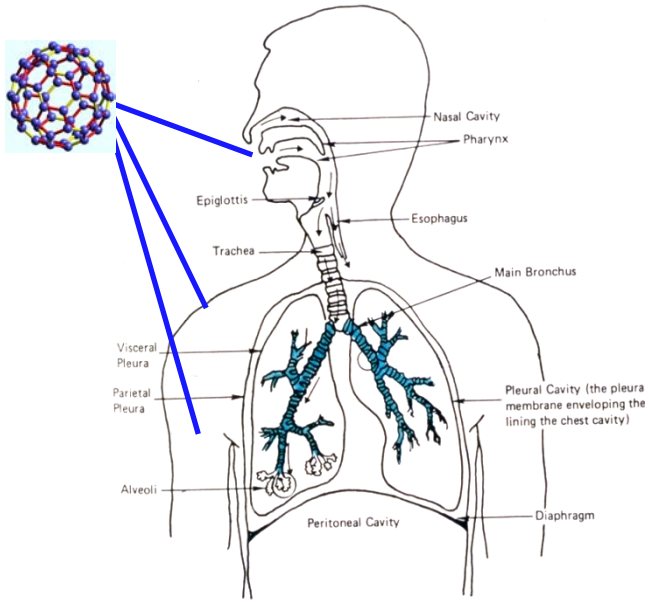
Designing Nanomaterials for Environmental Health and Safety

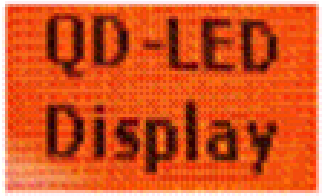


Robert Hurt
Brown University, Providence, Rhode Island

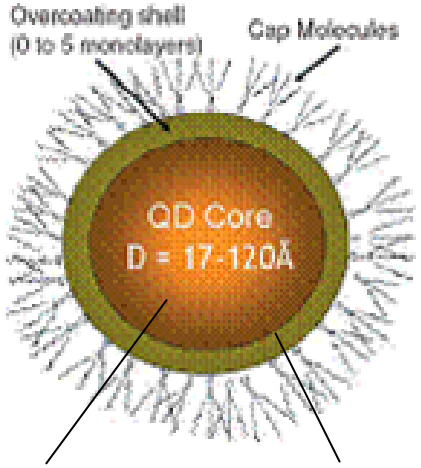
The Fifth U.S.-Korea Forum on Nanotechnology
Jeju Korea, April 17-18, 2008

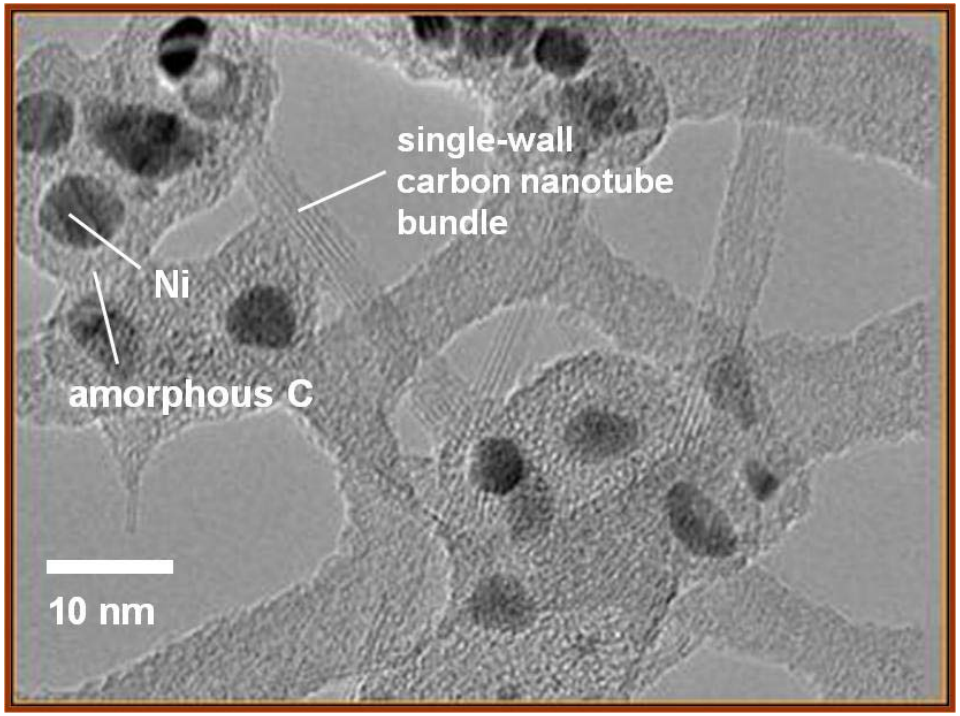
Nanomaterials are complex "chemical systems" that may include:

- surface functional groups
- adsorbed surface species, bound and free ligands
- byproduct phases or structures
- chemical toxicants imbedded within a passivating shell
- unreacted precursors, residual catalysts

