Nano EHS @ NIST

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Labs at NIST Partnering on NanoEHS

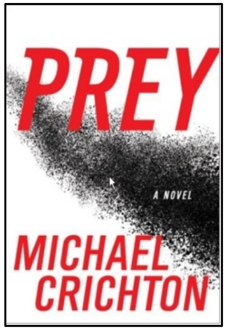
- Materials Science & Engineering Laboratory
- Physics Laboratory
- Manufacturing Engineering Laboratory
- Chemical Science & Technology Laboratory

- Center for Nanoscale Science & Technology
- Electronics & Electrical Engineering Laboratory

Nano EHS @ NIST

❖ What is the problem?

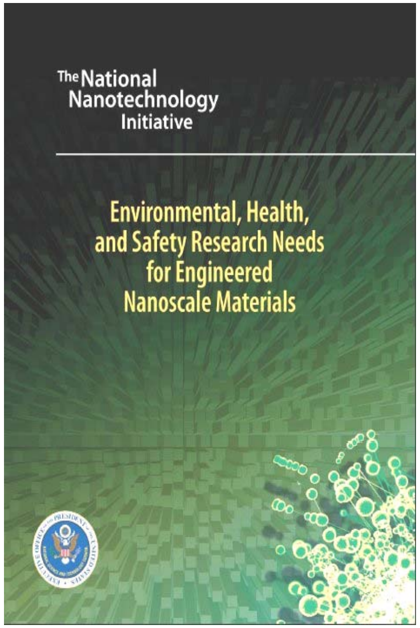
- Health and environmental risks of nanomaterials (real and perceived) are roadblocks for innovation and commercialization of nanotechnology.
- Data quality inhibits the ability to understand, predict, and manage potential risks of engineered nanoscale materials.
- Lack of certainty in nanoscale measurements impacts regulatory and policy decisions.



Nano EHS @ NIST

❖ How can NIST make an impact here?

- Develop a national-scale nano-metrology infrastructure that enables science-based decision-making
- Lead government and industry nano-metrology efforts to develop a unified approach to manage potential nanomaterial environmental, health, and safety risks

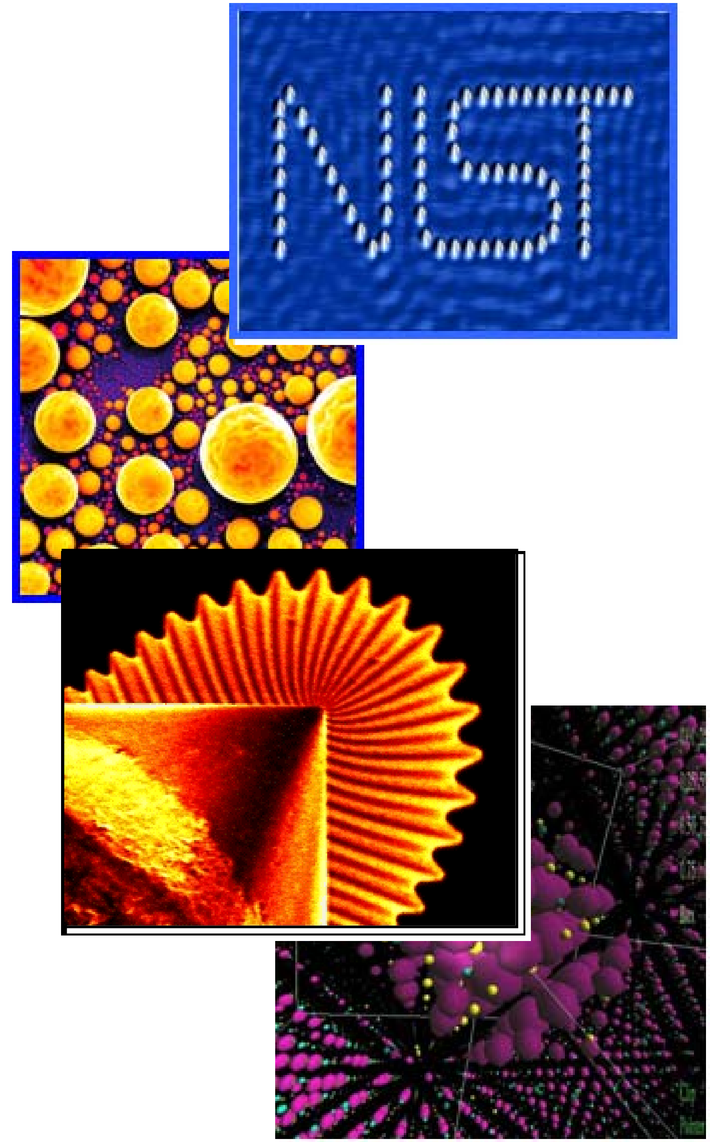


❖ Why should NIST be the one doing this?

- NIST identified by the NNI as the lead agency on nanoscale metrology to reduce scientific uncertainties associated with EHS
- Nano EHS potential showstopper for U.S. industrial competitiveness - NIST mission

Anticipated Outcomes of NIST Program

- **With our federal partners, we will**
  - **Provide a scientific basis to the health and environmental effects of nanotechnology**
  - **Enable US industry to safely develop, exploit, commercialize nanotechnologies**



OSHA 1971 35 2006

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

FDA

NATIONAL INSTITUTES OF HEALTH

NIOSH

USGS science for a changing world

Programmatic Outline of New NIST Work

Area	Year 1	Year 1 and Outyears	Outyears
I. Nanomaterial Classification	**Establish unifying definitions for classes of nanomaterials; develop roadmap for NIST work**	**Initiate national effort to develop standards**	**Deliver standards** **-reference materials** **-reference data** **-interlaboratory comparisons**
II. Nanomaterial Characterization	**Identify and critically evaluate existing nanoscale measurement methods, devices, instrumentation**	**Develop new and extend existing methods to meet measurement challenges**	**Deliver validated** **-instrumentation** **-measurement methods** **-protocols**
III. Validation of Toxicological Assessments	**Facilitate the assessment of state of the art toxicological measurements**	**Integrate classification scheme into toxicological assessment**	**Create and disseminate reference materials and protocols for nanomaterial toxicology**

What have we done leading up to this?

