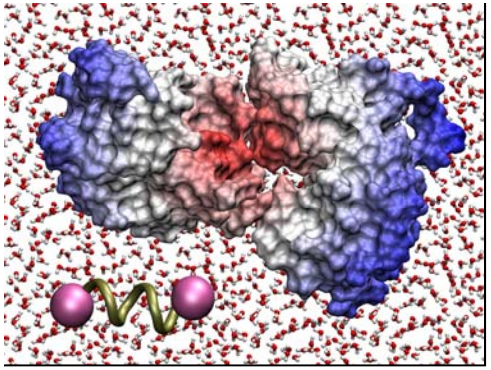
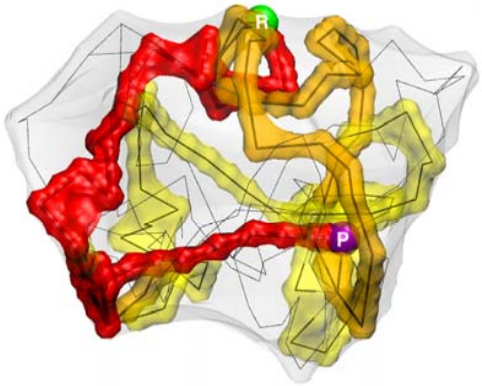


Center for Molecular Biophysics

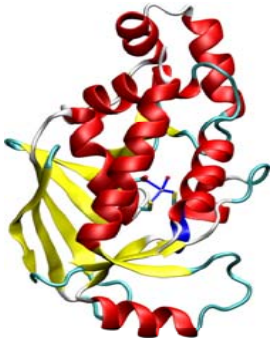
ORNL

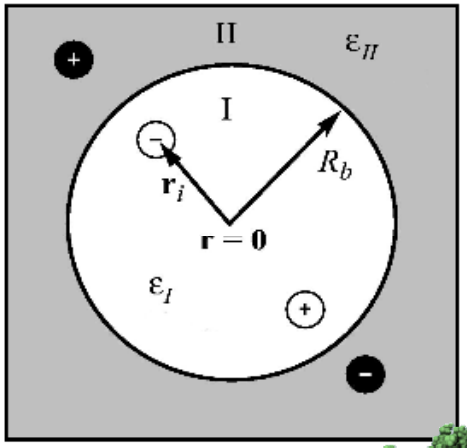
Oak Ridge National Laboratory

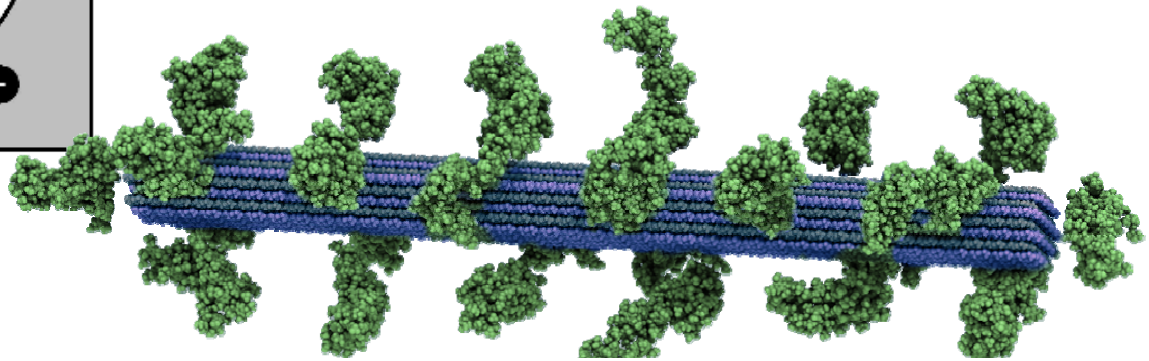


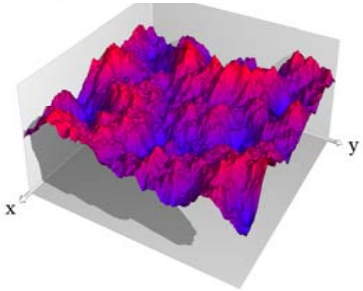
Molecular Simulation in the Energy Biosciences

Jeremy C. Smith



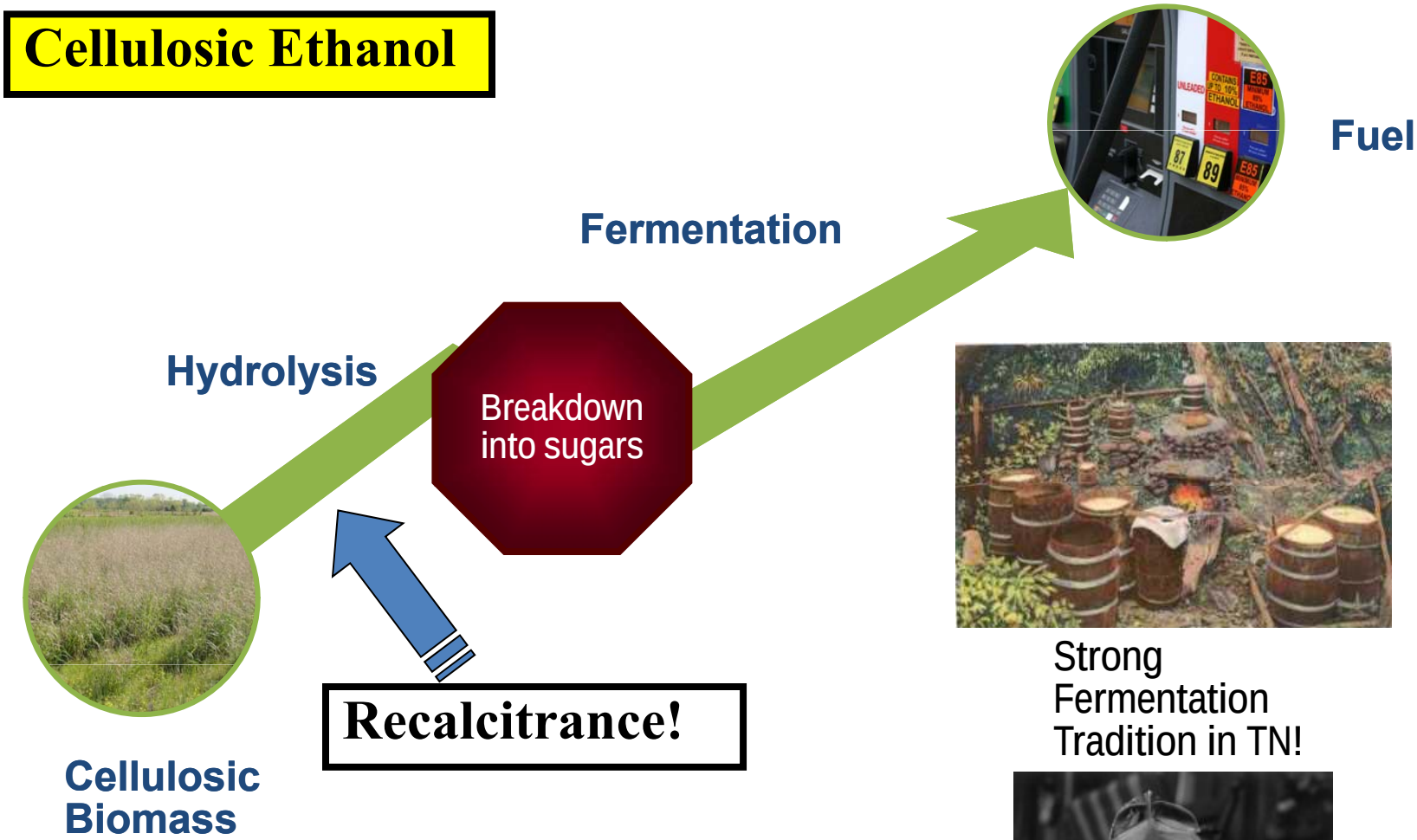




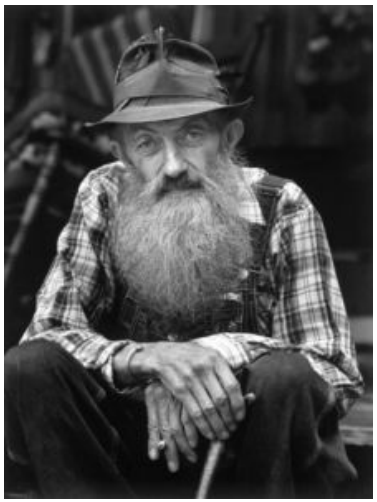


- **Cellulosic Ethanol**
- **Mercury Bioremediation**
- **Molecular Machines**

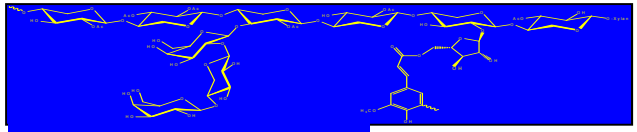
Cellulosic Ethanol



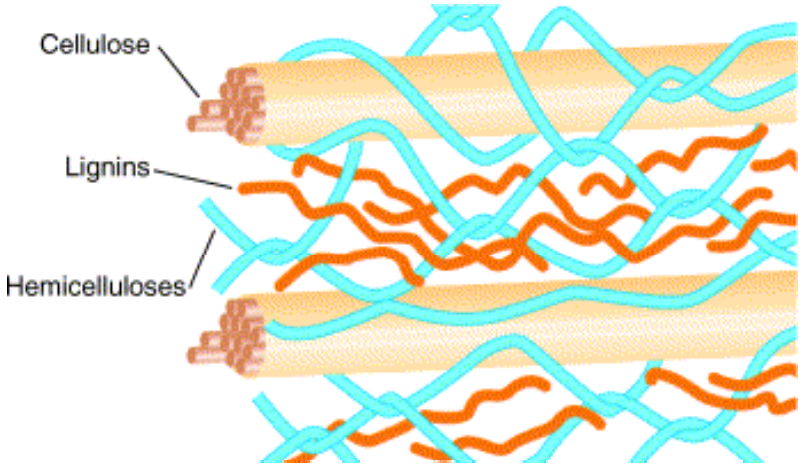
Strong Fermentation Tradition in TN!

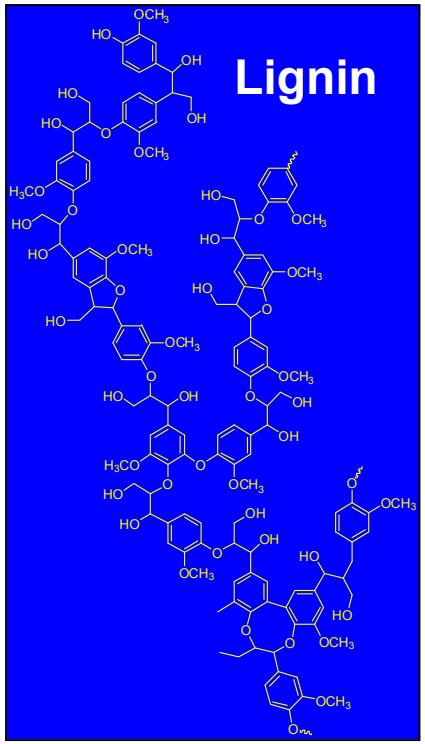


Lignocellulosic Biomass Exhibits Structural Complexity



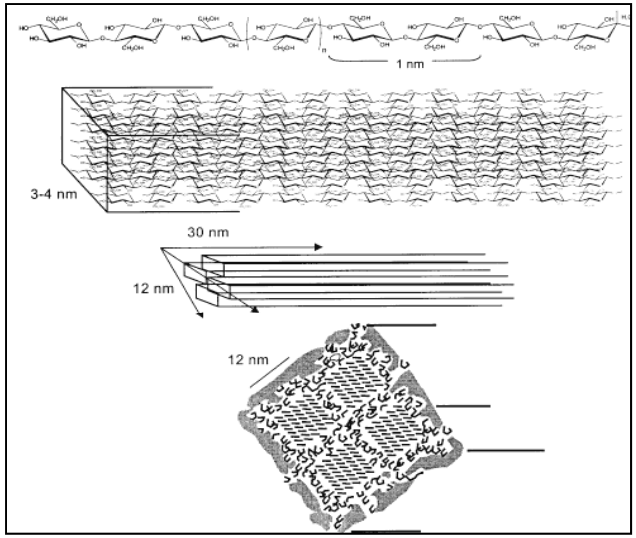
Hemicellulose





Lignin

Cellulose

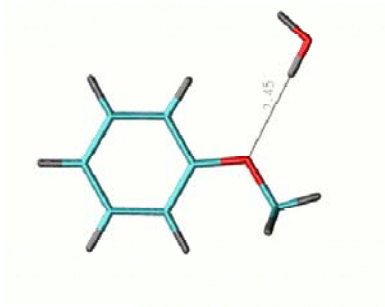


Simulation Model of Lignocellulose

1 nm

length-scale

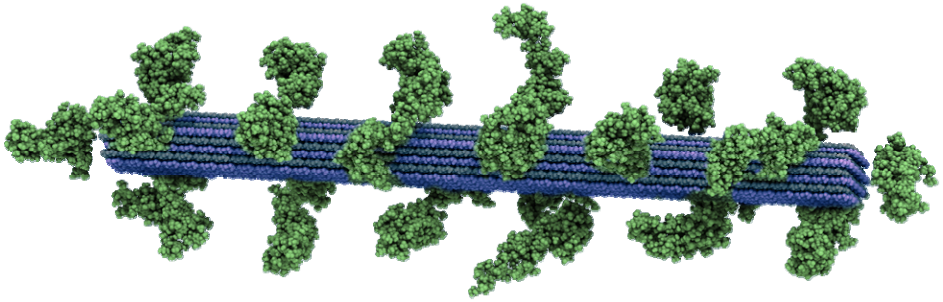
~1Å
atomic-level



~10Å
molecular-level

~100Å

supramolecular

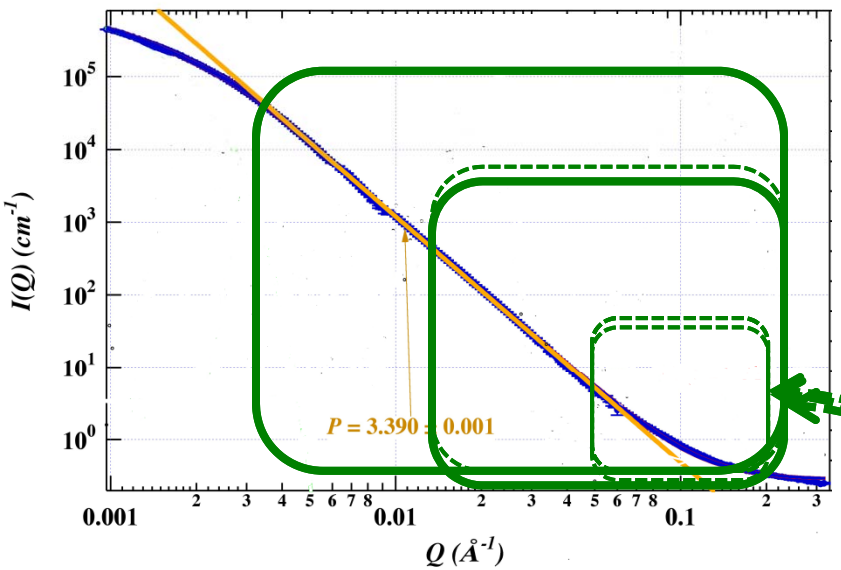


1 μm

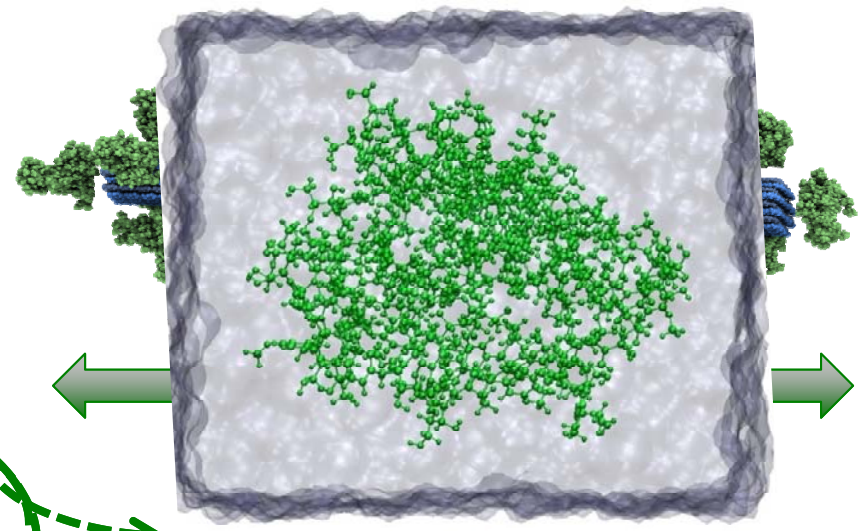
~1000Å
coarse-grained

Length-Scale Correspondence: Simulation and Experiment

Small-Angle Neutron Scattering



Simulation



100 Å / ~500k atoms

10 Å / ~50k atoms

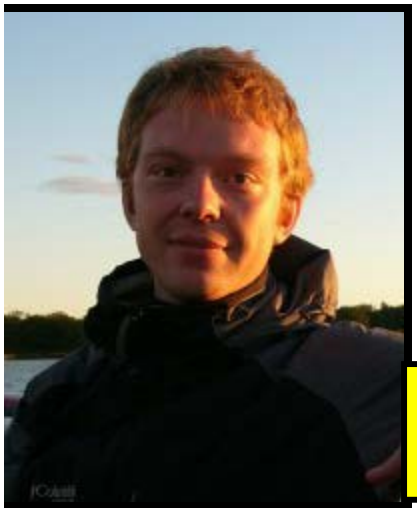
INCITE XT4

NSF Teragrid

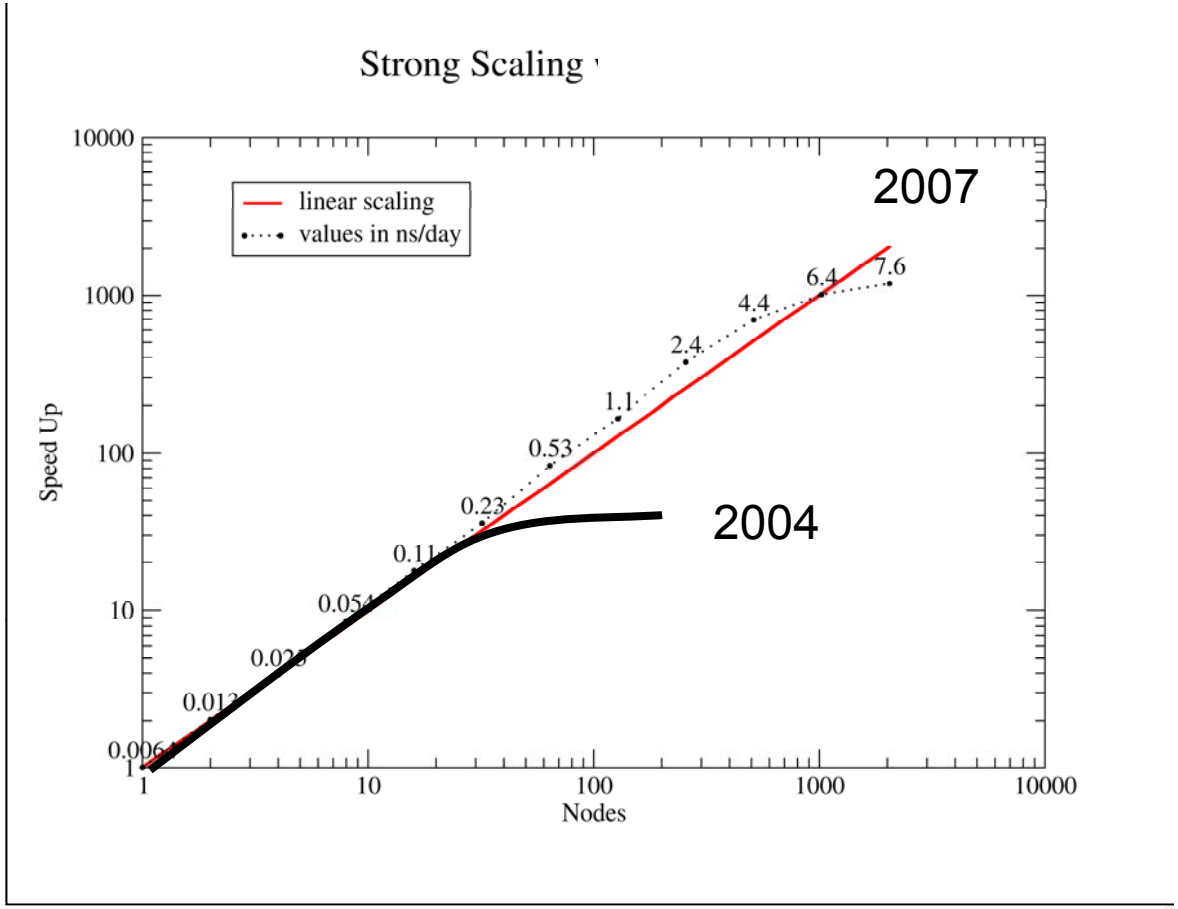
Center for Molecular Biophysics

ORNL

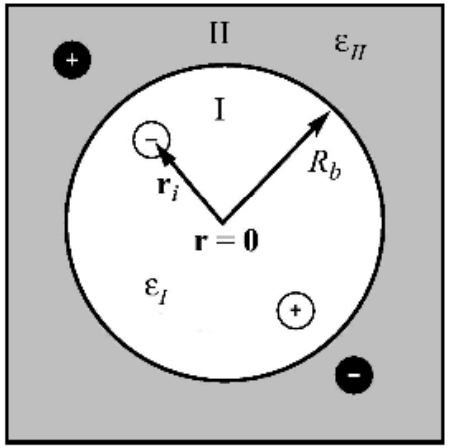
One Million Atoms – Molecular Dynamics



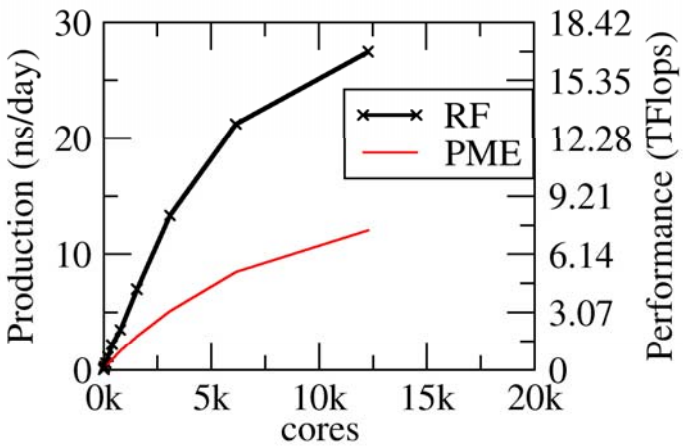
ROLAND SCHULZ



Long-Range Electrostatics

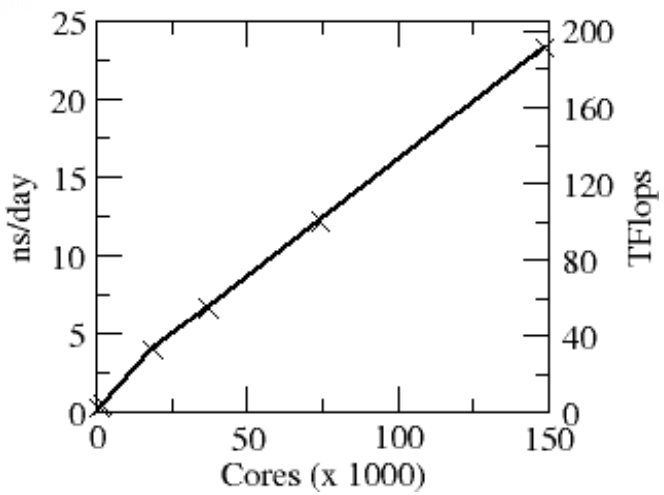


ROLAND SCHULZ



3.3 million atom system.

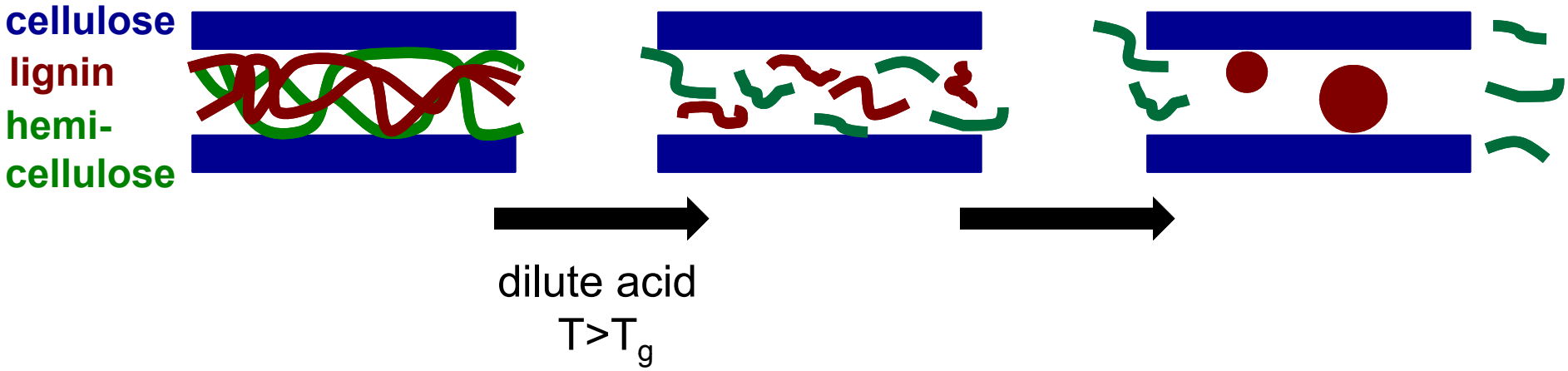
- **12 288 cores 27.5 ns/day = 16.9TFlops.**

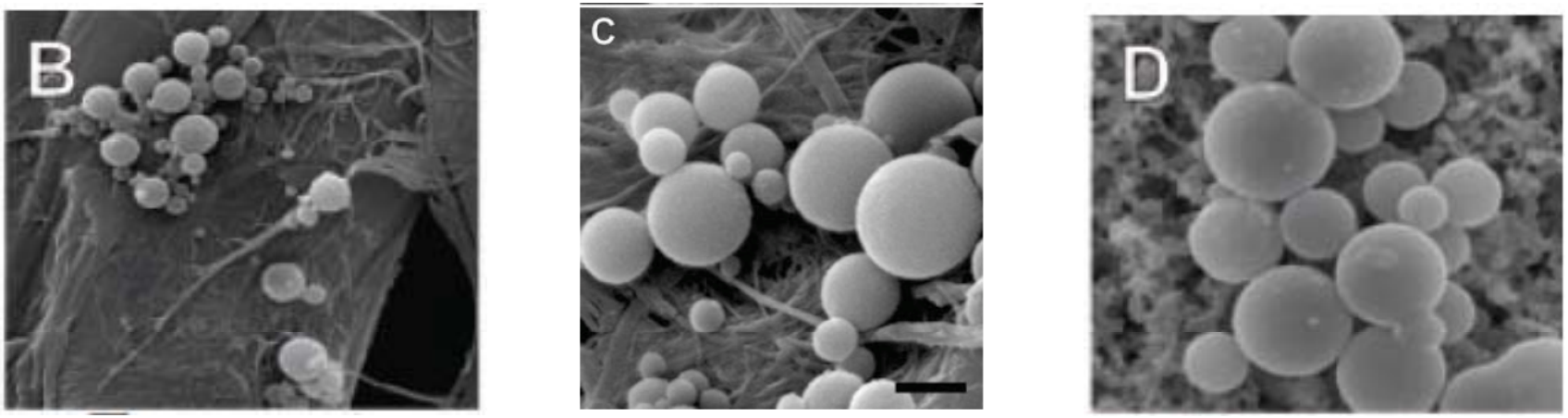


102 million atoms.

