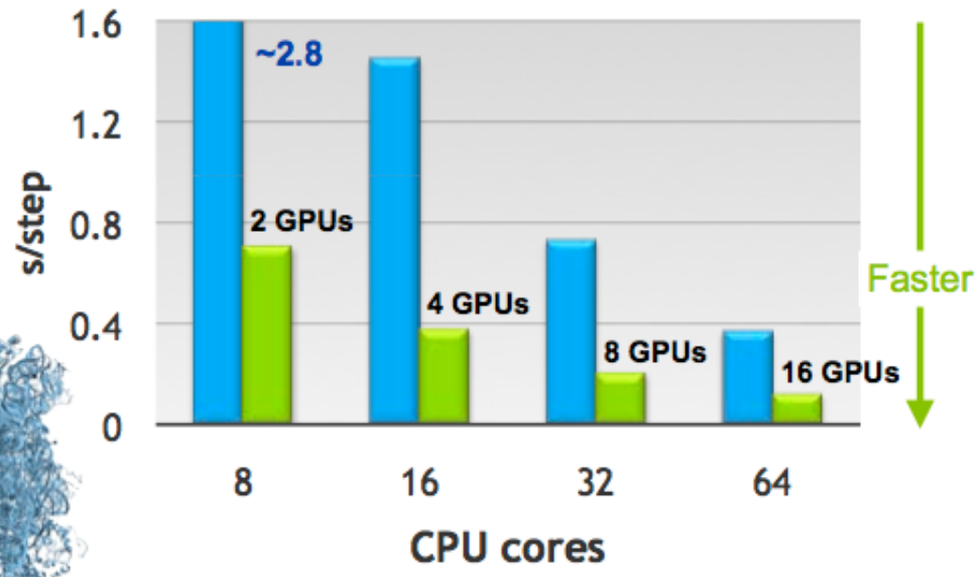
2006: Villin headpeace 2^4 atoms, 500 us: 2^5 CPUs via Folding @ Home: JCP **124**, 164902 (2006). . . . 10,000 trajectories (26 AA + ~5000 waters) . . .

2011: GPUs “Electrostatics only” calculations: 25-fold faster
MD simulations: 10^6 atoms ~ 4-fold faster . . . up to ~ 3 ns / day





Molecular dynamics simulation of protein insertion process



NCSA Lincoln Cluster performance
(8 Intel cores and 2 NVIDIA Tesla GPUs per node, 1 million atoms)

GPUs reduced time for simulation from **two months to two weeks!**

Klaus Schulten's **Keynote Lecture** from the 2010 GPU Technology Conference

Barriers: BUILD; EQUILIBRATE; PROPAGATE; ANALYZE

What software package(s) and force-fields do I use?

Starting structure?

How do I clean up the structure?

How do I set up a trajectory (time or space)?

How do I calculate scattering observables correctly?

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So many options . . .

Bio-simulation (All-atom MD packages):

Amber*
CHARMM*
NAMD*
GROMACS*
GROMOS
LAMPPS*
PINYMD*
HIPPO
GPIUTMD
DL_POLY*
ESPResSo
MacroModel*
MACSIMUS
MOLDY
MOSCITO
ProtoMol
TINKER*
MDGrape
Materials Studio (InsightII)*
. . .

Classical force fields:

Amber*
CHARMM*
CVFF
COSMOS-NMR
GROMACS*
GROMOS
OPLS*
ENZMIX
ECEPP/2
QCFF/PI
UFF
CFF*
MMFF
MM2, MM3, MM4*
XPOL
SIBFA
AMOEBA
VALBOND
DRF90
CG MD*
. . .

Methods & details*:

Thermostats
Barostats
Electrostatics (PBC)
Polarizability
Implicit Solvent
Langevin Dynamics
Replica Exchange
Parallel Tempering
Steered MD
Free-Energy Calculations
Umbrella Sampling
Normal Mode Analysis
VMD
Pymol
Chimera, O
APBS
Gaussian, Gamess, CPMD
Beowulf, GPU Clusters
Rosetta
PHYRE
Folding @ Home
TIP3, TIP3P, TIP4P, SPC, ST2
. . .

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Let's narrow the options

VMD →	www.ks.uiuc.edu/Research/vmd/
NAMD →	www.ks.uiuc.edu/Research/namd/
CHARMM (MD/MC) →	www.charmm.org/
CHARMM (FF) →	mackerell.umaryland.edu/CHARMM_ff_params.html
CGMD (Marrink) →	www.ks.uiuc.edu/Research/vmd/plugins/cgtools/
MMC (CHARMM & SASSIE) →	www.smallangles.net/sassie/SASSIE/SASSIE_HOME.html
SASSIE-web →	sassie-web.chem.utk.edu/sassie2
COURSE DOCS & FILES →	sassie-web.chem.utk.edu/trainining/ccp-sas_2105

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“Student Interests”

“Other MD project interests”:

--> the basics covered here:

topology, parameters --> FF (outline & dev.)
input files for MD runs
T & P control, MTS, NNL, PME, PBC
Analysis of runs (EQ, MTO)

. . . are transferrable

Let’s chat on Tues. & Wed. about setting up your systems as well.