- Members of Nanotechnology Environmental & Health Implications (NEHI) panel (NSET, NNI)
- Participating in & leading efforts in ISO, IEC, ASTM, IEEE
- Held **NNI-sponsored workshop** to initiate interagency, academic, industrial cooperation and consensus building
- Developing first **nano reference materials**
- Developing **analytical methods** to characterize nanomaterials
- Using characterized materials to **evaluate cellular uptake**, transport, stability, fate
- Developing **high-throughput multiplexed screening methods** for quantitative, reliable toxicity measurements
- Developing approaches to evaluate **environmental transport & fate**

All of these efforts seeded by other funds (IMS, ATP, STRS reprogramming) in prior years

NIST & Nanotechnology Standards

Nano@NIST

- **Standards**
  - Documentary standards
  - Reference materials
- **Nanomaterial Characterization: Nanoscale Metrology**
  - Chemical
  - Physical
- **Validation of Toxicological Methods: Support Understanding Environmental and Health Impacts**
  - High throughput tox screening
  - *In vitro* simulations of *in vivo* conditions
  - Fate of nanomaterials in environment

Nanotechnology Documentary Standards

ISO TC 229: Nanotechnologies - established 2004

- Chair and Secretariat with UK
- Three working groups:
  - WG 1: Terminology and nomenclature (Canada- Chair)
  - WG 2: Measurement and characterization (Japan- Chair)
  - WG 3: Health, Safety and Environmental Aspects of Nanotechnologies (USA/NIST – Chair)

ASTM E56: Standards and guidance for nanotechnology and nanomaterials - established 2004

- Six sub-committees:
  - E56.01 Terminology & Nomenclature
  - E56.02 Characterization: Physical, Chemical, and Toxicological Properties
  - E56.03 Environment, Health, and Safety
  - E56.04 International Law & Intellectual Property
  - E56.05 Liaison & International Cooperation
  - E56.90 Executive
  - E56.91 Strategic Planning and Review

Nanotechnology Documentary Standards

Nano@NIST

<u>IEC TC 113:</u> Nanotechnology standardization for *electrical and electronics products and systems* **- established 2006**

- **Secretariat: Germany, and Chair: US**
- **US TAG recently formed**
- **Emphasis on strong liaison with ISO TC 229**

<u>IEEE:</u> Standards activities under IEEE Nanotechnology Council addressing materials, devices and system-level interoperability

- **Part of IEEE Nanoelectronics Standards Roadmap initiative – March 2006**
- **Anticipatory standards philosophy**
- **Standards for nanoelectronics:**
  - **IEEE P1650 standard test method for measurement of electrical properties of CNTs- standard approved and adopted in 2005**
  - **Work underway on development of standard method for characterization of CNTs used as additives in bulk materials (IEEE P1690)**

Workshop at NIST (Feb. 2008) to coordinate nanotechnology standards groups; identify immediate and medium-term nanotechnolgy documentary standards needs.

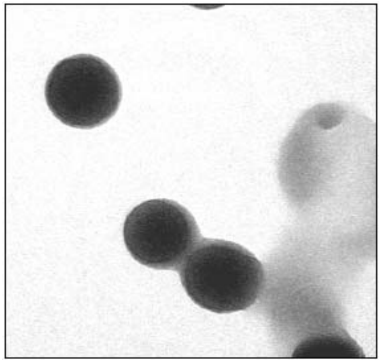
Roadmapping NIST's Nanoscale RM Program

- **Workshop: Standards for EHS Research Needs for Engineered Nanoscale Materials**
- Goal: Prioritization of NIST standards efforts – building the NIST roadmap for NanoEHS standards
- Dates: September 12-14, 2007, NIST
- NIST Organizers: Dianne Poster, John Small
- Outcomes:
  - Report in progress
  - Candidate nanomaterials identified and classified according to several parameters including:
    - risk of exposure
    - public perception
    - ability to mass produce with good quality
    - stability
    - well-studied materials
  - Some materials include: silver, TiO2, gold, C60, SiO2, ZnO, quantum dots, polystyrene, SWCNT/MWCNT, dendrimers

Nano Reference Materials

Current NIST Particle Size Standards: nm-µm Range

SRM	Type	Particle Diameter, nominal
1691	Polystyrene (0.5 % in H_2O)	269 nm
1963a	Polystyrene (0.5 % in H_2O)	100 nm
1964	Polystyrene (0.5 % in H_2O)	60 nm
1659	Silicon Nitride	200 nm to 10 µm
1978	Zirconium Oxide	330 nm to 2.19 µm
1988	Titanium Oxide	100 nm to 500 nm



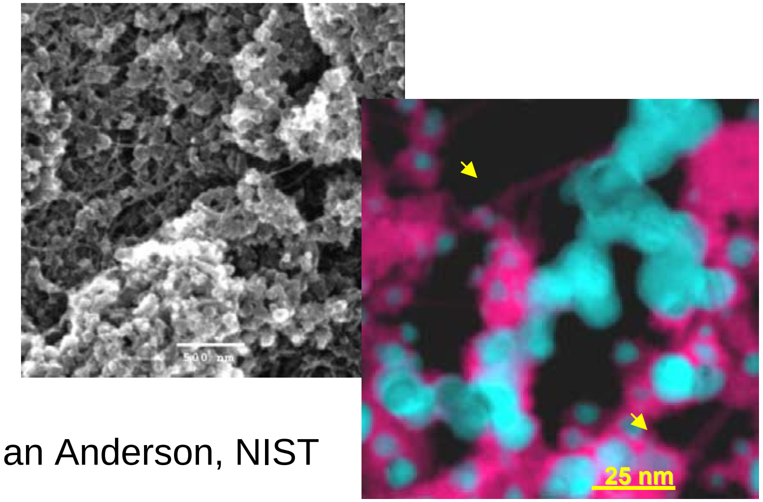
SRM 1963
100 nm spheres

SRMs for evaluating or calibrating instruments used for the determination of particle size (light scattering, electrical zone flow-through counters, optical and scanning electron microscopes, sedimentation systems)