- **Scales to 150,000 cores**
- **23.3 ns/day at 193TFlops.**
- **for pure water > 300TFlops..**

Biomass Pretreatment

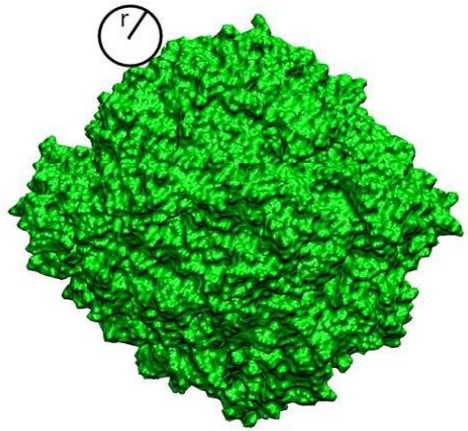




Are Lignin Aggregates Spheres?

LOUKAS PETRIDIS

Lignin Aggregates

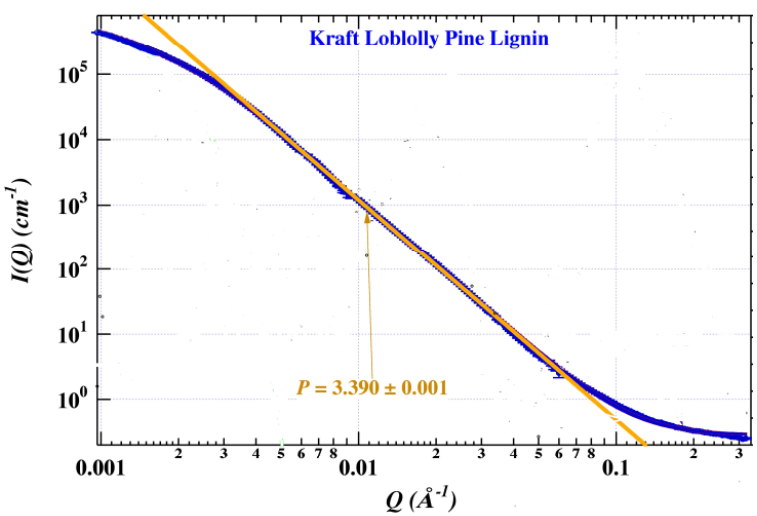


Small-Angle Neutron Scattering

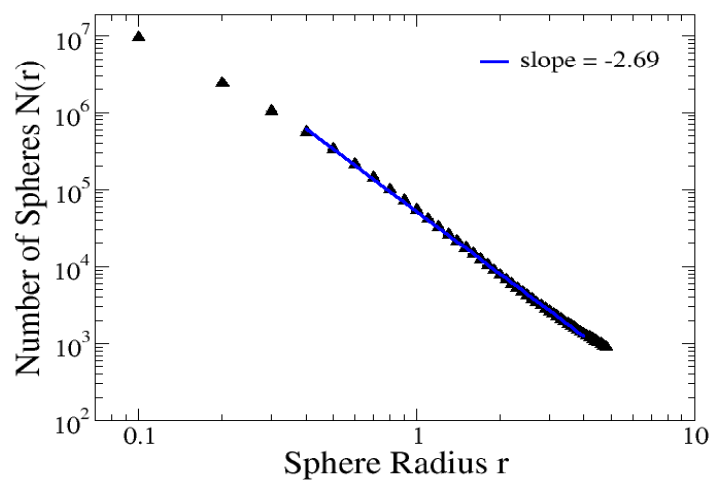
$$S(q) \propto q^{d_s - 6}$$

Molecular Dynamics

$$N(r) = r^{-d_s}$$

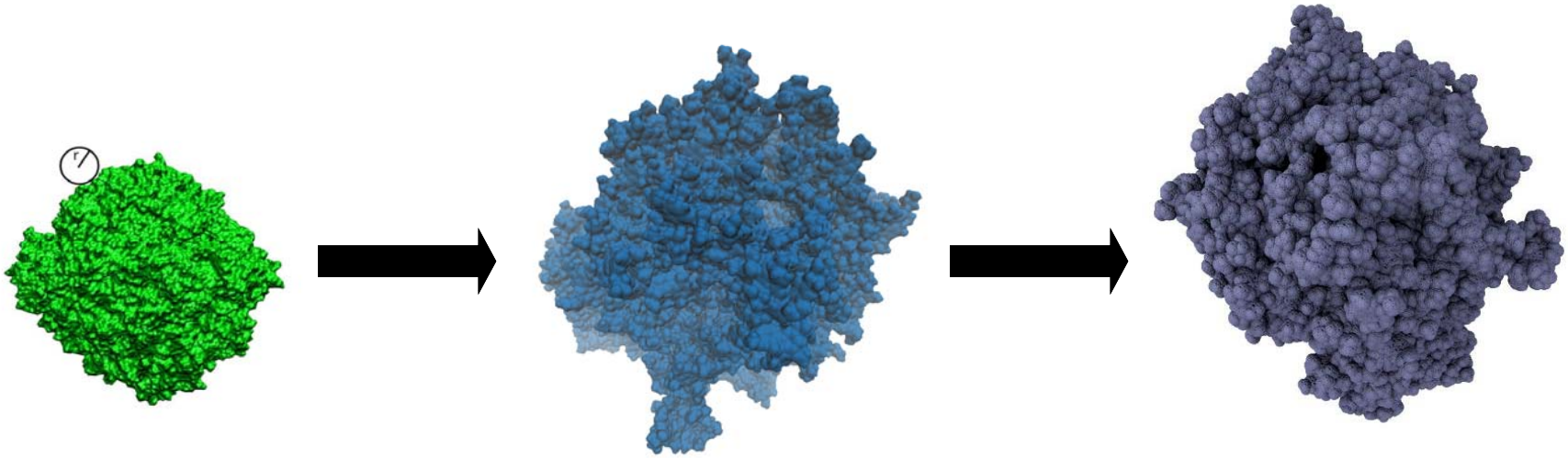


d_s=2.62±0.02

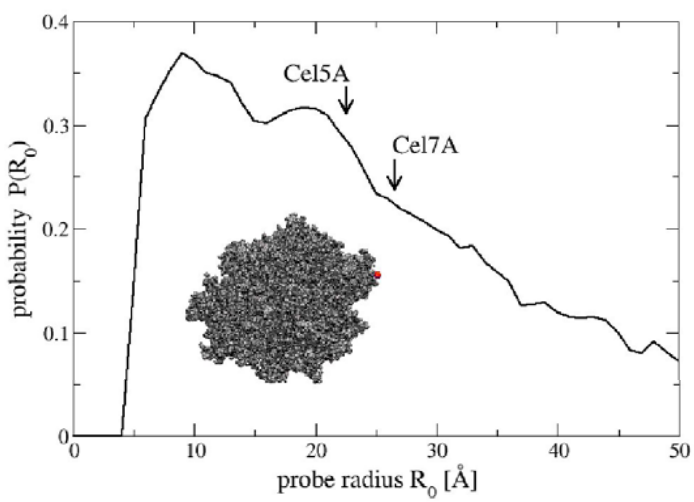


d_s=2.65±0.01

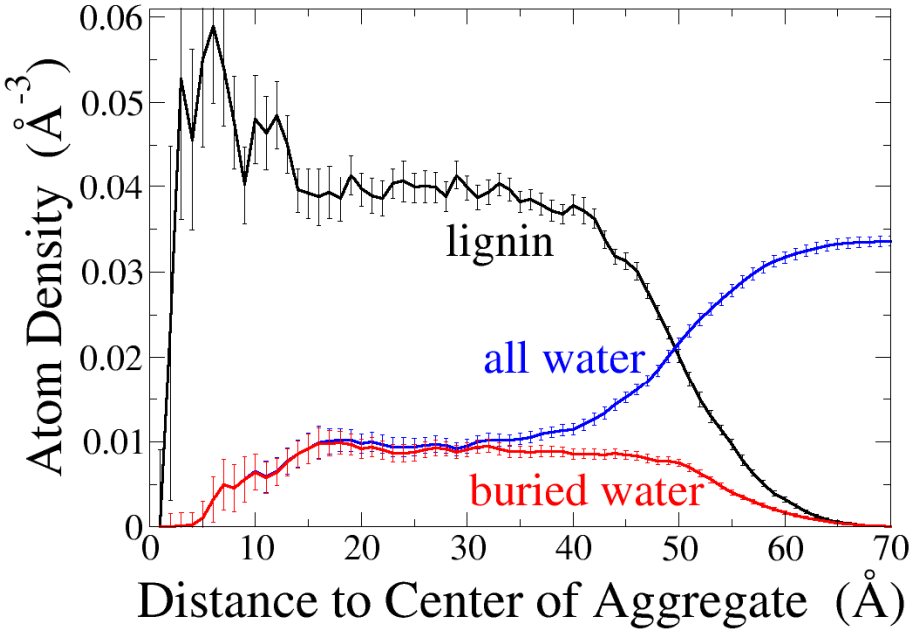
Surface Fractals over Three Orders of Magnitude

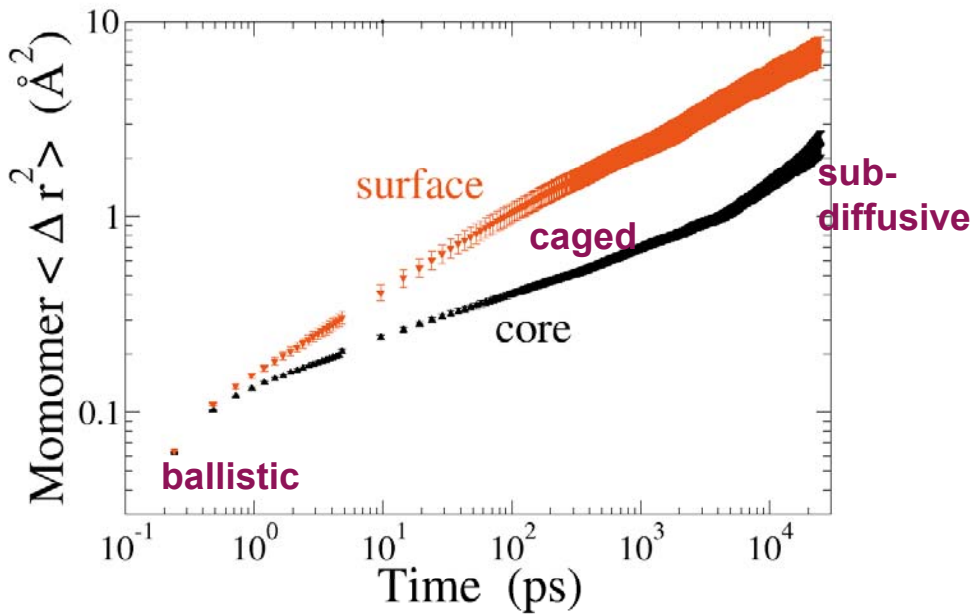


R_g=4.2Å R_g=42Å R_g=420Å



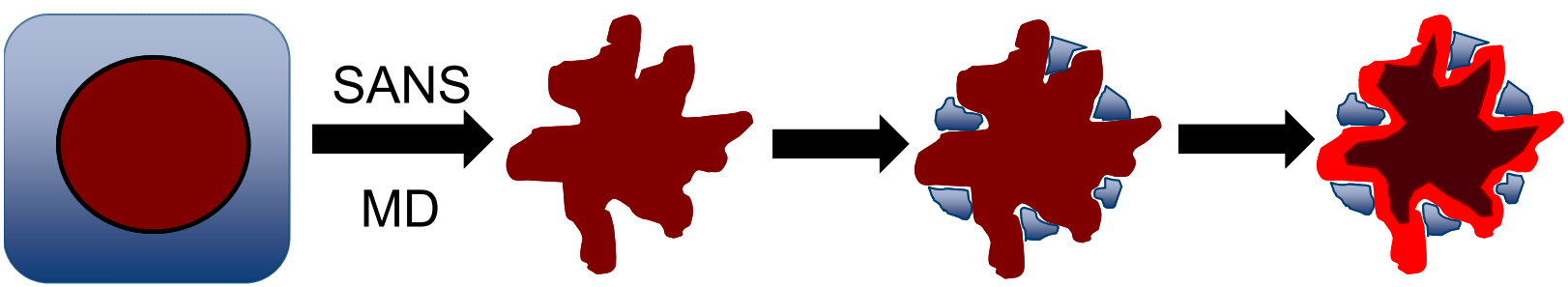
Enzyme:lignin interaction distribution





Extensive Water Penetration

Heterogeneous Chain Dynamics



rigid sphere

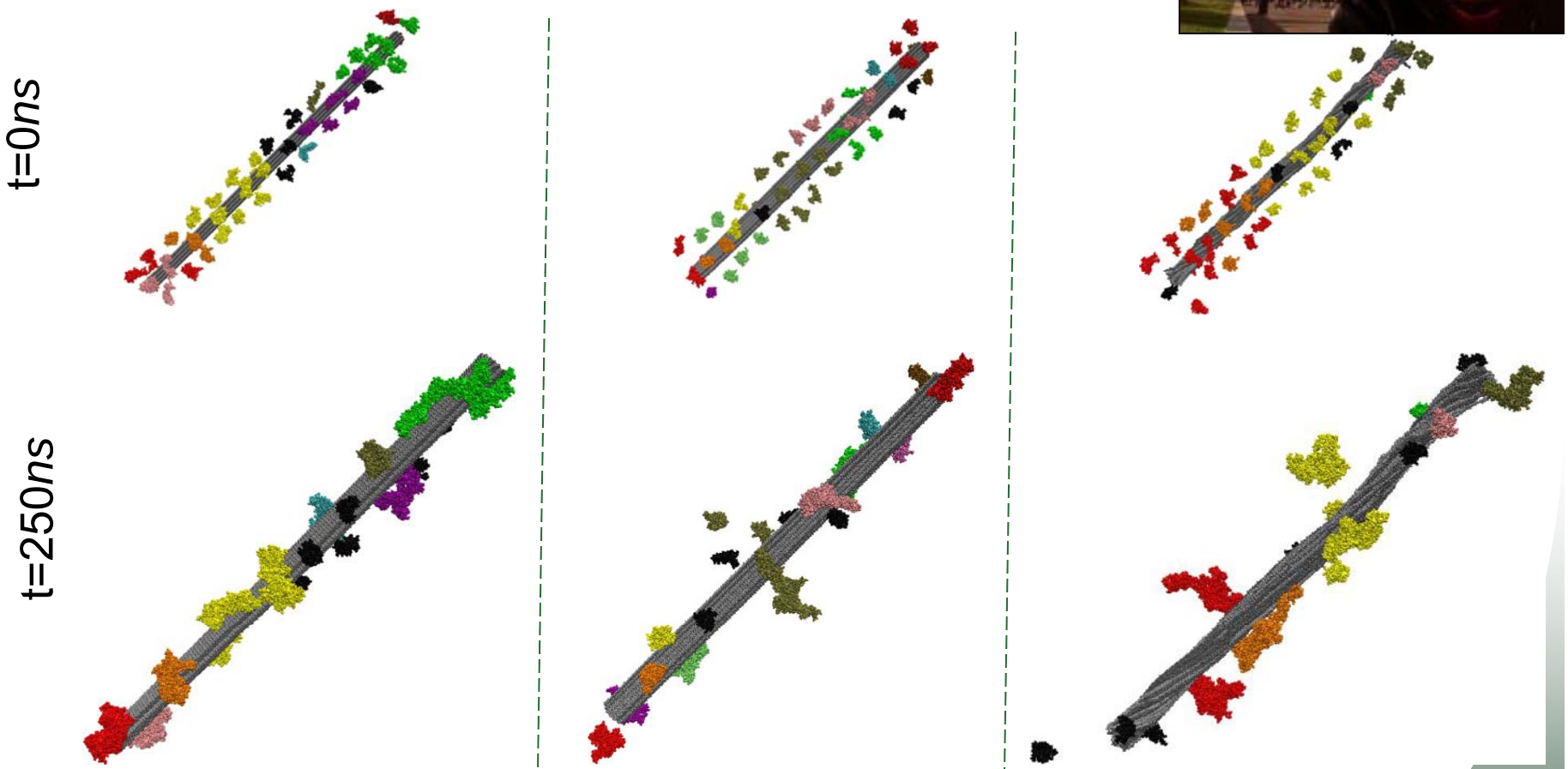
highly folded surface

water penetration

rigid core fluid surface

Lignin Aggregation & Precipitation onto Cellulose

BENJAMIN LINDNER



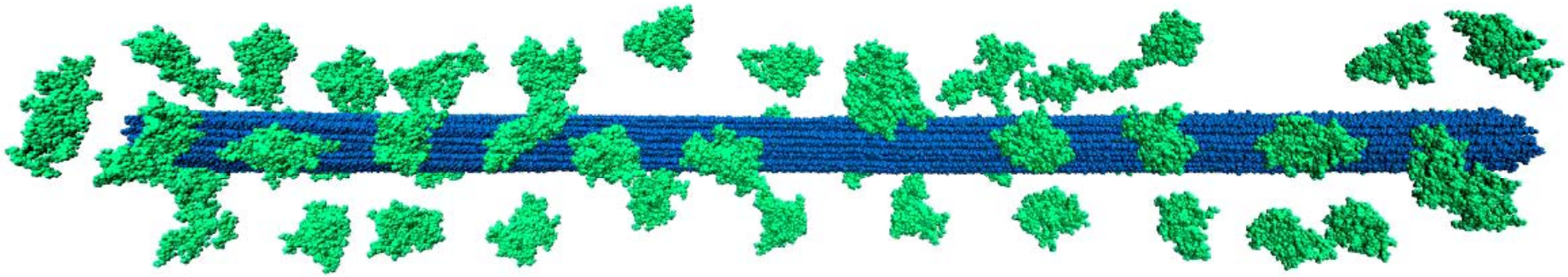
high concentration & crystalline cellulose

low concentration & crystalline cellulose

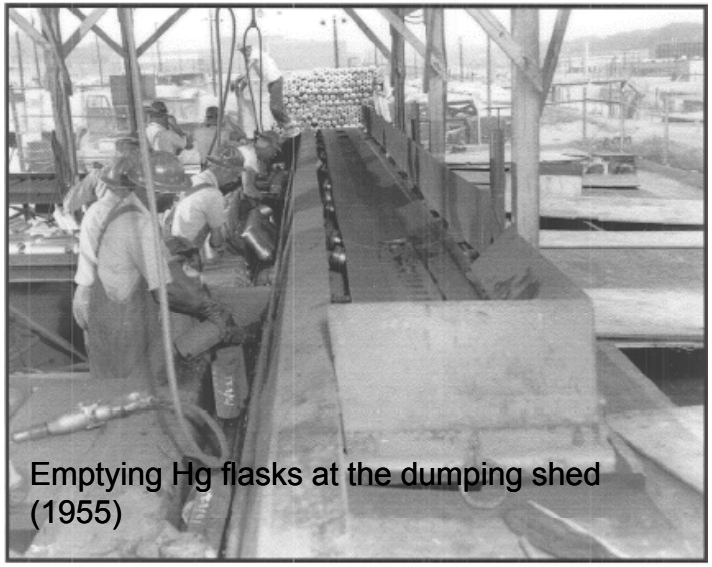
low concentration & semi-crystalline cellulose

Lignin Aggregation & Precipitation onto Cellulose

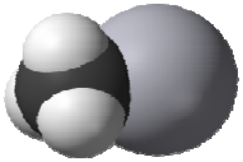
BENJAMIN LINDNER



Oak Ridge

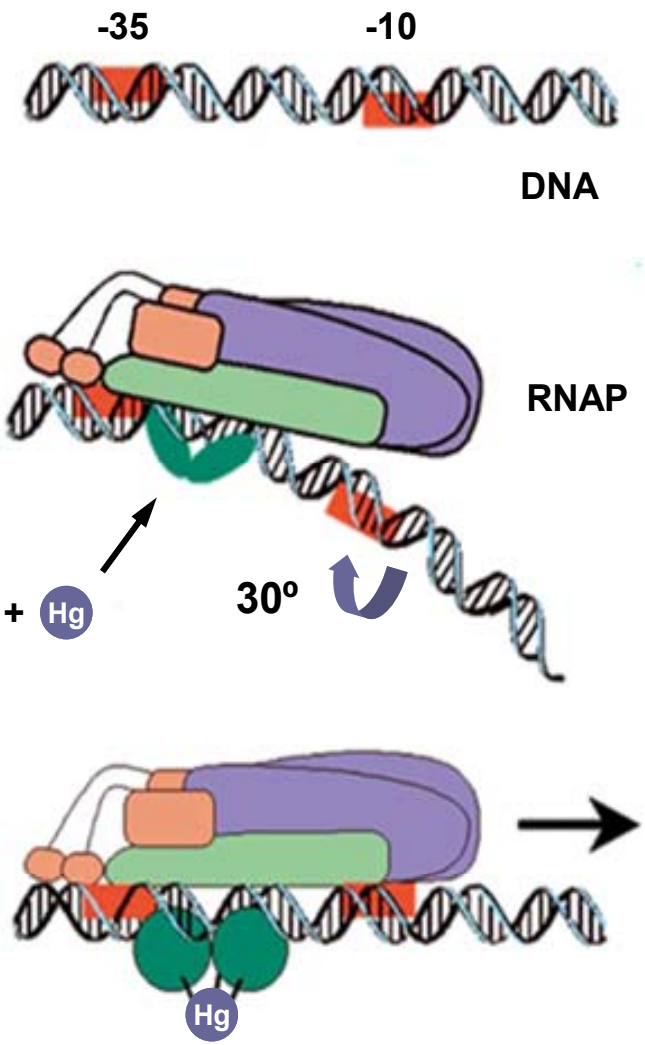


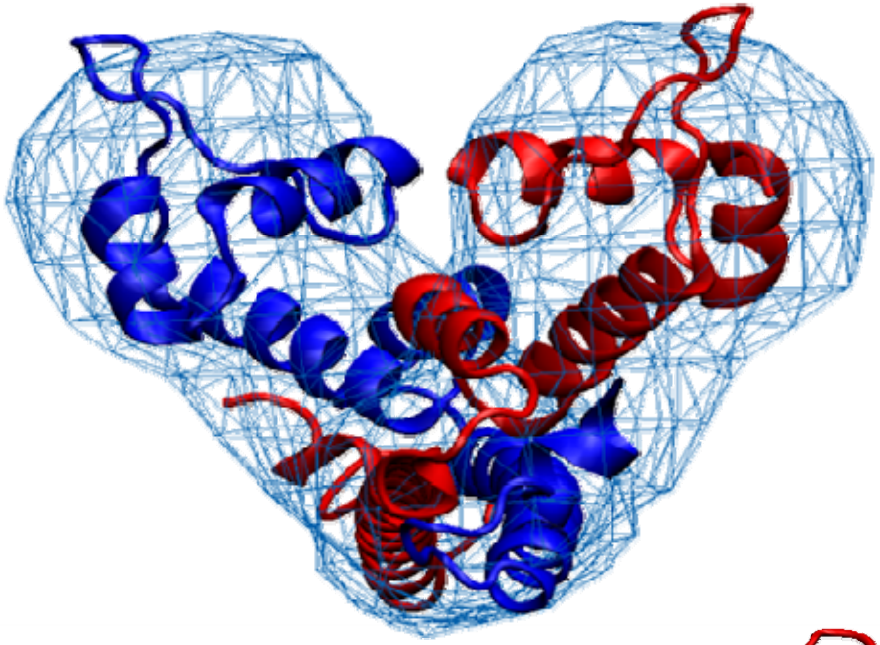
Toxic
Methylmercury
CH_3Hg^+

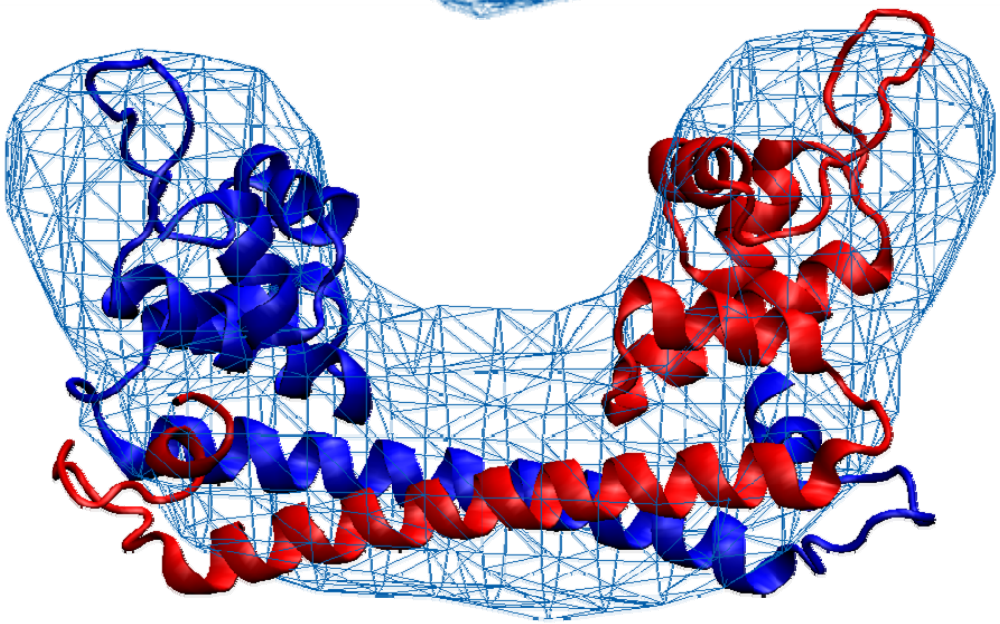


Inert
Hg(0)

