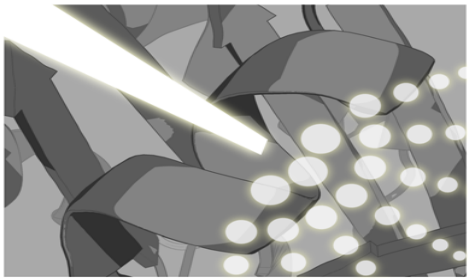
Oak Ridge National Laboratory

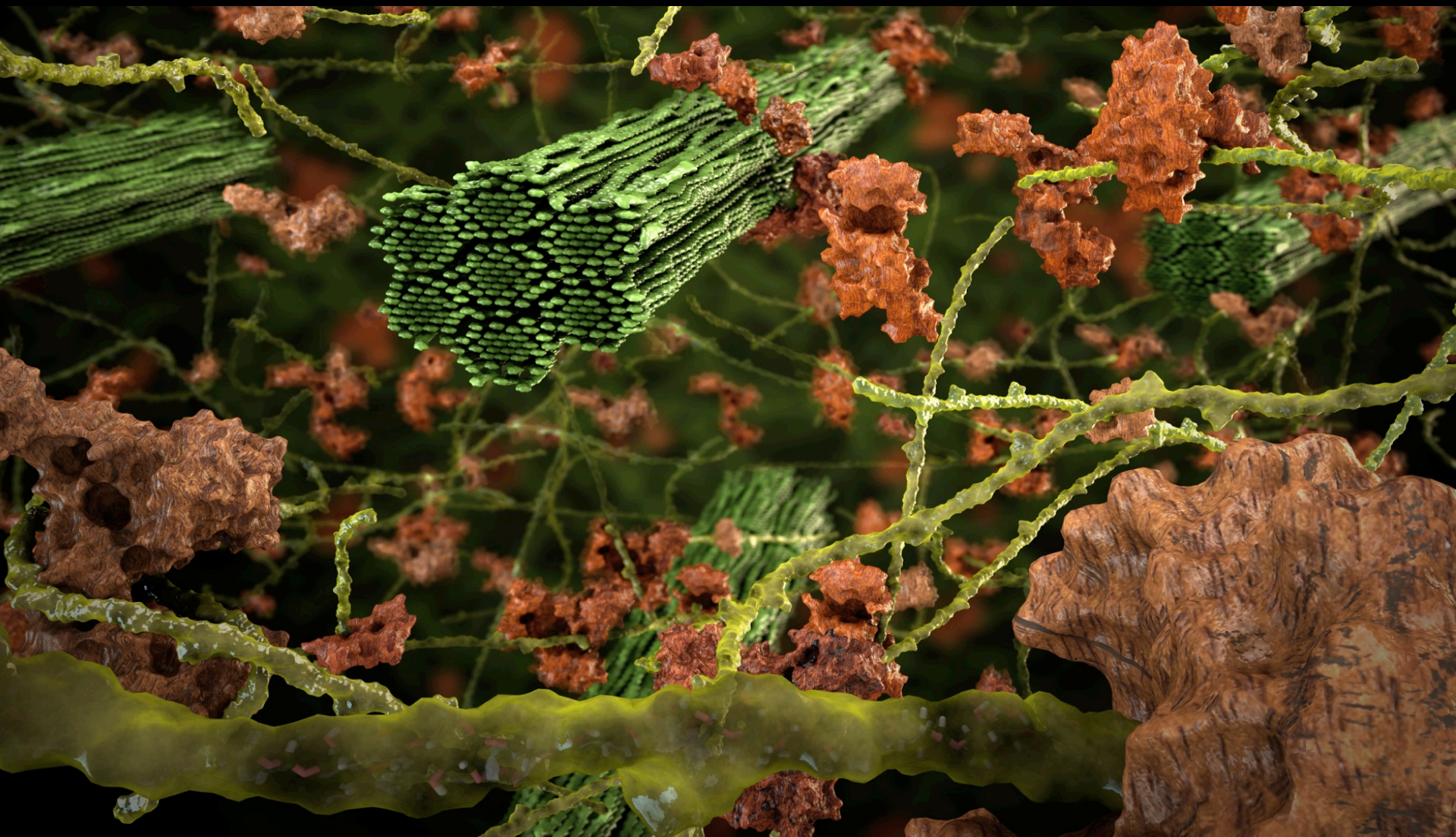
Managed by UT-Battelle for the Department of Energy

University of Tennessee



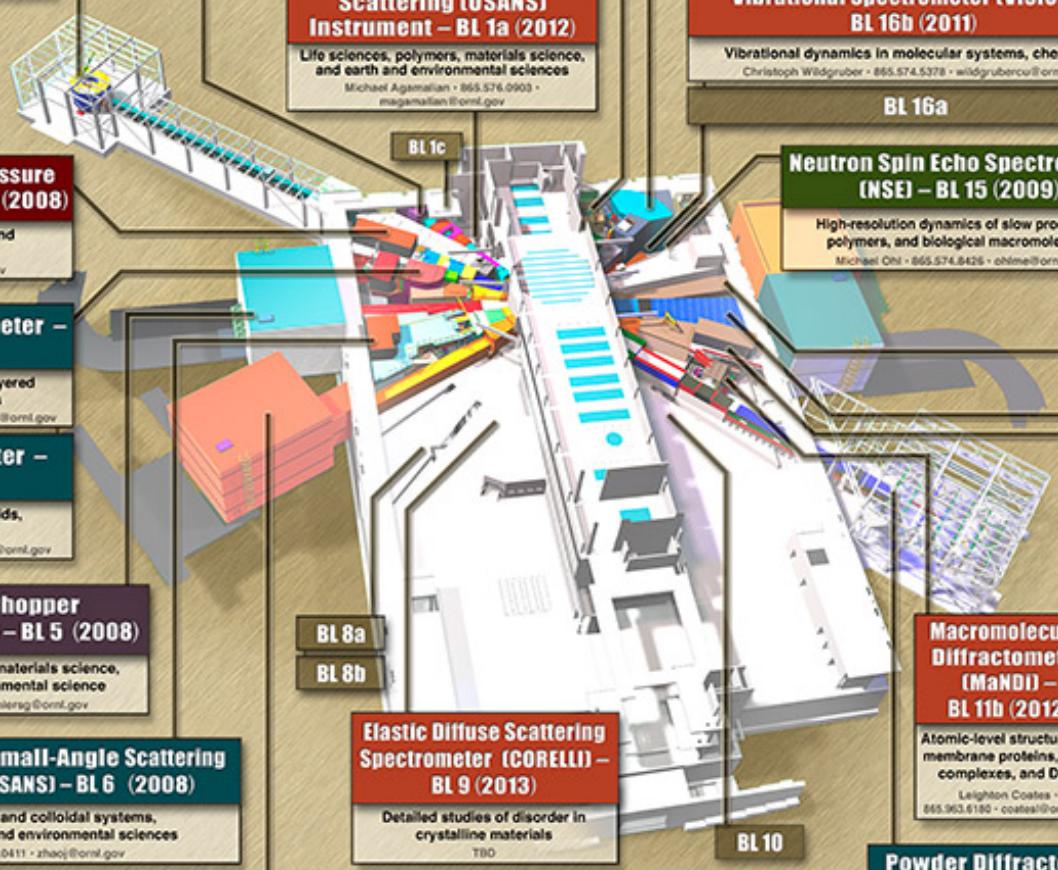
ORNL

Center for Molecular Biophysics



OAK RIDGE
National Laboratory

Spallation Neutron Source



Backscattering Spectrometer (BASIS) – BL 2 (2006*)
Dynamics of macromolecules, constrained molecular systems, polymers, biology, chemistry, materials science
Eugene Mamontov · 865.574-5109 · mamontove@ornl.gov

Nanoscale-Ordered Materials Diffractometer (NOMAD) – BL 1b (2010)
Liquids, solutions, glasses, polymers, nanocrystalline and partially ordered complex materials
Joerg Neuefeind · 865.241.1635 · neuefeindjc@ornl.gov

Wide Angular-Range Chopper Spectrometer (ARCS) – BL 18 (2007)
Atomic-level dynamics in materials science, chemistry, condensed matter sciences
Doug Abernathy · 865.576.5105 · abernathydl@ornl.gov

Fine-Resolution Fermi Chopper Spectrometer (SEQUOIA) – BL 17 (2008)
Dynamics of complex fluids, quantum fluids, magnetism, condensed matter, materials science
Garrett Granroth · 865.576.0900 · granrothge@ornl.gov

Ultrasmall-Angle Neutron Scattering (USANS) Instrument – BL 1a (2012)
Life sciences, polymers, materials science, and earth and environmental sciences
Michael Agamalian · 865.576.0903 · magamalian@ornl.gov

Vibrational Spectrometer (VISION) – BL 16b (2011)
Vibrational dynamics in molecular systems, chemistry
Christoph Wildgruber · 865.574.5378 · wildgrubercu@ornl.gov

BL 16a

BL 1c

Spallation Neutrons and Pressure Diffractometer (SNAP) – BL 3 (2008)
Materials science, geology, earth and environmental sciences
Chris Tulk · 865.576.7028 · tulkca@ornl.gov

Neutron Spin Echo Spectrometer (NSE) – BL 15 (2009)
High-resolution dynamics of slow processes, polymers, and biological macromolecules
Michael Ohl · 865.574.8426 · ohlme@ornl.gov

Hybrid Chopper Spectrometer (HYSPEC) – BL 14B (2011)
Atomic-level dynamics in single crystals, magnetism, condensed matter sciences
Mark Hagen · 865.241.9782 · hagenme@ornl.gov

BL 14a

Magnetism Reflectometer – BL 4a (2006)
Chemistry, magnetism of layered systems and interfaces
Haile Ambaye · 865.574.9096 · ambayeh@ornl.gov

Liquids Reflectometer – BL 4b (2006)
Interfaces in complex fluids, polymers, chemistry
John Ankner · 865.576.5122 · ankner@ornl.gov

Fundamental Physics Beam Line – BL 13 (2008)
Fundamental properties of neutrons
Geoffrey Greene · 865.574.8435 · greenegl@ornl.gov

Single-Crystal Diffractometer (TOPAZ) – BL 12 (2009)
Atomic-level structures in chemistry, biology, earth science, materials science, condensed matter physics
Christina Hoffmann · 865.576.5127 · hoffmanncm@ornl.gov

Cold Neutron Chopper Spectrometer (CNCS) – BL 5 (2008)
Condensed matter physics, materials science, chemistry, biology, environmental science
Georg Ehlers · 865.576.3511 · ehlersg@ornl.gov

BL 8a

BL 8b

Macromolecular Diffractometer (MaNDi) – BL 11b (2012)
Atomic-level structures of membrane proteins, drug complexes, and DNA
Leighton Coates · 865.963.6180 · coatesl@ornl.gov

Extended Q-Range Small-Angle Scattering Diffractometer (EQ-SANS) – BL 6 (2008)
Life science, polymer and colloidal systems, materials science, earth and environmental sciences
Jinkui Zhao · 864.574.0411 · zhaoj@ornl.gov

Elastic Diffuse Scattering Spectrometer (CORELLI) – BL 9 (2013)
Detailed studies of disorder in crystalline materials
TBD

BL 10

Powder Diffractometer (POWGEN) – BL 11a (2008)
Atomic-level structures in magnetism, chemistry, materials sciences
Jason Hodges · 865.576.7034 · hodgesj@ornl.gov

Engineering Materials Diffractometer (VULCAN) – BL 7 (2008)
Engineering, materials science, materials processing
Xun-Li Wang · 865.574.9164 · wangxl@ornl.gov

*Date shown is the scheduled commissioning date.

