



Recipient of the 2005 National Medal of Technology

Some thoughts on how chemical and physical modifications affect properties of selected nanomaterials

Driving Innovation Through Collaboration to Advance Humankind

National Nanotechnology
Initiative Workshop on
Nanomaterials and the
Environment
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recommendations and contributions: **Jim Field, Scott Boitano,**
Russell Mumper, Buddy Ratner , Farhang Shadman, Reyes Sierra,
Alexander Tropsha, and Victor Zhirnov

q Introduction

q Transport

q Transformation

q Thresholds

q Toxicity

q Metabolic

q Tools

q Research Challenges and Discussion

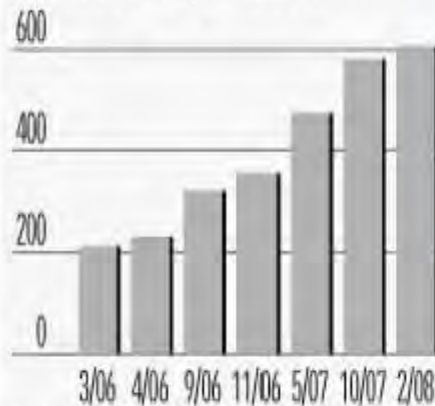
There Are Real Products!

- ~650 commercially available “nano” products
- cosmetics
- intended to be orally ingested or eaten

Nano's Nest Grows

The number of identified consumer nanotech products on the market is on the rise*

Number of products



*excludes non-consumer products on the market such as parts in car bodies and in certain batteries

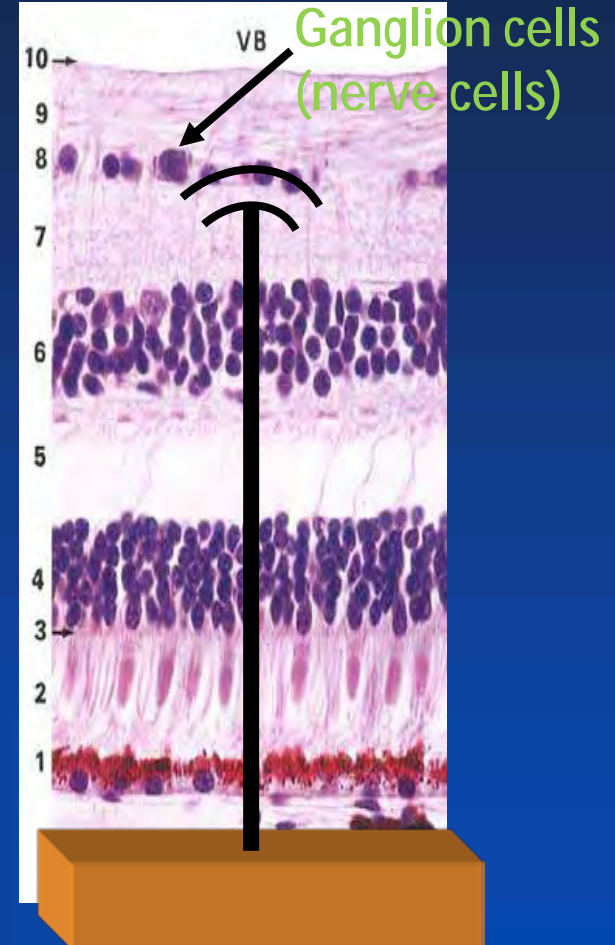
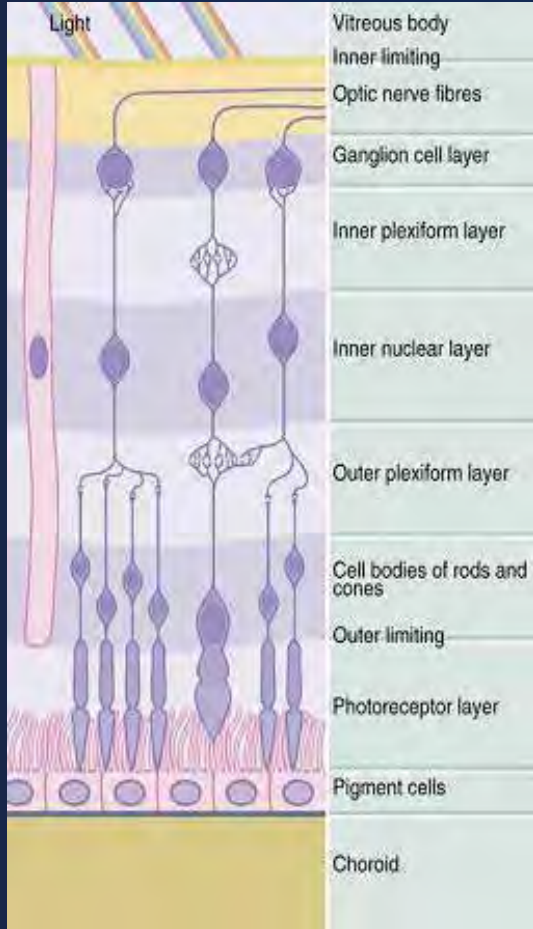
Source: Nanotechproject.org

Selected Applied Nanomaterial Families:

- q Lipid and polymer-based pharmaceutical drug and imaging carriers
 - Ø Various liposome products
 - Ø Nanocrystals
 - Ø Nanosuspensions for oral delivery of drugs
- q Metals Oxides
 - Ø Ceramics from oxides of zinc, iron, cerium, and zirconium
 - Ø Polishing agents for semiconductors
 - Ø Scratch resistant glass coatings
 - Ø Sunscreens and cosmetics
- q Nanoclays
 - Ø Naturally occurring clay particles
 - Ø Barrier films on bottles/cartons and other products
- q Nanotubes
 - Ø Fillers for plastics
 - Ø Exterior automobile components
 - Ø Coatings to reduce or dissipate static electricity