MerR

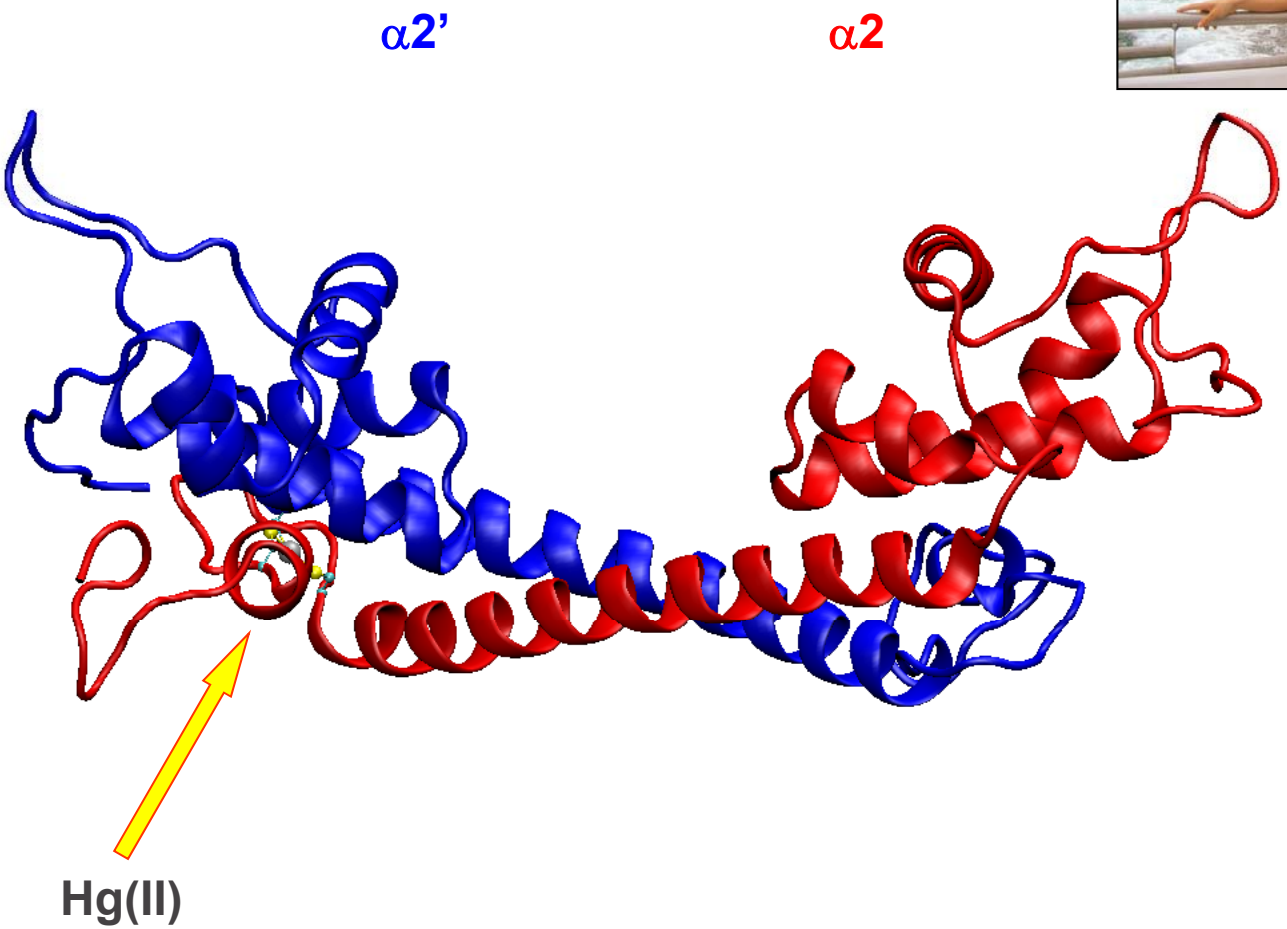






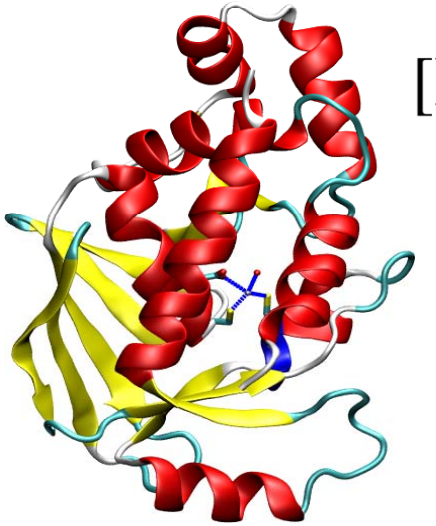
The MerR Machine

Hao-Bo Guo

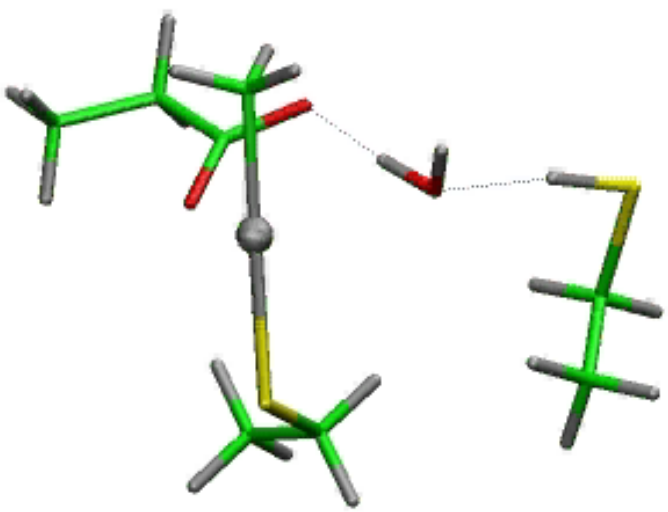


Catalytic Mechanism of MerB
Hg-C Protonolysis

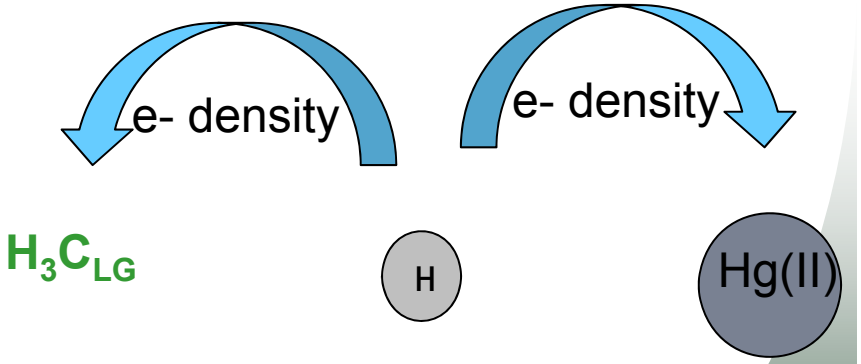
JERRY PARKS



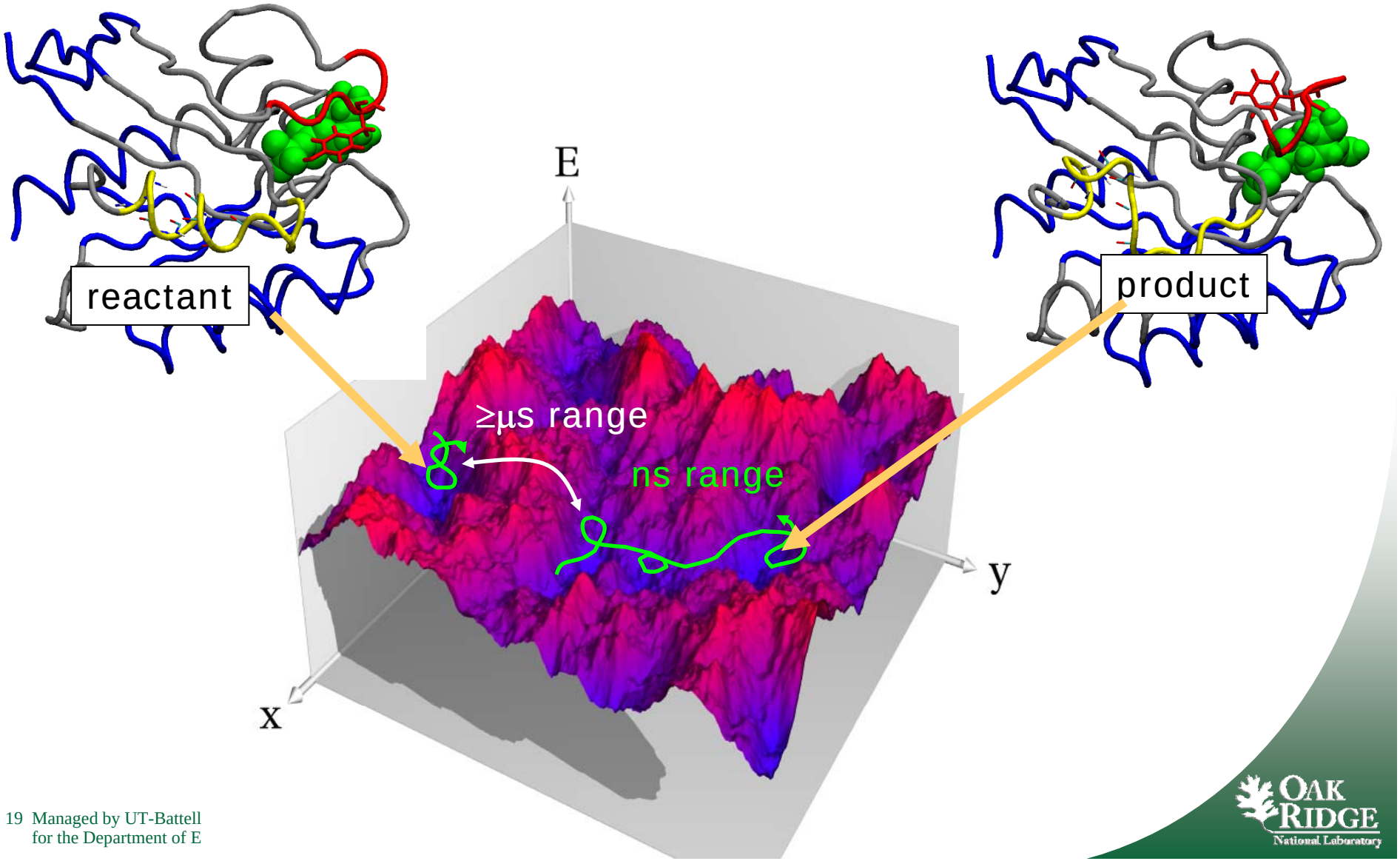
$$[\text{R-Hg(II)}]^{+} \xrightarrow{\text{MerB}} [\text{Hg(II)}]^{2+} + \text{R-H}$$



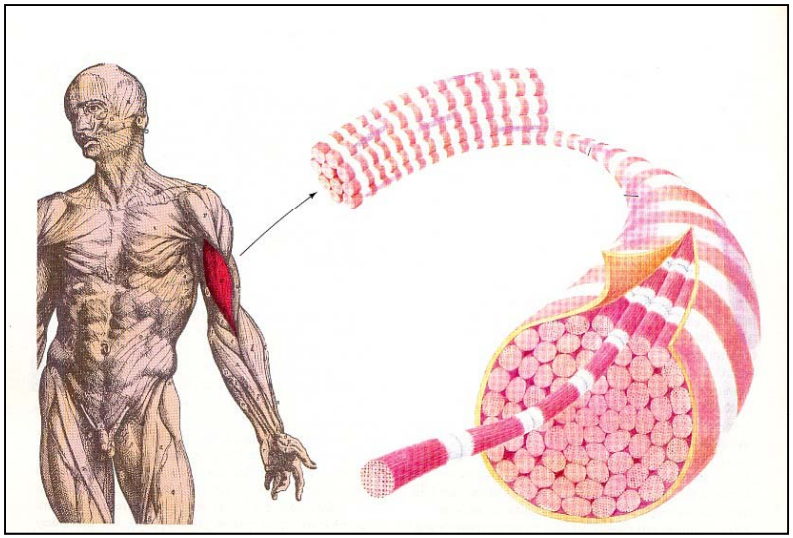
- **Thiol *bis*-coordination of Hg at Transition State Polarizes Attacking Proton.**

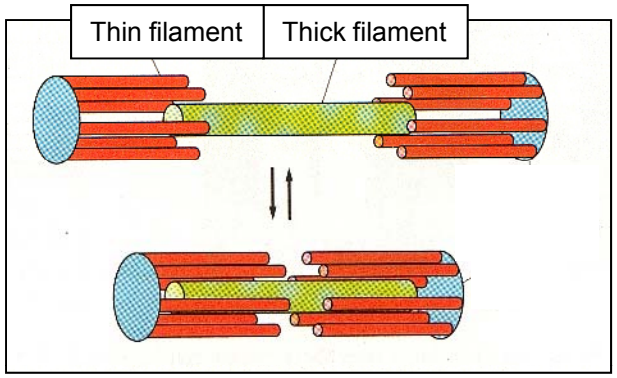


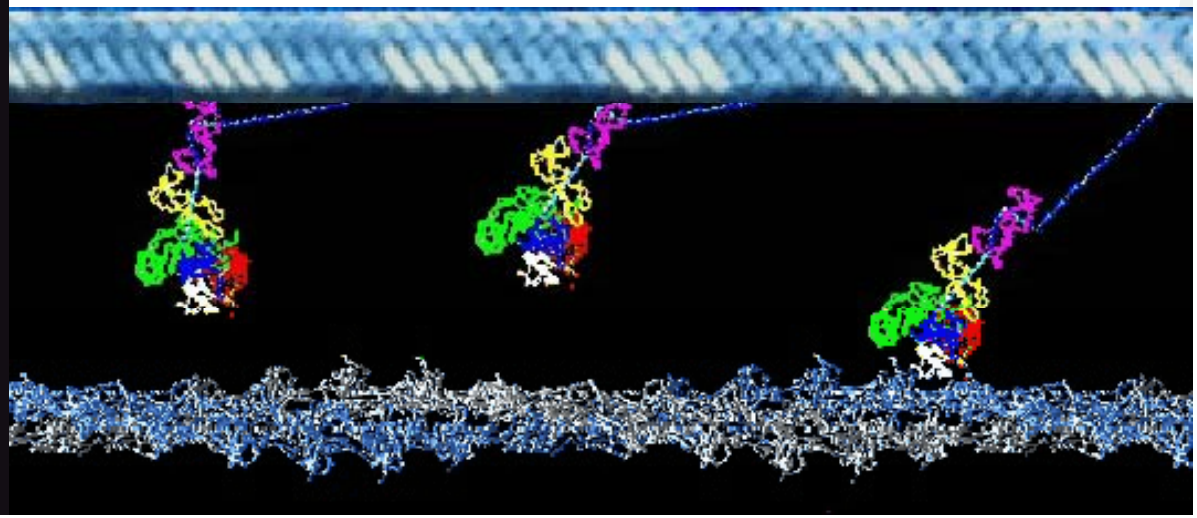
Large-Scale Functional Conformational Transitions



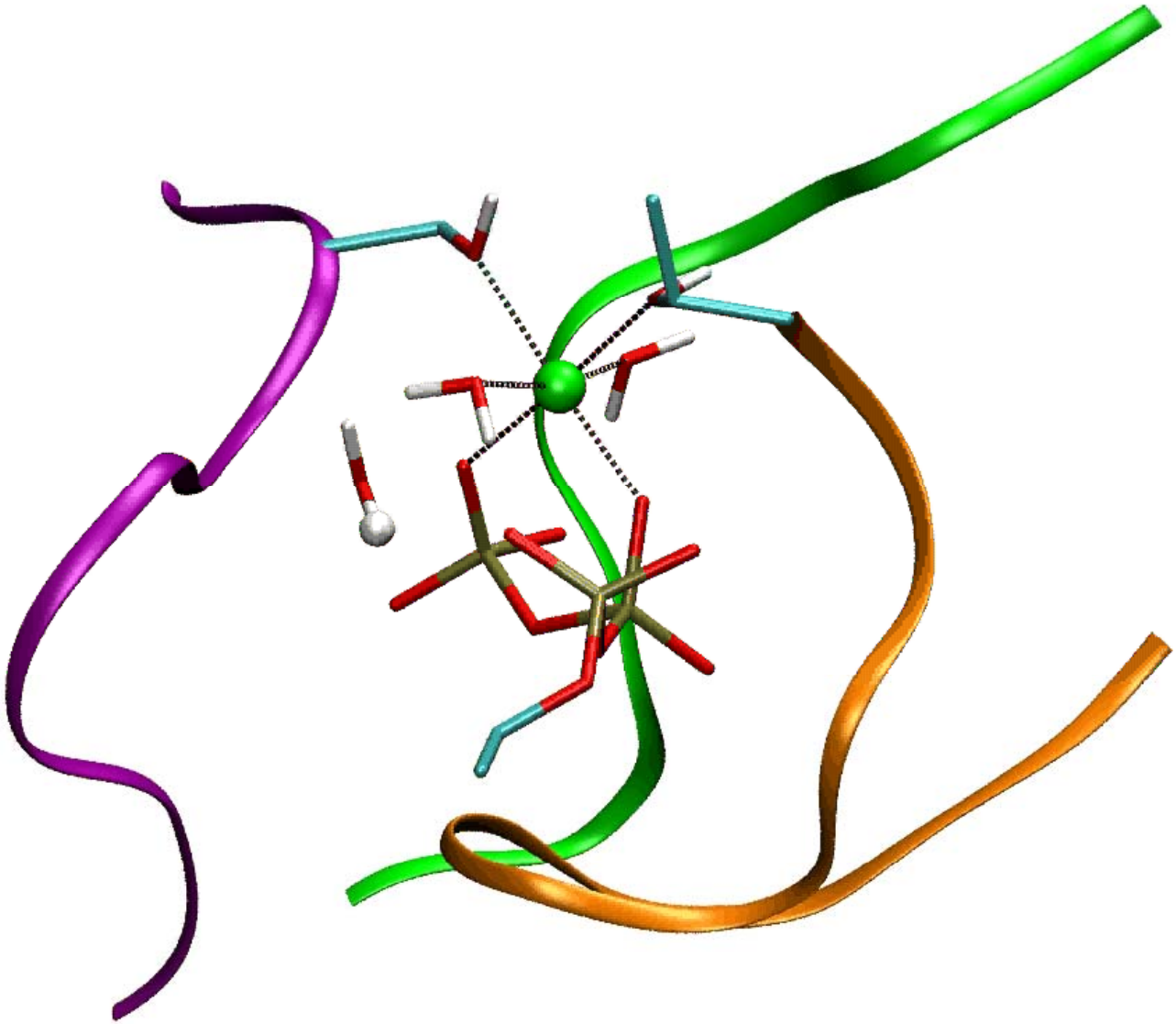
Muscle Contraction







ATP Hydrolysis by Myosin

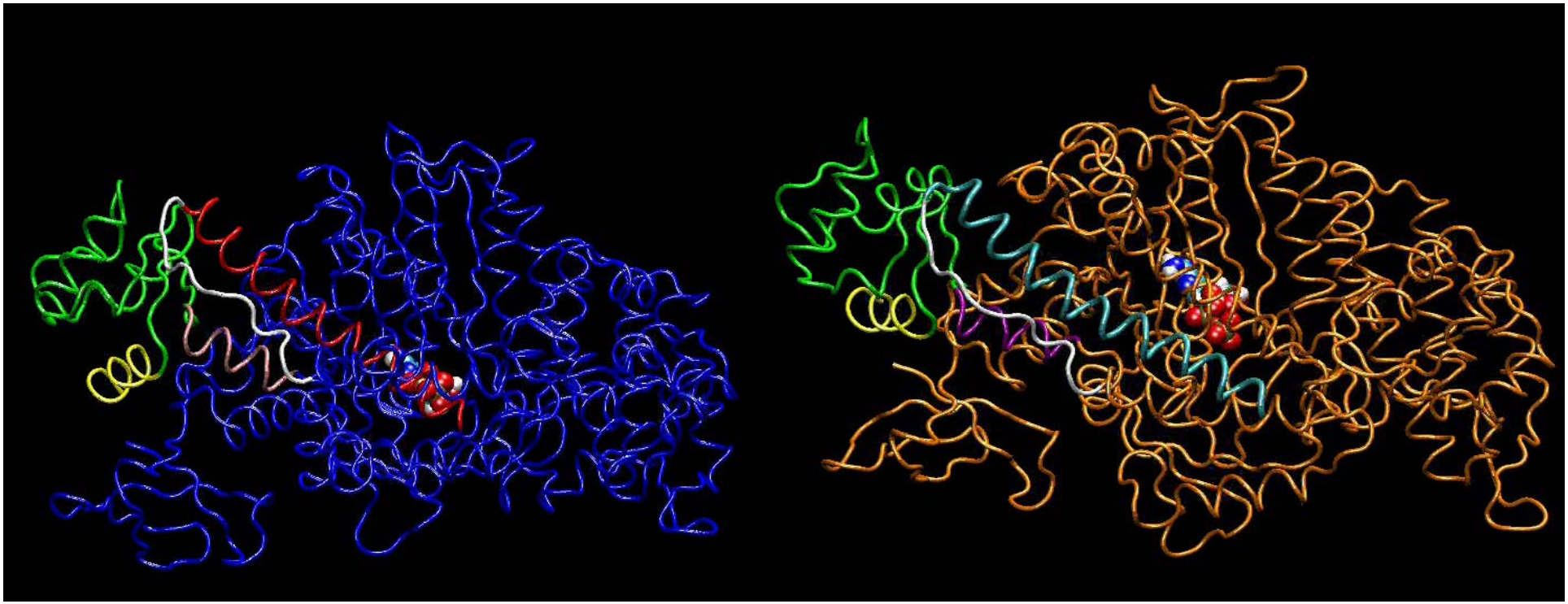


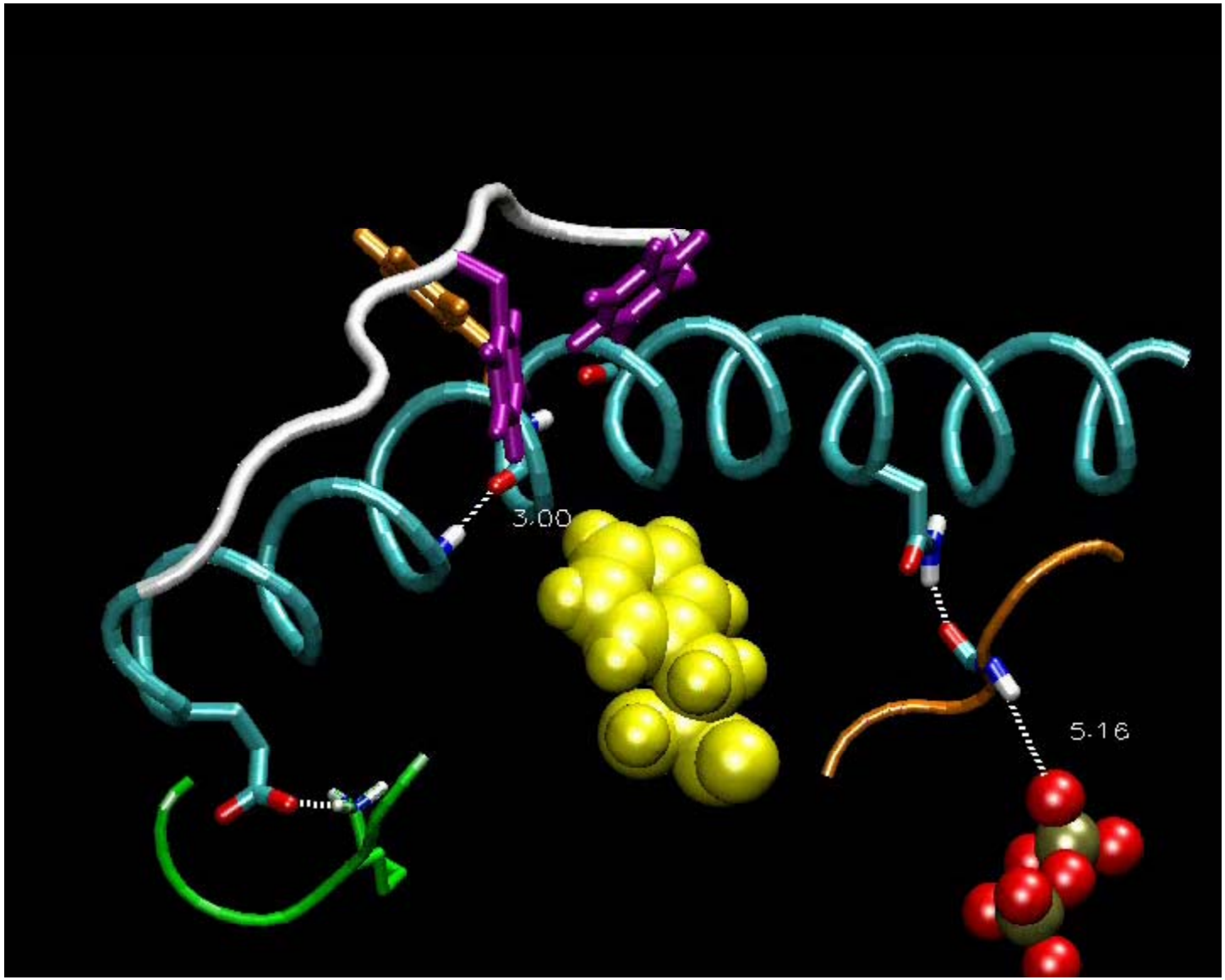
SONJA SCHWARZL

OAK RIDGE National Laboratory

BJORN WINDSHUEGEL

Dynamics of Muscle Contraction

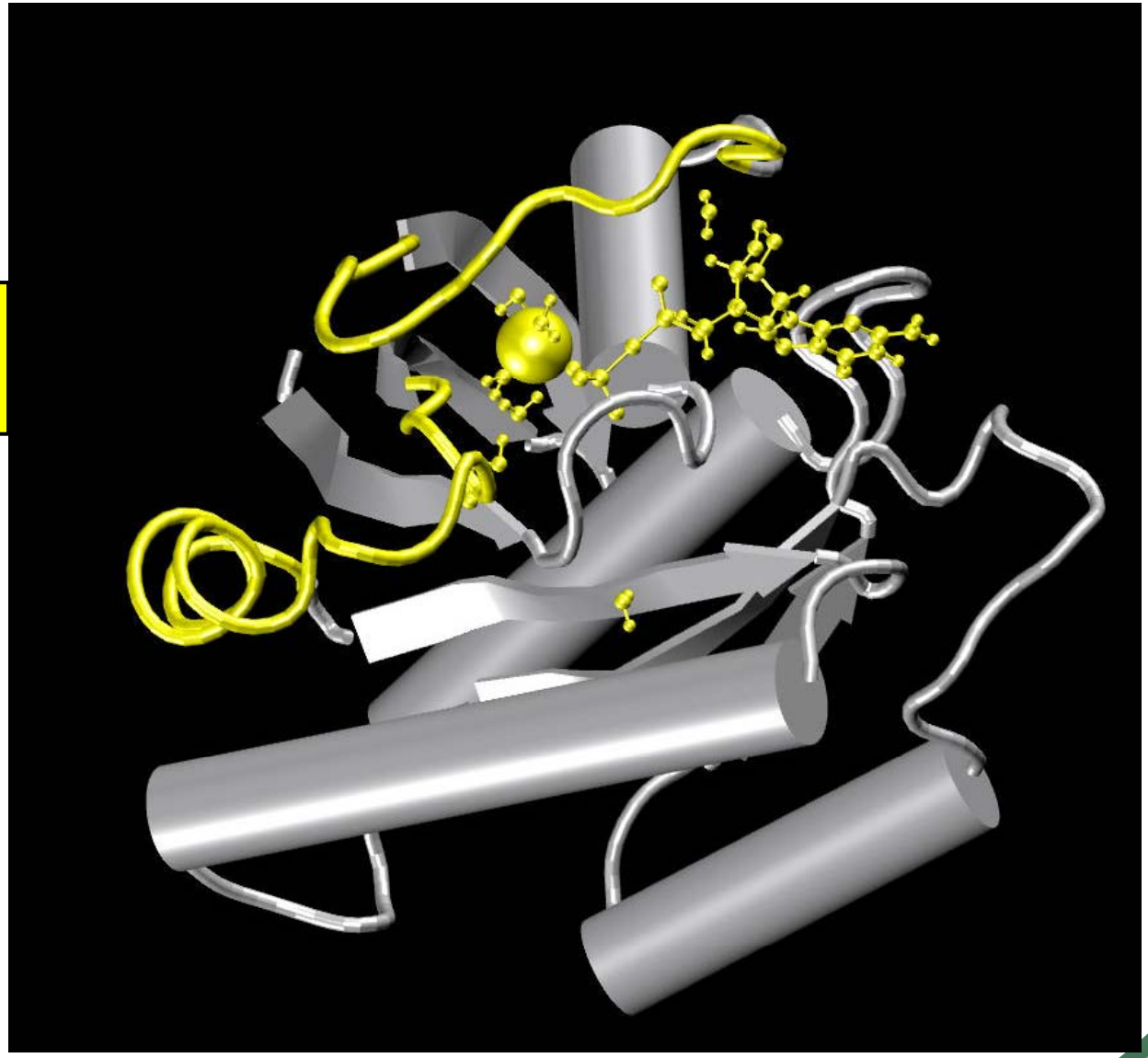



3.00
5.16

Ras p21

GTP-Bound Form

(ON)



