Nanomaterials in industrial and international context

Mark Bünger, Research Director

Lux Research, Inc.

Lux Research profile

- Primary research methodology: Focus on proprietary interviews and site visits
  - > 1,400 interviews last year
  - Site visits in 18 countries, China to Dubai
- Clients on five continents
- Delivers value via analyst inquiry, weekly intelligence reports, and semi-annual State of the Market reports
- Retainer-based services in solar, energy storage, nanomaterials, water and life sciences
- Source proprietary ideas from Lux Research Network of execs + scientists
- Diverse, 40-person team; Ph.D scientists to market researchers

Josh Wolfe,
Director, Lux Research

21st Century R&D Act signing in Oval Office

LR Chairman Peter Hebert on CNBC

LR President Matthew Nordan testifying before U.S. Congress

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Our journals and reports provide information and insight for corporations, governments, and universities

Alliances Director: Acquisitions, funding history, key investors, phase in development

Business Development Manager: Potential and current partnerships, new opportunities, competitors' interests and deals, licensing data, adjacent technologies, upfront and milestone payments

Legal/in-house counsel: IP position, past or current litigation

Research and Development: scientific references, new instruments and approaches

...plus market sizes, competitor comparisons, historical data, and more

Outline

- Nanotechnology in industry and commerce
- Nanotechnology investment and revenue internationally
- Nano EHS trends in science, perception, and regulation
- Recommendations for a way forward

"California can become 'the place to do nanotech' if we regulate it well. In China everything is nano, for better and for worse. We don't want nano to become the next "GMO" -- nano should keep its head held high."

Outline

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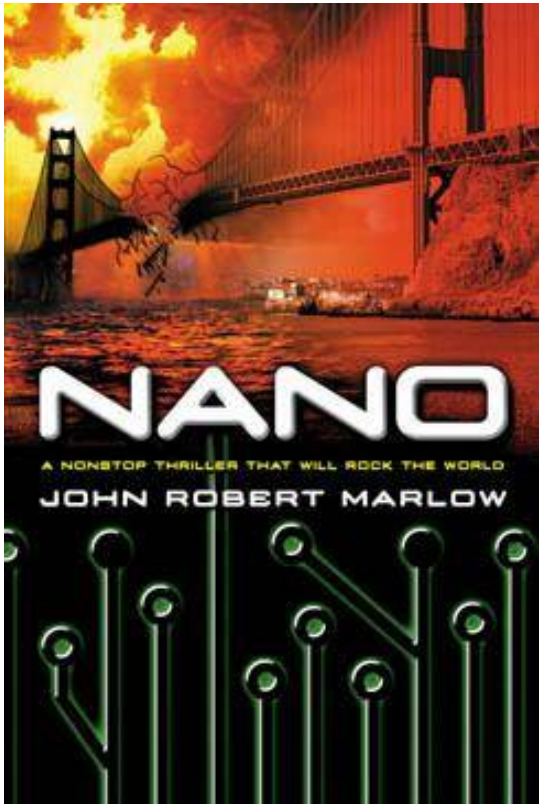
How most people see nanotech products today



Visionary but Scary

Imaginary

magic NANO

Mundane and Scary

Not nano

?

Visionary and Useful

Real

Mundane but Useful

Real

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Nanotech energy creation will emerge in niches

- Today: Flexible, inexpensive, powerful solar cells could make rooftops into generators -- and better align supply and demand
  - Konarka, Nanosys, Nanosolar
- Tomorrow: Nanoporous filters could reform natural gas onboard vehicles for fuel cell applications
- In years: White/industrial nanobiotech might create organisms or organic materials that produce H2 or EtOH in commercially meaningful quantities
  - Synthetic Genomics, Hydrogen Solar

nanosolar

Konarka

synthetic genomics

Hydrogen Solar

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Nanotech provides unparalleled improvement to energy distribution

- Today: Aerogel insulators reduce oil pipeline energy costs and logistics/installation costs
  - Aspen Aerogels
- Tomorrow: Batteries with nanostructured electrodes extend hybrid vehicle range 5x, achieving 180MPG and plugin recharging practical
  - Altair, A123
- In years: Carbon nanotube power cables would transmit energy hyperefficiently (10x Cu at 15% of weight)

ASPEN

A123 SYSTEMS

Altairnano

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State of the art and key developers in electronics nanotechnology

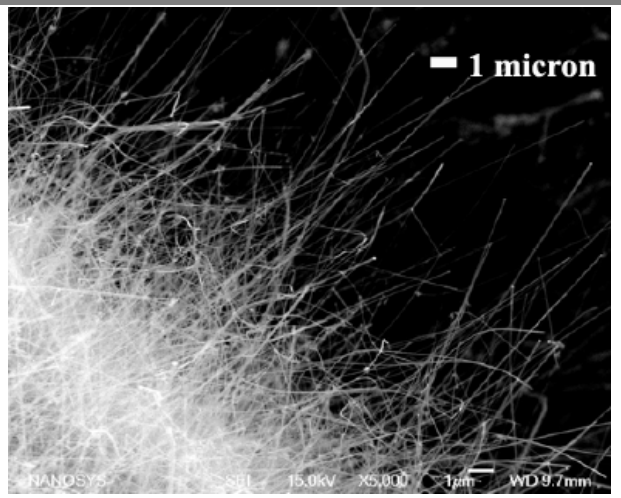
Application	Description	Readiness	Key companies
Transparent conductors	CNTs and metal NPs in a polymer matrix can replace costly indium tin oxide (ITO) in displays and solar PV panels	Development	Eikos, Unidym, Cambrios, Cima Nanotech, Nanofilm, Canatu,
Thermal management	Nanostructured devices can provide active cooling, while highly conductive features can provide thermal contact	Introduction	Nextreme, Applied Sciences, Nanolab, NovaCentrix, IMEC, NanoComp
Displays	CNTs, quantum dots, and nanoscale layers of polymers can improve the properties of displays, including flexibility	Development	Motorola, Samsung, Cambridge Display, QD Vision, Evident, Ntera
Memory technologies	As optical lithography hits its limits of resolution, emerging technologies offer the promise of extending Moore's law	Development	Nantero, EverSpin, NVE Corp., Samsung, Molecular Imprints, IMEC, HP
Printed electronics	RFID and flexible displays will drive the growth in electronics made by printing processes rather than lithography	Development	Kovio, NanoMas, Nano-C, Polyera, Nanoident, Five Star, Bayer, Cima
LEDs and optical components	Nanoscale engineering and NPs like QDs and dendrimers boost LED output and enable precision optical elements	Introduction	API Nanotronics, Nanocs, NanoGram, PPG, Lightwave Logic, NeoPhotonics
Energy storage	Nanostructured electrodes and NP electrode coatings can greatly improve performance for consumer devices	Introduction	Enable IPC, Cap-XX, Primet, Ionova, APowerCap Technologies, ZPower
Barrier coatings	Several efforts use NPs in attempts to create gas barrier coatings impermeable enough for OLED applications	Development	Nova-Plasma, Hybrid Plastics, IMRE (Singapore)
Packaging	Soldering and bonding at lower temperatures protects nearby components, plus other packaging improvements	Introduction	NovaCentrix, Ormecon, Nanodynamics, Reactive Nanotechnologies, Mayaterials
Lithography and process tools	Fullerenes target improved resists, anti-static packaging for semiconductor wafers, and nanoimprint lithography	Scale	Hybrid Plastics, Frontier Carbon, IMEC, Hyperion Catalysis, Nanocyl, Obducat

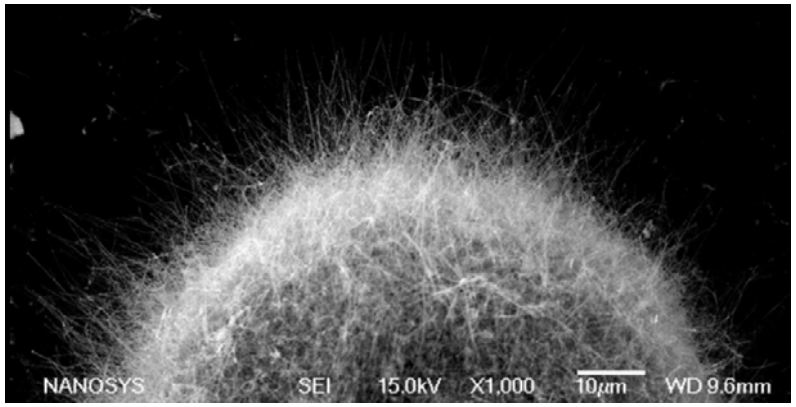
Nanotech in Electronics: Key companies

Name	Type	Country	Comments
Reactive Nanotechnologies	Private start-up	U.S.	Its NanoFoil technology is a thin film made of alternating nanoscale layers of aluminum and nickel for bonding various materials together in electronics **packaging**
Cambrios	Private start-up	U.S.	Silver nanowire dispersions provide a less costly **transparent conductor** alternative to the indium tin oxide (ITO) currently used in displays
Cambridge Display Technology (CDT)	Public (NASDAQ:OLED)	U.K.	Makes **displays** from thin films of engineered polymers, such as polyphenylene vinylene (PPV), between electrodes to emit visible light
Nantero	Private start-up	U.S.	Develops CMOS-compatible methods for producing carbon nanotube (CNT)-based semiconductor **memory** and logic devices
Lightwave Logic	Public (OTC:LWLG)	U.S.	**Optical components** based on the chromophore perkinamine which is embedded in a polymer, then aligned and spaced out using dendrimers
NanoMas Technologies	Private start-up	U.S.	Conductive metal nanoparticle inks that sinter into solid traces quickly at lower temperatures for **printed electronics**
Nextreme Thermal Solutions	Private start-up	U.S.	Thermoelectric cooling structures for **thermal management** made by stacking thousands of interleaved nanoscale layers within a thin-film single crystal
Ionova Technologies	Private start-up	U.S.	Cathode system for supercapacitors and lithium ion (Li-ion) **batteries** made of a nanostructured conductive material coated with a cobalt-free metal oxide layer
Nova-Plasma	Private start-up	Canada	Developing a flexible and transparent **high-barrier coating** with glass-like levels of gas permeation
Obducat	Public (Frankfurt:OBD)	Sweden	Nanoimprint lithography **processing tool** for manufacturing double-sided hard disk drive (HDD) patterned media and high-brightness LEDs

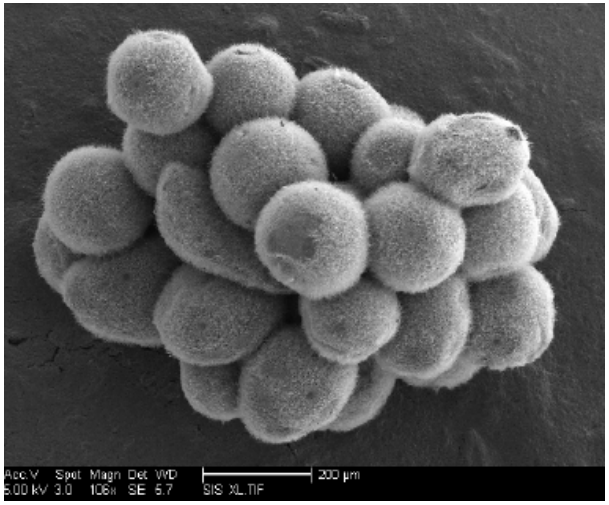
Nanowire Device Fabrication (with Kayte Fischer, Desai Lab, UCSF)

