


REUSE IN RHODE ISLAND  
*A State-Based Approach To Complex Exposures*




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## Nanotechnology – Human Health and Environmental Impacts

Jim Rice, Robert Hurt, Agnes Kane


*Brown University, Providence, Rhode Island*

NEWMOA Webinar, January 24<sup>th</sup>, 2012





Institute for Molecular and Nanoscale Innovation



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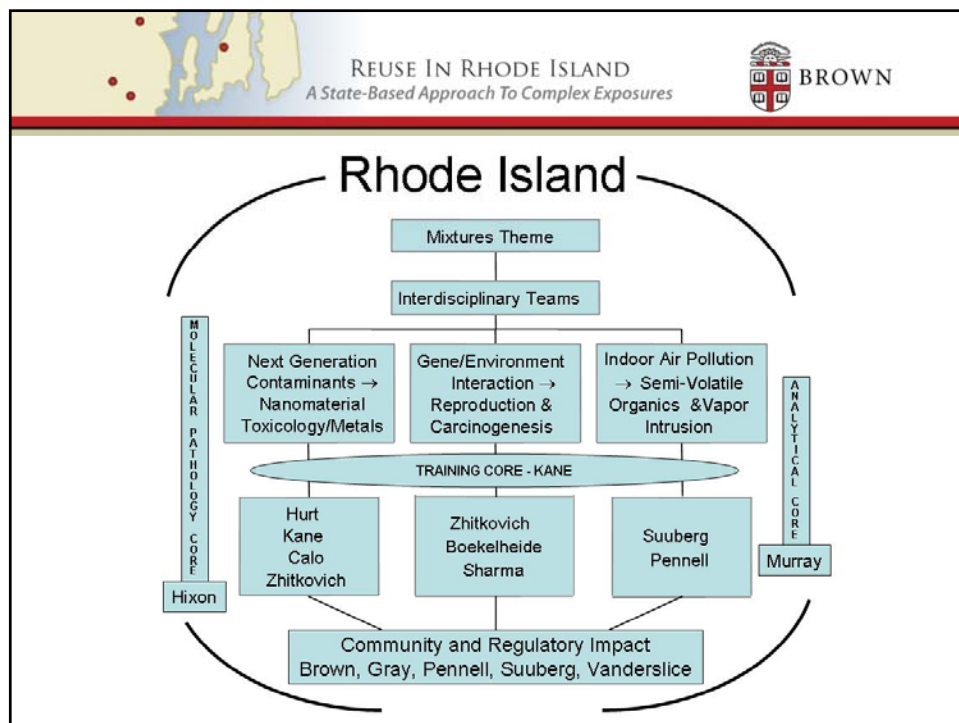
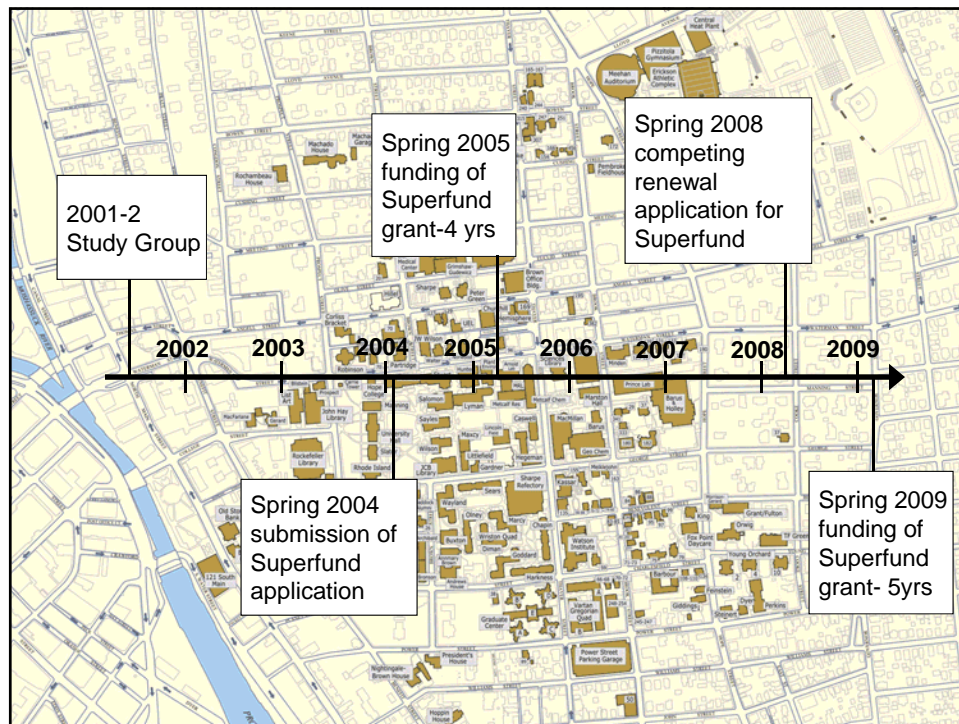
## The Superfund Research Program at Brown University



*Rhode Island is Our Laboratory*

Mission - To provide Rhode Island (and other states) with a responsive center of technical excellence that takes a research-oriented approach to resolving the complex scientific, engineering, and societal issues that arise when considering the reuse of hazardous waste sites

- **Focus on Mixed Exposures**
  - Environmental health and engineering research
  - Technology development
- **4 Biomedical and 3 Engineering Research Projects**
  - Tackle reuse of contaminated land in RI and other post-industrial states
  - Seek to understand the health effects of complex exposures
  - Focus on **Nanotechnology & Metals, Molecular Epidemiology & Reproduction, and Semi-Volatile Organics & Vapor Intrusion**
- **Research Translation and Community Engagement Cores**
  - Provide knowledge and services to professional and community stakeholders
  - Address basic and translational research issues, management decisions, and communication complexities inherent to reuse of hazardous waste sites






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## Partnerships at Regional NPL Sites

- Fisherville Mill NPL Site, Grafton, MA
  - In partnership with our Analytical core, the Fisherville Redevelopment Company, and Clark University, Jim Rice leads an effort aimed at helping to develop an efficient and reliable analytical testing method to determine whether bioremediation efforts are improving water quality in the Blackstone River.
- Centredale Manor NPL Site, N. Providence, RI
  - Attended October 2011 Dialogue Group Meeting with EPA, RI DEM, RI DOH, community activists, lawyers, etc.
  - Exploring opportunities for research; interested in partnering with Narragansett EPA labs to determine how remediation activity influences bioavailability of sediment contaminants
  - Partnering with WRWC through Community Engagement Core efforts – Questions about the Oxbow area; community education and risk communication; and what is happening downriver?

