Bionanotechnology: the role of measurements & standards

Eric B. Steel

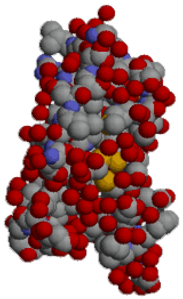
Acting Director, Program Office

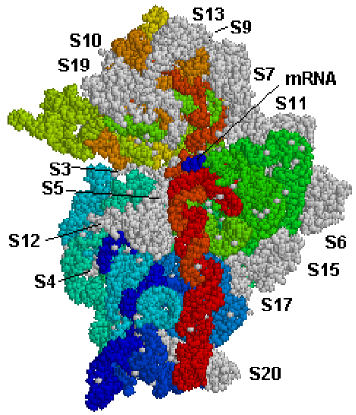
National Institute of Standards and Technology

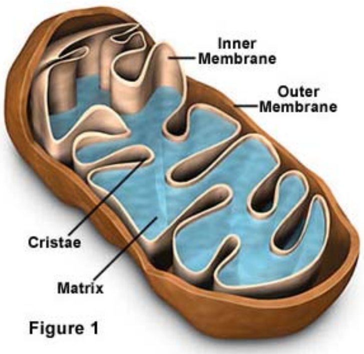
Gaithersburg, MD 20899

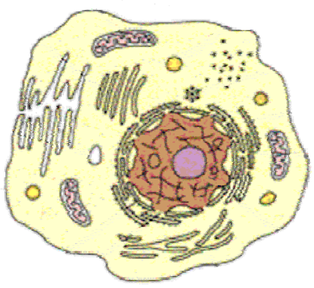
eric.steel@nist.gov

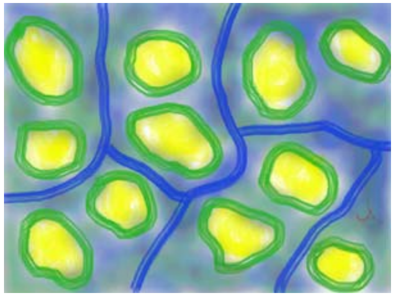
Scale in Biology











molecules *proteins*	**supramolecular complexes** *ribosomes*	**organelles** *mitochondria*	**cells** *liver cell*	**tissues** *liver*
1-10 nm	**10-100 nm**	**100 nm - 1 μm**	**1-10 μ m**	**macro**

Want to Know (measure)

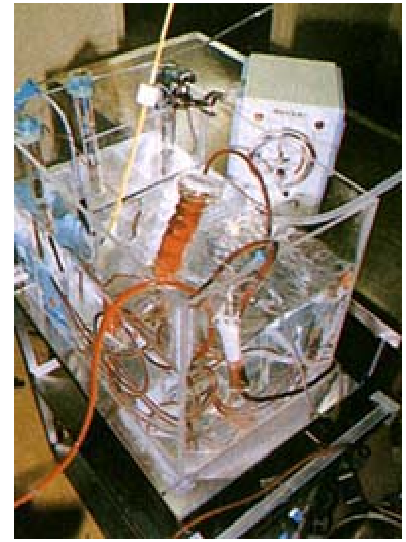
3D elemental, chemical, structure, properties

Want to Do (technology)

