Neutrons for the Nation

A report by the APS Panel on Public Affairs
July, 2018
Reporting by

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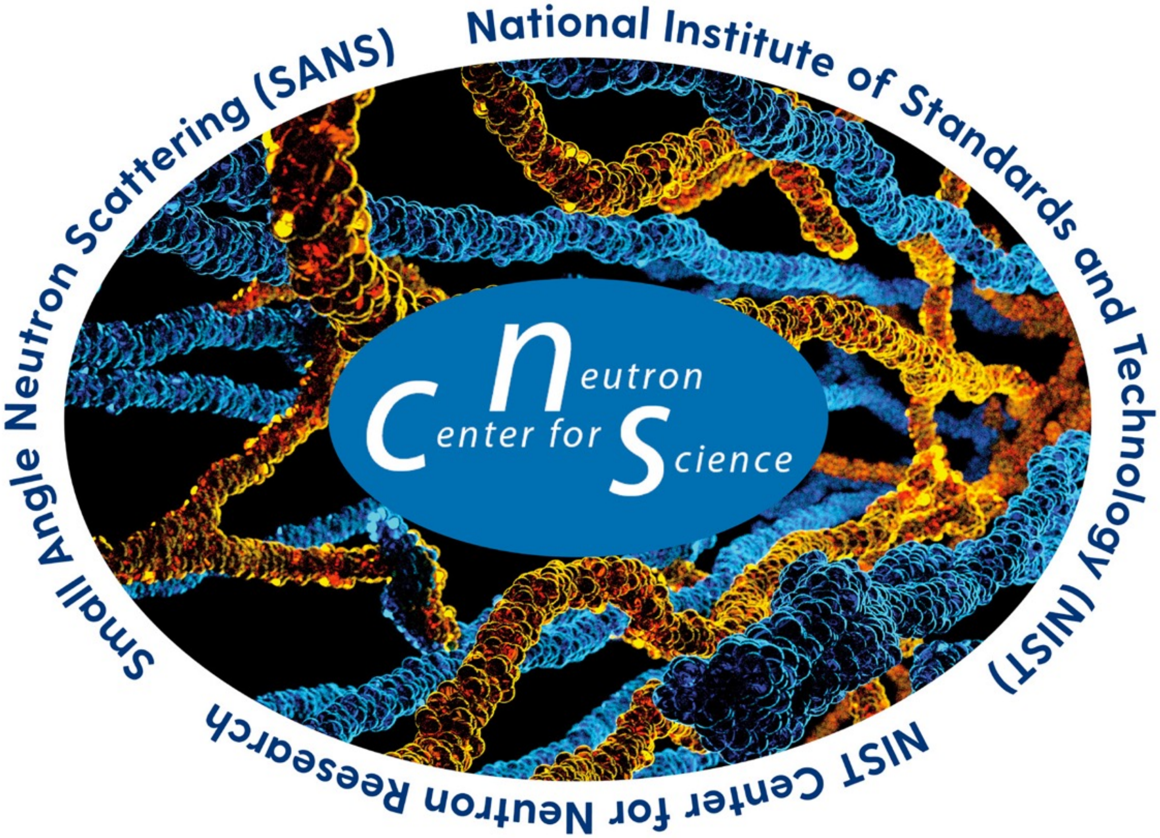
Physics and Astronomy
Biomedical Engineering
University of Delaware


Small Angle Neutron Scattering (SANS)
National Institute of Standards and Technology (NIST)
NIST Center for Neutron Reesearch
Neutron
Center for
Science

Committee Charge

Organized by the American Physical Society's Panel on Public Affairs (POPA), which produces reports on timely topics being debated in government so as to inform the debate with the perspectives of physicists working in the relevant issue areas.

This report focuses on the competing goals of:

1. Reducing nuclear proliferation risk
2. Maintaining intense controlled sources of neutrons for vital scientific and industrial work

Report Committee

- James Wells, Co-Chair, University of Michigan Physics Department
- Julia Phillips, Co-Chair, Sandia National Laboratory (retired)
- William Barletta, Massachusetts Institute of Technology Department of Physics
- Robert Birgeneau, University of California, Berkeley
- Robert Dimeo, National Institute of Standards and Technology
- Francesco Ganda, Argonne National Laboratory, Nuclear Engineering Division
- William Martin, University of Michigan, Nuclear Engineering & Radiological Sciences
- John Sarrao, Los Alamos National Laboratory
- Antoinette Taylor, Los Alamos National Laboratory
- Norman Wagner, University of Delaware, Chemical & Biomolecular Engineering

"Neutrons are essential, precious, and powerful."

Outline

- Quick background info
- 6 findings
- 4 recommendations
- Some future opportunities for science with neutrons

N4N Commentary on HEU

HEU fuel is classified as a “direct-use material” by the International Atomic Energy Agency (IAEA), whereas low enriched uranium (LEU) fuel, with less than 20% uranium-235, is classified as an “indirect-use material” that cannot be used for “the manufacture of nuclear explosive devices without transmutation or further enrichment” [1]. Hence, the policy objective of reducing/eliminating proliferation risks gave rise to the goal of converting HEU-fueled reactors to LEU-fueled reactors. However, while converting all research reactors to operate using LEU fuel would meet U.S. policy goals, it is not currently feasible to make this conversion and maintain the unique capabilities provided by existing facilities for critical scientific investigations and engineering applications. Those reactors that cannot be converted to LEU fuel without significantly degrading their capabilities are the high-performance research reactors discussed in this report. Therefore, there is a current challenge in meeting both the needs of the scientific and engineering communities and the U.S. policy goal to reduce proliferation risks.

Finding #1

Investigations performed at neutron sources are essential components of R&D in numerous areas of science and engineering

U.S. industry relies on neutron scattering and imaging for discovery, development, and processing of superior materials.

- Advanced Polymers – molecular engineering
- Biopharma – stable formulations for drug delivery
- Oil and gas – recovery
- Green Energy – fuel cell performance
- Engines & generators - Turbine blades
- Aircraft- corrosion detection
- Shull Wollan Center (ORNL) and n-SOFT (NIST) enable U.S. based manufacturers to solve manufacturing challenges
- LANSCE (LANL) semiconductor irradiation damage
- Europe and Japan have complementary facilities

Finding #2

Neutron scattering is often an essential part of a broader experimental study that uses a complementary suite of tools (e.g., light sources, high performance computers). Thus, neutron sources play a key role in overall U.S. innovation capacity.

1. **Materials Science and Engineering:** Neutron scattering is used to investigate the crystal structure, composition, and defects in materials, such as metals, ceramics, polymers, and nanomaterials. Researchers can study how materials behave under different conditions (e.g., temperature, pressure) to optimize their properties for specific applications.
2. **Condensed Matter Physics:** Neutron scattering is crucial for studying condensed matter systems, including magnets, superconductors, and other quantum materials. It helps scientists understand the magnetic and electronic properties of materials, as well as their phase transitions and quantum behaviors.
3. **Biology and Biophysics:** Neutron scattering can provide valuable insights into biological molecules like proteins and nucleic acids. By studying the structural arrangement and dynamics of biomolecules, researchers can better understand their functions and potential implications for diseases and drug design.
4. **Chemistry:** Neutron scattering is used to analyze molecular structures, chemical reactions, and intermolecular interactions. It is particularly useful for studying hydrogen and other light elements, providing crucial information for designing new materials and improving chemical processes.

5.**Earth and Environmental Sciences:** Neutron scattering can be applied to study various aspects of geological materials, soils, and environmental samples. Researchers use it to investigate pore structures, water absorption, and other properties relevant to soil and environmental science.

6.**Nuclear Physics:** Neutron scattering plays a fundamental role in nuclear physics, especially in understanding nuclear structures, interactions, and reactions. It helps researchers probe the structure and behavior of atomic nuclei, shedding light on the fundamental forces that govern matter.

7.**Cultural Heritage Conservation:** Neutron scattering can be used to analyze artifacts and historical objects to determine their composition and degradation mechanisms. This is crucial for conservation and restoration efforts in the field of cultural heritage.

8.**Energy Research:** Neutron scattering is used in energy-related research to study materials for energy storage (e.g., batteries), fuel cells, and nuclear reactor materials. Understanding the structure and behavior of these materials is vital for improving energy efficiency and sustainability.

These examples demonstrate the versatility and significance of neutron scattering across various scientific disciplines, enabling researchers to gain valuable insights into the properties and behaviors of a wide range of materials and systems.

Source: Open AI, ChaptGPT (3.5)

Finding #3

The United States has lost important capability in neutron R&D in the last two decades and is no longer the world leader. The United States cannot afford to lose its remaining capacity and capability without significant detriment to the quality and quantity of science, engineering, and even medical and manufacturing processes that rely on neutron sources.

■ MAP

MAJOR NEUTRON SCATTERING FACILITIES WORLDWIDE

Map of the major neutron scattering facilities worldwide and the number of neutron scattering and imaging instruments from each region in 2017 [37]. A major neutron scattering facility is defined in this report as having eight or more beam instruments and a thermal power of 10 MW or more if the source is reactor based. Pins (📍) denote reactor-based facilities and stars (★) represent spallation neutron sources. Green, orange, and red symbols represent facilities that are currently operational, under construction, and not operational at present, respectively.