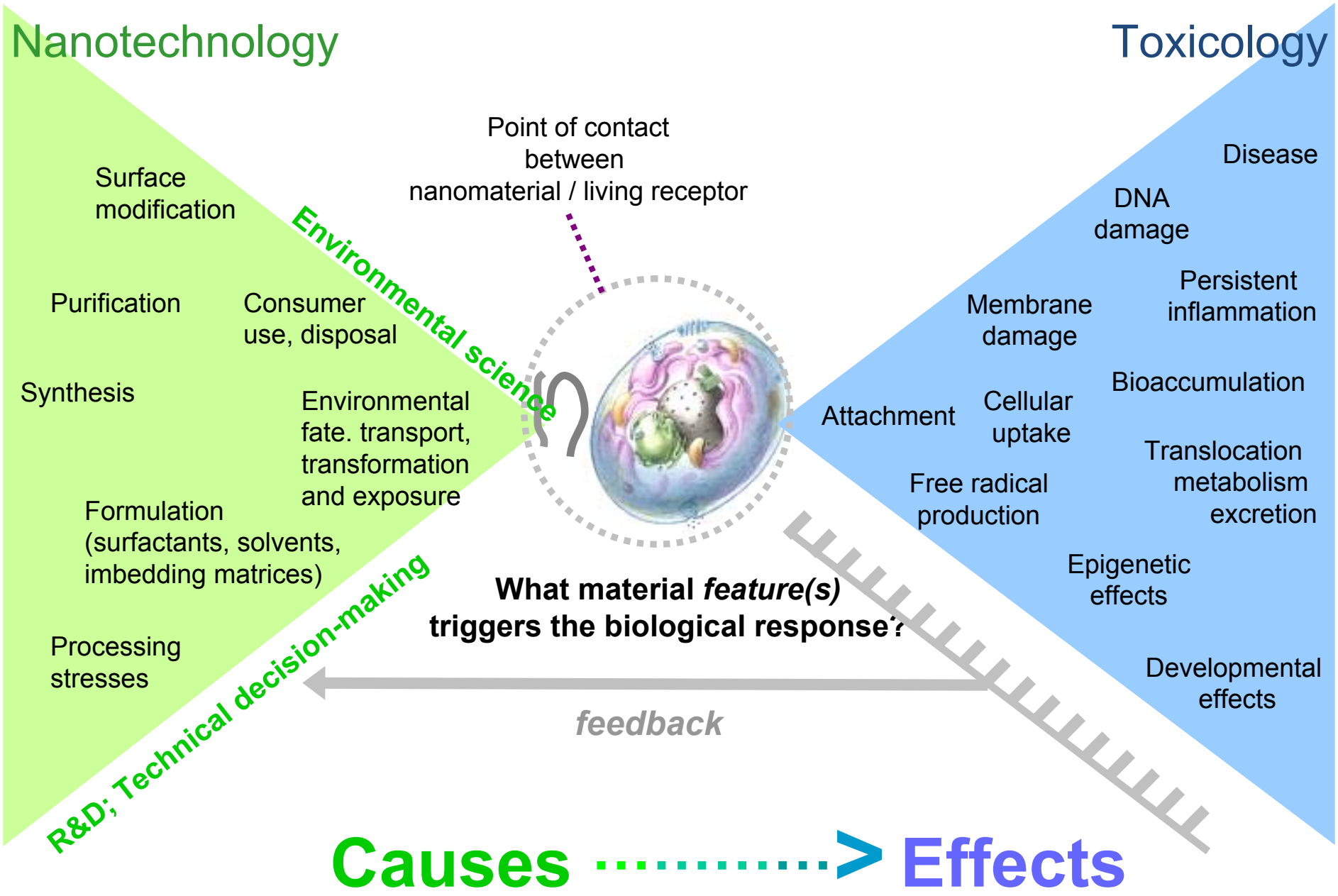


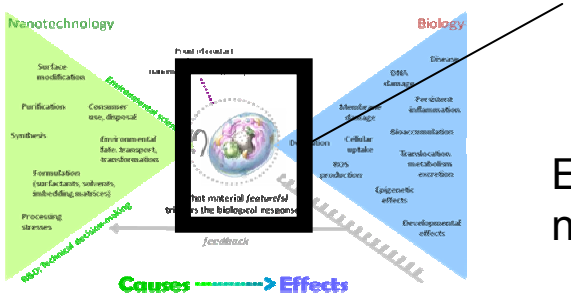
Quantum dot fluorescence, example LED display application, and core/shell structure





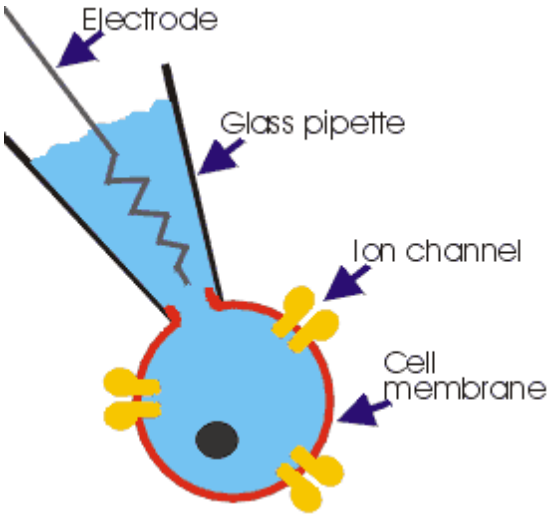
Commercial single-wall nanotube sample


Nanotechnology
Toxicology
Point of contact
between
nanomaterial / living receptor
Surface
modification
Purification
Consumer
use, disposal
Synthesis
Environmental
fate. transport,
transformation
and exposure
Formulation
(surfactants, solvents,
imbedding matrices)
Processing
stresses
Environmental science
R&D; Technical decision-making
Disease
DNA
damage
Persistent
inflammation
Membrane
damage
Bioaccumulation
Attachment
Cellular
uptake
Translocation
metabolism
excretion
Free radical
production
Epigenetic
effects
Developmental
effects
What material feature(s)
triggers the biological response?
feedback
Causes
Effects

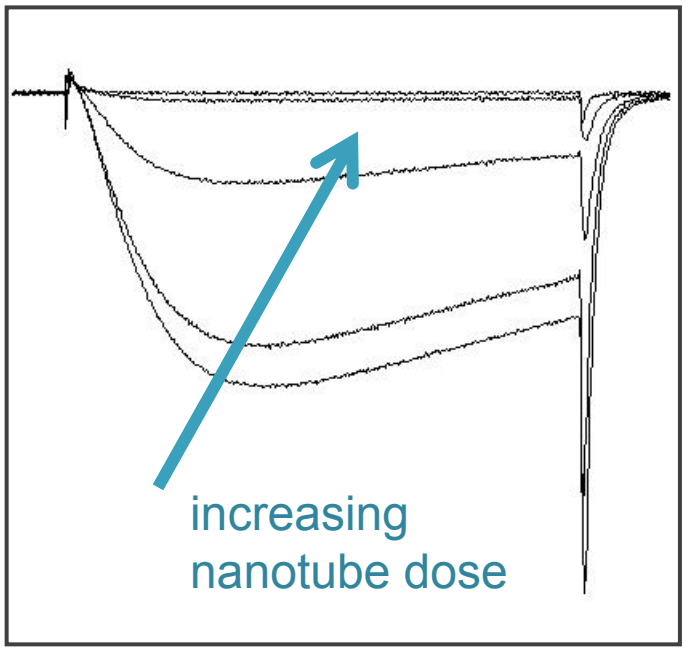


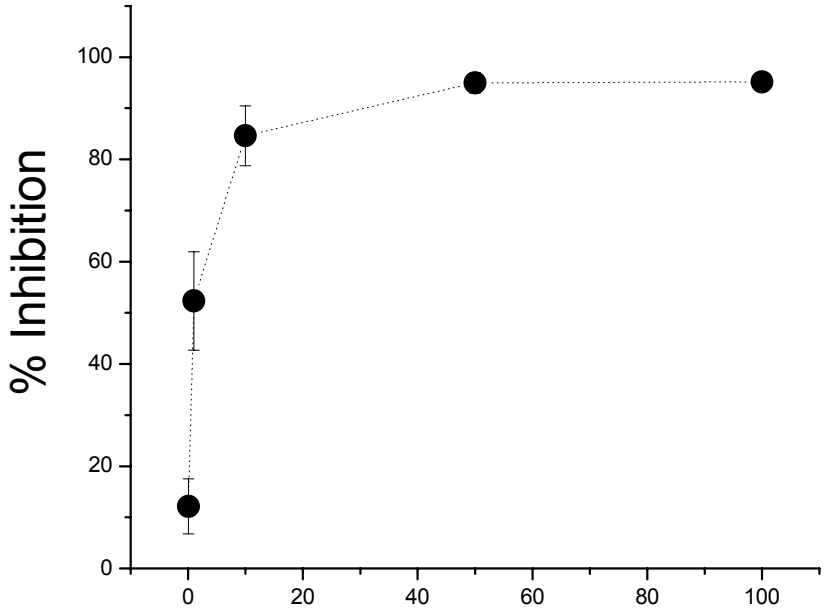
What material feature is the trigger for the biological response?

Example: Effect of carbon nanotubes on electrically active cells
(Lorin Jakubek w/ Prof. Diane Lipscombe, Neuroscience, Brown)



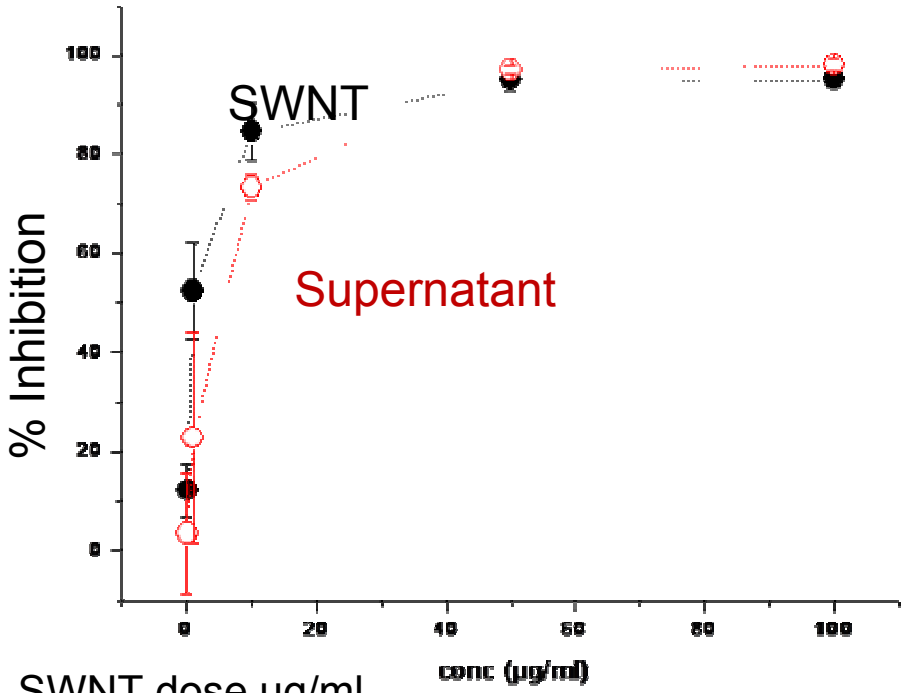
Current in cells transfected with voltage-gated calcium channel