LEGEND

SNS TPC	SING I	SING II
DOE Grant	DOE NP	Non U.S.

OAK RIDGE National Laboratory

NEUTRON SCIENCES

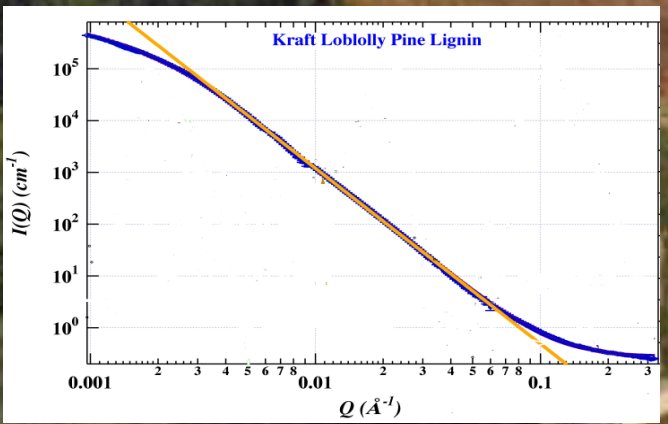
06-G00400H/arm

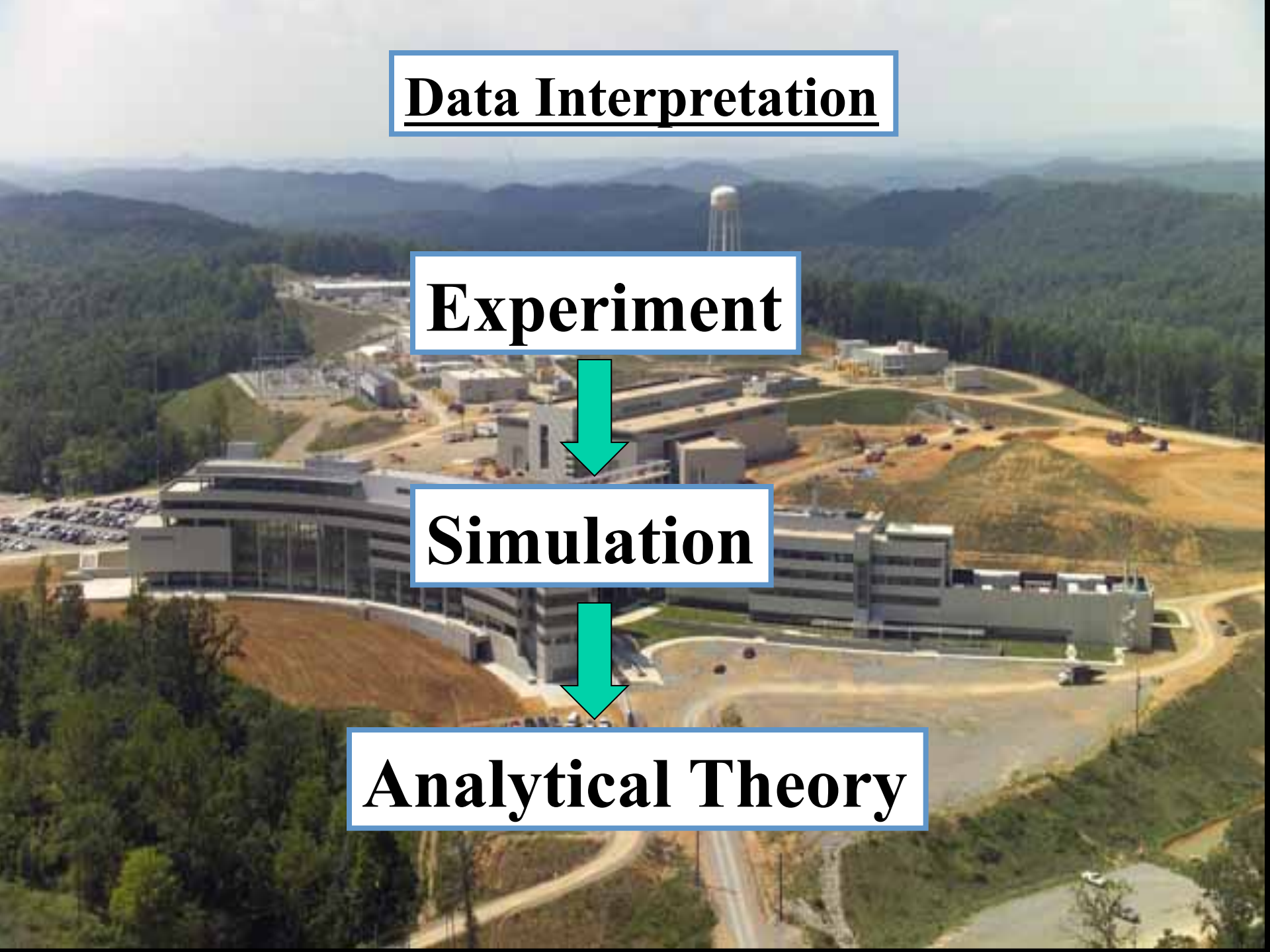
Spallation Neutron Source

Data Acquisition

Data Reduction

Data Interpretation




Data Interpretation
Experiment
Simulation
Analytical Theory

Cellulosic Ethanol

Fermentation

Fuel

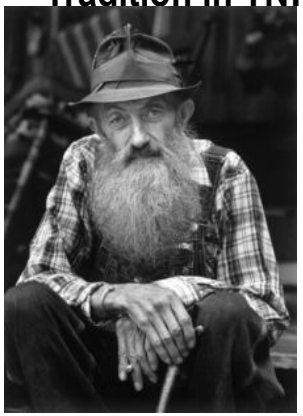
Hydrolysis

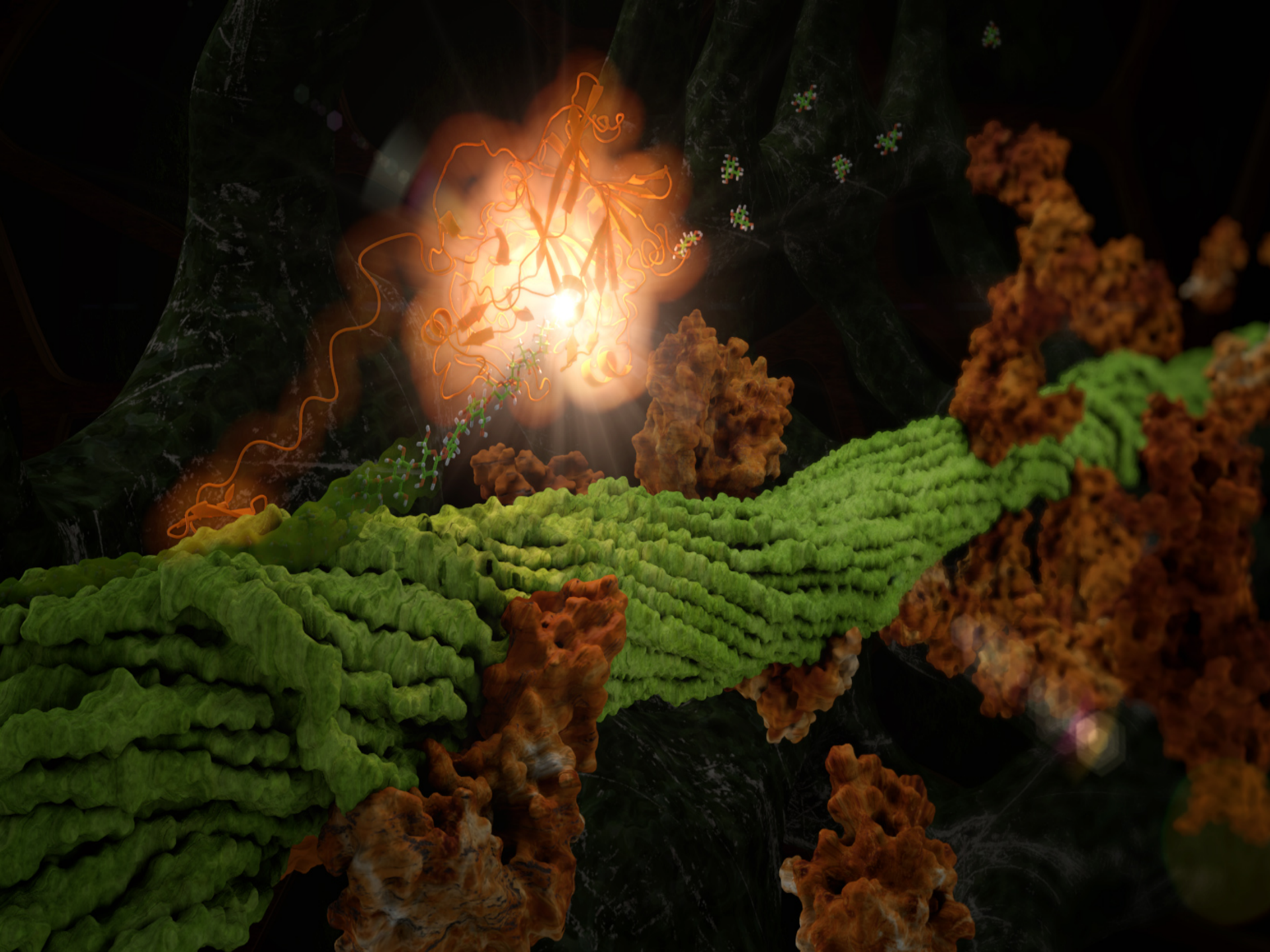
Breakdown into sugars

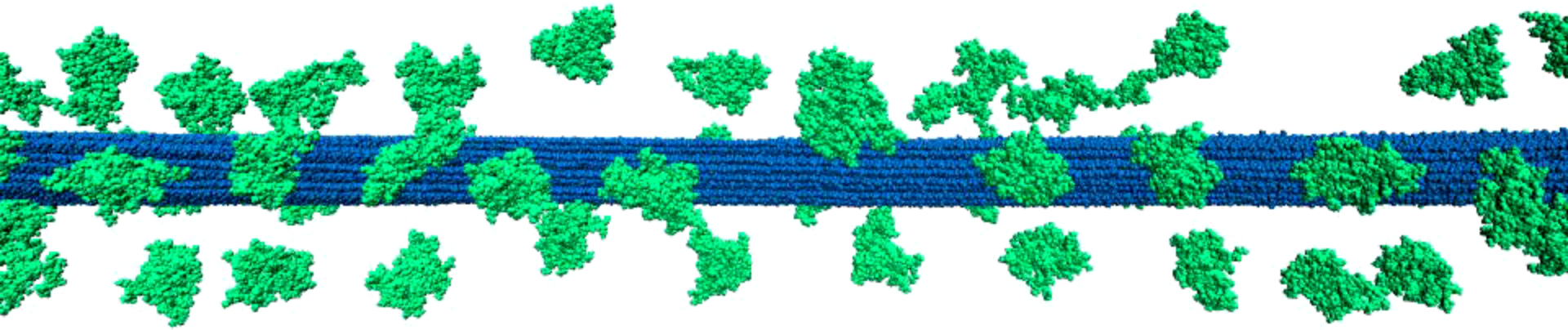
Cellulosic Biomass

RECALCITRANCE!