Nanowire Dimensions:
- 40-90 nm diameter
- 5-40 μm length





Novel 3D nanowire coating technique applied to silica beads



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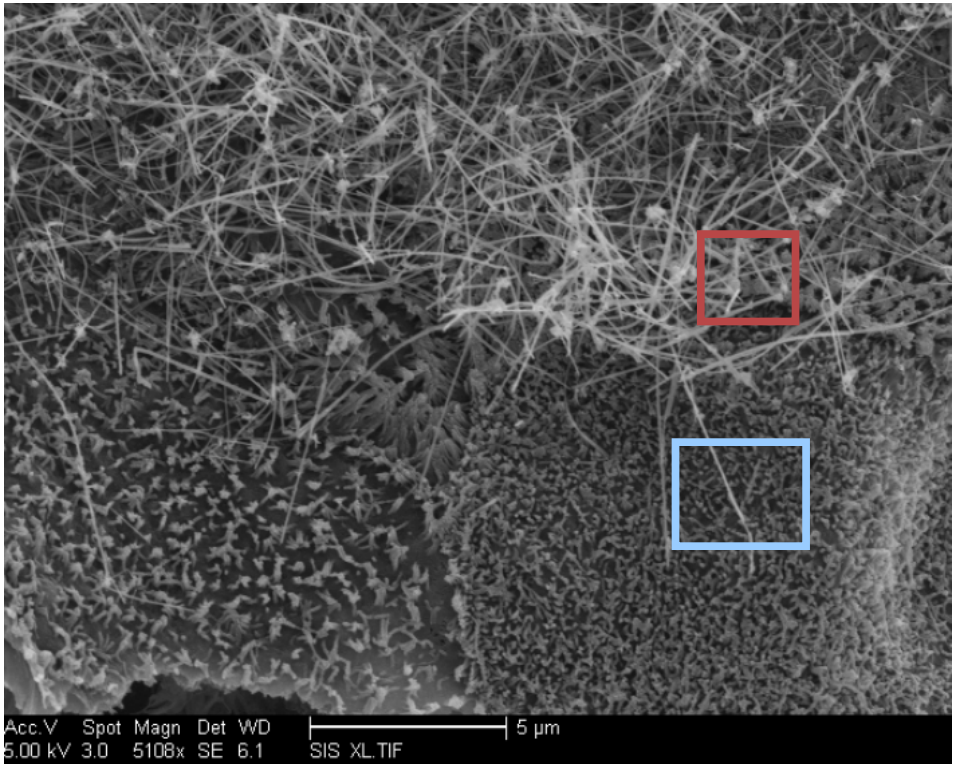
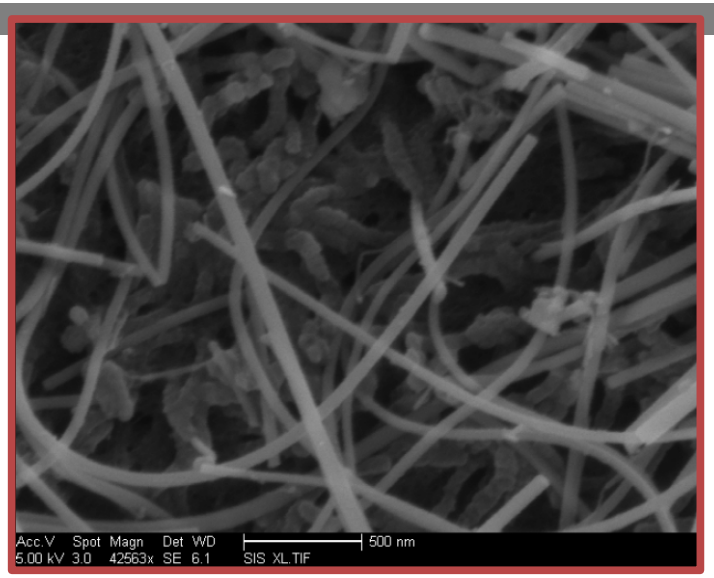
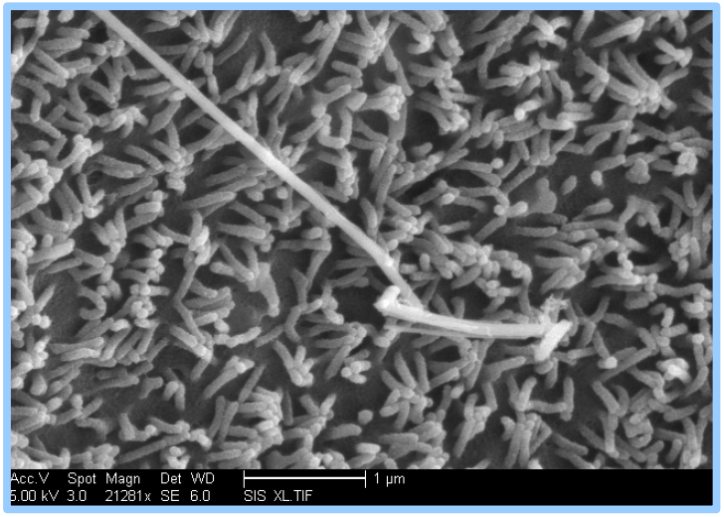
Cell-Nanowire Interface







Nanoscale features allow interdigitation with microvilli, leading to increased van der Waals force

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Adhesion Under Shear Flow

Nanowires continue to adhere under high shear flow

NANO LETTERS

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Biomimetic Nanowire Coatings for Next Generation Adhesive Drug Delivery Systems

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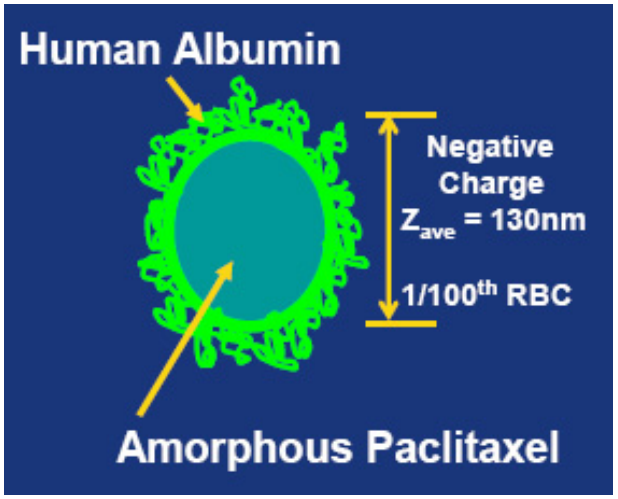
ABSTRACT

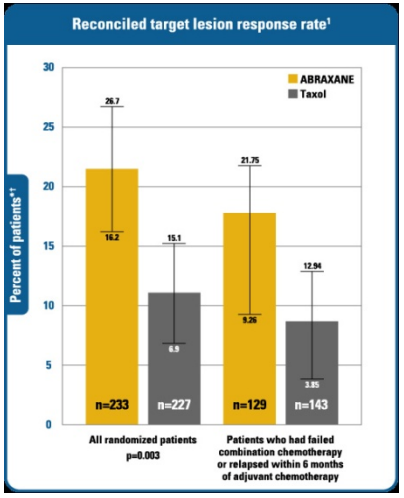
Without bioadhesive delivery devices, complex compounds are typically degraded or cleared from mucosal tissues by the mucous layer.[1−3] While some chemically modified, microstructured surfaces have been studied in aqueous environments,[4,5] adhesion due to geometry alone has not been investigated. Silicon nanowire-coated beads show significantly better adhesion than those with targeting agents under shear, and can increase the lift-off force 100-fold. We have shown that nanowire coatings, paired with epithelial physiology, significantly increase adhesion in mucosal conditions.

Because of their easy accessibility, large surface area, and rich blood supply, mucous membranes (mucosae), such as intestinal, nasal, ocular, vaginal, and buccal tissues, are frequently targeted for therapeutic drug delivery.[1,6] However, the mucosae present significant barriers to permeation, including a 1−450 μm motile mucous gel layer, tight

transit time in conjunction with chemical degradation produce a relatively low concentration gradient at the cellular surface and thus reduced compound absorption. Specific epithelial targeting agents, such as lectins, adhere to glycosaminoglycans on the cell surface; because these sugars are found in the mucous layer as well, competition between the mucous

Nanoparticulate reformulations are battling cancer





APP AMERICAN PHARMACEUTICAL PARTNERS, INC.™

ABRAXIS ONCOLOGY

- **What it does:** Formulates drugs into nanoparticles with improved solubility and bioavailability
- **How it works:** Mechanical milling or chemical processes yield nanoparticles; polymers/stabilizers/surfactants keep them dispersed
- **Stage of development:** Four drugs on market now; many more in pipeline
- **Who's developing it**: APP, Baxter (U.S.), Elan (Ireland), Solubest (Israel), Eurand (Italy)

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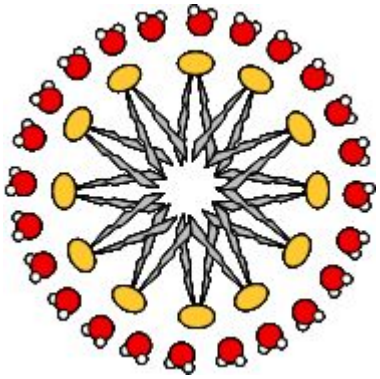
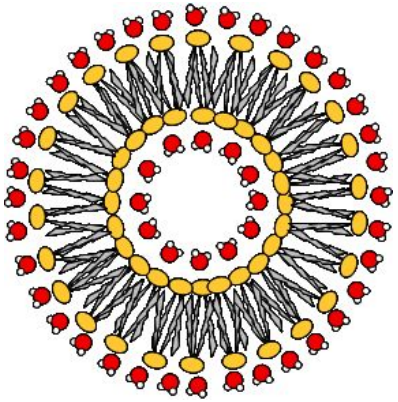
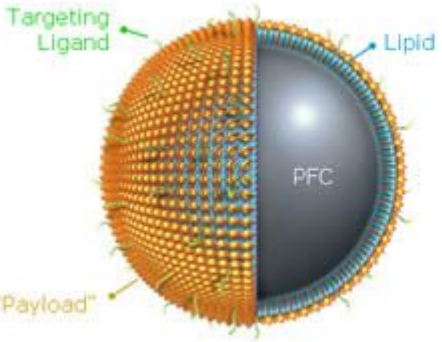
Polymeric nanoparticles are targeting genetic disease

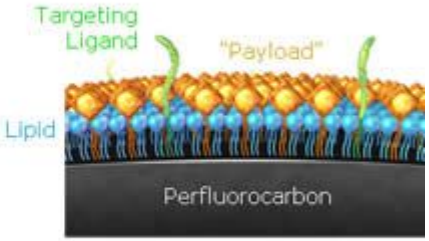


Micelle



Liposome





Nanoemulsion (Kereos example)

- **What it does:** Protects active from being attacked by immune system and/or enables triggered release by emedding drug in void or surface of nanosphere
- **How it works:** Phospholipid or polymer monolayer surrounds spherical core; active may be enclosed within core or "dissolved" into GRAS/DMF monolayer
- **Stage of development:** $100m+ drugs on market (J&J Doxil liposomes)
- **Who's developing it**: Wide variety; key ones include J&J, Gilead (liposomes); Nanocarrier, Nutralease, Samyang (micelles); Kereos (nanomeulsions)

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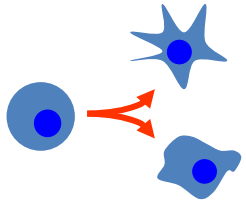
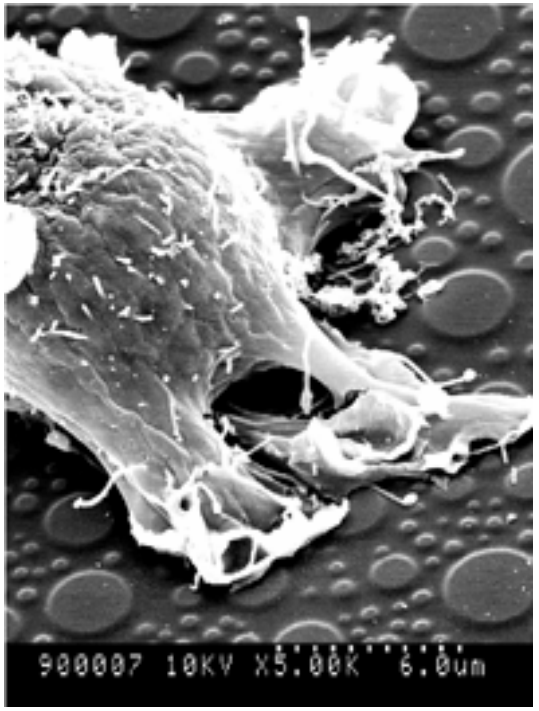
Nanotextured materials offer chemical-free control of stem cells

- Preferential differentiation
  - Stem cells adopt bone, muscle or cartilage based on substrate pattern alone -- no biological or chemical signaling (Dalby, Univ Glasgow)
- Maintenance in pre-differentiated state
  - Difficult to proliferate stem cells without inducing differentiation
    - Mouse feeder cells contaminate hESCs with mouse proteins -- all existing Federally-acceptable stem cell lines are contaminated
  - Nanotextured surfaces can facilitate proliferation without differentiation (see F Besenbacher, Univ Aarhus (DK), others)





SEM image of human fibroblast producing large processes in response to polymer islands 95 nm high (Source: Dalby)

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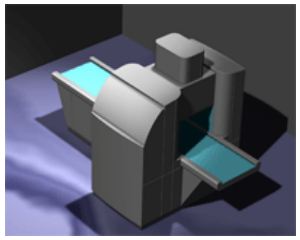
Noninvasive cancer therapy: Magforce

- 15nm dia FeO nanoparticles injected directly into tumor site. Alternating magnetic field (similar to MRI) heats up nanoparticles, destroying tumor from inside with minimal damage to surrounding tissue
- Therapy system and nanoparticles are classified as medical devices, not pharmaceuticals
- Currently in Phase I-III trials versus several types of solid tumors:
  - Glioblastoma multiforme successfully completed with 14 patients (March 2003 - June 2004)
  - Glioblastoma and Astrocytoma, Grade III brain tumor recurrence: 65 patients
  - Prostate carcinoma recurrence after therapy
  - Esophagus carcinoma

magforce® NANOTECHNOLOGIES



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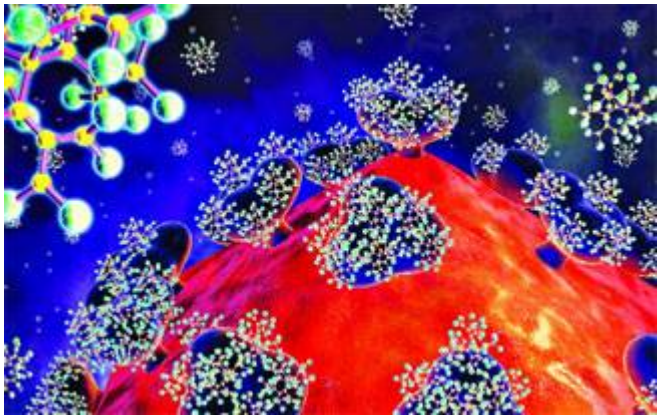
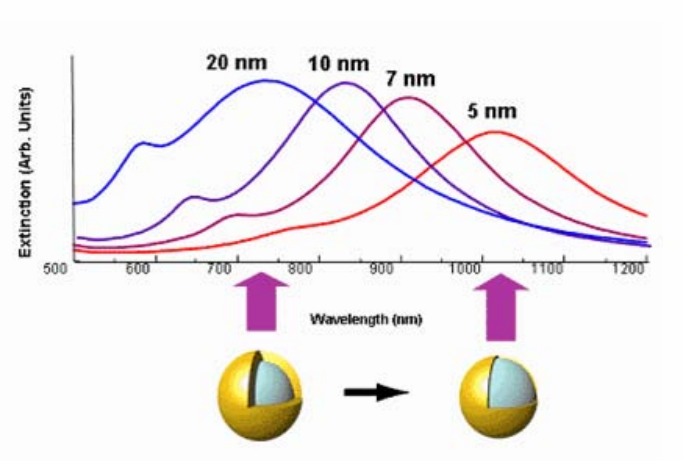
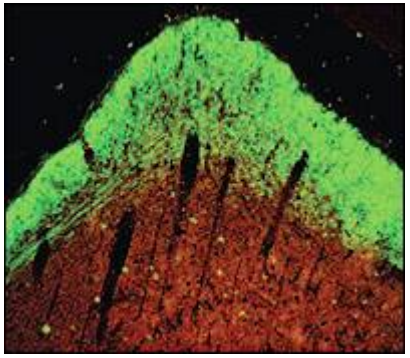
More examples, more conditions