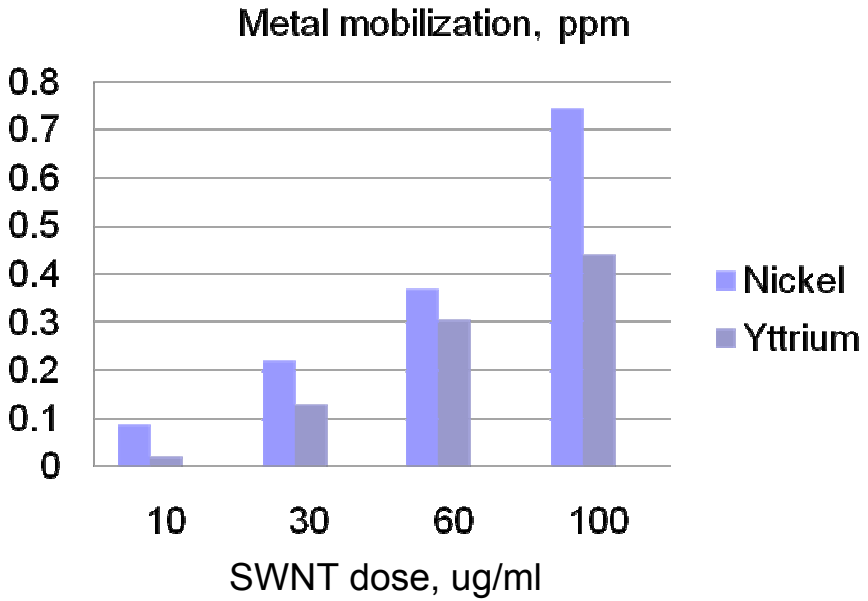


IMNI

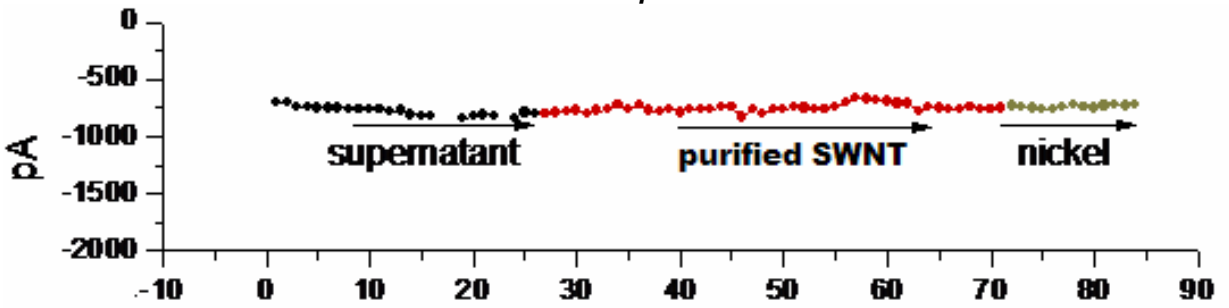
How do SWNTs inhibit neuronal calcium channels?



SWNT dose ug/ml

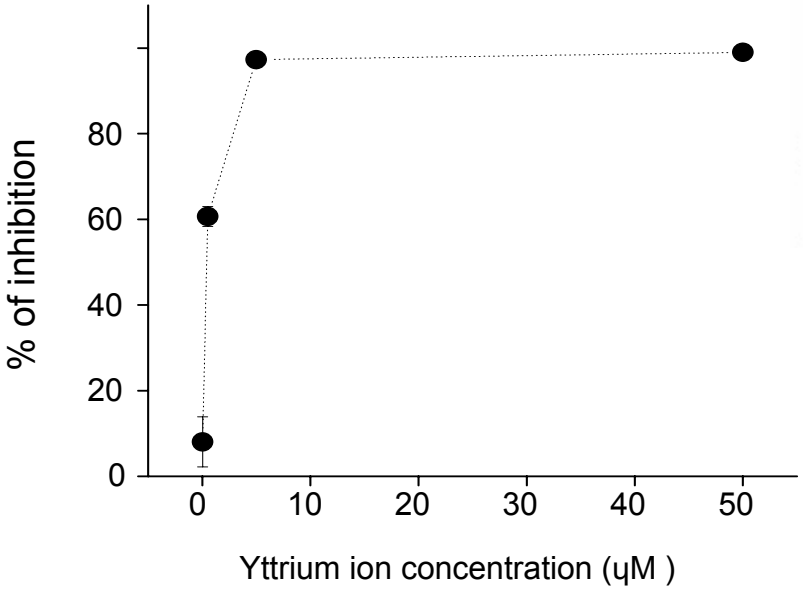


no inhibition from purified SWNTs or soluble Ni

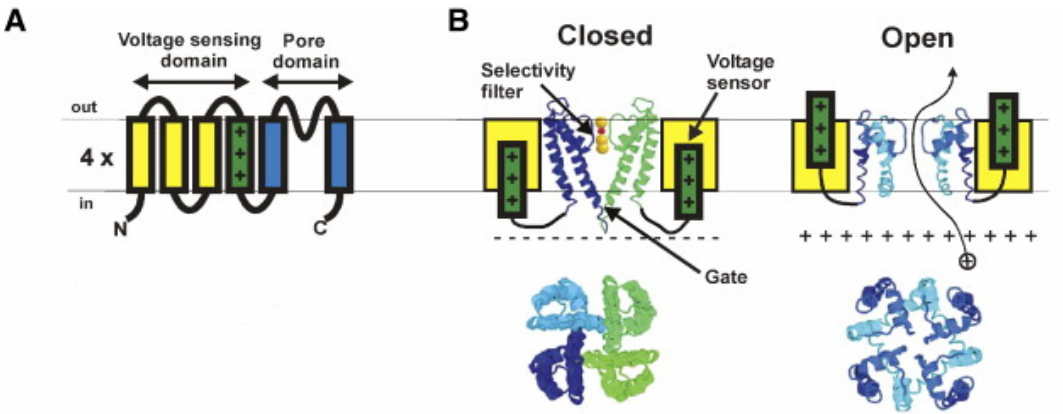


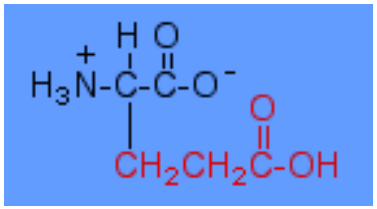
IMNI

Calcium Ion Channel Inhibition is due to Mobilized Yttrium!