5



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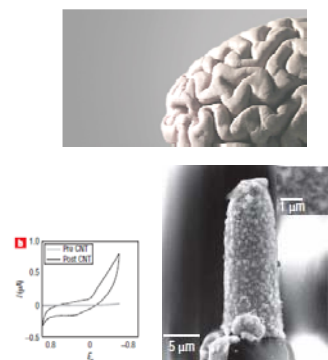
## How Can You Interact With Us?

- **We provide/seek two-way professional to professional communication of relevance**
  - Official State partners (Rhode Island Departments of Health and Environmental Management)
  - Other non-governmental partners (RI Bar Association, NEWMOA, Metcalf, etc.)
- **We host translational seminars, conferences, webinars, symposiums. For example:**
  - *Addressing the Complex Site: Mixed Pollutants Across Environmental Media* Symposium at the American Chemical Society National Meeting (Fall 2012)
  - *Social, Economic, and Psychological Costs of Contamination* Workshop (May 2012)
  - *Fate and Transport and Toxicology of Nanomaterials* Webinar co-sponsored by NEWMOA (Jan. 2012)
  - *Epigenetics and Fetal Origins of Health and Disease* Symposium (Oct. 2011) - 79 attendees (DOH, academia, healthcare, non-profits); 23 RNs awarded continuing education credits
  - *Environmental Health and Chemical Exposures: Law and Science* Seminar co-sponsored by The RI Bar Association (2010)
  - *Waiter, there's a phthalate in my soup! Reporting on the Science & Impacts of Toxic Chemicals* Seminar for journalists co-sponsored by Metcalf Institute for Marine & Environmental Reporting (2010)
- **We aim to involve our investigators & students in translational research/communication activities.**
  - Monthly seminar series
  - Planning informal lunches with State partners, i.e., RIDEM and RIDOH
  - We would like to get students more engaged with actual hazardous waste sites
- **We search for creative and practical research activities and funding opportunities/partnerships.**
- **Contact Us:**
  - Website <http://www.brown.edu/Research/SRP/>
  - James Rice, PhD, Engineering State Agencies Liaison, [James\\_Rice@brown.edu](mailto:James_Rice@brown.edu)

**nature nanotechnology**

Carbon nanotube coating improves neuronal recordings

Keefer et al., 2008

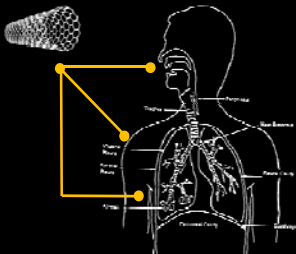


The image shows a brain, a carbon nanotube coating, and a graph of current (I) versus voltage (V). The graph compares 'Pre CNT' and 'Post CNT' recordings, showing improved performance after coating.

**The New York Times**

In Study, Researchers Find Nanotubes May Pose Health Risks Similar to Asbestos

May 21, 2008

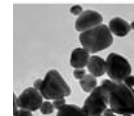


The diagram illustrates the human respiratory system, highlighting the lungs and the potential for nanotube inhalation, which is compared to asbestos risks.

## The Nanotechnology Movement

### Definition

the systematic manipulation of matter on the length scale 1-100 nm to produce useful new engineered structures, materials, or devices.



### History

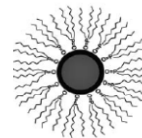
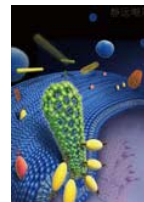
- R. Feynman, 1959, "There's plenty of room at the bottom"
- Kroto, Smalley, Curl, Fullerene C60 synthesis, 1985
- Sumio Iijima, 1991, nanotube synthesis

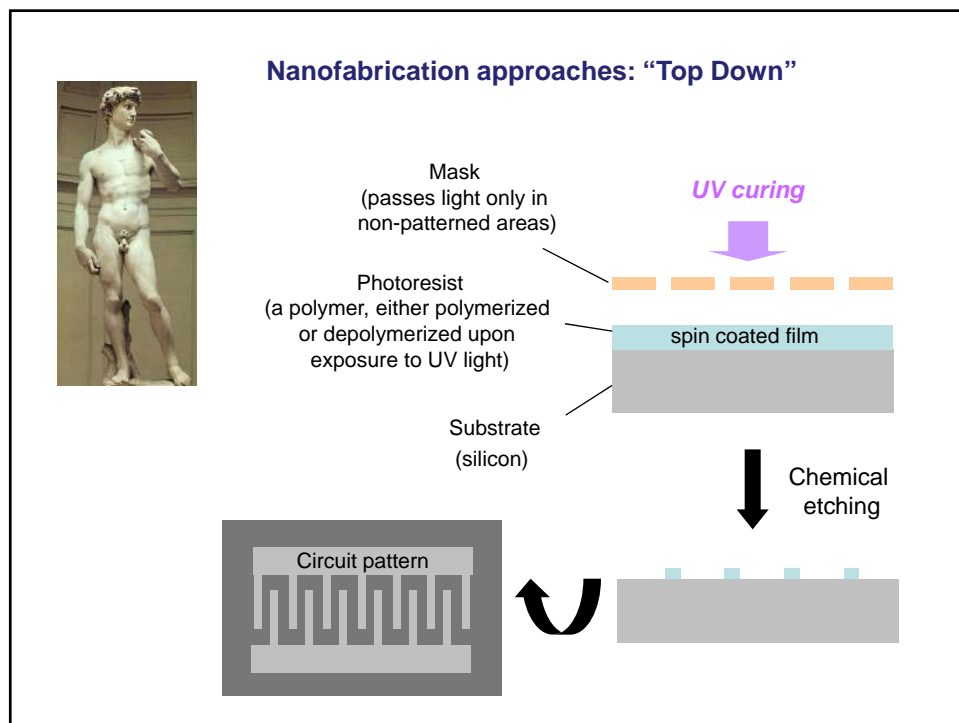
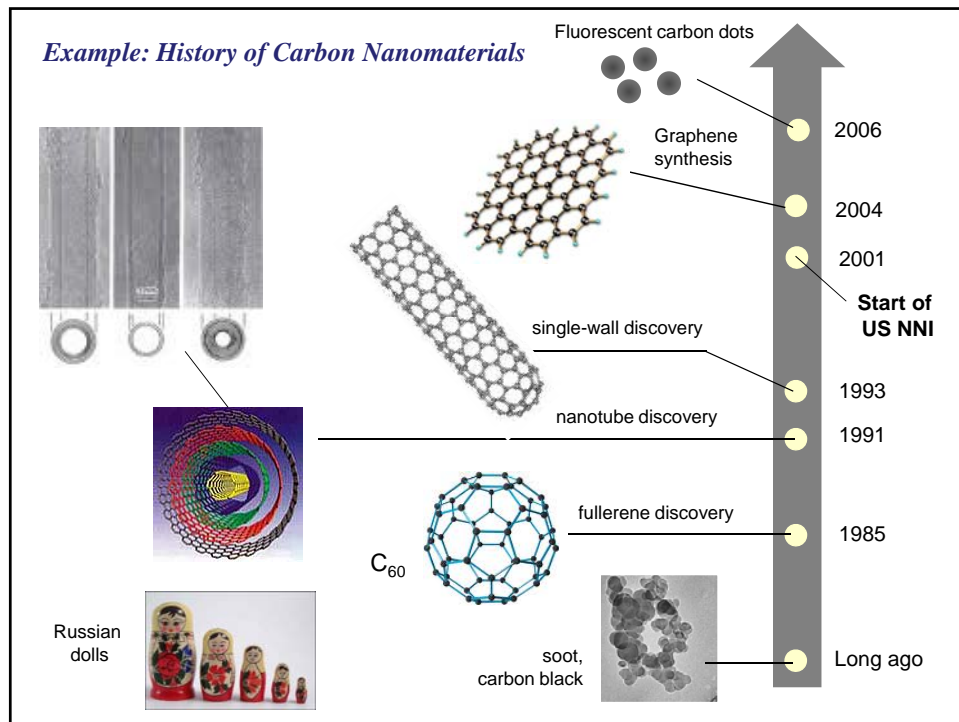
### Nanotechnology today