Ras p21

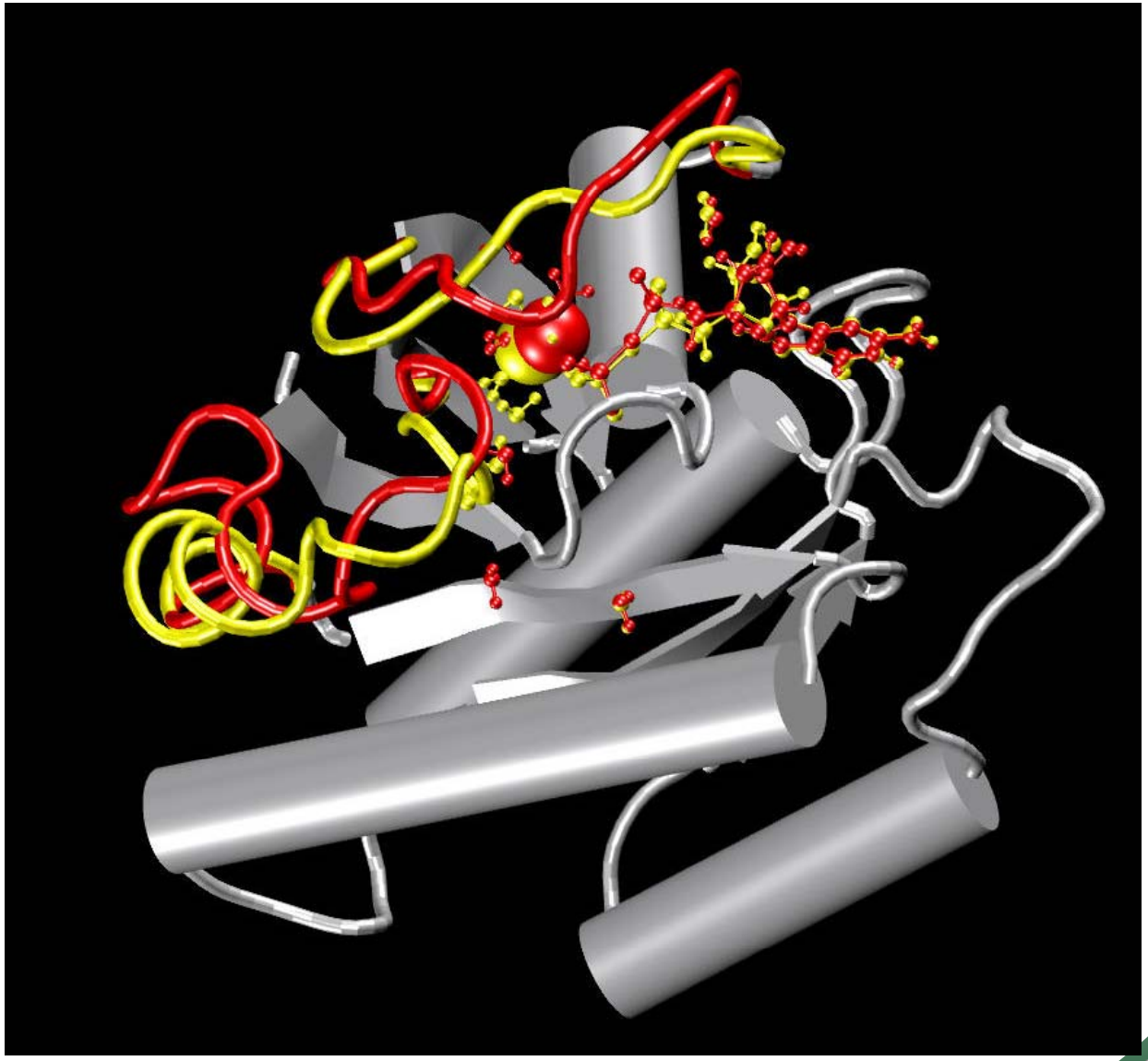
GTP-Bound Form

(ON)

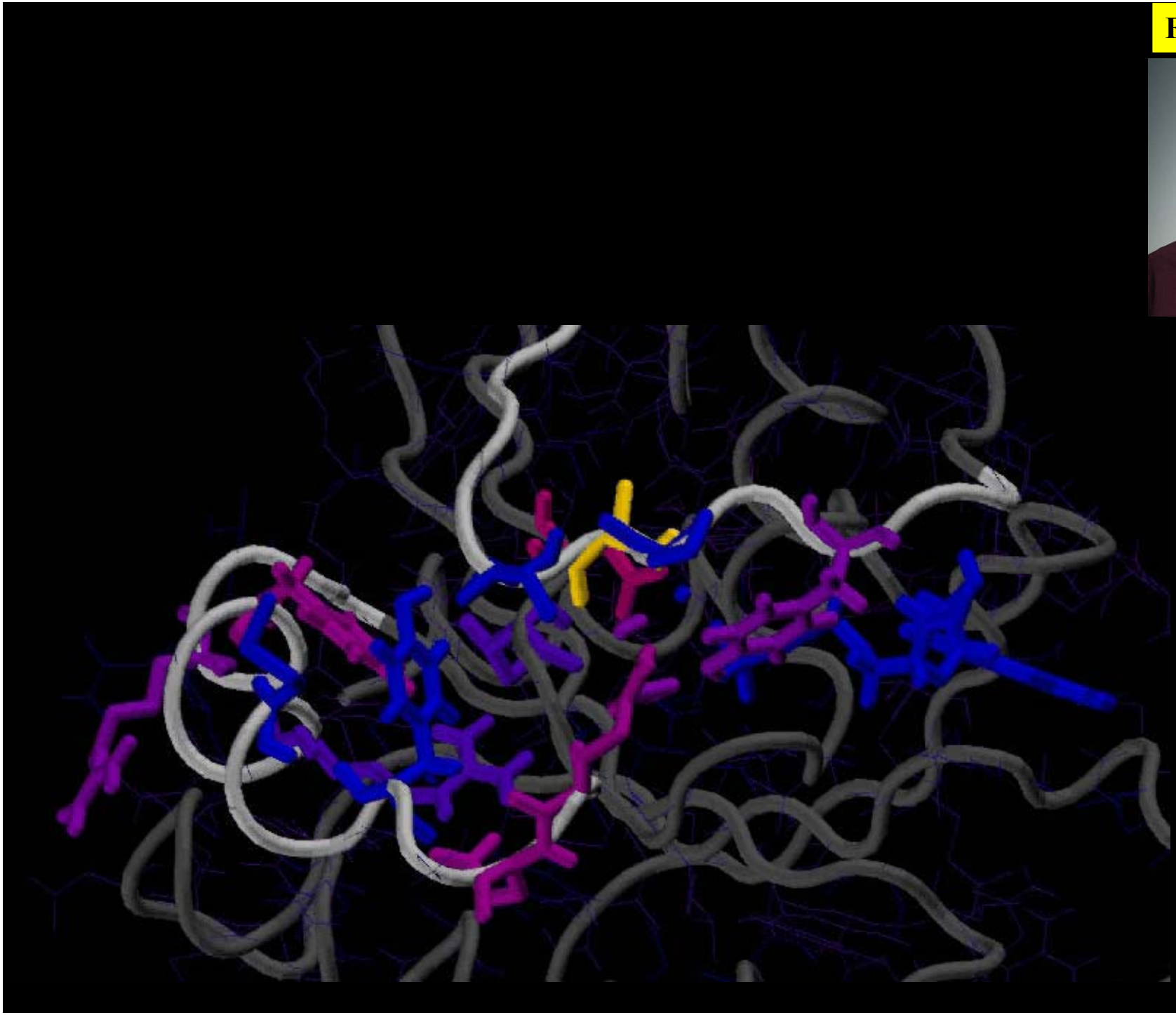
↓

GDP-Bound Form

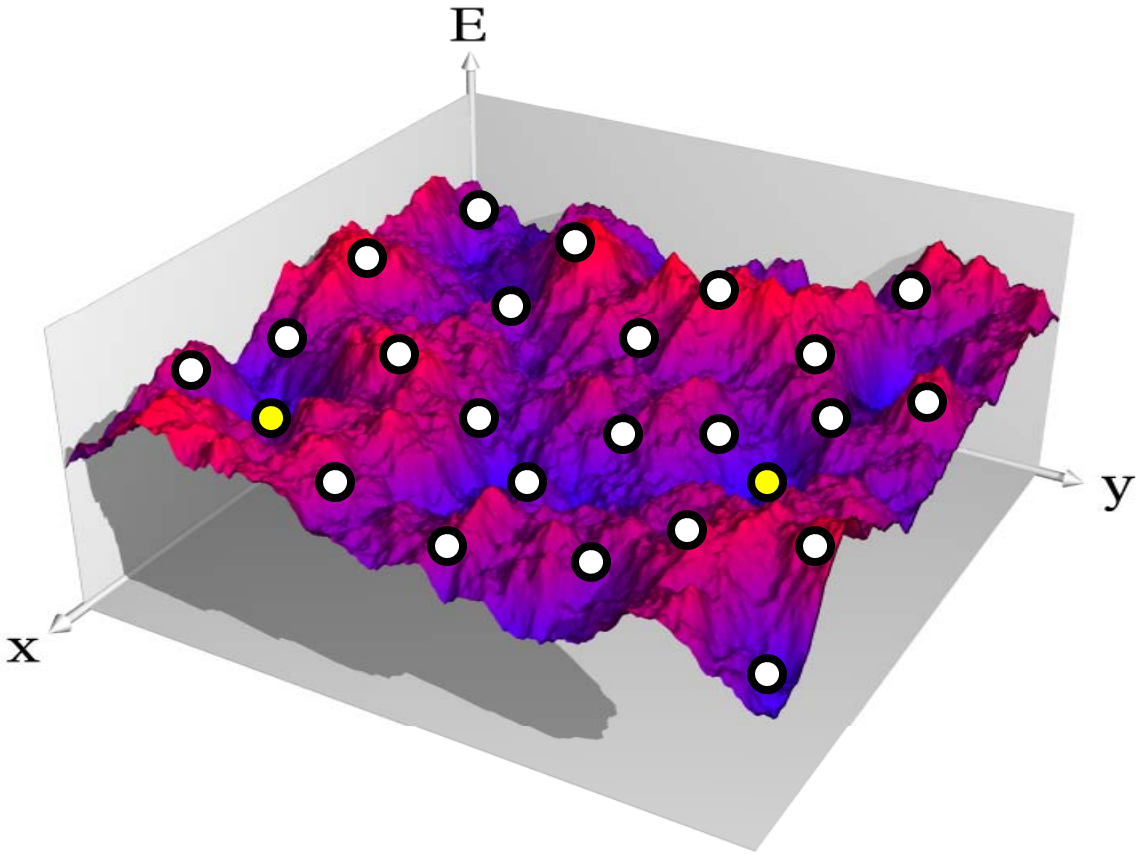
(OFF)