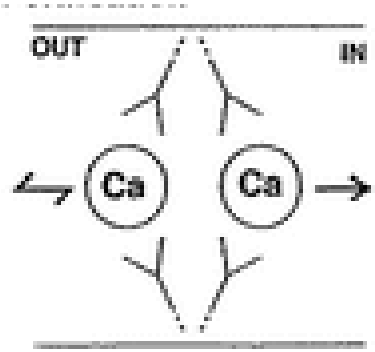


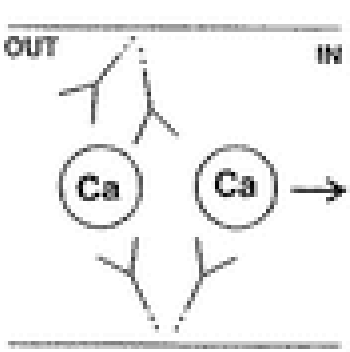
General channel structure



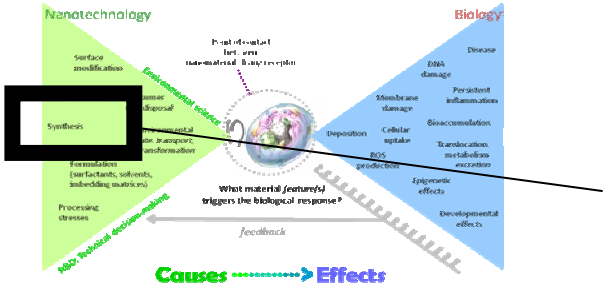


EEEE (glutamate) peptide sequence is highly preserved in Ca channels



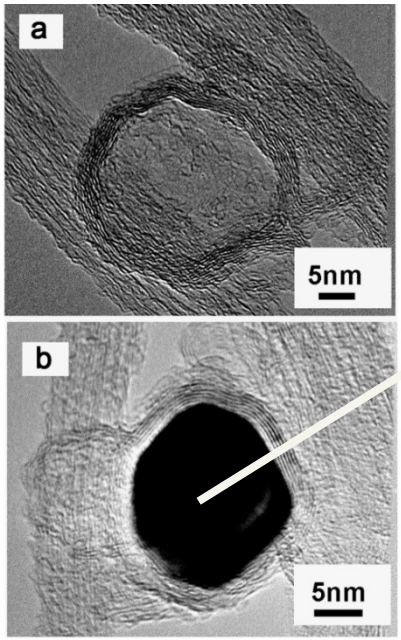


IMNI

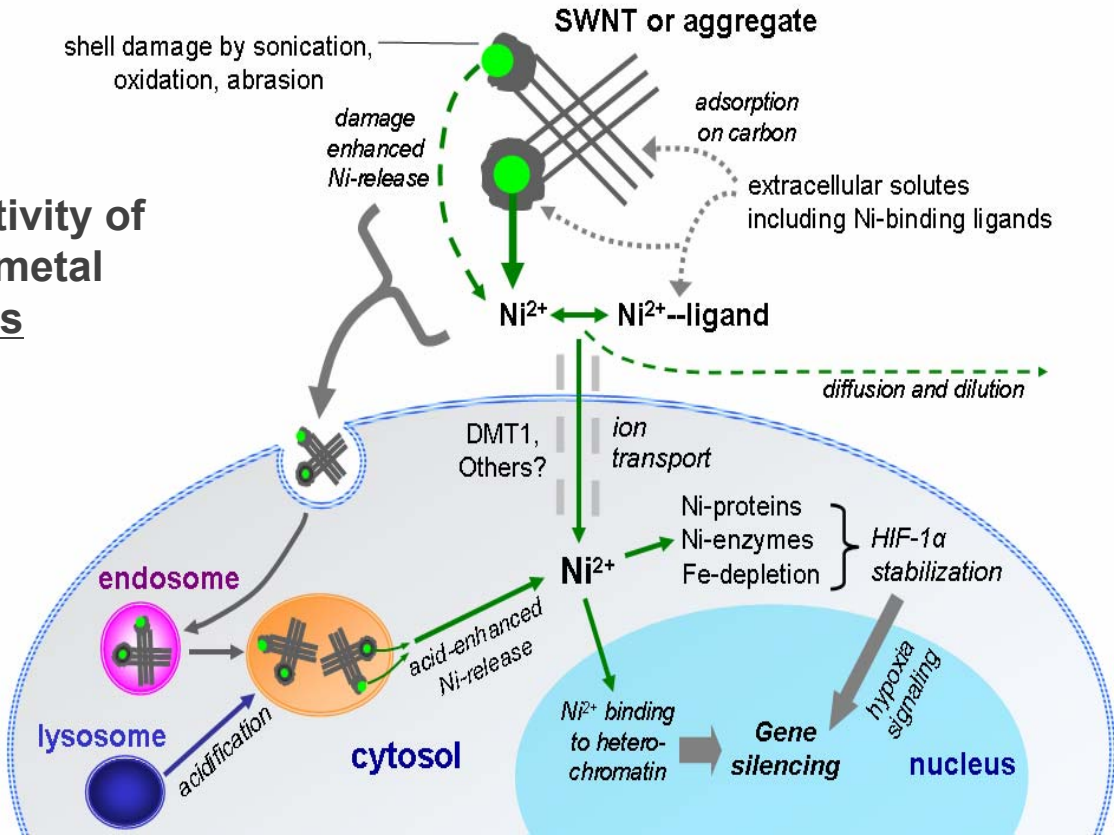


Synthesis: **Bioavailability of Nickel in Single-Wall Carbon Nanotubes**

Liu, Gurel, Morris, Murray, Zhitkovich, Kane, Hurt
Advanced Materials, 19 2790 (2007)



biological activity of C-imbedded metal is not obvious

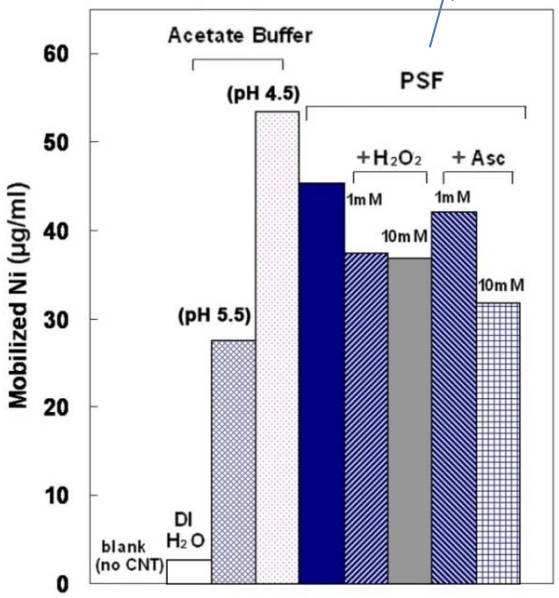


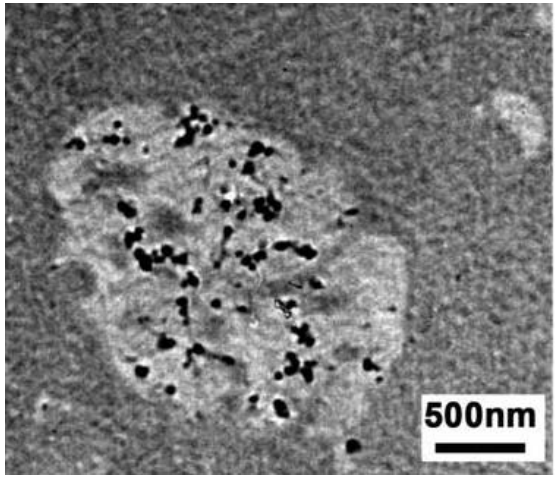
BROWN

Cellular Response to CNT Nickel

Effect of fluid media

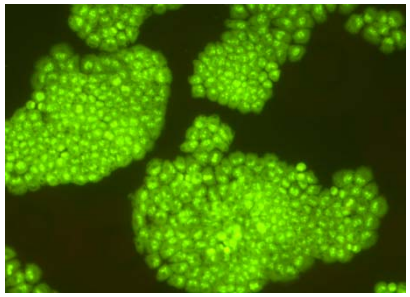
PSF: Phagolysosomal Simulant Fluid



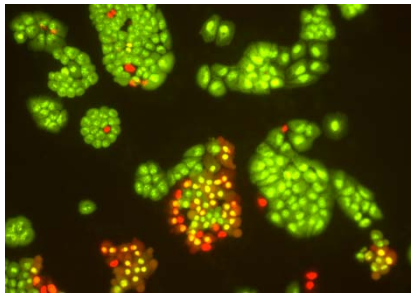


SWNTs inside lung epithelial cell vesicle by thin-section TEM

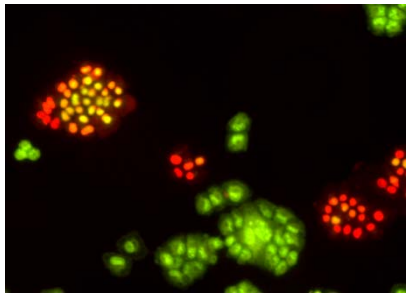
Soluble Ni dose-response in human lung epithelial cells (48 hrs)