Company: StarPharma
Condition: HIV
Particle: Dendrimer
Mechanism: Receptor blocking
Stage: Clinical Phase II



Company: Nanospectra
Condition: Cancer
Particle: Gold nanoshell
Mechanism: EPR, IR heating
Stage: entering Phase I



Company: 3DM Puramatrix
Condition: Nerve damage (tissue scaffold)
Particle: synthetic peptide
Mechanism: in-vivo self-assembling hydrogel
Stage: small mammal studies

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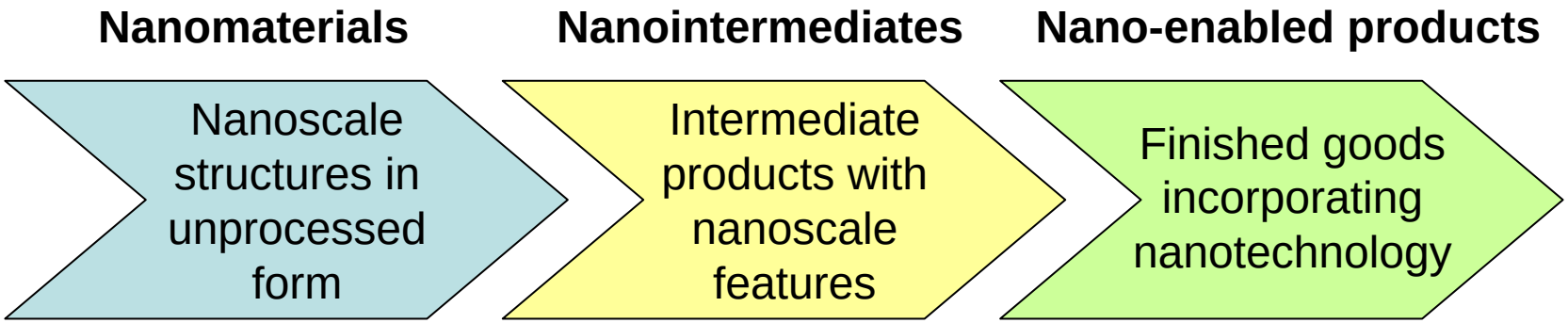
The nanotechnology value chain

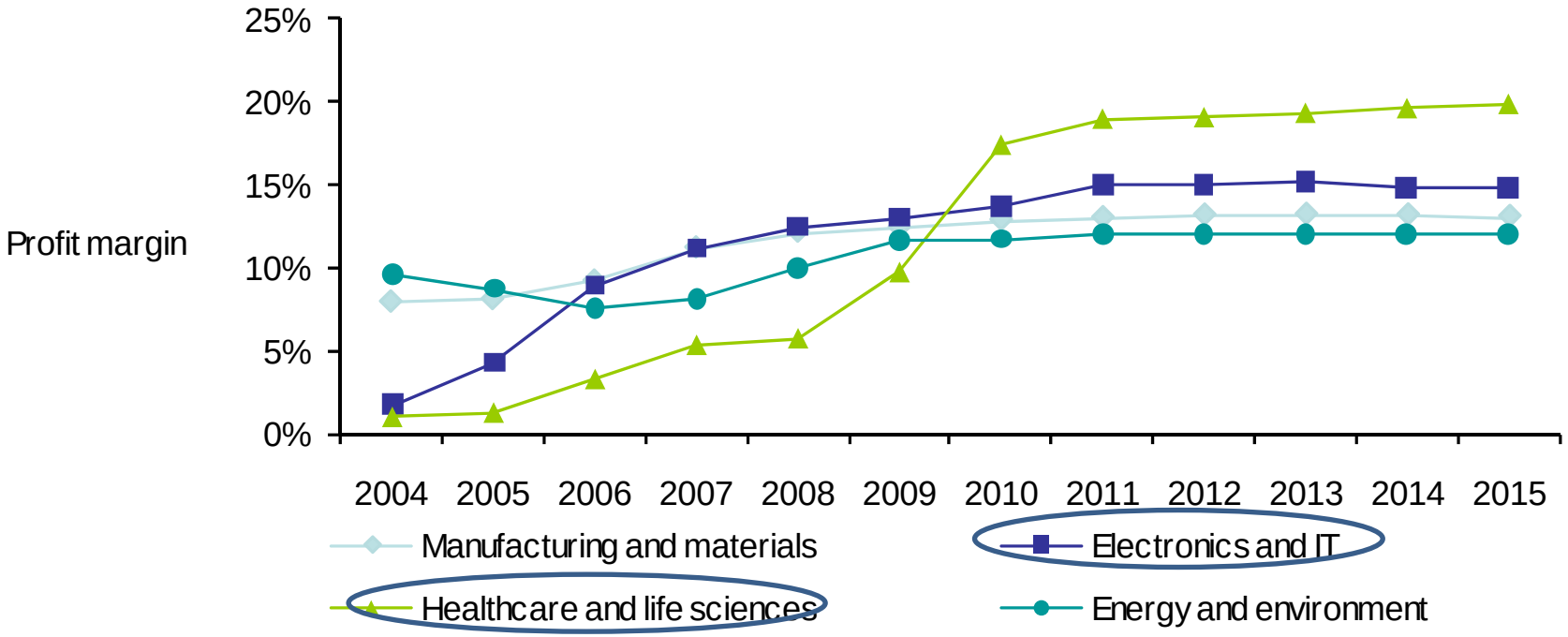


Nanoparticles, nanotubes, quantum dots, fullerenes, dendrimers, nanoporous materials…

Coatings, fabrics, memory and logic chips, contrast media, optical components, orthopedic materials, superconducting wire…

Cars, clothing, airplanes, computers, consumer electronics devices, pharmaceuticals, processed food, plastic containers, appliances…

Electronics- and healthcare-based nanointermediates do especially well



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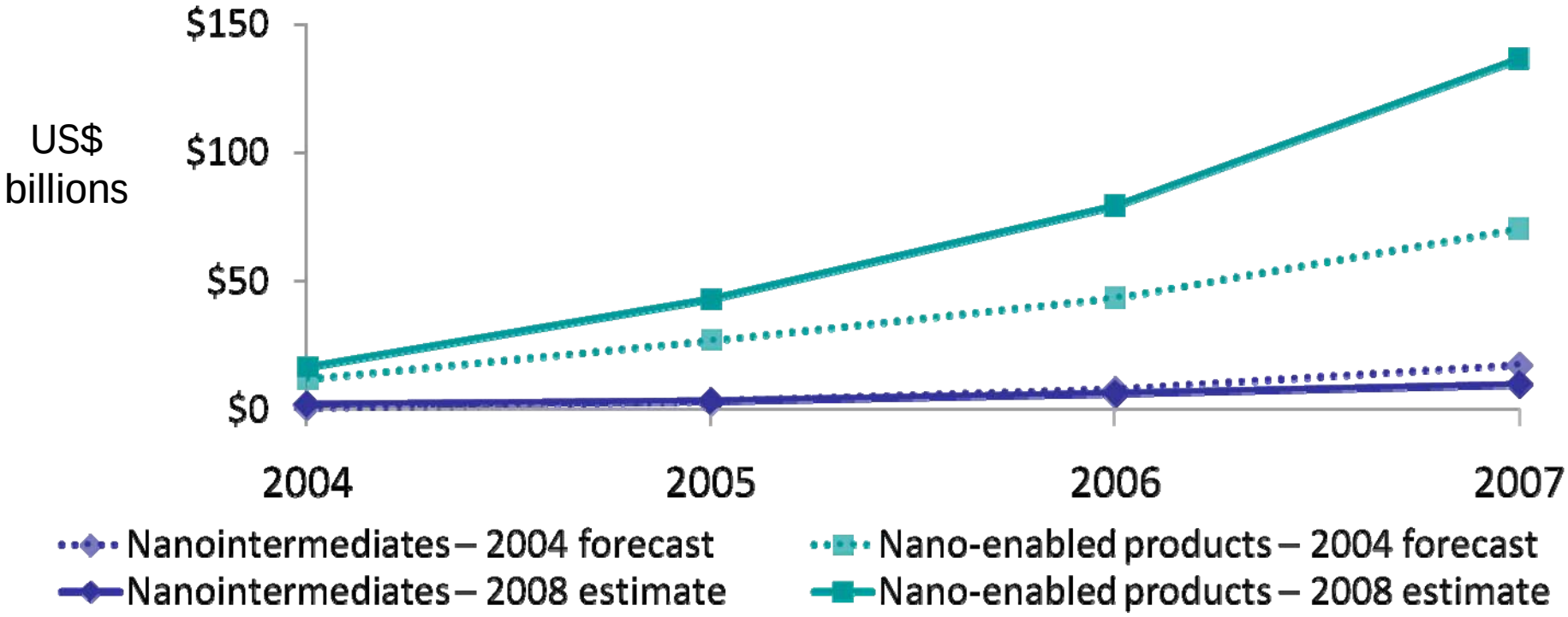
Benchmarking 2004 forecast against current estimates



Compared to projection, nanointermediates are much smaller percentage of nano-enabled products

> More incremental innovations and fewer (high-value) disruptive ones
> Incremental improvements to more different product categories