Strong Fermentation Tradition in TN!



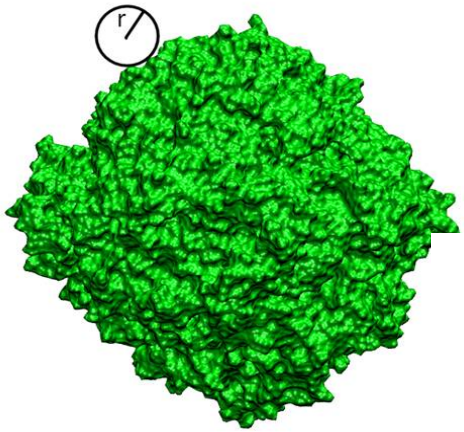




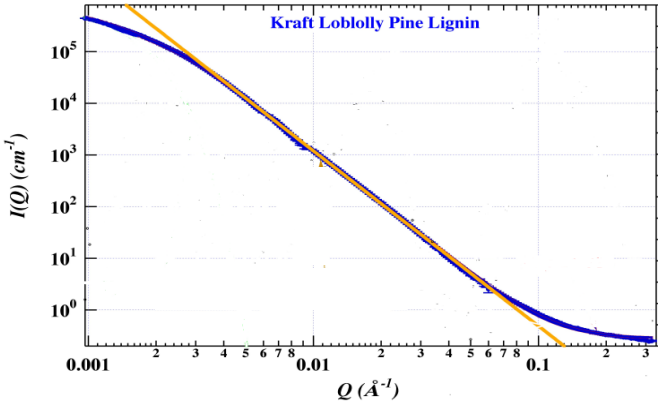
Biomacromolecules, In Pres

Lignin Aggregates

LOUKAS PETRIDIS
VENKY PINGALI



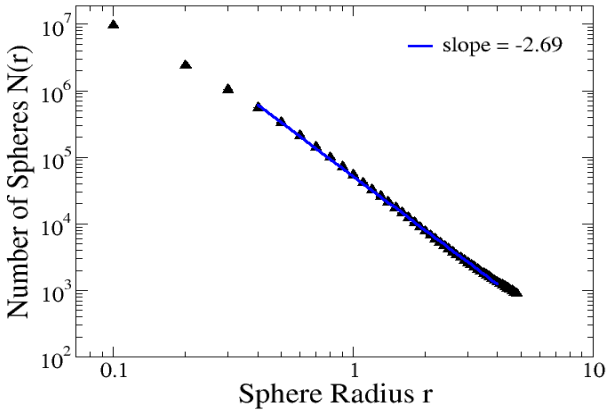
Small-Angle Neutron Scattering



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

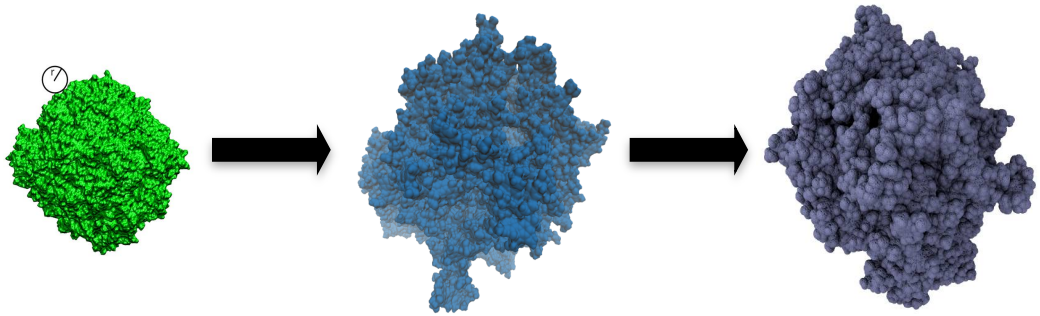
d_s= 2.62±0.02

Molecular Dynamics



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

d_s=2.65±0.01

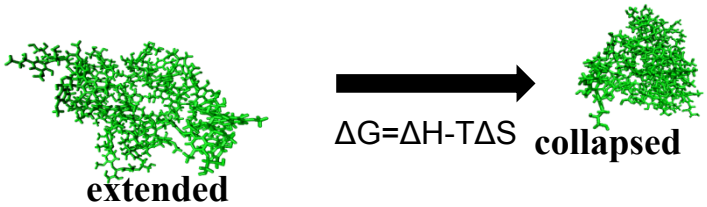


R_g=4.2Å R_g=42Å R_g=420Å

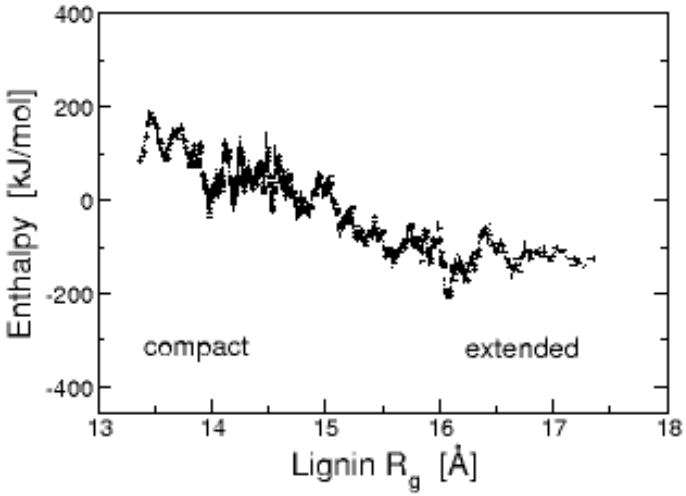
PRE 83(61):061911 (2011)

Why does Lignin Collapse at Room Temperature?

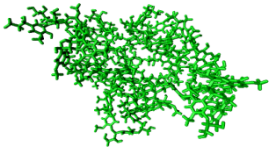
LOUKAS PETRIDIS



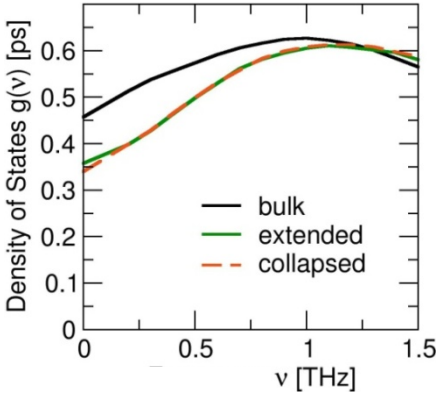
- **Enthalpy**
- ΔH ≈ +200 kJ/mol **Unfavorable**

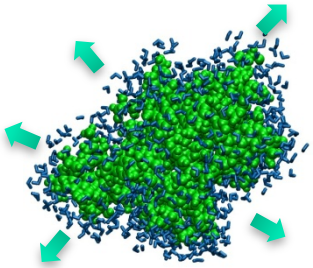


- **Lignin configurational entropy**
- $-T\Delta S_{conf} \approx +10$ kJ/mol **Unfavorable**



- Hydration **water translational & rotational entropy**
- $-T\Delta S_{t+r} \approx -100$ kJ/mol **Favorable**





- Hydration **water compressibility**
- $-T\Delta S_{fluc} \approx -300$ kJ/mol **Favorable**

Collapse Driven by Removal of Entropically Unfavorable Water Molecules from Lignin Surface to Bulk

JACS 133 20277 (2011)