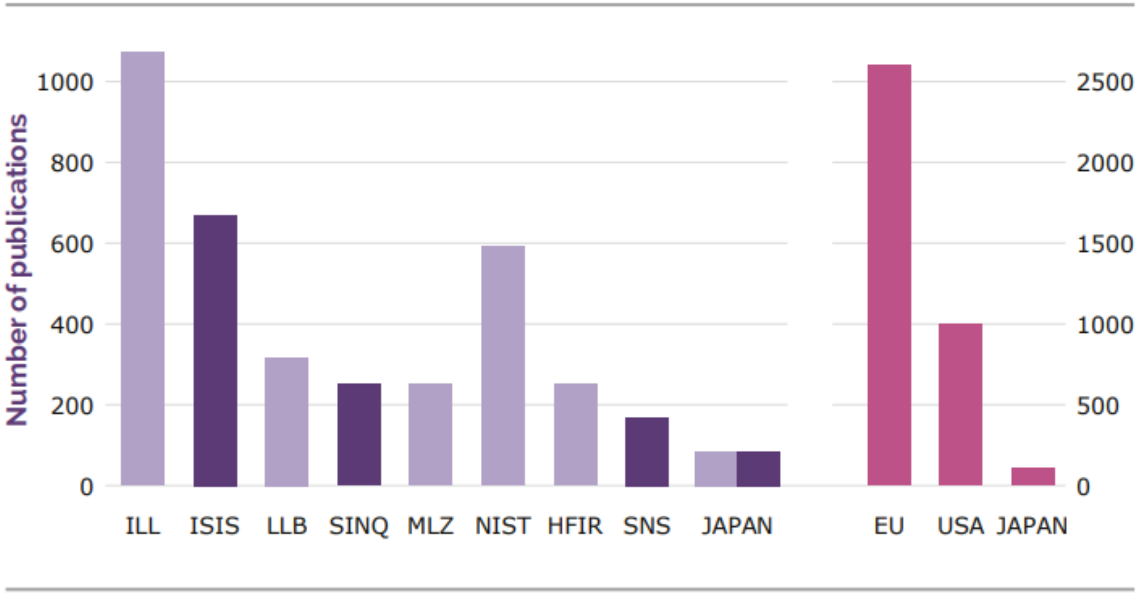


Figure 6. Publication output of major neutron sources

The number of publications of major sources in Europe and the rest of the world, integrated from 2008 to 2014. Light violet columns are reactor sources and dark violet columns are spallation sources. On the right, fuchsia columns show the data consolidated into the three regions of the world identified by OECD in 1999 as requiring a MW-class spallation source. Note the different scales.

Neutron scattering facilities in Europe, Present status and future perspectives, ESFRI Physical Sciences and Engineering Strategy Working Group, Neutron Landscape Group, ESFRI Scripta Volume I, Published by Dipartimento di Fisica - Universita degli Studi di Milano, September 2016, ISBN: 978-88-901562-5-0

Finding #4

Reactor fuels containing HEU represent a risk for proliferation, which should be considered when planning for the future infrastructure for neutron R&D.

Finding #5

Current HEU-fueled research reactors provide unique R&D capabilities relative to other neutron sources available today. Eliminating them without developing and deploying alternative methods of producing neutrons with the same properties (e.g., from high-density LEU-fueled reactors and/or a new generation of spallation sources) would compromise U.S. innovation capacity

In summary, considering all major facilities, the United States currently has about one-third of the neutron scattering instruments of Europe and one-half those of the Asia-Oceania region

Finding #6

World-class neutron science and engineering require the comprehensive benefits of spallation facilities, research reactors, and high-performance instrumentation. While there is some overlap in the capabilities provided by spallation and reactor sources, each provides certain capabilities that cannot now be duplicated by the other type of source

Recommendation #1

The United States should continue to support its diversity of neutron R&D capabilities, including both research reactors and spallation sources, for scientific, engineering, and economic capacity and capability. Decisions regarding potential new neutron sources should be guided by the principle of reducing and ultimately eliminating the use of HEU while retaining or enhancing current neutron capabilities.

Recommendation #2

The United States should sharply increase its investments in neutron instrumentation development and deployment to partially compensate for the country's dramatic decrease in neutron R&D capacity and capability in recent decades; to offset any loss of capability arising from the elimination of HEU fuel from research reactors; and to complement continuing investments in complementary tools such as light sources and high-performance computing.

Recommendation #3

The United States should reaffirm its commitment to the timely development and deployment of high-density LEU fuels for use in existing highperformance research reactors. Any transition from HEU to LEU reactor fuel must not compromise neutron research and engineering capabilities, especially those that cannot be duplicated using spallation sources. The United States should also consider options to cost-effectively maintain reactor performance and simultaneously reduce HEU consumption while awaiting a suitable LEU fuel.

Recommendation #4

The United States should initiate an effort to competitively design and build a new generation of LEU-fueled high-performance research reactors that would satisfy all needs presently met by current HEU-fueled U.S. high-performance research reactors and provide new capabilities.

“Neutrons are essential, precious, and powerful.”

The Scientific Justification for
a U.S. Domestic High-Performance Reactor-Based Research Facility

DOE BES https://doi.org/10.2172/1647598

REPORT OF THE BASIC ENERGY SCIENCES ADVISORY COMMITTEE
U.S. Department of Energy/Office of Science/July 2020
Revision 10-28-2020
Prepared by the BESAC Subcommittee to Assess the Scientific Justification
for a U.S. Domestic High-Performance Reactor-Based Research Facility

3 recommendations:

#1 Operate "as is": This is the least desirable option. Investment in fuel conversion or instrumentation without replacing the pressure vessel leaves an unacceptable risk of a short life of the reactor

#2 Replace the Pressure Vessel: Pursue this approach immediately with the goal that the fuel conversion and pressure vessel replacement be performed during the same shutdown. The significant risk of HFIR failure will be removed, and important capabilities will result.

#3 Pursue study of a new high-flux reactor in parallel with the shorter term replacement of the pressure vessel and conversion of HFIR to LEU fuel.

The Scientific Justification for
a U.S. Domestic High-Performance Reactor-Based Research Facility

DOE BES https://doi.org/10.2172/1647598

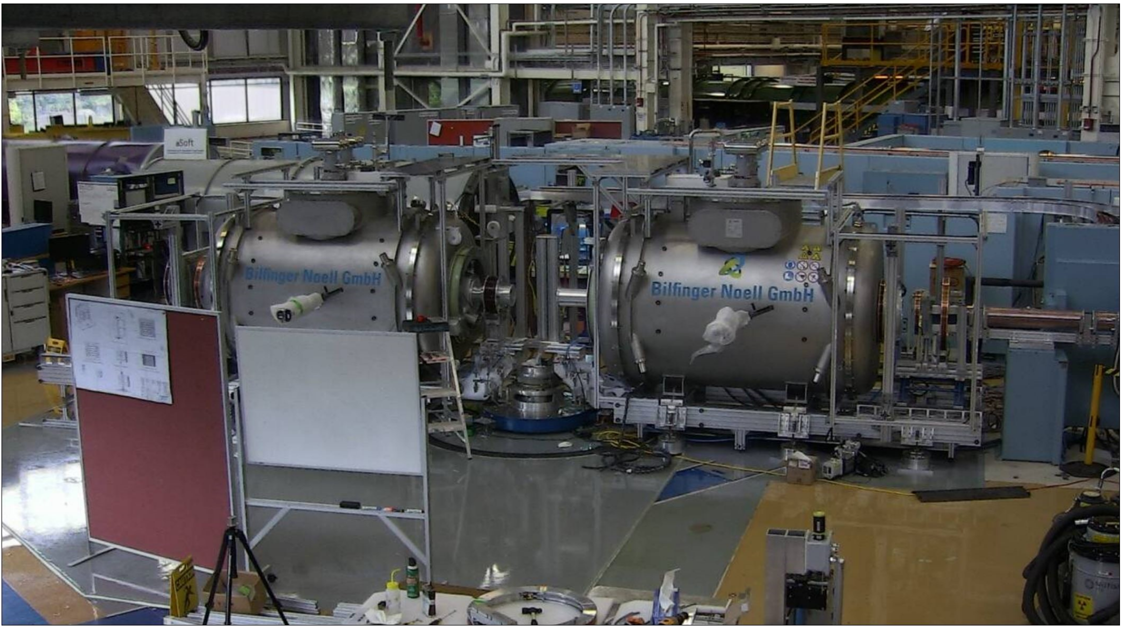
Finally, there is always the possibility that, for either technical or political reasons, HFIR will have to be closed down and the vessel replacement and HEU- LEU conversion proposed above will not be possible. Indeed, our country has already suffered a major loss with the permanent closure of the High Flux Beam Reactor at Brookhaven National Laboratory. Because of the long times involved between the initial design and the final commissioning of such a reactor, DOE must have an alternative strategy. Specifically, DOE needs to initiate a scoping study for a green field research reactor optimized to perform neutron studies and isotope production that are uniquely suited to a very high flux reactor such as HFIR. The reactor would be designed to operate on LEU fuel. Reactor and fuel assembly designs should be evaluated to optimize simultaneously reactor performance and fuel assembly manufacturability. Further, the design should, to the extent possible, be optimized for neutron needs as currently understood and for flexibility of configuration to enable future, currently unanticipated, applications. Beginning this process now will allow time to evaluate options and proceed with planning and approvals in time to ensure continuing availability of a multiply capable high flux research reactor in the U.S

vignettes on soft matter & biophysics

20th Century Paradigm:	3D Structure <-> Function
21st Century Paradigm:	**4D** Structure <-> Function

(x,y,z,**t**)

World-Class NSE



Mid-scale RI:1 (M1:IP): A world-class Neutron Spin Echo Spectrometer for the Nation: UD-NIST-UMD Consortium