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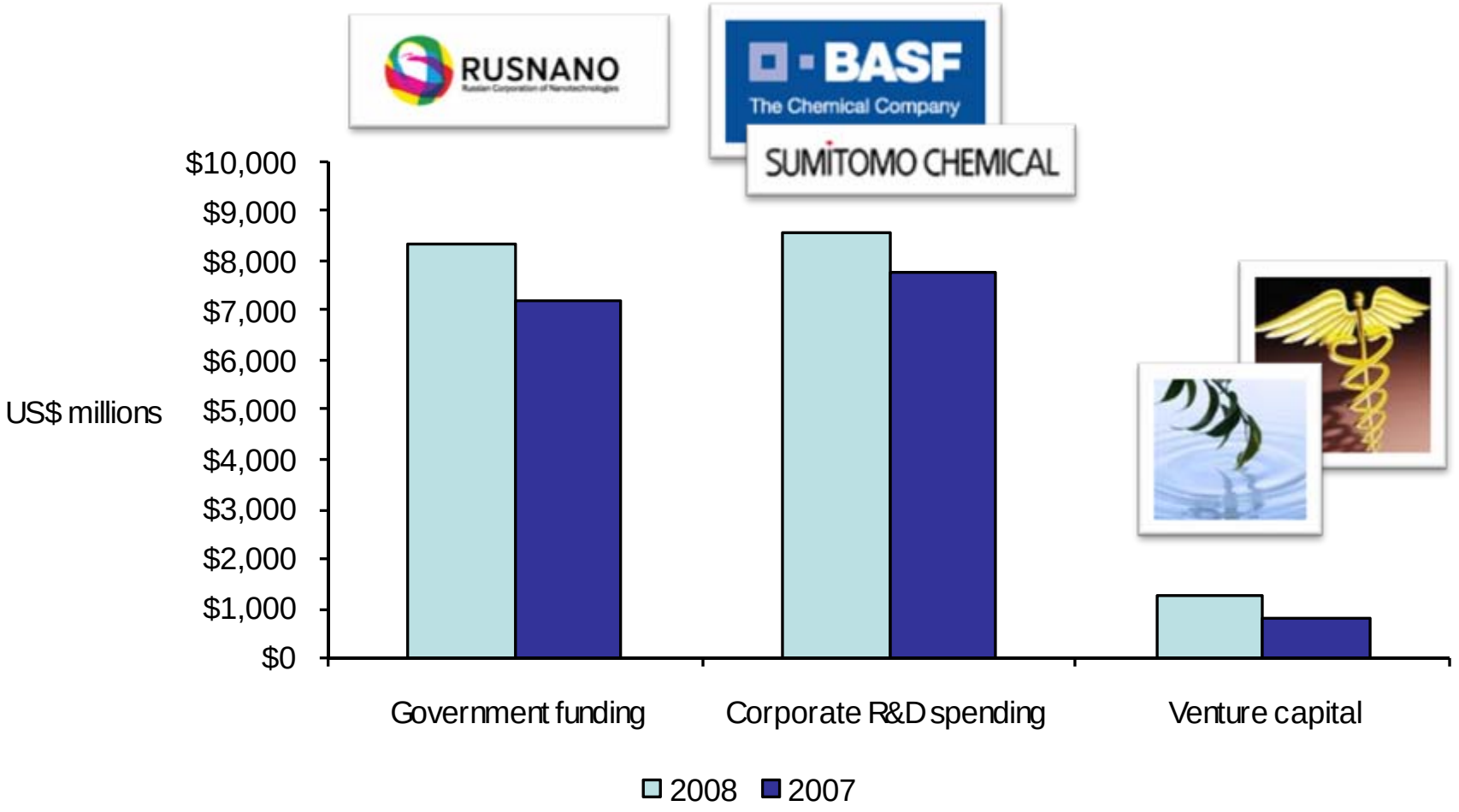
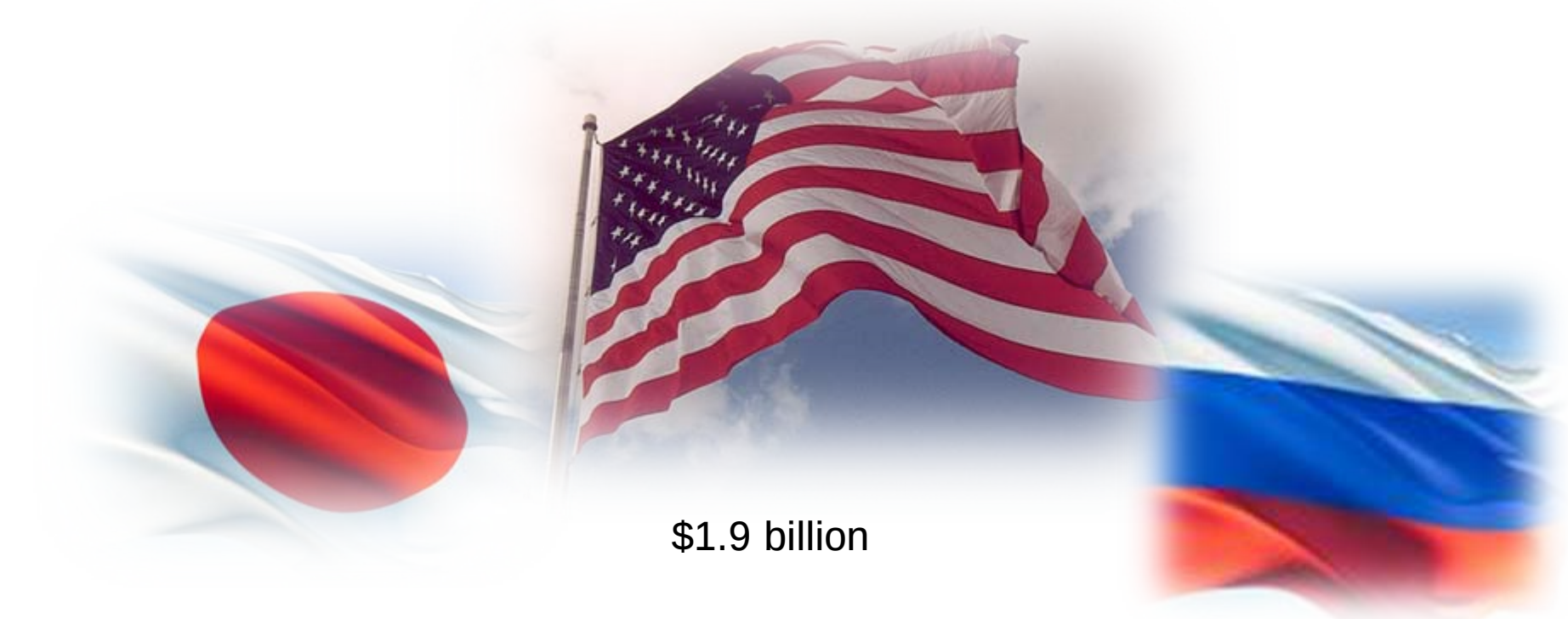
A full force of funding



U.S. , Japan, and Russia account for 52% of $8.4 billion government spending



$1.9 billion

$1.7 billion

$0.8 billion

Russia bumps Germany for 3rd place

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U.S., Japan, and Germany account for 74% of $8.6 billion corporate spending

$2.7 billion

$2.9 billion

$0.8 billion

Japan jumps over U.S. for top spot

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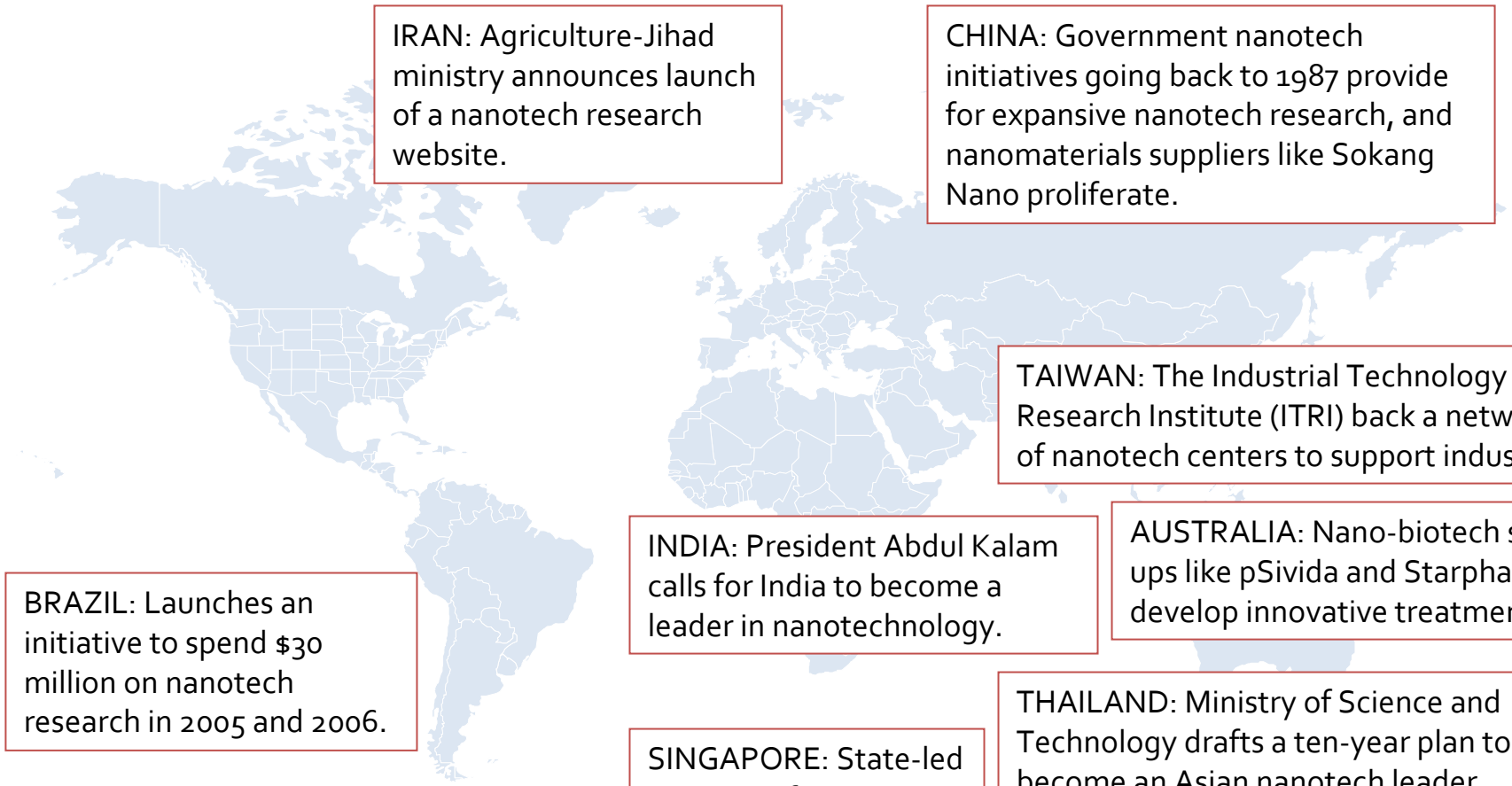
Nanotechnology is not limited to large or advanced economies



IRAN: Agriculture-Jihad ministry announces launch of a nanotech research website.

CHINA: Government nanotech initiatives going back to 1987 provide for expansive nanotech research, and nanomaterials suppliers like Sokang Nano proliferate.

TAIWAN: The Industrial Technology Research Institute (ITRI) back a network of nanotech centers to support industry.

INDIA: President Abdul Kalam calls for India to become a leader in nanotechnology.

AUSTRALIA: Nano-biotech start-ups like pSivida and Starpharma develop innovative treatments.

BRAZIL: Launches an initiative to spend $30 million on nanotech research in 2005 and 2006.

THAILAND: Ministry of Science and Technology drafts a ten-year plan to become an Asian nanotech leader.

SINGAPORE: State-led initiatives focus on nanoelectronics applications.

Source: Lux Research

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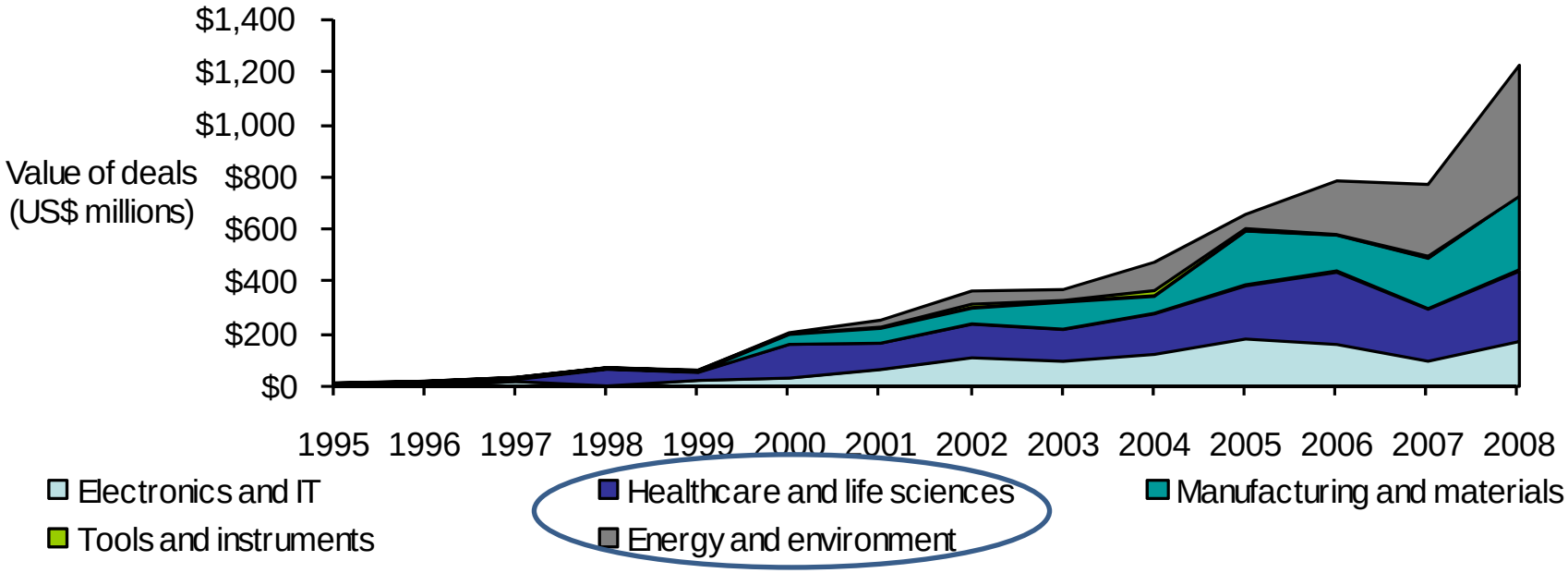
VCs splurge as investments jump 60% in 2008