- over 60,000 scientific papers / yr
- over 1,300 industrial products (as of 2010)

### The U.S. National Nanotechnology Initiative (NNI)

- first passed in 2001, reauthorized in 2008
- now ~ 2.1 billion \$ / yr (2012)
- four phases envisioned:
  1. passive nanostructures
  2. active nanostructures
  3. three dimensional nanosystems
  4. molecular nanosystems





### Nanofabrication approaches: "Bottom Up"

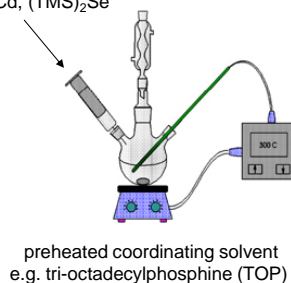
(brick)



Bottom-up, or self-assembly, approaches use chemical or physical forces operating at the nanoscale to assemble basic units into larger structures.

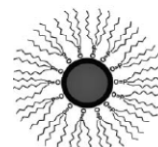
#### Example

organometallic reagents,  
e.g.  $\text{Me}_2\text{Cd}$ ,  $(\text{TMS})_2\text{Se}$



rapid nucleation  
of  
fine particles

cooling



Most nanoparticles have "coatings" that stabilize them and limit growth

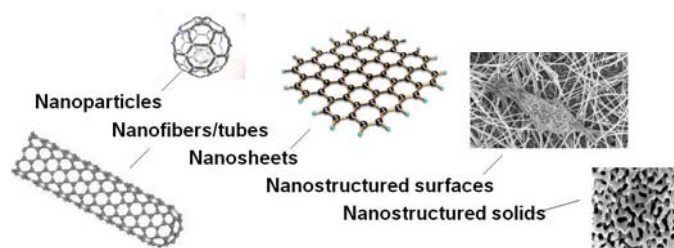
### Nanomaterials Today

Geometry x Chemistry = almost limitless diversity, complexity

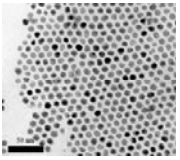
- Equi-axed forms (nanoparticles)
- One-dimensional forms (fibers and tubes)
- Two-dimensional forms (plates and disks)
- Nanostructured surfaces
- Nanostructured solids

Periodic Table of Elements

\* Lanthanide Series  
\* Actinide Series







**Some specific examples of nanomaterials**

	<b>Equi-axed forms (particles)</b>	<b>1D materials (fibers, tubes)</b>	<b>2D materials (plates, disks)</b>
<b>metals</b>	Silver, gold nanoparticles Iron, cobalt, nickel magnetic nanoparticles copper nanoparticle conducting inks	nanowires	
<b>semiconductors</b>	CdSe quantum dots	Si, ZnO semiconducting nanowires, nanorods	
<b>ceramics</b>	zinc oxide, titanium dioxide pigments and sun screens, cerium oxide catalysts	electrospun ceramic nanofibers for composite fillers	nano-clays
<b>carbons</b>	fullerenes, carbon black, nanohorns	carbon nanotubes nanofibers	graphene few-layer graphene graphene oxide
<b>polymers</b>	biodegradable polymer nanobeads for medical applications, dendrimers	electrospun polymer nanofibers	

**Nanotechnology in Industry**

Now (1,300 products)





*Metal oxides*



Components for next-generation batteries, fuel cells, computer chips, displays, structural materials, cosmetics, implants, drug delivery vehicles, paints, self-cleaning windows, and much, much more.....




The Woodrow Wilson Center "Project on Emerging Nanotechnologies" maintains a database of consumer nano-products <http://www.nanotechproject.org/>

## Human Exposures

Four primary exposure routes are:

- inhalation
- dermal (skin) exposure
- ingestion
- injection / implantation

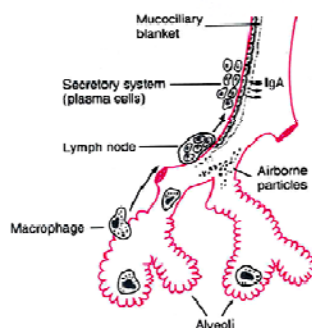
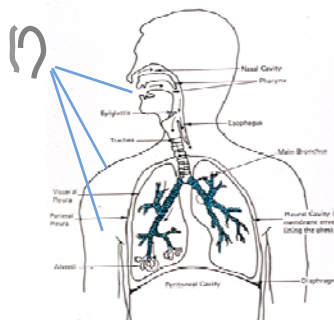
Some nanomaterials become easily airborne

- dry powders, mists from sonication, spraying

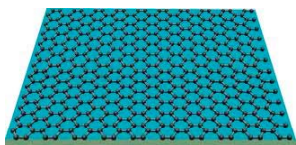
Particles < 5-10  $\mu\text{m}$  are respirable

Nanomaterials may permeate the skin, or migrate up the olfactory nerve to the brain, but possibly in low doses

Nanoparticles can be ingested in food, beverage, or by swallowing after clearance from the lung



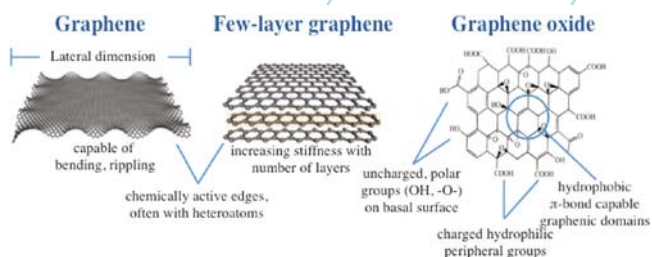
## Exposure Example: Graphene



Above: monolayer epitaxial graphene  
silicon substrate for nanoelectronics  
→ likely not a significant exposure risk

