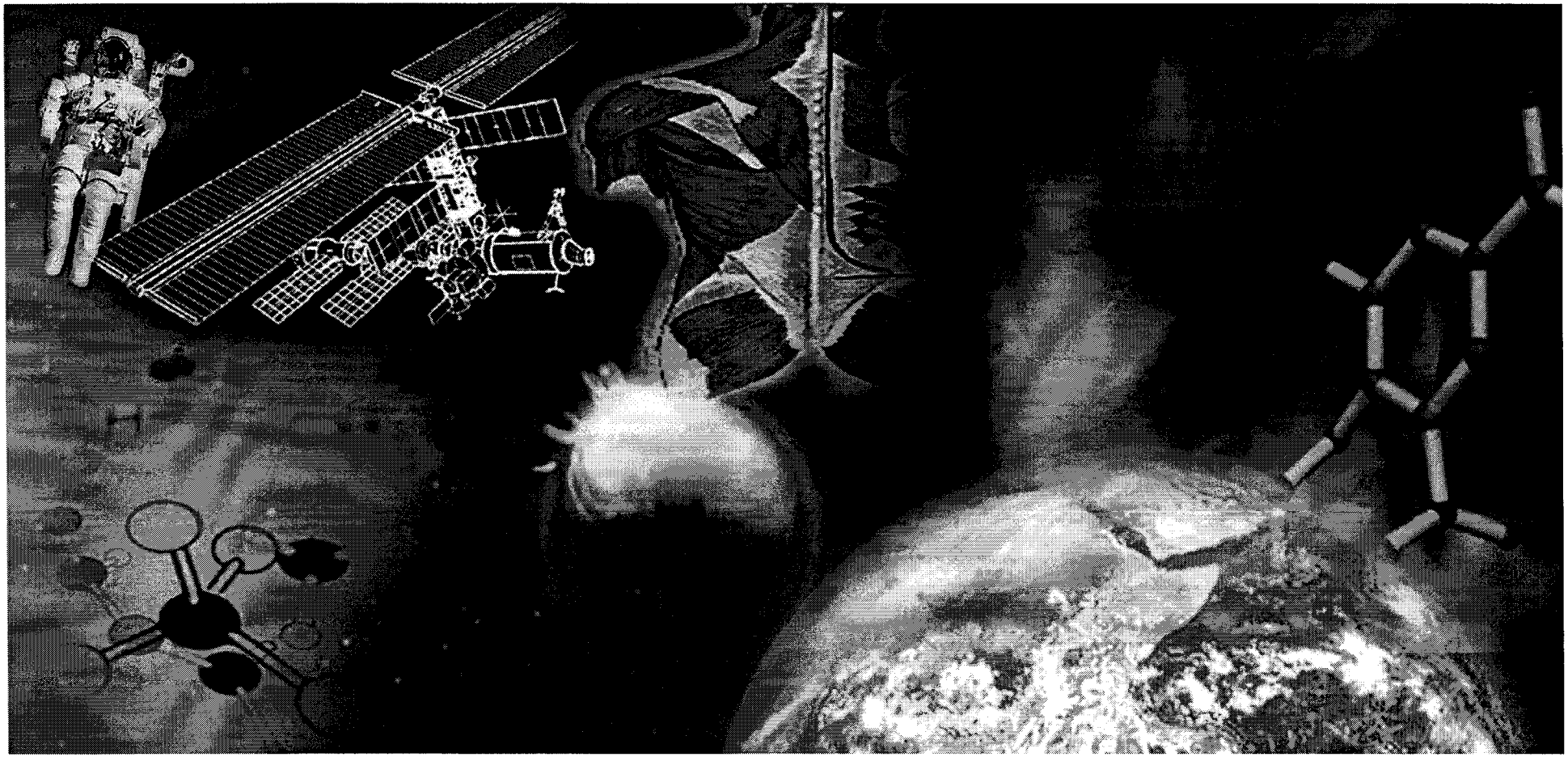


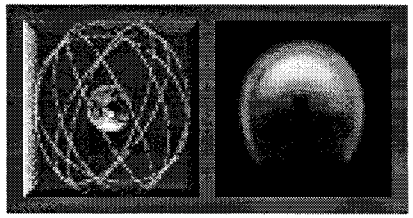
Biomolecular Systems Research Program

Physical Sciences Division
Office of Biological and Physical Research (Code U)

JPL

John W. Hines, Manager *Darrell Jan, Deputy Manager*
Biomolecular Physics and Chemistry Program