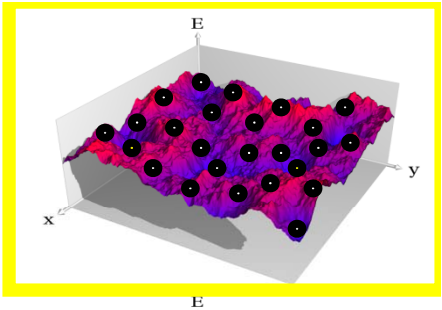


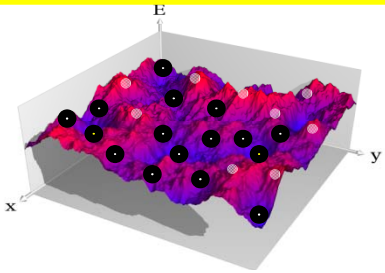
FRANK NOE

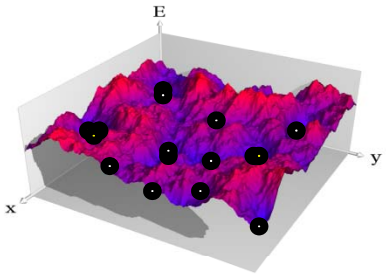


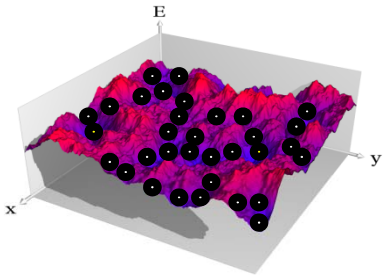
Sampling:
Uniform Distribution

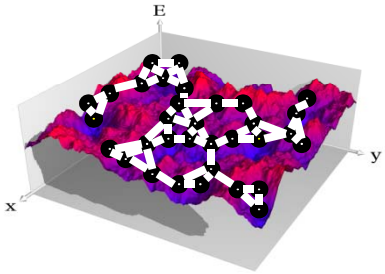




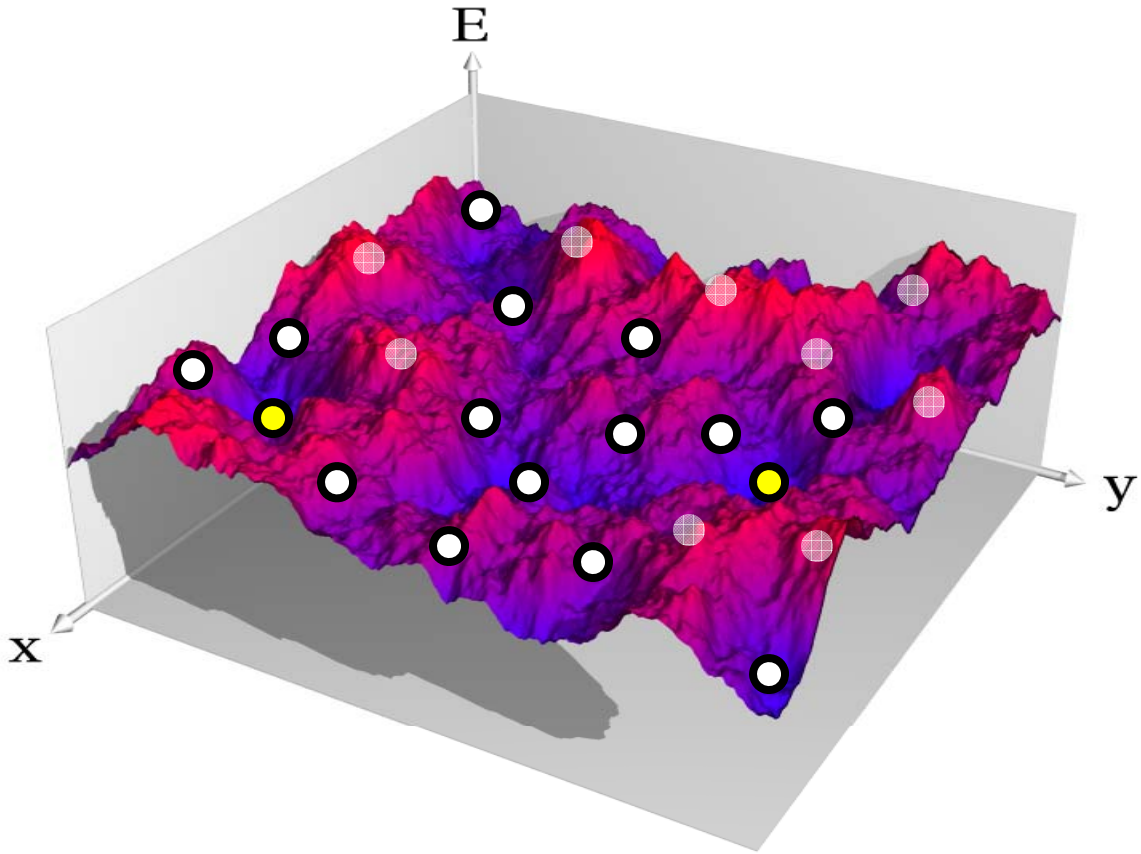


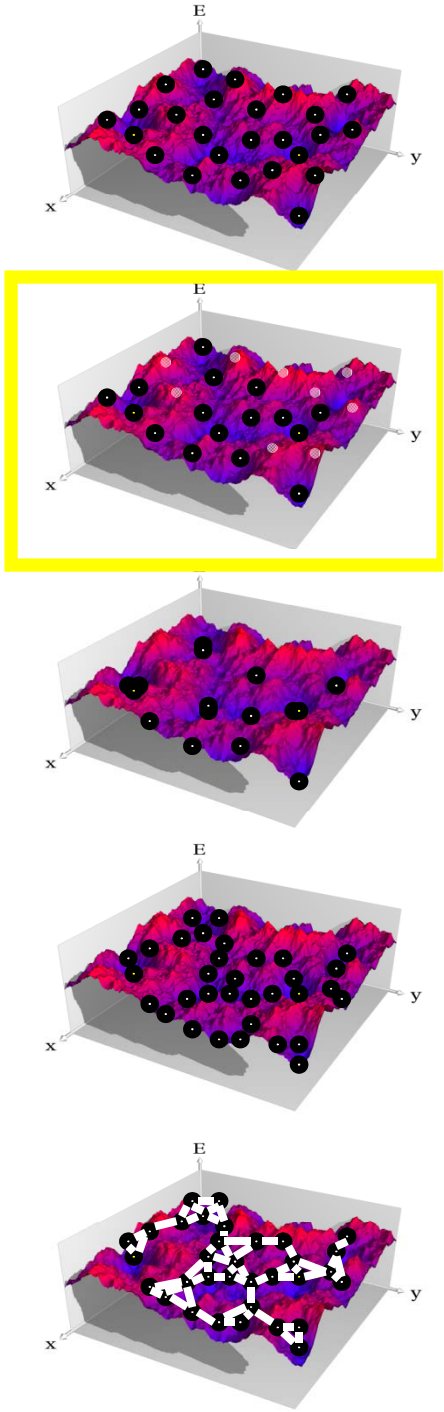




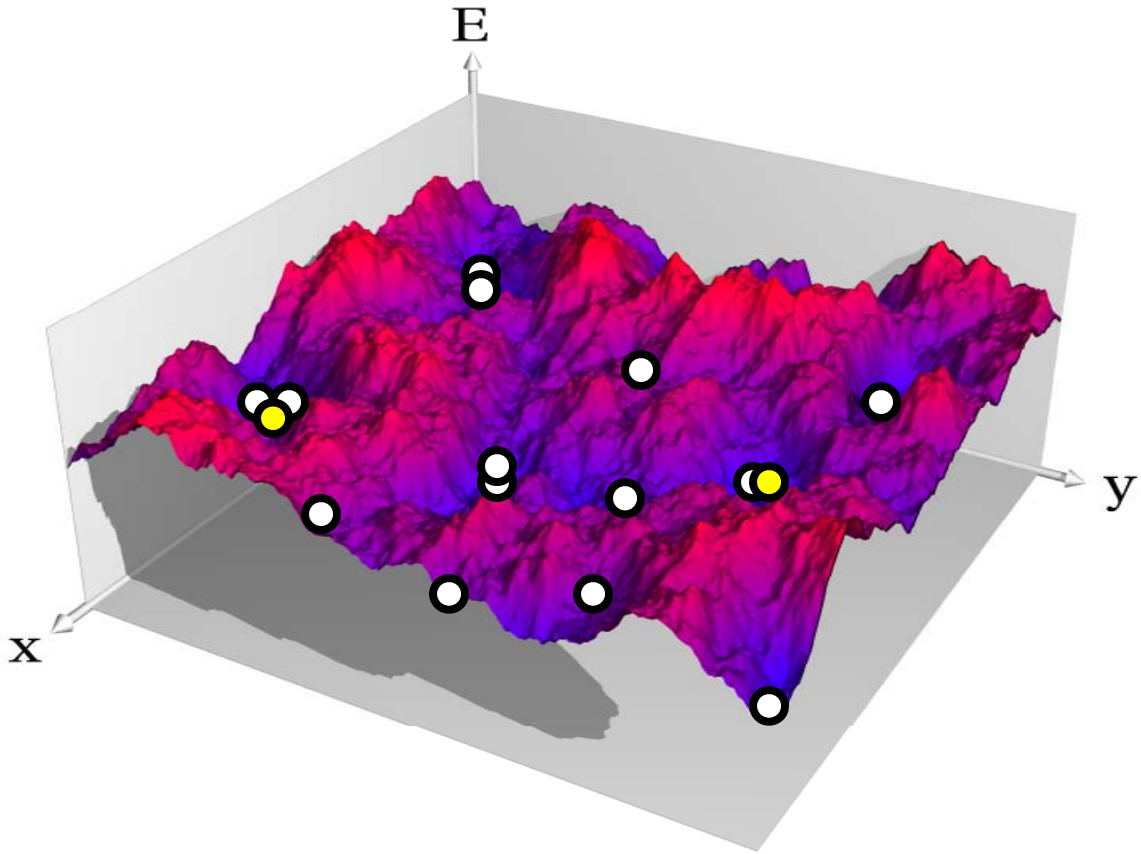


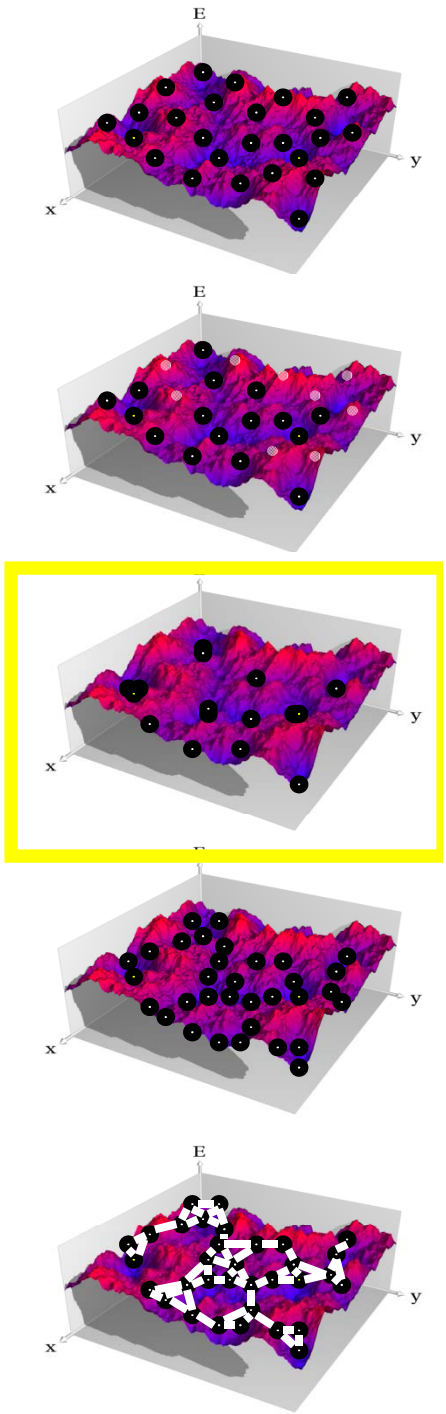
Sampling:
Exclusion of „Bad Structures“



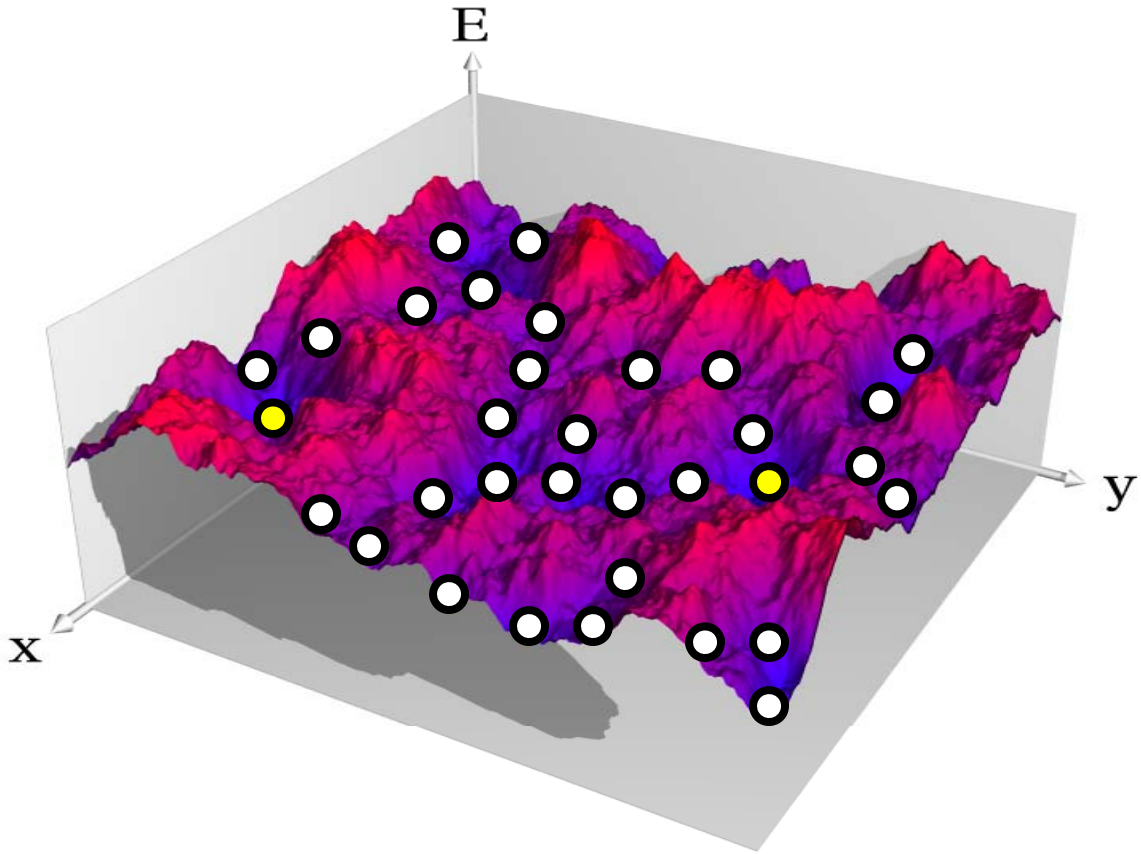


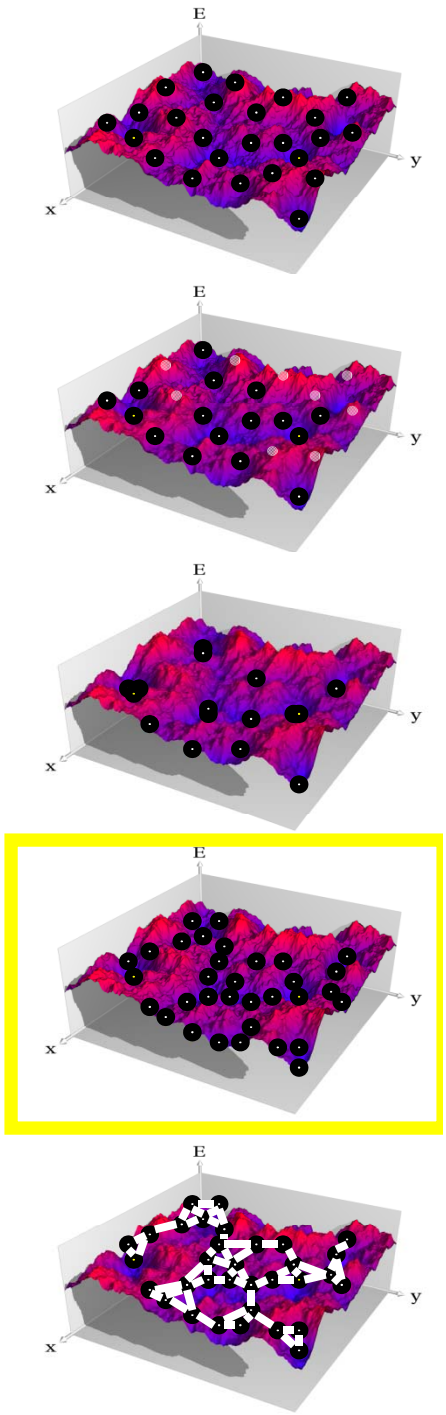
Sampling:
Fail-Fast Minimization



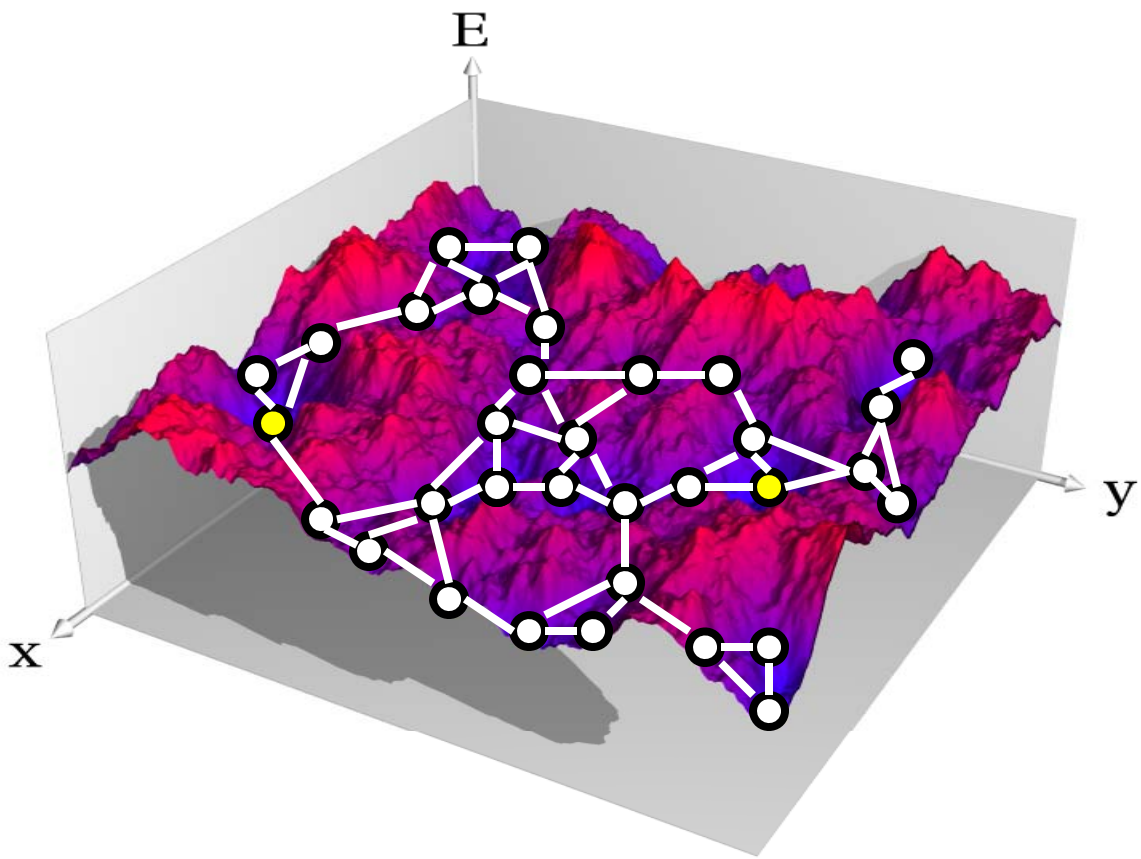


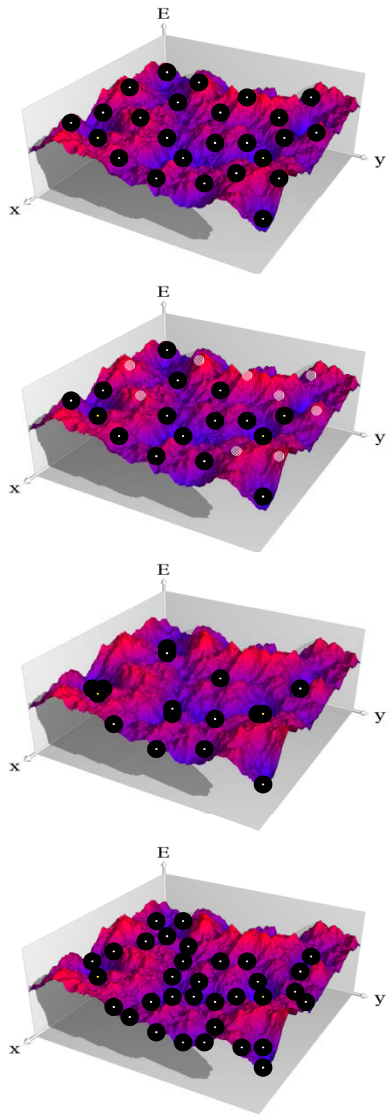
Sampling:
Increase Density of Low-Energy Points

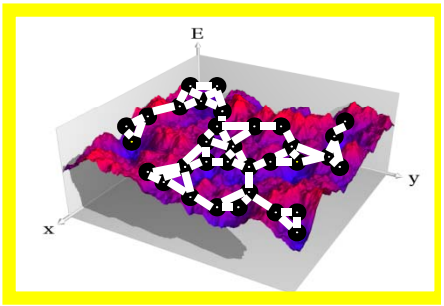




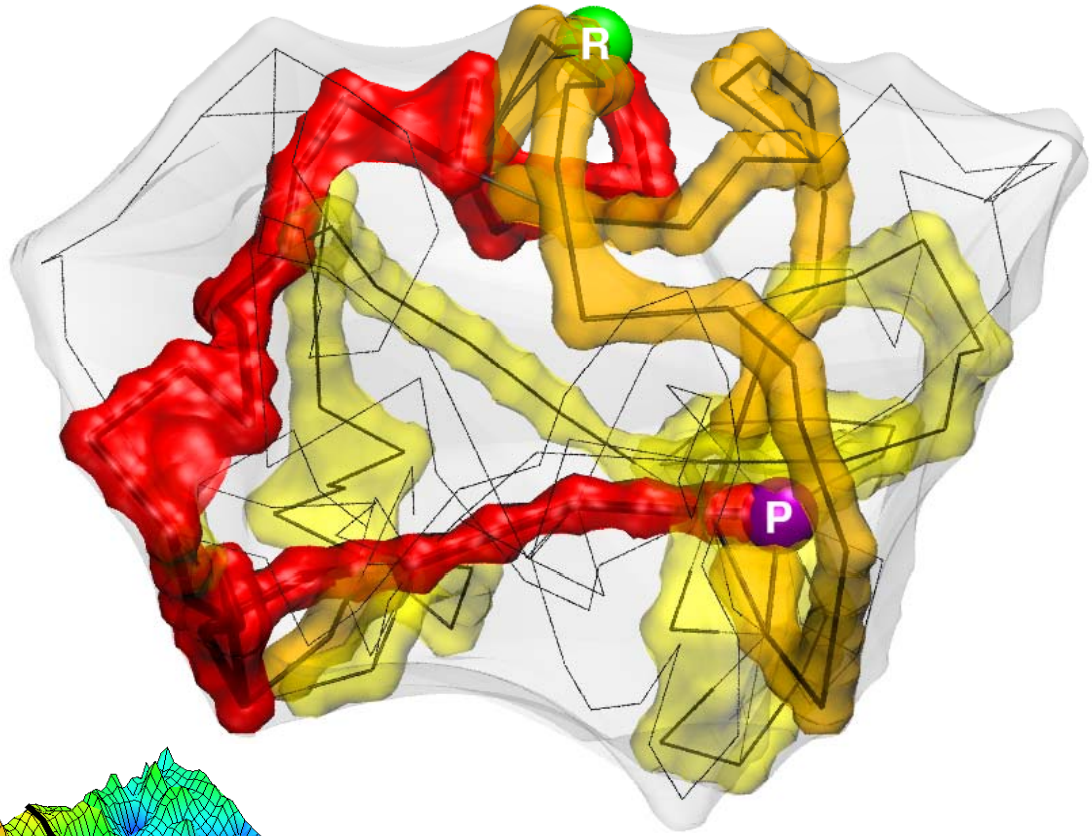
Transition Network: Edges between Neighbours