State-of-the-Art Application: Nanomaterial Based Retinal Prosthesis Project

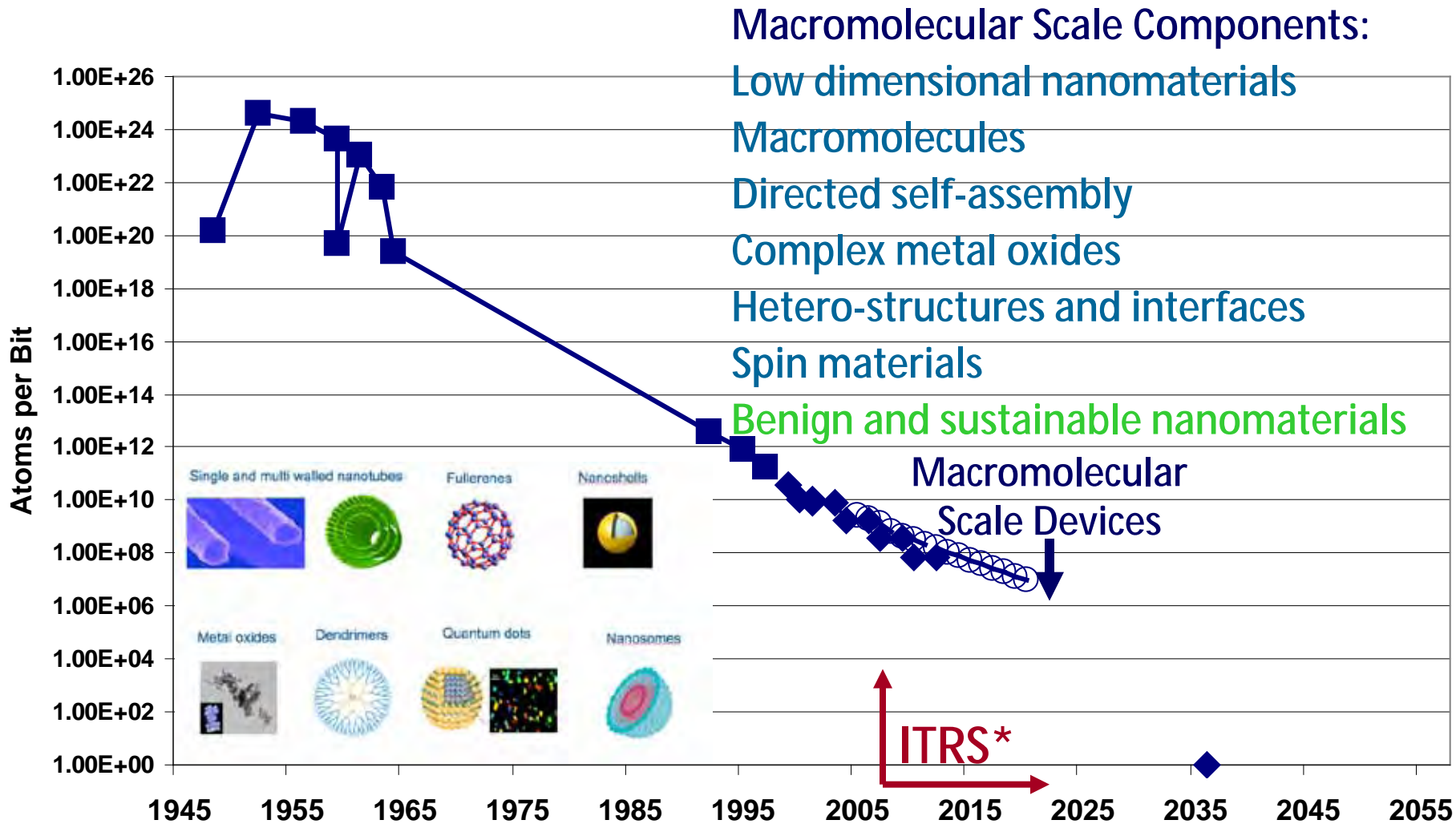


Implantation of Carbon Nanotube Bucky Paper into the Sub-Retinal Space of an Albino Rabbit immunologically well-tolerated

Ref.: David J. Loftus, NASA Ames Review, 2003



State-of-the Art: Functional Nanomaterials May Enable Macromolecular Scale Devices



ITRS*: International Technology Roadmap for Semiconductors

Revised 2006 from: D. Herr and V. Zhirnov, Computer, IEEE, pp. 34-43 (2001).