Nano Reference Materials

Proposed RM: Carbon Nanotubes

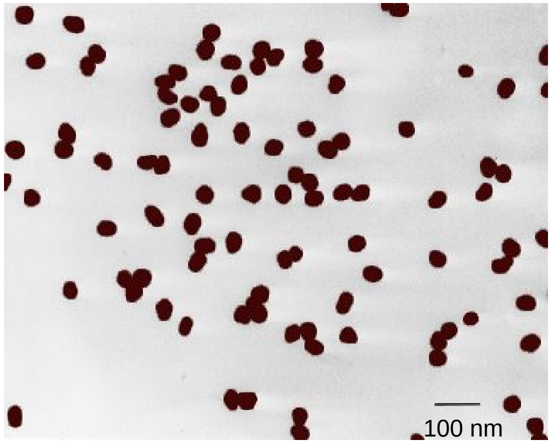
- Material obtained from vendor analyzed using >15 techniques (will result in paper in *NIST Jour. Res.*)
- NIOSH used materials in their tests
- Determined sample heterogeneity too high for RM
- Other company provided new test material
- Research on in-house production



Ian Anderson, NIST

RM: Au nanoparticles

- RM in conjunction with NIH/NCL
- Release planned for FY08
- 10 nm, 30 nm, and 60 nm mean particle size
- Currently in stability testing



www.huck.psu.edu

Nano Characterization: Building our Capabilities

The vast majority of data in the literature on tox testing of nanomaterials involves poorly characterized samples-

What characteristics are important for tox testing?

- Many groups working to develop classification matrix to prioritize characterization for tox testing
- ISO developing a document to provide guidelines on nanocharacterization for toxicology
  - Size
  - Shape
  - Chemical Composition
  - Chemical Spatial Mapping
  - Homogeneity
  - Aspect Ratio
  - Stability …

Nano Characterization: Building our Capabilities

Methods Evaluated in Development of Initial RM for Nanocharacterization

I. Analytical Measurements

Cold-neutron prompt gamma-ray activation analysis (CNPGAA).
Instrumental neutron activation analysis (INAA).
Thermogravimetric analysis (TGA)

II. Information Measurements

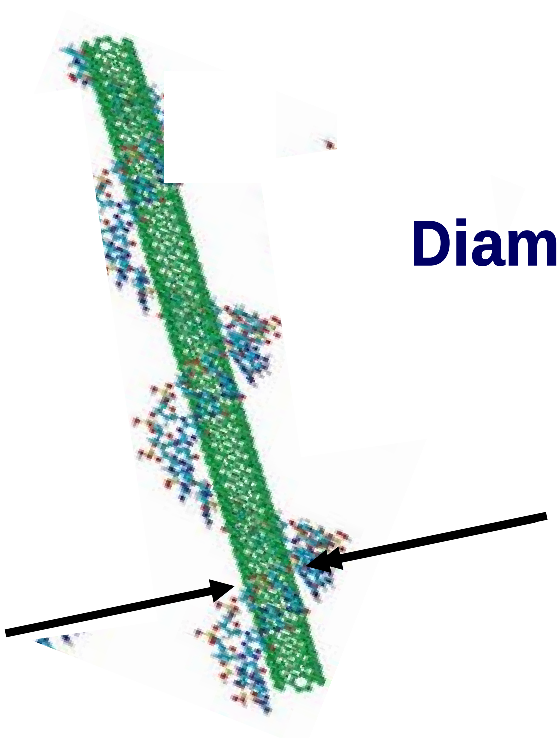
Absorption Spectroscopy
Atomic Force Microscopy
Cold-neutron prompt gamma-ray activation analysis
Dispersion and Fractionation
Dispersion Stability by UV-visible Spectroscopy
Electrical Conductivity
Helium Ion Microscopy
Inductively Coupled Plasma Source Mass Spectrometry
Instrumental neutron activation analysis
Mobility
Near Edge X-ray Absorption Fine Structure
Pyrolytic Detector
Raman Spectroscopy
Scanning Electron Microscopy
Surface Area
Transmission Electron Microscopy