Control

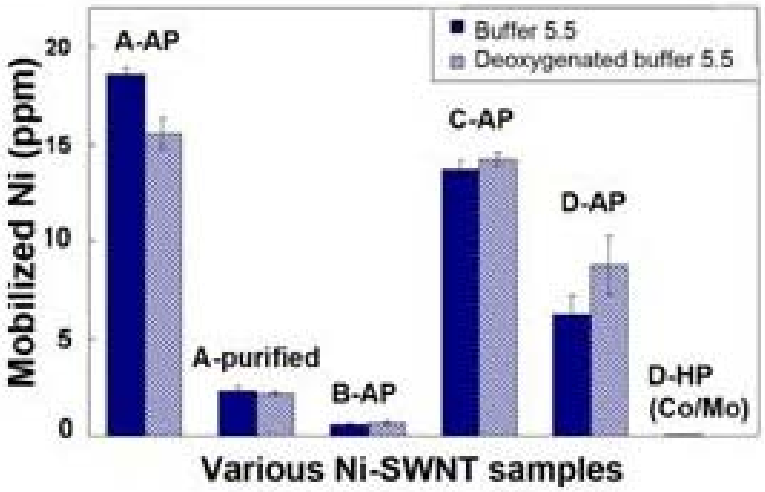


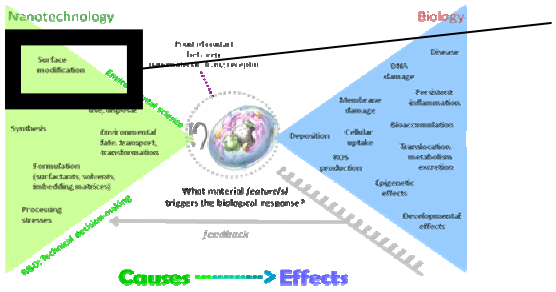
3 ppm (ug/g)



6 ppm (ug/g)

Effect of CNT source / type





Surface modification

Effect of CNT hydrophobicity

[Guo, Von Dem Busche, Buechner, Kane, Hurt ; *Small,* in press]

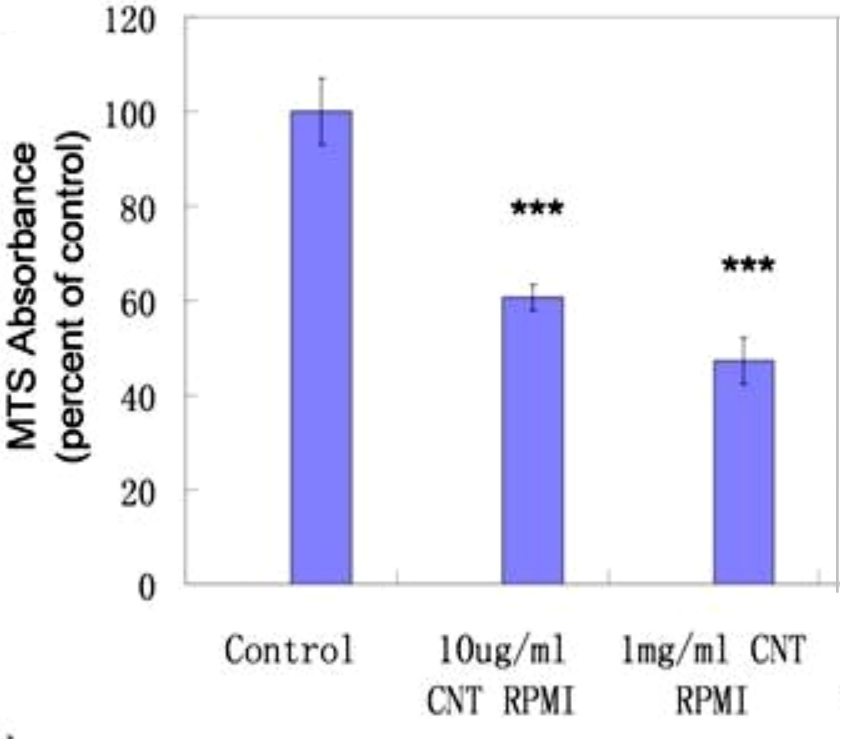
Simple Experiment

SWNTs + Cell culture medium

SWNT removal by centrifugal ultrafiltration

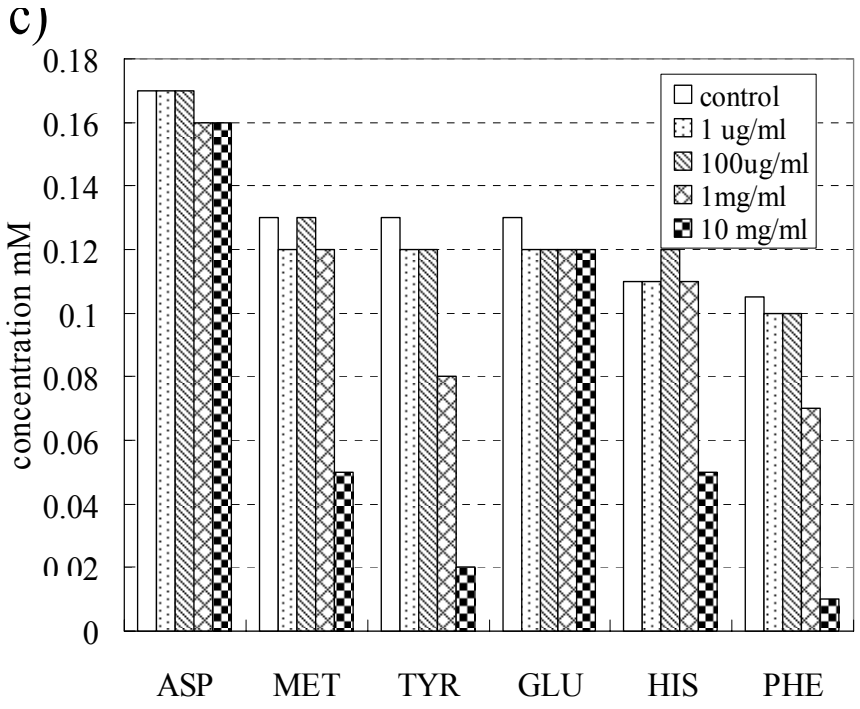
solute profiling and cell culture in “exposed” media