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If you wouldn't mind . . .
. . . BIO/STRUCTURE course . . .

Let's not argue about

force-field 1 -vs- force-field 2
water model 1 -vs- water model 2
NAMD -vs- CHARMM -vs- AMBER -vs- ???
classical MD -vs- ab-initio MD
single-chain Nose-Hoover -vs- Nose-Hoover chains
phase space coverage (MD or MC)

etc.

although, you are free to "chat" about your feelings and questions during labs, breaks . . .

"HOW TO" . . .
Start you on the path

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Details ... there are a lot of them coming!

At our shoulder in our group . . .

You will go through many of the same problems described in the lectures (and others) in the lab sessions.

WEB: lectures/labs/worked_examples, etc.

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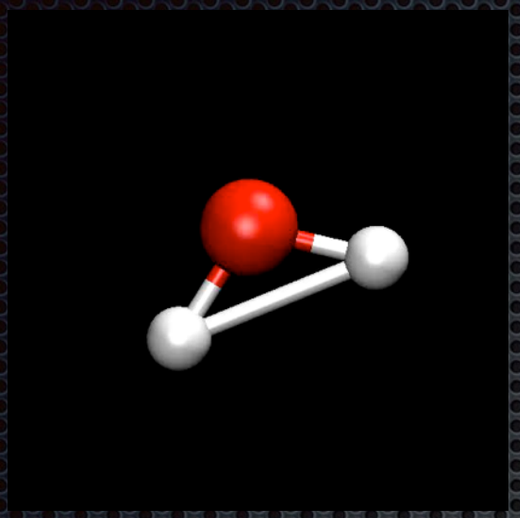
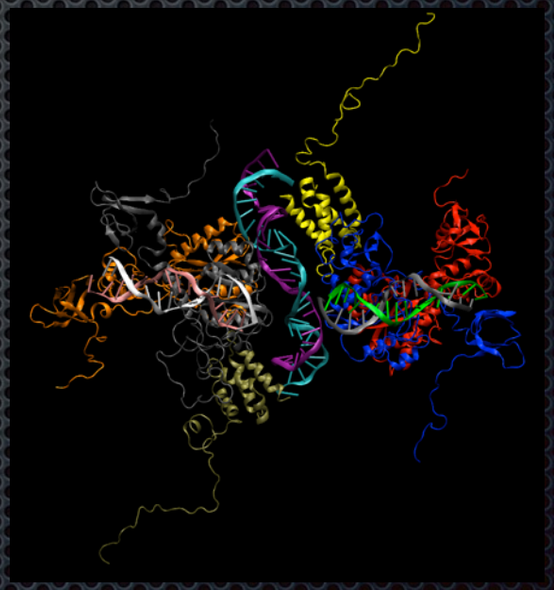
Tuesday

Introduction & background

Oxygen atom to protein-dna complex in 9 slides





minimize structures in vacuo

The building scripts you will input are generic and can be expanded to any system (FF)

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Wednesday

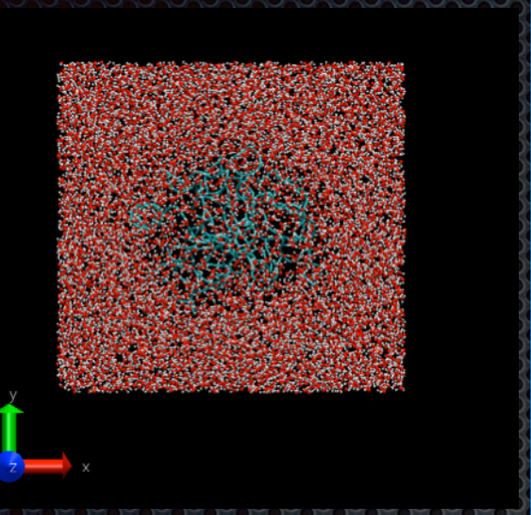
Solvate, PBC, relax, & NVT/NPT dynamics runs