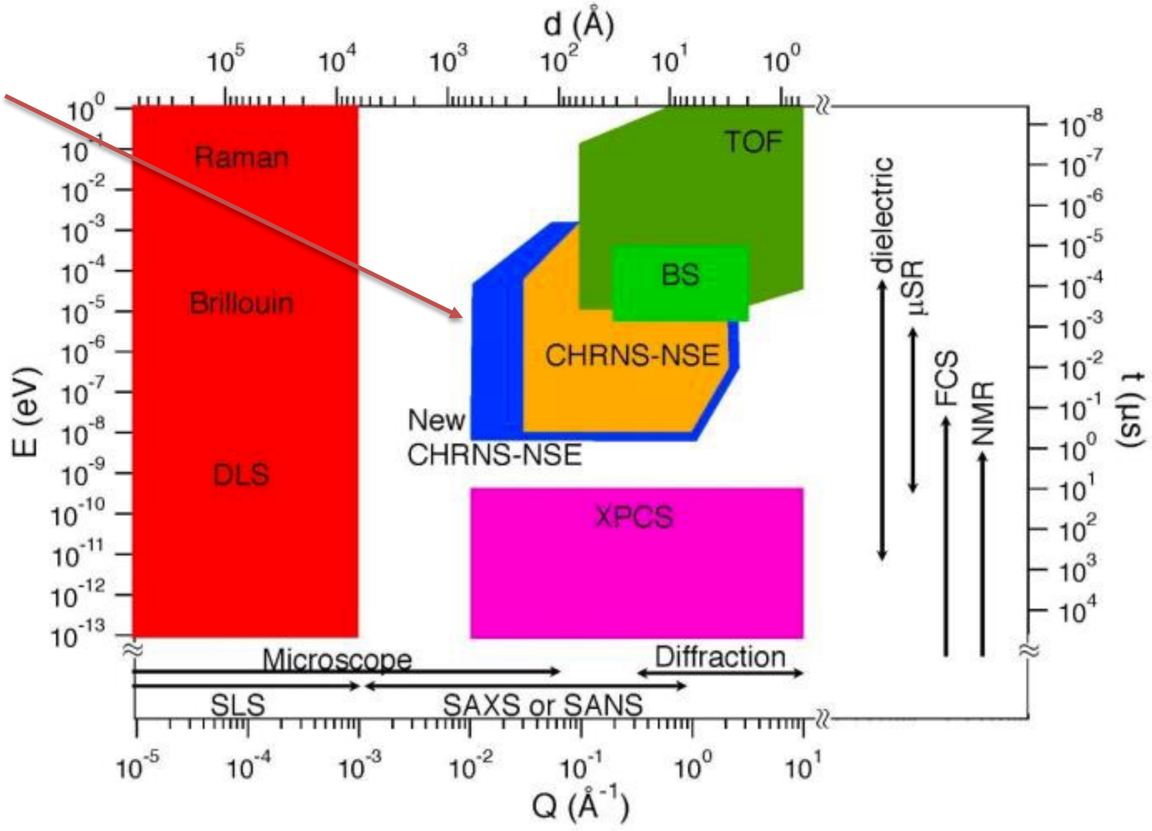
Award # **1935956 Start 10/1/2019, 5 years**

Principal Investigator:	Wagner, Norman J.
Project Manager:	Brocker, Christoph
Lead Institution:	University of Delaware
Cognizant PO:	G.X. Tessema

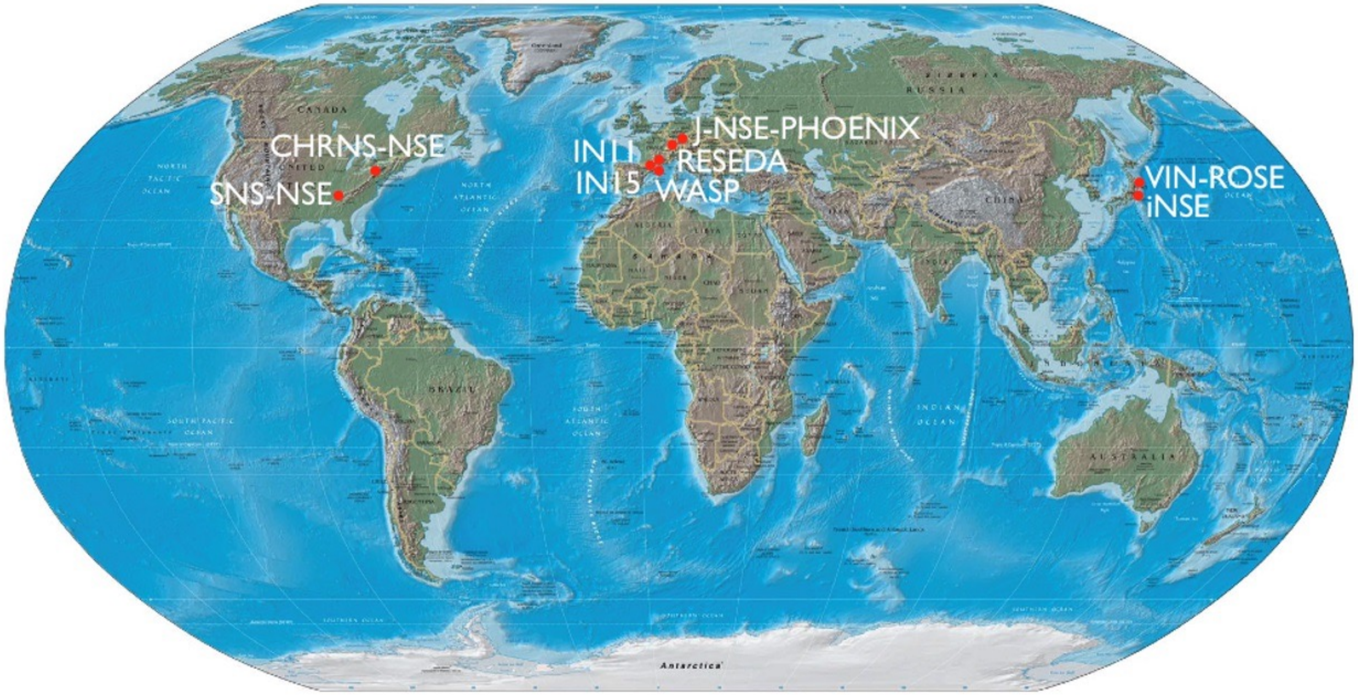
- **2.5x Fourier Time >300 ns (700ns)**
- **~10x flux**

NIST Center for Neutron Research

NSE Length and Time Scales- Big Picture

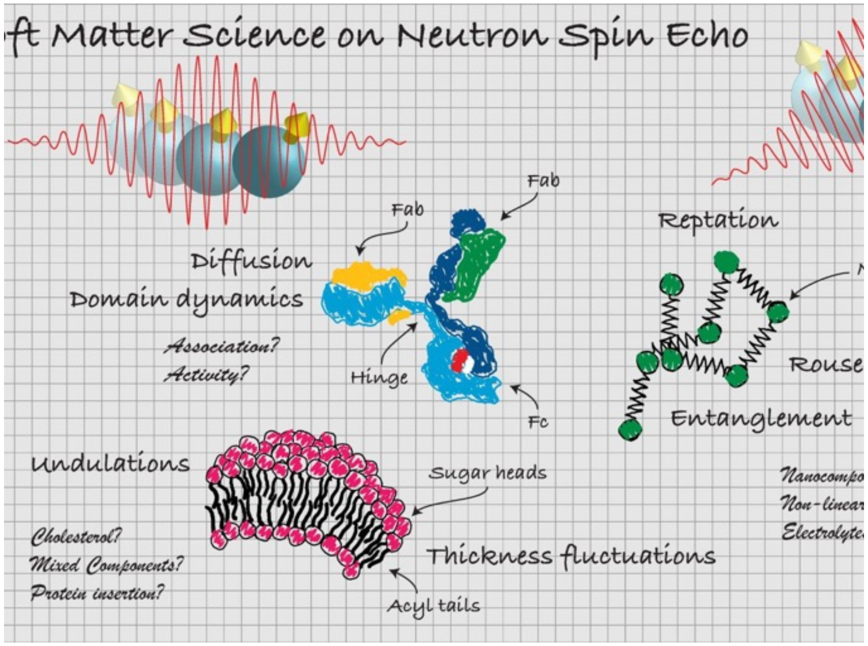


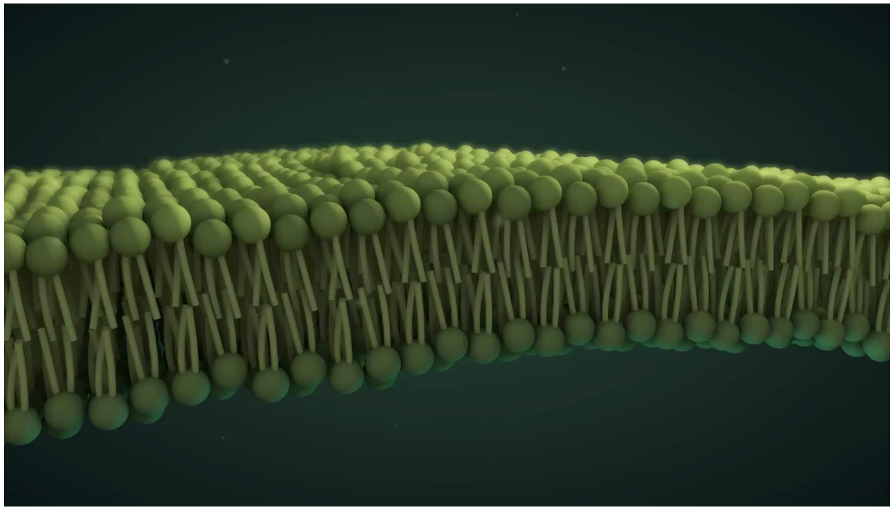
NSE Instruments World Wide



Hypothesis

Accessing longer time scales allows us to probe relevant dynamics on the nanoscale – on longer length scales- bridging dynamics and structure