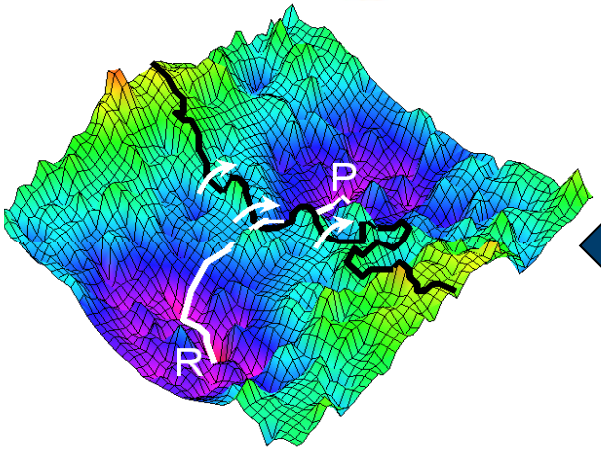




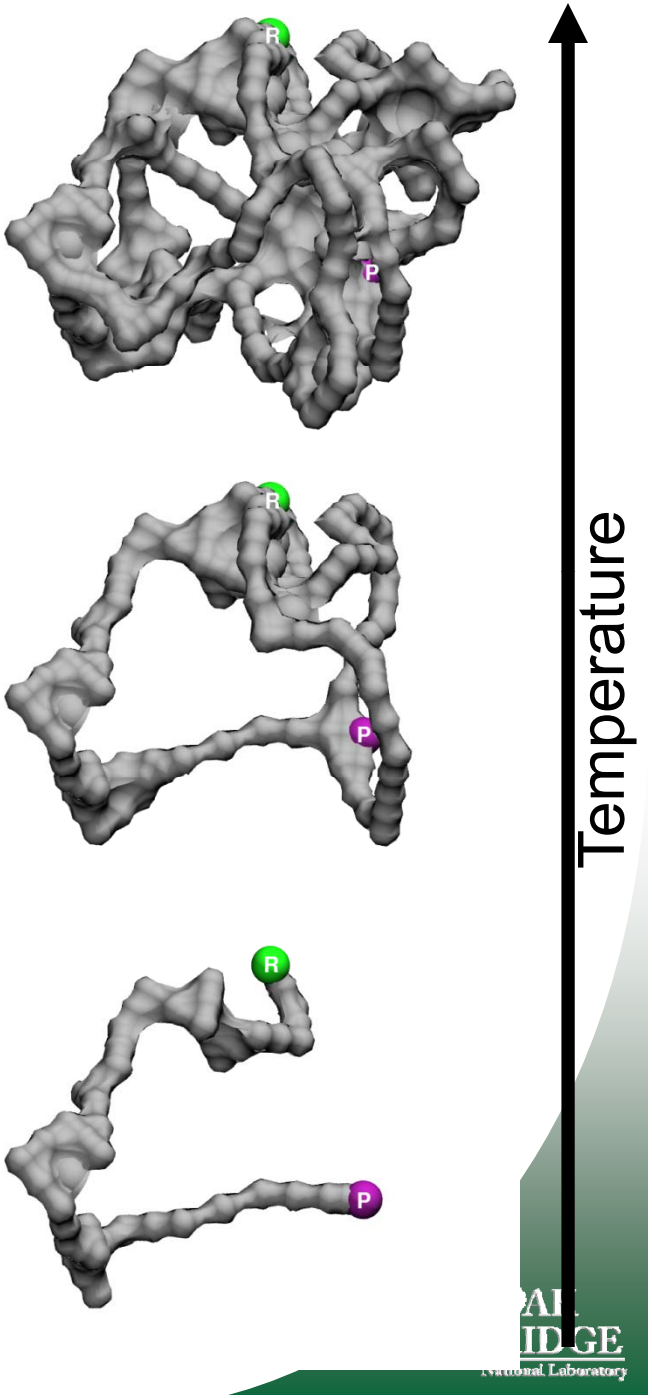


Connectivity of Network of Best Paths



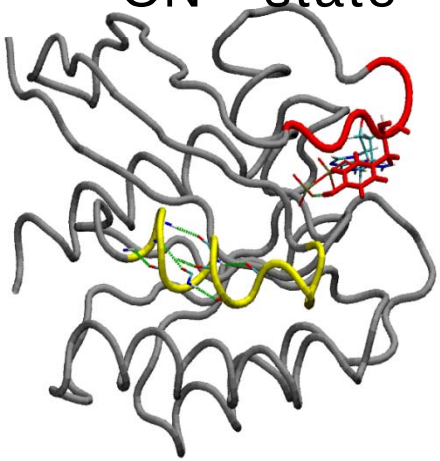


Watershed

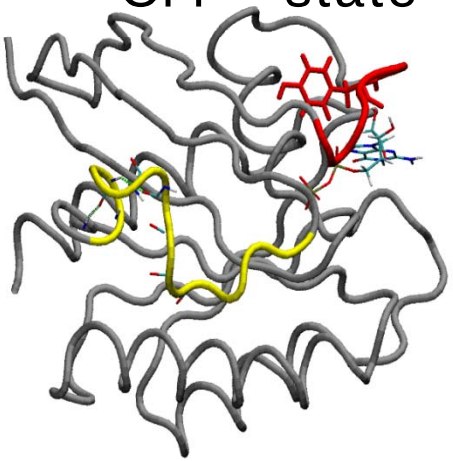


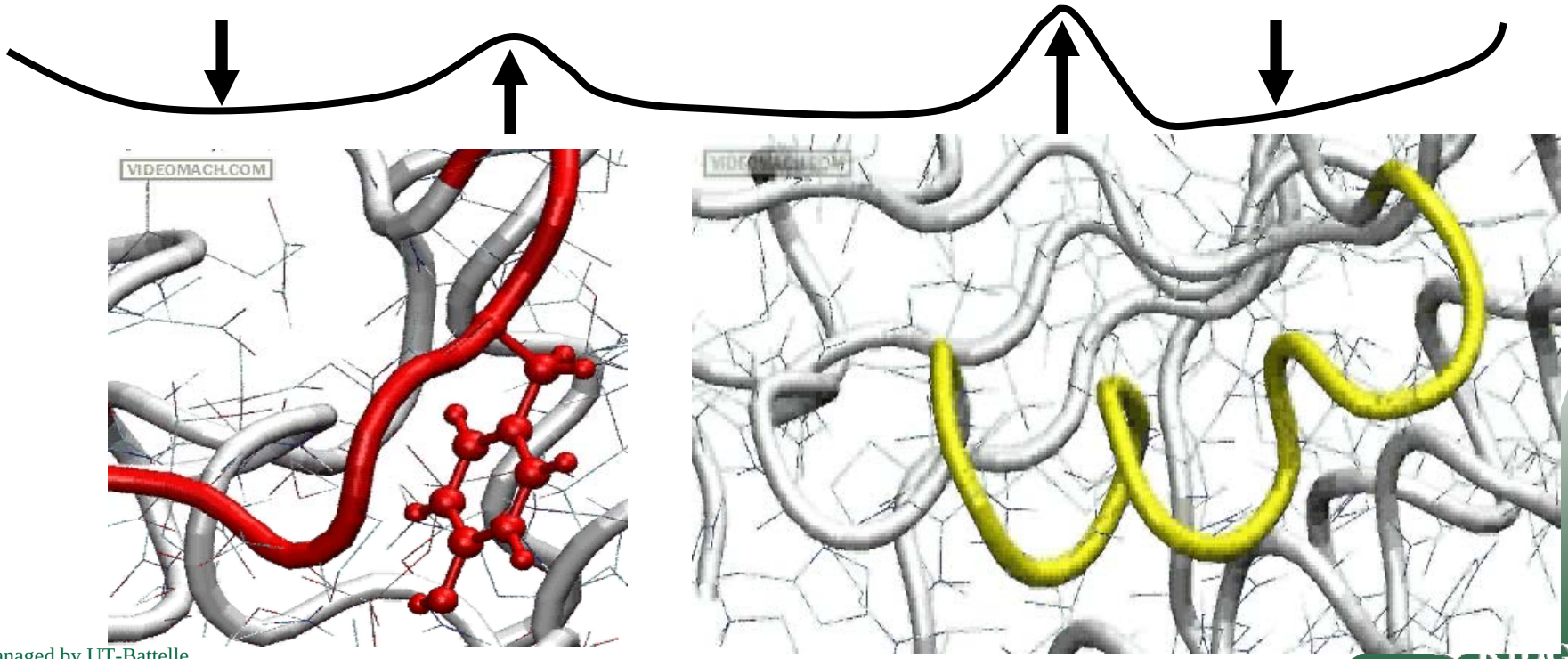
Ras Molecular Switch

ON - state

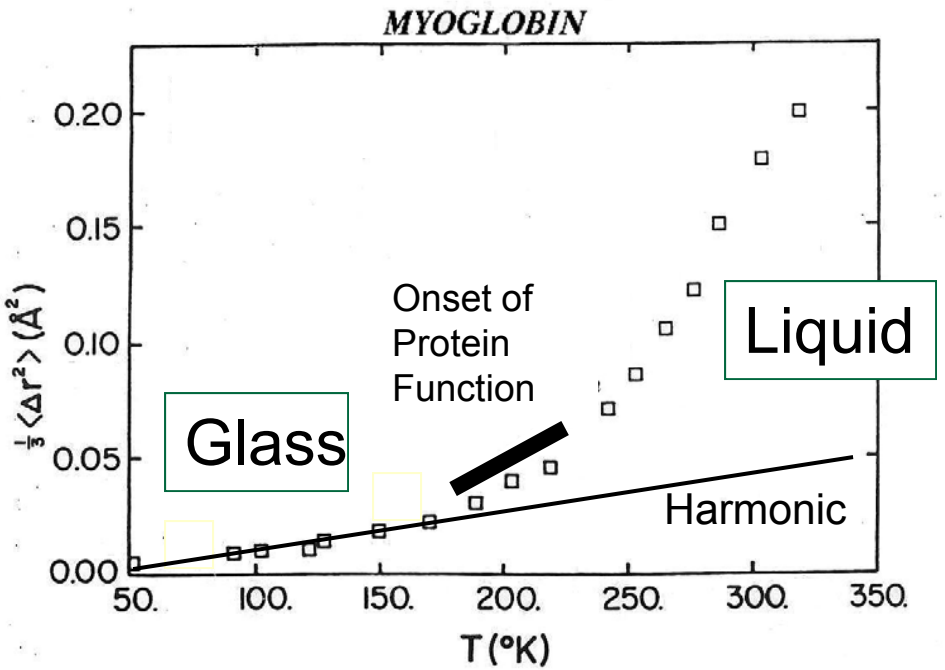


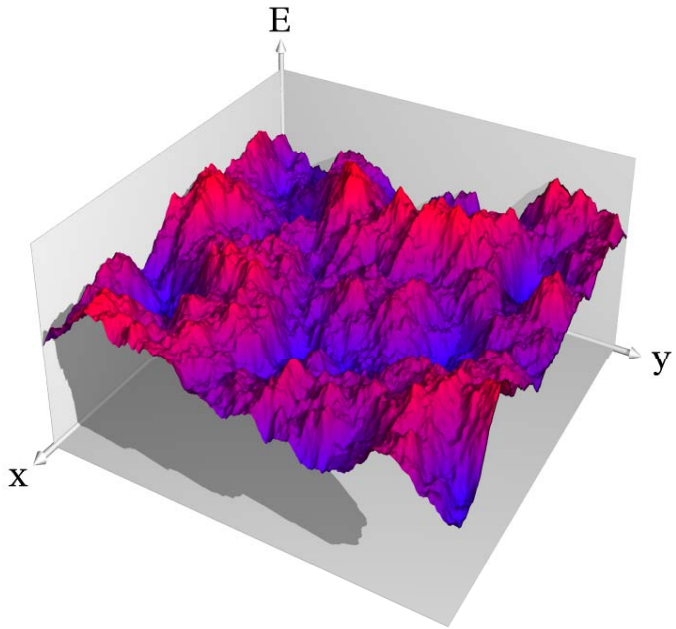
OFF - state





The Protein Glass Transition

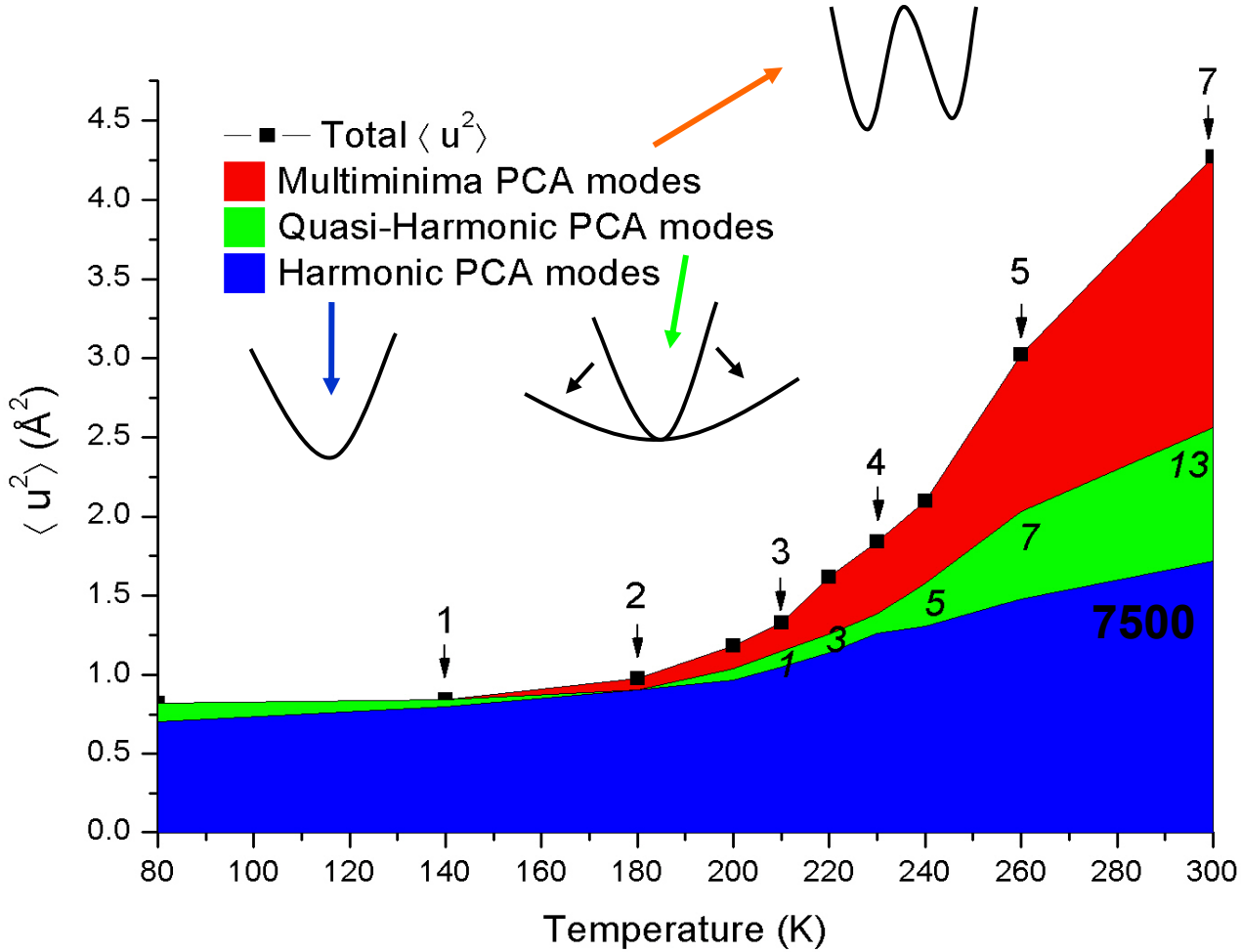




Principal Component Analysis of the Myoglobin Glass Transition

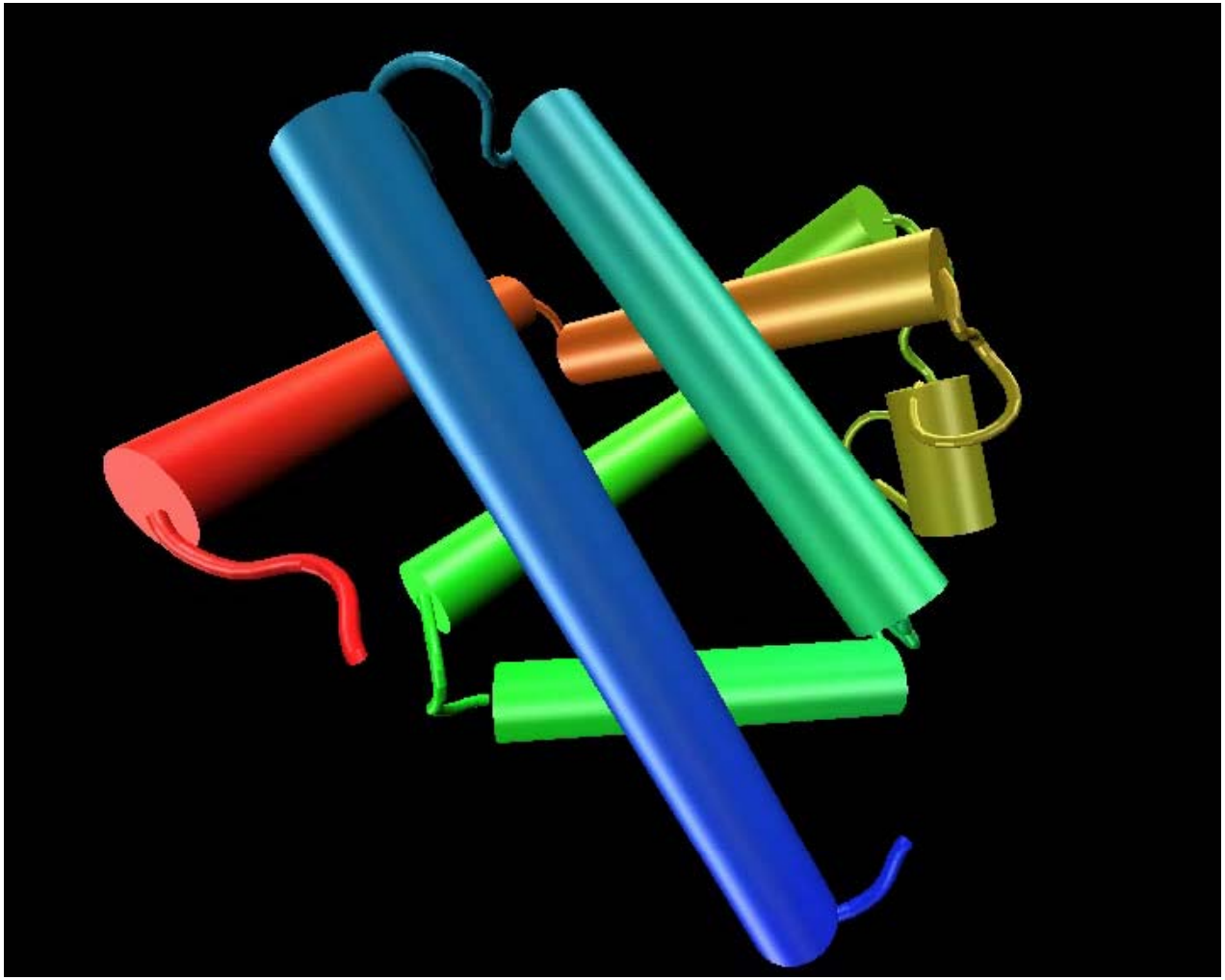
$$A_{ij} = \left\langle \left(r_i(t) - \bar{r}_i\right)\left(r_j(t) - \bar{r}_j\right)\right\rangle$$

ALEX TOURNIER



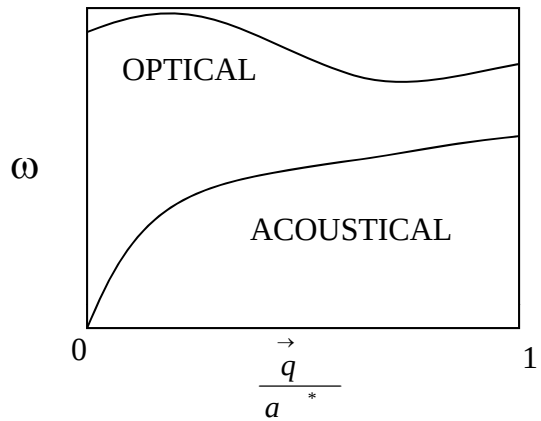
OAK RIDGE National Laboratory

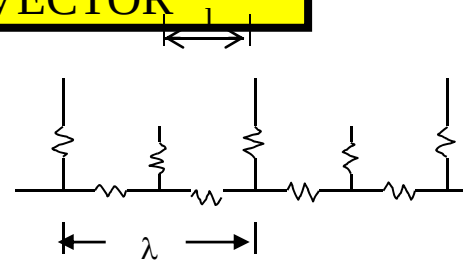
Mode Incipient at Myoglobin Glass Transition



Lattice Vibrations

- PERIODIC in TIME and SPACE.
- DISPERSION RELATIONSHIP between FREQUENCY and WAVEVECTOR

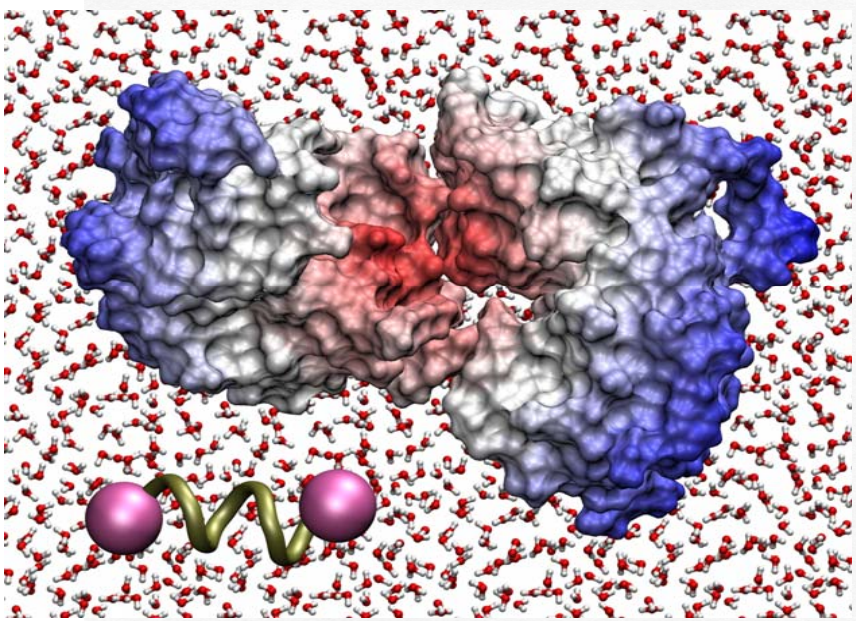


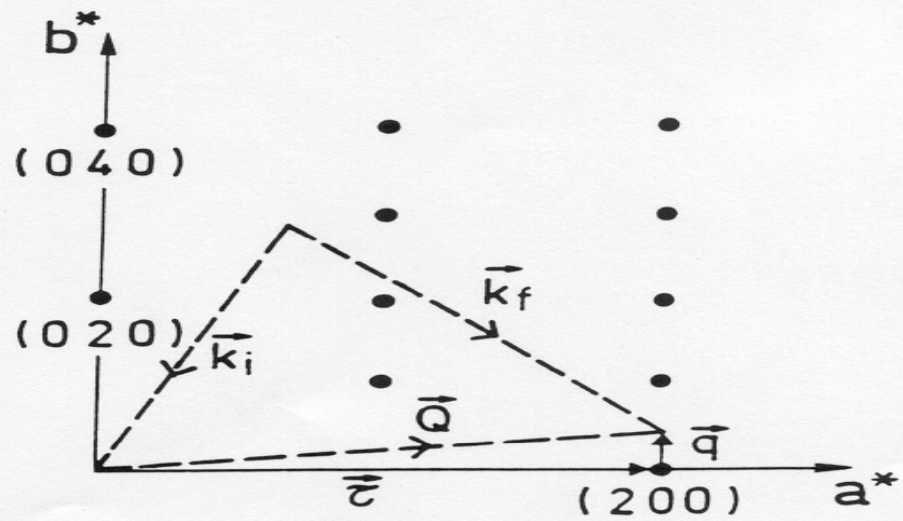


$\Theta = 180^o = \pi$

$\lambda = 2l$

$q = \pi / l$



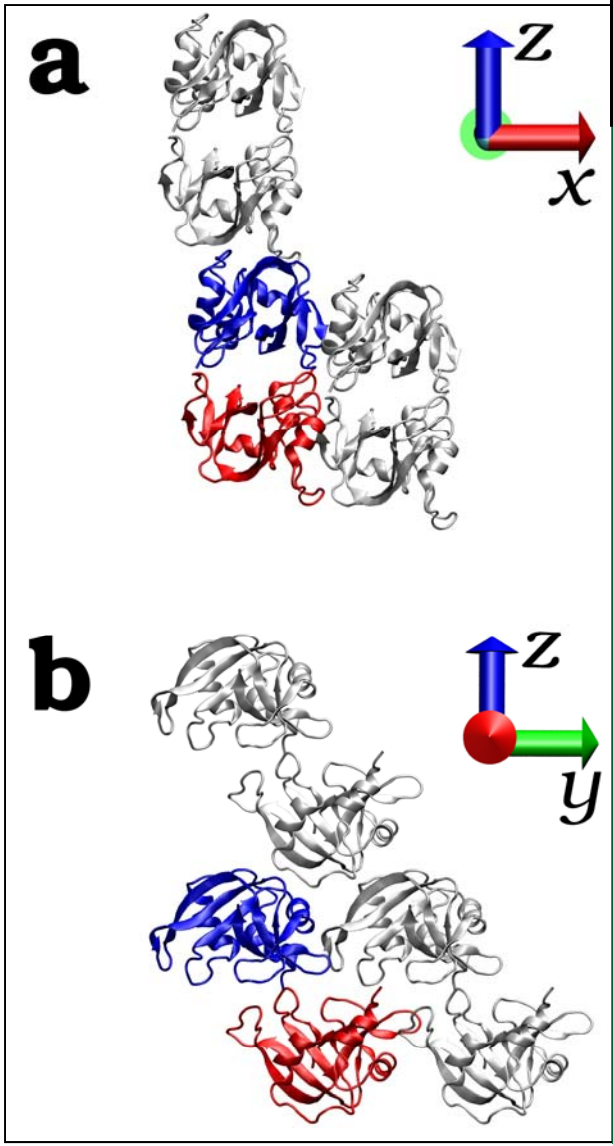


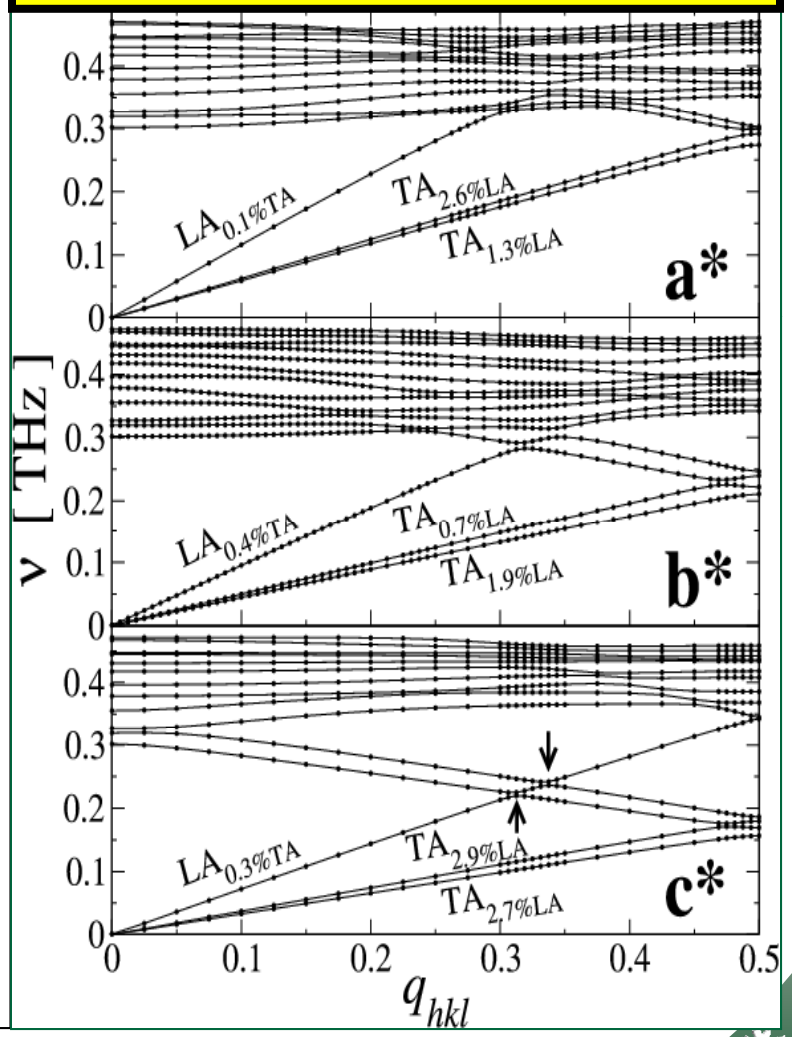
COHERENT INELASTIC NEUTRON SCATTERING

LARS MEINHOLD

Monoclinic Ribonuclease A:

Phonon Dispersion Relations





Co-workers

Alex Johs
Benjamin Lindner
Frank Noe
Hao-Bo Guo
Lars Meinhold
Thomas Neusius
Jerry Parks
Loukas Petridis
Roland Schulz
Sonja Schwarzl
Goundla Srinivas
Alex Tournier
Bjorn Windshuegel

Collaborators

Mark Gordon (Iowa State)
Barbara Evans, Dean Myles,
Xiaolin Cheng, Volker Urban,
William Heller, Hugh O'Neill,
Liyuan Liang (ORNL)
Stefan Fischer (U Heidelberg)
Anne Summers (U Georgia)
Sue Miller (UCSF)
Hong Guo (U Tenn)

Funding

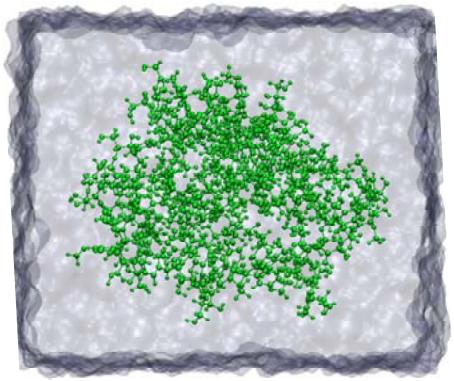
DOE OBER (Bioenergy Science Center,
ORNL Subsurface SFA,
ORNL Biofuels SFA,
ORNL LDRD)
ASCR/OBER SciDAC/GTL
BES EPSCOR.
DFG Sachbeihilfe
NSF SCALE-IT IGERT,
Biological Systems Cluster.

OAK RIDGE National Laboratory

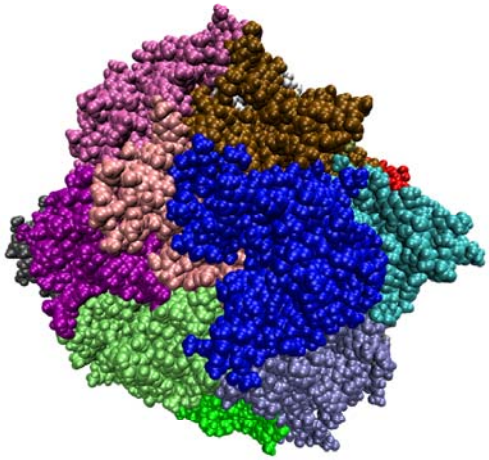
Models Based on Experimental Data

- bulk chemical composition
- linkage distribution
- degree of branching
- molecular weight
- no optical activity

25 distinct molecules



constrained to aggregate

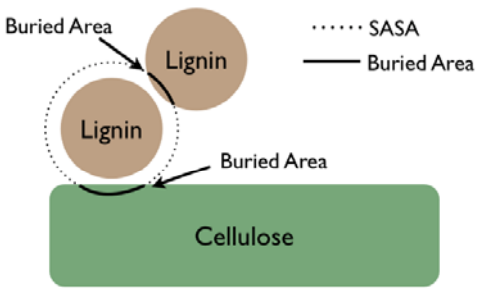


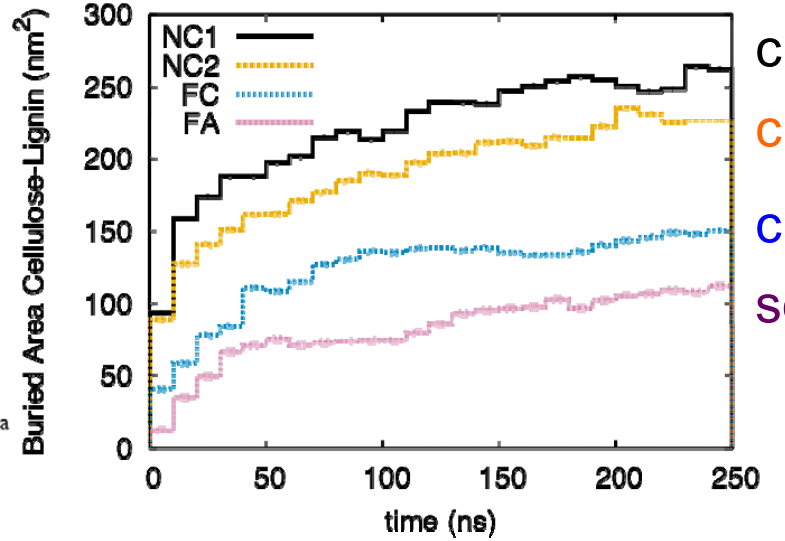
Interaction Potential*

Time-Evolution

Larger Contact Area for Crystalline and Concentrated Models

Lignin Precipitation onto Cellulose





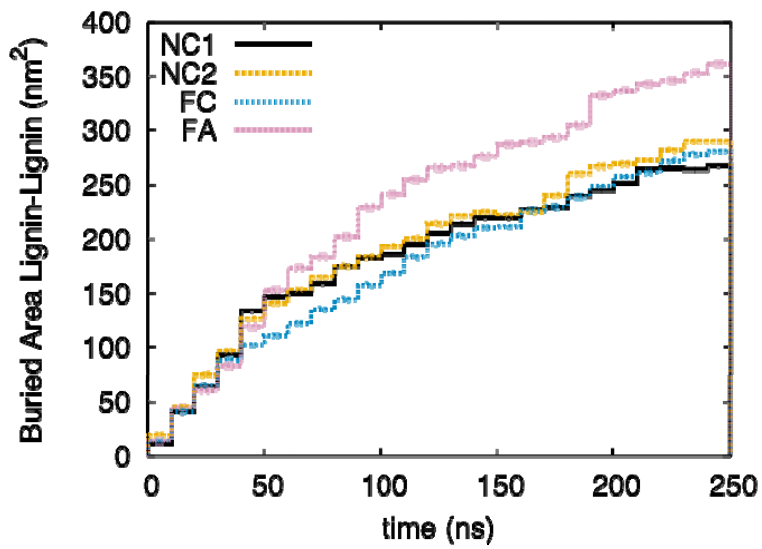
crystalline & concentrated I

crystalline & concentrated II

crystalline & dilute

semi-crystalline & dilute

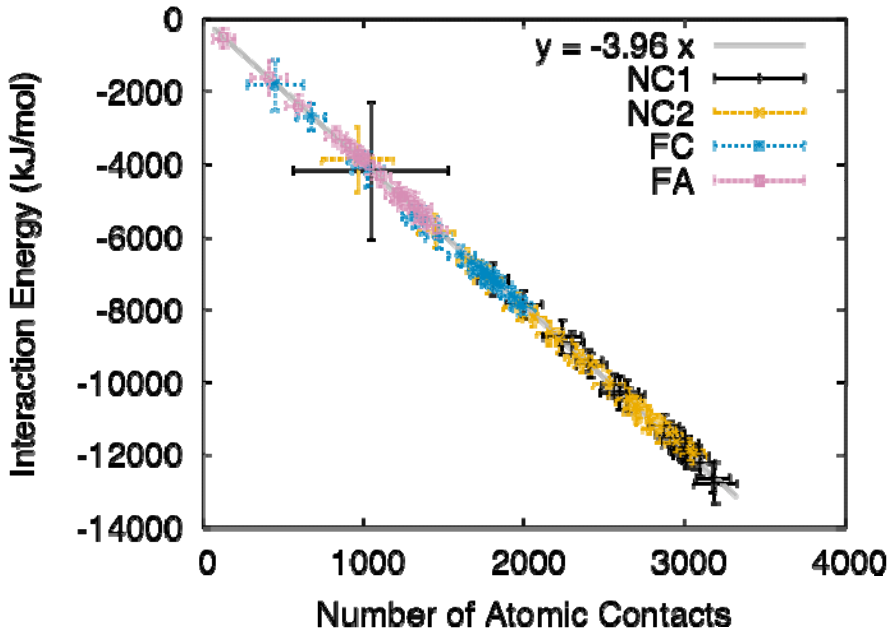
Lignin Aggregation



semi-crystalline & dilute

crystalline concentrated &dilute

Interaction Energies

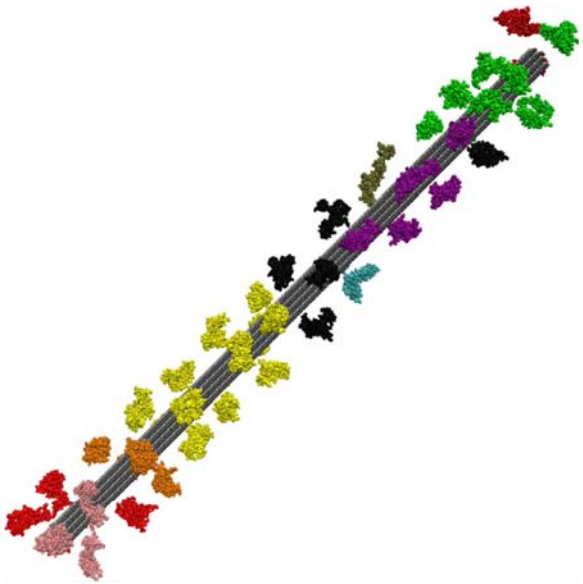


Cellulose:Lignin interaction energy is same for all models

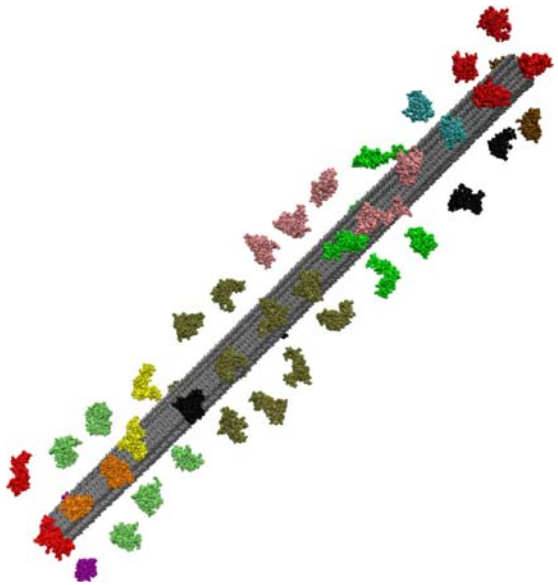
Interface	Interaction Energy Density
water : crystalline cellulose	-94 ±2 kJ/mol/nm^2
water : semi-crystalline cellulose	-107±2 kJ/mol/nm^2

Cellulose:Water interaction energy is more favorable for semi-crystalline cellulose

