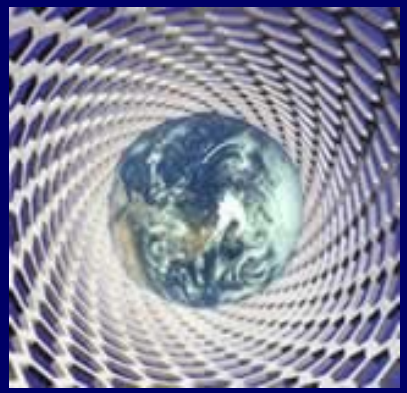
NATIONAL CANCER INSTITUTE

NCI Alliance for
Nanotechnology
in Cancer

"Engineering safe nanoparticles"



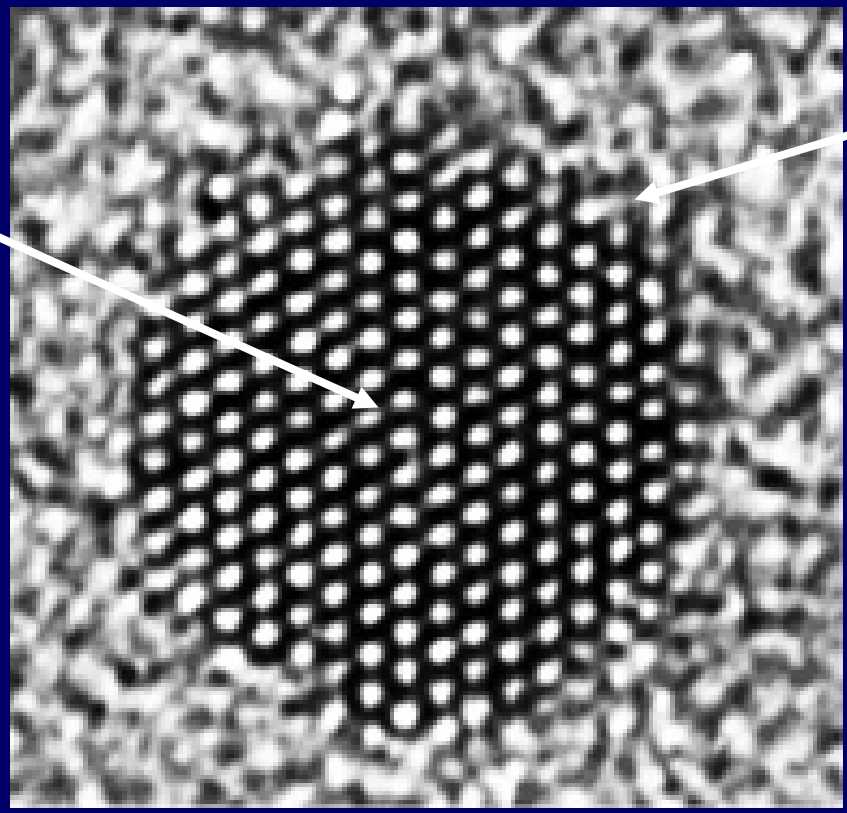
CBEN
Center for Biological and Environmental Nanotechnology

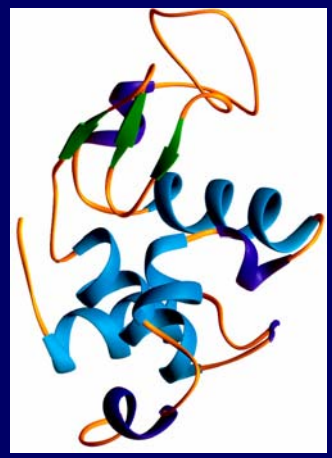
Dr. Vicki Colvin
Director, CBEN
Professor of Chemistry
Rice University