Control, shape, change operation, kill very specifically

Public Concern, Fear

Jay Vacanti, 1997

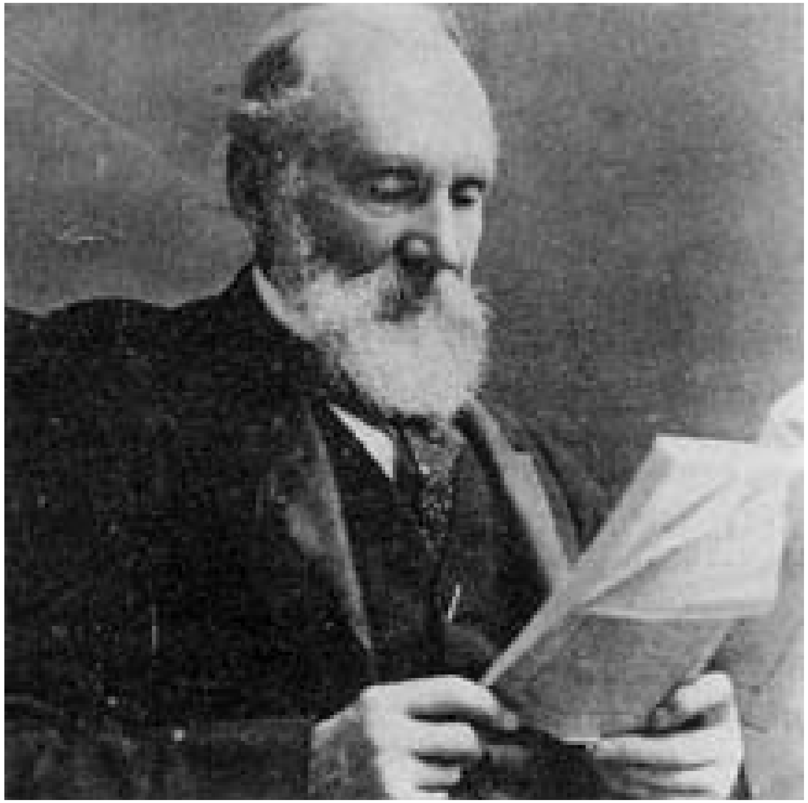


bio-artificial liver

gray goo problem

Metrology

The science of measurement; a system of measures



“When you can measure what you are speaking about, you know something about it. But when you cannot measure it, your knowledge is of a meager and unsatisfactory kind. It may be the beginning of knowledge, but you have scarcely advanced to the stage of science.”

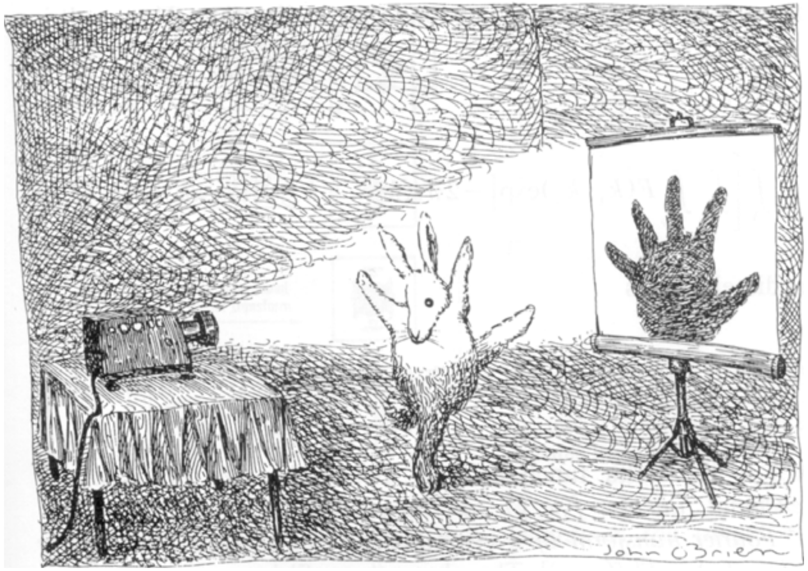
William Thomson, Lord Kelvin

NIST works closely with government, universities, and industry to develop the Nation’s metrology infrastructure necessary for scientific, technical, and economic advances – such as nanotechnology.

Measurements

- When we get a number, graph, image, etc.
  - Do we know if it is real?
  - Can we distinguish the measurement from the instrument/sample/environment/… dependent artifacts?
  - Can we distinguish signal from noise?

- Do we know how variable or precise it is?
- Do we know how accurate it is?
- Can we characterize and determine our uncertainty in our measurement?