NASA

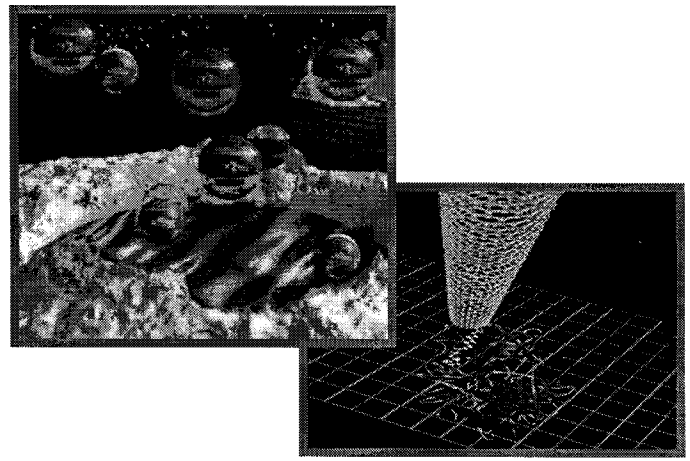


Division of Physical Sciences Research

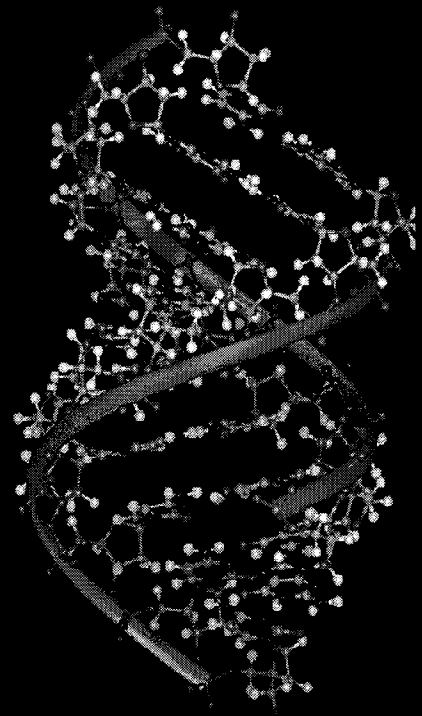
Organization

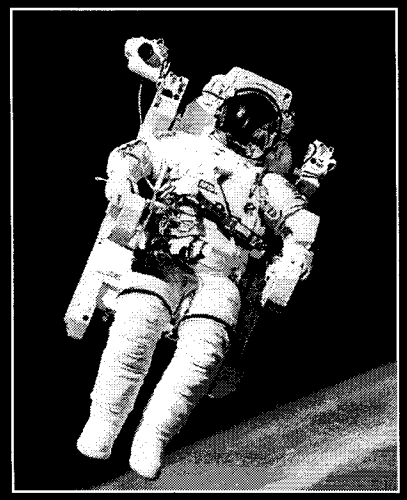
- Fundamental Microgravity Research
  - Fundamental physics
  - Materials science
  - Fluid physics
  - Combustion science
  - Exploration research
- **Biomolecular Physics & Chemistry**
  - **Atomic and molecular processes in biosystems**
  - **Biological sensing phenomena**
  - **Cellular components assembling mechanisms**

- Biotechnology & Earth-based Application
  - Cellular biotechnology
  - Macromolecular biotechnology
  - Earth-based applications



BIOMOLECULAR SYSTEMS RESEARCH PROGRAM





John W. Hines
Program Manager
Darrell L. Jan
Deputy Program Manager

Biomolecular Systems Research Program

NASA's Biomolecular Systems Research Program is an integrated research program focused on developing molecular level technologies to monitor cellular signals and processes with applications to crew health and safety, basic biology research, life detection, planetary protection, and nanotechnology

NASA has the capability to create a unique cross-disciplinary research program bringing the basic sciences of Physics, Biology, and Chemistry together with a wide range of Engineering Disciplines and Information Technologies. The resulting synergy and the access to Space will ensure that the Agency's contribution to Biological and Biomedical Research will be significant and long lasting.

Biomolecular Systems Research Program

- Monitor cellular signatures and processes at the molecular level
  - Conduct long-term scientific research
  - Develop enabling technologies
  - Deliver prototype micro- and nano- systems for the detection, imaging, recognition and monitoring of biological signatures and processes at the molecular level
- Conducted in partnership with the National Cancer Institute (NCI)
- Cross-cutting Research: NASA Applications Include
  - Astronaut health and safety (Bioastronautics)
  - Biological Research (Fundamental Biology)
  - Detection of molecular signatures of life (Astrobiology)
  - Processing of biology related information (Bioinformatics)
  - Molecular scale systems engineering (Nanotechnology)
  - Planetary protection (Space Science)
- NCI APPLICATIONS are primarily in the area of in-vivo and minimally invasive methods for the early detection and treatment of cancers.

Biomolecular Systems Research Program
Background/History

- *First NASA/NCI Workshop on Bio Molecular Systems*, June 2-4th 1999, Pasadena.
  - Dan Goldin, Richard Klausner, David Balitmore, Edward Stone
  - Organized by Carol Dahl and Leon Alkalai

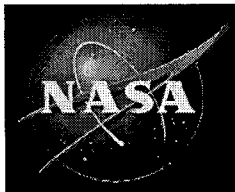
- *NASA/NCI Bio-Molecular Systems and Technology Working Group Meeting*, Washington, DC, April 13-14th, 2000
  - NASA/NCI Memorandum of Understanding

"*... define opportunities and critical directions of research needed to advance the development of technologies and informatics tools to enable minimally-invasive detection, diagnosis, and management of disease and injury ... technological breakthroughs in these areas will enable the development of revolutionary systems needed to support common and unique objectives of NASA and NCI ...*"

BSRP PROGRAM IMPLEMENTATION

- Extramural collaborative NASA/NCI research program:"Fundamental Technologies for the Development of Biomolecular Sensors.
  - peer-reviewed research and technology development projects
  - open solicitation (Broad Agency Announcement) released by NCI.
- Intramural NASA element: Biomolecular Systems Research Program (BSRP).
  - managed by Biomolecular Physics and Chemistry LCPO at Ames Research Center.
  - concentrated at Ames Research Center (ARC) and the Jet Propulsion Laboratory(JPL).
  - intramural projects are intended to complement the Extramural element and bridge the gap between fundamental R&D and NASA/NCI programs and mission objectives.