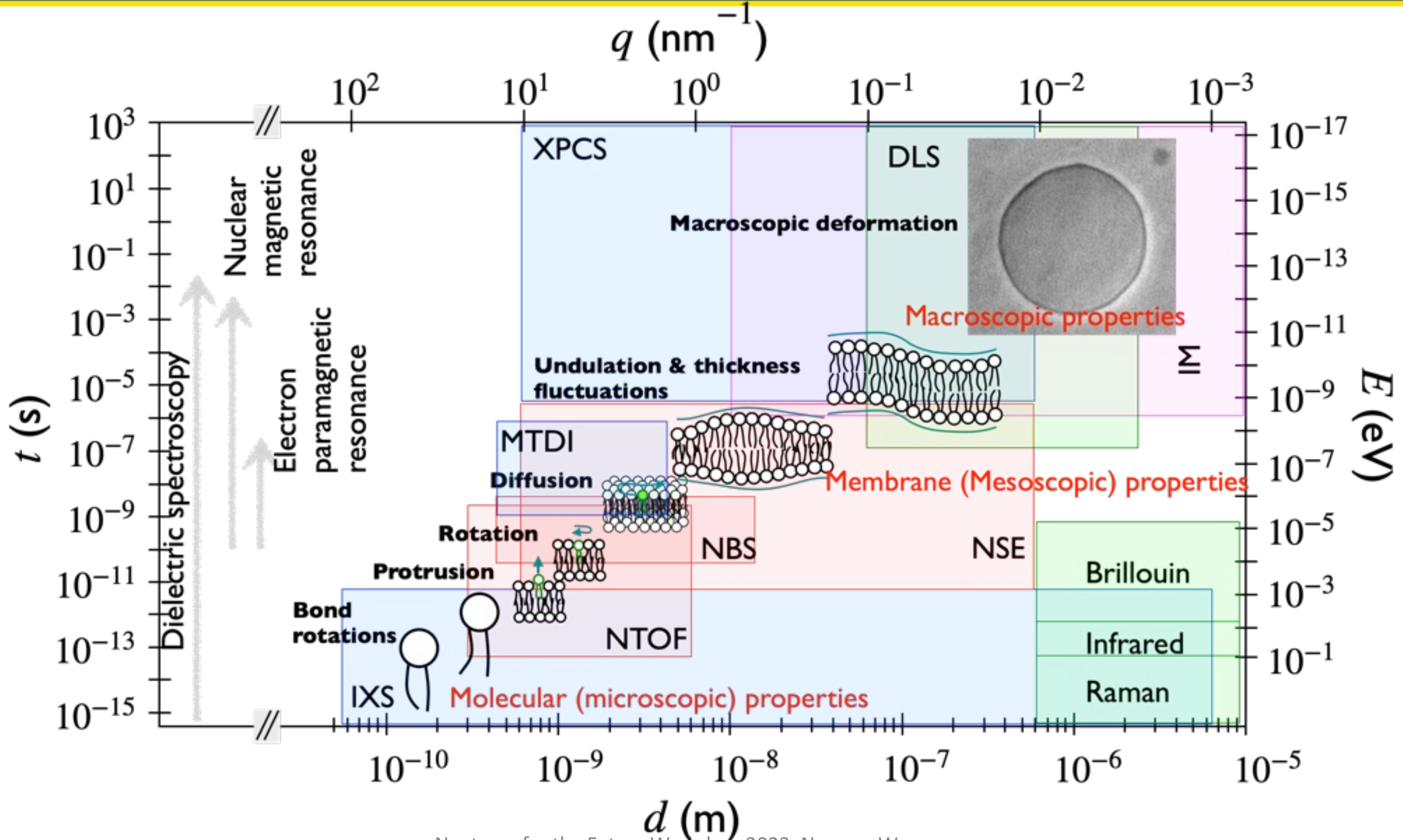




M. Nagao, E.G. Kelley, A. Faraone, M. Saito, Y. Yoda, M. Kurokuzu, S. Takata, M. Seto and P.D. Butler. Relationship between Viscosity and Acyl Tail Dynamics in Lipid Bilayers. *Physical Review Letters.* Published online Aug, 12, 2021. DOI: 10.1103/PhysRevLett.127.078102

UNIVERSITY of DELAWARE

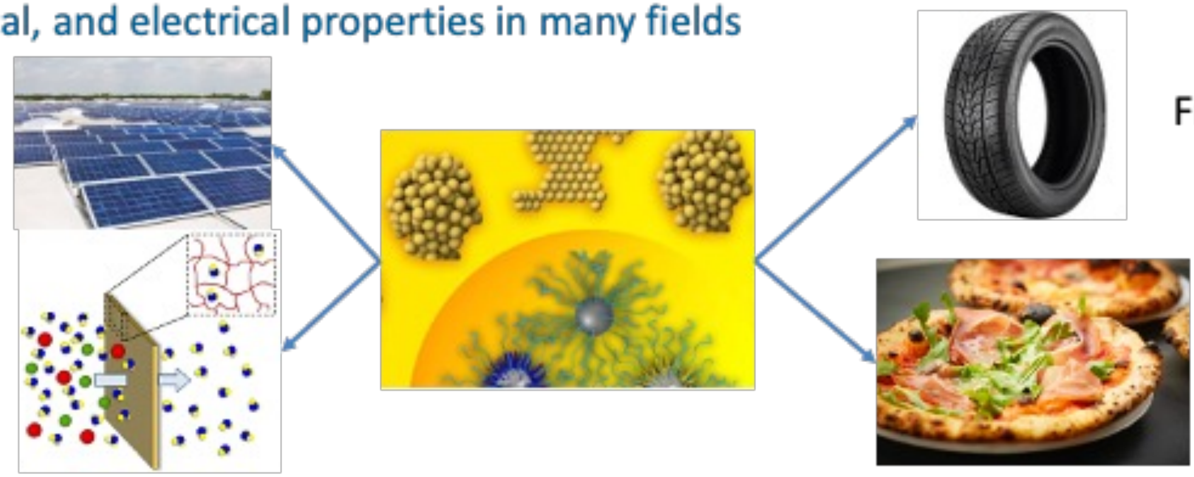
"Neutrons are essential, precious, and powerful."



Neutrons for the Future Workshop 2023, Norman Wagner

Polymer Nanocomposites

- Addition of nanoparticles to a polymer melt can improve thermomechanical, optical, and electrical properties in many fields



Solar Panel

Membranes

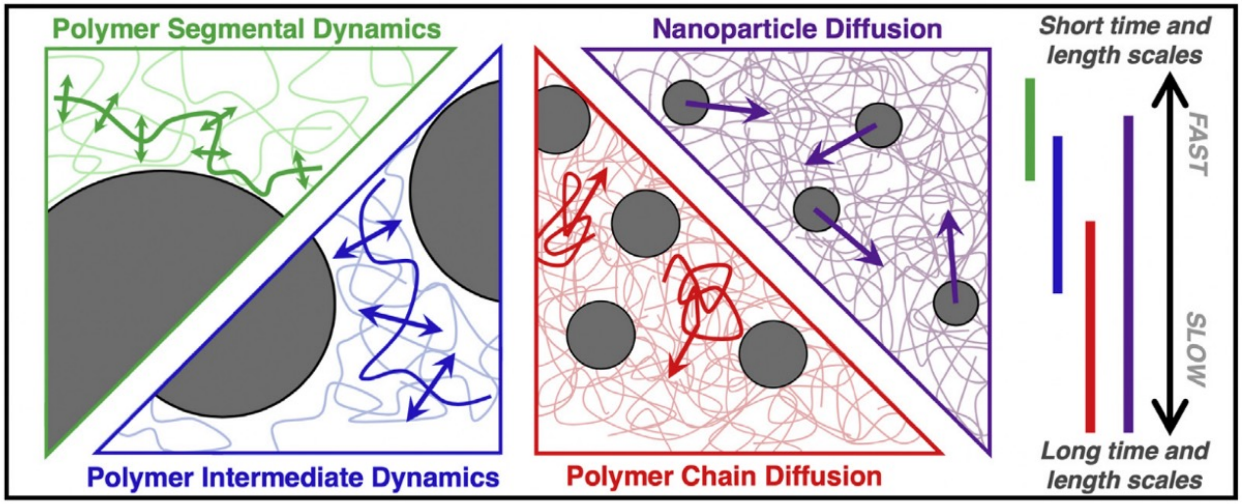
Filled Rubbers

Food Packaging

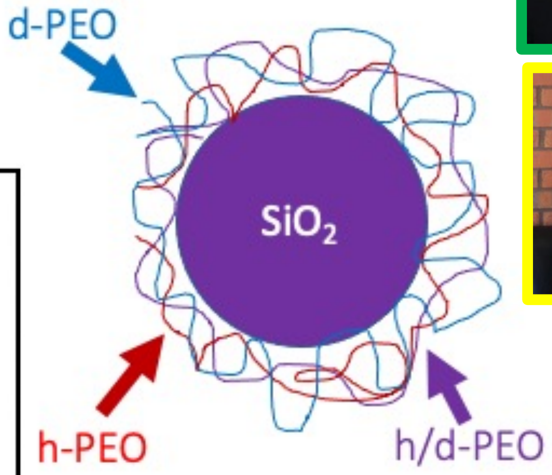
Kumar, S. K. et al., *Macromolecules* **2017,** *50* (3), 714-731.1
https://www.nist.gov/programs-projects/polymer-membranes
http://www.jeccomposites.com/knowledge/international-composites-news/continuous-fiber-reinforced-thermoplastic-plates-industry

Nanocomposites: Mechanism

Hypothesis: Nanoparticles affect polymer structure and dynamics through adsorbed segments and/or confinement

