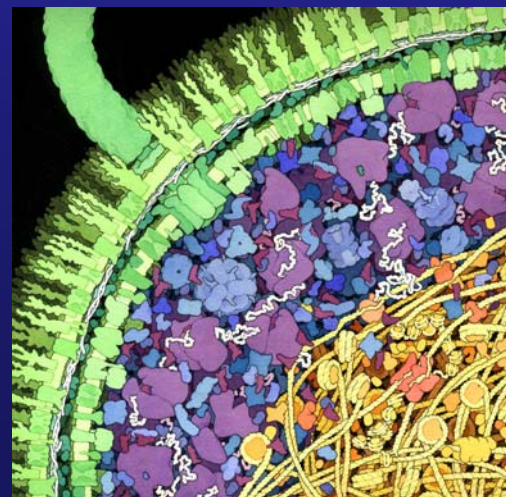
NANOMEDICINE ROADMAP INITIATIVE

Project Launch Meeting

NIH, Masur Auditorium, Bldg 10, Bethesda, MD
Tuesday, May 4, 2004



NANOMEDICINE ROADMAP INITIATIVE RFA IS IN TWO PARTS

- Part 1 – Nanomedicine Initiative Description and Research Objectives
- Part 2 – Solicitation of the Concept Development Memo

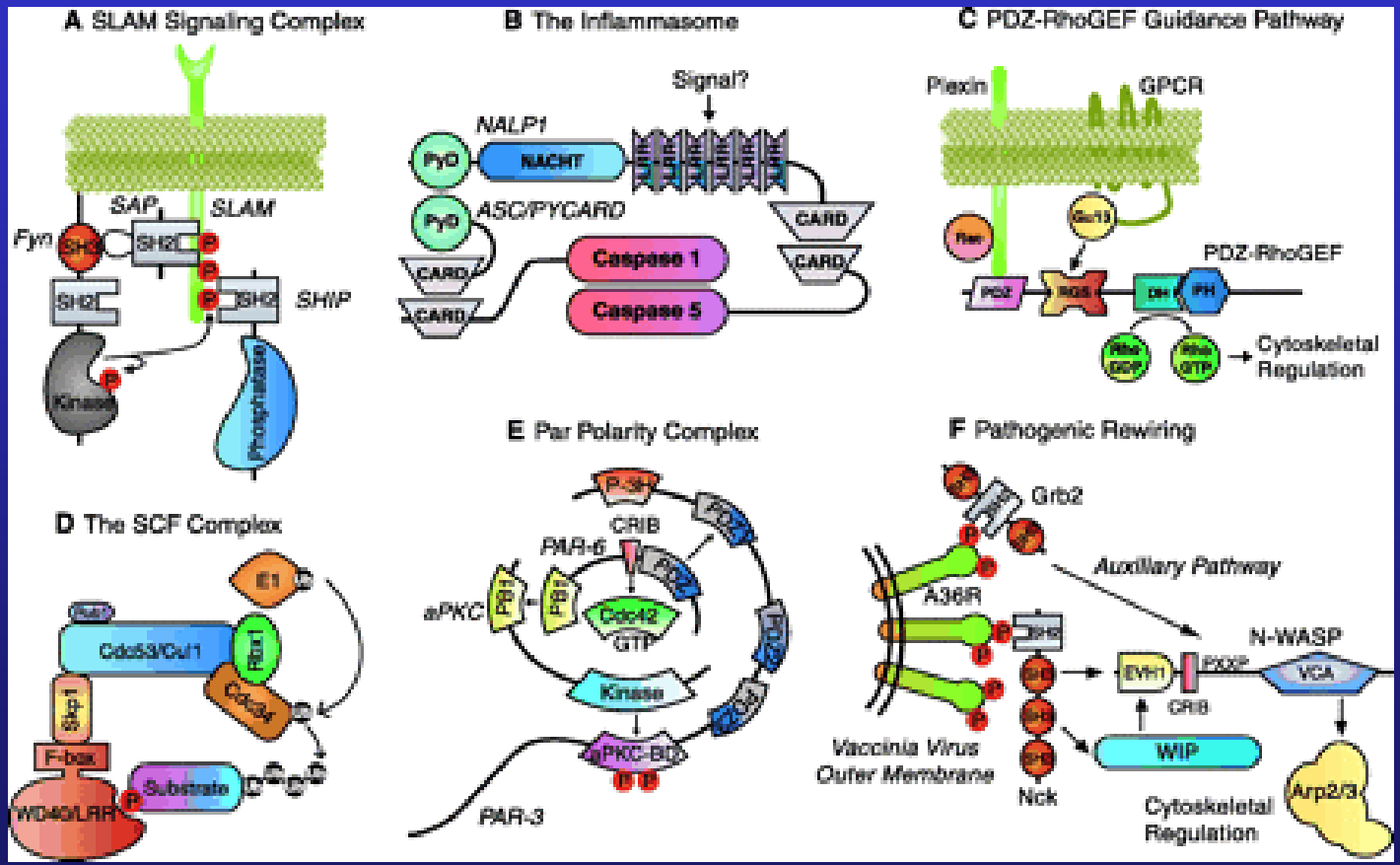
THE NANOMEDICINE ROADMAP

The overarching goal is to create the *conceptual and literal interface* between biology and medical devices *at the scale* of biomolecular processes.

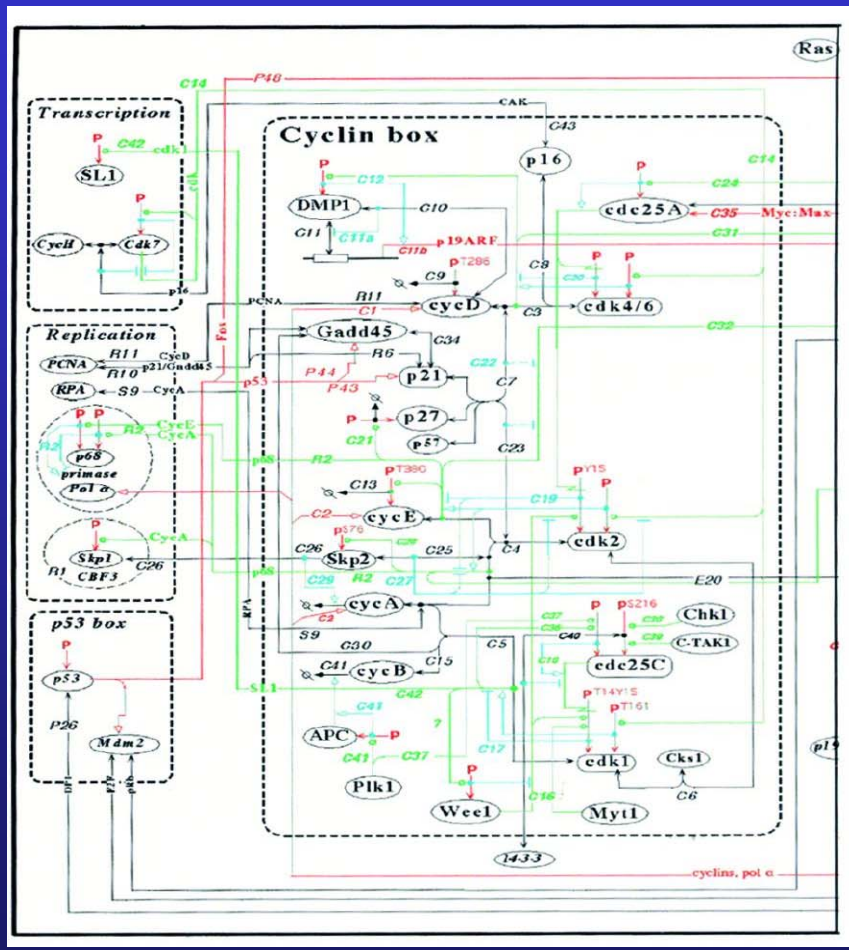
To achieve this goal, Nanomedicine Development Centers will:

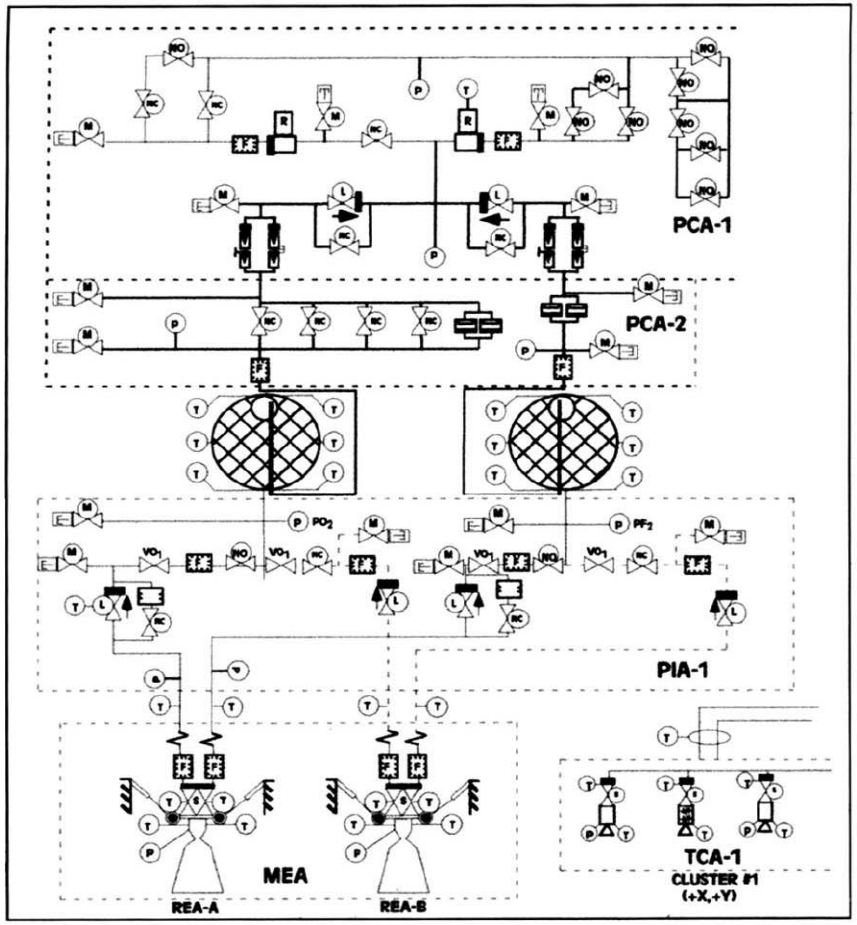
- enable comprehensive measurements on biological molecular system components and their interactions
- combine these measurements using analytical tools to achieve fundamental understanding of biological processes
- use that knowledge to drive the design of new nanomachines and technologies to interact with living systems to improve human health.