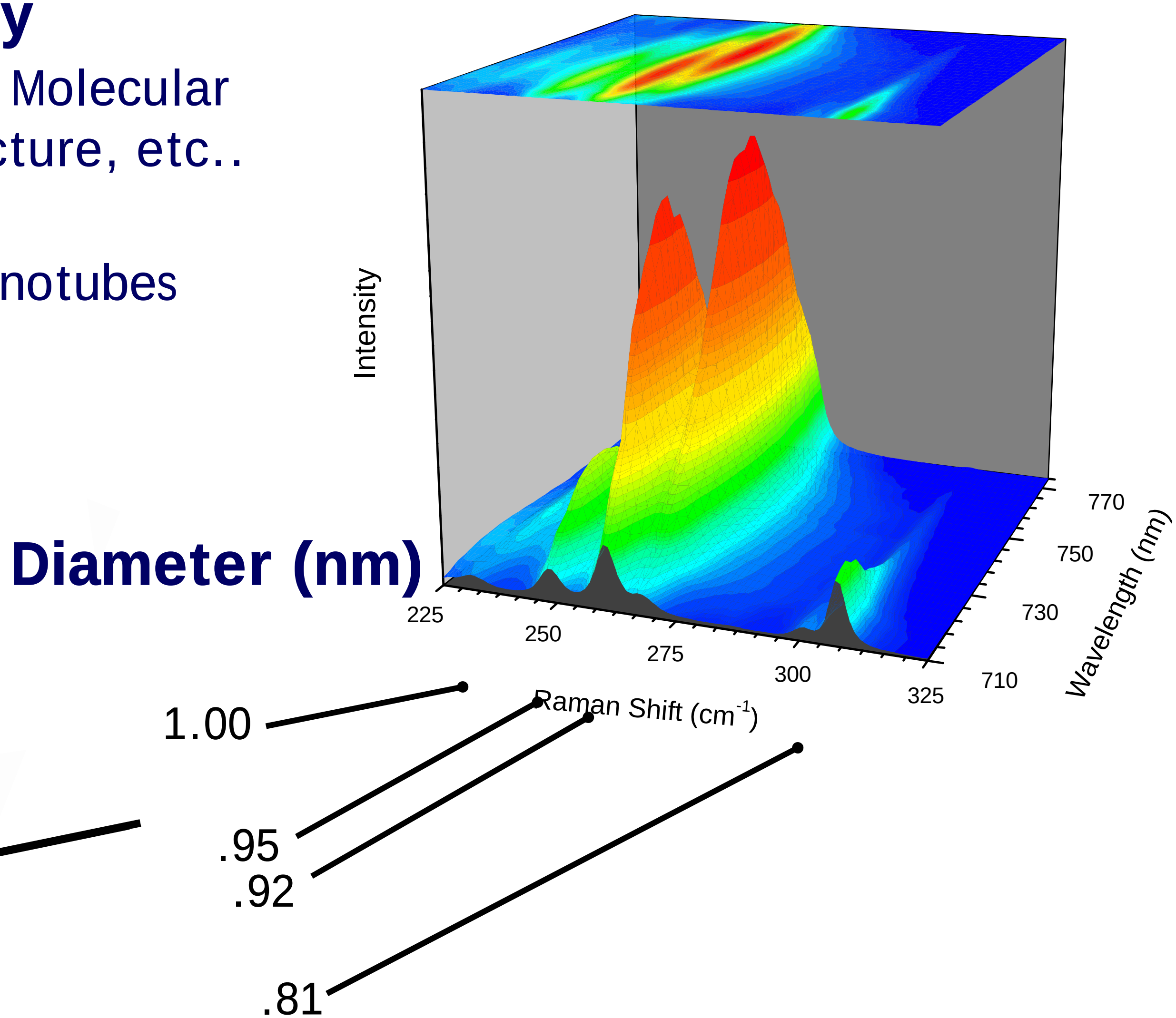
Nano Characterization: Raman Spectroscopy

Raman Spectroscopy

Chemical Composition, Molecular Structure, Crystal Structure, etc..

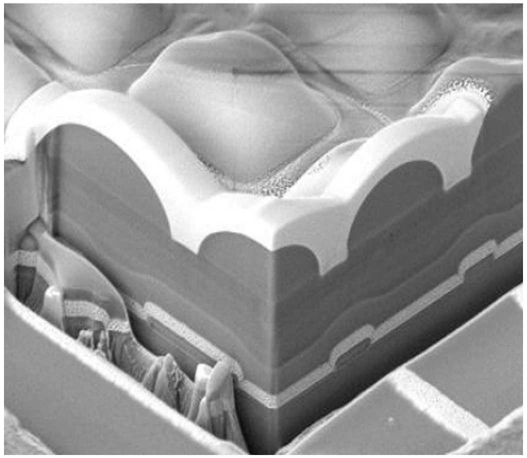
DNA-Wrapped Carbon Nanotubes

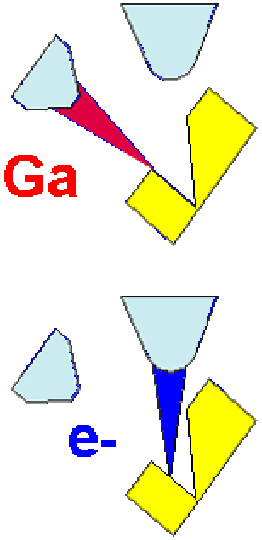




3-D Chemical Imaging

FIB cross section



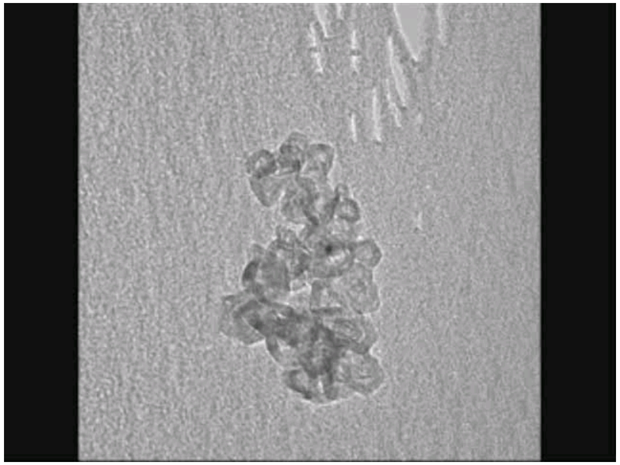


5 μm

- cut with ion beam
- image/X-ray map with SEM
- repeat…

Serial Focused Ion Beam (3D FIB)

TEM tilt series



50 nm

- TEM based
- tilt sample
- ~ 160 projections
- chemistry by EELS
- 3D reconstruction