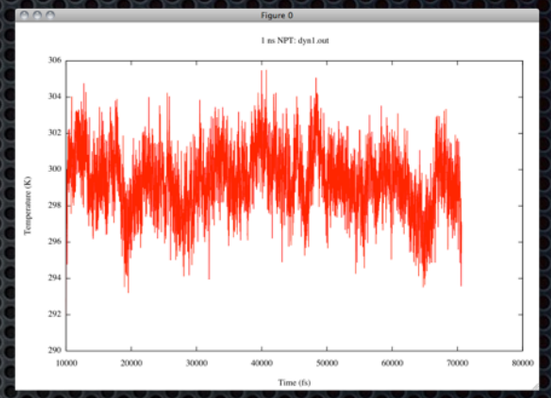
Analyze (check) runs for EQ & analyze trajectory

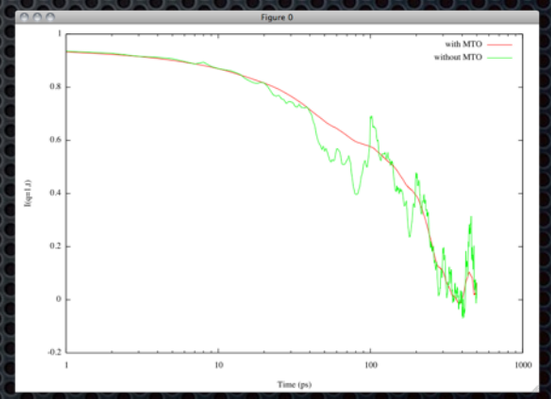
MMC via SASSIE-web

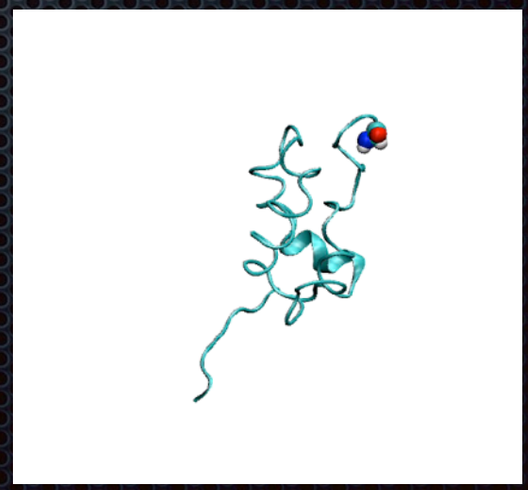
Calculate SAXS/SANS

Analyze Results









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Thursday

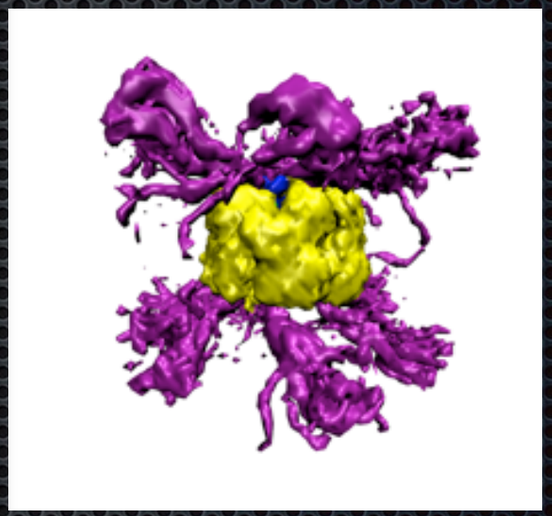
MMC of IDP/ID-NA: Complexes

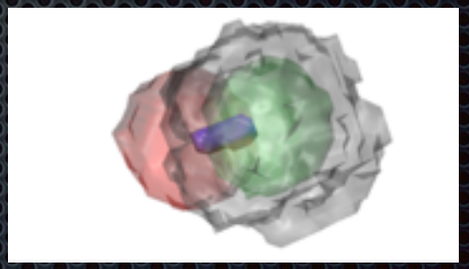
Calculate SAXS/SANS

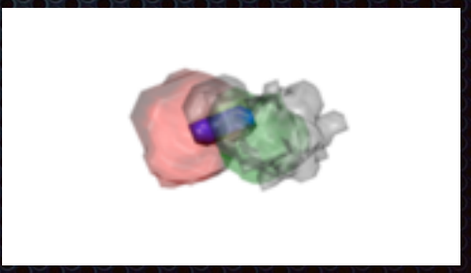
Analyze Results

Advanced Tricks

Student Projects







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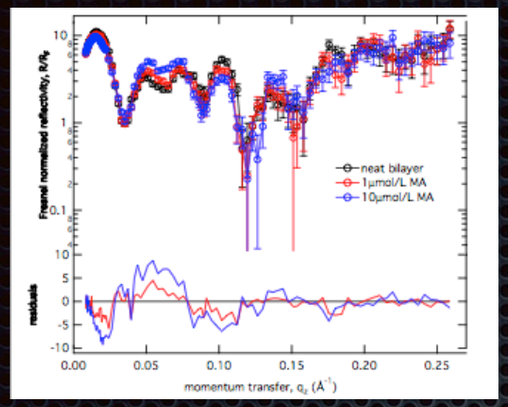
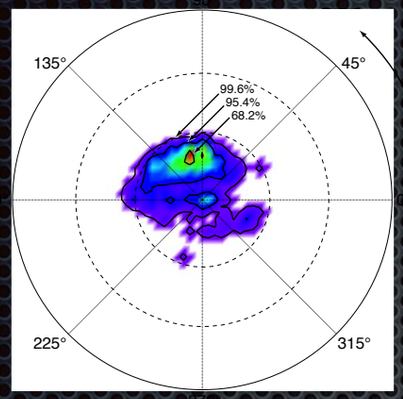