Effect of Pretreatment on Biomass Structure

X-Ray

Neutron

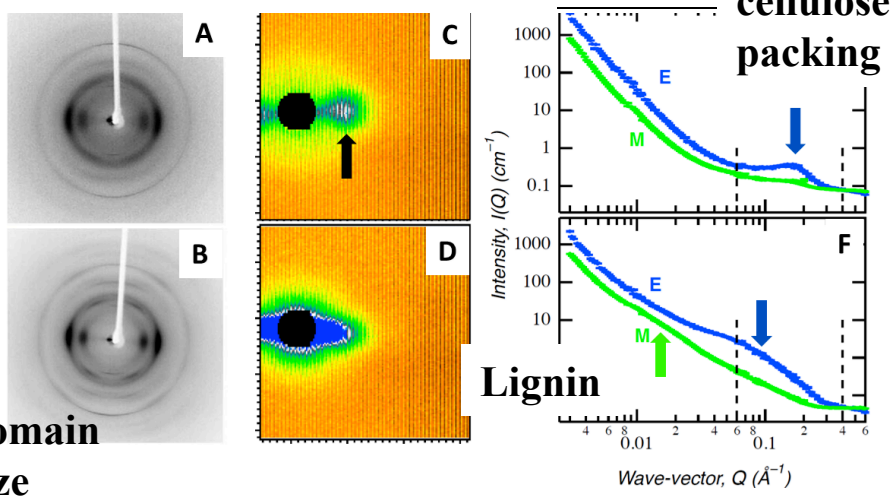
Side-by-side cellulose fibril packing

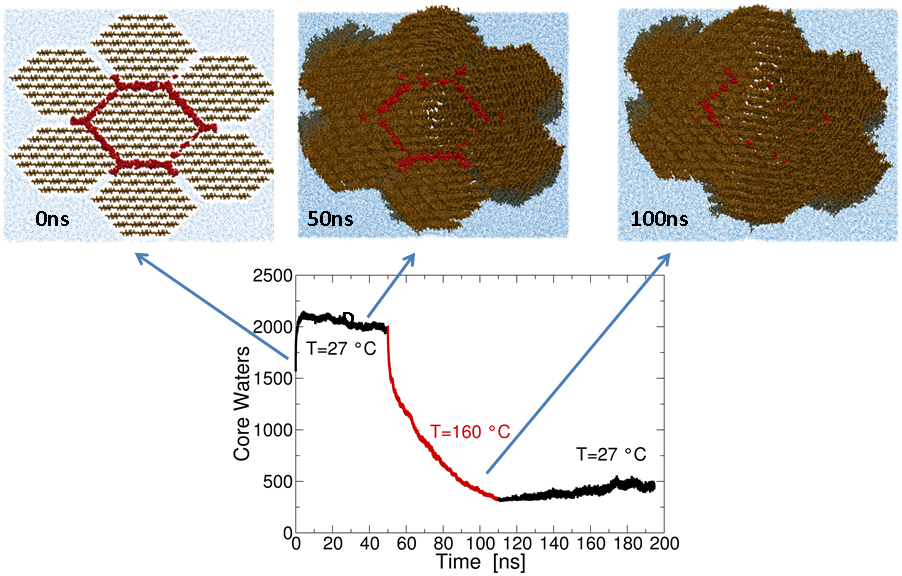
Untreated

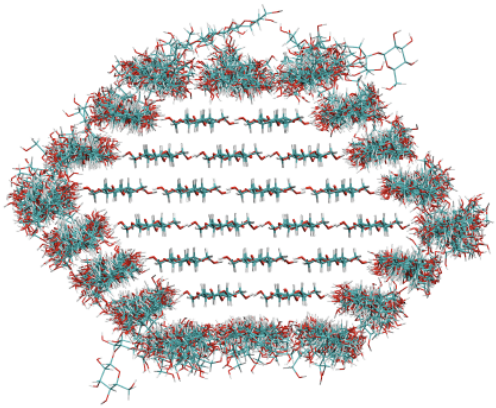
Pretreated

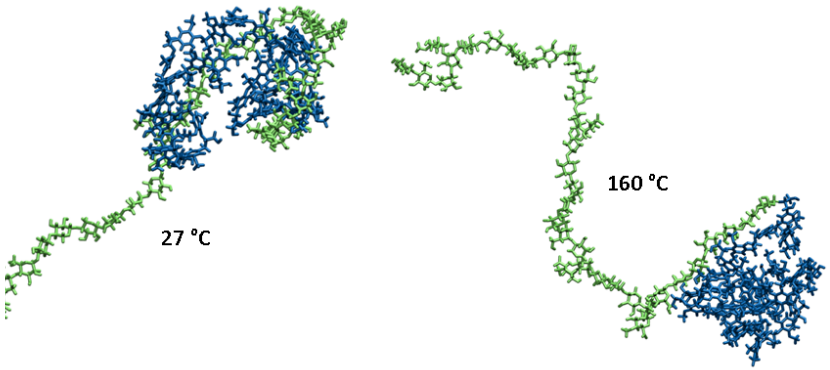
Lignin

Domain Size









Langan et al, submitted

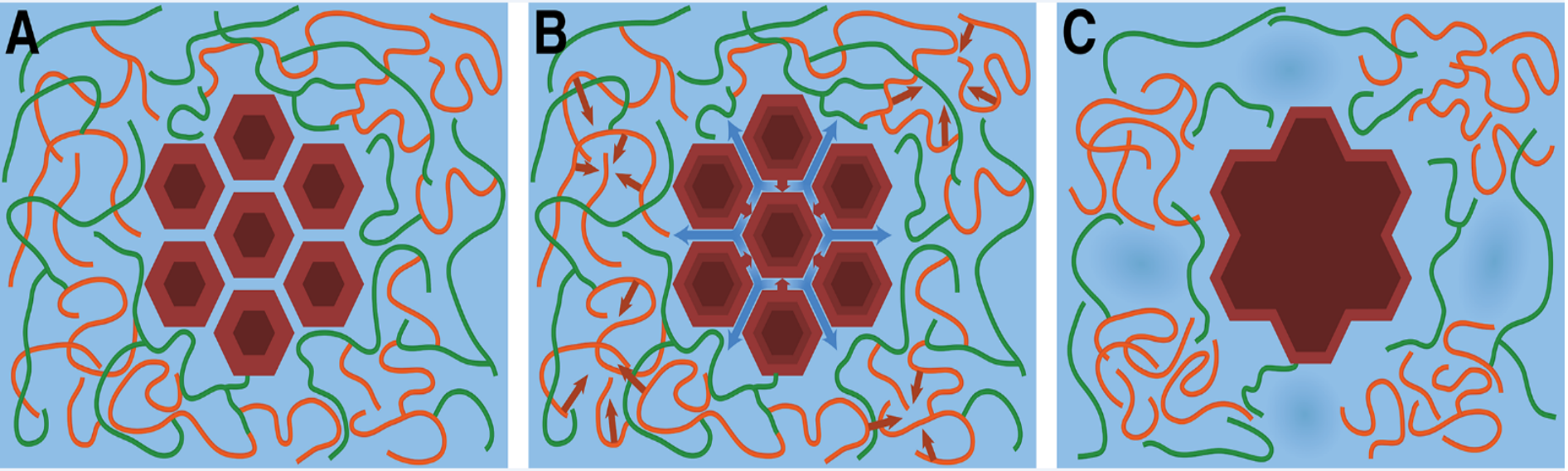
Steam Explosion Pretreatment

matrix phase separation

T↑

T↓

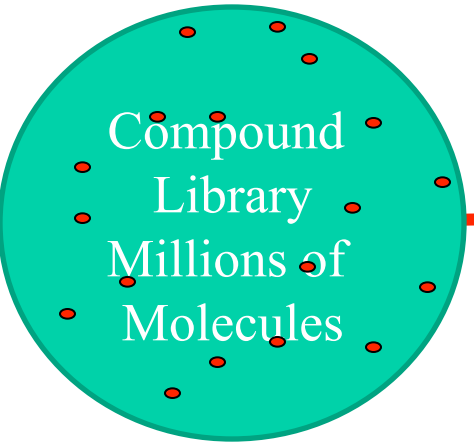
lignin globules collapsed

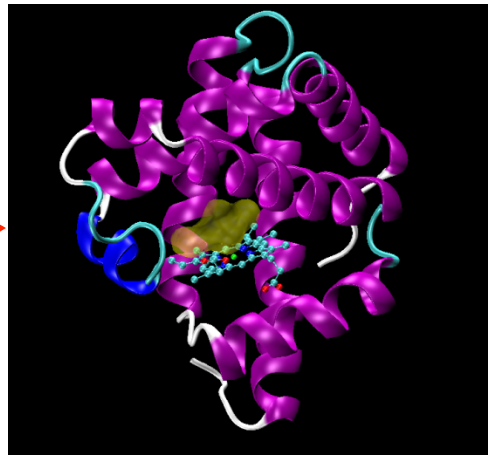


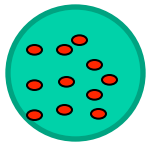
core water molecules expelled

cellulose fibril bundles remain dehydrated and more ordered

Structure-Based Computational Ligand Binding





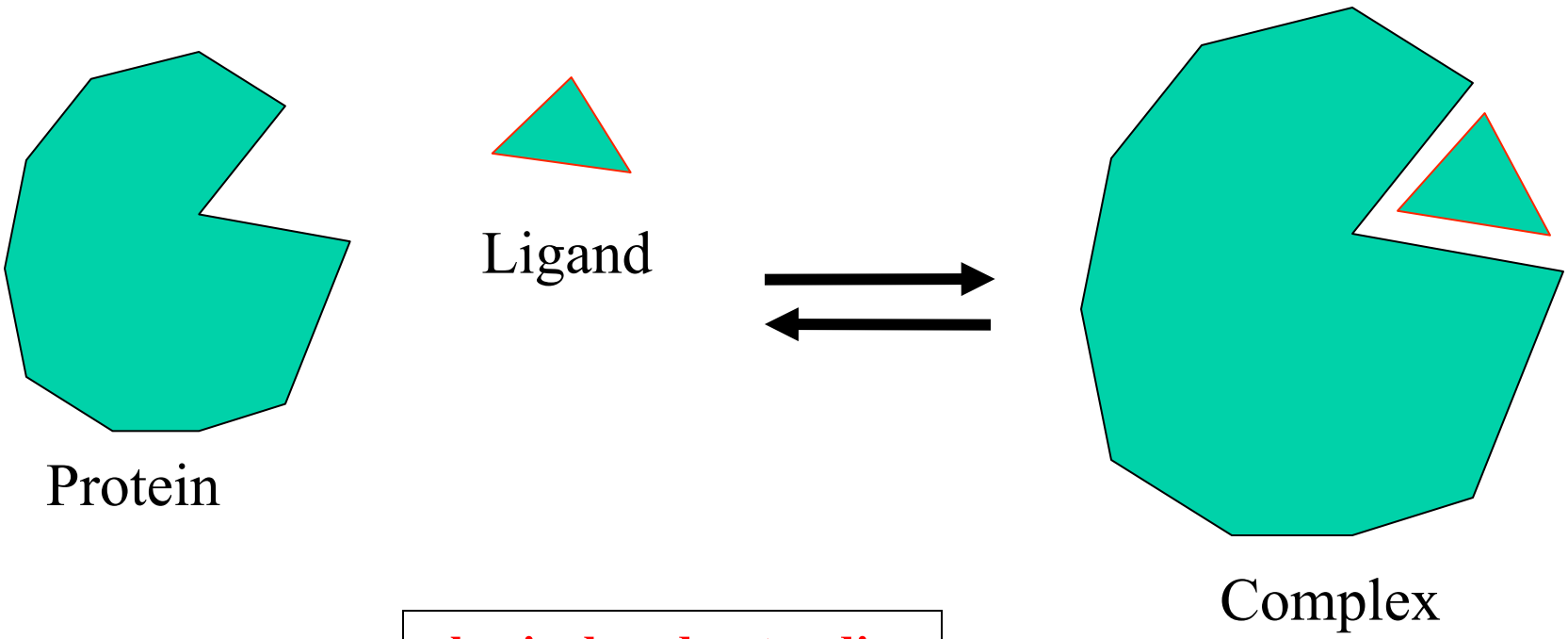


Enrichment Factor ~12 with Autodock Vina

Enrich a collection of compounds with molecules most likely to bind to the target