Overview State-of-The-Art

- q Introduction

- q **Transport**

- q Transformation

- q Thresholds

 - q Toxicity

 - q Metabolic

- q Tools

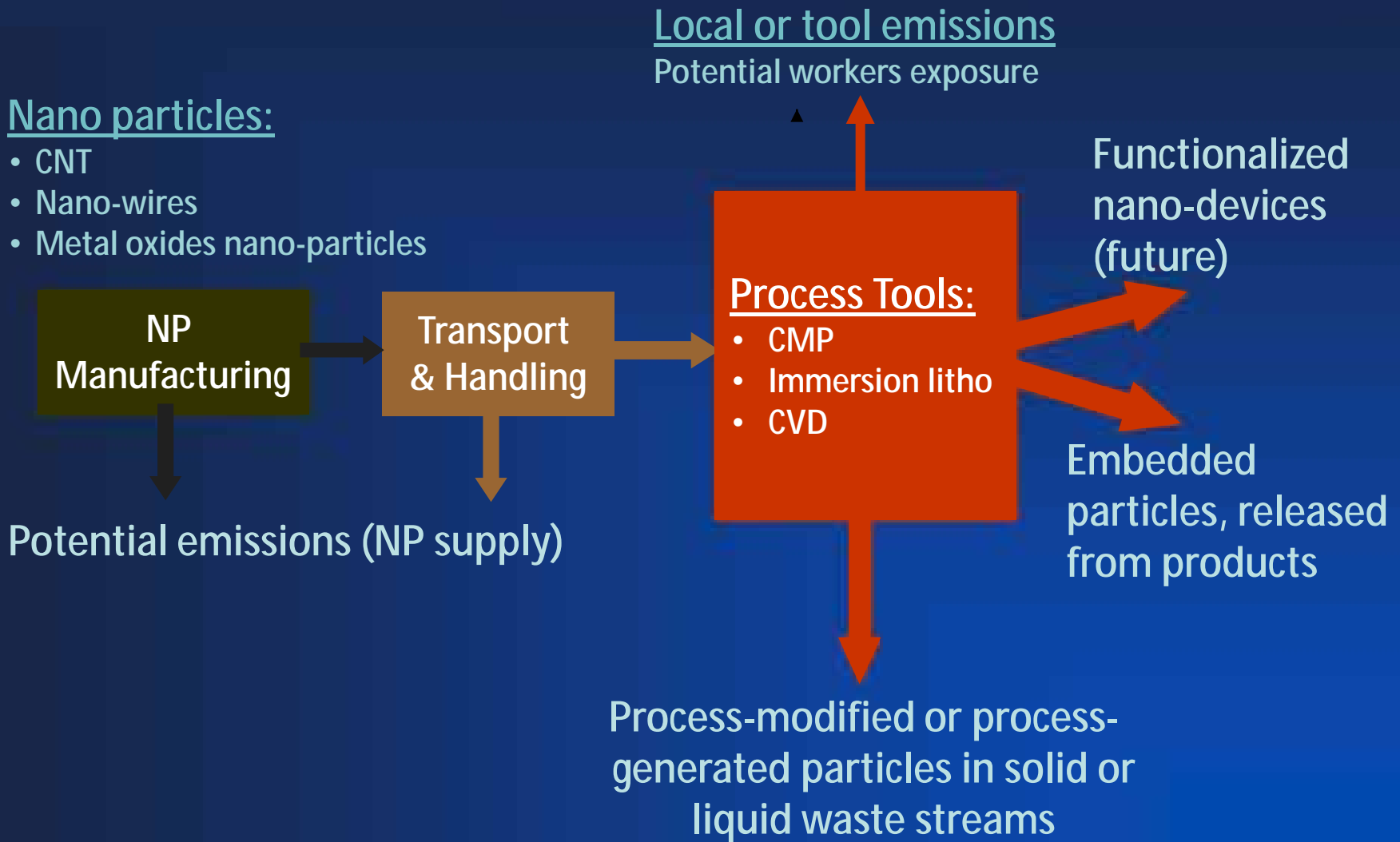
- q Research Challenges and Discussion



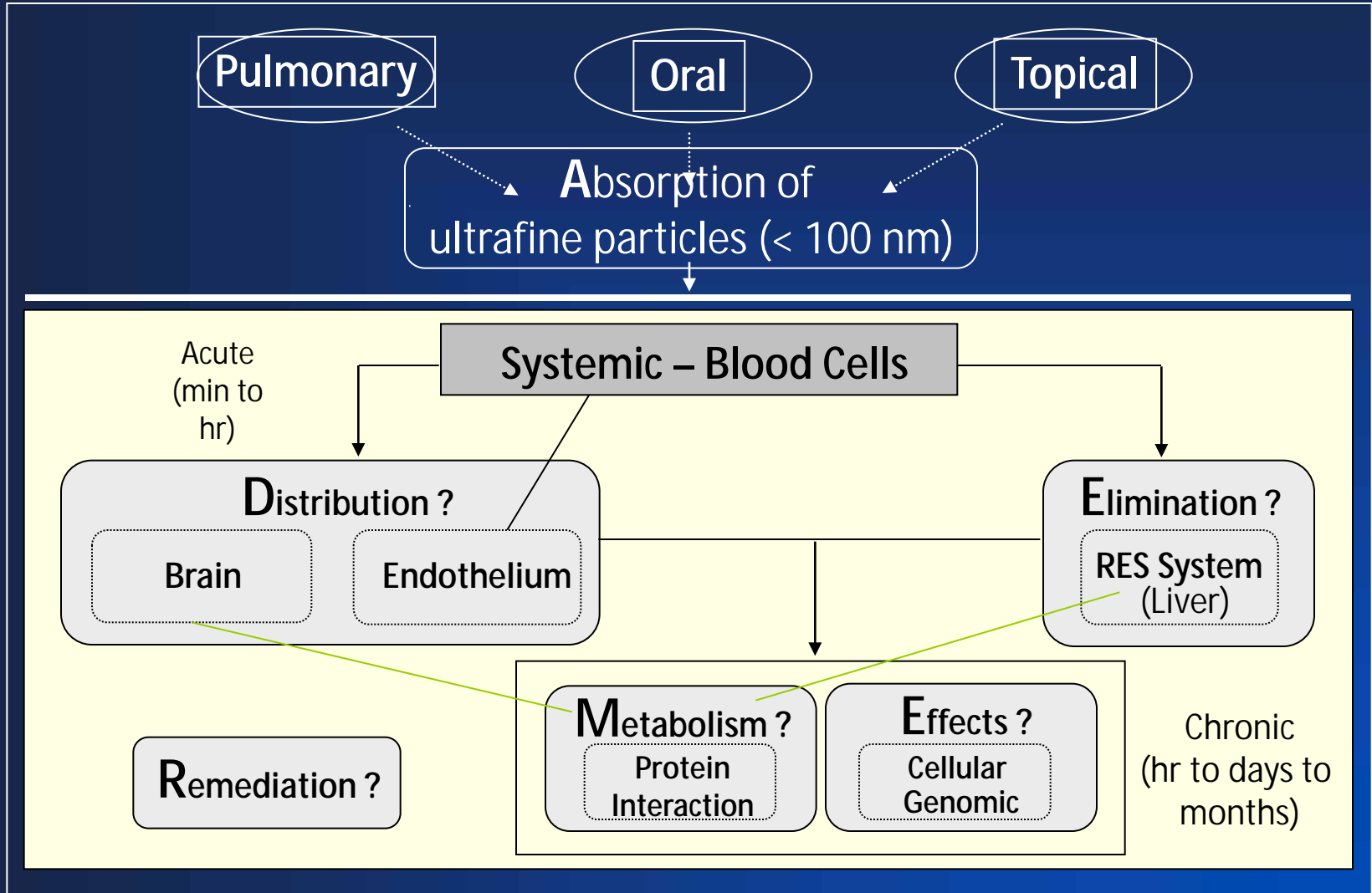
Potential Opportunities for Nano-Particle Exposure and Transport

Nano particles:

- CNT
- Nano-wires
- Metal oxides nano-particles



JRC In-Vivo Exposure and Transport Mechanisms





Nanoparticle Dynamics and Transport: The Emergence of Brownian Motion

Courtesy of Chih-Ming Ho, UCLA]

Consider neutrophil phagocytosis, in which a 10-20 μm neutrophil chases a \sim 1 μm *S. aureus* in our blood stream.

This represents an example of a distributed intelligent network of autonomous systems composed at the nano-level with adaptive emergent behaviors



State-of-the Art: Potential for Assembling a Lab-in-a-Particle, with Micro-batteries