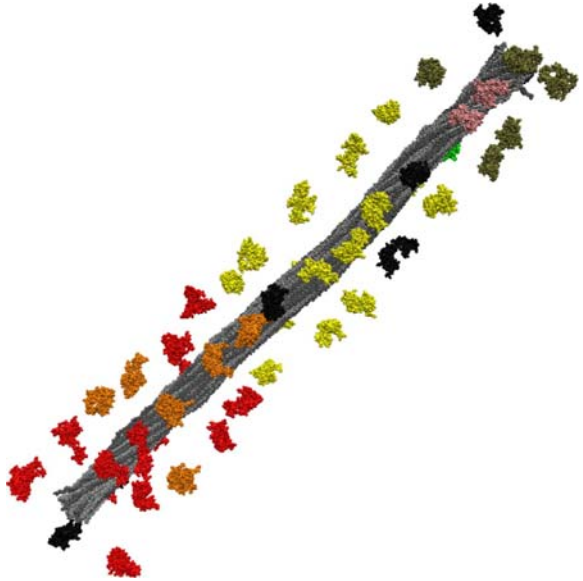
2. Factors Influencing Aggregation (?): Concentration & Cellulose Crystallinity



high concentration & crystalline cellulose (2 simulations)



low concentration & crystalline cellulose

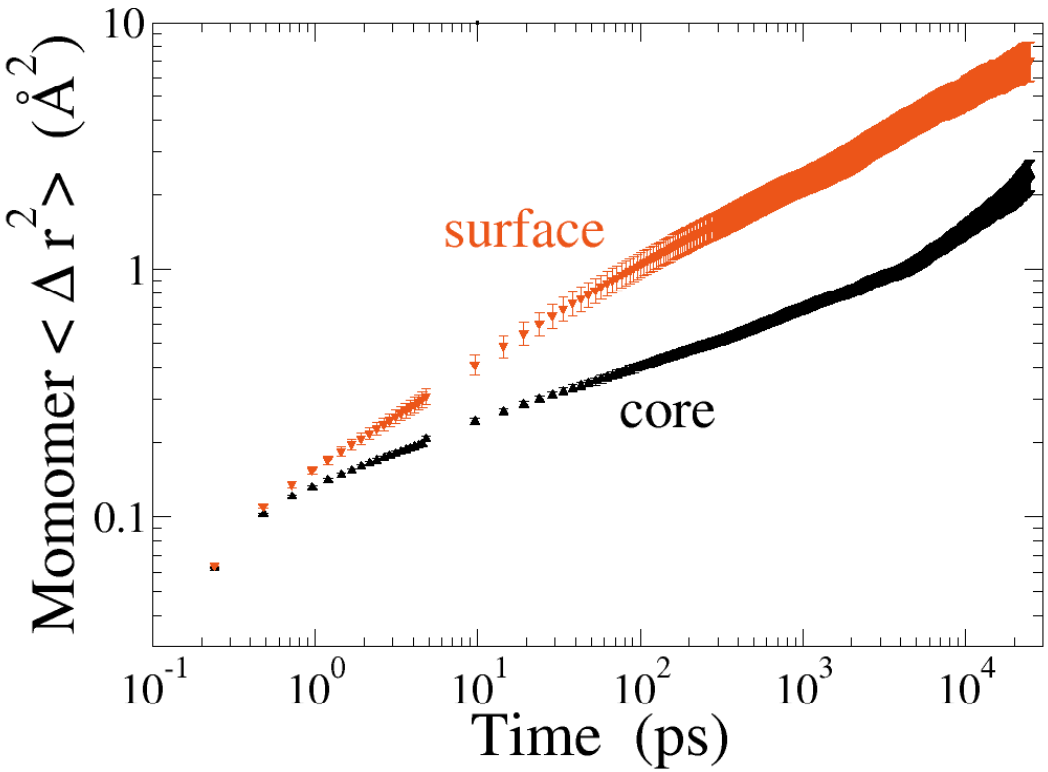


low concentration & semi- crystalline cellulose

4 Simulations

lignin:cellulose = 0.54:1.00, lignin molecules same in all simulations

Heterogeneous Chain Dynamics

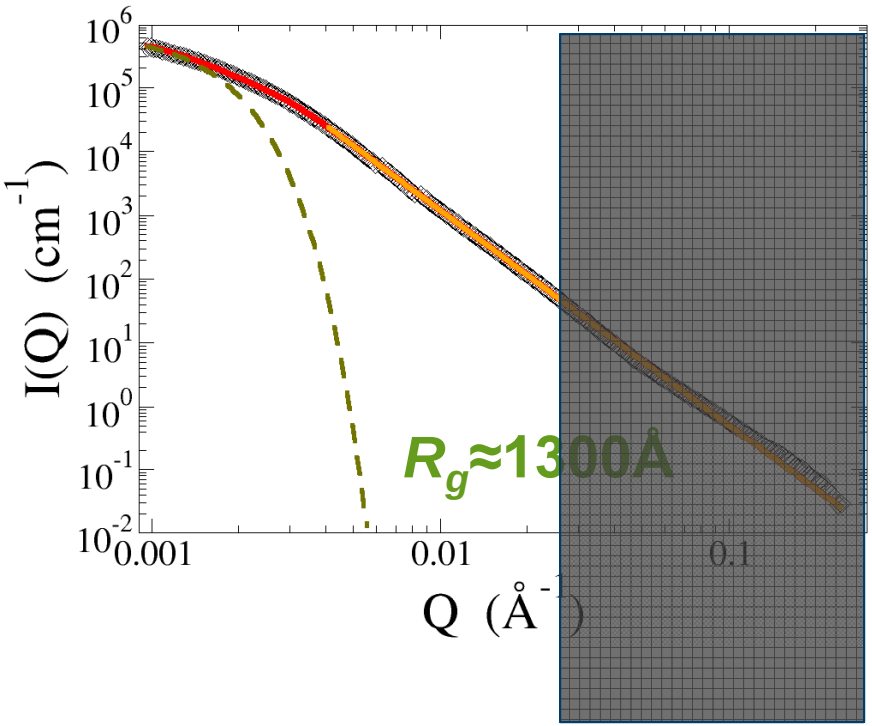


enhanced monomer mobility at the surface

nanoscopic lignins have reduced T_g

SANS&MD: Highly-Folded Self-Similar Surface

SANS

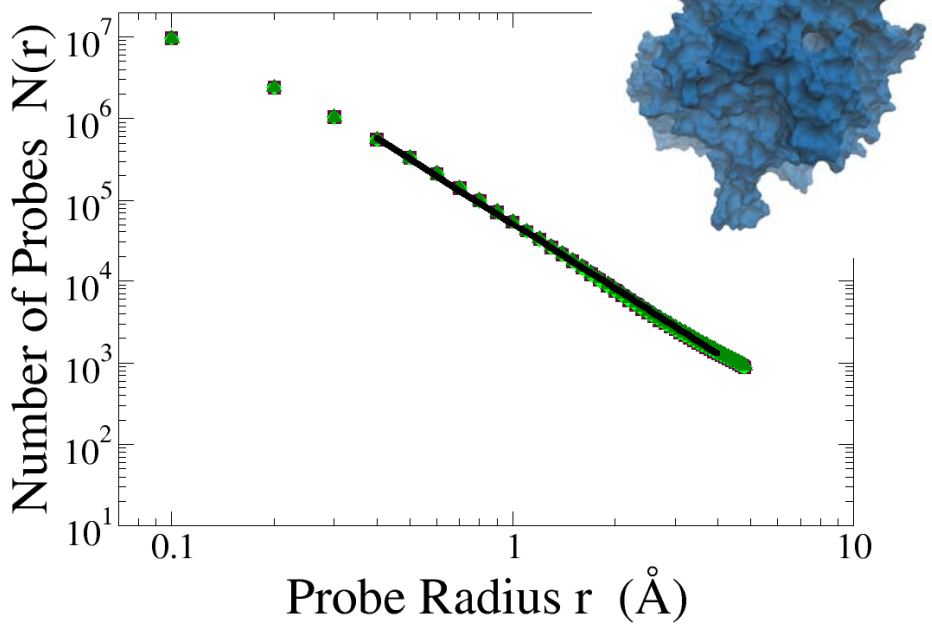


overlap
SANS-MD

D_{aggr}=130Å

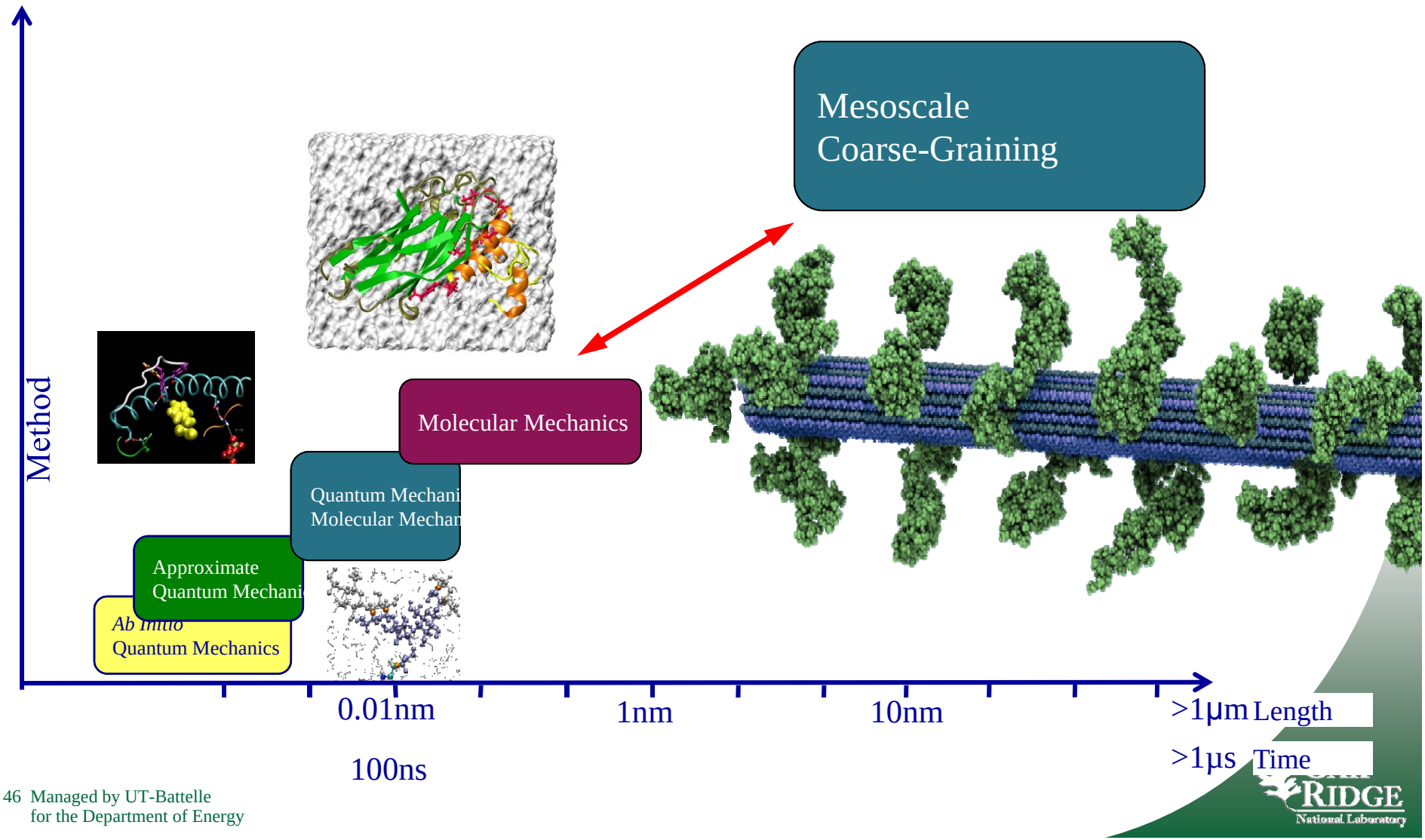
r

MD



Center for Molecular Biophysics

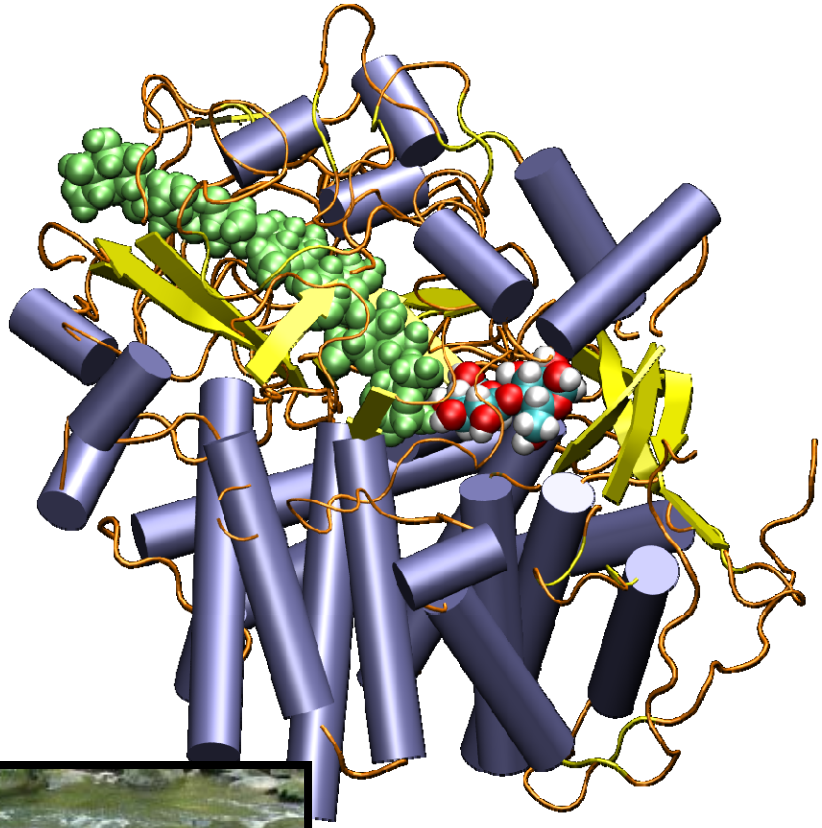
Multiscaling

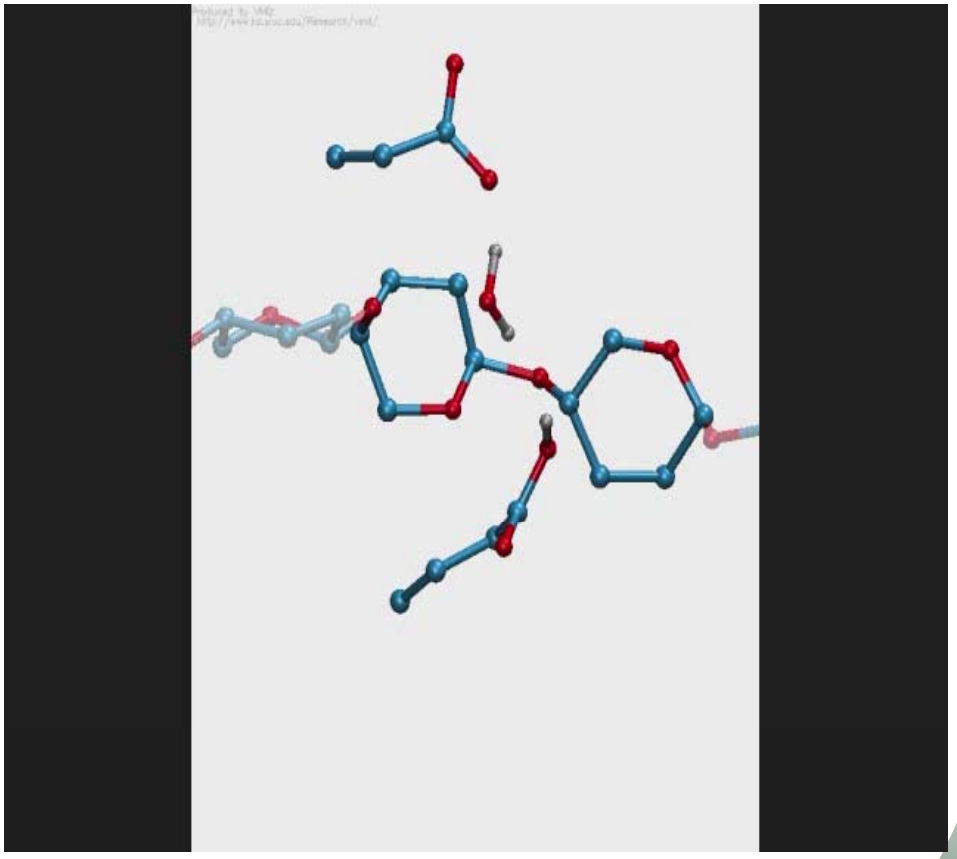


Center for Molecular Biophysics

Catalytic Mechanism of Cellulase *CelS*

Oak Ridge National Laboratory





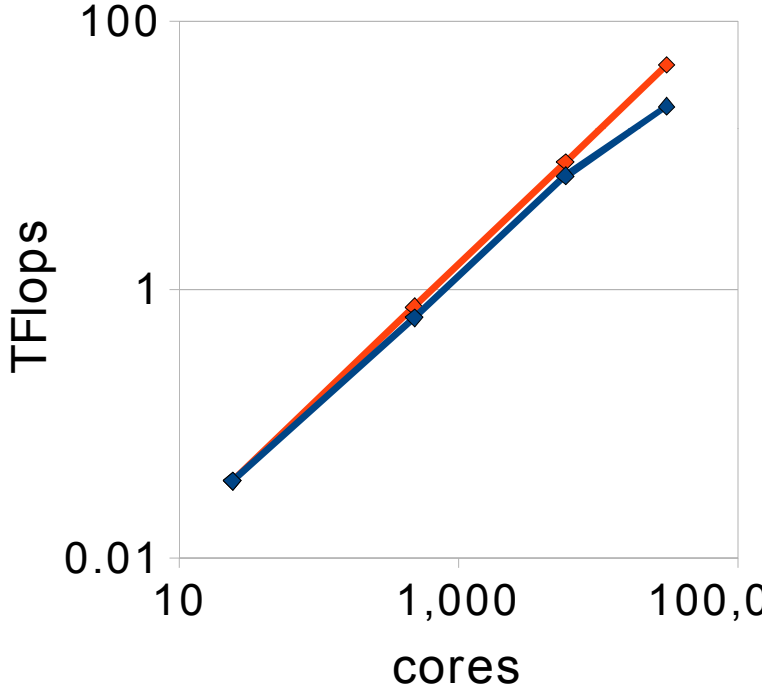
MOUMITA SAHARAY

Oak Ridge National Laboratory

Molecular Dynamics Scaling

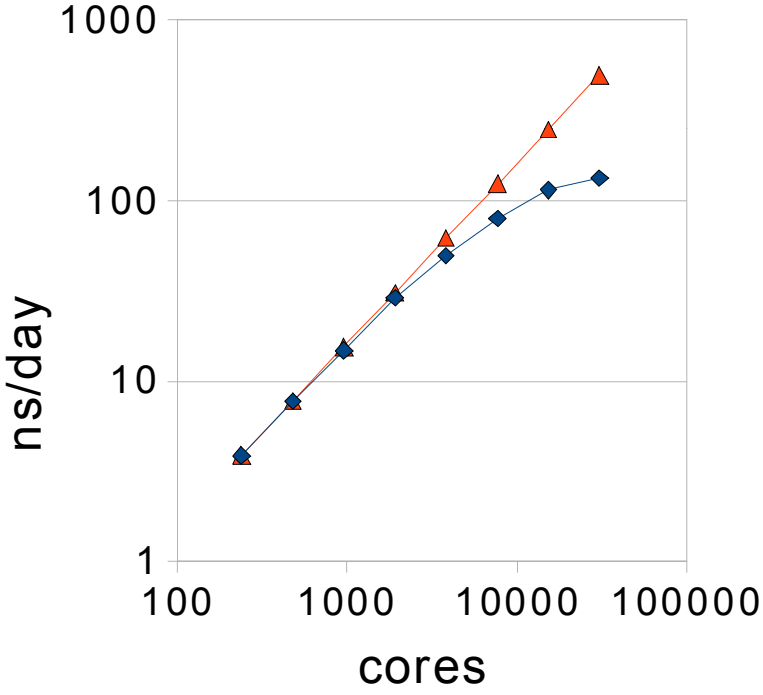
Weak Scaling

175 atoms/core



Strong Scaling

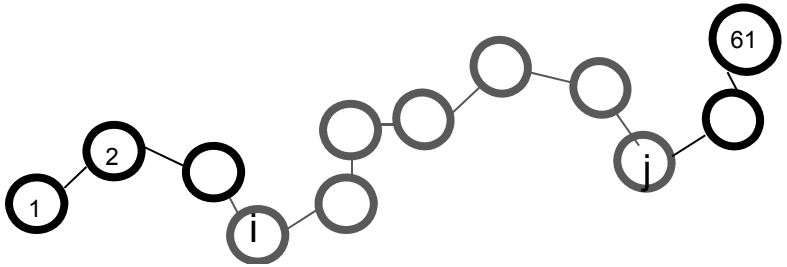
5.4 million atoms

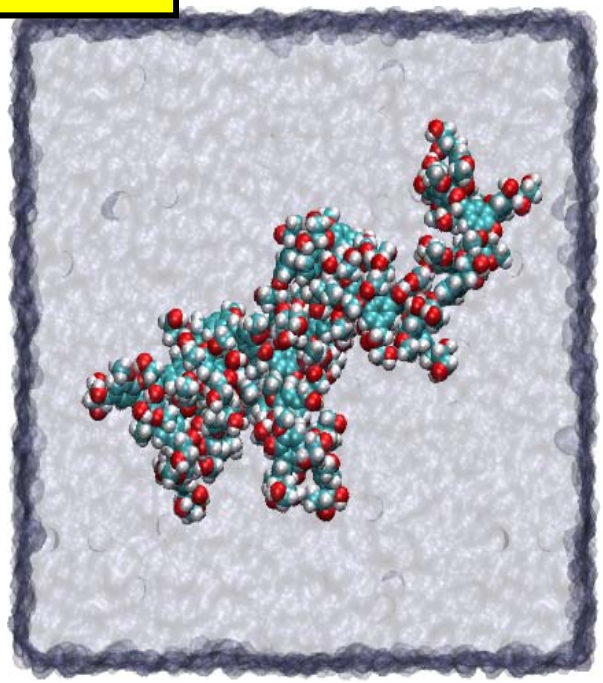


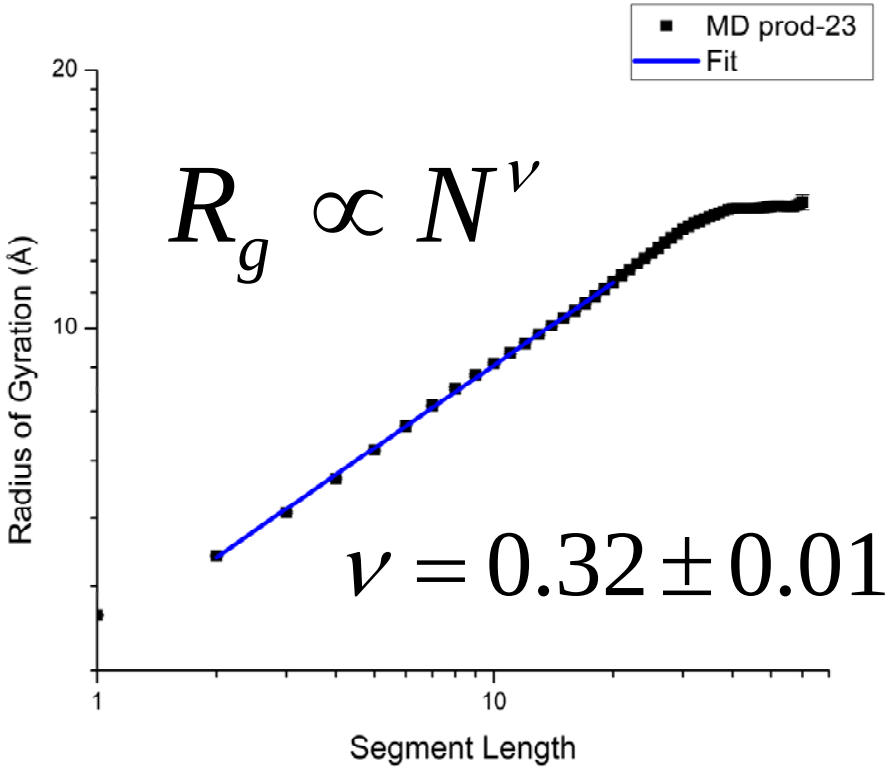
LOUKAS PETRIDIS

Lignin

R_g=Segment Radius of Gyration

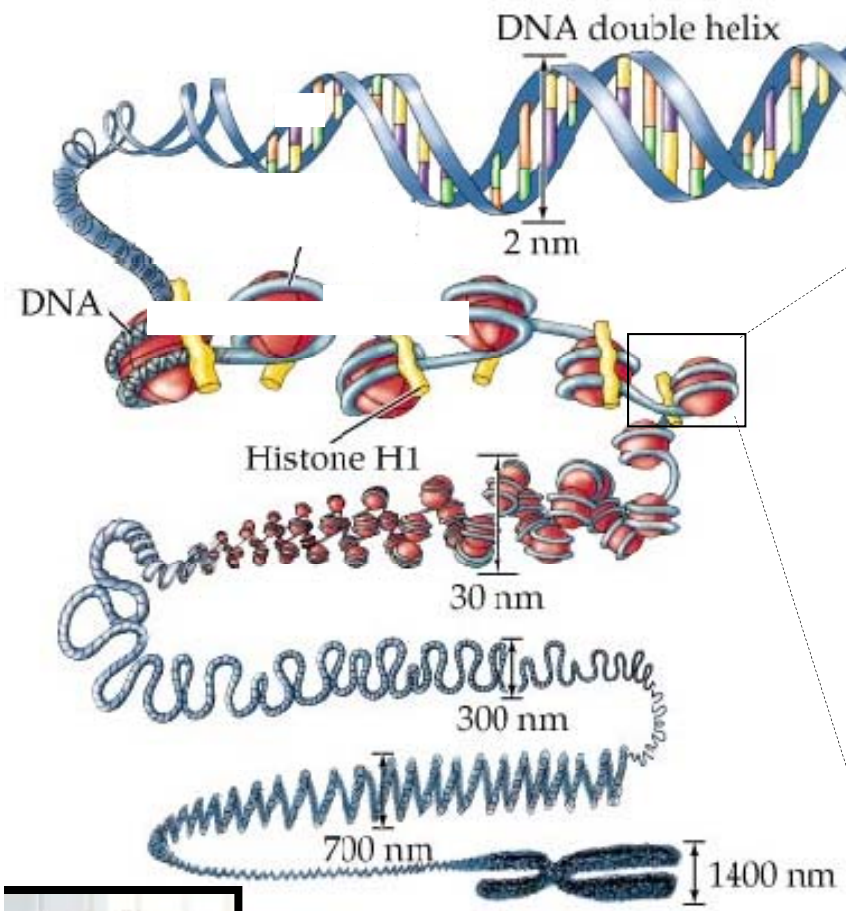


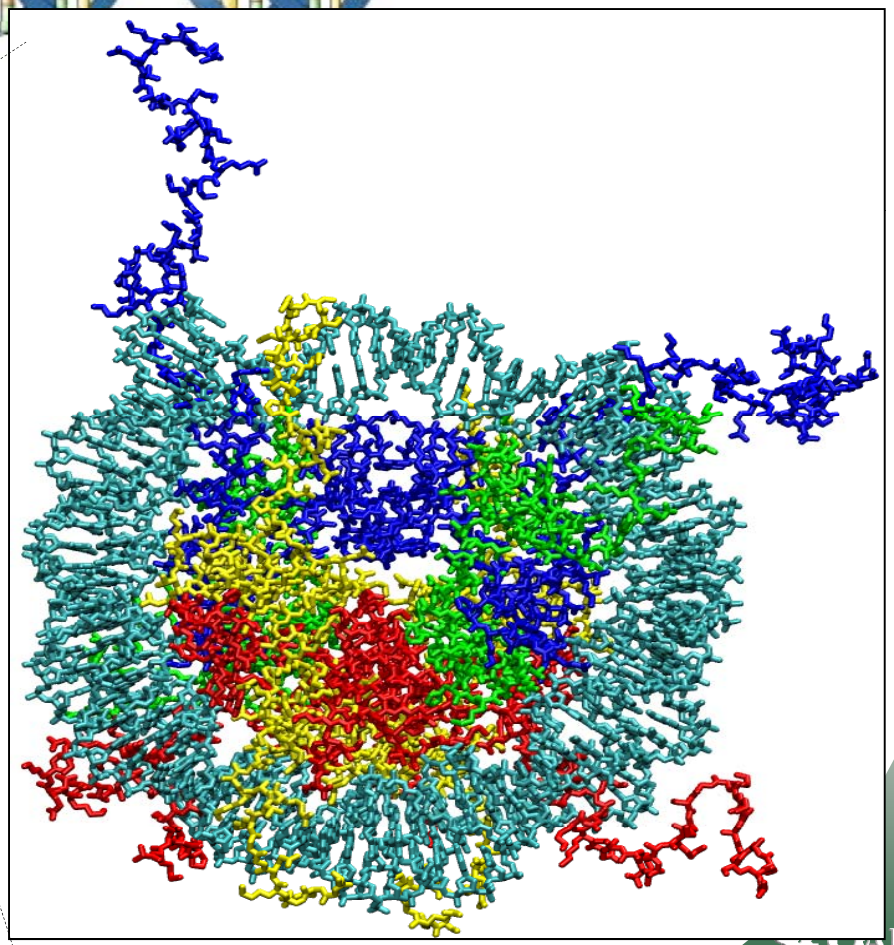




Center for Molecular Biophysics

The Nucleosome



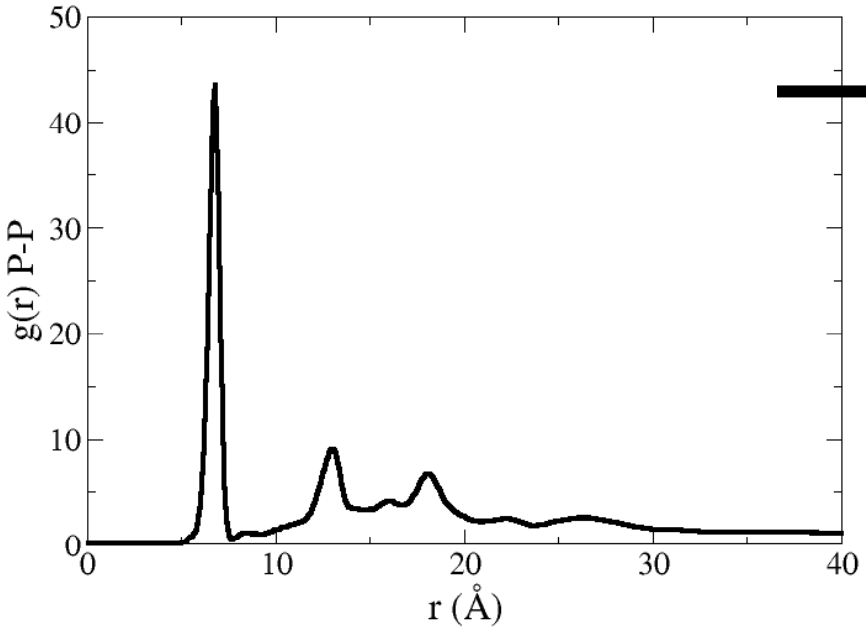


Karine Voltz

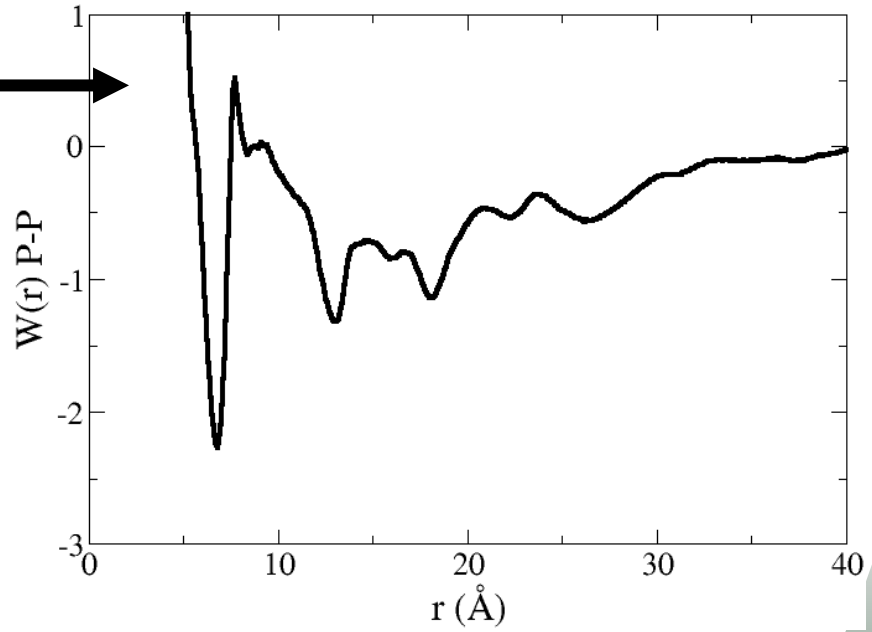
Oak Ridge National Laboratory

Boltzmann Inversion

Radial Distribution Function, g(r)