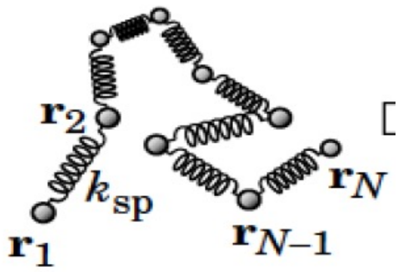


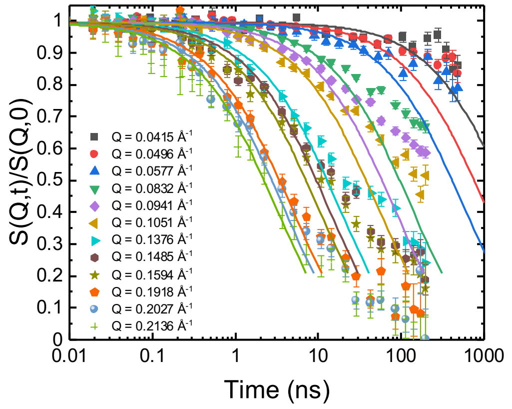
SiO$_2$ in h/d PEO for NSE

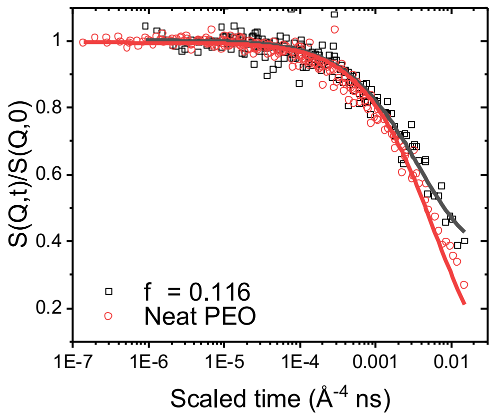


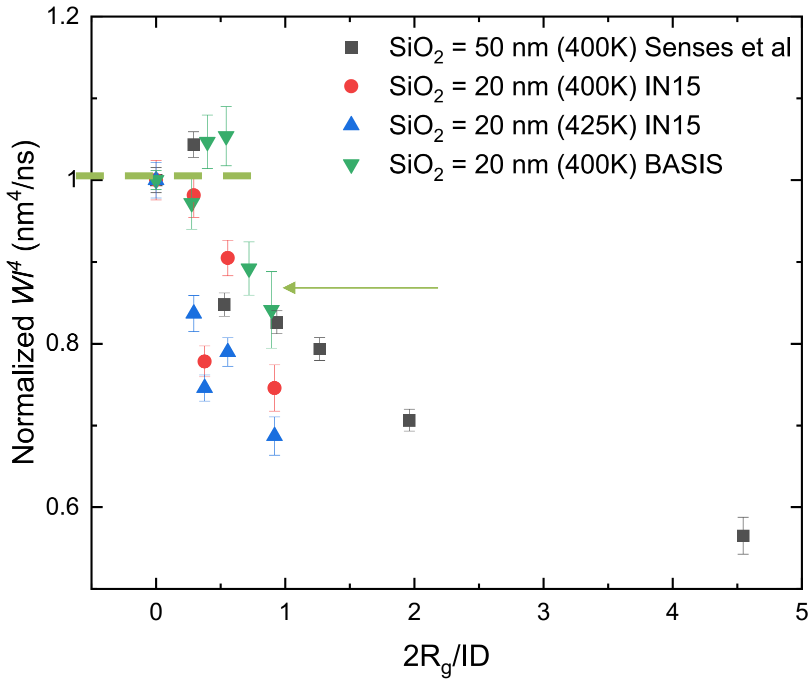
Bailey, E. J.; Winey, K. I., Dynamics of polymer segments, polymer chains, and nanoparticles in polymer nanocomposite melts: A review. *Progress in Polymer Science* **2020,** *105*.

NSE Accesses Rouse Motion

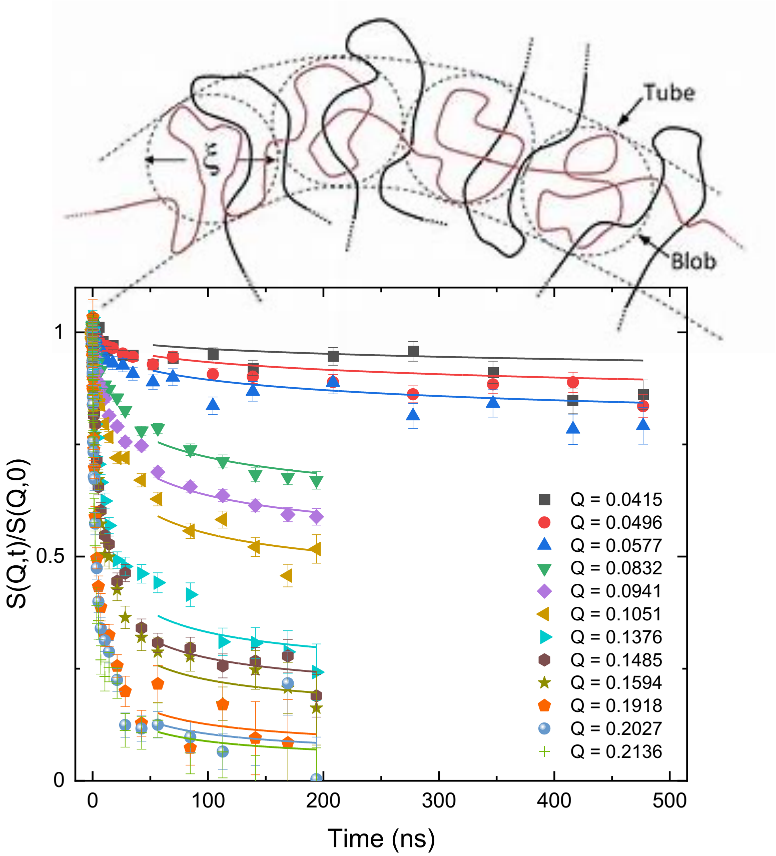




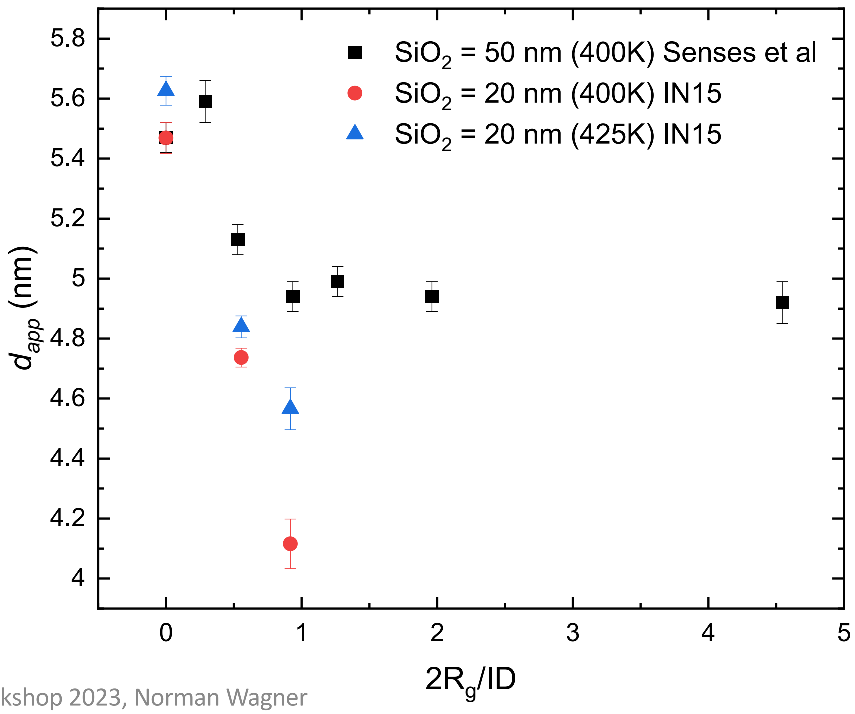




NSE Accesses Rouse & longer time motion

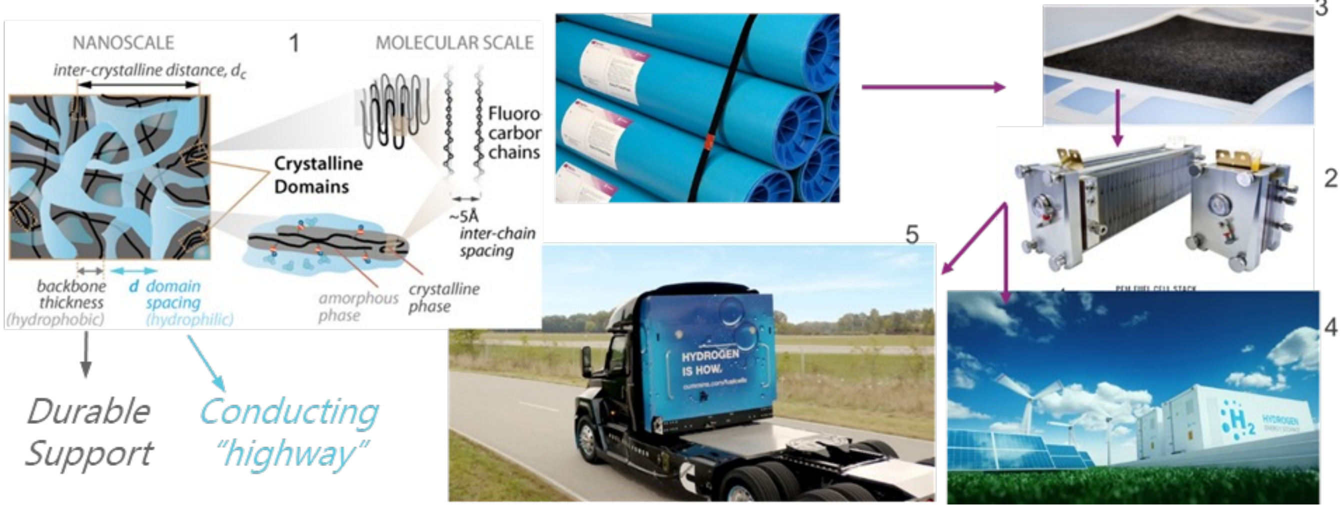


Reptation Tube Size (IN15)



Hydrogen Economy

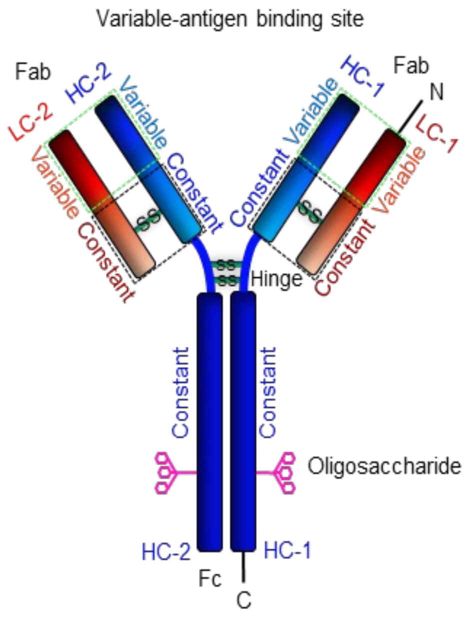
Advanced Material Design → **Commercial Membrane Fabrication** → **High Efficiency Devices**