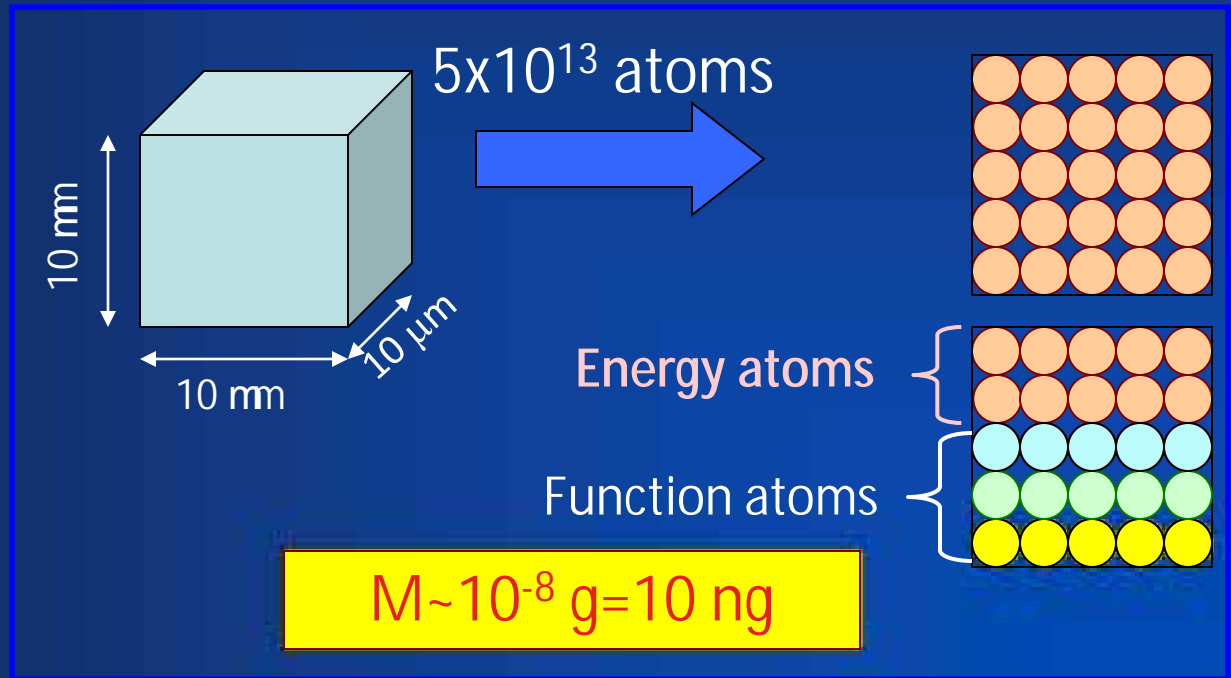
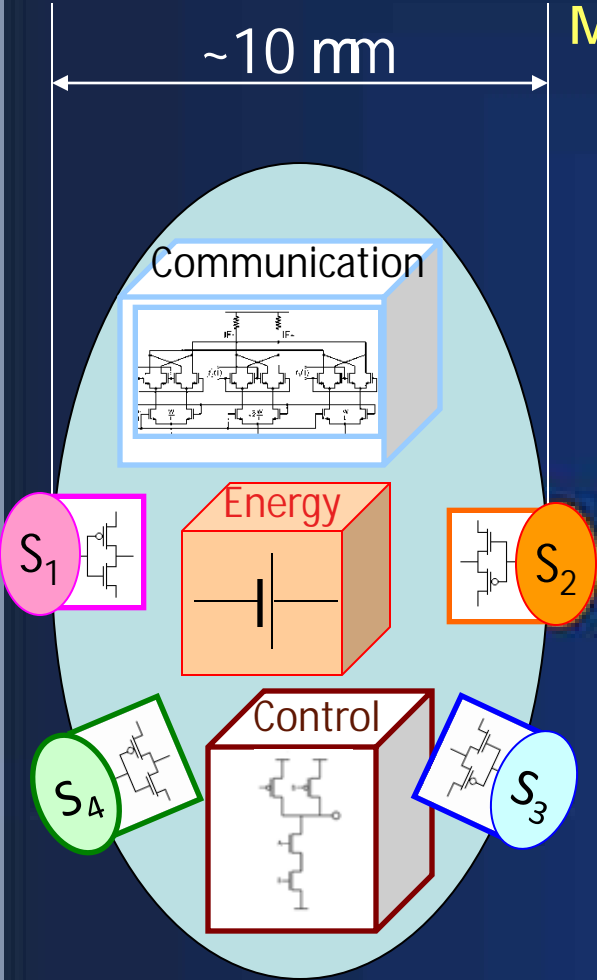
Ex. Early diagnostic and treatment tools for long duration space missions

Major functional blocks:

- Sensing
- Communication
- Control and Motion
- Energy

Constraints and Trade-offs:

Very limited space needs to be divided between sensors, power supply & electronic components



At this scale, we are literally designing with atoms



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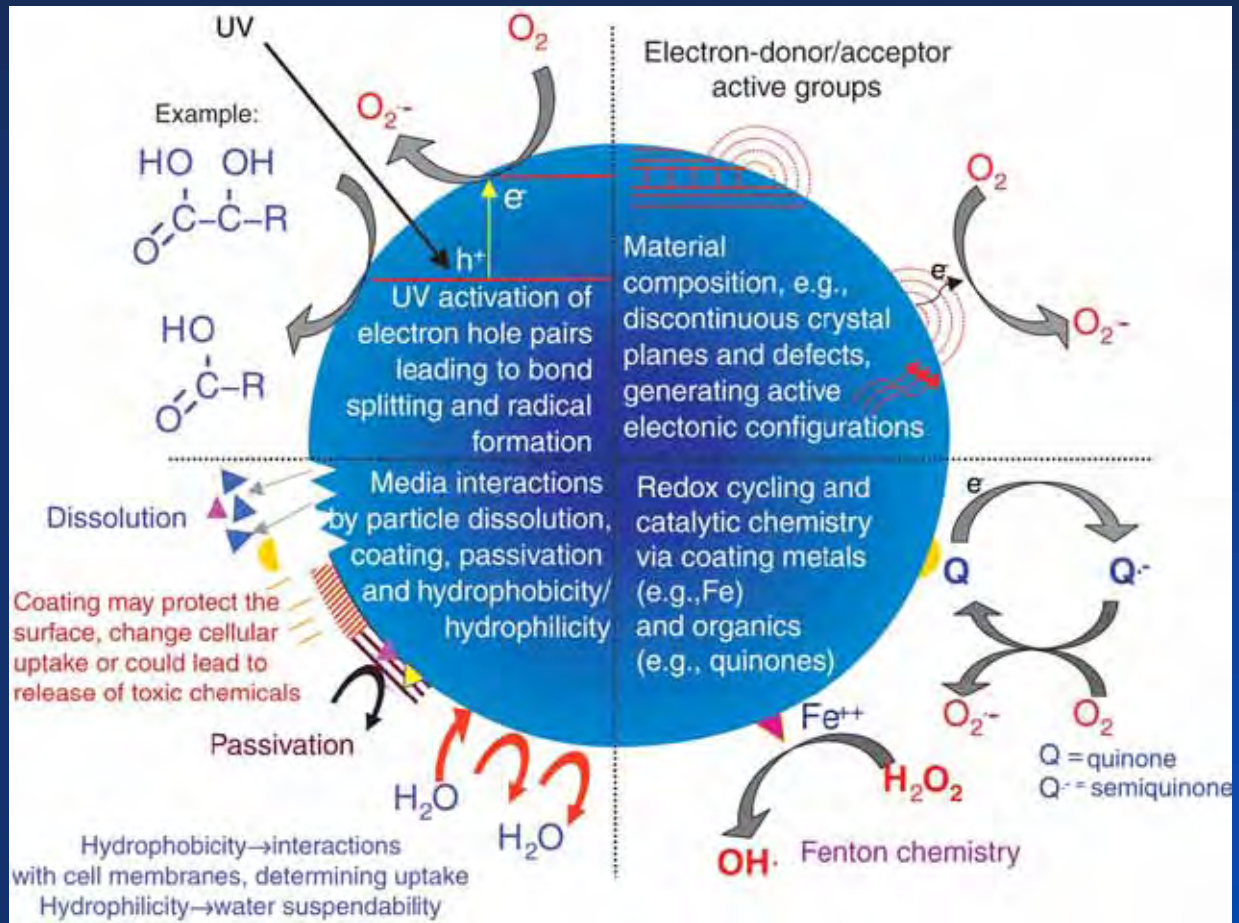
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Attribute Transforming Reactions