*Graphene* – the single-atom-thick sheet of  $\text{sp}^2$ -hybridized carbon first isolated from graphite in 2004

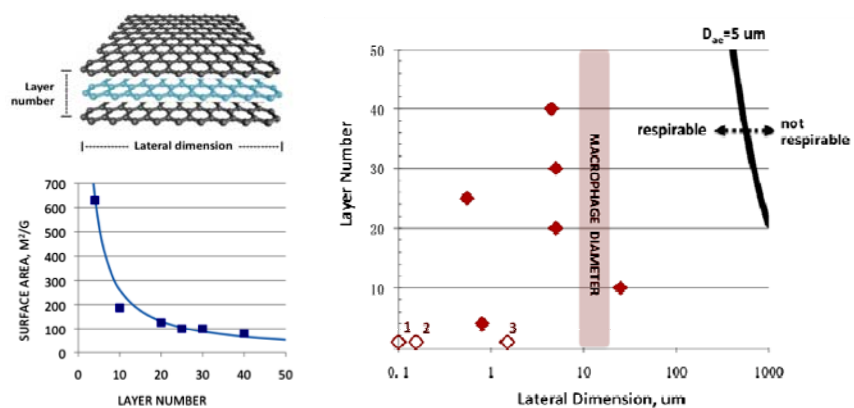
## Related forms, however.....



Typically produced as bulk dry powder  
Typically produced as aqueous suspension, which can be used in biomedicine or aerosolized

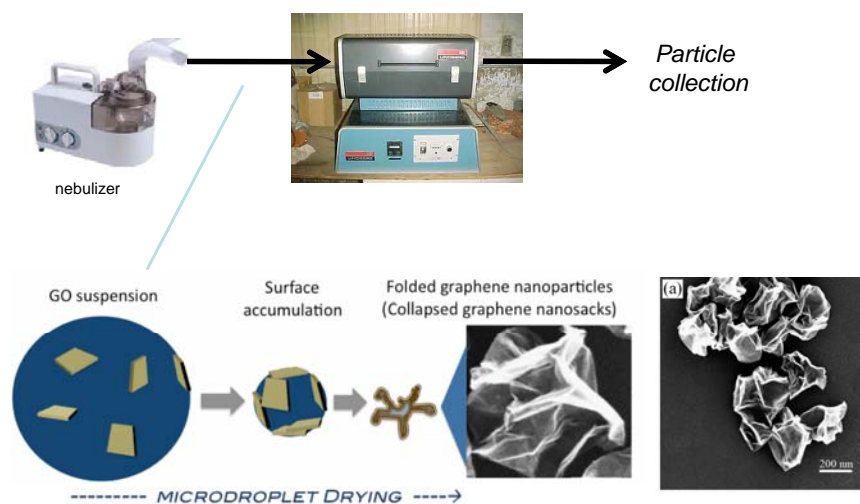


### Many “Few-Layer-Graphene” Samples are Potentially Respirable



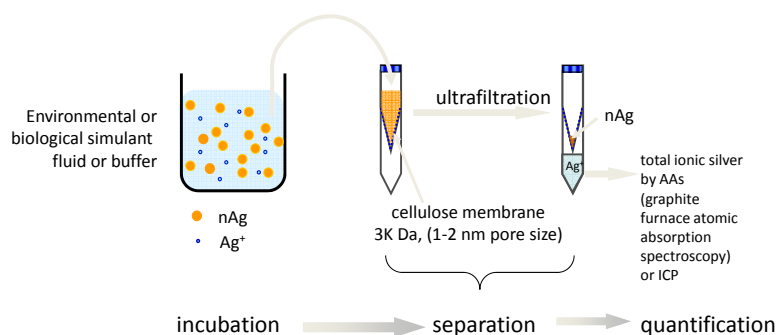
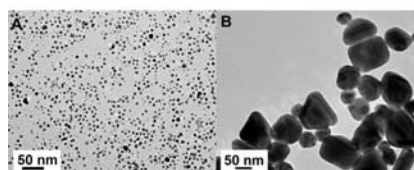
....and some are larger than macrophages and may not be cleared from the lung

### Graphene Oxide Solutions May Be Aerosolized to form Respirable “Crumpled Graphene Nanoparticles”



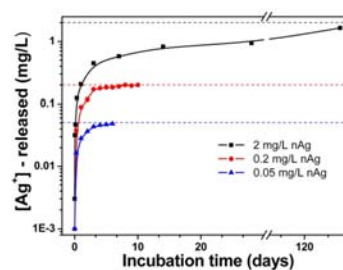
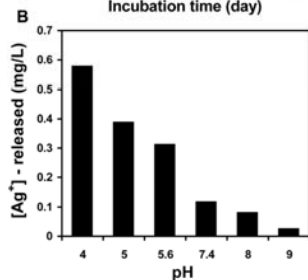
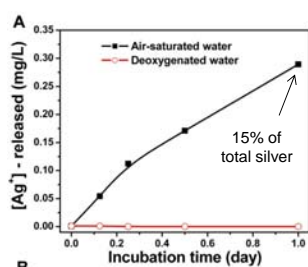


### A general measurement method for ion-nanoparticle partitioning

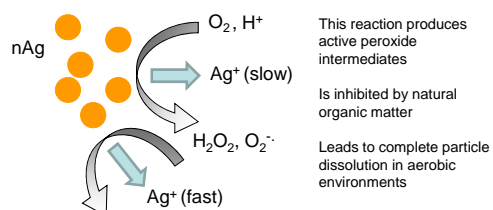


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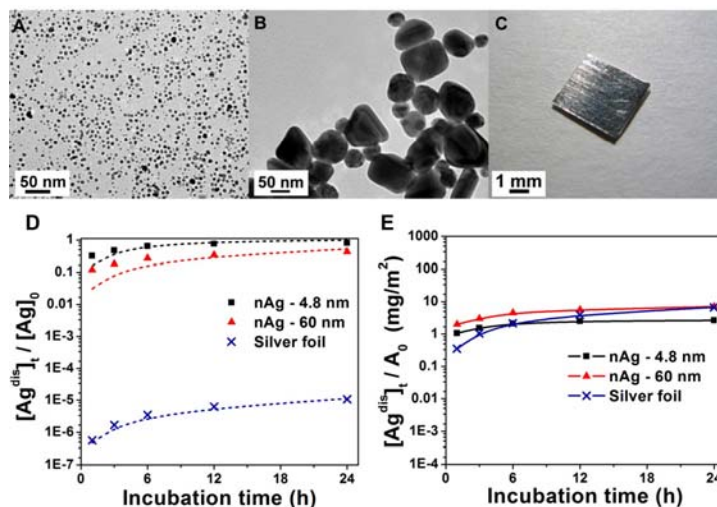
### Results: ion-particle partitioning in nanosilver



*nAg particles are not persistent in the presence of O<sub>2</sub> !*

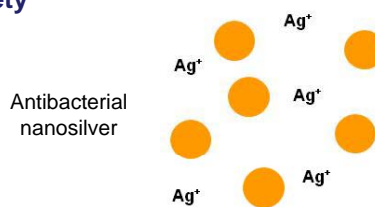
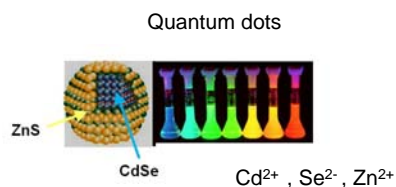


If nano-silver oxidatively dissolves, why doesn't bulk silver?