PACIFIC BIOSCIENCES

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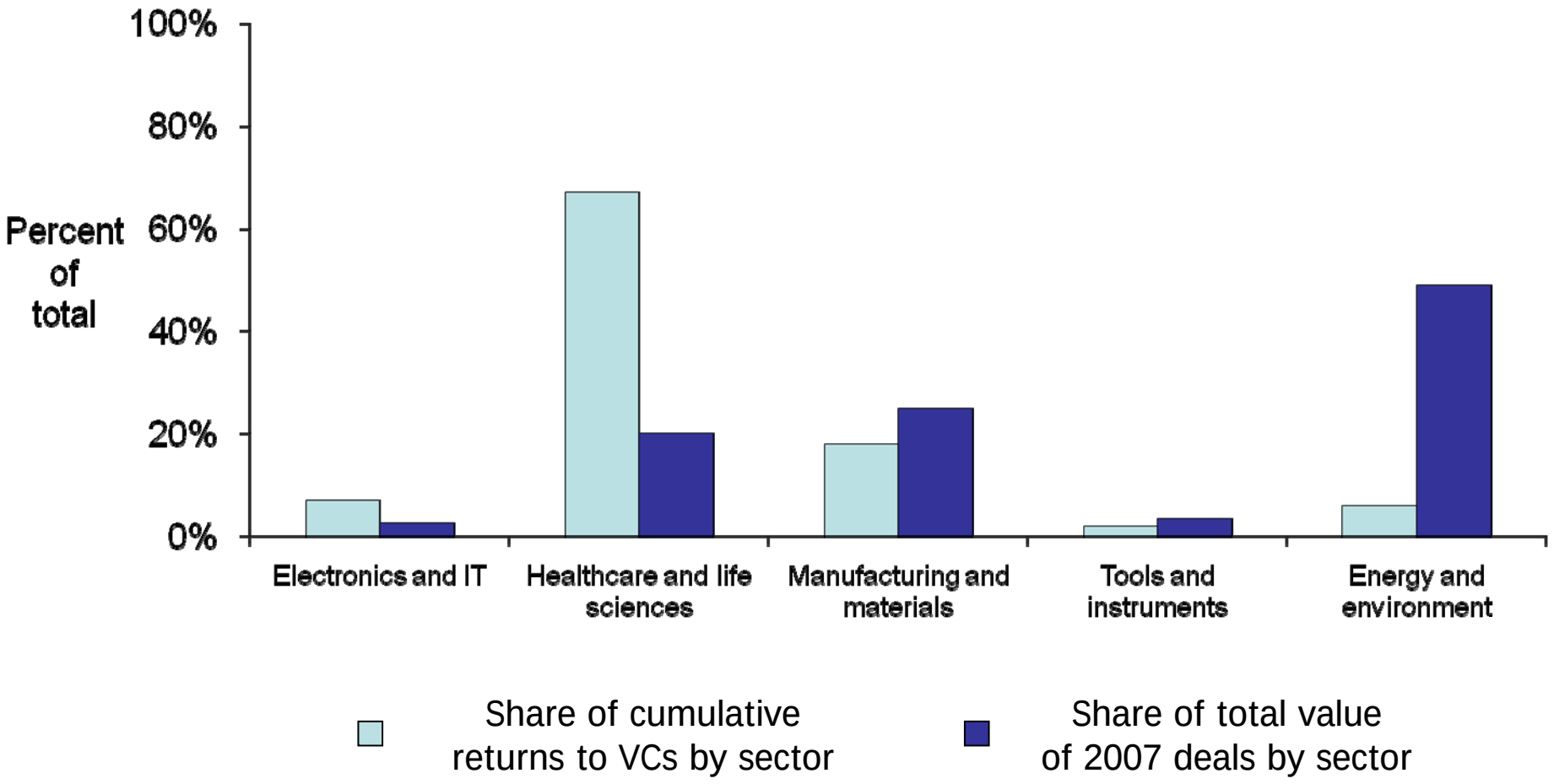
VC investments aren't informed by exits



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Lux Research evaluated countries on two axes: nanotech activity and development strength

Criterion	Description
Nanotech initiatives	Qualitative assessment of the operational status, effectiveness, and coordination of nanotechnology initiatives at the national, regional, and local levels
Nanotech centers	Number of dedicated government and university nanotech facilities in country with a focus on either R&D or commercialization
Government spending	Amount of funding at regional and national levels specifically allocated to nanotechnology in 2008
Risk capital	Qualitative assessment of availability of risk capital to fund new ventures, taking into account institutional venture capital, government grants, and subsidized loans
Corporate nanotech funding	Estimated spending by established corporations on nanotechnology R&D in 2008, at purchasing power parity
Nanotech publications	Number of articles in scientific journals on nanoscale science and engineering topics from 1995 through 2008
Issued international patents	Number of international patents on nanotech-enabled inventions issued from 1995 to 2008 to entities based in country
Active companies	Qualitative score; considering both number and quality of companies active in nanotech, including large corporations, small and midsize companies, and start-ups

Criterion	Description
High-tech manufacturing as percent of GDP	Value of domestic output for high-tech chemicals, information technology products, pharmaceuticals, and life sciences products for most recent year available divided by GDP in that year
R&D spending as percent of GDP	Gross domestic R&D spending from both government and private-sector sources divided by GDP, for most recent year available
Technology and science workforce	Number of R&D personnel per $1,000 of GDP at purchasing power parity, for most recent year available
Science and engineering Ph.D.'s	Number of science and engineering Ph.D. graduates as a percent of total population, most recent year available)
Expatriation of highly educated	Percent of highly educated leaving country in 2008
Infrastructure	Composite metric composed of electricity availability (2%), mobile phones per capita (2%), Internet hosts per capita (2%), Internet users per capita (2%), and abundance of roads (2%), for 2008

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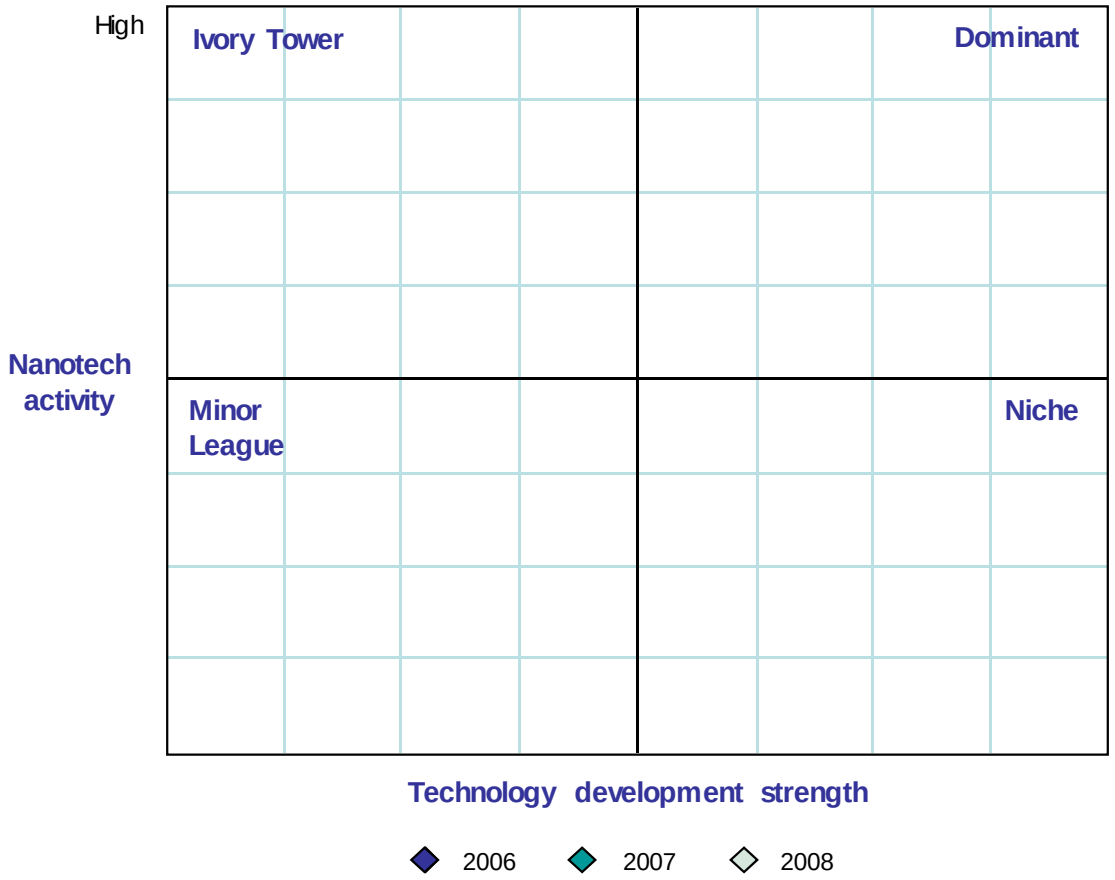
Evaluated countries on activity and development strength



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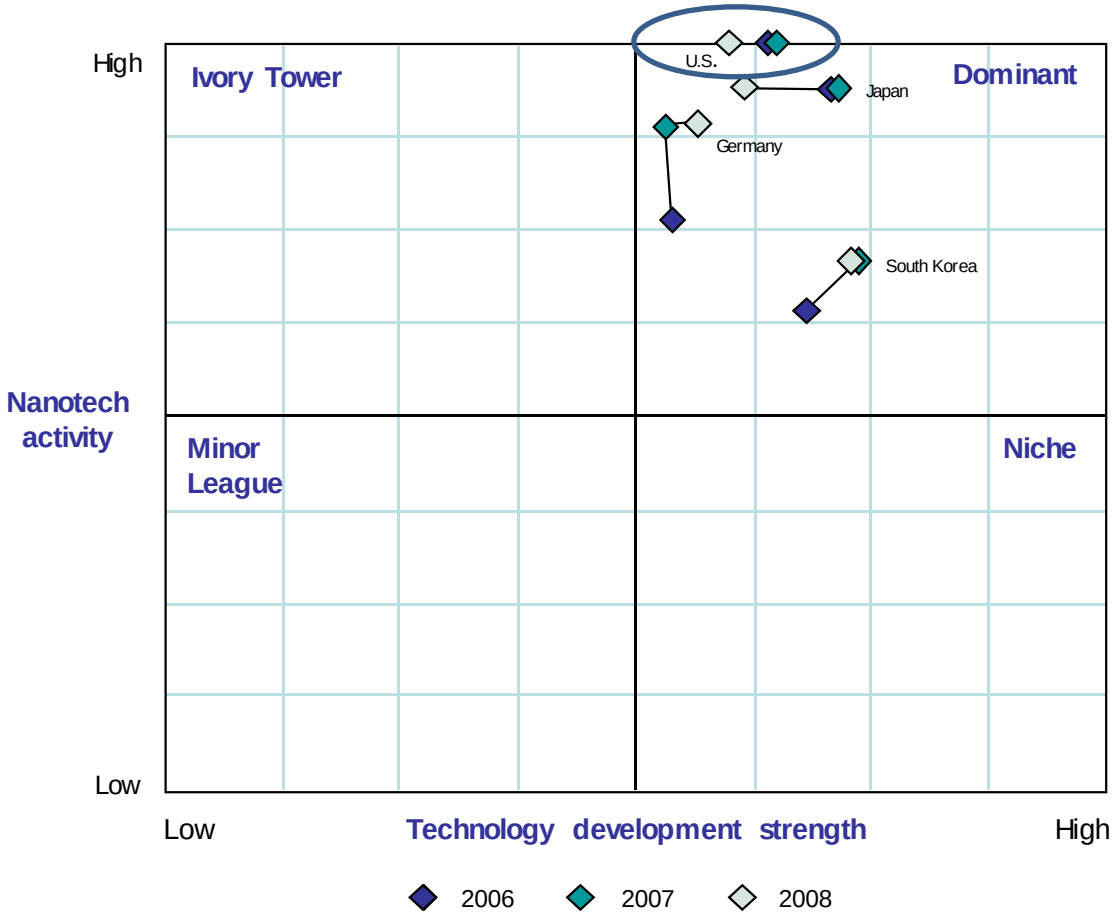
U.S. still leads the pack



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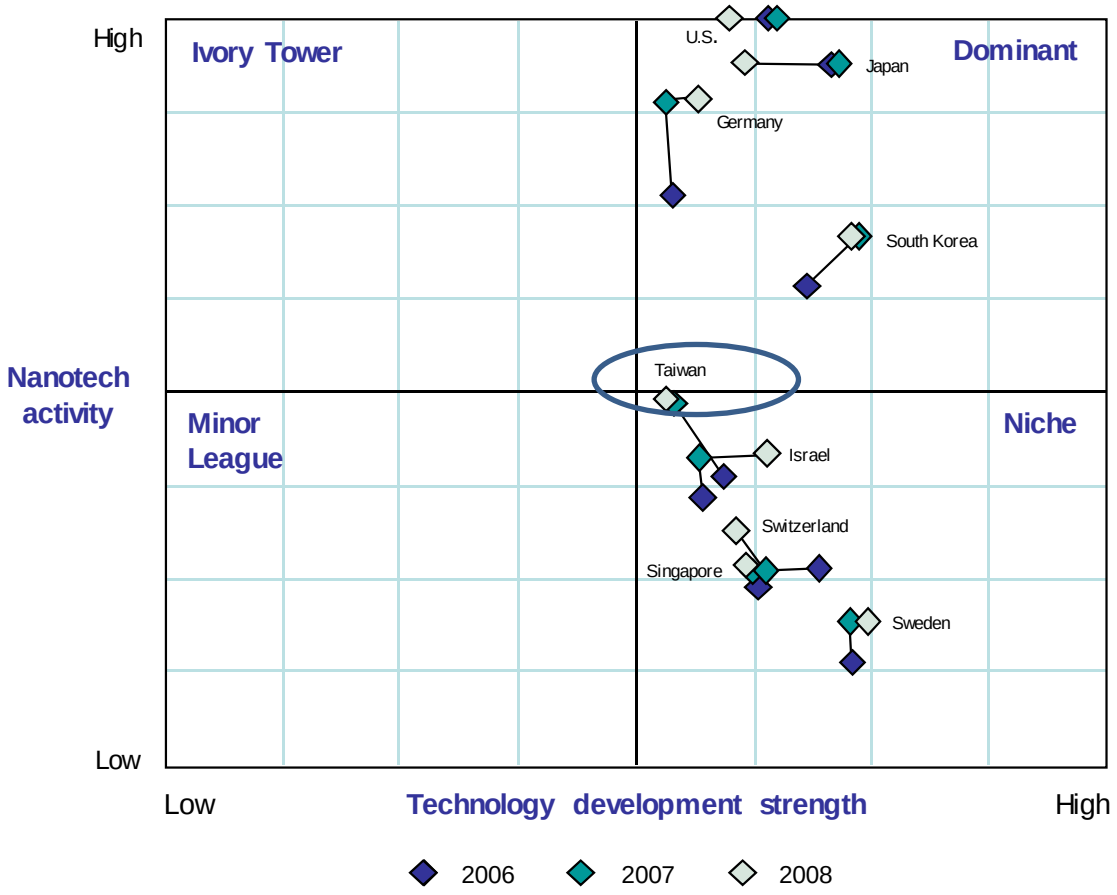
Taiwan fails to break through