→

Ligand Binding



physical understanding

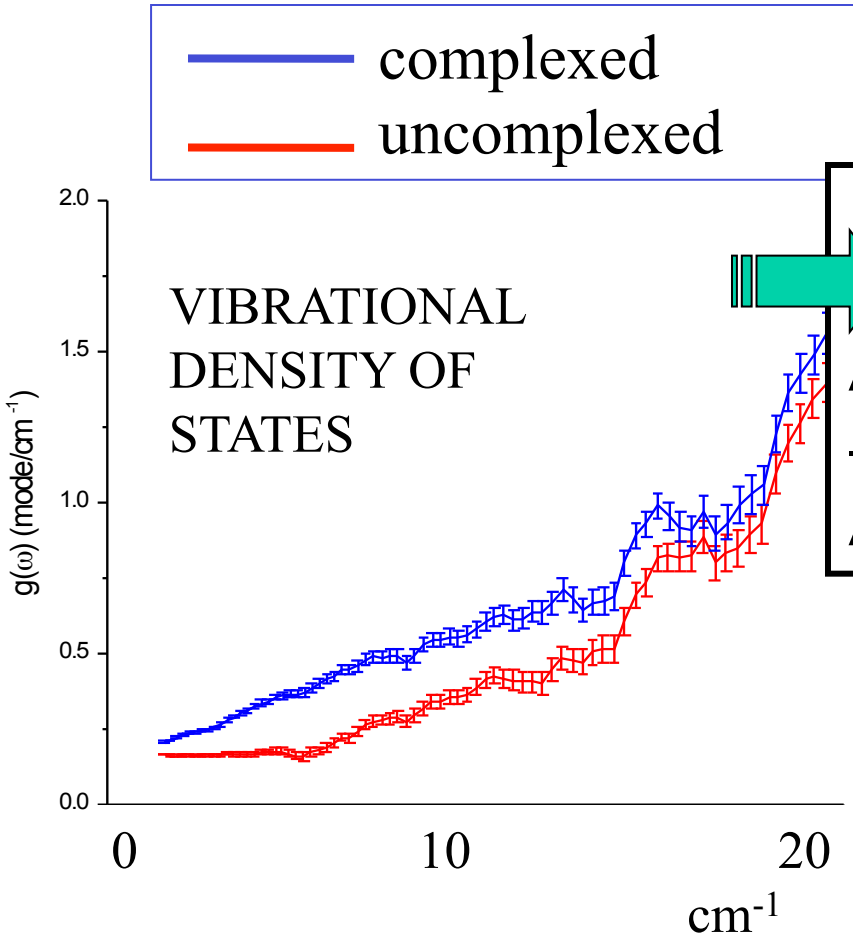
vibrational changes?

$$g_{\exp}(\omega) = \lim_{q \to 0} \frac{6\omega}{\hbar q^2}(e^{\hbar\omega/kT} - 1)S(q, \omega)$$

g(ω) = vibrational density of states (probability distribution of frequencies)

TORSTEN BECKER
ERIKA BALOG

Vibrational Change on Methotrexate Binding to Dihydrofolate Reductase



Vibrational Thermodynamics

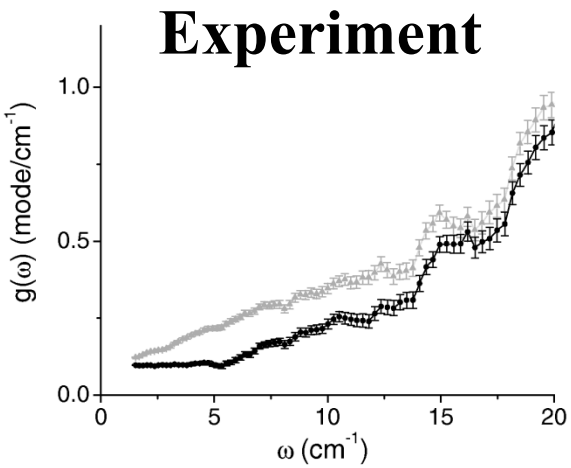
ΔG_{vib} = -4.0 ± 1.0 kcal/mol

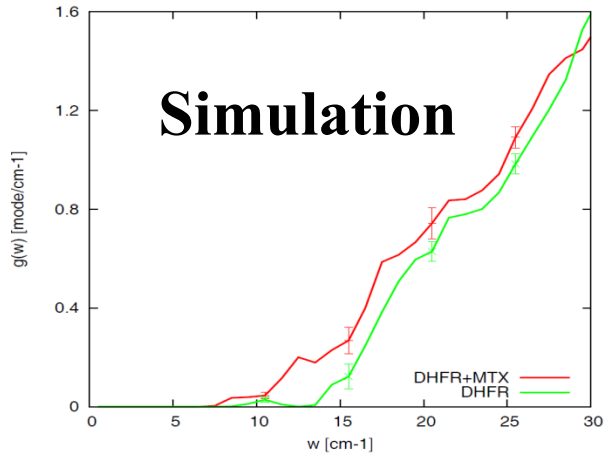
$-T\Delta S_{vib}$ = -6.0 ± 1.5 kcal/mol

ΔH_{vib} = +2.0 ± 0.5 kcal/mol

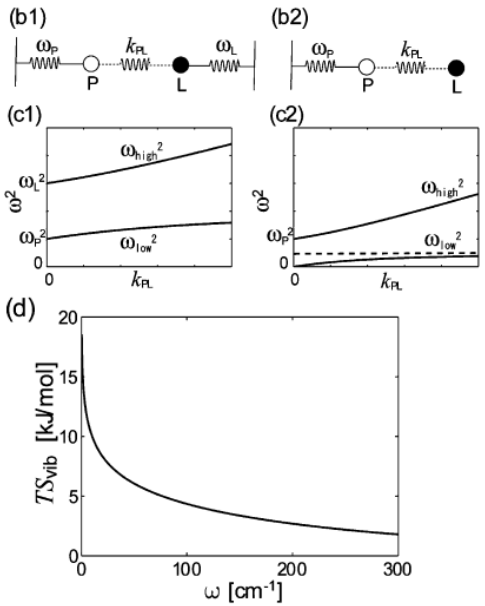
PRL 93 028103 (2004)
JPCB 114 1479 (2010)
JPCB 115 6811 (2011)

KEI MORITSUGU

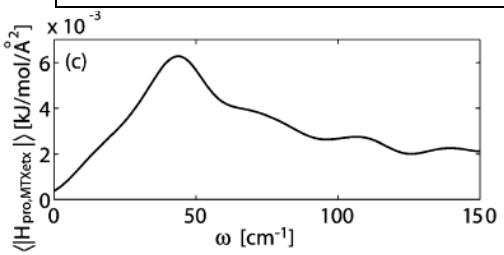




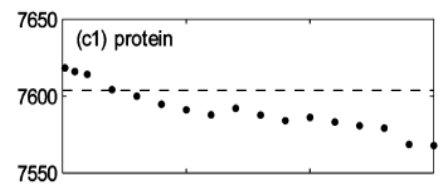
(b) calculation



Coupling constant of ligand external motion



Entropy loss on progressive formation of interactions



Entropy gain from coupling between protein and ligand external motion

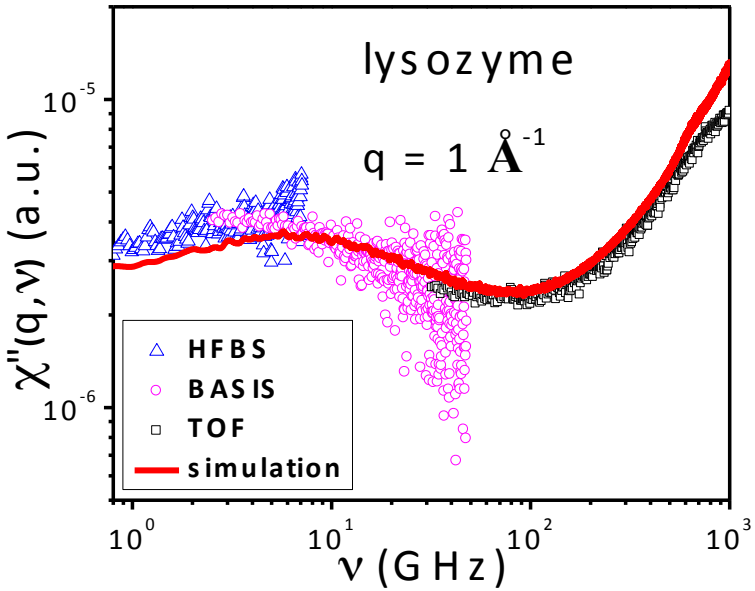
>

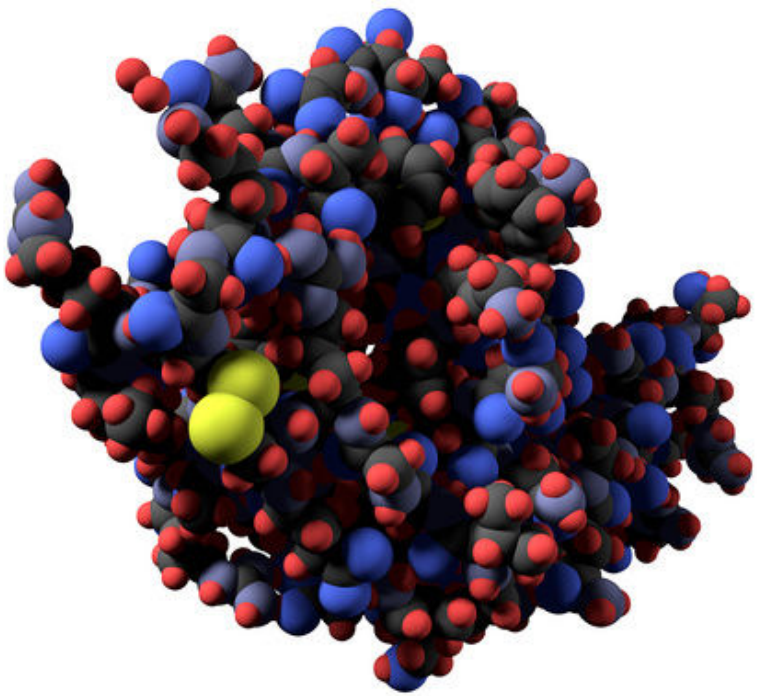
Entropy loss on formation of interactions within bound complex

JPCB 115 6811 (2011) JPCB 114 1479 (2010)

Dynamic Neutron Susceptibility of a Globular Protein

LIANG HONG





$$\chi''(q,\omega) = S(q,\omega)/n_B(T)$$

$\chi''(q,\omega)$: dynamic susceptibility
$S(q, \nu)$:dynamic structure factor
$n_B(T)$: Bose factor

PRL 107 148102 (2011)

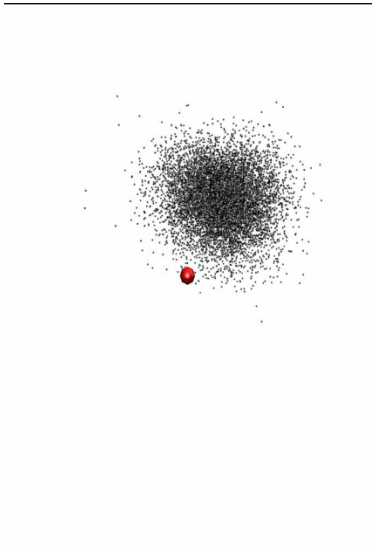
PRL 108 238102 (2012)