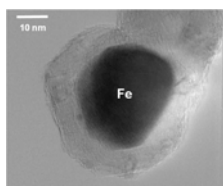


Answer: it can! (but slowly – about 1 nm/day)

Leaching, or ion-particle partitioning,  
Is a major theme in nanomaterial safety



Carbon nanotubes



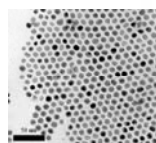
$Fe^{2+}$ ,  $Ni^{2+}$ ,  $Y^{3+}$ ,  $Co^{3+}$ ....

ZnO

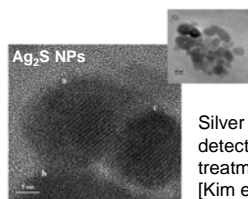


Ni

NiO

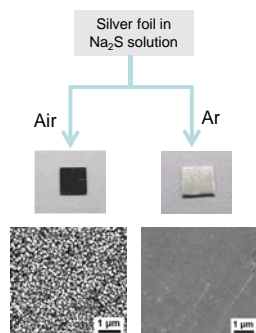
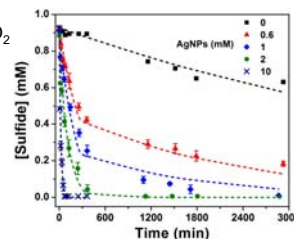


## Nanosilver “corrodes” by dissolution – does it also “tarnish”?

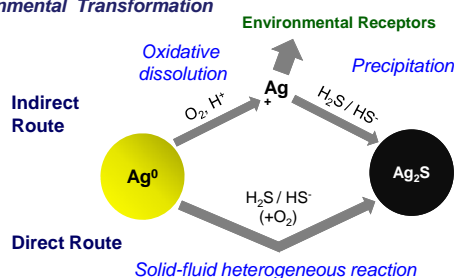


Silver sulfide nanoparticles detected in waste water treatment sludge [Kim et al., ES&T, 2010]

In the lab, nanosilver reacts with sulfide in the presence of  $O_2$

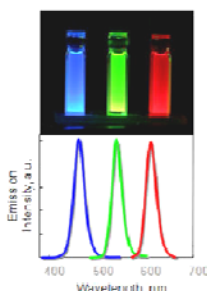
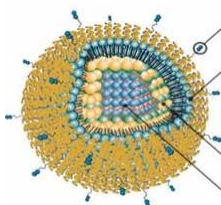


### Competing Pathways of Environmental Transformation



## Nano-Enabled Consumer Products

### Example: Quantum Dot Composites for Energy-Efficient Lighting



CdSe quantum dots absorb short-wavelength light and emit longer wavelength light -- thus they red-shift the LED spectrum without the losses that simple filters would cause



Seth Coe-Sullivan, Sc.B. eng. '09  
Chief Technical Officer, QD Vision

A “quantum dot optic”

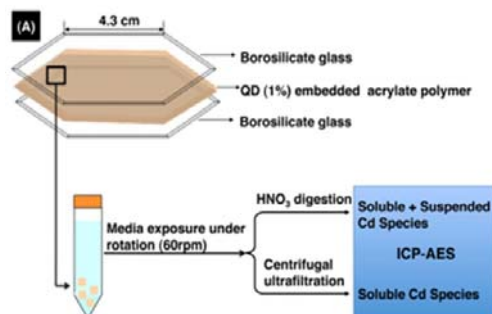


“Emotionally satisfying” LED lighting

### Nano-enabled Products

#### Example: End-of-Life Behavior of the Quantum Dot Optic

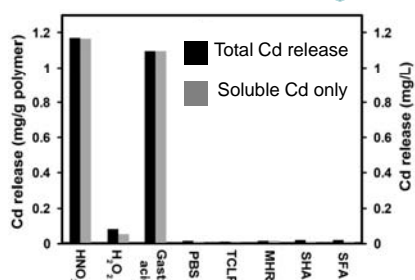
- Do Cd, Se leach from the optic after disposal?
- Are QD nanoparticles released to the environment through degradation processes?



The QD optic releases small amounts of Cd and Se through water infiltration and quantum dot dissolution

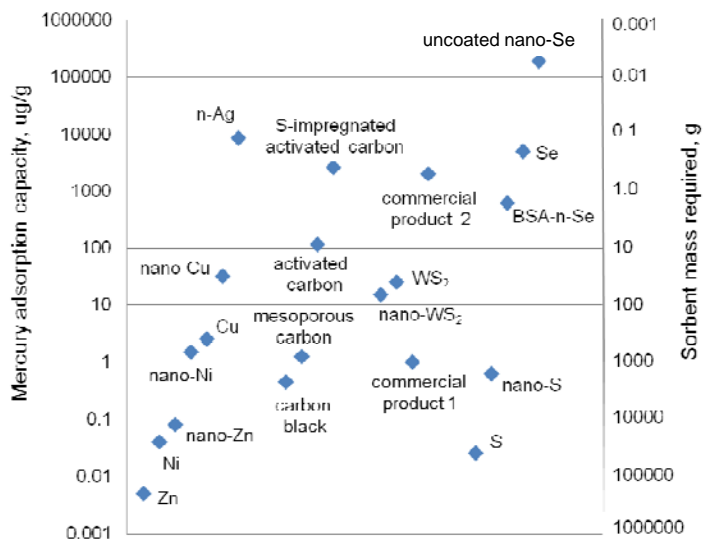
There is no evidence of nanoparticle release, or unique "nanospecific" risk

Results



#### Example environmental Application: Nanomaterials for Hg vapor capture

Some types of nano-selenium have ultrahigh activity for Hg vapor capture





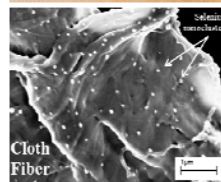
## Nano-selenium formulations offer self-sensing and mercury detection



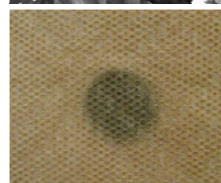
Colloidal form



nanoclusters  
supported  
on cellulose



controlled  
demonstration  
of indicator  
function



Nano-sorbent has the advantage of optical reporting:

*Self-sensing function* - is the sorbent spent?