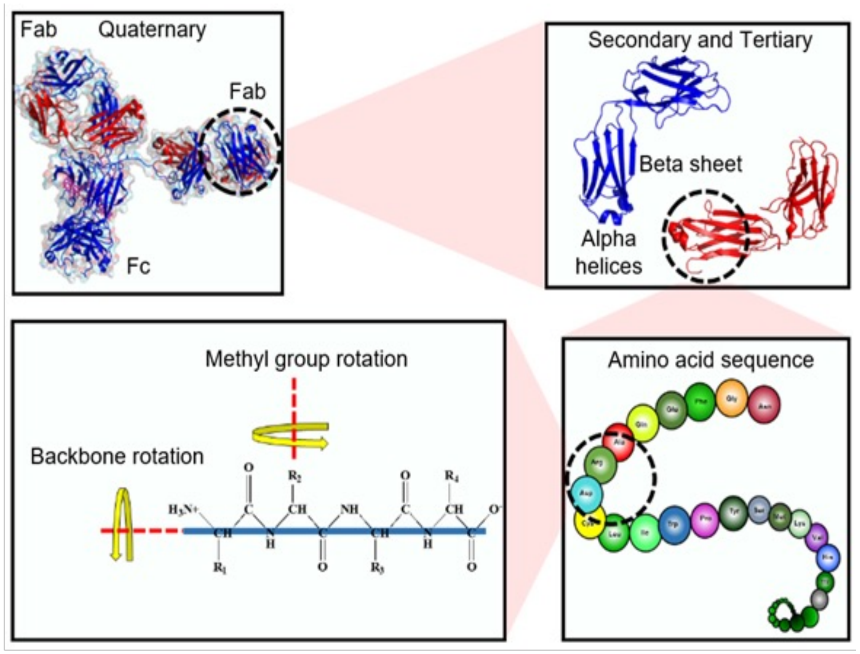


Jack Rooks

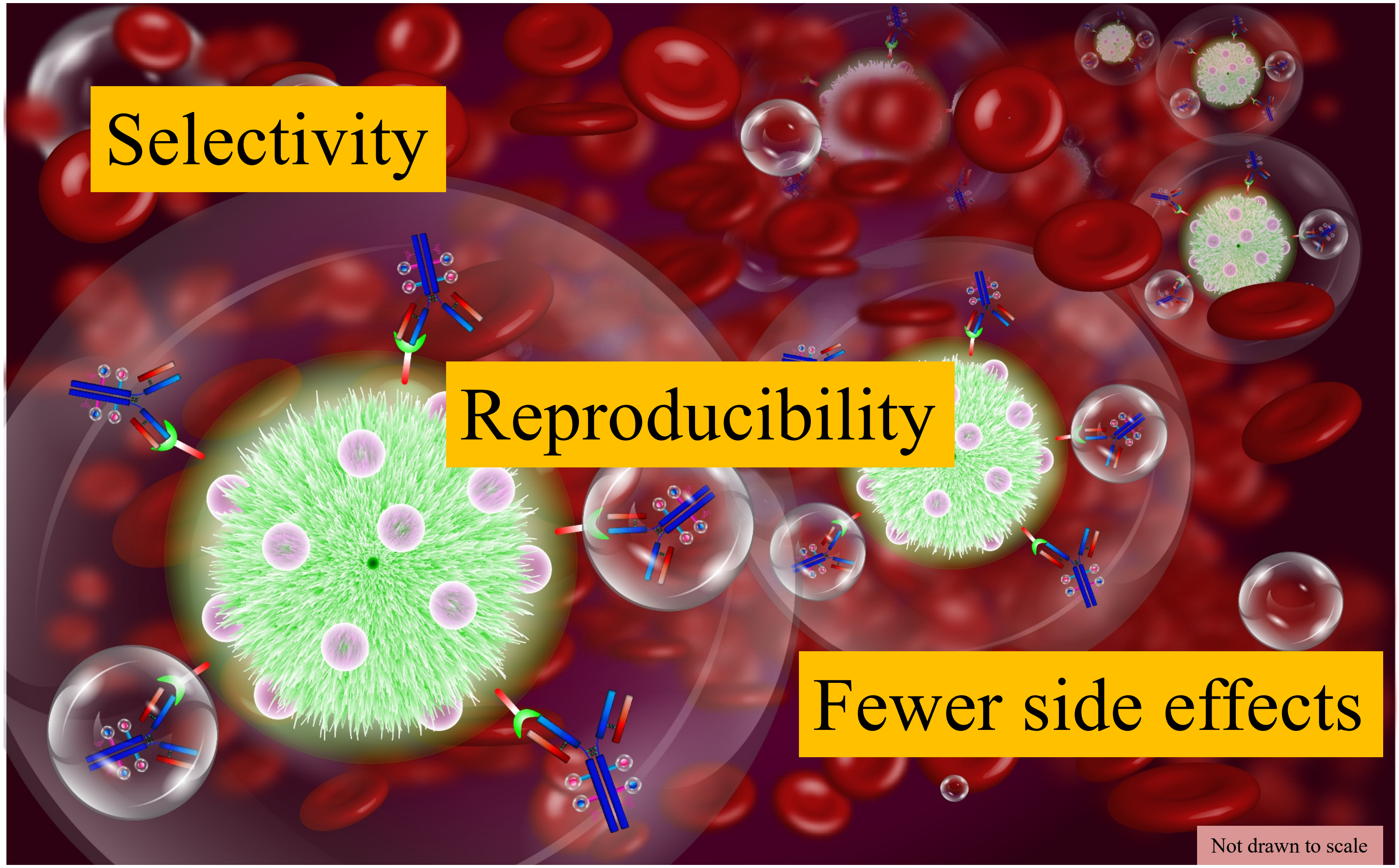
OAK RIDGE National Laboratory | HIGH FLUX ISOTOPE REACTOR | SPALLATION NEUTRON SOURCE

Monoclonal Antibody





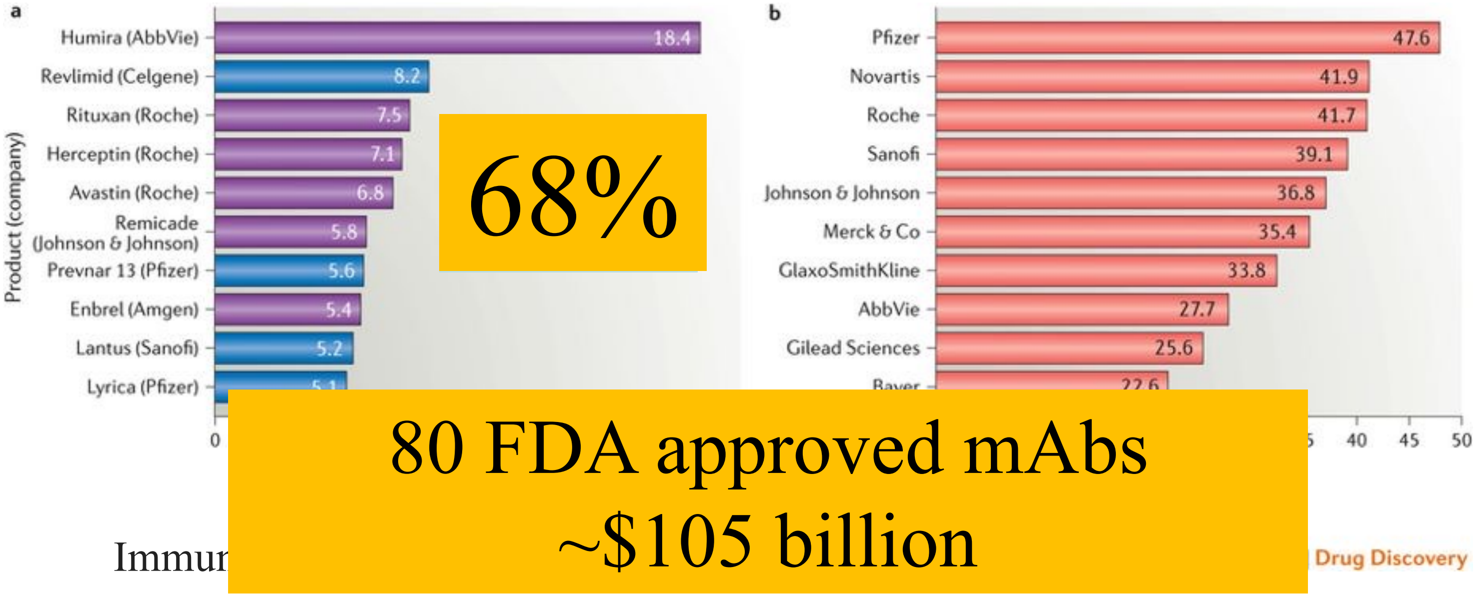
❑ Monoclonal antibodies for targeted therapies



Nayem et al. (2019) (in prep)

❑ Biopharmaceuticals

Nature review: Top 10 pharmaceutical drugs and companies (2017)

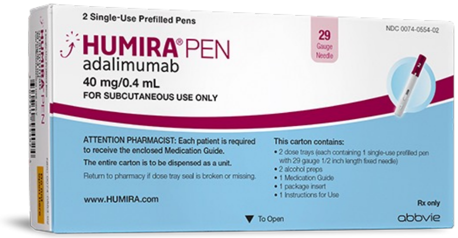


68%

80 FDA approved mAbs
~$105 billion

Immun

$18 billion of sales in 2017



- Rheumatoid arthritis
- Poriatic arthritis
- Crohn’s disease
- Ulcerative colitis
- Plaque psoriasis
- Hidradenitis suppurative

Nayem et al. (2019) (in prep)

Urquhart, Lisa. "Market watch: Top drugs and companies by sales in 2017." (2018): 232.

