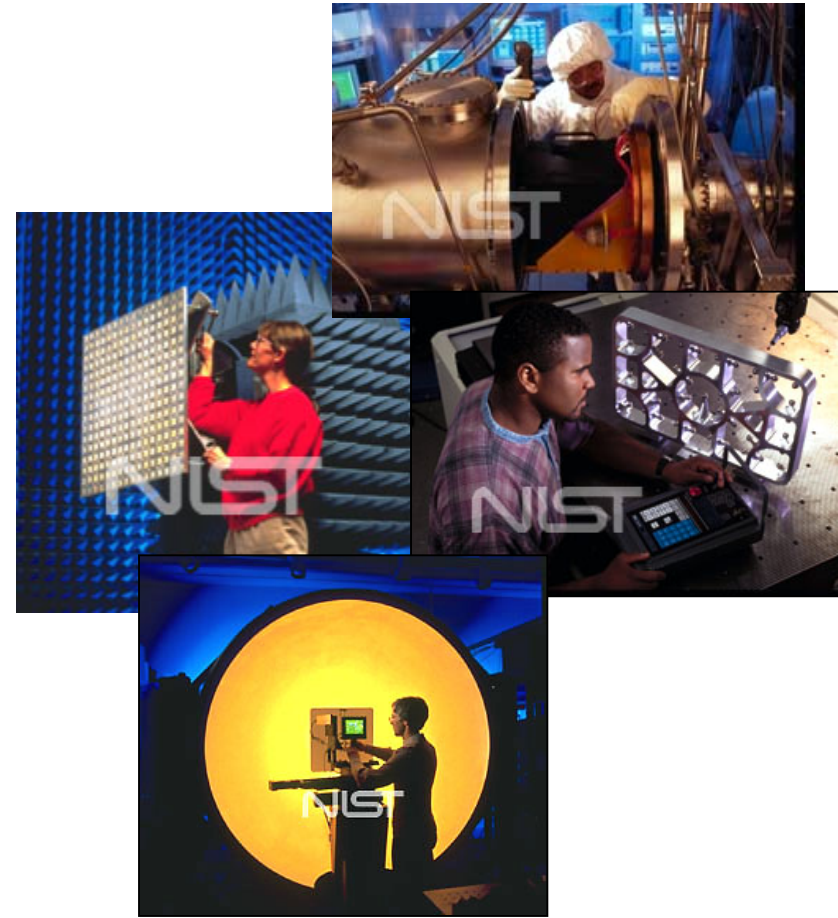


National Institute of Standards & Technology (NIST)

Non-regulatory agency
established in 1901 in the US
Department of Commerce.

Mission: to promote US
innovation and industrial
competitiveness by advancing
measurement science, standards
& technology



NIST: Basic Statistics

- ~ 3,000 employees
- ~ 2,800 associates and facilities users
- ~ 1,300 field staff in partner organizations
- Two main campuses- Gaithersburg, MD and Boulder, CO
- FY15 Budget: ~\$700M for Laboratory Programs
- 8 NIST strategic partnerships including the Joint Quantum Inst. & Inst. for Biotechnology & Bioscience Research



Gaithersburg, MD



Boulder, CO



IBBR, Rockville, MD



NIST Program in Biomanufacturing

Program coordinator: Mike Tarlov, tarlov@nist.gov

- Measurement science, standards, and data to support development, manufacturing, & regulatory approval of protein therapeutics
 - Extensive stakeholder input & interactions (regulatory, biopharma, instrument vendors, academia)
 - Relevant, innovative and robust tools
 - Open data sharing, crowd-sourcing approach



Partners and Stakeholders:



NIST Biomanufacturing Program Areas

Protein Stability/Biophysical

Particulates, Aggregation

- (Surrogate Protein Particle SRM 1989)
- Flow microscopy
- AFFF, SEC

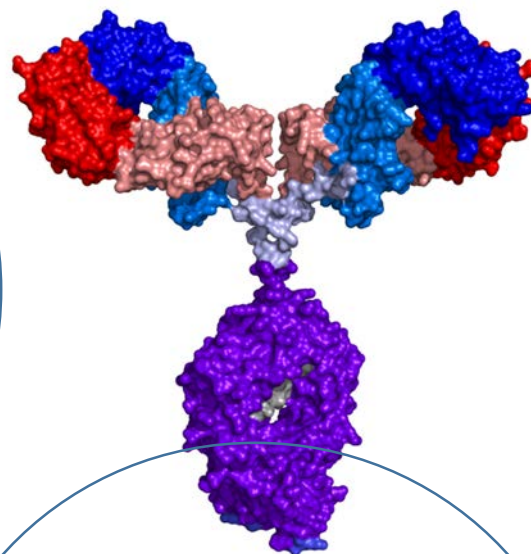
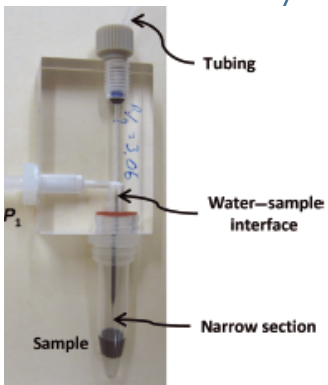
Stability predicting tools