Nanomaterial features

Highly crystalline

Huge surface areas





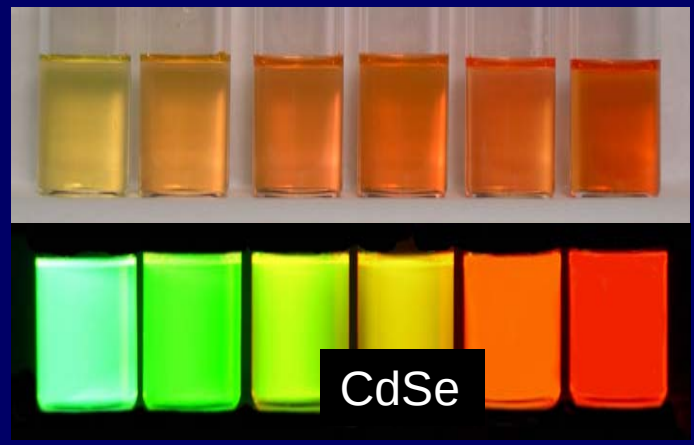
C-sixty
1nm

Cadmium Selenide nanocrystal
6 nm

Lysozyme
3 nm

Nanotechnology and Cancer

GO

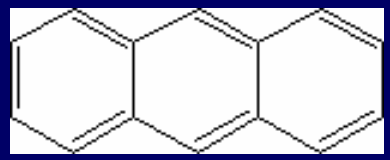


STOP

- Public fear of nanotechnology
- Sweeping claims about safety or danger by scientists

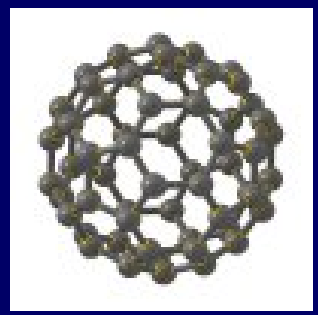
Make safety and testing part of early stage research

Central Question



Molecular

?

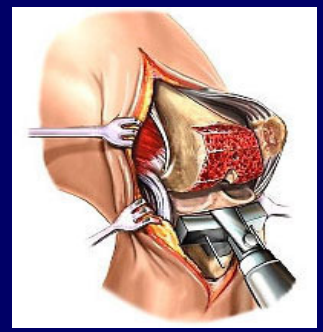


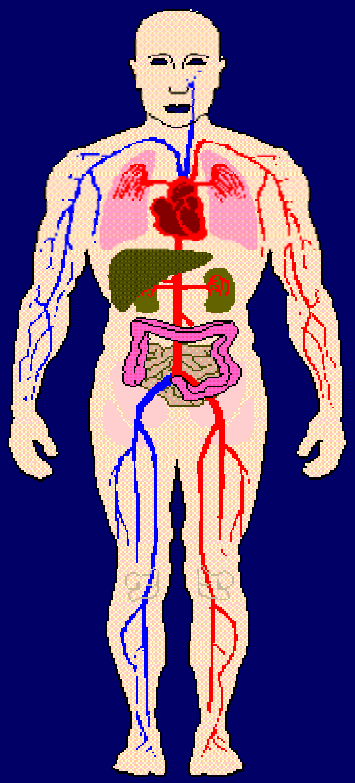
Foreign particles

Will biocompatibility be more like a molecular question, or like a larger particle?

Disease results from foreign particles

Auto-immune diseases: Wear debris is generated by orthopedic implants. Patients with such implants have a statistically significant rise in the incidence of auto-immune diseases.

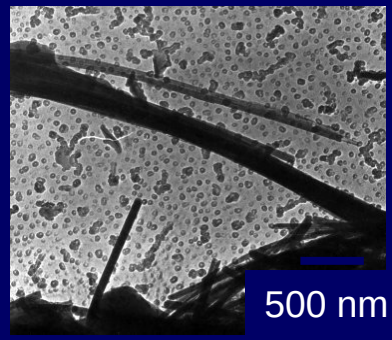




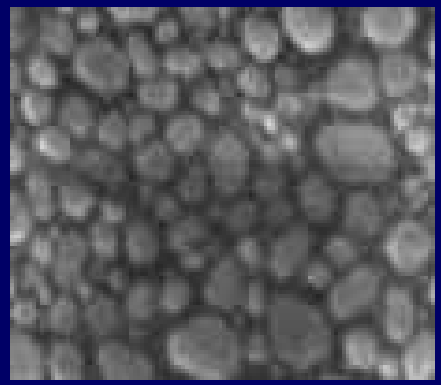
Tissue Damage: Industrial workers who breathe particulate matter (i.e. silica dust) develop fibrosis in their lungs, and other respiratory problems.