BPC Program Structure



BioMolecular Physics and Chemistry Program
JW Hines, Program Manager; D. Jan (JPL), Dep.

ARC Program Staff

Program Management Specialist
P. Fung

Grants/Contract Coordinator - A. Chu

Resources Mgr - D. Fencl

Admin Asst/Support - J. Fishman

Technology Development Manager
M. Flynn

JPL Program Staff

Technology Coordinator(s)

Biological Sciences - G. Bearman

Physical Sciences - L Alkalai

JSC Program Liaison
N. Pellis

Program Management and Administration

Systems Integration/Applications

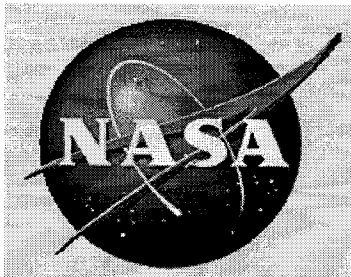
Leveraging and Collaborations

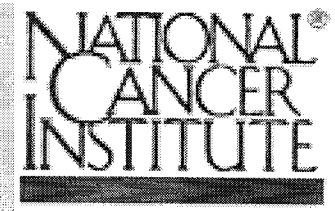
Biomolecular Systems Research Program
BSRP

Biosciences and Engineering Institute

Intramural Program

Extramural Program





Broad Agency Announcement No. N01-CO-17016-32

Fundamental Technologies for Development of Biomolecular Sensors

Issue Date: January 3, 2000

Due Date: April 30, 2001

Issuing Office: Treatment, Biology, and Sciences Section

National Cancer Institute

[In association with the NASA Office of Biological and Physical Research]

Fundamental Technologies for Development of Biomolecular Sensors

NASA and NCI are jointly seeking innovations in fundamental technologies that will support the development of minimally invasive biomolecular sensor systems that can measure, analyze, and manipulate molecular processes in the living body.

Specific areas of interest include novel:

- molecular recognition chemistries, materials, chemical composites, nanoparticles, nanostructures, agents, and devices suitable for in vivo use.
- strategies for in vivo signal generation and amplification.
- dynamic signal acquisition systems suitable for non-invasive, dynamic signal acquisition from deep tissues and systems of reduced scale suitable for manned space missions.
- tools for feature definition and extraction, including computational and mathematical approaches.
- approaches and multifunctional technology platforms to create an interface between in vivo detection and targeted intervention, including nanostructures/devices and novel materials and composites.

Proposals are encouraged from investigators from a variety of disciplines including, but not limited to, nanotechnology, chemistry, physics, engineering, biomedical research, and computational sciences; particularly as multidisciplinary teams.

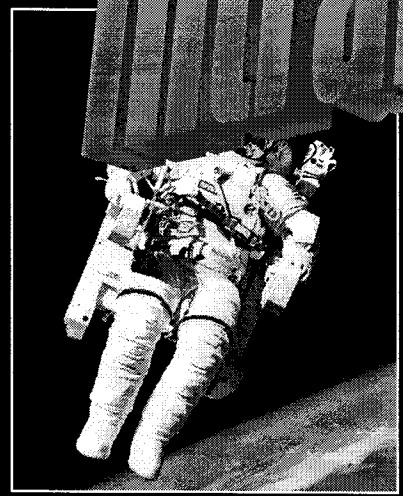
Fifty-Five Proposals Received.
Peer Review held 24-27 July, 2001
Est Awards = 1Q FY2002

BIOMOLECULAR SYSTEMS RESEARCH PROGRAM

NASA

Intramural Program

NATIONAL RESEARCH COUNCIL



Intramural Program Objectives

- Directed and focused effort
  - Supports NASA/NCI Collaboration and develops NASA Center core competencies (ARC & JPL)
  - Takes advantage of NASA center expertise, facilities, and knowledge of NASA applications.
  - Higher Technology Readiness Level than the Extramural program and directed at NASA missions.
  - Emphasizes system integration and technology infusion.
  - Facilitates the orderly and efficient transition from the extramural grants to NASA applications
  - Provides a pathway and process by which new and emerging technologies can be validated and integrated.

BSRP Intramural Program Elements

- Research into the development of biomolecular sensors and systems
- Areas of Technology Development
  - Biomolecular Signatures
  - Biomolecular Signal Amplification
  - Sensors and Manipulators
  - Biomolecular Informatics
  - Biomolecular Imaging
  - Integrated Biomolecular Systems
- Development of instrumentation platforms
- Prototype hardware and systems
- Testbeds and Specialty laboratory capabilities
- Unique leveraging or collaboration opportunities
- Technology interface with molecular community

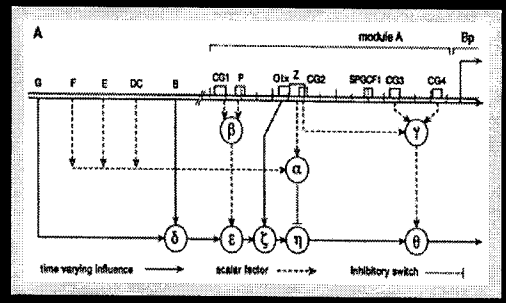
-Biosignatures

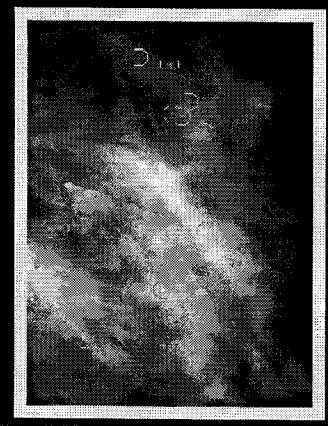
Signal Amplification

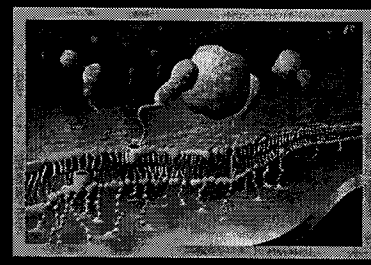
Biomolecular Sensors and Effectors:

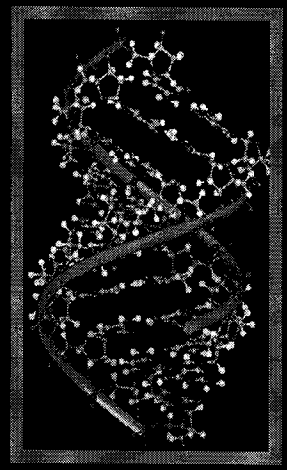
Biomolecular Imaging

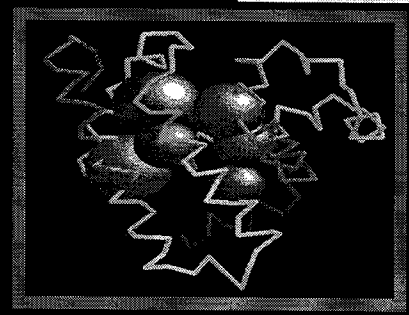
Bioinformatics/ Info. Proc.

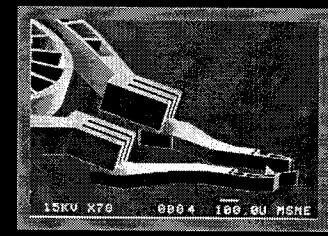


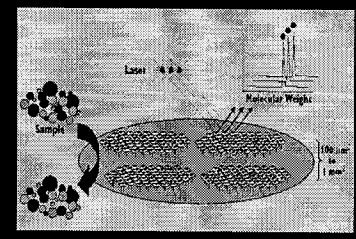


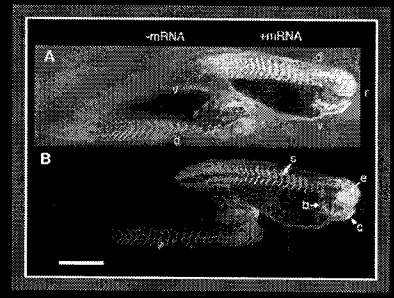


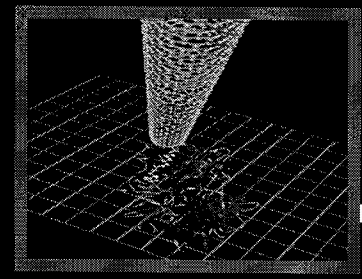


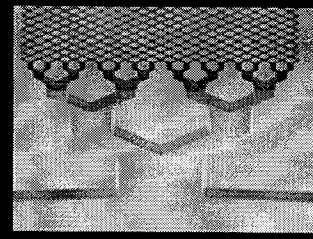


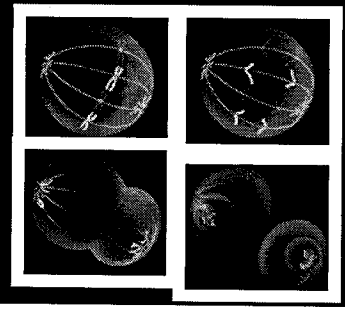


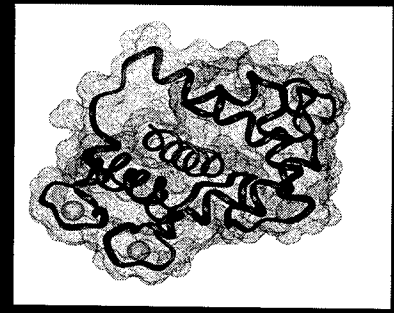


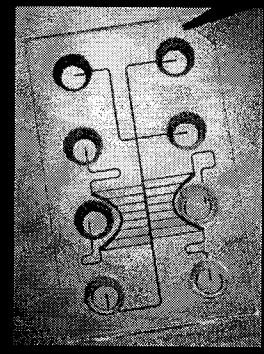








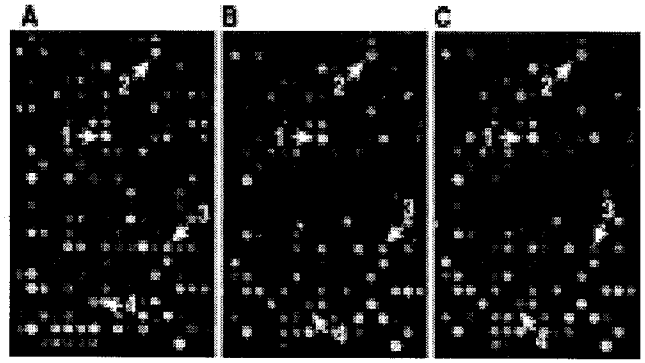




Biomolecular Signatures

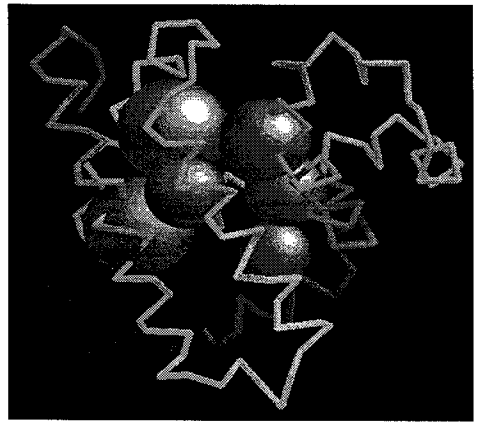
- Identification of signatures of life via thermodynamics and kinetics of metabolism
- Detection of molecular level structures and anomalies
- Detection of chemical disequilibria and microscale chemical analyses
- Models for biological metabolism
- Genomic and protein signatures indicative of disease