Emerging Complexity Of Biology



Need to understand biological systems





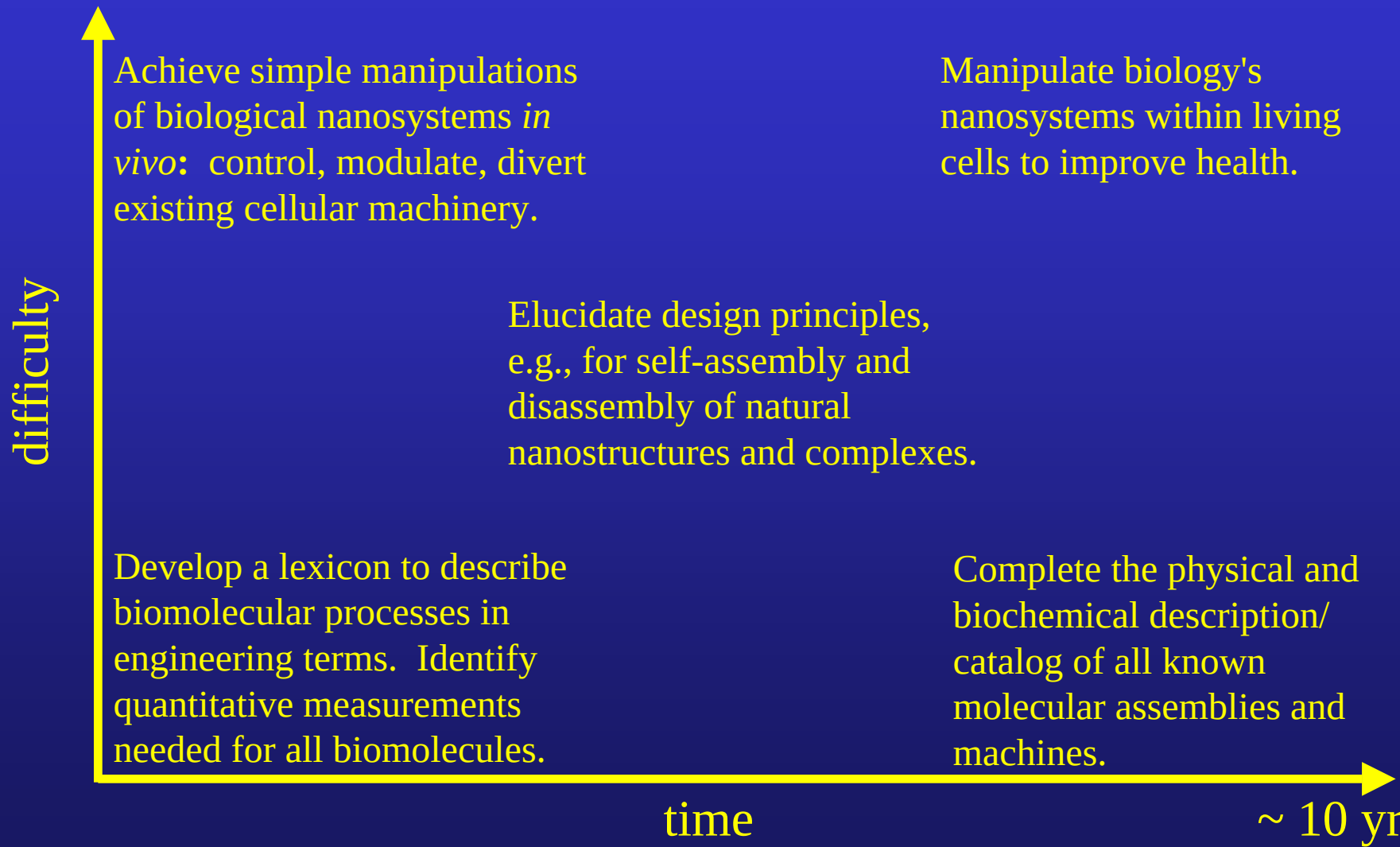
Brent *Cell*, 2000

The Biological Data Of The Future

- Destructive
- Qualitative
- Uni-dimensional
- Low temporal resolution
- Low data density
- Variable standards
- Non cumulative

- Non-destructive
- Quantitative
- Multi-dimensional and spatially resolved
- High temporal resolution
- High data density
- Stricter standards
- Cumulative

CONCEPTUALIZING THIS INITIATIVE



A TEN-YEAR PROCESS

1. determine what additional measurements and analytical and computational tools are needed to understand biological system design at the molecular level
2. develop, refine, and apply those measurements to biological systems to elucidate design principles
3. engineer molecular structures, assemblies, and organelles for treating diseased or damaged cells and tissues