Akisue, T. Journal of Biomedical Materials Research (2002) 59(3) p.507.
Maloney, W. J. Journal of Biomedical Materials Research (1998) 41(3) p. 371.

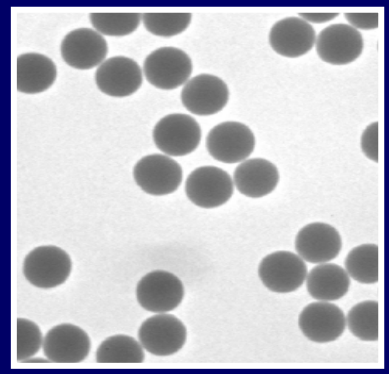
Ultra-fine Particles & Engineered Nanomaterials



Asbestos

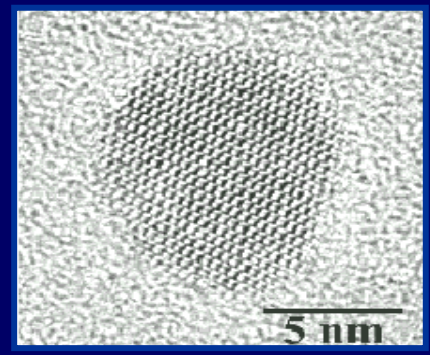


Crystalline particles



Silica colloids

Nanocrystals



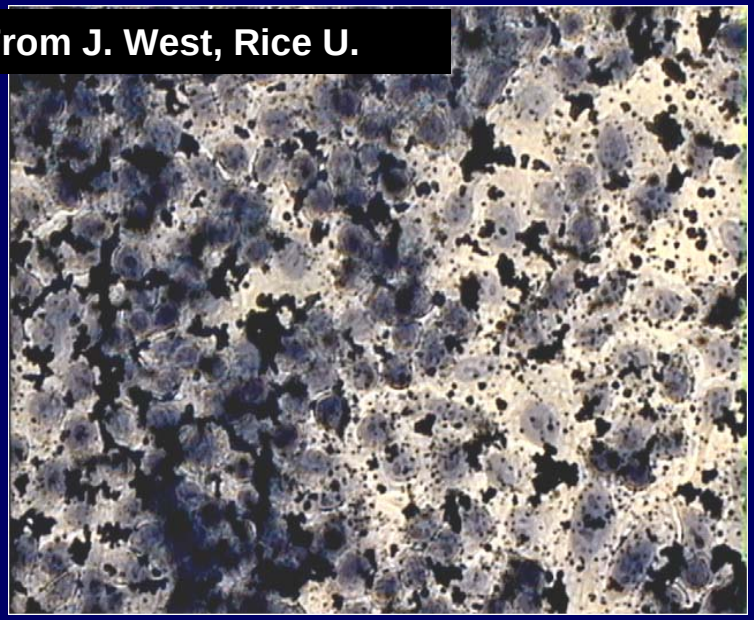
Diameter < 100nm
Complex composition
Exposure significant
Microns to sub-microns
Ill-defined surface chemistry

Diameter << 100 nm
Pure materials
Small quantities
Monodisperse
Controlled surface chemistry

Data on aerosol generated nanoparticles does not easily extrapolate to engineered nanoparticles

General observations for nanoparticles

From J. West, Rice U.



100 nm particles, intercellular space

Bruchez, Alivisatos et al Science 281 (1998) p. 2013

10 nm particles, inside cell

- **Receptor mediated endocytosis**
  - o d > 100 nm colloids don't
  - o d < 50 nm do
- **High reactivity of nanoparticle surfaces**
  - o Strong oxidizing/reducing agents
  - o Free radical activity

In-Vitro Cytotoxicity

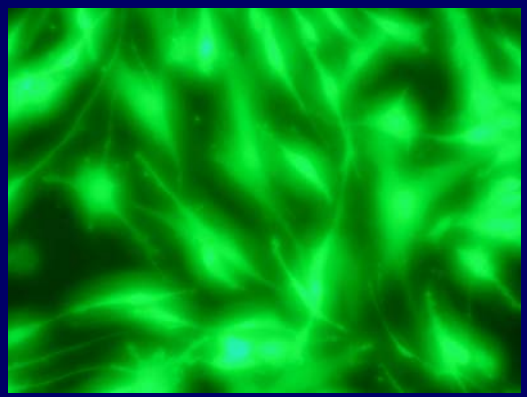
C_{60} colloidal Particles (4 ppm)