*Mercury finder function - where was the spill / break?*



## Smart boxes, bags for safe recycling



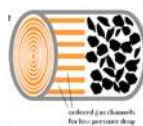
## Technologies for permanent Hg sequestration



### Retail drop-off boxes



### Power plant flue gas capture



## Cartridge-based air-cleaning for NASA spaceflights



## Consumer spill and disposal kits

# The Nanostructured Sorbent as a Platform Technology



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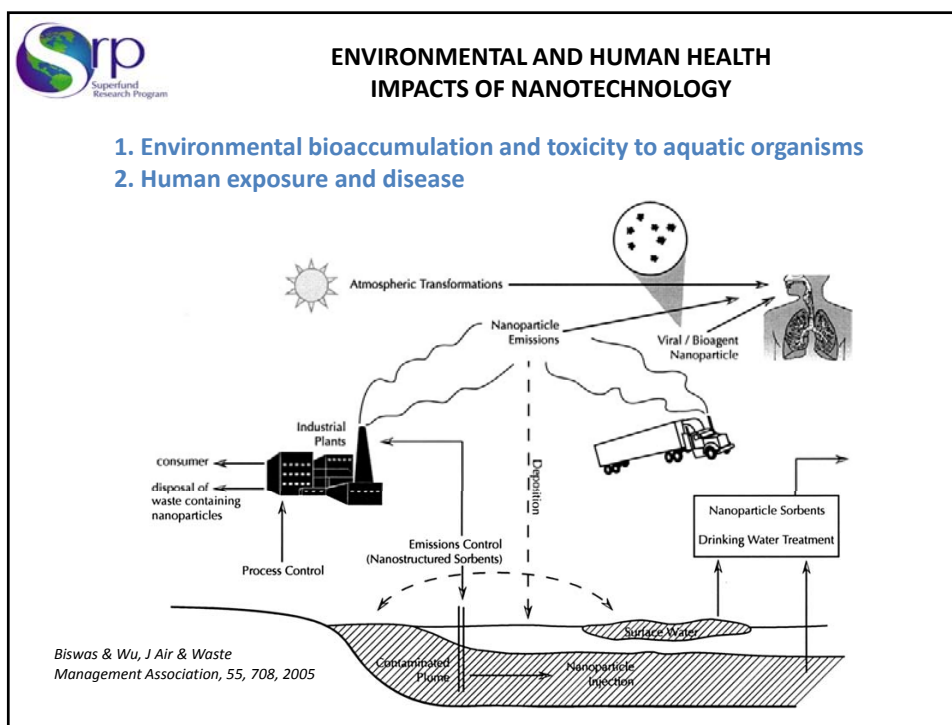
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Financial support from the US EPA Science to Achieve Results Program, the NSF NIRT program, and the NIEHS Superfund Research Program grant at Brown is gratefully acknowledged



*The Laboratory for Environmental and Health Nanoscience*





## 1. ENVIRONMENTAL BIOACCUMULATION AND TOXICITY TO AQUATIC ORGANISMS



October 28, 2011: The Environmental Protection Agency issued a proposed \$101 million cleanup plan for the Centredale Manor superfund site in North Providence.

Dioxins  
TCE, PCE  
Metals (Pb, Cd, Cu, As)  
SVOCs: PAHs  
PCBs



Benzene



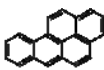
Toluene



Ethylbenzene



Pyrene



Benzo(a)pyrene



- Carbon black nanoparticles and carbon nanotubes have  $sp^2$ -hybridized graphenic carbon surfaces
- High surface area for adsorption of PAHs by  $\pi$ - $\pi$  bonding

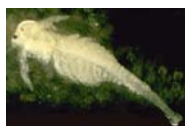
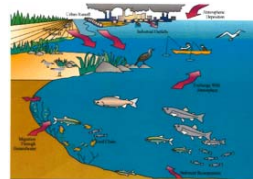
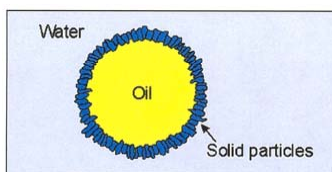
*Delgado et al. J Mater Chem 18, 1417, 2008*

## NANOPARTICLE-BASED DISPERSANTS FOR ENVIRONMENTAL REMEDIATION OF POLYCYCLIC AROMATIC HYDROCARBONS

Deepwater Horizon Disaster, 2010



Pickering emulsion stabilized by particles



Bioaccumulation in simplified aquatic food chain

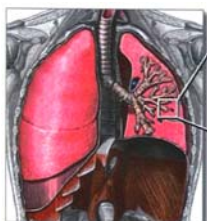
*brine shrimp → killifish larvae → adult fish*



**Hypothesis: Nanoparticle-based dispersants will stabilize oil-water emulsions, adsorb aromatic hydrocarbons, and decrease their toxicity and bioavailability.**

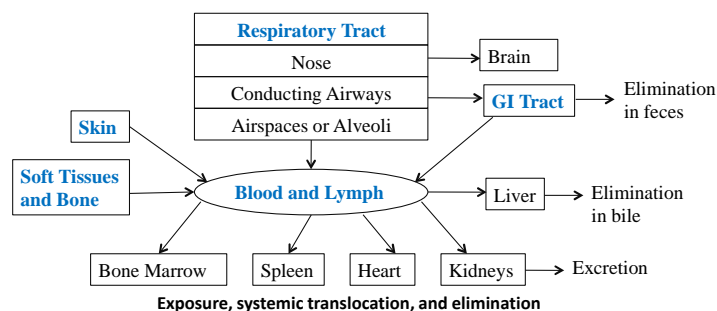
## 2. INHALATION AND SYSTEMIC TRANSLOCATION OF NANOPARTICLES

**Exposure** → **Dose** → **Response**



Galya Orr, Pacific Northwest National Laboratory

Alveoli or airspaces



## POTENTIAL CHRONIC TOXICITY OF NANOMATERIALS

NEL et al. SCIENCE 311: 622-627, 2006

TISSUE TARGET	DISEASE
Macrophages and inflammatory cells	granulomas chronic inflammation fibrosis or scarring
Lungs	cancer, mesothelioma
Blood vessels	stroke, heart attack
Immune system	autoimmune disease leukemia, lymphoma
Nervous system, brain	heart arrhythmia brain injury