Gene Expression



Source: *Science*, Vol. 283, No. 5398, Jan 1999, pp. 83 - 87

Protein structure & function

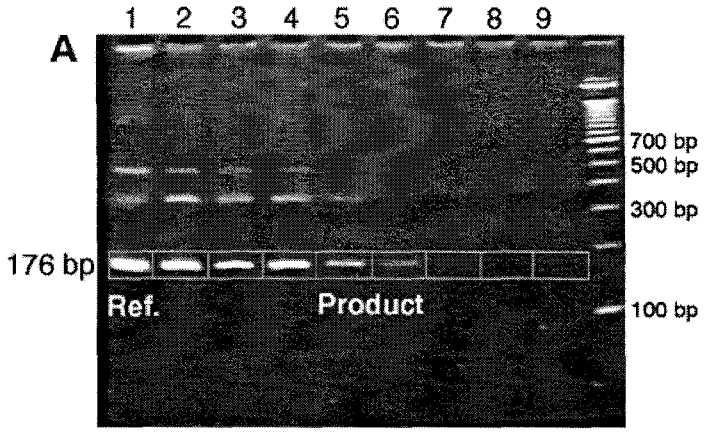


Genetic Alterations & Signatures

Signal Amplification

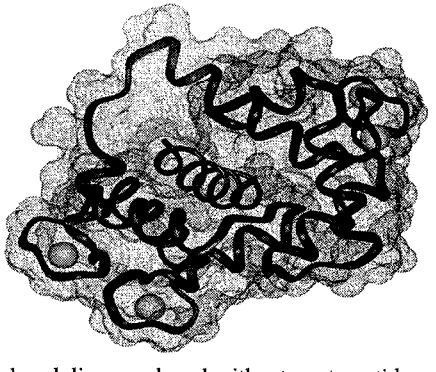
- Single, specific molecule detection among high background noise
- sensitivity enhancers
- Utilization of biological amplification or self-amplification of target molecules.
- Amplification methods to increase the probability of finding target molecules.
- Signal enhancement from targeted molecules

On-chip PCR



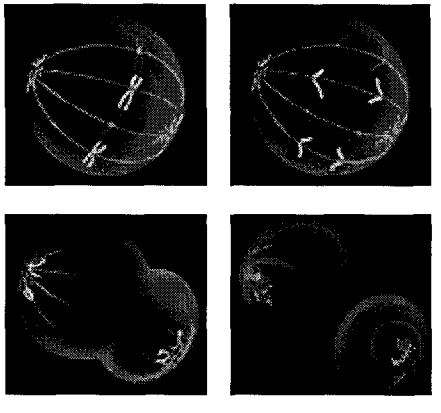
Source: *Science,* vol. 280, pp. 1046-1048. May 15, 1998.

Protein Labeling



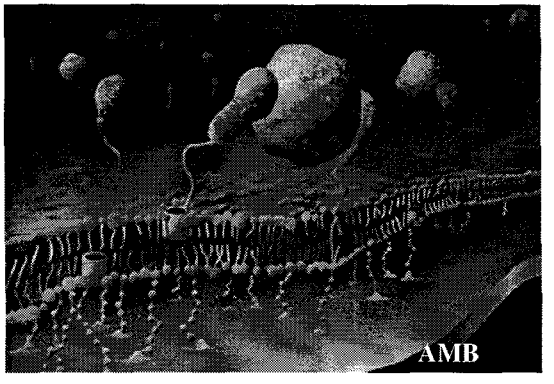
calmodulin complexed with a target peptide

Cell replication (mitosis)

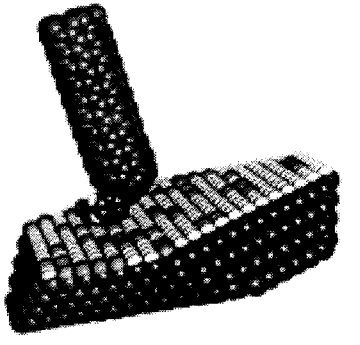


Biomolecular Sensing and Manipulation

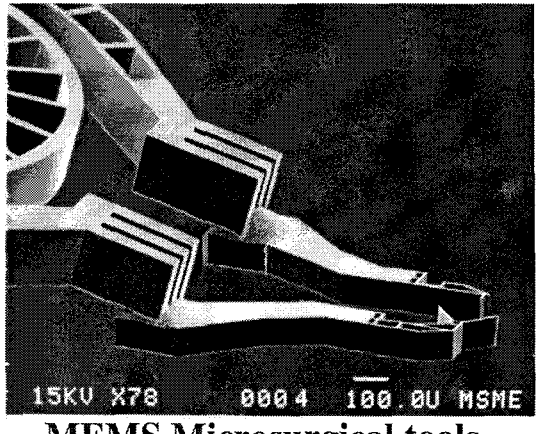
- Biomolecular Probes
- Nanotube-based actuators and force sensors
- Biologically-Based and Biomimetic Sensors
- Molecular Engineered Biosensors
- Molecular Manipulators
- Single Molecule Sensing and Recognition