Selected Attributes

- q Composition
- q Size
- q Shape
- q Biopersistence
- q Surface chemistry
- q Release of chemicals



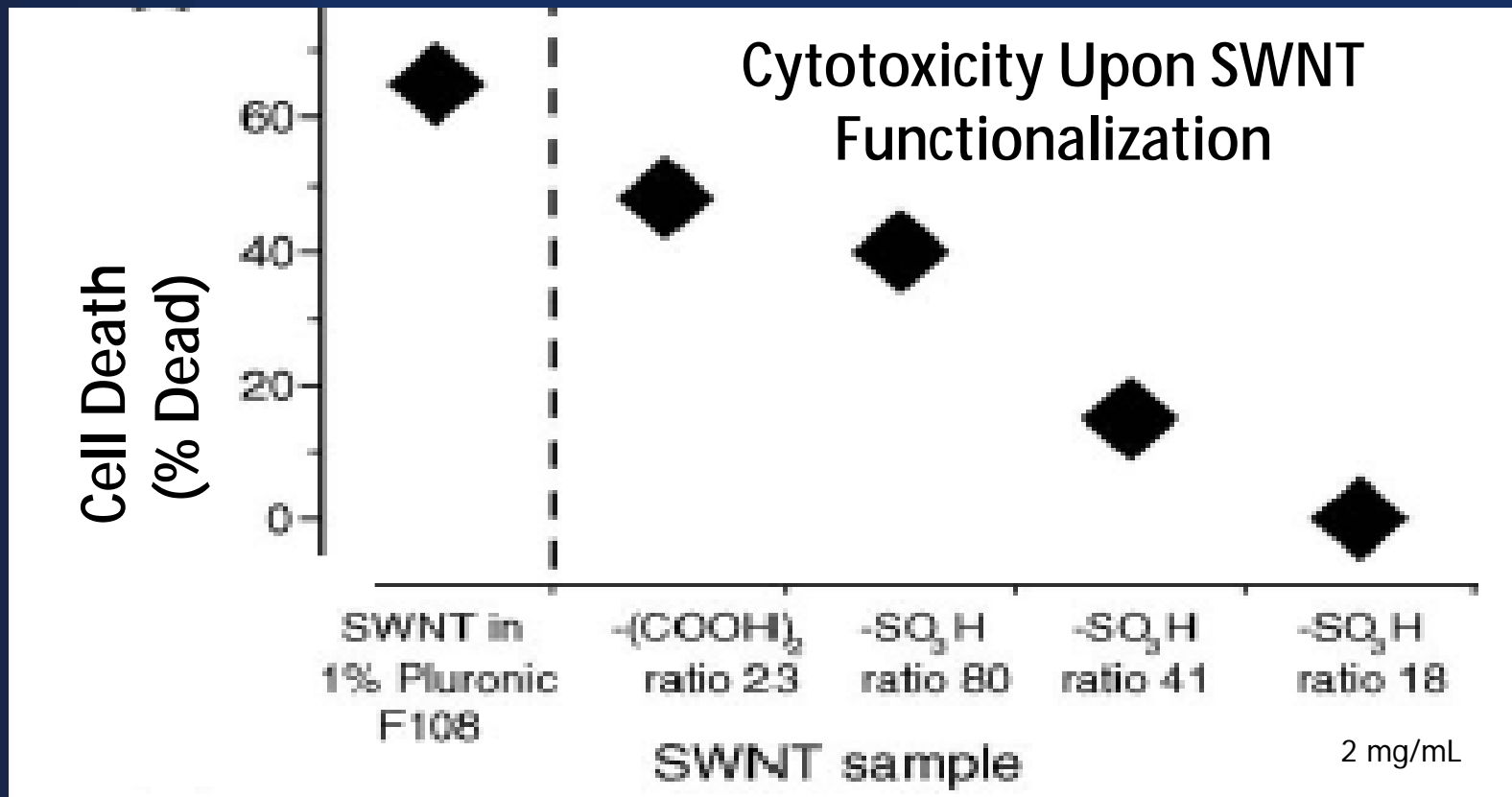


State-of-the-Art:

Nanoparticle Transformations and Toxicity

Covalent functionalization of the nanotube sidewall attenuates cytotoxicity.

Courtesy of the Strano Group/MIT



No cytotoxicity found 24 hours after introducing DNA-wrapped SWNT (HeLa Cells)