TEM nanotomography

FIB of Biological Material

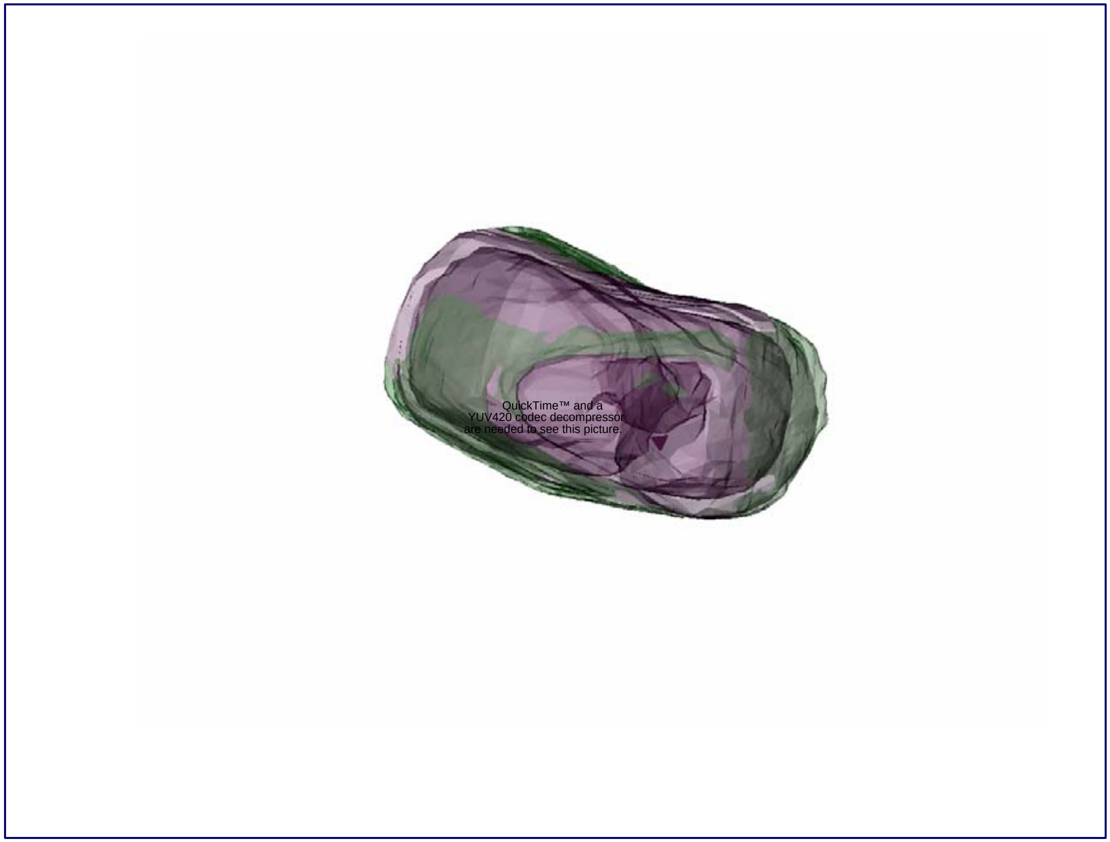
Si-Red, P-Green, O-Blue

Diatom T. Pseudonana

Eukaryotic unicellular marine algae

3-4 mm in diameter, 5-9 mm in length

Finely structured silica shell



- Only 50 &100 nm clusters detected
- No 5 & 10 nm quantum dots detected
- Cannot resolve 50 nm clusters separated by 250 nm

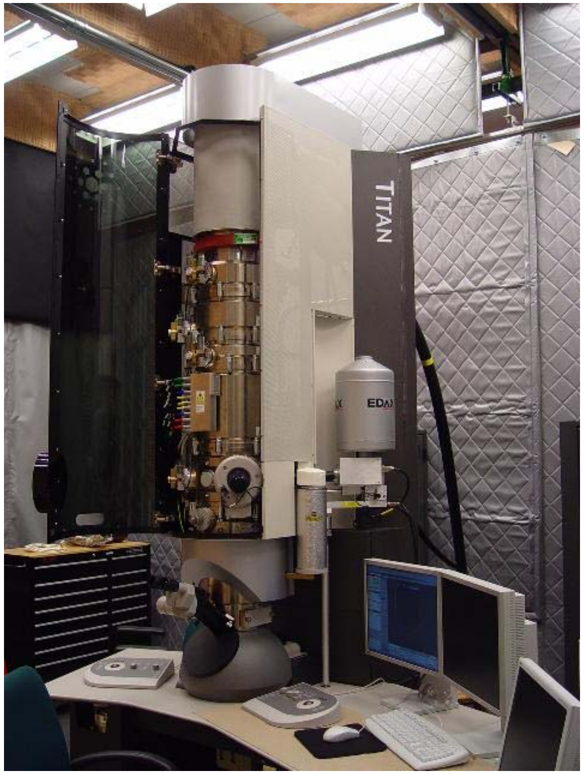
X-ray mapping & SEM imaging every 250 nm in z-direction

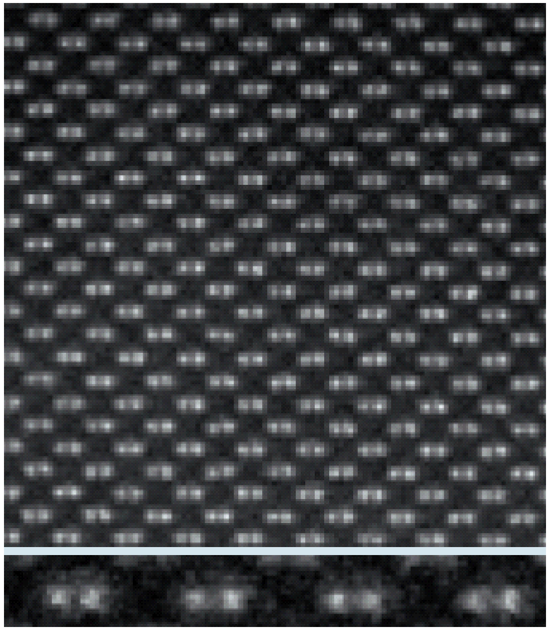
3D Si volume reconstructions of a diatom