❑ Stability of mAb-based drug products

Research

Purification

Formulation

Filing

Storage

Shipping

Administration

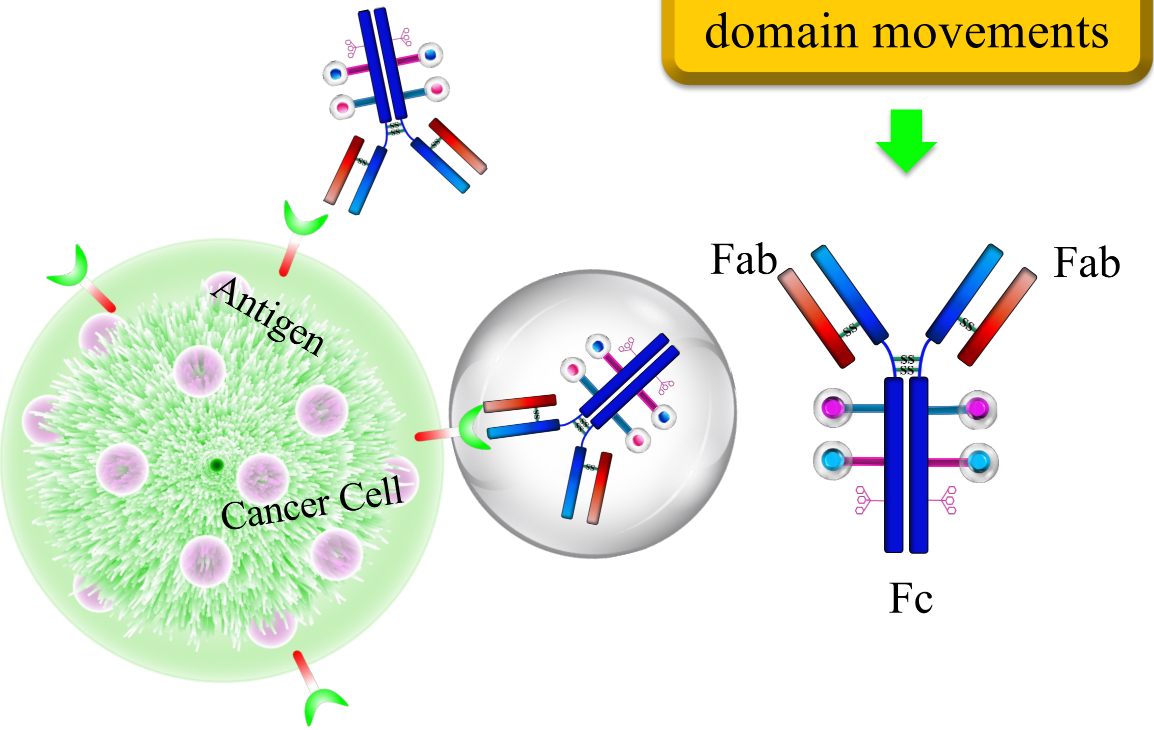
- Biophysical properties

- structure, dynamics, protein-protein interactions, solution viscosities etc.

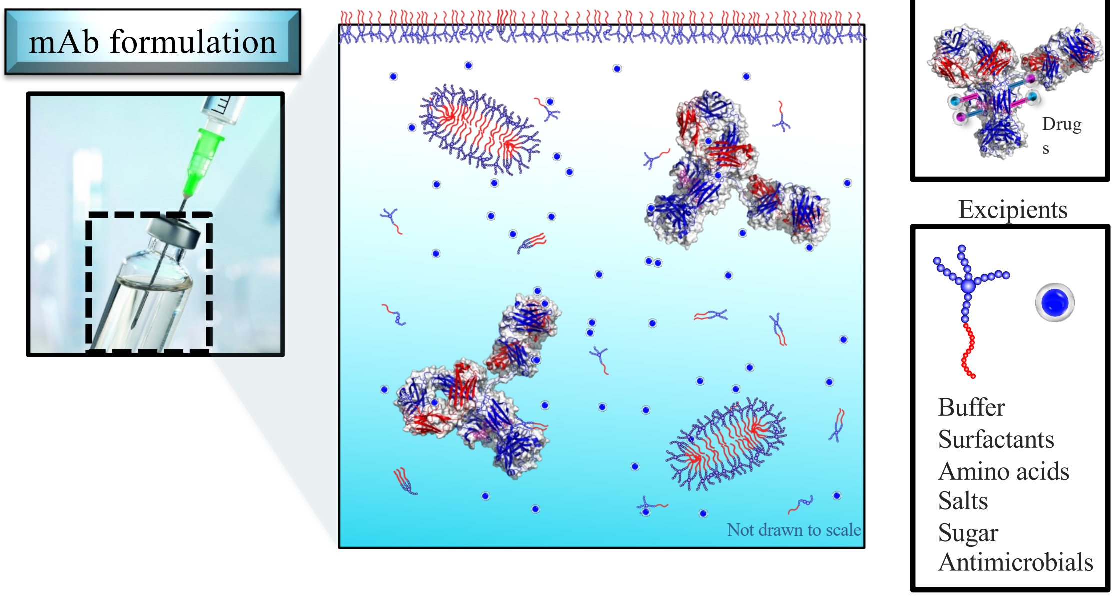
- Aggregation propensities
- Excipients (e.g. surfactants)
- Buffer conditions (e.g. pH)
- Protein concentrations

☐ Importance of internal dynamics: bio-functionality

Hinge-bending domain movements



❑ Importance of conformational stability of therapeutic mAb



mAb formulation

Protects mAbs at the air-water interface

Active pharmaceutical ingredients (APIs)

Excipients

Buffer
Surfactants
Amino acids
Salts
Sugar
Antimicrobials

Filing

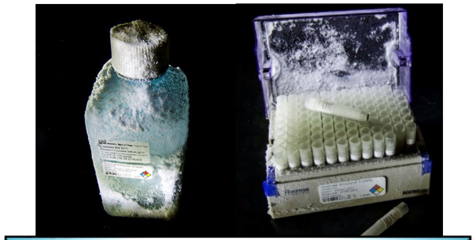
Storage

Transport

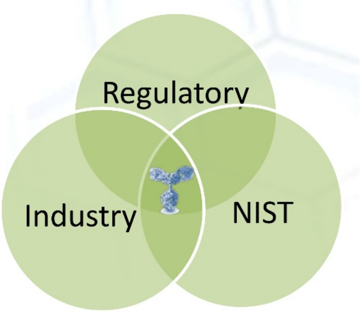
Administration

☐ The model therapeutic mAb: NISTmAb

A <u>widely characterized</u> <u>publicly available</u> monoclonal antibody for development of <u>novel methods for characterizing</u> therapeutic mAbs.



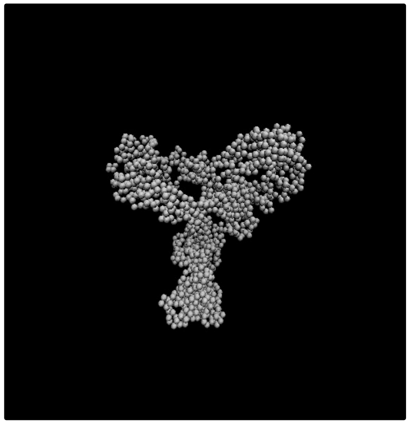
The NISTmAb reference material



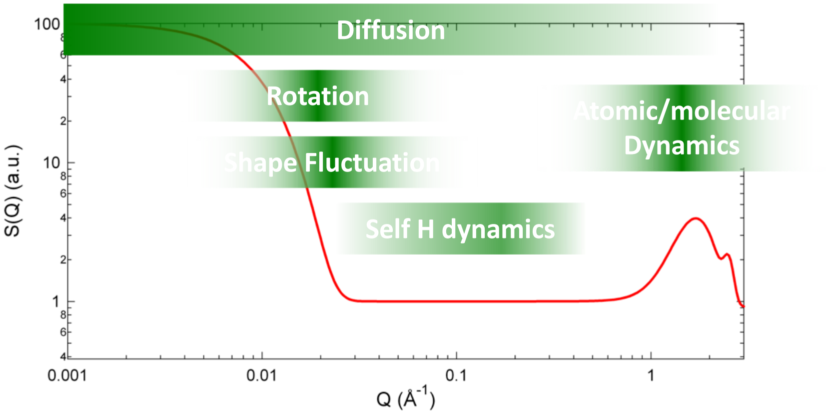
AMGEN
MedImmune
nibrt
FDA
University of Birmingham
Pfizer Wyeth
National Institutes of Health
Boehringer Ingelheim
SANDOZ
Agilent Technologies
Thermo Scientific
BRUKER
Genentech A Member of the Roche Group
biogen idec
Janssen
NOVAVAX
PROTEIN METRICS
Lilly

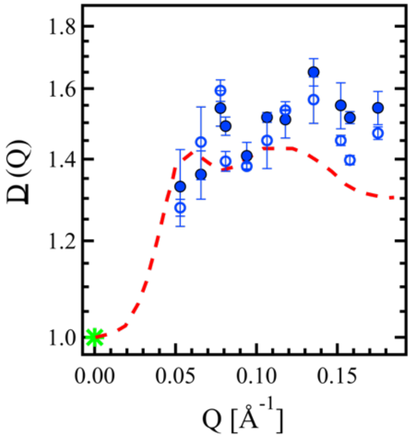
Schiel, John E., Darryl L. Davis, and Oleg Borisov, eds. *State-of-the-art and Emerging Technologies for Therapeutic Monoclonal Antibody Characterization: Monoclonal antibody therapeutics: structure, function, and regulatory space; Volume 2. Biopharmaceutical characterization: the NISTmAb case study; Volume 3. Defining the next generation of analytical anf biophysical techniques*. American Chemical Society, 2014.

Types of Dynamics



Dr. Joseph Curtis, NIST





At length scales larger than the macromolecular size: Diffusion.

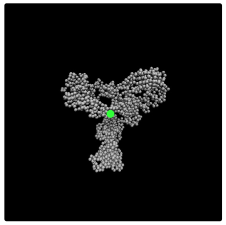
At length scales of the order the macromolecular size: Rotations and shape fluctuations.

Where the incoherent signal is dominant: Self H dynamics (translations, rotations, vibrations,…)

At the structural peaks: Atomic/Molecular Dynamics.