Biomimetic ion channel sensors



Nanoscale sensing

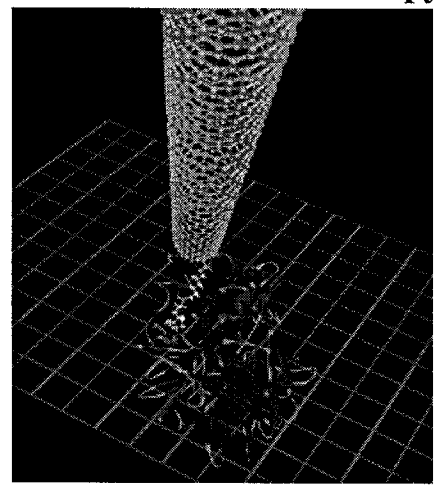


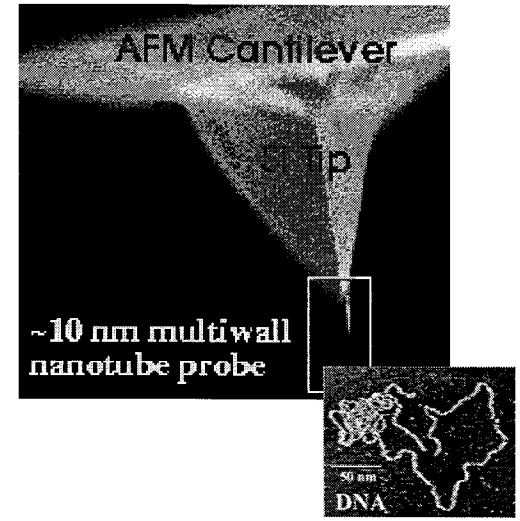
MEMS Microsurgical tools

Biomolecular Imaging

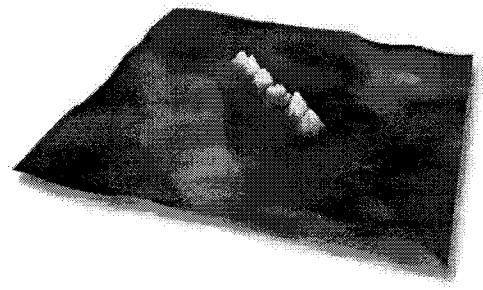
- New technologies for imaging protein expression in cells
- Nanoscale imaging to resolve protein or DNA structure, correlate with function
- Image cellular activities
- Development and refinement of optical/electromagnetic techniques

Carbon-nanotube-based chemical force microscopy



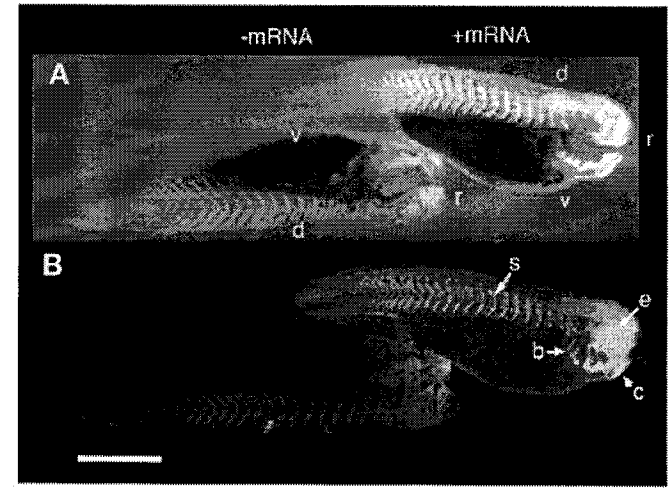


C. M. Lieber, Harvard



STM image of DNA helix

Contrast Enhancers

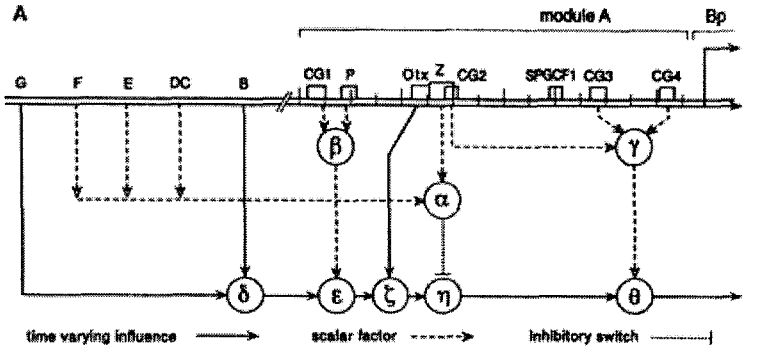


Biomolecular Informatics

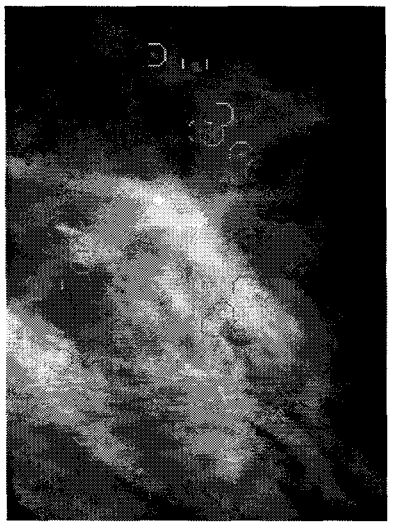
Data + modeling-> knowledge

- Data: Pattern recognition, data mining, data fusion
- Modeling: genomics, kinetics of biological processes and cellular function
- Knowledge Discovery: real-time medical diagnostics and treatment