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 - q **Toxicity**

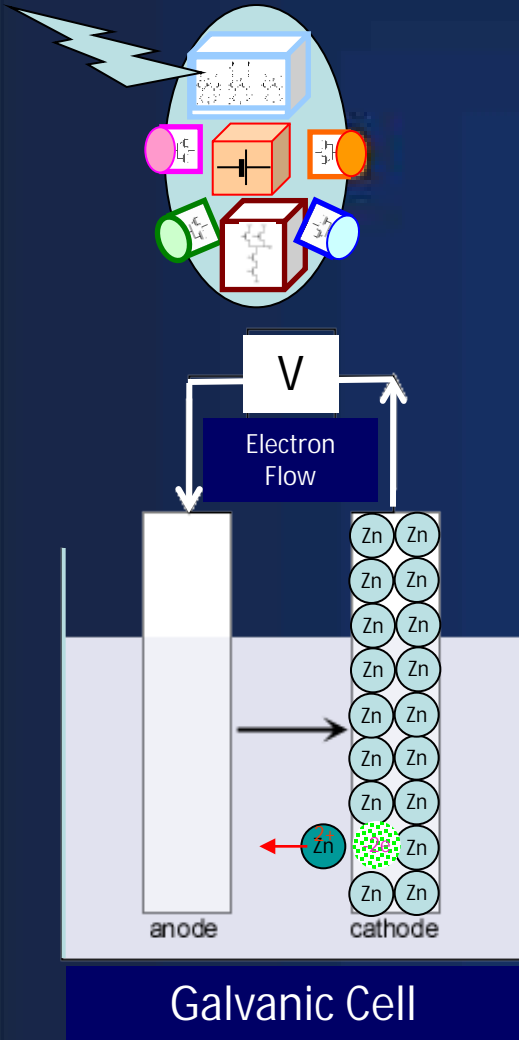
 - q **Metabolic**

- q Tools

- q Research Challenges and Discussion

SRG Integrated Micro-scale Power Sources

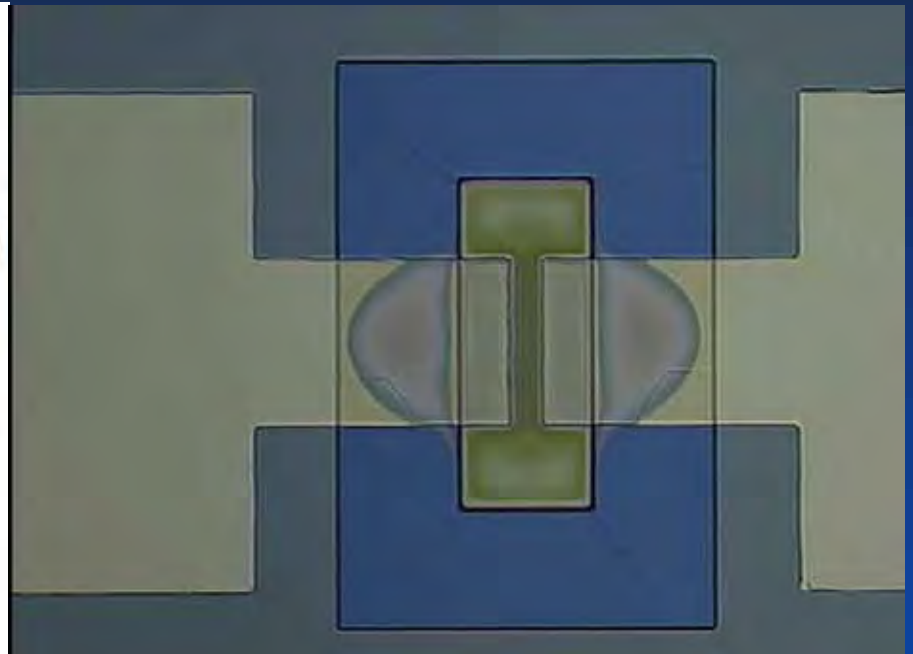
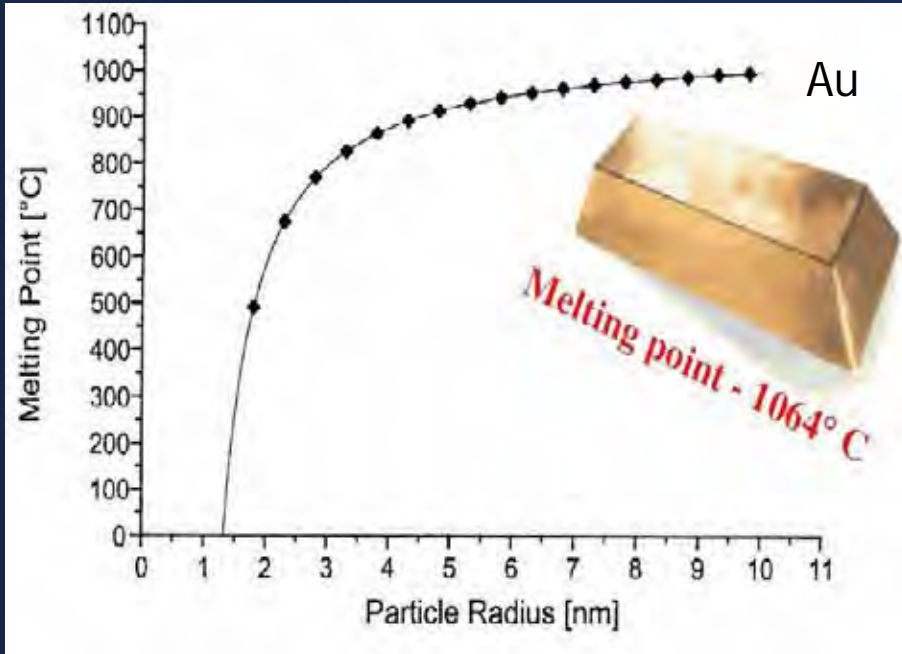
Choice and scaling limits of micro-batteries



Negative electrode Material	E^0 (V)	Max Energy J/cm ³	Max total mass in 10 mm cube	Recommended (typical) Dietary Intakes	U.S. EPA Drinking Water Regulations
Al ³⁺ / Al	1.7	4.9E+04	3x10 ⁻⁹ g	2x10 ⁴ n/a	5x10 ⁻⁵ g/L
Mg ²⁺ / Mg	2.4	3.3E+04	2x10 ⁻⁹ g	6x10 ⁶ 0.3 g/day	~10 ⁻² mg/l
Mn ²⁺ /Mn	1.2	3.1E+04	7x10 ⁻⁹ g	7x10 ³ 2x10 ⁻³ g/day	5x10 ⁻⁵ g/L
Zn ²⁺ /Zn	0.8	1.6E+04	7x10 ⁻⁹ g	7x10 ⁵ 10 ⁻³ g/day	5x10 ⁻³ g/L
Fe ²⁺ /Fe	0.4	1.2E+04	8x10 ⁻⁹ g	4x10 ⁴ 10 ⁻³ g/day	3x10 ⁻⁴ g/L
Cd ²⁺ /Cd	0.4	6E+03	9x10 ⁻⁹ g	6x10 ² 17x10 ⁻⁶ g/day	5x10 ⁻⁶ g/L



State-of-the-Art: Metal Nano-particles as Potential Pb Bump Replacements



K. J. Klabunde, "Nanoscale Materials in Chemistry", Wiley/Interscience publishers, New York (2001).

D. Huang, F. Liao, S. Molesa, D. Redinger, and V. Subramanian, *J. Electrochemical Soc.*, 150, G412-G417 (2003).

Ex. Droplet on Demand patterning of organically coated **Cu** nanoparticles enables low temperature **[130 C]** sintering, enhanced conductivity, i.e. better than lead.

What is the ESH impact of organically coated 3 nm Cu particles?