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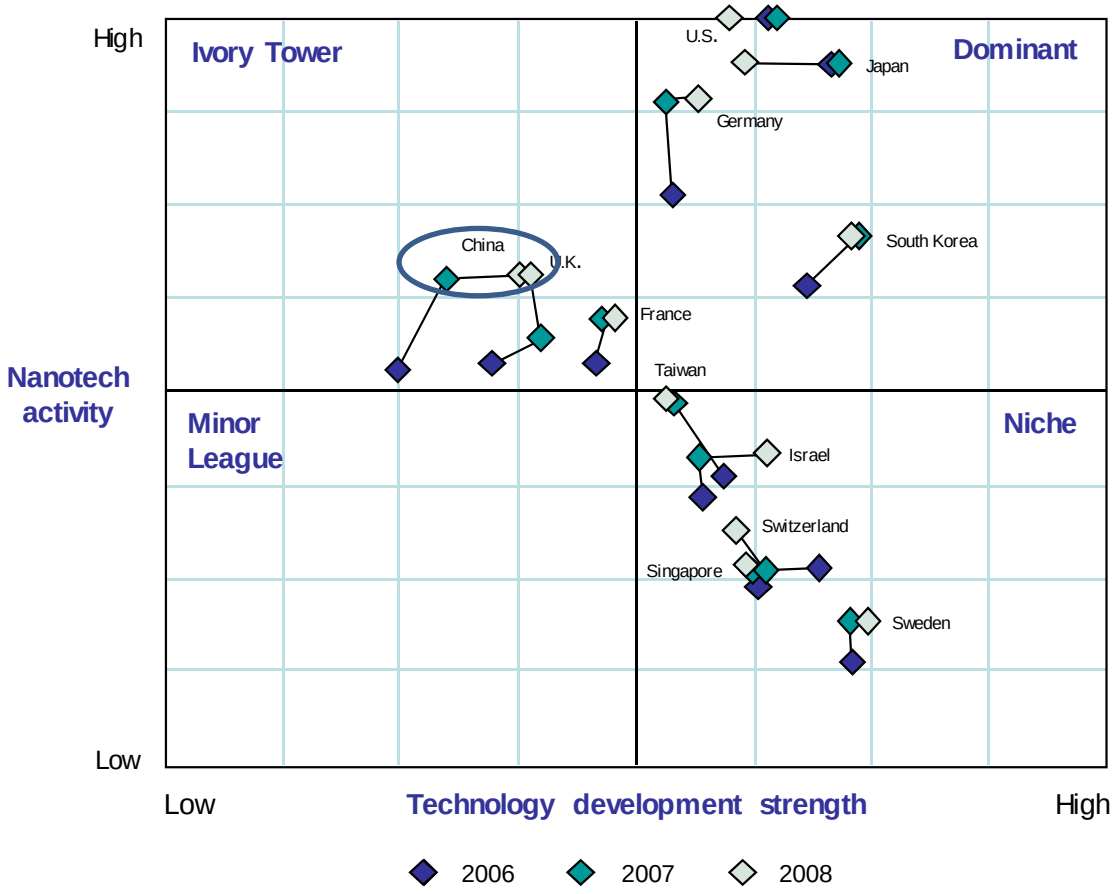
China increases development strength



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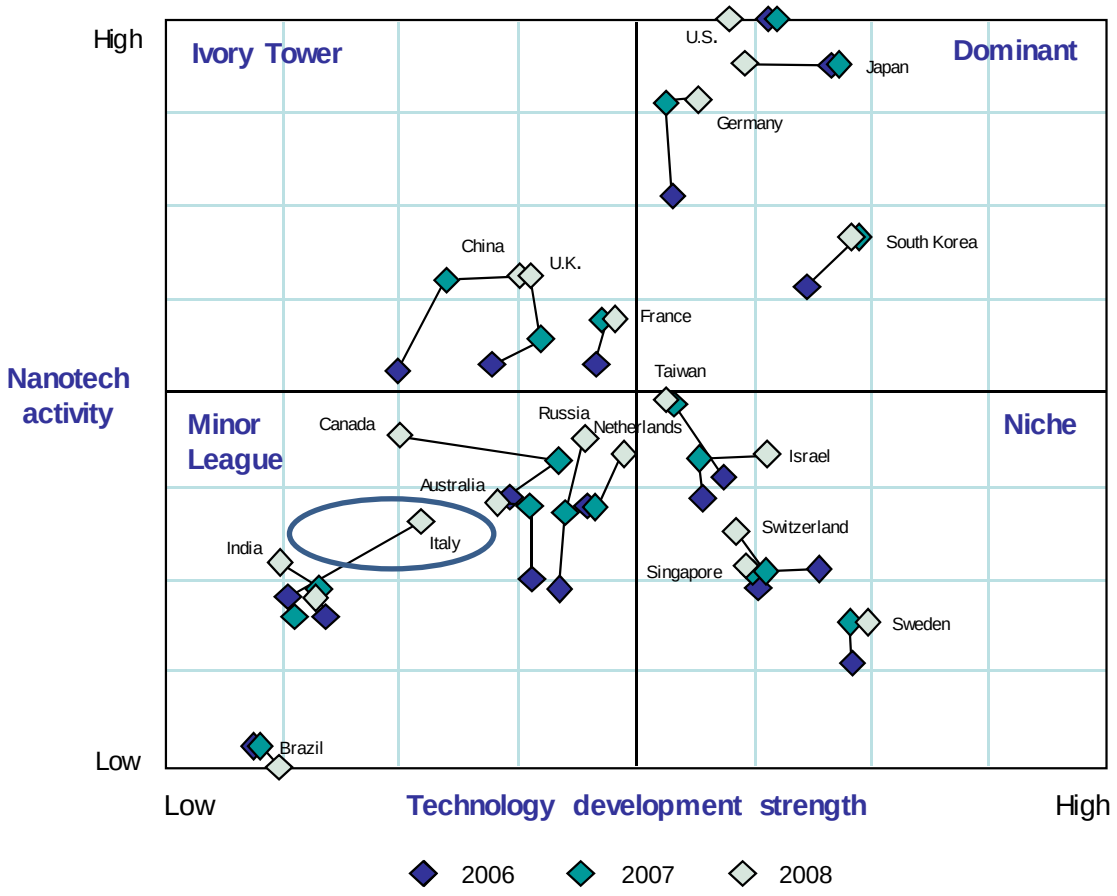
Italy gains momentum



Outline

- Nanotechnology in industry and commerce
- Nanotechnology investment and revenue internationally
- **Nano EHS trends in science, perception, and regulation**
- Recommendations for a way forward

All technologies carry risks; we must (and usually do) learn to manage them

The Technology	Internet and cell phones	Genetically-modified organisms	Stem cells
The Bad	• Viruses • Privacy • Piracy • Porn • ADD • Brain cancer	• Frankenfoods • Jumping genes • Economic displacement	• Religious issues
The Good	• Google • iPhone • YouTube	• Insulin • Less pesticide • Drought tolerance	• Nerve repair • Cancer treatment • More to come

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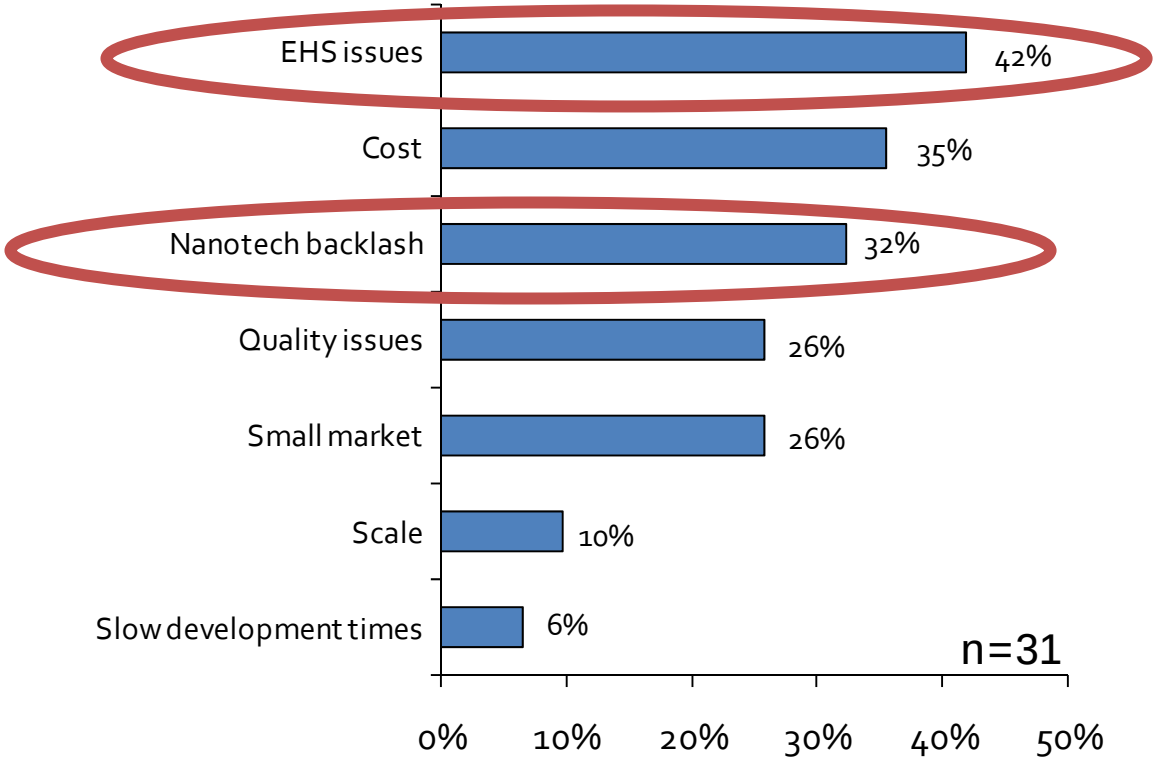
Corporate nanotech leaders cite growing cynicism

"What are the challenges facing nanotech development and commercialization today?"



Three aspects of nanomaterial safety

Real Risks

Nanomaterials might have negative effects on people or the environment

Rat exposed to cobalt nanoparticles on the left side, bulk cobalt on the right side

Best case: Nanomaterials prove to be more dangerous than ordinary substances in only a handful of cases

Worst case: Studies show that many nanomaterials have elevated hazard and are more difficult to control

Perceived Risks

Nanotechnology might come to be seen as unsafe – irrespective of actual harm

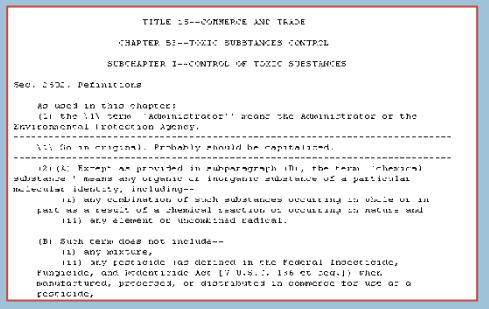
Protest of the use of Nano-Tex fabric treatment outside an Eddie Bauer store

Best case: Consumers appreciate the benefits nanomaterials can offer and embrace the technology

Worst case: Nanotech comes to be seen as synonymous with danger and consumers are reluctant to accept it

Regulations

Regulations might – rightly or wrongly – slow or block commercialization



TITLE 15--COMMERCE AND TRADE

CHAPTER 53--TOXIC SUBSTANCES CONTROL

SUBCHAPTER I--CONTROL OF TOXIC SUBSTANCES

Sec. 2602. Definitions

As used in this chapter:

(2) the \1\ term ''Administrator'' means the Administrator of the Environmental Protection Agency.

\1\ So in original. Probably should be capitalized.

---

(3)(A) Except as provided in subparagraph (B), the term ''chemical substance'' means any organic or inorganic substance of a particular molecular identity, including--

(i) any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature and

(ii) any element or uncombined radical.