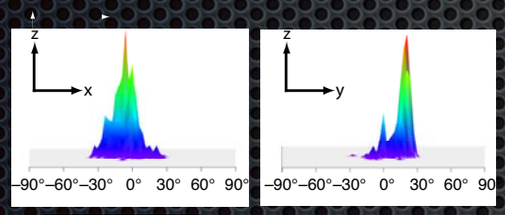
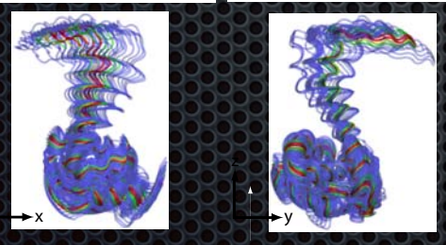






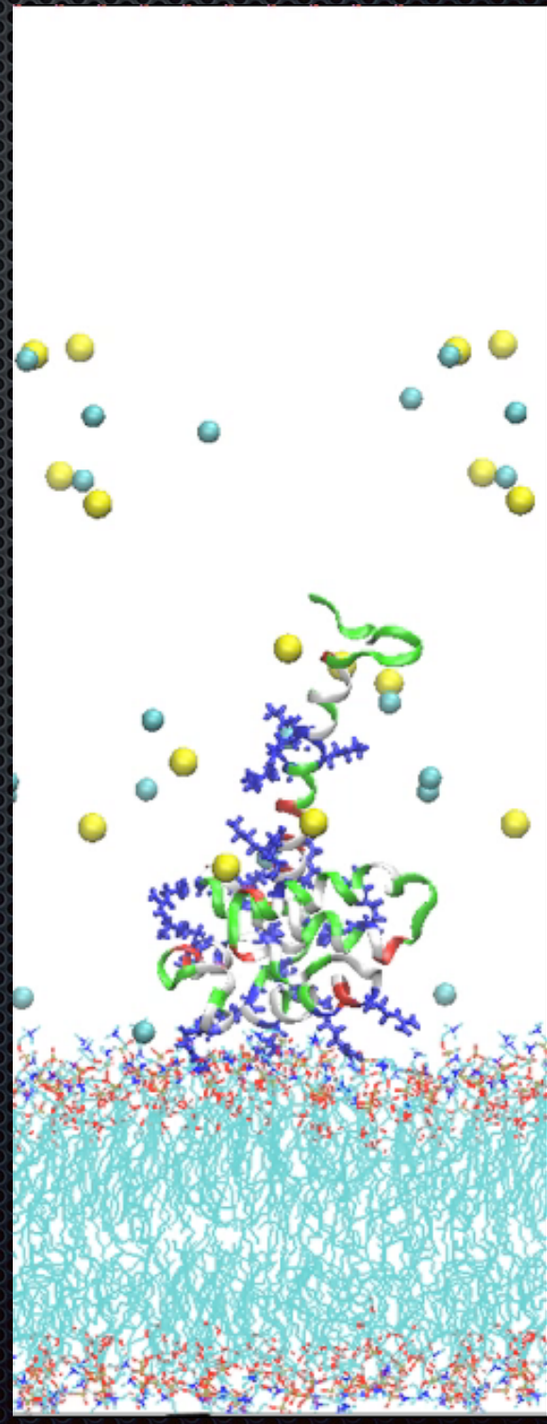


Summary

Steps are Transferrable to almost all MD/MC “Engines”

Complete Structure, Modern FF, Representative Equilibrium

Sample & Converge Observable(s)



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Today: “Build Structures & Run”

9:30 AM - 10:30 AM: Coordinates to Structure

~10:30 AM - 10:45 AM: Break

10:45 AM - Noon: Lab 0: Software Installation & SASSIE-web

Noon - 1:00 PM: LUNCH

1:00 PM - 2:45 PM: LAB I: VMD and PDB Scan

2:45 - 3:00 PM: Break

3:00 - 5:00 PM: LAB II: PSFGEN / NAMD

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