BEGINNING A TEN-YEAR PROCESS

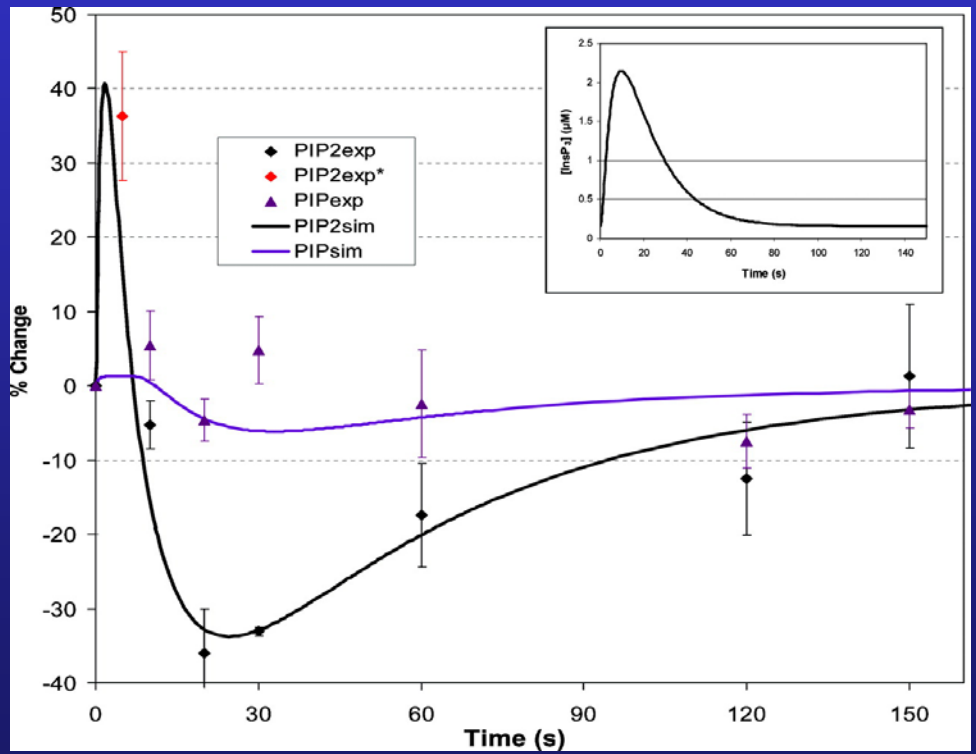
- We need a more quantitative analysis of biomolecules and their interrelationships.
- To understand design, we need to measure, in living systems, physical parameters such as force, stoichiometry of subunits, kinetics, material requirements, energy utilization and transduction
- *Collecting this comprehensive data set requires:*
  - *a coordinated effort to develop uniform standards,*
  - *a lexicon of engineering terms and definitions applicable to biological processes and structures, and*
  - *data systems to collect and analyze the data.*

BEGINNING A TEN-YEAR PROCESS

continued…

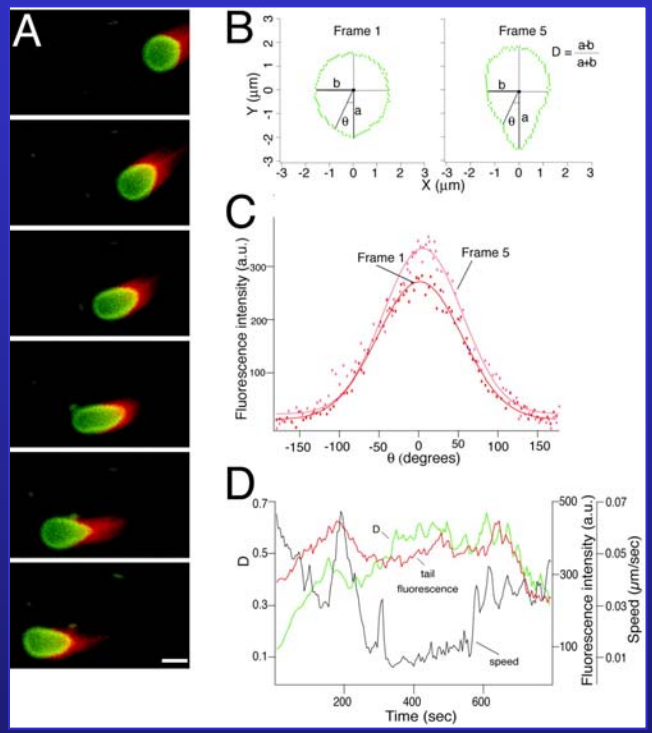
- As we develop this lexicon we will discover gaps in our ability to collect essential data.
- To complete the analyses, new tools and strategies will be discovered and applied.
- The endpoint of this activity will be a characterization of biomolecular systems in a format that will interface seamlessly with engineering specifications required to create blueprints for the design of new nanomachines or structures.
- Tools for measurement will be closely related to tools for manipulation.