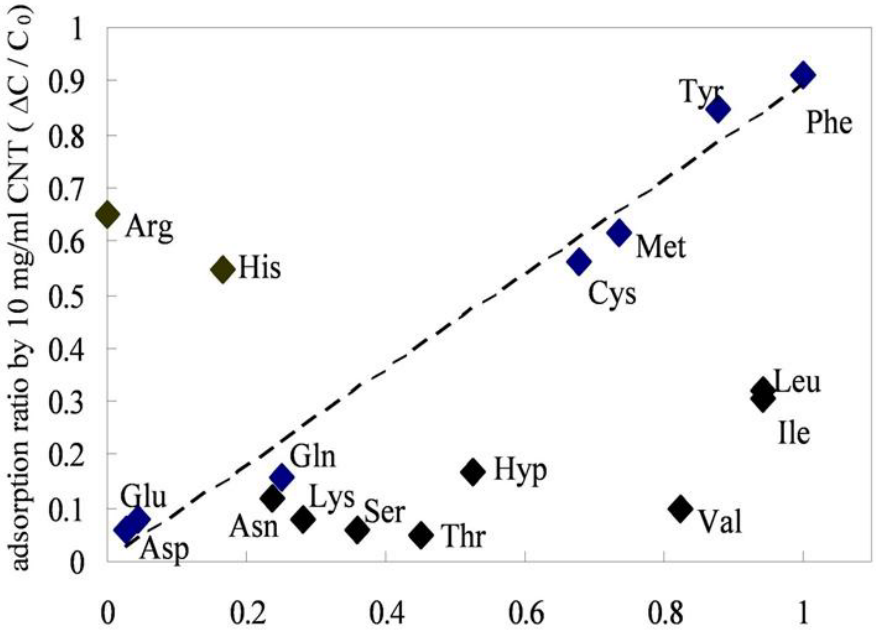
Viability of HepG2 liver cells



IMNI

Amino acid profiling after dose-dependent SWNT exposure

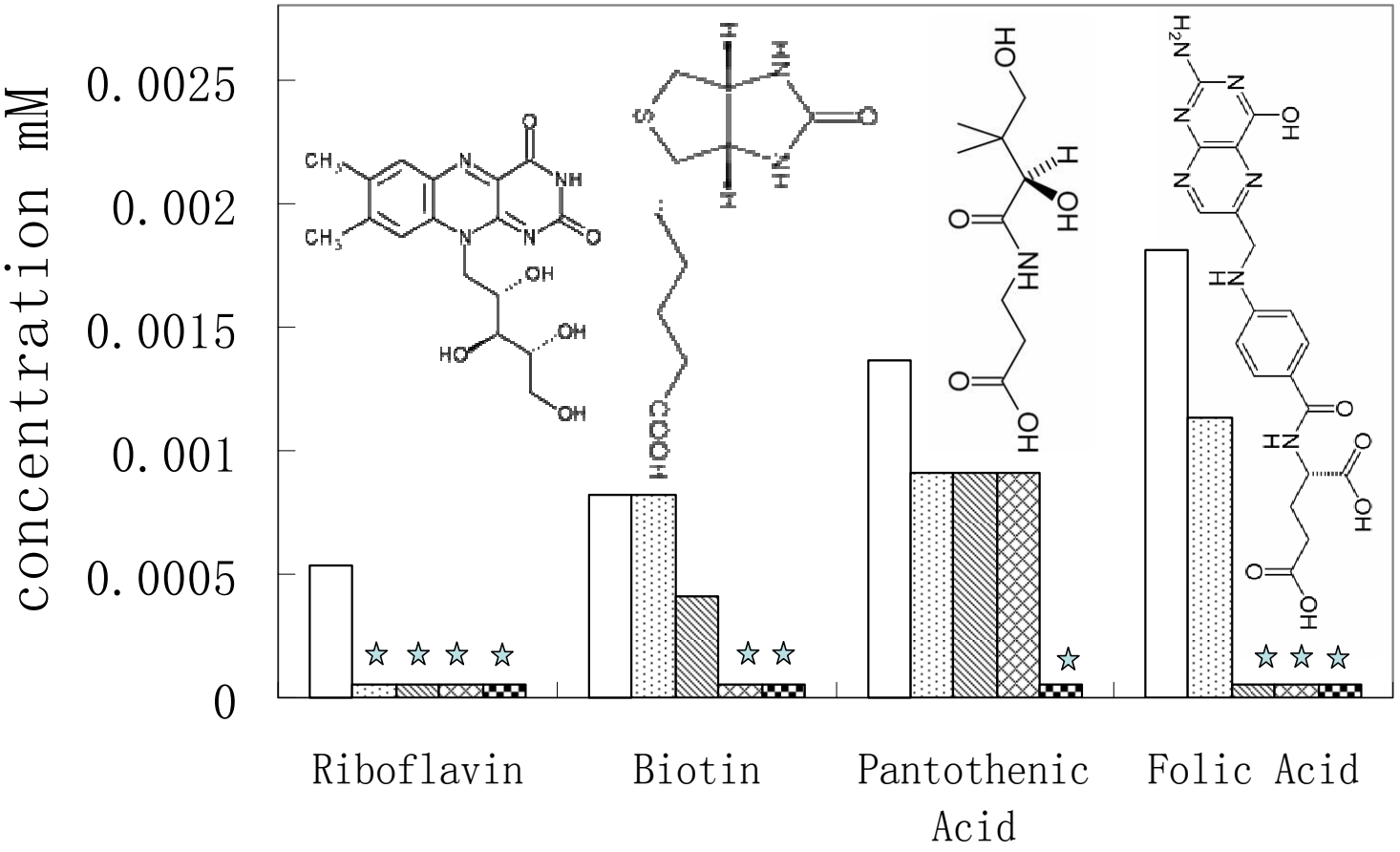




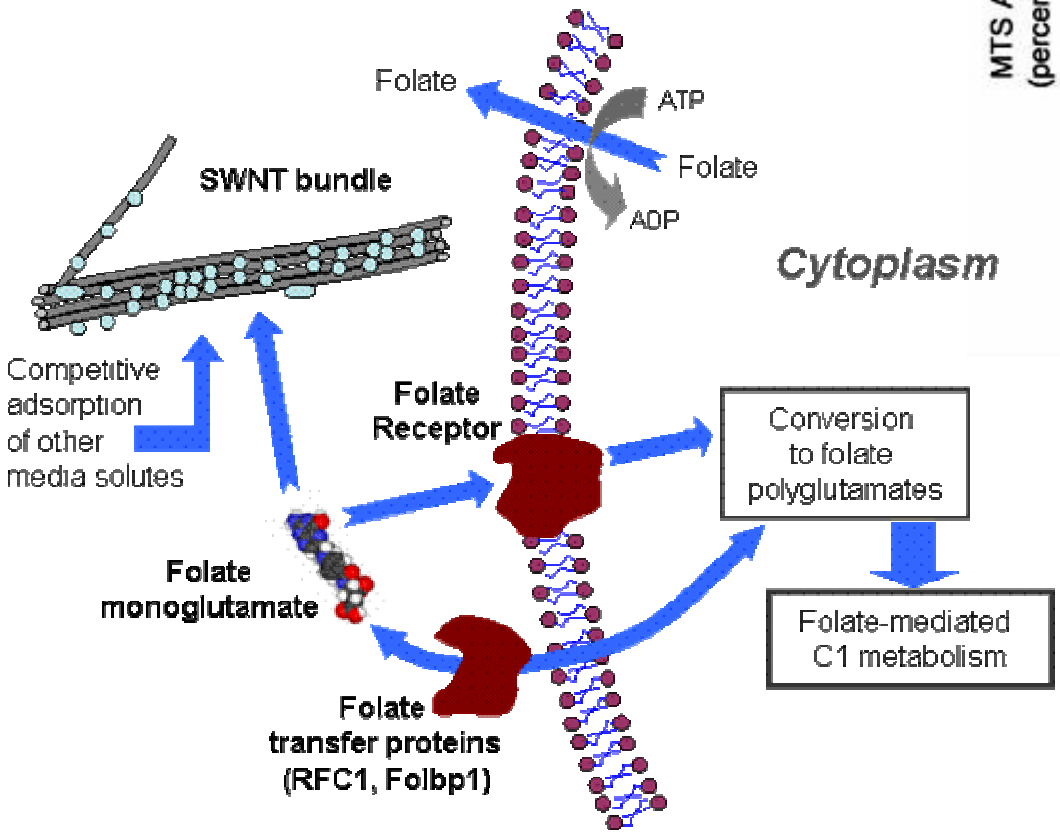
Hydrophobicity index
of Black and Mould, 1991

IMNI

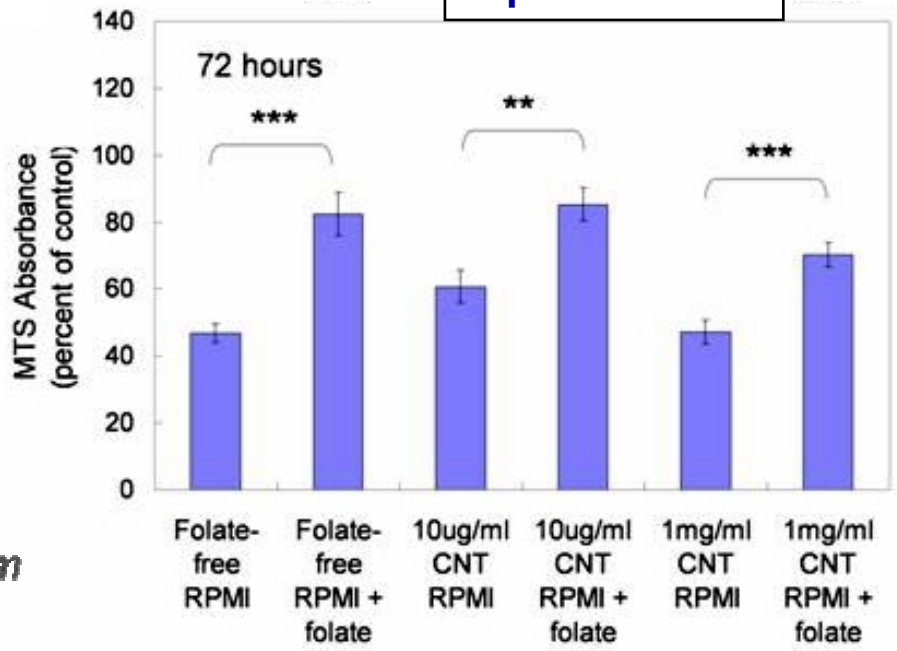
Some vitamins are depleted at CNT doses as low as 10 ug/ml !