## Occupational Carcinogens

Agent	Industry	Target Site
Arsenic	Glass, metal, pesticide	Lung, Skin
Asbestos	Construction	Lung, Pleura, Larynx
Benzene	Chemical	Leukemia
Beryllium	Aerospace	Lung
Cadmium	Dyes, batteries	Lung, Prostate, Kidney
Chromium (VI)	Metal plating, welding	Lung, Nasal Sinus
Nickel	Metallurgy, alloys	Lung, Nasal Sinus
Crystalline silica	Mining, glass, pottery	Lung
Sulphuric acid mists	Metallurgy	Larynx
Benzo[a] pyrene	Coal gasification, paving and roofing	Lung

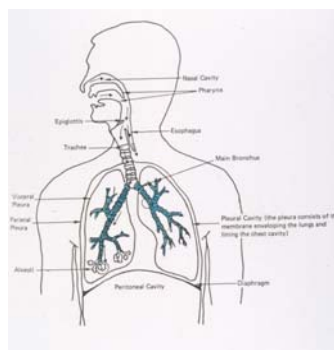
*P. Boffetta, Epidemiology of environmental and occupational cancer, Oncogene 23: 6392-6403, 2004.*

## THE ASBESTOS-CARBON NANOTUBE ANALOGY

### History of Asbestos-Related Diseases

*Becklake, Am. Rev. Resp. Dis. 114:187-227, 1976*

Disease	Established Casual Association
Asbestosis	1930
Lung Cancer	1955
Mesothelioma	1965
Cancer of Larynx	2006
Nanodiseases	????



- The Potential Environmental Impact of Engineered Nanomaterials.

*Vicki L. Colvin, Nature Biotechnology, October, 2003*

- Ethical and Scientific Issues of Nanotechnology in the Workplace

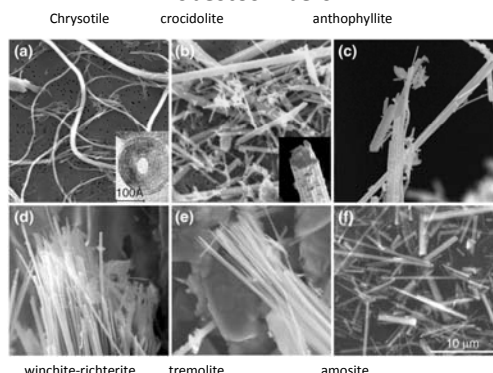
*Paul A. Schulte and Fabio Salamanca – Buentello, Environ Health Perspect, 2007*

- Researchers Find Nanotubes May Pose Health Risks Similar to Asbestos

*The New York Times, May 21, 2008*

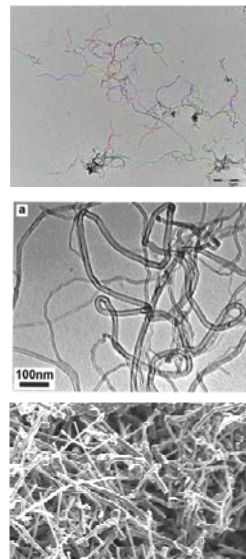
## The Asbestos-Carbon Nanotube Analogy

### Asbestos Fibers



U.S. Geological Survey

### Carbon Nanotubes



### Properties of Fibers Relevant for Biological Activity

1. Surface reactivity
2. Durability and biopersistence
3. Fibrous shape and dimensions

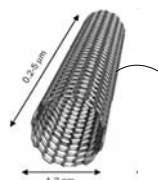
## Properties of Fibers Relevant for Biological Activity

### 1. Surface Reactivity of Asbestos Fibers and Carbon Nanotubes



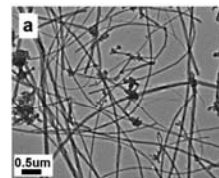
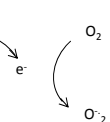
Crocidolite asbestos  
 $\text{Na}_2\text{Fe}^{2+}_3\text{Fe}^{3+}_2(\text{Si}_6\text{O}_{22})(\text{OH})_2$

Fenton chemistry:  
 $\text{H}_2\text{O}_2 \xrightarrow{\text{Fe}^{2+}} \text{OH}^{\bullet}$



Reilly et al (2007) JNM, 48: 1039-1042

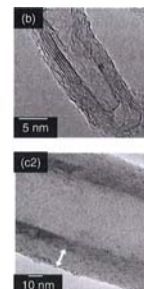
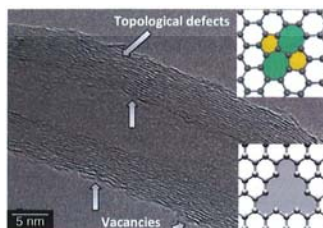
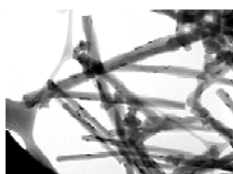
Surface e<sup>-</sup> donor:



Carbon nanotubes

### Surface Defects and Impurities in Carbon Nanotubes

Iron Catalyst Residues





## Properties of Fibers Relevant for Biological Activity

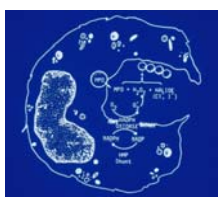
### 2. Biopersistence



Fiber	T 1/2 in vivo (days)	Carcinogenicity
Crocidolite asbestos $\text{Na}_2\text{Fe}^{2+}_3\text{Fe}^{3+}_2(\text{Si}_6\text{O}_{22})(\text{OH})_2$	> 600	+
Wollastonite $\text{CaSiO}_3$	21	-
Fiberglass CaO: 38% $\text{SiO}_2$ : 60%	77	-

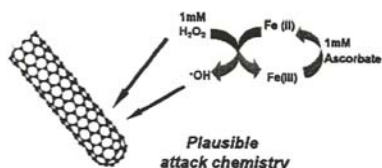
Biopersistent mineral fibers are toxic and carcinogenic in rodents

Bernstein et al., *Inhalation Toxicol*, 2005  
Macdonald & Kane, *Fund. Appl. Toxicol.*, 1997

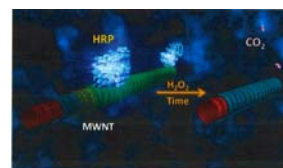


Phagocytic Vacuole:

- Low pH (4.5)
- Endogenous ROS, Fe



Carboxylated Carbon Nanotubes are Oxidatively Degraded at Low pH  
*Liu et al. Carbon*, 2010