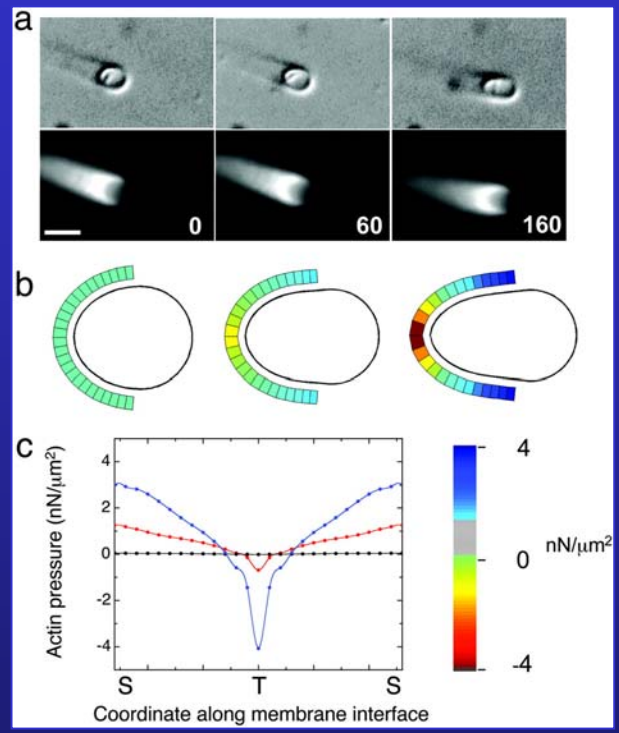
"…A mathematical model of phosphoinositide turnover based on this data predicted that PIP_2 synthesis is also stimulated by bradykinin, causing an early transient increase in its concentration. This was subsequently confirmed experimentally."



Kinetic analysis of receptor-activated phosphoinositide turnover.
Chang Xu, James Watras and Leslie M. Loew. J. Cell Biology, 2003, **161**:779-791

Changes in vesicle shape reflect changes in the forces generated by the polymerizing actin gel, and vesicles thus can be used as sensitive spatial and temporal force sensors. Here we characterize the spatial distribution and temporal dynamics of actin-based polymerization forces exerted on a phospholipid membrane.





Compression forces generated by actin comet tails on lipid vesicles
Paula A. Giardini, Daniel A. Fletcher and Julie A. Theriot PNAS, 2003, **100**:6493-6498

Probing polymerization forces by using actin-propelled lipid vesicles
Arpita Upadhyaya, Jeffrey R. Chabot, Albina Andreeva, Azadeh Samadani, and Alexander van Oudenaarden PNAS, 2003, **100**:4521-4526

CONTEXT FOR THIS INITIATIVE

The Nanomedicine Roadmap Initiative…

- depends on progress in the other *New Pathways to Discovery* Initiatives, requires building interdisciplinary *Research Teams of the Future*, and will benefit from *Re-engineering the Clinical Research Enterprise.*
- is a long-term, trans-NIH initiative widely applicable to the scientific and medical communities served by all of the NIH Institutes and Centers.

CONTEXT FOR THIS INITIATIVE
(continued)

The Nanomedicine Roadmap Initiative…

- is distinct from the several other nanoscience and nanotechnology research programs and opportunities supported by the NIH (www.becon.nih.gov/nano.htm), and
- complements NIH participation in the National Nanotechnology Initiative by providing unique knowledge about biological system design that will be used to engineer devices for use in other fields.

FLEXIBLE RESEARCH AUTHORITY

FY2004 L/HHS Appropriations Act and Conference Report

- …enter into transactions (other than contracts, cooperative agreements, or grants) to carry out research in support of the NIH Roadmap Initiative
- …may utilize such peer review procedures (including consultation with appropriate scientific experts) as the Director determines to be appropriate to obtain assessments of scientific and technical merit.

Implementation

- rapid turn-around
- intensive consultation with scientific community re. science & structure
- formulation process stimulates new partnerships
- review by team composed of NIH staff and review consultants

SCOPE OF CENTERS

- multidisciplinary -- biology, clinical, math, physics, chemistry, engineering, computational …
- biomedical focus of model system/theme -- e.g.,
  - pathway, motor system, transport
  - cell type, disease model
- toxicity, biocompatibility -- goal is to develop particles, materials and devices that can be used in vivo.
- broad (but not comprehensive) technological approach
- generality of tools (broadly applicable)
- design of tools: throughput, comprehensive measurement (à la HGP)
- operate as network of centers