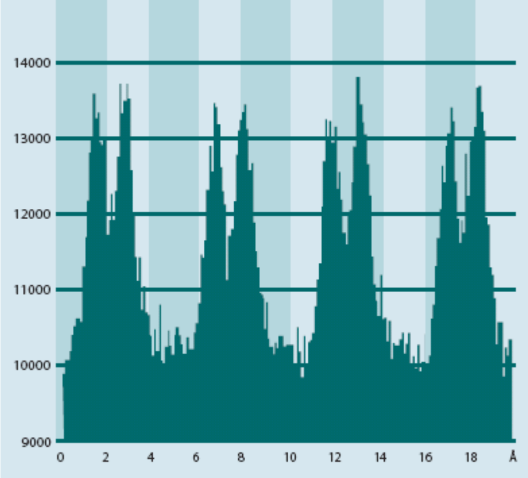
Simulated Sample Conditions: fixed with osmium tetroxide; resin embedded; quantum dot exposed/labeled

Nano Characterization: Advanced Imaging

3D Chemical Imaging with aberration-corrected monochromated AEM to improve resolution



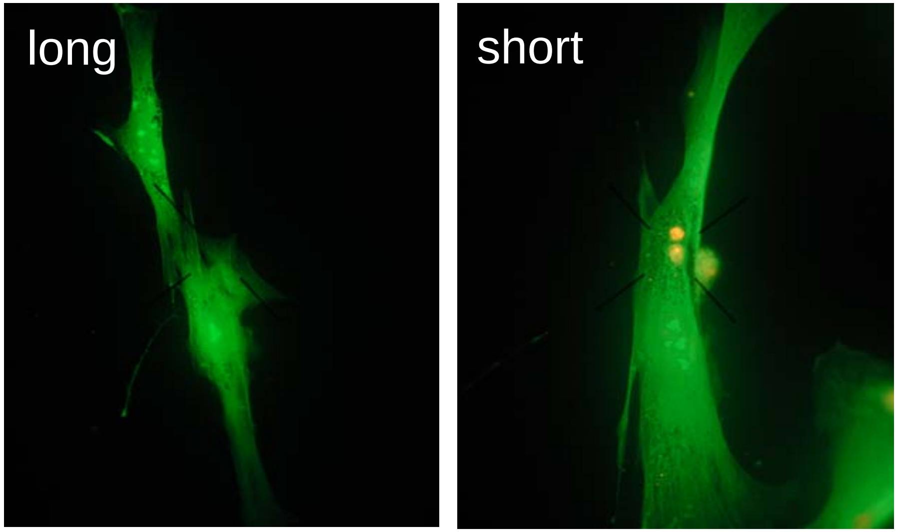




0.136 nm Si “dumbbells”
as seen in STEM

- 80 keV to 300 keV
- 0.07 nm probe
- HRTEM information limit < 0.1 nm
- Monochromator to provide < 0.2 eV
- EELS spectral resolution with < 0.2 nm probe

Evaluating cellular uptake, fate

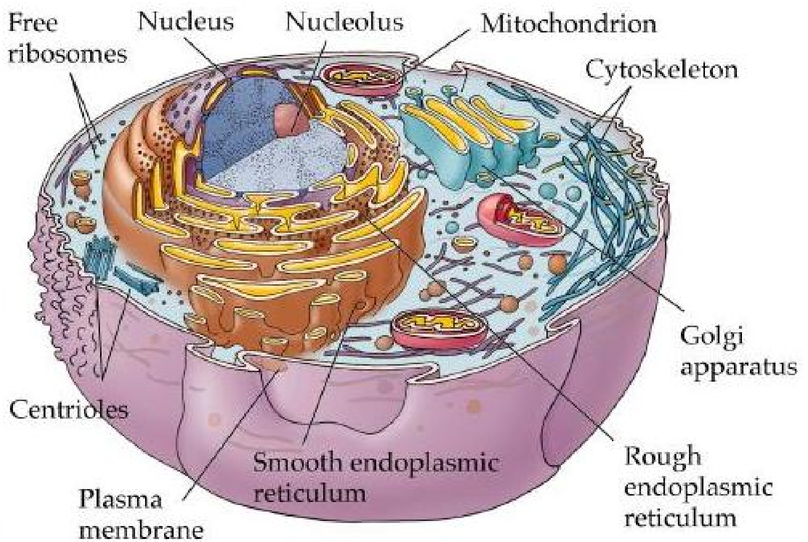


DNA-wrapped single-walled carbon nanotubes (SWCNTs) shorter than about 200 nanometers readily enter into human lung cells and may pose increase health risk.

- ❖Concentration-dependent effect of shorter SWCNTs on cells
- ❖SWCNTs longer than 200 nm did not enter cells

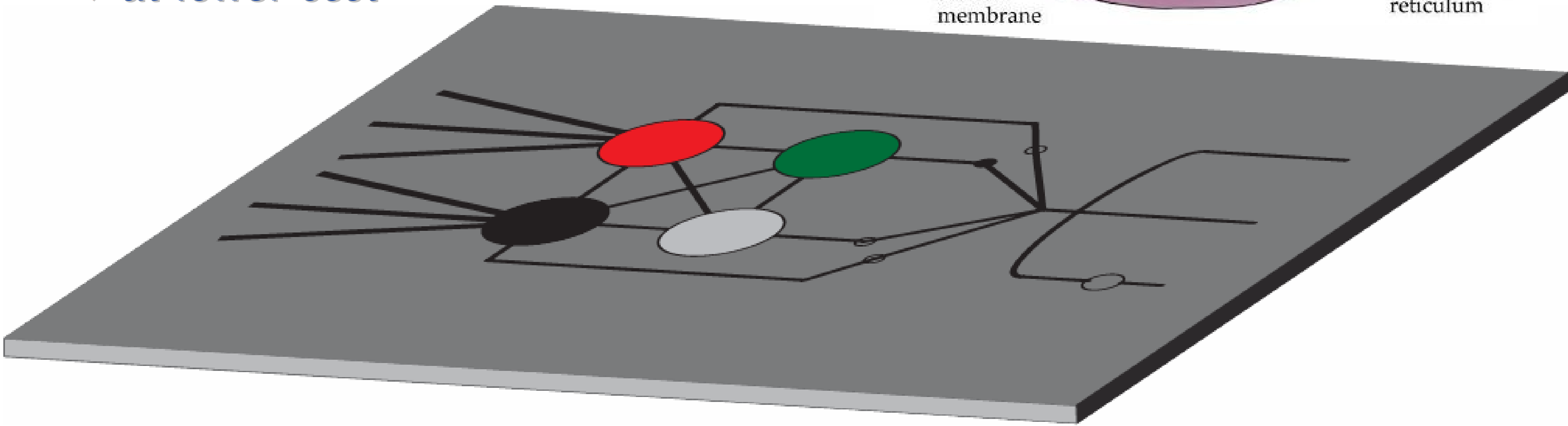
*M.L. Becker, J.A. Fagan, N.D. Gallant, B.J. Bauer, V. Bajpai, E.K. Hobbie, S.H. Lacerda, K. B. Migler and J.P. Jakupciak. Length-dependent uptake of DNA-wrapped single-walled carbon nanotubes. *Advanced Materials*, published on-line : 20 March 2007