PRL 110 028104 (2013)

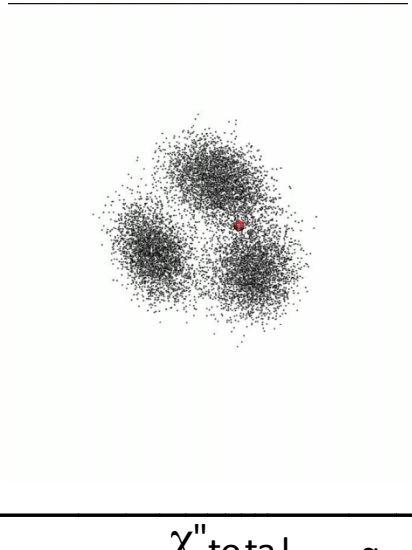
LIANG HONG

Three Classes of Motion

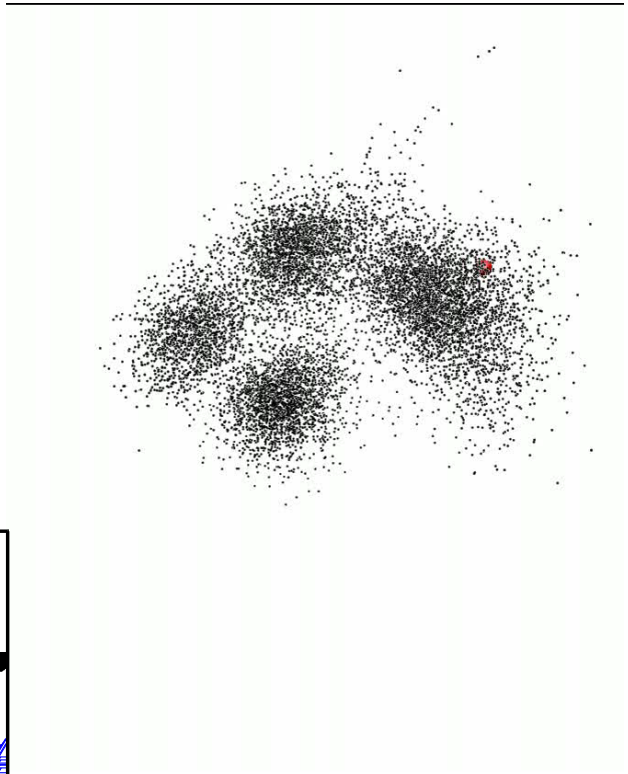
Localized diffusion

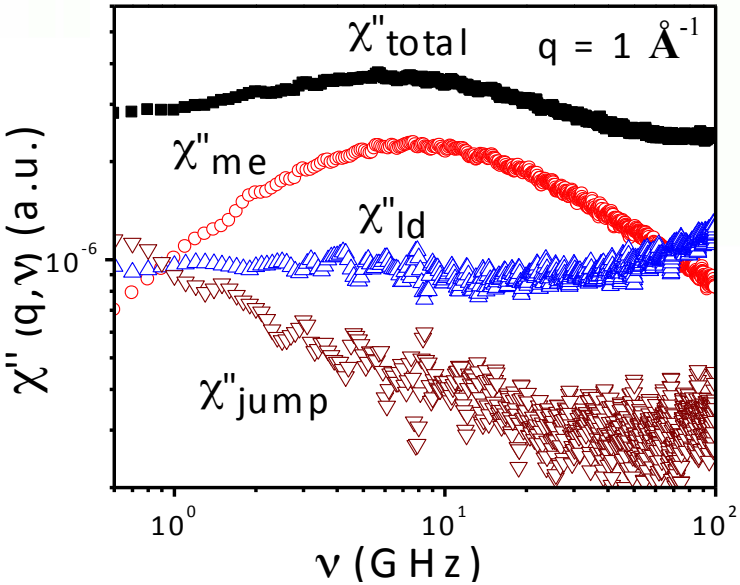


Methyl rotation



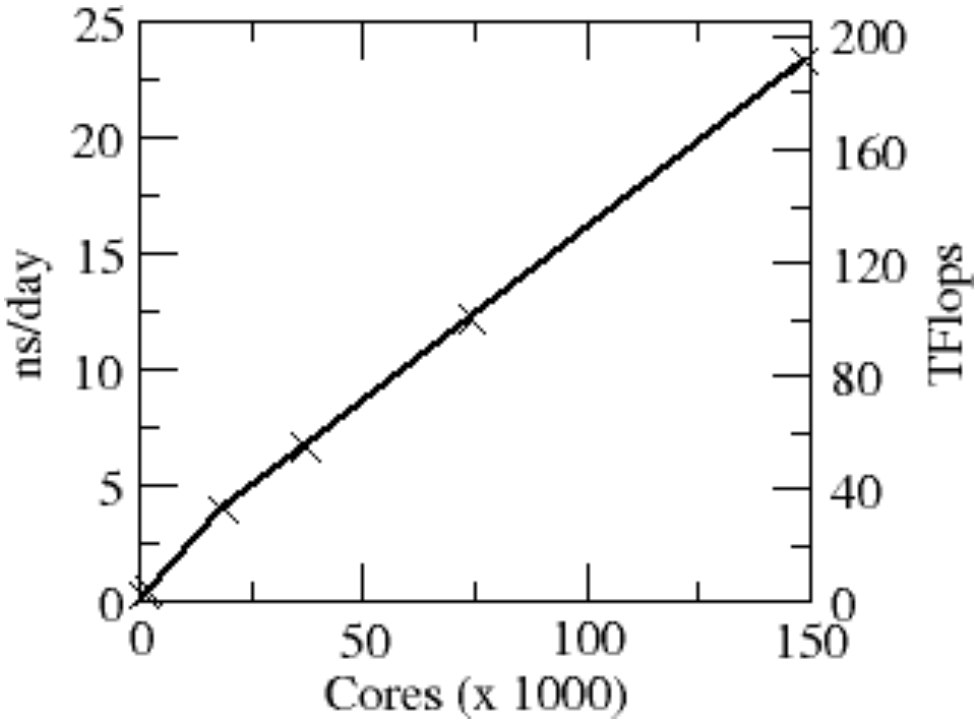
Non-methyl jumps

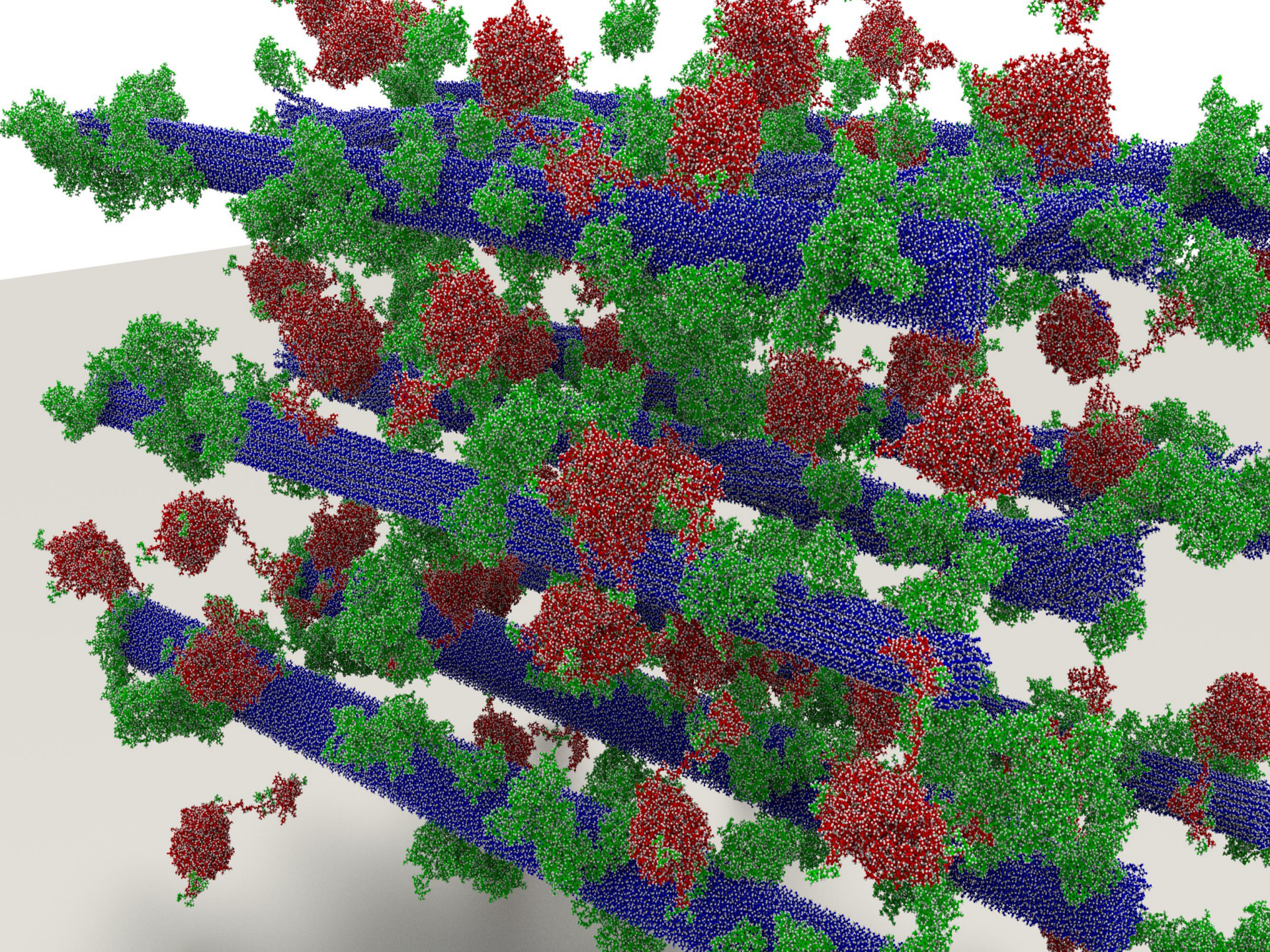


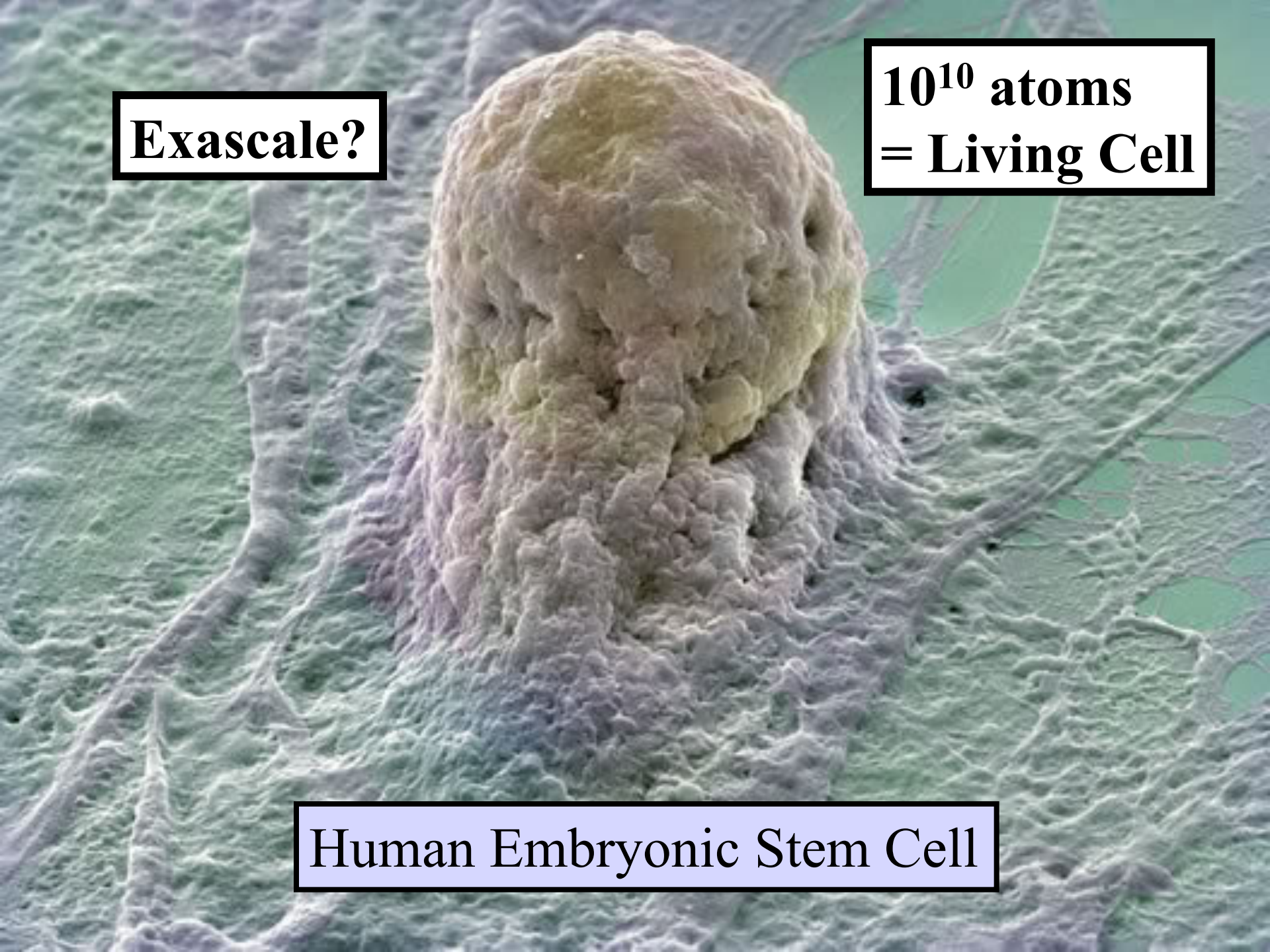