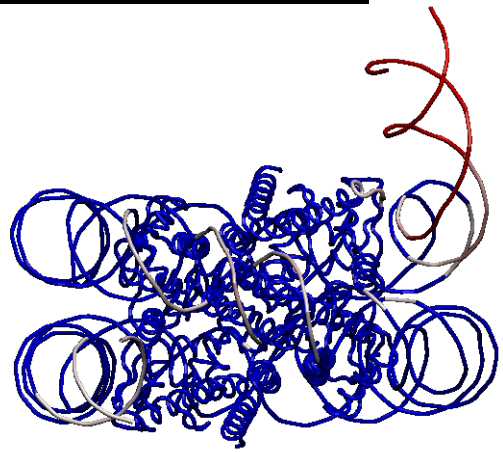
Boltzmann Inverse, W(r)

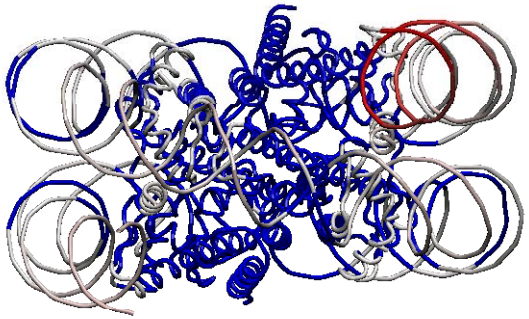


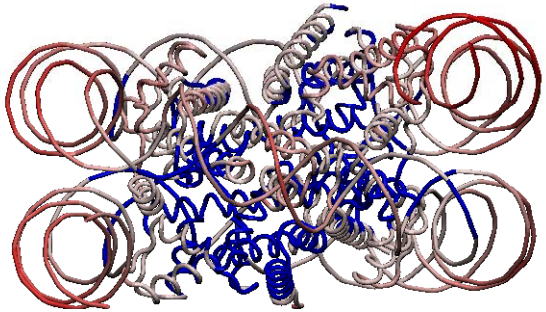
$$W(r) = -k_B T \ln g(r)$$

Center for Molecular Biophysics

Microsecond Dynamics



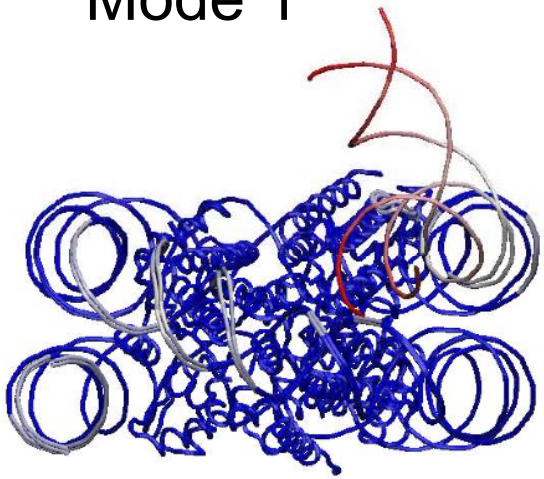


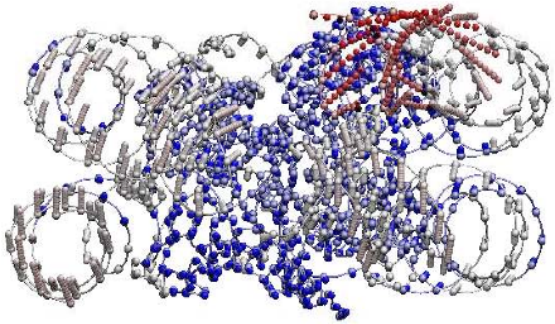


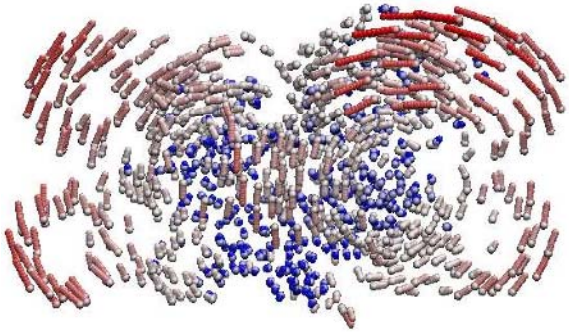
Mode 1

Mode 2

Mode 3







detachment perpendicular to nucleosome plane

detachment parallel to the nucleosome plane

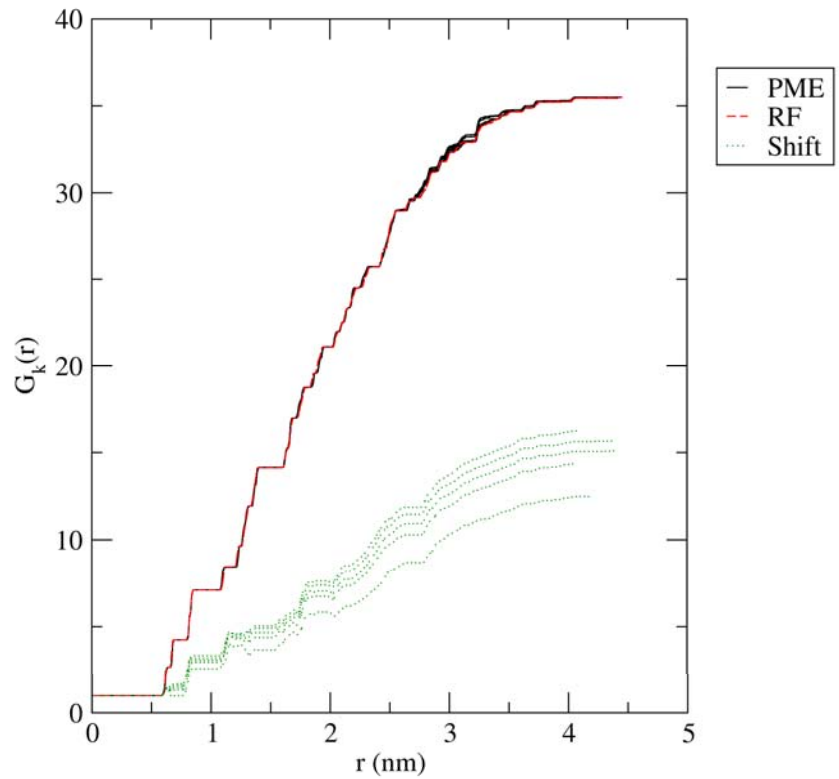
scissor motion

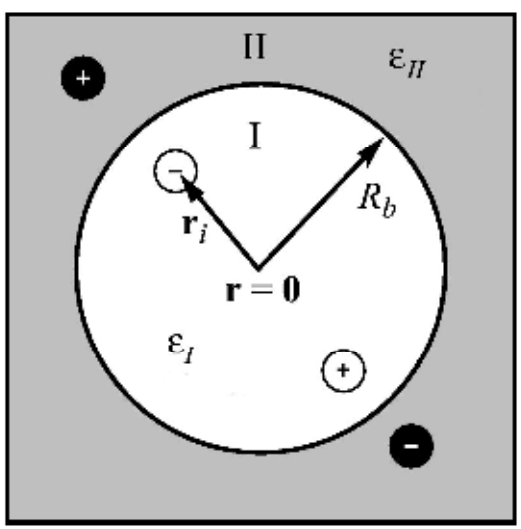
Oak Ridge National Laboratory

Electrostatics

Kirkwood G Factor $G_k(r) = \sum_{r_{ij}<r} \frac{\boldsymbol{\mu}_i \cdot \boldsymbol{\mu}_j}{\mu^2}$

1. Shift Truncation (fast, not accurate)
2. Particle Mesh Ewald (slow, accurate)
3. Reaction Field (fast, accurate?)

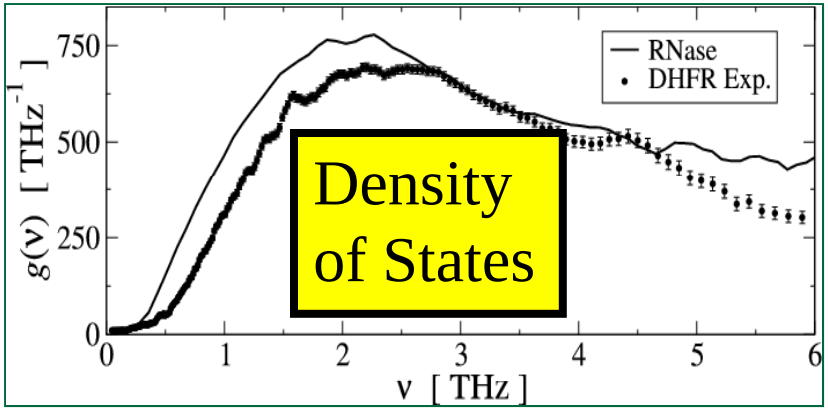


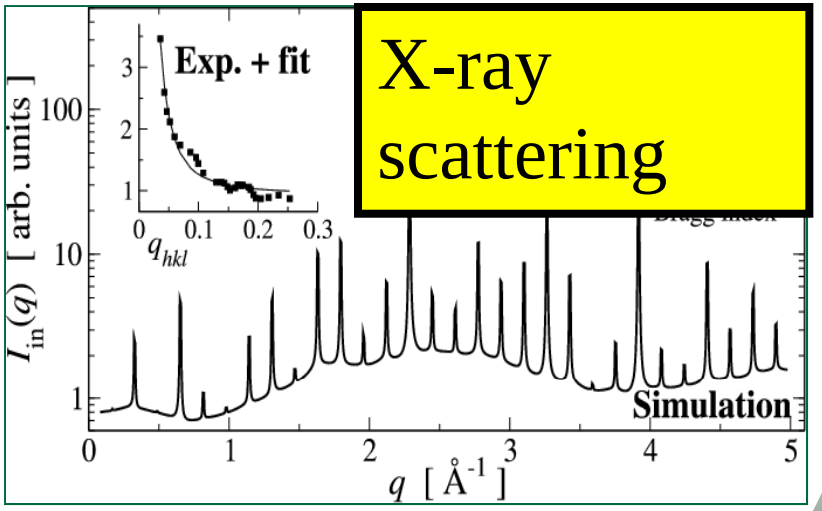


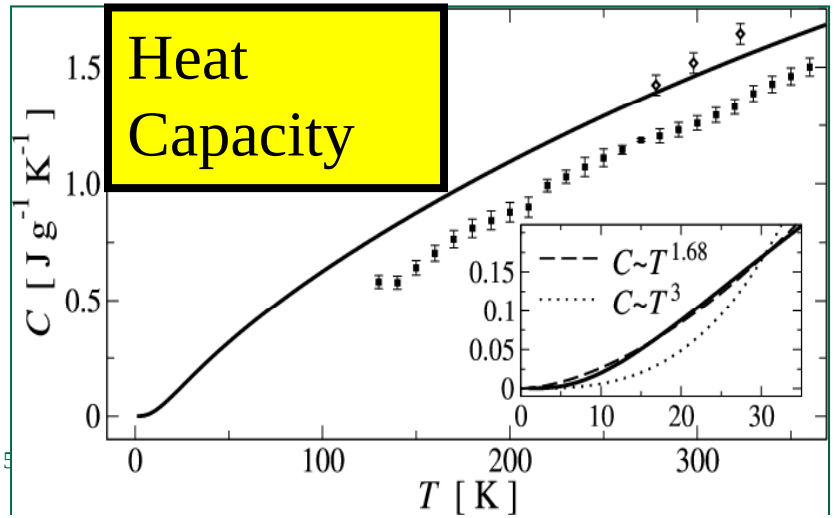
- RF cuts simulation time to ≈1/3 cf PME (10k cores)
- RF improves scaling

Monoclinic Ribonuclease A

LARS MEINHOLD

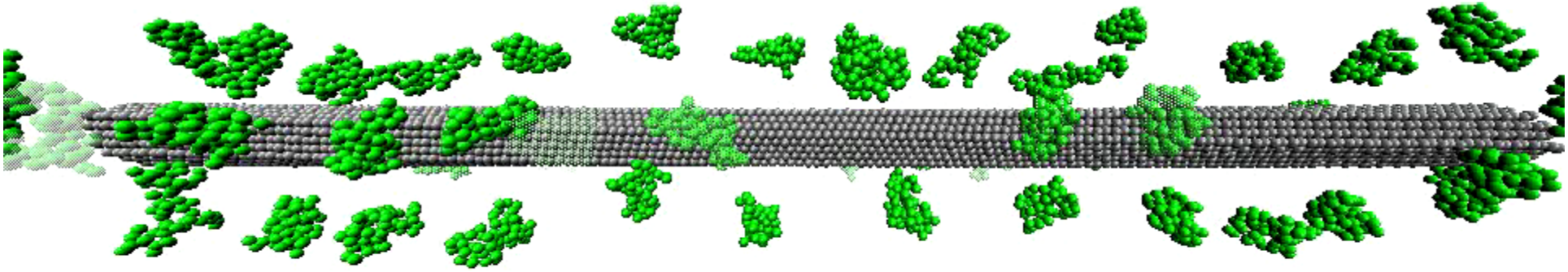




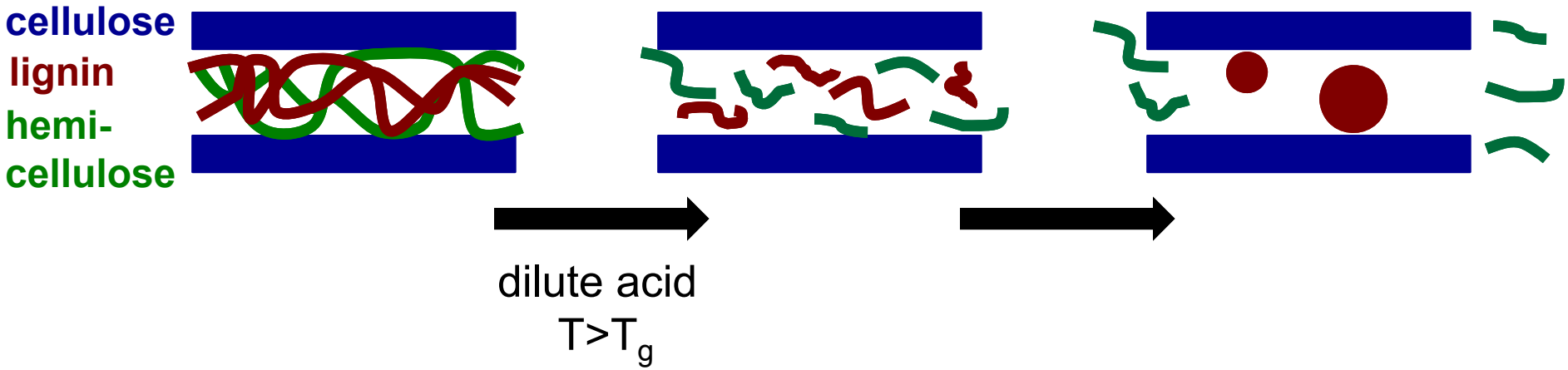


Lignin Precipitation on Cellulose

BENJAMIN LINDNER



Lignin Aggregation *after* Pretreatment

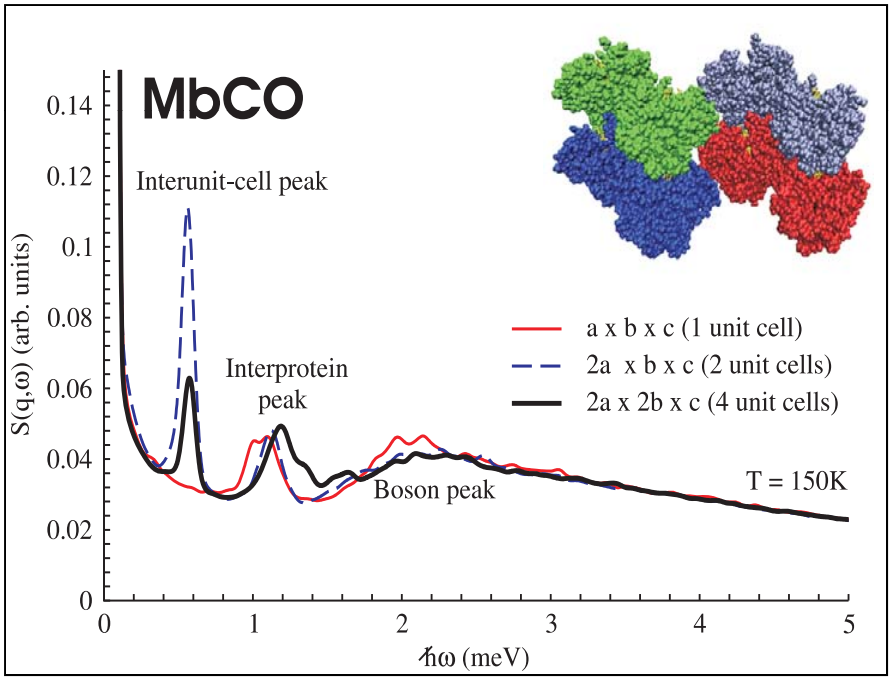


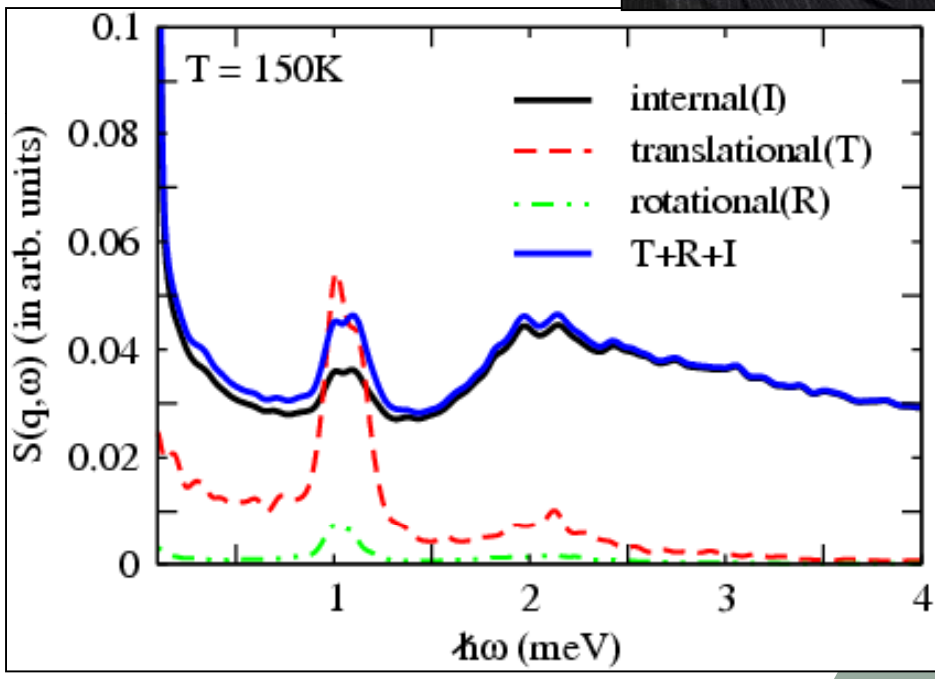
Inhibitory effect of lignin is determined by

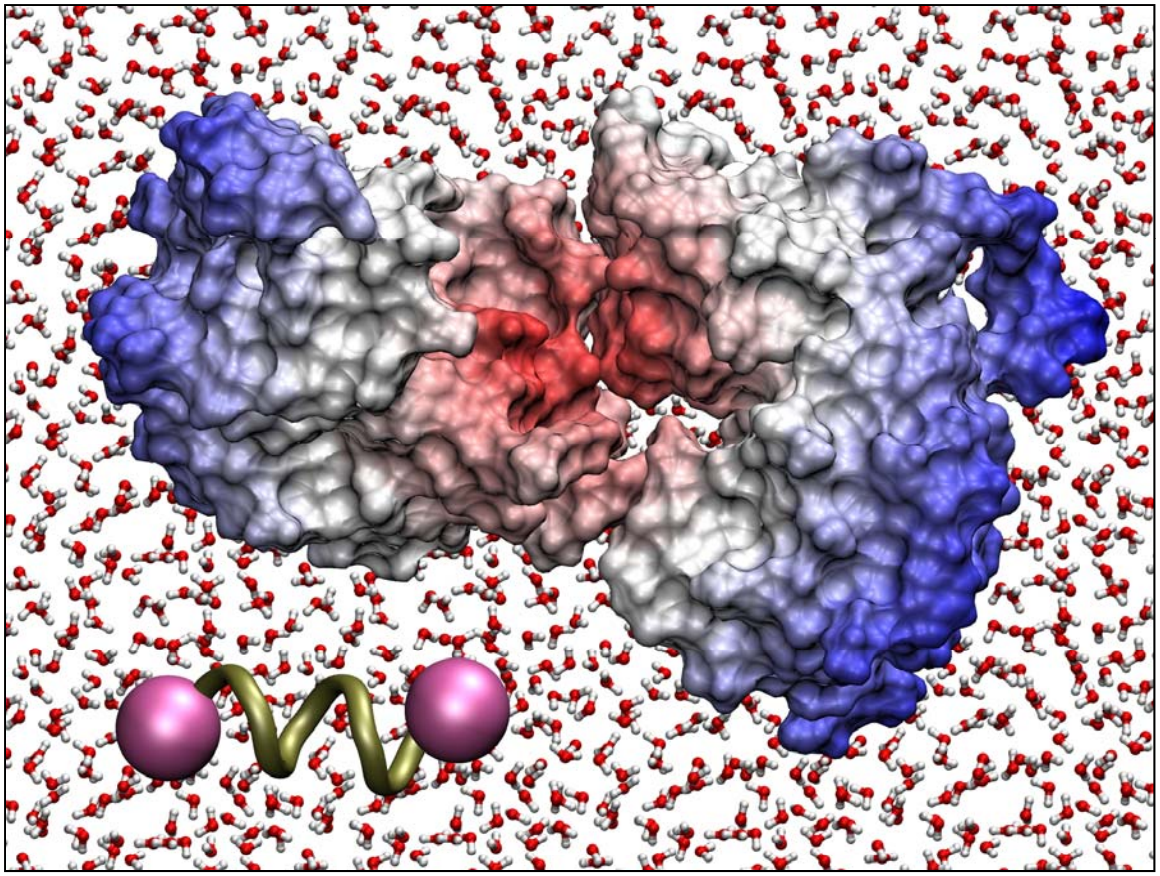
1. Structure of the aggregates
2. Factors influencing Lignin re-precipitation on cellulose

Molecular Dynamics Simulation of Protein:Protein Interactions at 150K

VANDANA KURKAL-SIEBERT





PRL 100 138102 (2008)

Protein:Protein Interactions