+

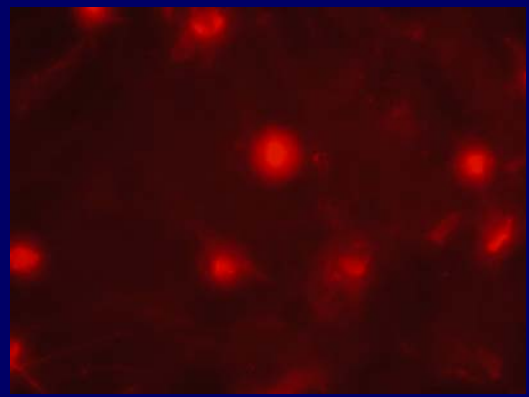
DMEM

HDP cells, seeded
(Human Diploid Fibroblasts)

48 Hours



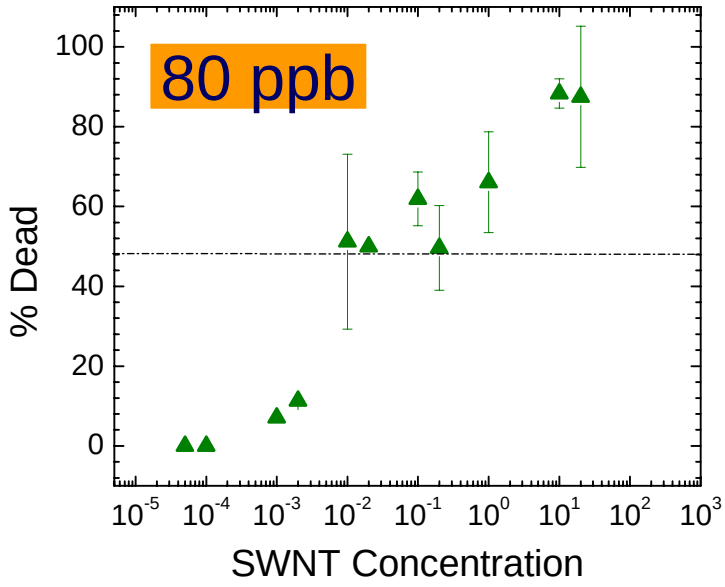
Live

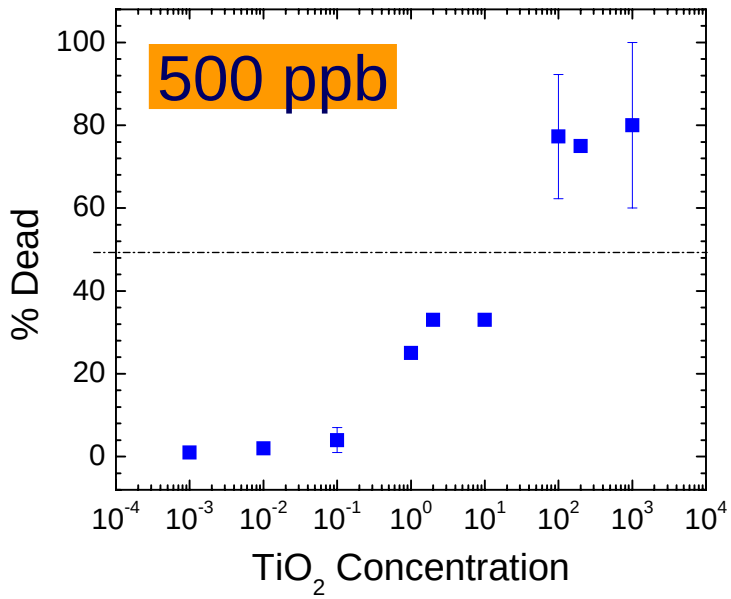


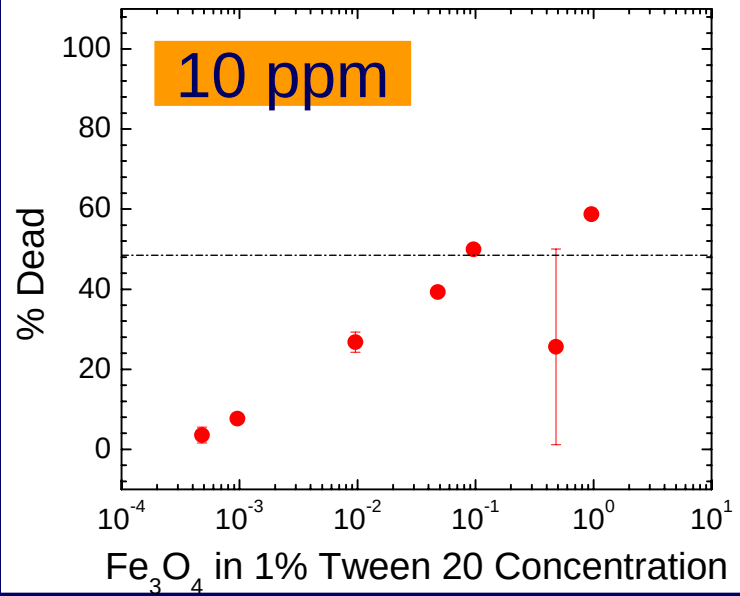
Dead