(B) Such term does not include--

(i) any mixture,

(ii) any pesticide (as defined in the Federal Insecticide, Fungicide, and Rodenticide Act [7 U.S.C. 136 et seq.]) when manufactured, processed, or distributed in commerce for use as a pesticide,

Text of the Environmental Protection Agency's Toxic Substances Control Act

Best case: Existing regulatory frameworks case be painlessly adapted to manage nanomaterials

Worst case: Risks drive regulators to impose stringent testing requirements on all nanomaterials

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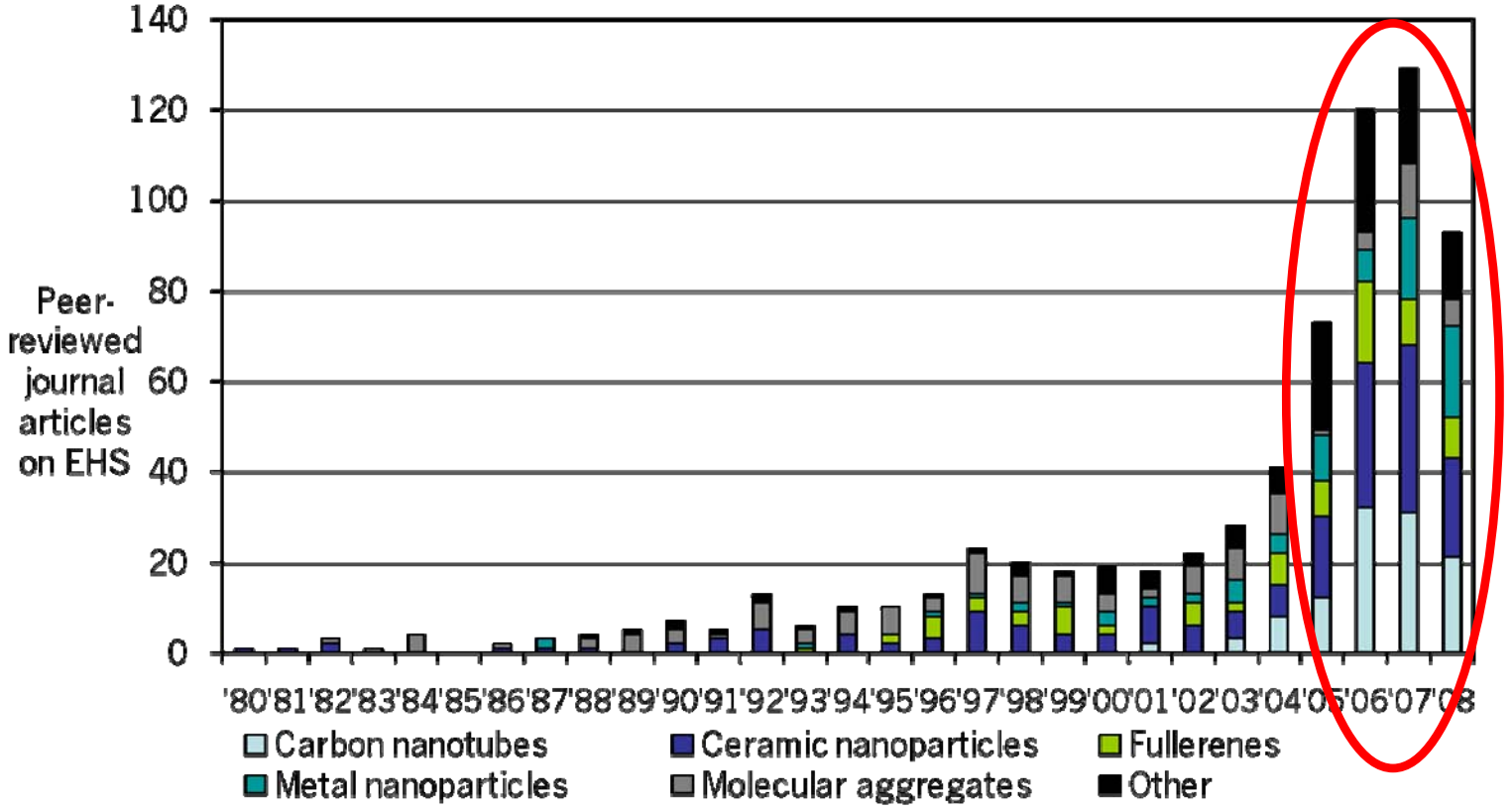
… but uncertainties exist around each.

Real risks



- Published research into nanotech EHS has increased dramatically since 2004 – 64% of all papers since 1980

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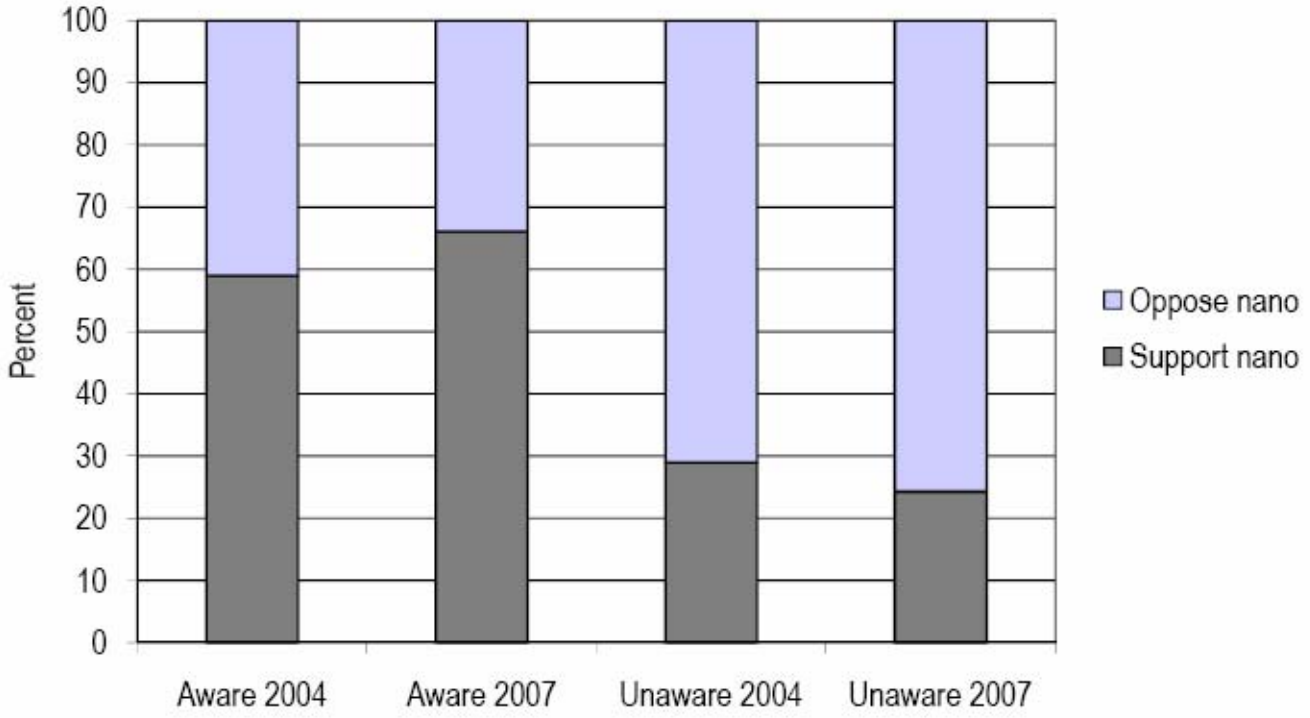
Consumers know little about nano but are optimistic

Researcher(s)	Year	Description	People	Region	Awareness	Attitude	Key finding
BMRB Social Research	2004	Face-to-face survey	1,005	U.K.	Low		Of those who could define it, 68% thought it would improve life
Cobb & Macoubrie	2004	Telephone survey	1,536	U.S.	Low		78% thought benefits would outweigh or be equal to risks
Currall, et al.	2004	Web-based survey	4,543	U.S.	n/a		Average respondent was “quite positive” on a scale of 1 (extremely negative) to 6 (extremely positive)
Scheufele and Lewenstein	2004	Telephone survey	706	U.S.	Low		52% supportive of nanotech, with more-aware respondents more supportive
Lee, Scheufele, and Lewenstein	2004	Telephone survey	706	U.S.	Low		Benefits outweigh risks; both knowledge of and emotion about nanotech affect by how much
Gaskell, et al. (Eurobarometer)	2005	Face-to-face survey	25,000	Europe	Low		40% optimistic about nanotech, 5% pessimistic, 42% don’t know the effect
Macoubrie	2005	Face-to-face focus groups	177	U.S.	Low		After discussions completed, 50% of participants were mostly or quite positive

SUPPORT: NOT MUCH HAS CHANGED

Percentage of people who "overall support (or oppose) the use of nanotechnology"



Note: DK/NA responses varied between 4 and 19 respondents and are not plotted here.

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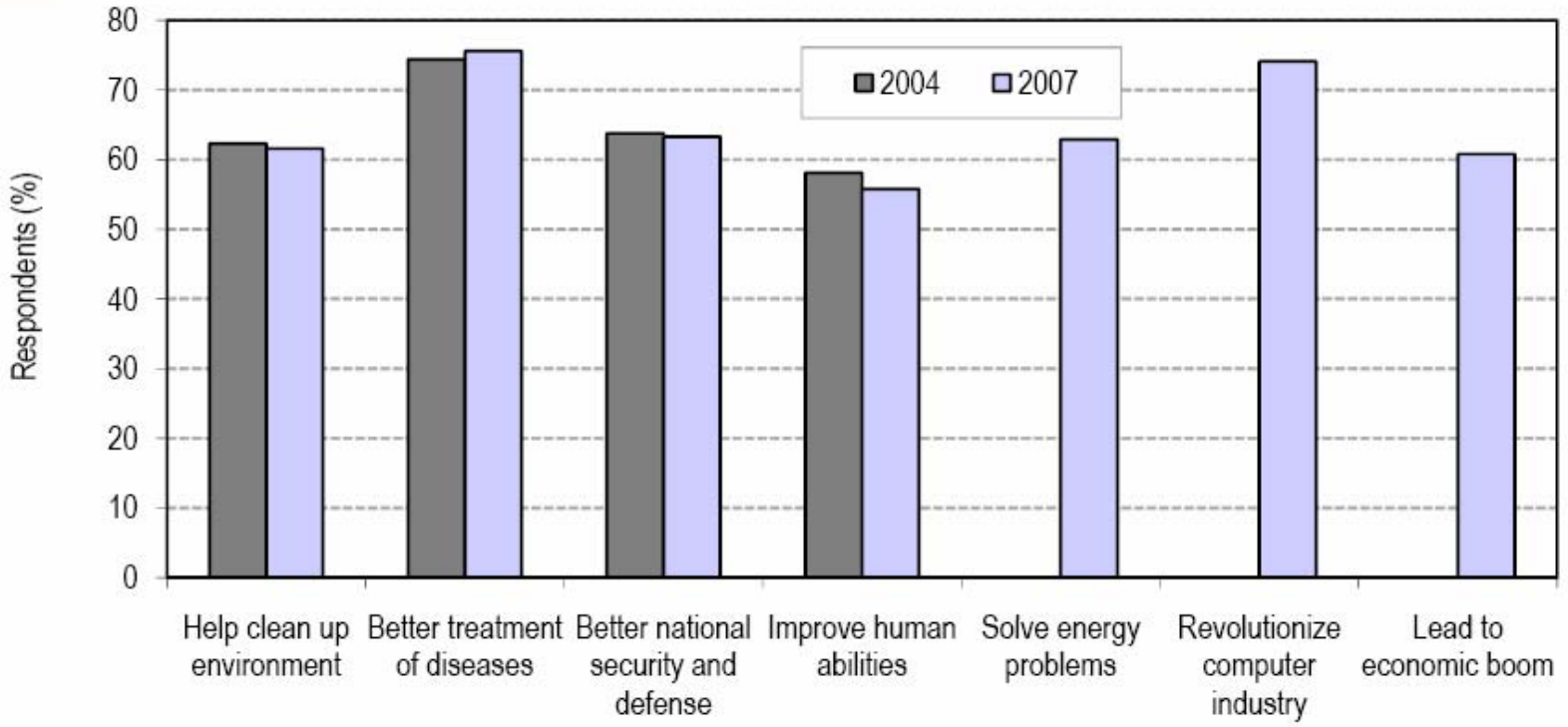
PERCEIVED BENEFITS: 2004 and 2007