Drawing by John O’Brien, The New Yorker Magazine (1991)

Nano-Measurements

What to measure… How good are we?

- Bulk vs. Nanoscale
  - Example: particle number vs. mass measurements
- Imaging vs. Schematic
  - When we shift to schematics and cartoons it is because we cannot see (image) these features
  - Common in nano

Mass vs. Particle Number Distribution for Characterization

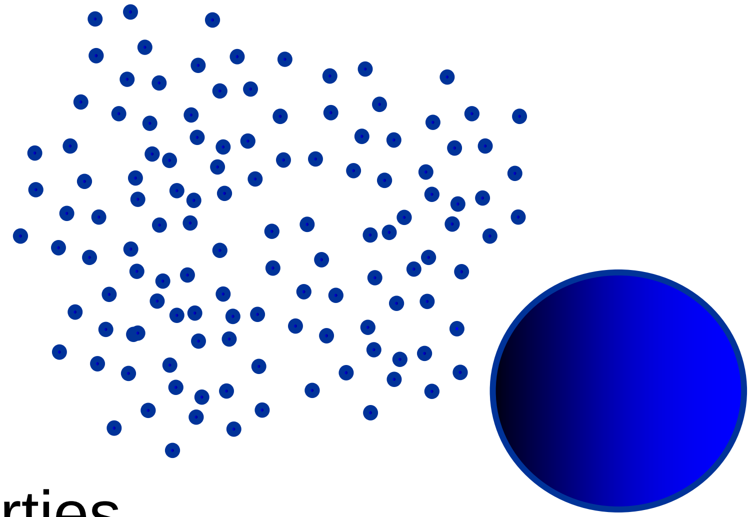
- For polydisperse, multimodal specimens
  - Large mass of a small fraction of particles may control **bulk** characterization results (except macroscopic surface analysis)
  - **Nanoanalysis** results will tend to be weighted by particle number
- A nanogram of material:

  one 10 μm particle, or

  10^3 1 μm particles, or

  10^6 0.1 μm particles or

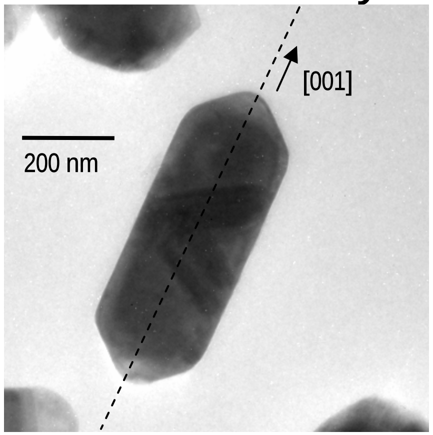
  10^9 10 nm particles



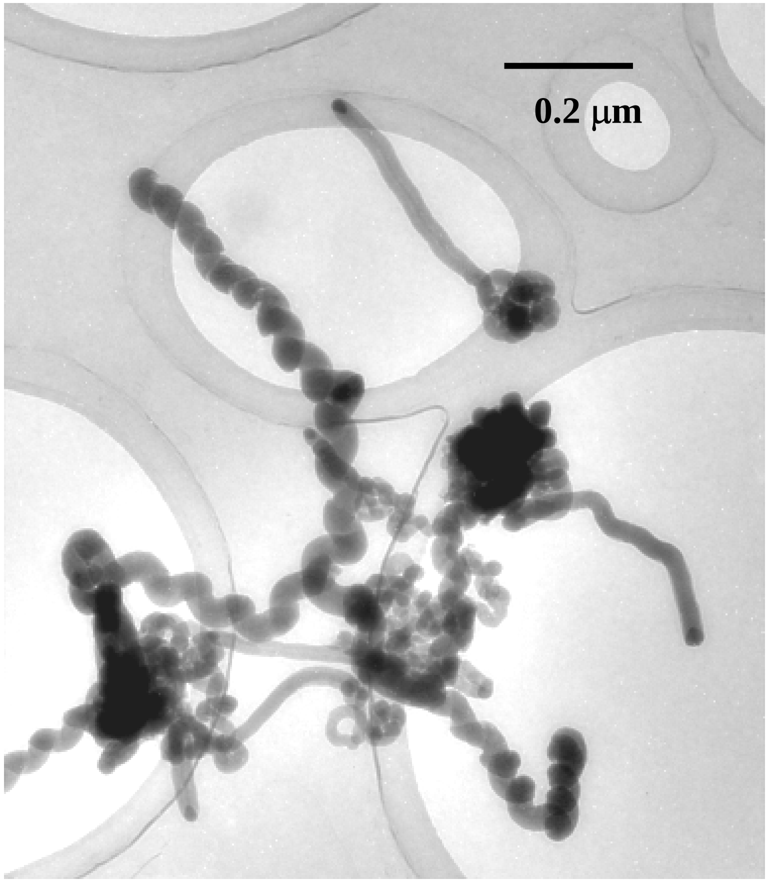
- Physical and chemical properties may vary with size (basis for nanotech)

What does size mean?

- Often one average “diameter” is reported for each particle
- Morphology
  - Size distribution
  - Shape
  - Surfaces
  - Crystalline form
  - Chirality



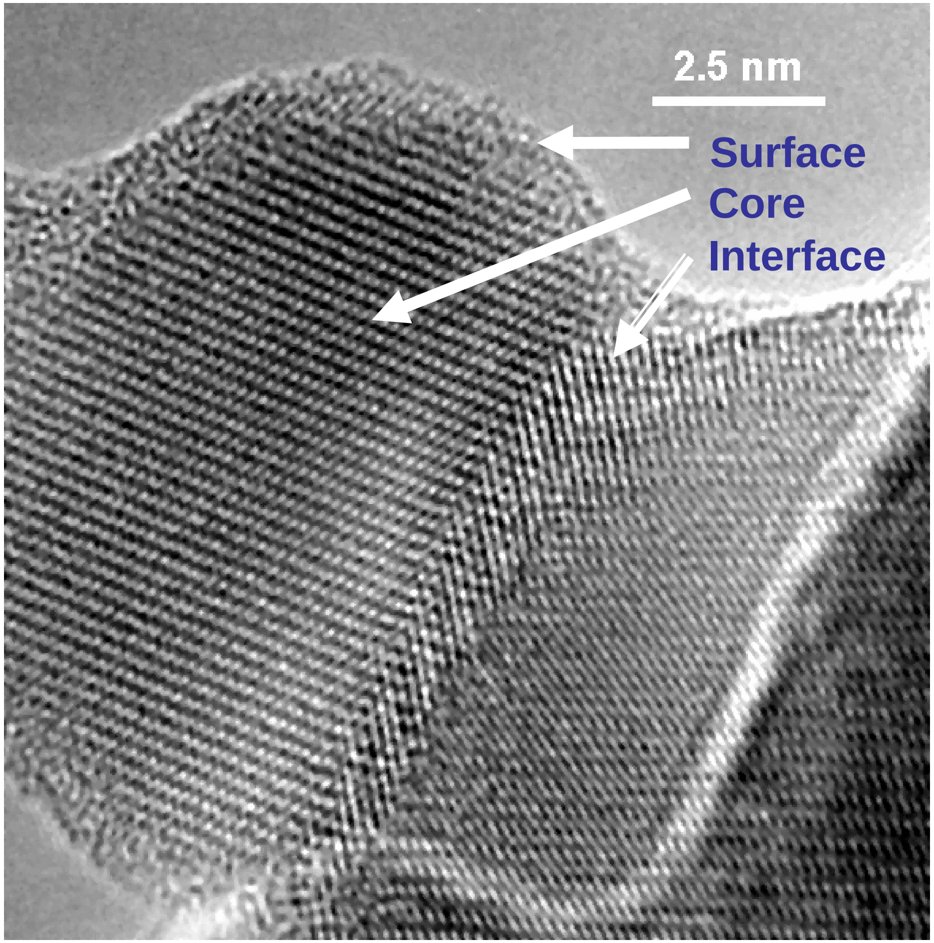
TiO_2 particles courtesy of Millenium Chemicals Micrograph courtesy Shirley Turner, NIST