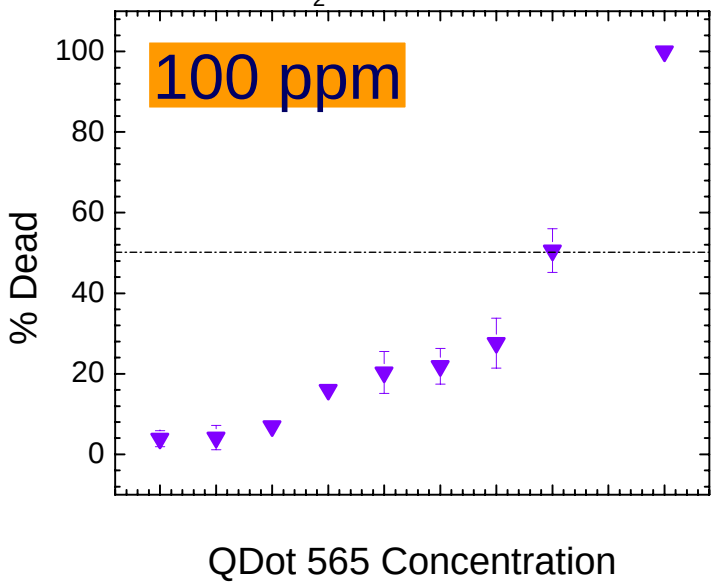
1) Nolan J S; Packer L **Monolayer culture techniques for normal human diploid fibroblasts**. METHODS IN ENZYMOLOGY (1974), 32(Part B), 561-8.
3) LIVE/DEAD Viability/Cytotoxicity Kit (L-3224). Molecular Probes Operation Manuel. p. 1. 1999.