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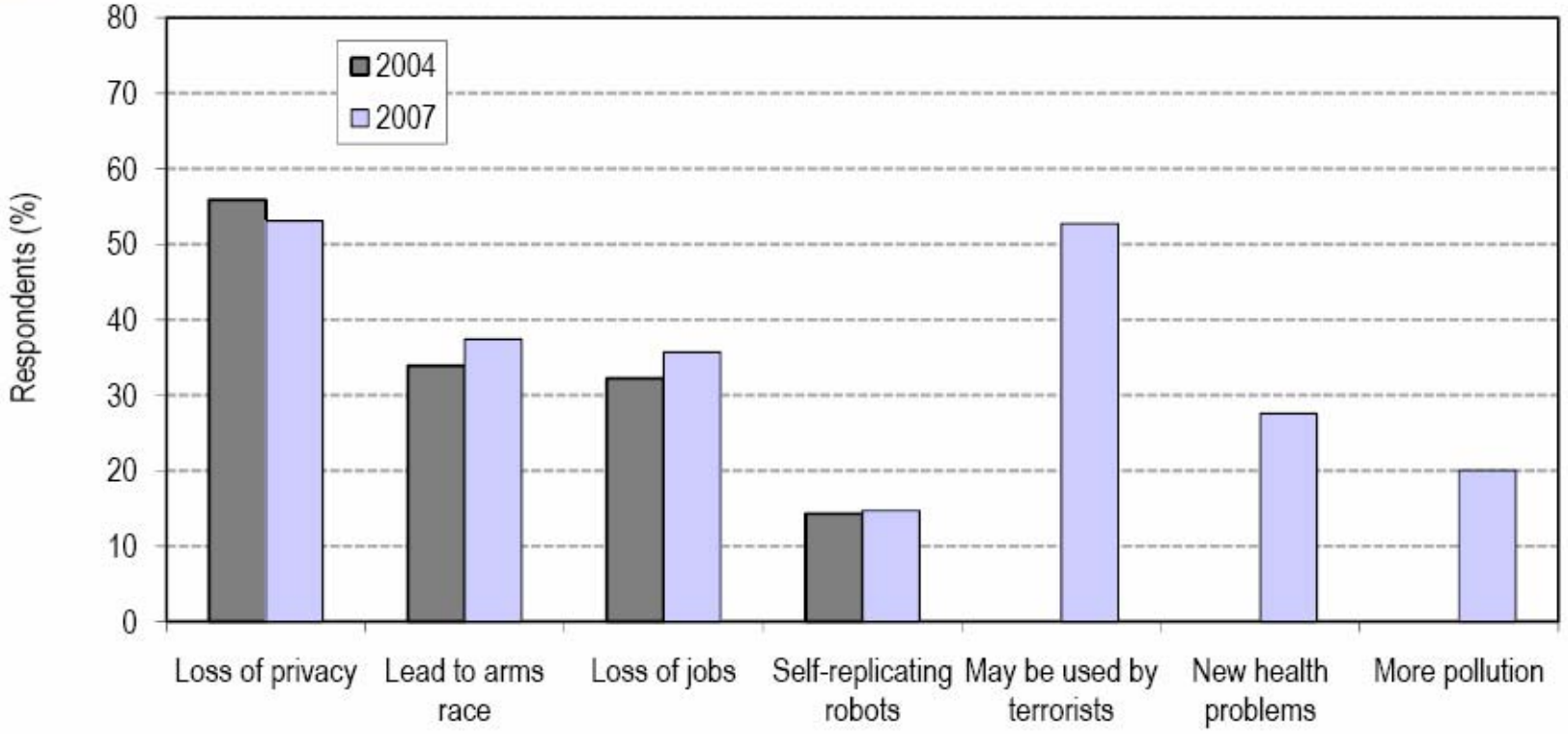
PERCEIVED RISKS: 2004 and 2007



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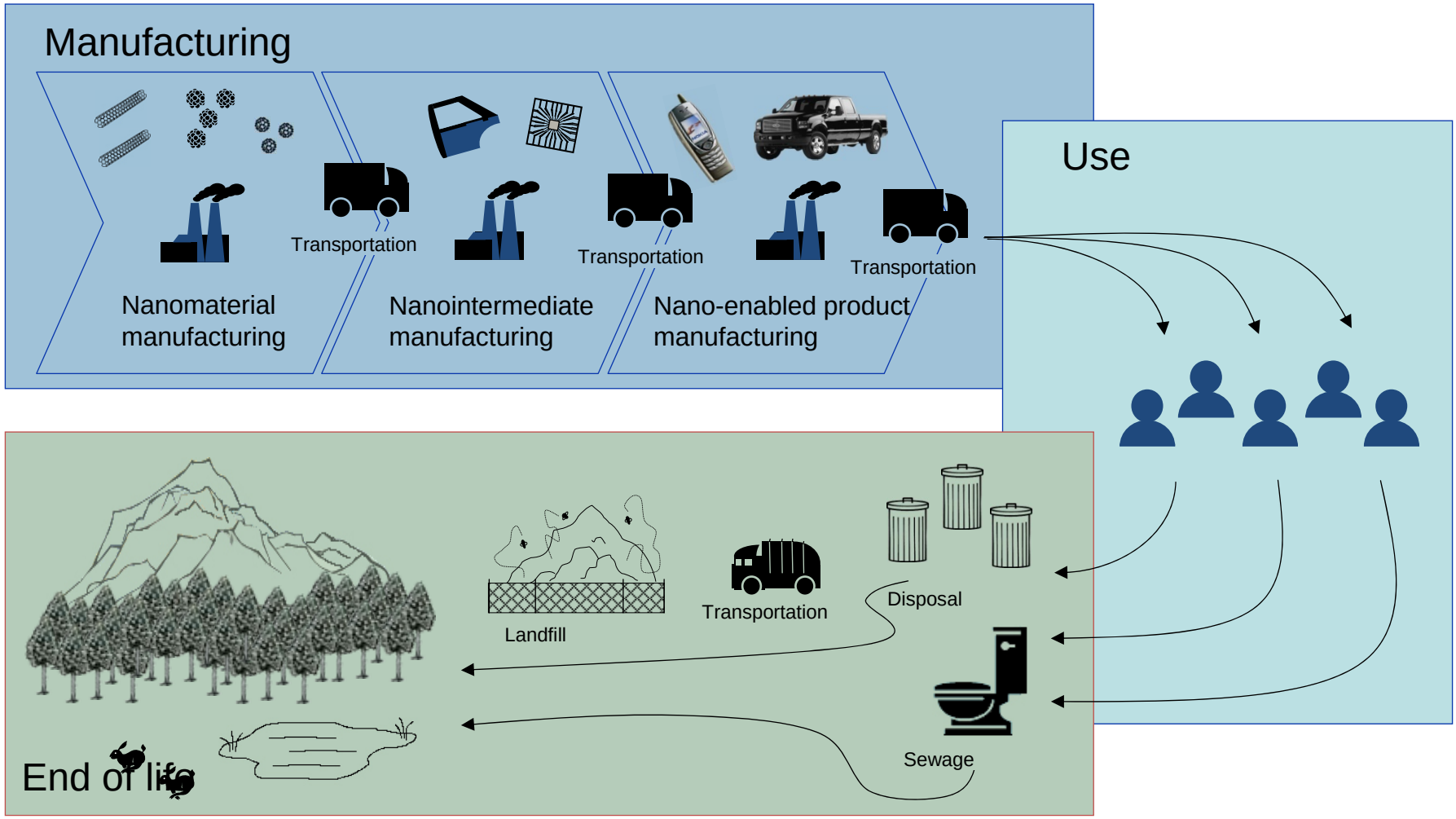
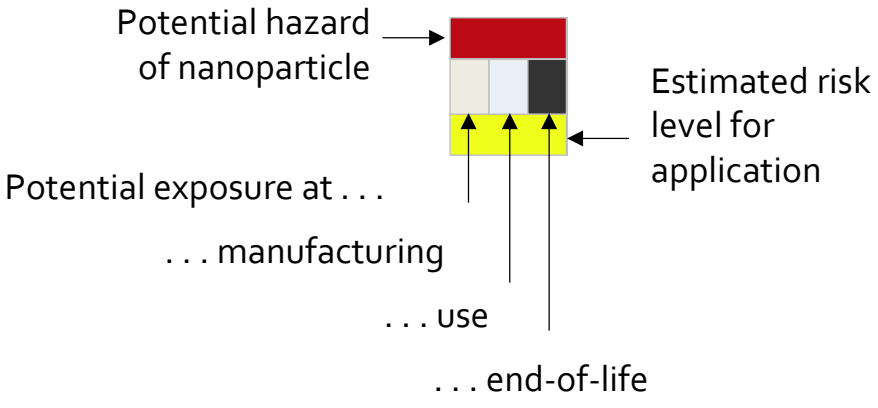
Regulation

- Regulatory agencies are looking for data before making any nano-specific regulations
  - Data has been slooooooow in coming
- Lawyers are ramping up nanomaterials practices because of murkiness in existing regulations
- Local governments eye regulations (Berkeley, Cambridge, Wisconsin, Canada)


Manufacturing
Transportation
Transportation
Transportation
Nanomaterial manufacturing
Nanointermediate manufacturing
Nano-enabled product manufacturing
Use
Landfill
Transportation
Disposal
Sewage
End of life

Lux Research estimates hazard and exposure by life cycle, material, and application

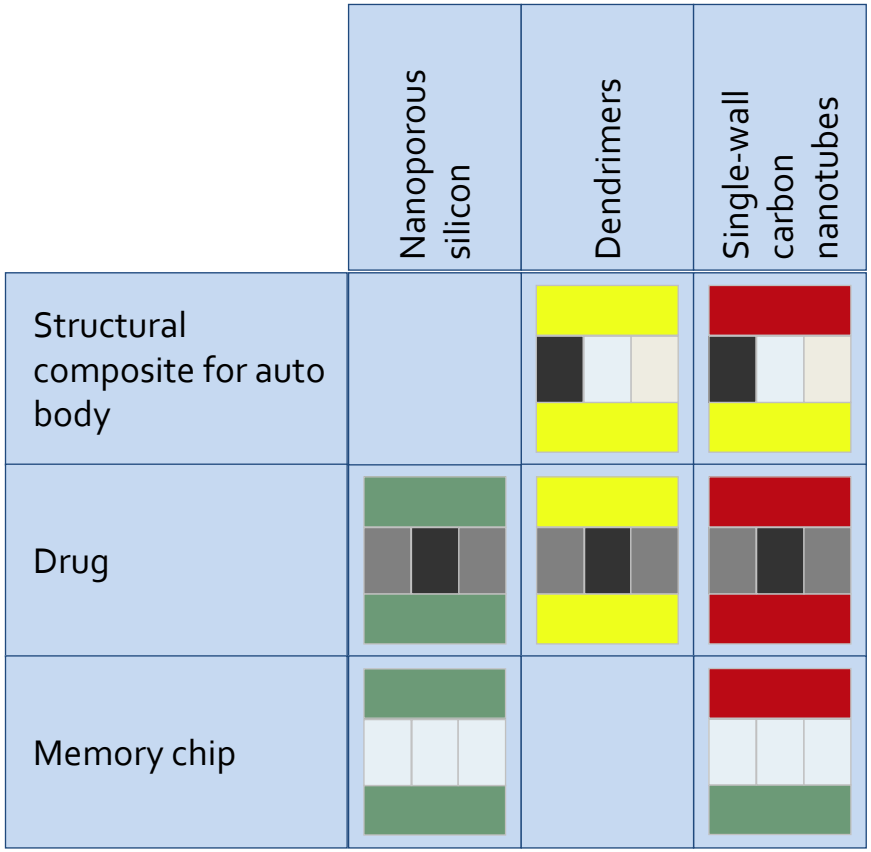


Hazard/risk level:

- High
- Medium
- Low

Exposure:

- High
- Medium
- Low



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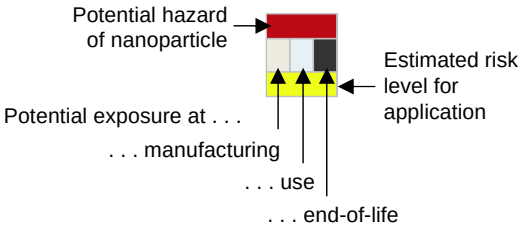
...for dozens of applications



Hazard/risk level:

Low Medium High

Exposure:

Low Medium High

	Single-walled carbon nanotubes	Multi-walled carbon nanotubes	Nanoclay particles	Cadmium-selenide quantum dots	Zinc oxide nanoparticles	Titanium dioxide nanoparticles	Dendrimers	Fullerenes	Nanocrystalline drug formulations	Silicon nanowires
In vivo imaging										
Structural composite for automotive body										
Sunscreen additive										
Food additive										
Display backplane										
Polishing agent										
Memory chip										
Printer toner										
Drug										
Flexible solar cell										

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Other nano-EHS observations

- The number companies producing or directly handling nanoparticles will continue to grow.
  - A "do not touch" policy would risk losing increasing amounts of business
- Nanoparticles should not be treated as a class of materials by regulators or insurers.
  - Make a value vs risk assessment and update as EHS knowledge grows.
- Larger companies know what they're doing; small(er) companies….not so sure.
  - Approach coverage of small companies carefully for nanoparticles with significant risk, or significant uncertainty. Learn from large companies.
- End of Life issues are lagging in terms of data development and understanding.
  - The biggest risk for insurers at the nanoenabled product part of the value chain. Need to build internal policies while this knowledge gap is addressed
- **The landscape will be a lot clearer in 3-5 years; stay engaged now**

Outline

- Nanotechnology in industry and commerce
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- **Recommendations for a way forward**

Nanotech EHS: Recommendations

- Nanotech companies should volunteer information about their nanomaterials to agencies and publics when and before they request it

- Regulators should tighten the feedback cycle for information gathering to less than 1 year

- Investors must scrutinize the EHS policies of nanomaterials companies (and ANY companies) they fund

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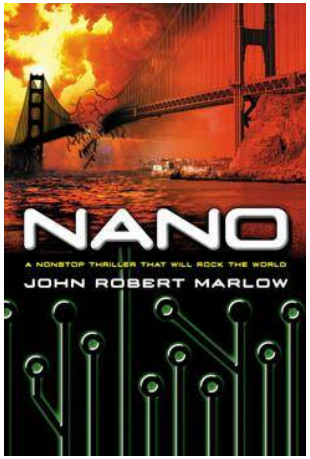
What's the outlook over the next five years?

- Global economics force nanotech developers to aim at near-term applications to generate cash
- Electronic materials become all the rage
- New industry clusters emerge
- 2009 administration changes in U.S. accelerate regulations
- Flood gates open for food and personal care applications
- Nanotech overtakes entire industries, and the term "nano" fades from view

How did we get here? Where do we go next?



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Thank you

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For more information, please see:
http://www.luxresearchinc.com/info/nanomaterials