- Neutron scattering
- Raman and Red edge spectroscopy

Rheology

- Micro-viscosity
- Shear effects

μViscometer

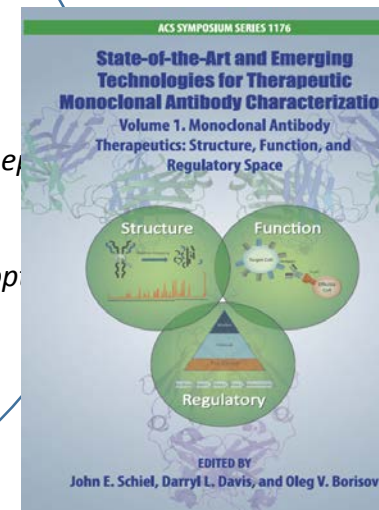


Protein Structure

(NISTmAb RM 8671)*

- Primary structure, modifications
 - Mass spectrometry
 - MS library
 - Peptides, glycans, glycopeptides, all modifications
- Protein folding
 - FT-IR, DSC/fluorimetry, Raman optical activity
- Higher-order structure
 - HDX-MS
 - NMR
 - Neutron scattering

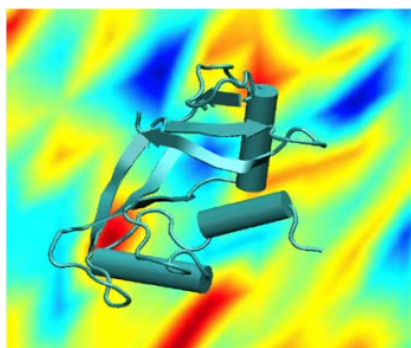
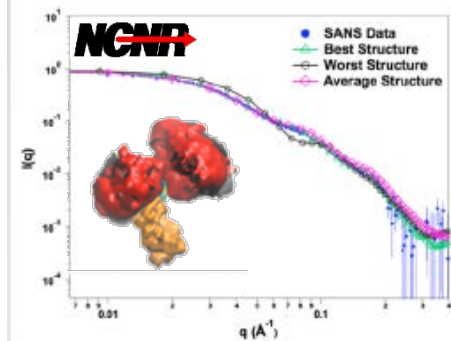
ACS Book
Based on NISTmAb



Production Cell Variability

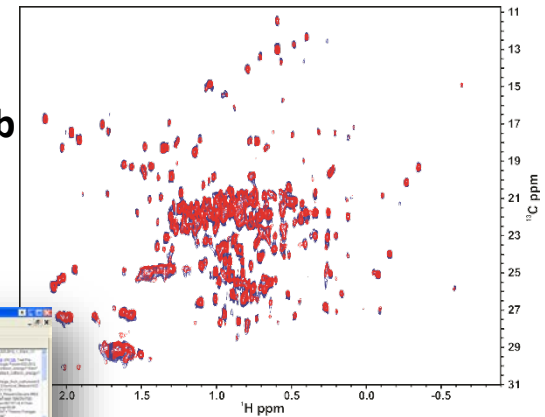
- Cell line ID
 - Multiplex PCR
- Production cell expression
 - Fluorescence imaging
- Host cell
 - MS Library
 - HCP peptides, glycans, metabolites

Neutron Scattering of Therapeutic Proteins

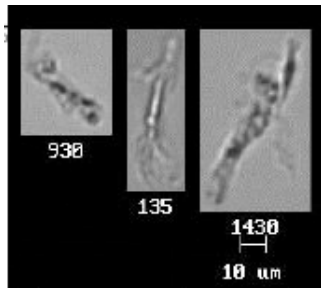
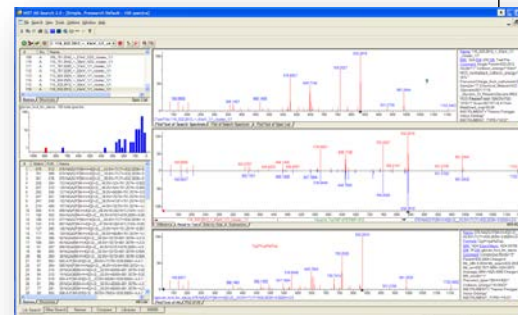


Protein in Freeze-Dried Formulation

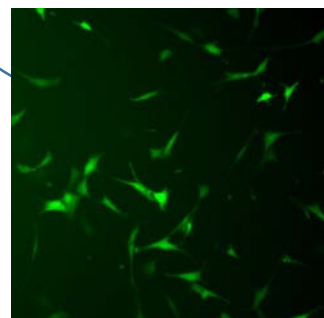
2-D NMR of NISTmAb



MS-Library of Therapeutic Antibodies



Protein Particle Standards



NIST Benefit

- Convenes stakeholders from across biopharmaceutical industry, academia & FDA so that NIST can better:
 - Assess current and future measurement and standards needs of industry
 - Learn of regulatory drivers shaping industry
 - Stay informed of new cutting-edge measurement technologies and methods
 - Communicate what NIST does to customers
 - Forge potential partnerships

NIST Characterization Efforts

(Stability, Identity, Purity, Concentration)

- **Separation Science**
 - SEC, RP, HIC, CEX, WAX
- **Mass spectrometry and LC-MS**
 - Peptide mapping, middle down, and intact
 - PTM analysis
 - Sequence Variant
 - Glycoanalysis
 - HCP's
- **Mass spectral database**
 - Peptide MS/MS
 - Glycan MS/MS
- **Certification of Total Protein Concentration**
 - AAA
 - Peptide IDMS
- **Future potential certified values**
 - Extinction coefficient
 - Monosaccharide content
- **Higher Order Structure**
 - NMR
 - XRD
 - HDX-MS
 - Small angle neutron scattering (SANS)
 - Small angle x-ray scattering (SAXS)
- **Biophysical Measurements**
 - AUC
 - SEC-MALS/DLS
 - AFFF
 - CD
 - FTIR
- **Fc binding assays**
- **Rheology**