Carbon Nanotubes courtesy of Richard Cavicchi and Shirley Turner, NIST

Areas of Interest in Nanoparticles

- Where
  - Inside
  - Outside
  - Next Door
  - Across the Street
- What
  - Homogeneous vs. Heterogeneous
  - Phase: Crystalline, Amorphous, Liquid, Gas, Void
  - Morphology, Faceting
  - Physical and Chemical Properties



Yttria particles courtesy Nanophase Technologies Corporation. Image courtesy of John Henry Scott, NIST

And then there is BIOLOGY!!!

- Incredible number of interrelated variables
- Easy to set out of equilibrium
- Hard to control parameters
- Hard to model
- Hard to run real experiments
- Hard to get sufficient population data
- Hard to understand short vs. long term effects

To paraphrase President Bush…

This is hard work.

Standards -- types

- Documentary (paper)
  - Guides, Methods, Glossaries, Specifications,…
- Materials
  - Reference Materials
    - In-house, Consensus, Absolute
    - Calibration (help instrument give the right answer)
    - Quality Assurance (help us know if the analysis is correct – often concentration, matrix, “form” sensitive (e.g. chiral form))
- Data
  - Reliable reference data used in theory, modeling etc.
    - e.g. human genome data, protein structure database, …
  - Algorithms/models or ways of using data