PRL 107 148102 (2011)

Molecular Dynamics Scaling
150M atoms

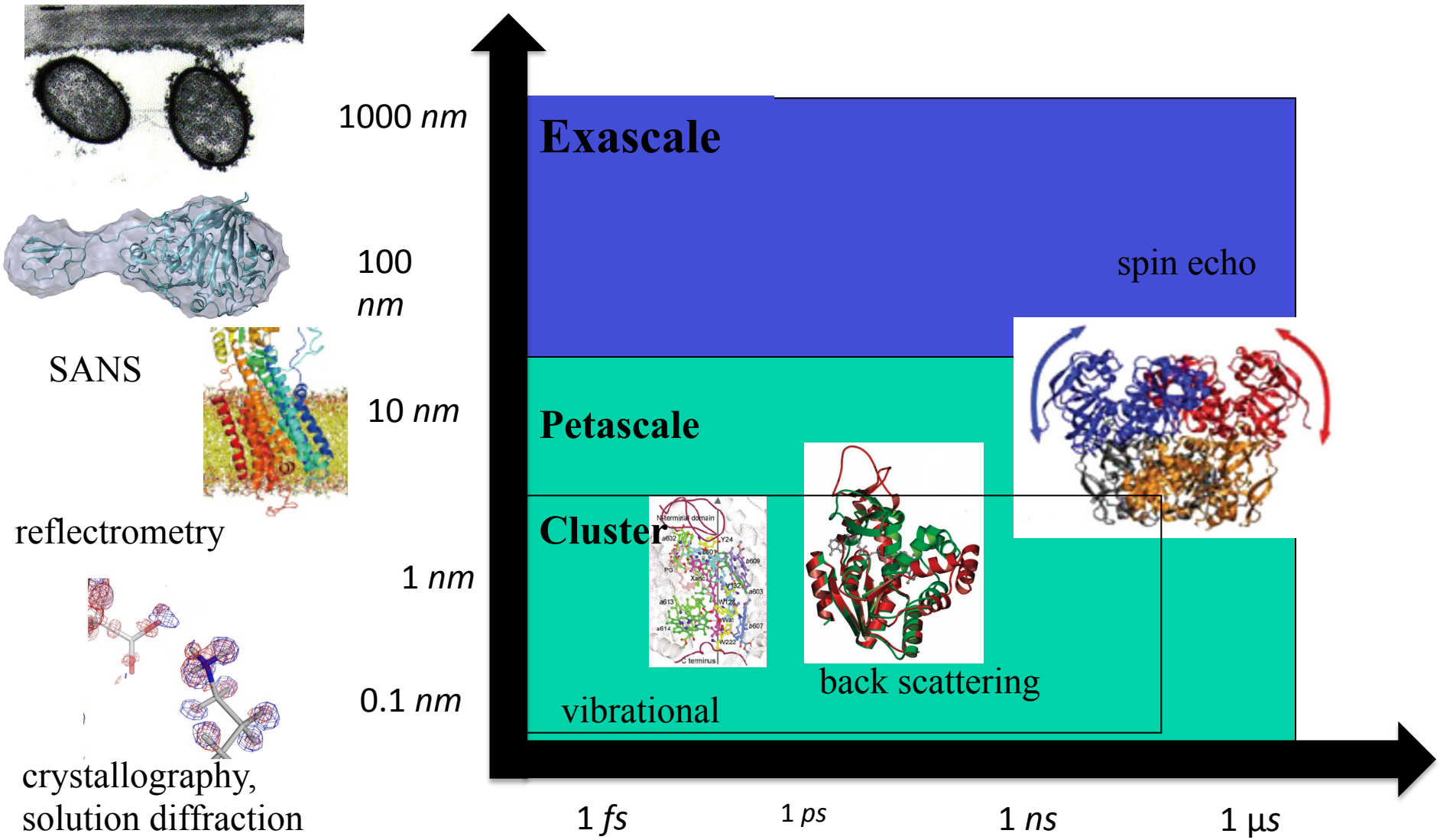





Exascale?
10^{10} atoms
= Living Cell
Human Embryonic Stem Cell

Multiscale Structure and Dynamics

Combining Unique Strengths of ORNL



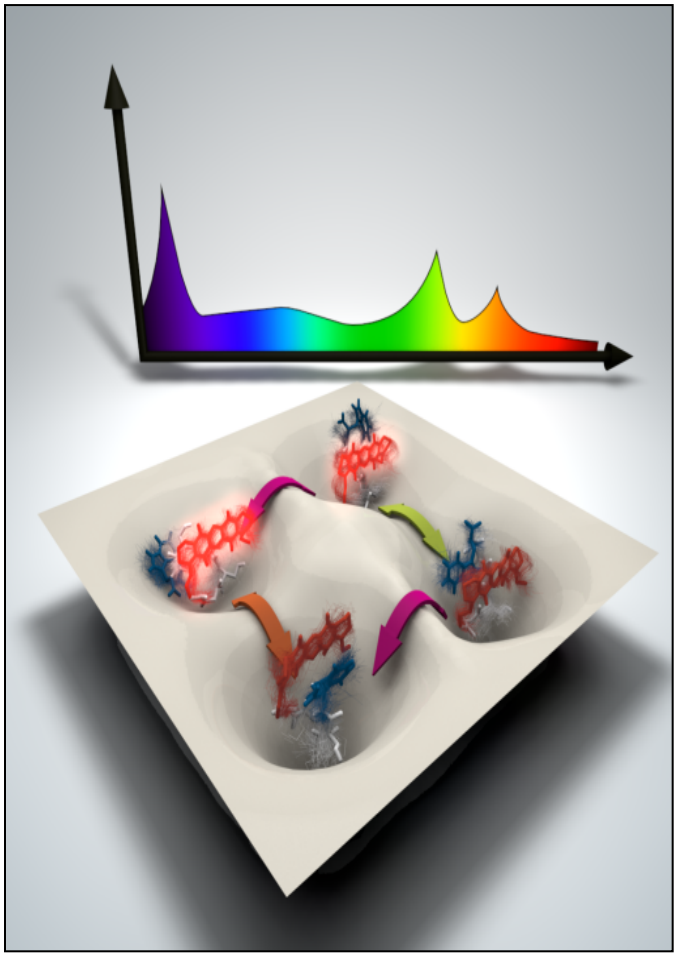
But…

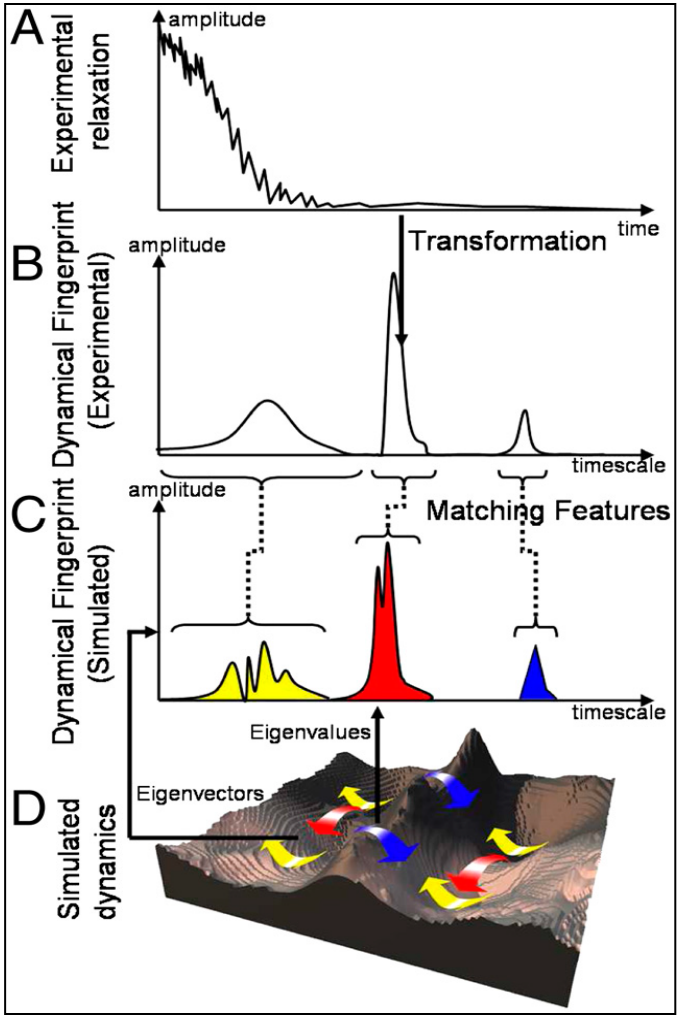
Microsecond Timescale Limitation!