Gene Regulation Computational Models



Source: Science, Volume 279, Number 5358 Issue of 20 Mar 1998, pp. 1896 - 1902

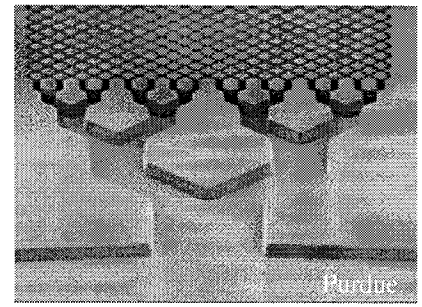


Source: Stanford University

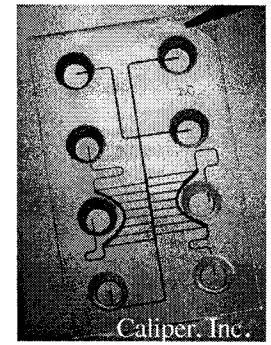
High Resolution Mammography Imaging: Data Intensive Computing and Visualization

Integrated Biomolecular Systems

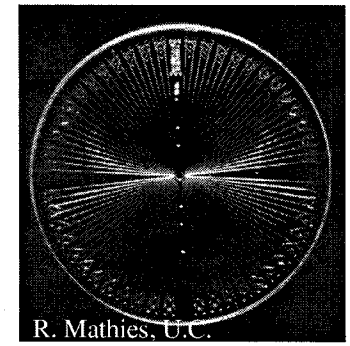
- Micro/Nanoscale biochemical sensors
- Microsurgical tools
- Microscale gene expression monitoring
- Bio-Astronautics: Human health, capability & environmental monitoring
- Intervention delivery and monitoring
- Biomimetic micro/nanosystems
- Molecular self-assembly and organization
- Power source, telemetry integration
- *In-vivo* sample acquisition and processing
- Nanoexplorer prototypes

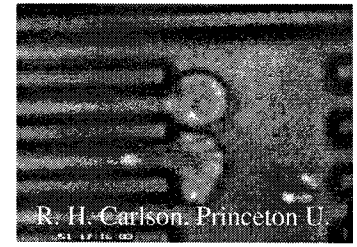


Microfluidic circuits

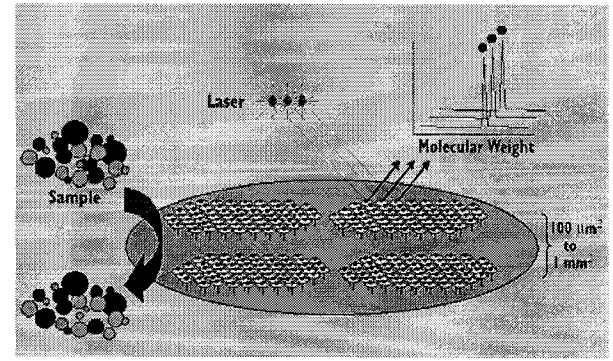


Microelectrophoresis





Cellular (WBC) Motility Characterization



Silicon-based immunological probes and biochemical sensors

BSRP FY01 Intramural Awards

ARC Selectees

Title	PI
Nanopores for Gene Sequencing	Viktor Stolc
Solid Surface DNA Sequencing	Viktor Stolc
Biosensor Nanovesicles	Eduardo A.C. Almeida
High-Throughput Metabolic Profiling by Multidimensional NMR and Mathematical Modeling of Metabolic Networks	Shoudan Liang
A New Ultrasensitive Technique for the Detection of Organisms and their Biomarkers	D. Summers
Technology Development of Miniaturized Far-Infrared Sources for Biomolecular Spectroscopy	Cun-Zheng Ning
High Resolution Imaging of Biological Samples	M. Meyyappan
Development of NASA-Specific Bioinformatics Environment	Andrew Pohorille
Computational Tools for Reconstruction and Discovery of Metabolic, Signal Transduction and Evolutionary Pathways	Andrew Pohorille
Fluorometric detection of microorganisms on sterilized surfaces	Chris McKay
Microbial Assay Technologies for Space (MATS): A Coordinated Ecosystem Response Assay Technology	L. Prufert-Bebout

JPL Selectees

The pharmacokinetics of the blood-brain barrier: applications in chemotherapy and astronaut health	Lambert, James
MEMS Ion Channel Sensors (MICS)	Nadeau, Hendrickje
Remotely coupled DC power for driving nanotubes	Siegel, Peter
Molecular complexes within cellular networks	Shapiro, Bruce, Mjoljness, Eric
Biomolecular imaging with atomic force microscope mediated Raman spectroscopy	Mark Andersen, Thomas Pike

NASA BioScience

and

Engineering Institute

Cooperative Agreement Notice
NASA BioScience and Engineering Institute

* Soliciting Proposals to Become a NASA BioScience and Engineering Institute (NBEI)

*DRAFT RELEASE:

Comments are invited from the community and should be directed to Dr. Don Roth at NASA Headquarters by June 1, 2001