Competitive Folate Pathways and Biological Implications



Effect of folate replenishment

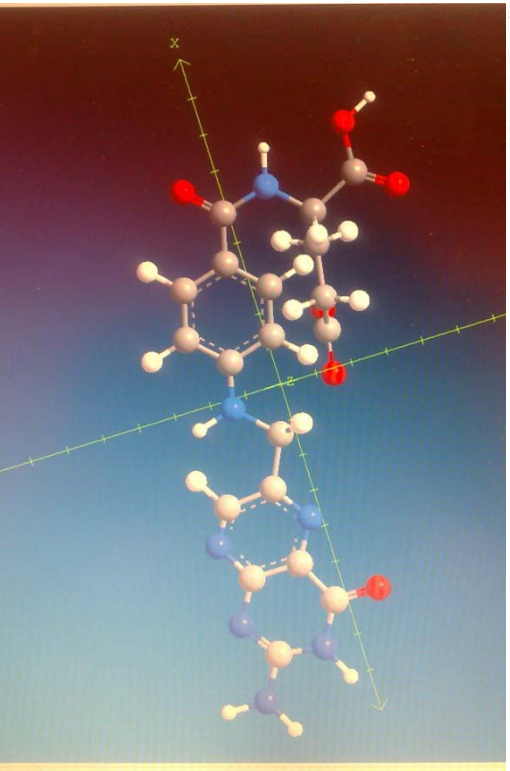


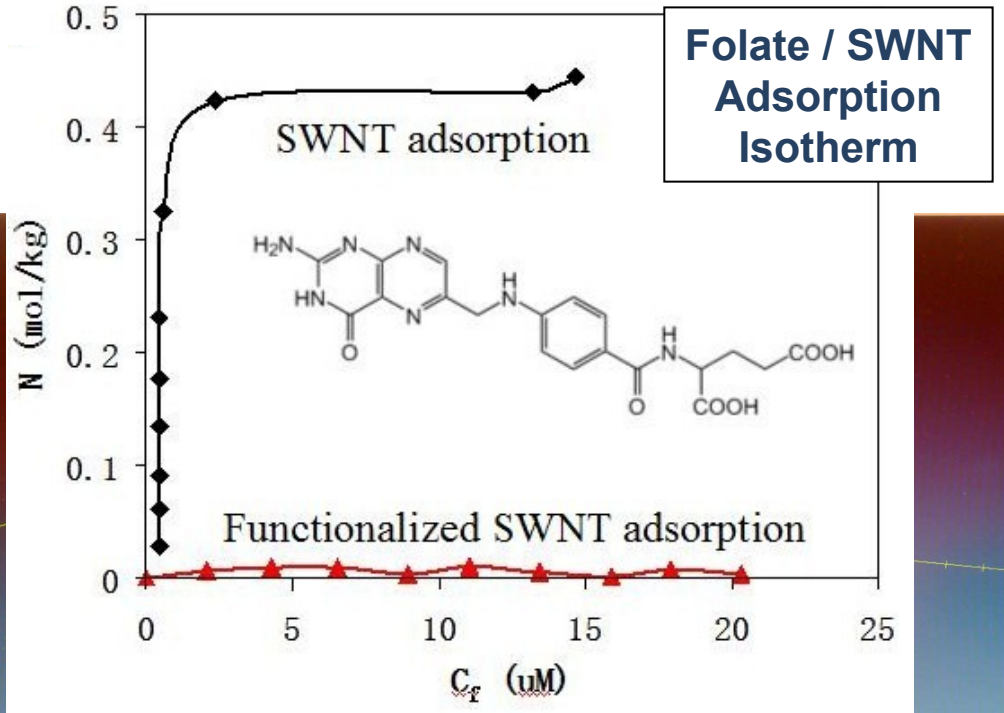
Institute for Molecular and Nanoscale Innovation

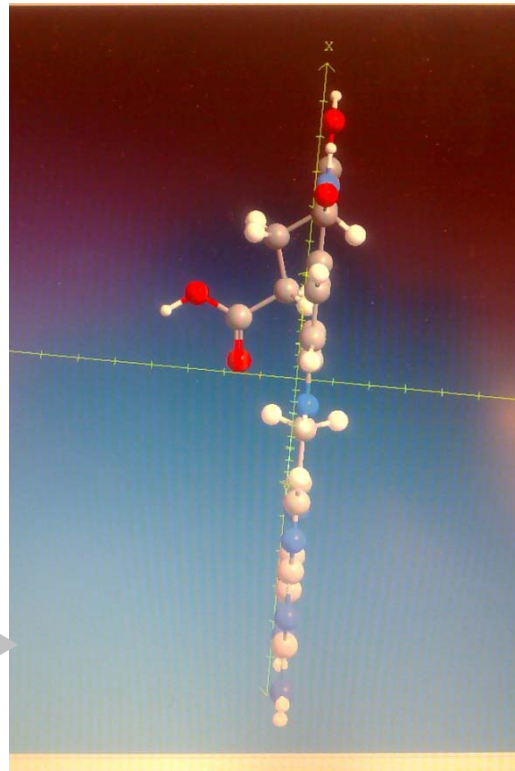
IMNI

Result: A new "starvation mechanism" driven by hydrophobic depletion of essential micronutrients

Adsorption of Essential Micronutrients by Carbon Nanotubes and Its Implications for Nanotoxicity Testing, Guo, Von Dem Bussche, Buechner, Kane, Hurt , *SMALL* in press