❑ Evaluating timescales of internal dynamics via MD simulation

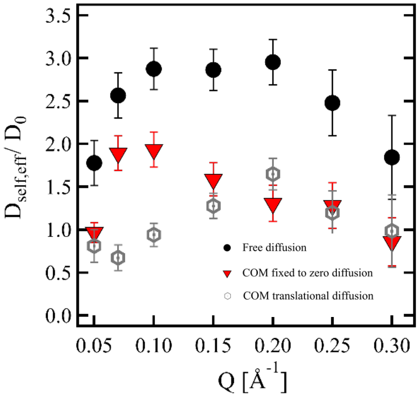
Free diffusion



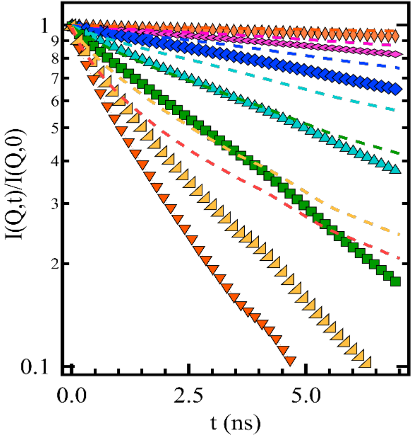
Translational + rotational + internal

COM fixed to zero

Rotational + internal



Intermediate scattering function



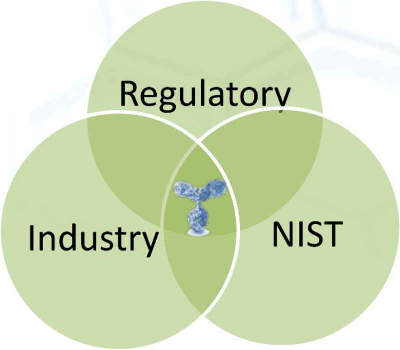
The normalized ISFs as a function of Q

MD simulation: Up to 7 ns timescale, internal dynamics contribute ~55% to the overall diffusion of one NISTmAb.

Joseph Curtis (NIST) & José Villanuev

❑ Model therapeutic mAb: NISTmAb

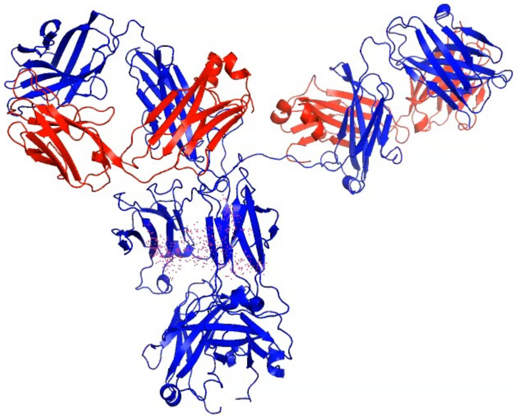
A global partnership to advance
biopharmaceutical analytics



Regulatory

Industry

NIST



The NISTmAb reference material

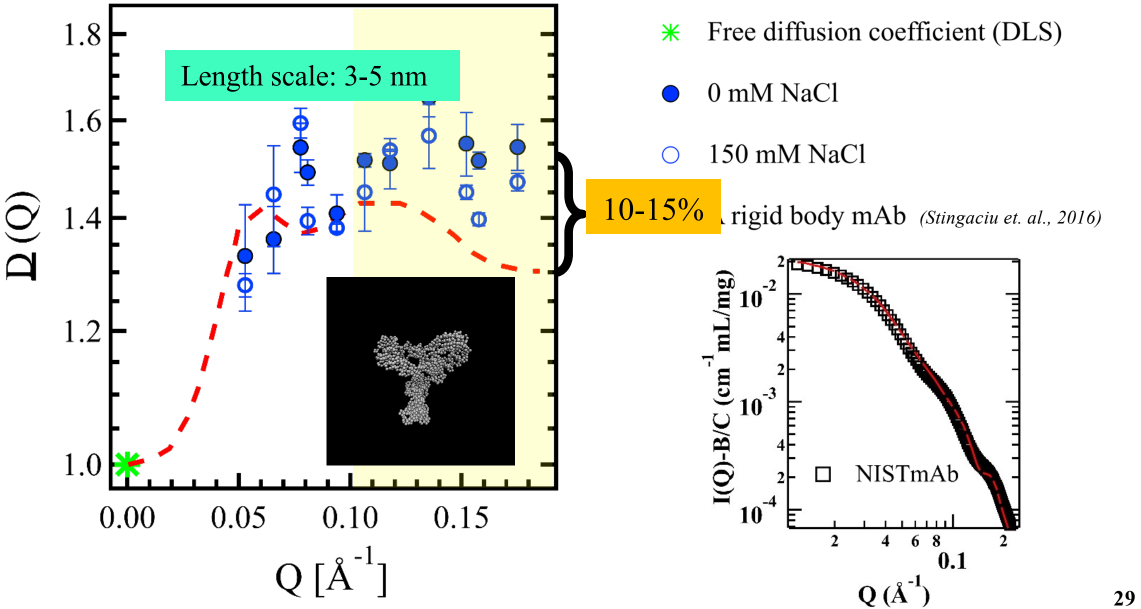
Jansser
NOVAVAX
PROTEIN METRICS
AMGEN
MedImmune
Genentech
A Member of the Roche Group
Boehringer Ingelheim
SANDOZ
biogen idec
Lilly
nibrt
FDA
Pfizer Wyeth
NATIONAL INSTITUTES OF HEALTH
UNIVERSITY OF BIRMINGHAM
Thermo SCIENTIFIC
BRUKER
Agilent Technologies

Nayem et al. (2019) (in prep)

Schiel, John E., Darryl L. Davis, and Oleg Borisov, eds. *State-of-the-art and Emerging Technologies for Therapeutic Monoclonal Antibody Characterization: Monoclonal antibody therapeutics: structure, function, and regulatory space; Volume 2. Biopharmaceutical characterization: the NISTmAb case study; Volume 3. Defining the next generation of analytical anf biophysical techniques*. American Chemical Society, 2014.

❑ Shape modulated effective free diffusion coefficient

In the NSE Q range, internal dynamics contribute to 10-15%.



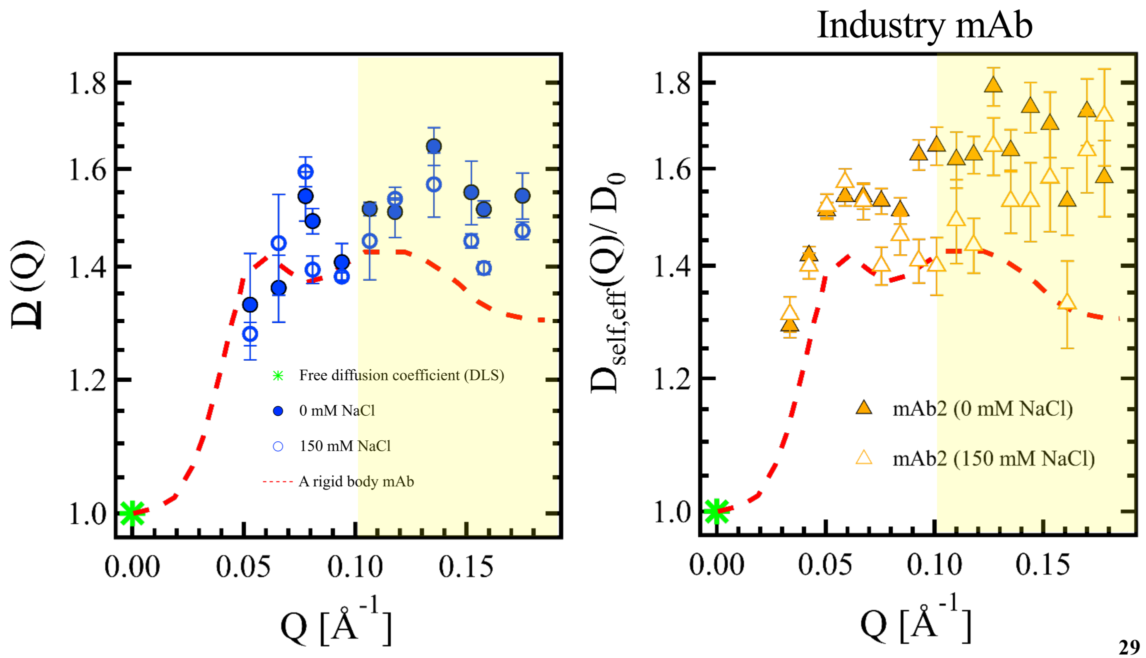
Length scale: 3-5 nm

10-15%

Nayem, J. et.al. *PNAS* (**2020**) (In prep)

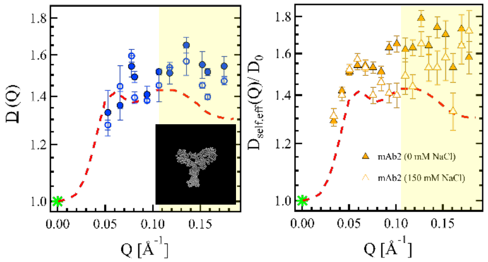
❑ Shape modulated effective free diffusion coefficient

Industry mAbs are more flexible compared to NISTmAb

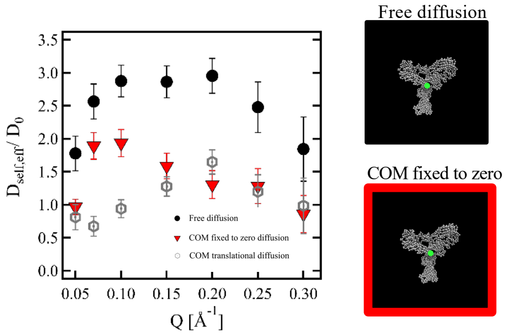


Nayem, J. et.al. *PNAS* (**2020**) (In prep)

❑ Conclusions



- In the NSE scales, internal hinge bending domain dynamics contribute **9-17%** to the total diffusion.
- Industry mAbs are **more flexible** than the NISTmAb
- The large deviation between DLS center of mass diffusion and NSE diffusions is due to the **anisotropic shape**.



- Internal motion contributes to **55%** to the overall motion of a NISTmAb proteins. This overestimation has to do with the force field
- Center of mass self-translational diffusion is **shape and size dependent**.

"Neutrons are essential, precious, and powerful."