Zhao et al. *J. Phys. Chem. A*, 115:9536, 2011

Enzymatic Degradation by Horseradish Peroxidase

## Properties of Fibers Relevant for Biological Activity

### 3. Fibrous Shape and Dimensions

Long Fibers Induce Frustrated Phagocytosis and Impair Clearance

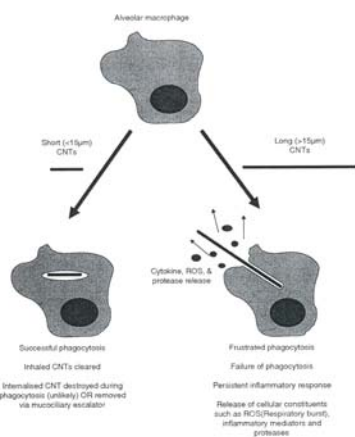
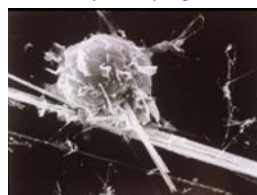
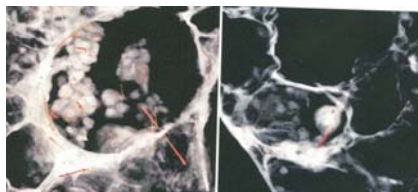


Figure 3. The importance of CNT length to their clearance by alveolar macrophages. Short CNTs (<15 µm) are easily cleared by macrophages, whereas longer CNTs (>15 µm) are not engulfed by macrophages, and frustrated phagocytosis ensues.

Incomplete or Frustrated Phagocytosis by Macrophages



Penetration into Alveolar Walls



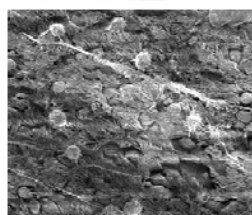
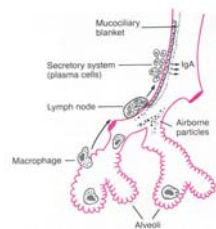
J. Brain, Harvard School of Public Health

Johnston HJ, Hutchison GR, Christensen FM, Peters S, Hankin S, et al. "A Critical Review of the Biological Mechanisms Underlying the in Vivo and in Vitro Toxicity of Carbon Nanotubes: The Contribution of Physico-chemical Characteristics." *Nanotoxicology* June 4.2 (2010): 207-46.

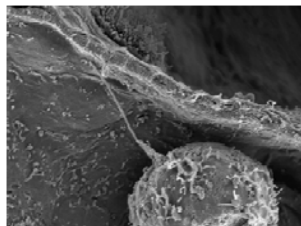
## Intratracheal Instillation of CNTs Causes Impaired Lung Clearance and Translocation to the Pleural Space

### Lung Clearance Mechanisms

Daniele, Immune defenses of the lungs, 1988



Long carbon nanotubes on the mucociliary escalator after 7 days



Frustrated phagocytosis of a carbon nanotube by an alveolar macrophage after 7 days

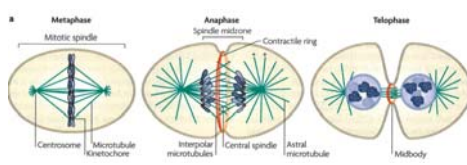
### Penetration Into the Pleural Space



Robert Mercer, NIOSH SEM

## PROPERTIES OF FIBROUS NANOMATERIALS AND CARCINOGENICITY

### Asbestos Fibers and Carbon Nanotubes Induce Micronuclei And Mitotic Abnormalities in Human Lung Epithelial Cells



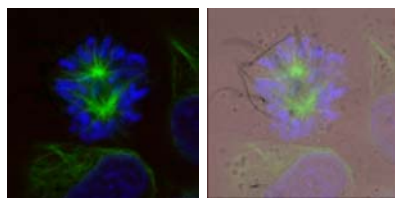
Glazier, Nat. Rev. Mol. Cell Biol. 10:9, 2009

Microtubules-green fluorescence; nuclei and chromosomes-blue fluorescence

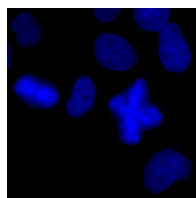


Carbon nanotube localized in midbody. Confocal microscopy- fluorescence and DIC.

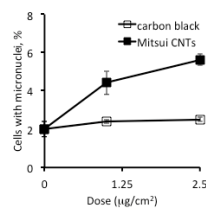
Carbon nanotubes induce multinucleated daughter cells.



Carbon nanotubes interfere with chromosomal segregation. Confocal microscopy- fluorescence and DIC.

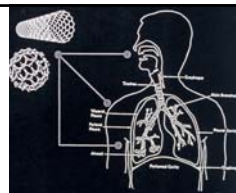
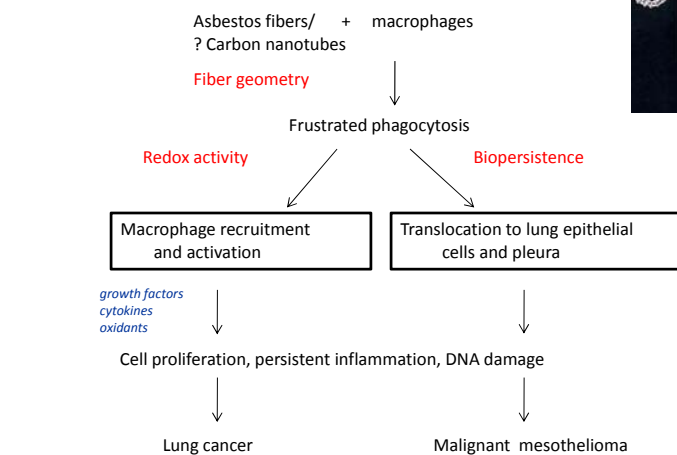


Asbestos fibers induce multipolar mitoses.



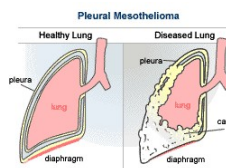
Lagging chromosomes produce micronuclei in daughter cells- 48 hours after exposure to CNTs.

### Physicochemical Properties of Fibers Associated with Carcinogenicity



#### Unresolved questions:

- Do carbon nanotubes translocate to the pleura following inhalation?
- Is their surface activity modified in vivo?
- Does acute toxicity predict chronic disease endpoints?



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## Summary

1. Nanotechnology has significant promise for energy generation, electronics, medicine, aerospace, defense, and environmental remediation.
2. Environmental toxicity and adverse human health effects are potential implications of nanotechnology.
3. The physical and chemical properties of nanomaterials responsible for cell toxicity are related to geometry, length, surface redox reactivity and biopersistence.
4. Commercial carbon nanotubes induce DNA damage and mitotic abnormalities in lung epithelial cells and mesothelial cells similar to asbestos fibers.
5. Engineers will be able to design less toxic, biocompatible and biodegradable nanoparticles for commercial applications that will minimize adverse environmental and health impacts.



### Collaboration Between Kane and Hurt Labs:

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