Selected Attributes of Copper

q **As a nutrient:**

- q **Function:** Enzyme activity, iron absorption, healing process, hair, skin & cells
- q **Deficiency:** Retarded growth, skin and respiratory problems, anemia
- q **Sources:** Organ meat, seafood, nuts, seeds, wheat bran, cereals, whole grain products, cocoa products
- q **RDU [Adults]:** 900 mg/day [9E-4 g/day]

q **As a toxin:**

- q **Adverse effects of excessive consumption include:** Gastrointestinal distress and liver damage
- q **UL [Adults]:** 10,000 mg/day [1E-2 g/day]



Exposure Potential of an Ink-jet Printed Copper Bump Process

RDU [Adults]: 900 m³/day [9E-4 g/day]

UL [Adults]: 10,000 m³/day [1E-2 g/day]

Copper/Entity	Cu (g)
Cu particle [coated; 3 nm diameter; ~89 atoms; ~1.5E-22 Moles]	9.3E-21
Cu/Ink-jet drop [~1E6 particles/drop]	9.3E-15
Cu/Chip [~1E3 pad/chip]	9.3E-12
Cu/Wafer [~100 chips/wafer]	9.3E-10
Cu/Day [@5000 wafers/week]	6.7E-07
Cu/Year	2.4E-04

But, mass may not be a sufficient dose metric.



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State-of-the-Art: Selected Tools

Secondary Ion Mass Spectrometry (SIMS)

Time-of-flight (ToF) SIMS; Static SIMS

Helium ion microscope

Virtues of the Helium ion microscope include:

High resolution (measured here to be about 1nm)

Excellent definition of different materials

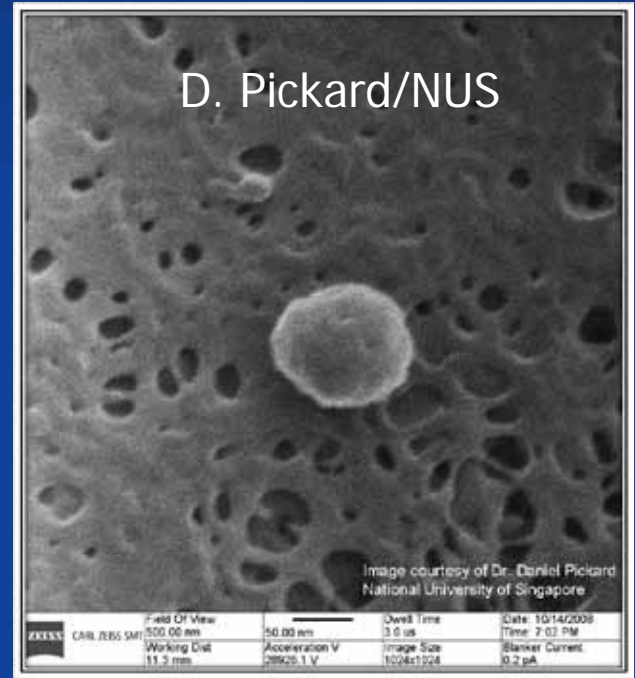
Images hard and soft materials

e.g. Cryptic epitopes

Macro- and nanoscale topography, with amazing surface detail and an astonishing depth of field