Validation of Toxicological Methods: Support Understanding Environmental and Health Impacts

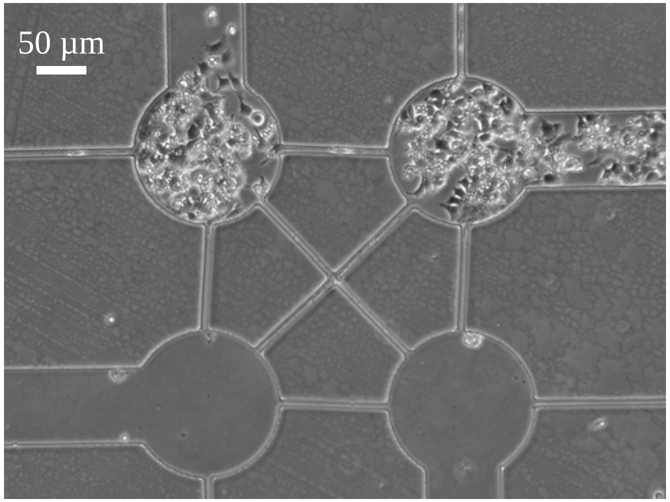


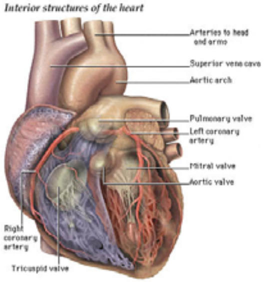
High-throughput screening methods: Toxicity Test Laboratory on a Chip

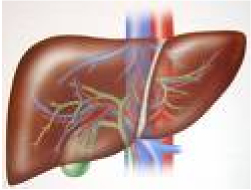
- **Many tests run in parallel**
  - more reproducible
  - faster results
  - better understanding
  - at lower cost



In vitro systems approach



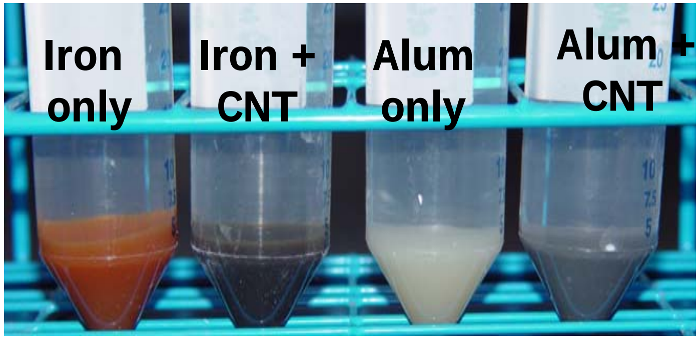




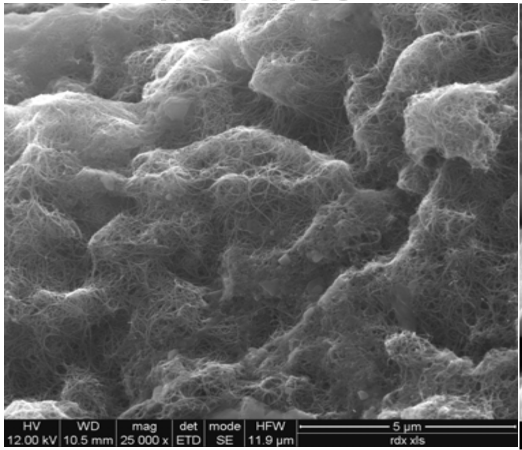
Microfluidic models of in vivo systems can be used to study ‘downstream’ toxic effects of nanoparticles

Environmental Transport and Fate

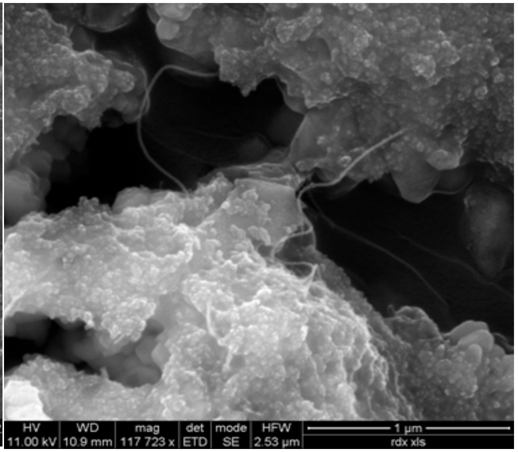
Carbon Nanotube release from production plant into municipal water supply



Iron floc



Alum floc



Validation of Toxicological Methods: Support Understanding Environmental and Health Impacts