ALL must be measurement based

Timelines for Standards

Time

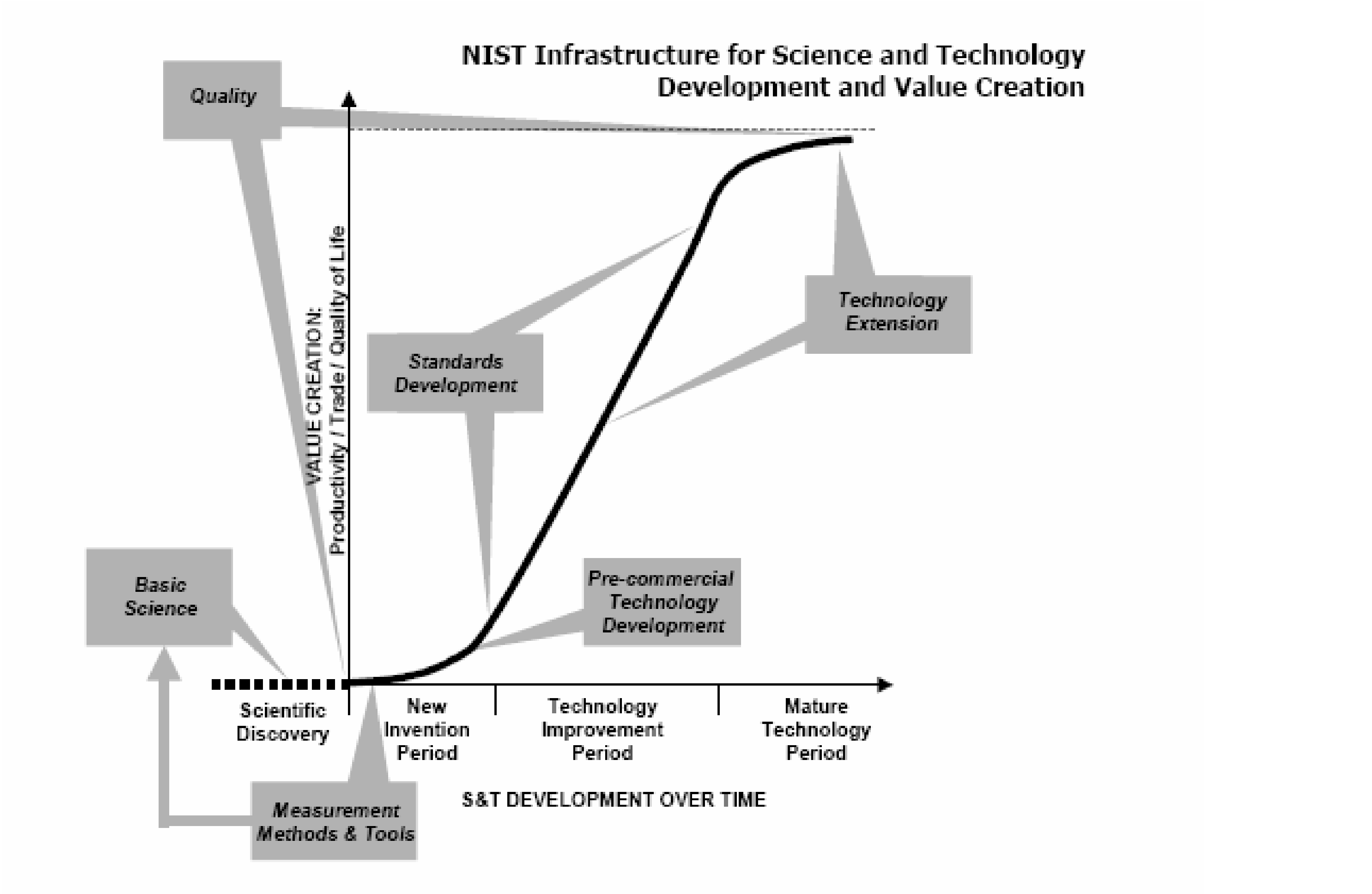
Increasing difficulty

- Research
- Draft protocol
- Interlaboratory comparisons
- Guidelines
- Draft method
- Standard method
- Applied method
- Rewrite
- Accreditation/Conformity Assessment

- Whatever you can get
- In-house materials
- Consensus materials

- Reference materials
- Certified materials
  - Calibration
- Certified materials
  - QA material
- Proficiency testing material

Relationship of measurements and standards to new technology

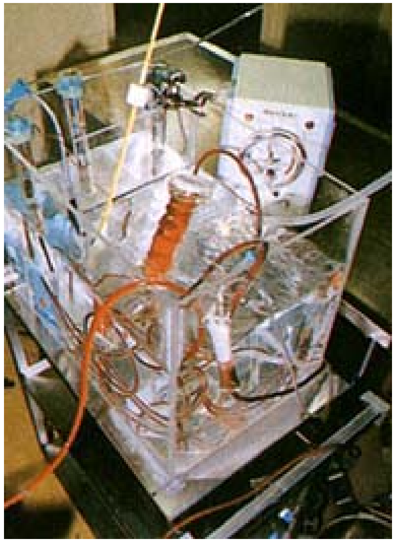


What measurement sensitivity on a mass scale?

	Name	Symbol	Factor	Name	Symbol
10^{24}	yotta	Y	10^{-1}	deci	d
10^{21}	zetta	Z	10^{-2}	centi	c
10^{18}	exa	E	10^{-3}	milli	m
10^{15}	peta	P	10^{-6}	micro	µ
10^{12}	tera	T	10^{-9}	nano	n
10^{9}	giga	G	10^{-12}	pico	p
10^{6}	mega	M	10^{-15}	femto	f
10^{3}	kilo	k	10^{-18}	atto	a
10^{2}	hecto	h	10^{-21}	zepto	z
10^{1}	deka	da	10^{-24}	yocto	y

Public Concern, Fear

Jay Vacanti, 1997



bio-artificial liver

gray goo problem