In-Vitro Screening for Nanoparticles

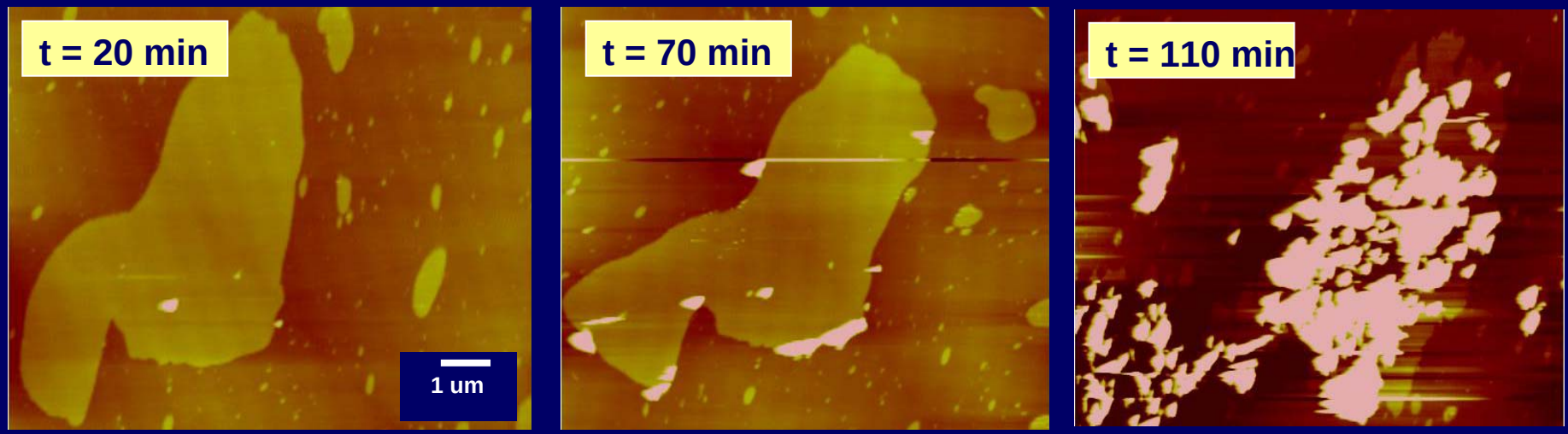






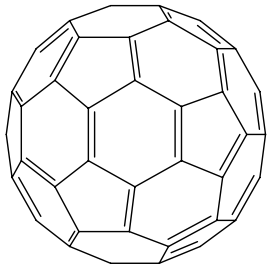


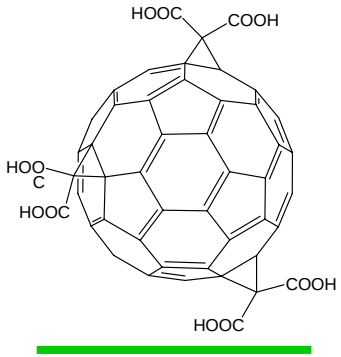
Mechanisms for nanoparticle toxicity

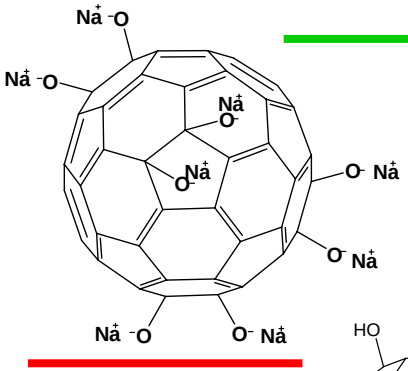


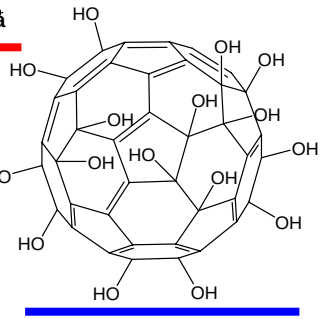
- Surfactant coated nanoparticles are not biocompatible
- Surface chemistry that makes particles lipophilic
- Reactive core materials that can generate free radicals