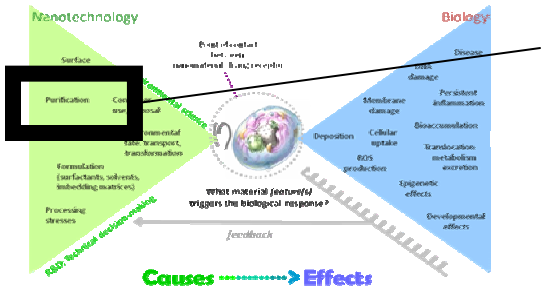






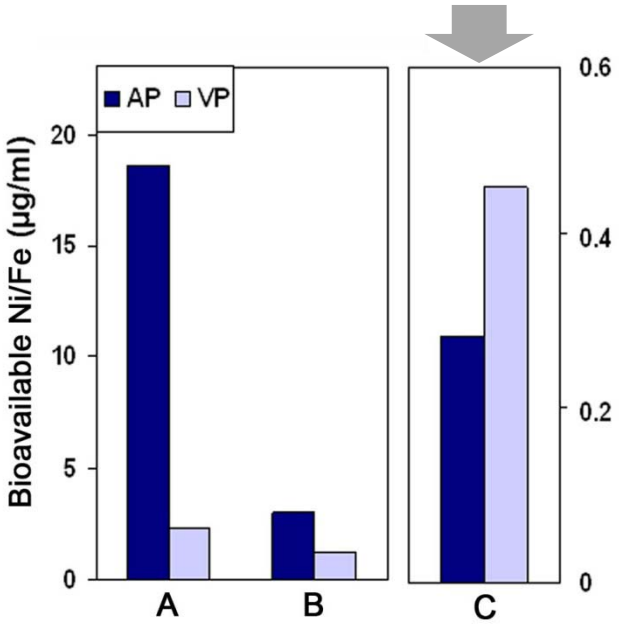
Folate monoglutamate

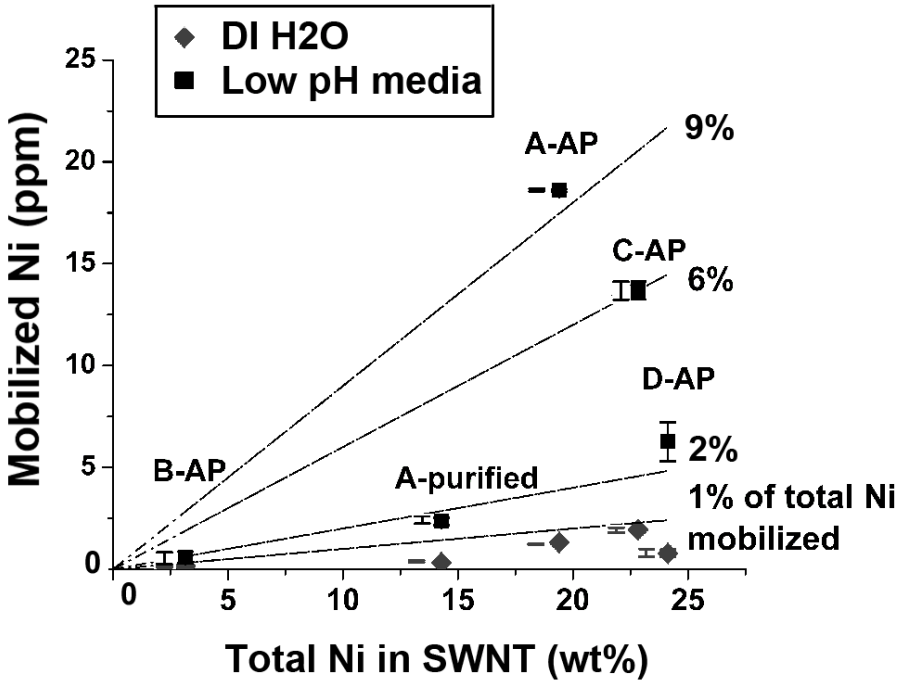
top view *side view*



Purification → Example: targeted removal of *bioavailable* metal as a detoxification strategy for nanotubes

purification ***increases*** bioavailable metal !



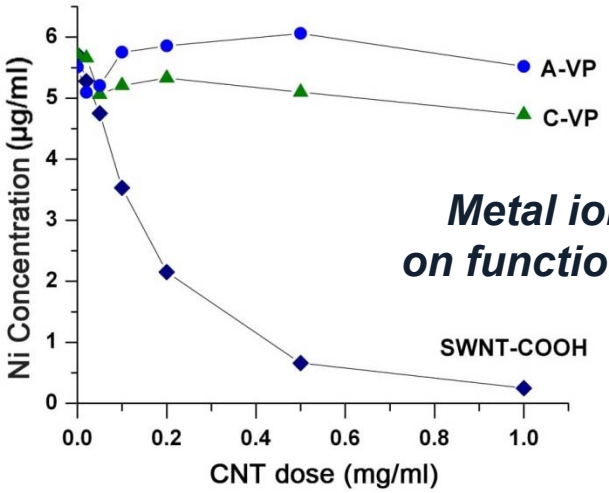


Question 1:
What is origin of bioavailable metal in “purified” CNTs ?
(and why does “purification” sometimes ***increase*** it?)

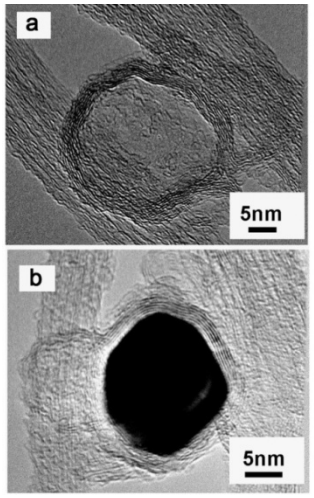
Question 2:
How can we target the bioactive portion of the metal for removal (and detoxification)

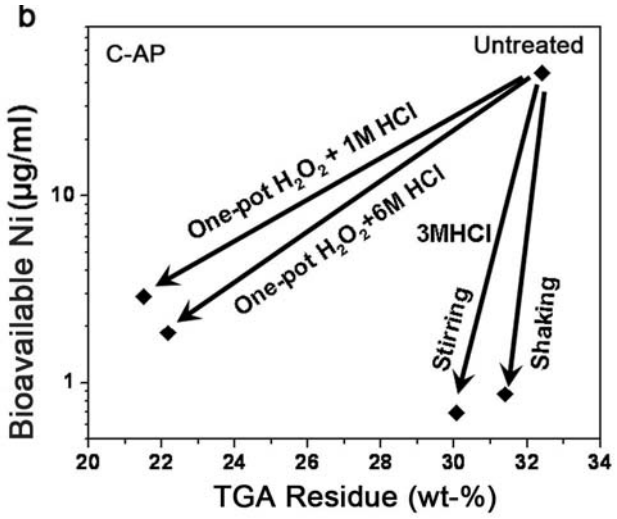
IMNI

Purification do's and don'ts

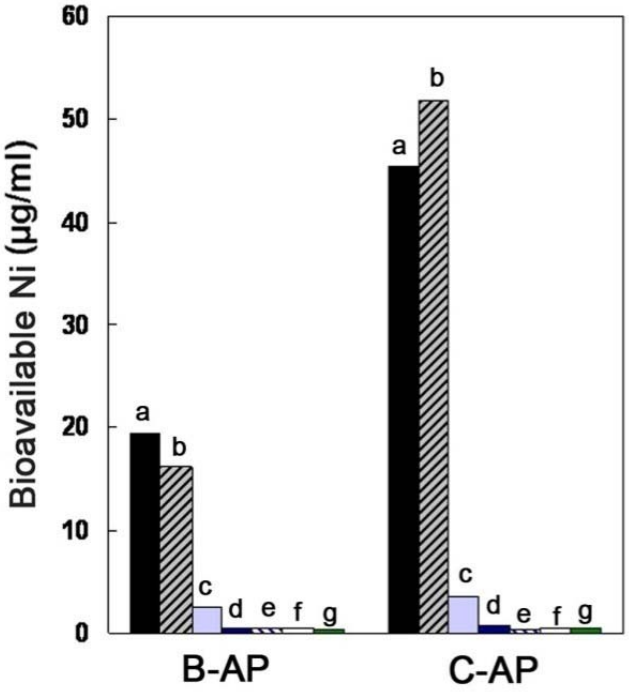


Metal ion re-deposition on functional groups (don't)





Oxidation during or after acid wash (don't)



Last step wash with non-oxidizing acid (do)

Summary

- Carbon nanotubes can block neuronal calcium ion channels through release of trace amounts of yttrium!
- Carbon nanotubes can also release toxicologically significant amounts of nickel – a known carcinogen that acts through epigenetic modification
- Single-wall carbon nanotubes can inhibit cell growth by adsorbing folic acid and other micronutrients (even without contacting cells!)
- The mechanisms above can be suppressed by proper purification (purification designed for detoxification) and by surface modification for hydrophilicity
- There are many other opportunities to make nanomaterials safer by understanding biomolecular mechanisms and modifying the nanomaterial *features* that trigger those mechanisms.

Contributors

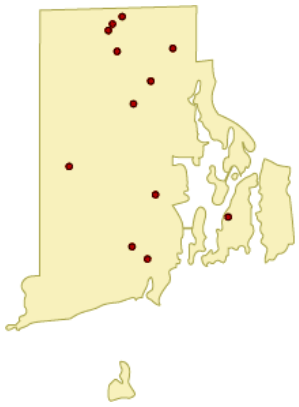
Materials Chemistry
Prof. Robert Hurt
Indrek Kulaots,
Lorin Jakubek
Lin Guo
Xinyuan Liu
Daniel Morris
Aihui Yan

Pathobiology
Prof. Agnes Kane
Charles A. Vaslet
Annette Von Dem Bussche
Kevin McNeil
Michelle Buechner
Jodie Pietruska
Ashley Smith

Neuroscience
Prof. Diane Lipscombe
Jesica Raingo

Financial support at Brown:

- US EPA (STAR Grant RD83171901)
- NSF NIRT grant (DMI-050661)
- SBRP grant at Brown (NIEHS P42 ES013660)
- NIEHS R01 on Nanotoxicology



This research is funded by
U.S. EPA - Science To Achieve Results (STAR) Program
Grant # RD-83171901-0