New Concepts Needed….

Dynamical Fingerprints

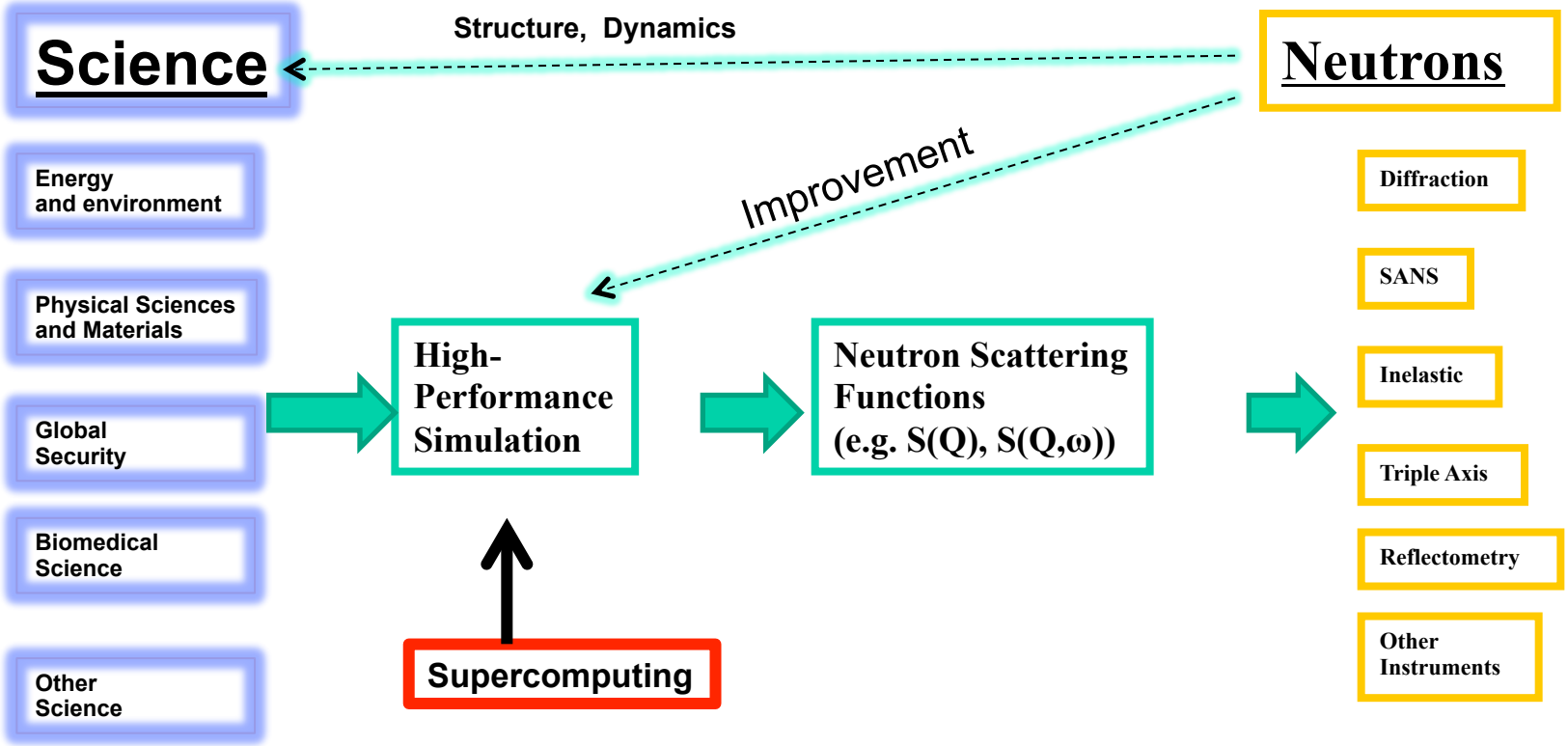
FRANK NOE





JCP 134 244108 (2011)
PNAS 108 4822 (2011)

JCTC 2, 840-857 2006



Real Time Exascale Neutron Experimental Design and Interpretation

Center for Molecular Biophysics

ORNL

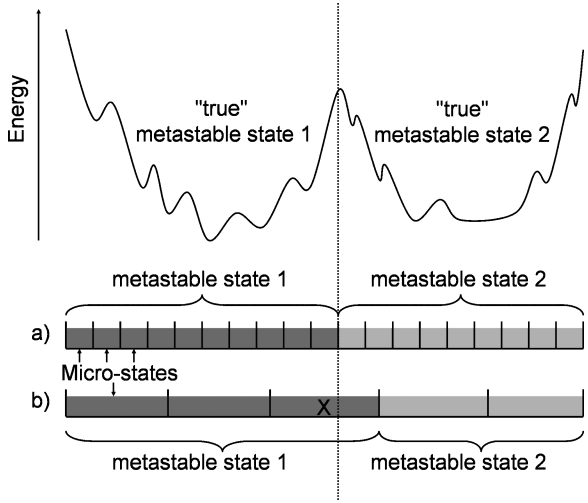
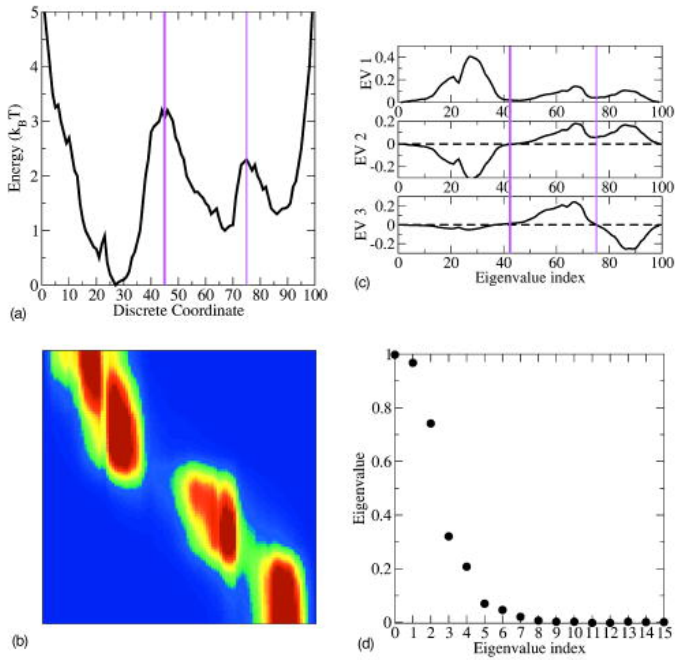
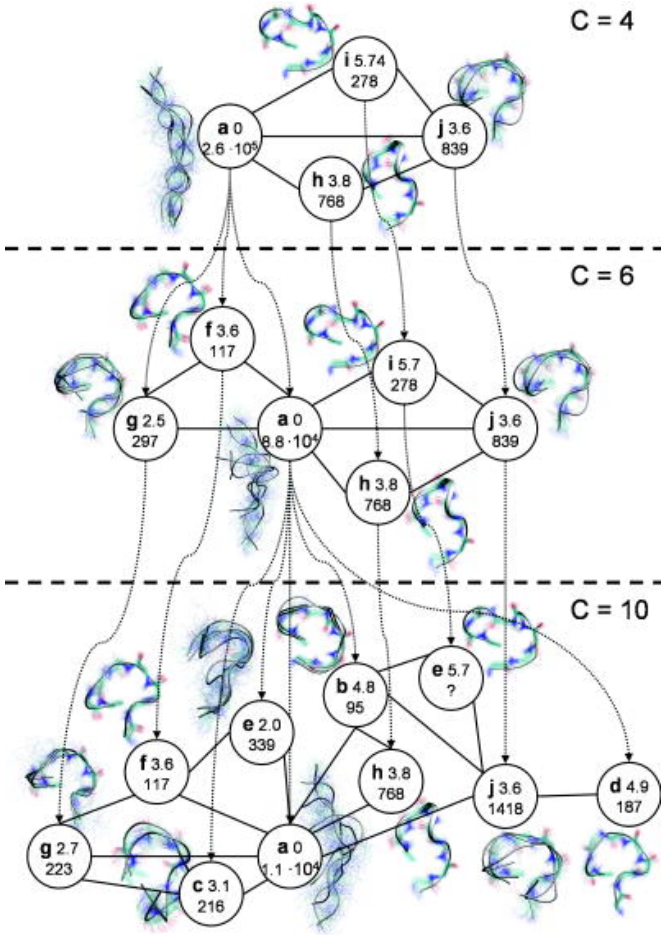
Oak Ridge National Laboratory

Co-workers

Torsten Becker
Barbara Collignon
Sally Ellingson
Jerome Baudry
Loukas Petridis
Roland Schulz
Benjamin Lindner
Dennis Glass
Xiaohu Hu
Barmak Mostofian
Amandeep Sangha
Liang Hong
Yinglong Miao
Yi Zheng
Jerry Parks

Collaborators

Ilia Horenko, Frank Noe
Christof Schuette (FU Berlin)
John Chodera (Memorial Sloan Kettering)
Erika Balog (U. Budapest)
Kei Moritsugu (RIKEN, Tokyo)
Dwayne Elias, Mircea Podar, Alex Johs, Liyuan Liang, Alexei Sokolov, Barbara Evans, Hugh O' Neill, Venky Pingali, William Heller, Paul Langan (ORNL)
Judy Wall (U. Missouri)
Anne Summers (U.Ga)
Sue Miller (UCSF)
Ahmed Zewail (CalTech)
Akio Kitao (U. Tokyo)
Dieter Richter, Ralf Biehl, Michael Ohl, Melissa Sharp (FZ Juelich)
Salim Shah (Georgetown U Med Center)

Funding: DOE(BER, BES, ASCR),NSF, NIH

Transition Networks Of Metastable States