D. Joy/ U Tenn.

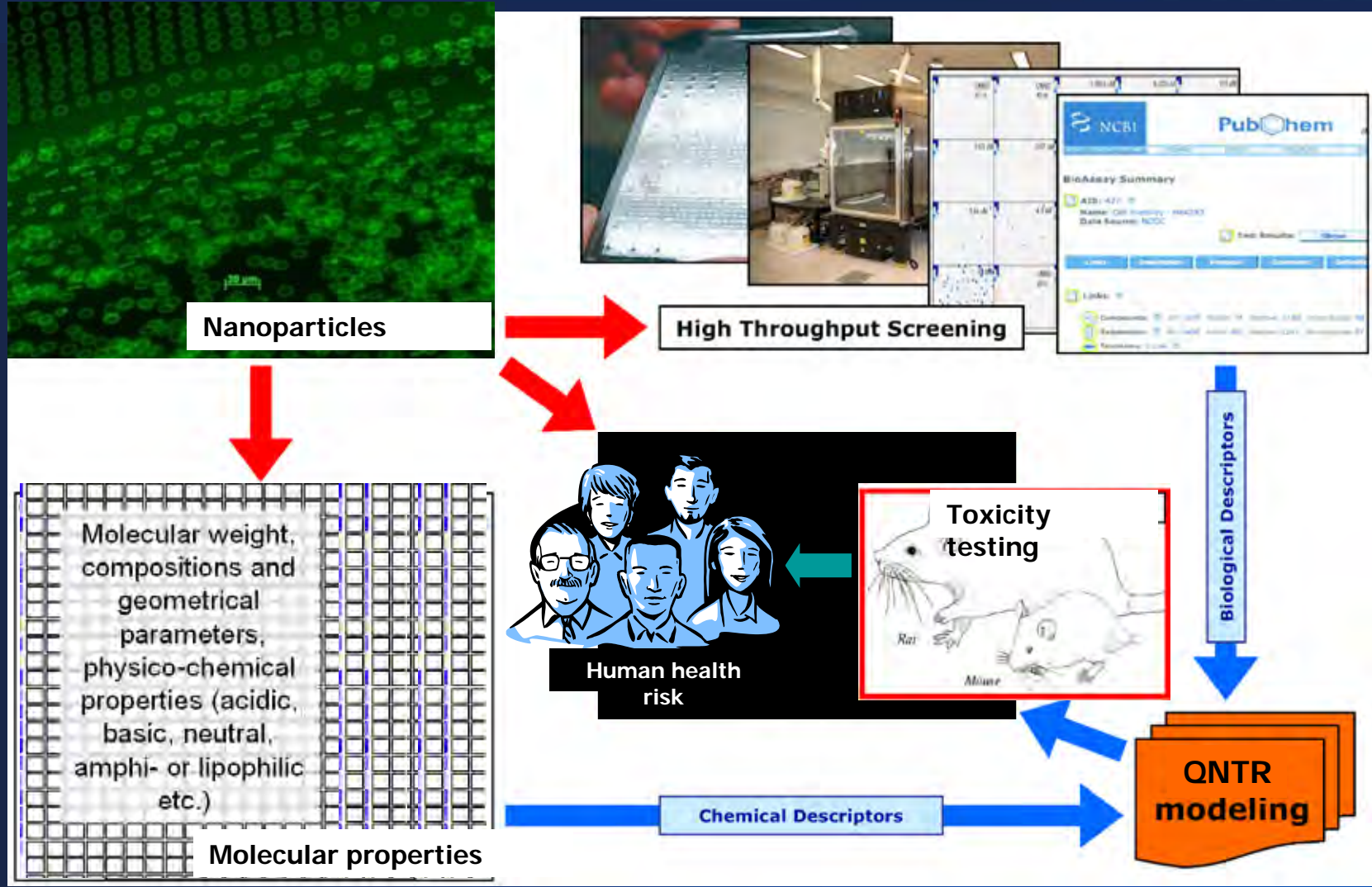


D. Pickard/NUS

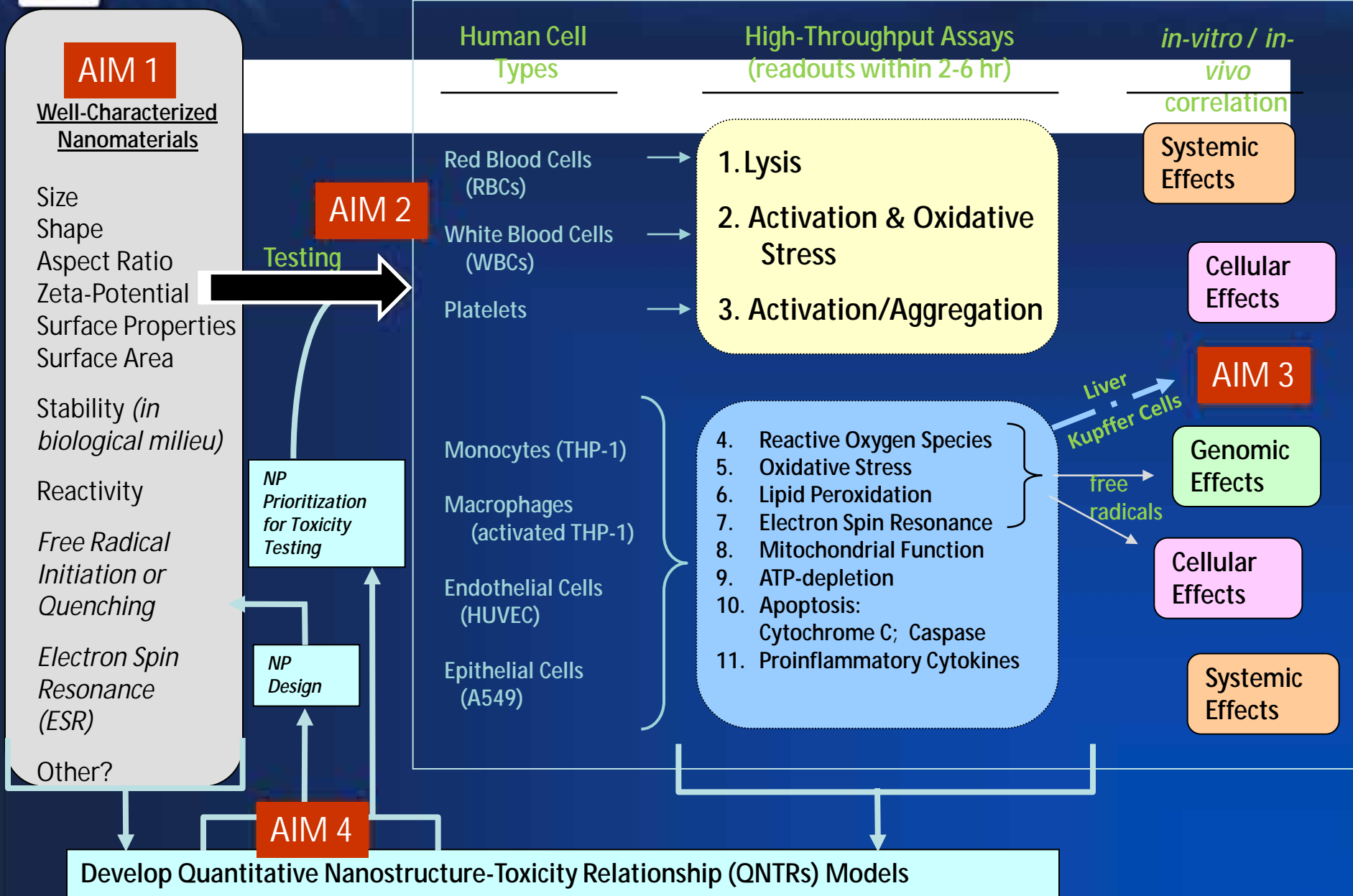
Image courtesy of Dr. Daniel Pickard
National University of Singapore

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SRC Predictive (Computer-Aided) Nanotoxicology



JRC Predictive (Computer Aided) Nanotoxicology





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- q **Research Challenges and Discussion**



Some Guiding Comments

- q Phil Sayre: "Support responsible innovation and regulatory decision making."
- q Leonard Robinson: "Reduced uncertainty will free markets."
- q Paul Westerhoff: We need predictive tools.
- q Hendrik Emons: "Make decisions based on sound knowledge."



q When are nanoscale material systems hazardous or helpful?

q Consider options with net ESH and societal performance benefits.

q The research and development communities need:

q Non-destructive sub-nm imaging/characterization tools;

q Foundational and appropriate mechanistic information in-situ;

q Screening protocol options that enable detection, synergistic effects, and hierarchical hazard assessment;

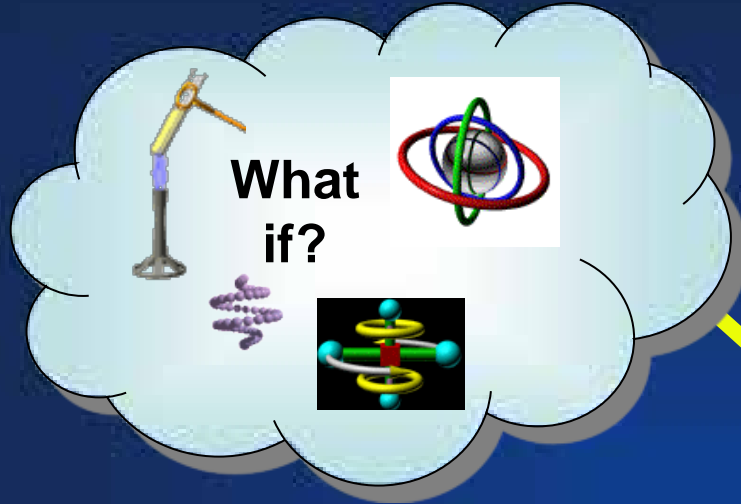
q Tools that enable efficient data mining of sparse knowledgebases;

q A predictive material by design capability.

q Consider concurrent optimization of ESH and performance factors.



Discussion



Thank You





Additional Challenges

- q What Materials should be studied? *the field is advancing so quickly...*
- q Material Quality and Consistency? *manufacturing processes are still emerging...*
- q Time to Complete the Studies? *toxicological testing takes years...*
- q Relevant Exposures? *duration of exposure, route, kinetics, ...*
- q Amount of Material Available for Testing? *often small quantities, very expensive...*
- q Are these 'Well-Characterized' materials? *the FDA requires this for human use...*
- q Are the nanoparticles stable under testing conditions? *what are we studying...*
- q How to measure nanoparticles in the body? *whole NPs, ingredients, etc.*
- q How is the Dose expressed? *as mass, surface area, particle concentration...*