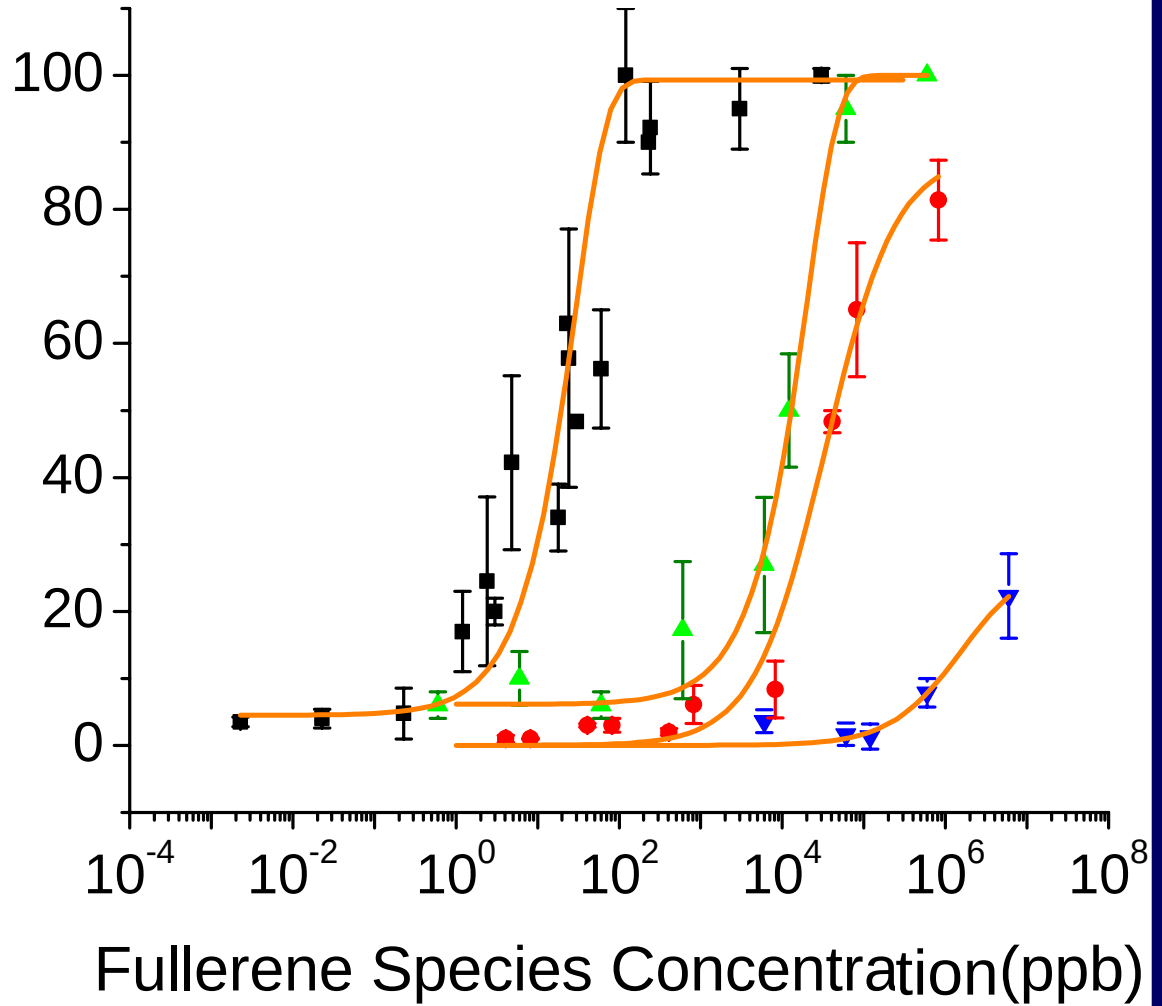
Structure-activity relationships for C_{60}





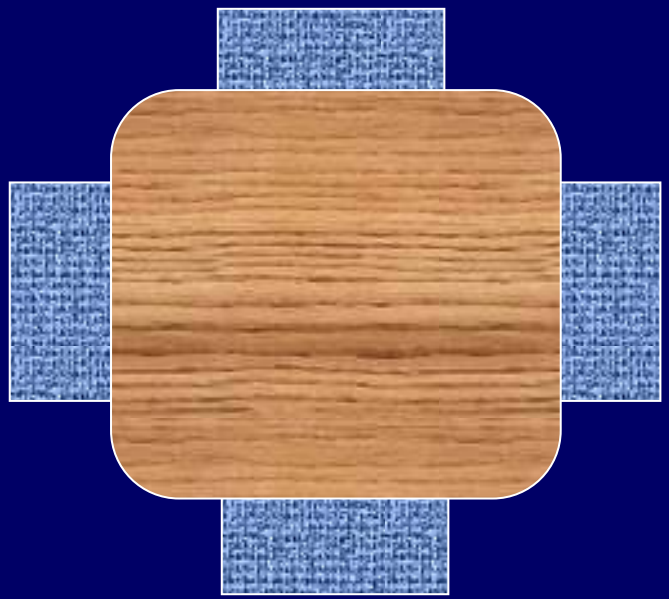






Public policy and partnerships

International Council on Nanotechnology



- All parties have a seat at the table
  - Academia, Industry,
  - Non-governmental, Government
- Consensus building activities
- Concrete policy work
  - Terminology standards
  - Laboratory health and safety
  - Hazards assessment framework

Ensuring Nanoparticle Safety

- Surfaces matter more than composition.
  Safety will not be only a function of core composition, but more about the surface

- Nanoparticle toxicity can be turned on and off
  We can engineer nanoparticles to be biocompatible, or not, through appropriate control over the surface

- Safe nanotechnology needs non-technical effort.
  Partnerships between industry, non-governmental organizations, and academia are developing to shepherd this new area.

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