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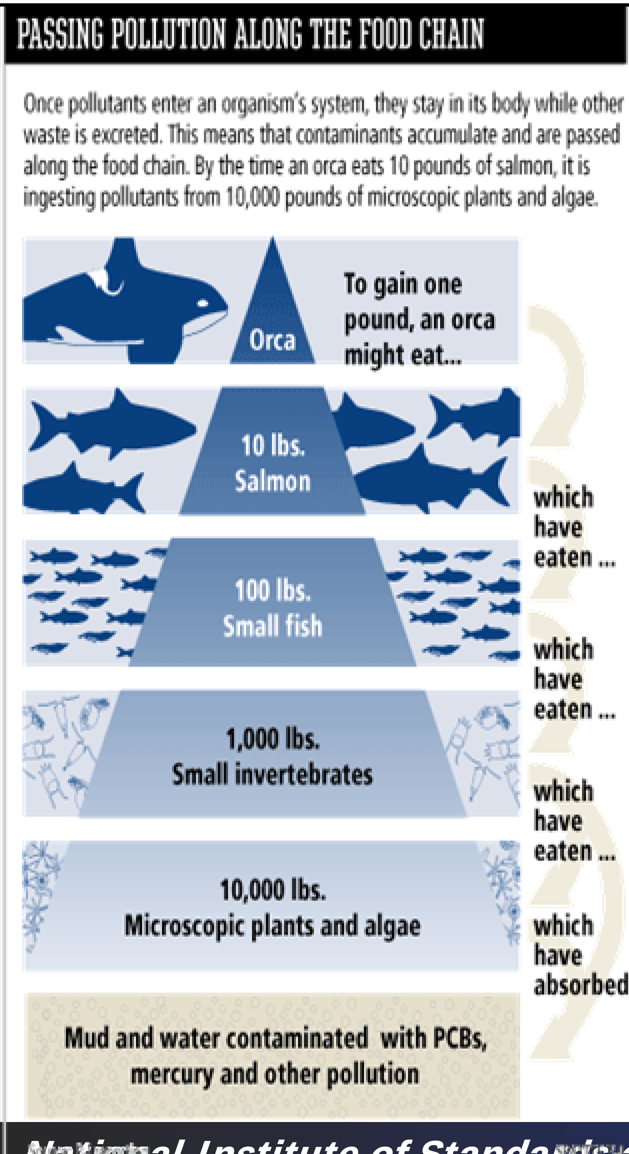
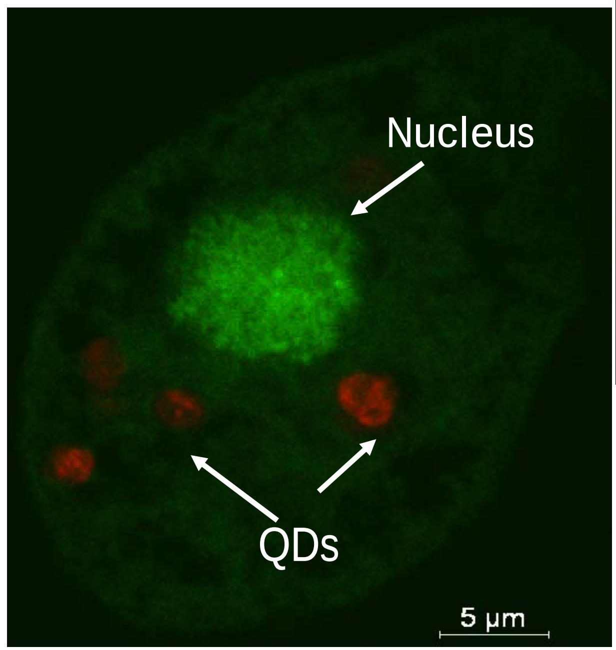
Nanomaterials in the Food Chain



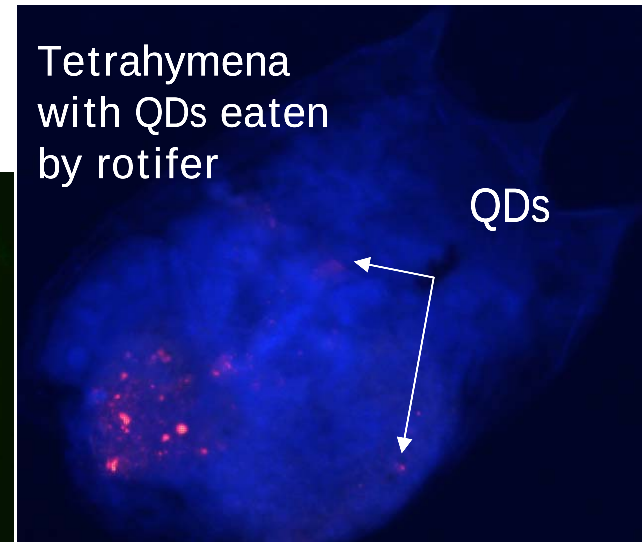
Passed up food chain

Tetrahymena (single cell eukaryote)



QDs internalized in vesicles

Tetrahymena eaten by rotifers (freshwater microorganisms)



QDs in undigested tetrahymena but also found distributed in rotifer

Internal & External Partnerships

External Coordination

- **Nanomaterial Classification**
  - Assembling large interagency task force to assess needs
  - Working closely with a number of standards organizations
  - Organizing workshop to coordinate documentary standards activities
- **Nanomaterial Characterization**
  - Drawing on NIST experts in standards development and state of the art physical science measurement capabilities
  - leveraging the expertise and infrastructure that has resulted from the NCI-NCL partnership
  - Seeking partners in nanomaterial production
- **Validation on Toxicological Measurements**
  - Developing new technology platforms to support/enhance in vitro measurements
  - Seeking partners in tox measurement and in vivo assays primarily from federal and academic sector initially

Internal Coordination

- New NIST journal club
- NIST Nano Standards group
- Joint visits to potential external partners (NIOSH, UAB, EPA, FDA…)

Strong Internal & External Partnerships

Success of this program depends largely on our ability to coordinate and communicate in our internal program;

and to leverage external partnerships in areas outside of our core mission

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