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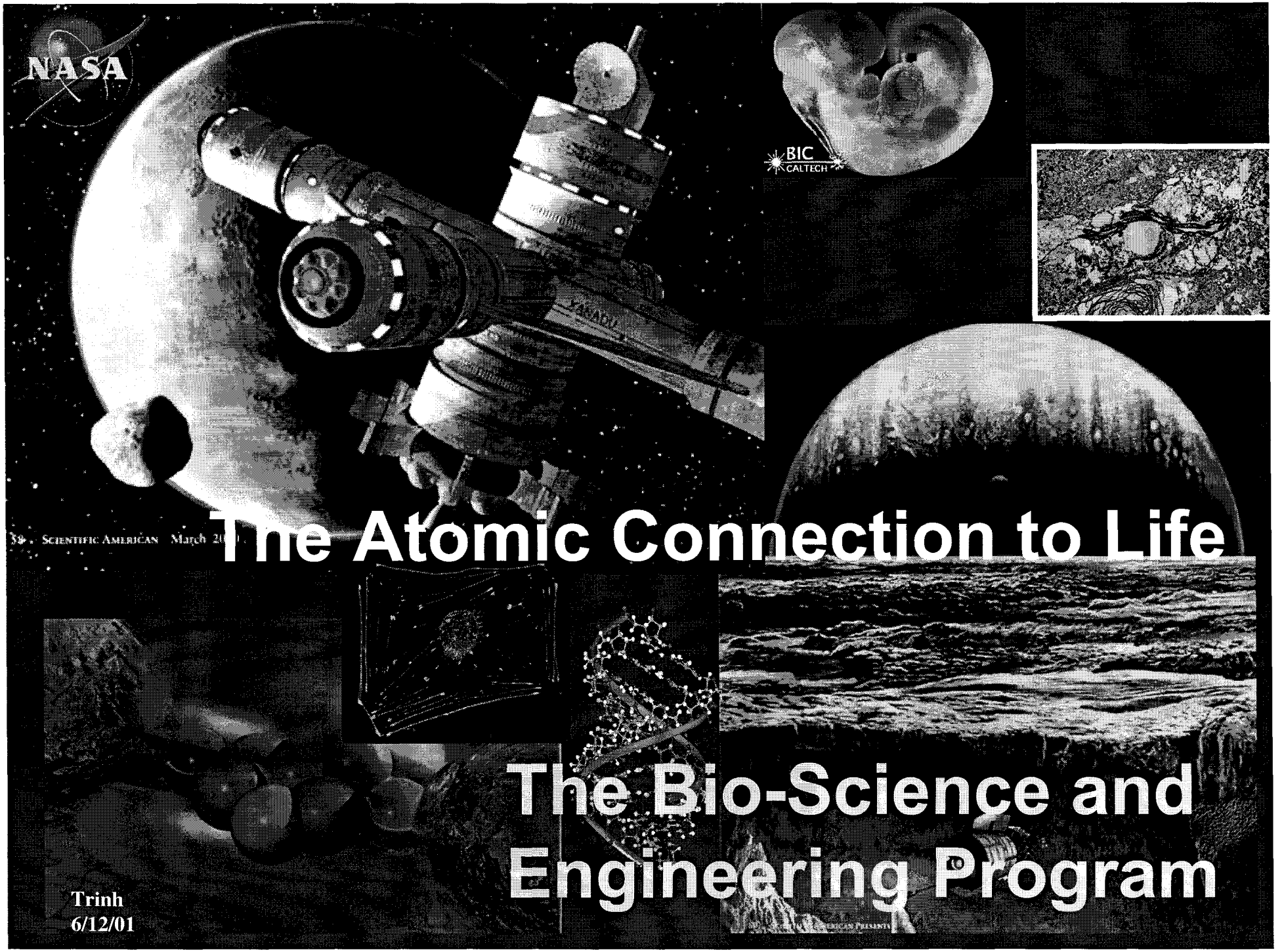
Notices of Intent Due: 8/9/01
Proposal Due Date: 9/9/01
Selections Announced: 1/11/02


NASA
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SCIENTIFIC AMERICAN March 20
The Atomic Connection to Life
The Bio-Science and Engineering Program
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6/12/01

The Bio-Science and Engineering Program

NASA- funded researchers have made ground-breaking advances in atomic and condensed matter physics, in colloidal physics and chemistry, and in cellular and macromolecular biotechnology. The theoretical understanding and the experimental tools thus made available can be fruitfully directed toward the study of biological systems to probe the transition from matter to life.

Scientific Insight generated by Microgravity-based Research

- Near convection-free environment leads to self-assembly of structures not possible at 1-g. Modeling of colloidal systems under these circumstances will drive the understanding of large-scale biological self-assembling systems.
    - Physical stimuli such as shear flow influence gene expression of specific cells. The microgravity environment may lead to the isolation of specific physico-chemical processes affecting molecular signals driving up and down regulation.
- Microgravity-like environments enhance cellular assemblies leading to structures with functional capabilities approaching those of integral organs. The understanding of the specific controlling physical processes will allow an enhancement of tissue engineering techniques on Earth and in space.
    - Mass and heat transport conditions in Microgravity significantly alter crystal growth processes for small macromolecules. Identification of the controlling factors will enhance the impact of applications of structural biology.
- Interfacial processes dominate in the reduced-gravity environment. Conversely, molecule-level interactions at interfaces may be more accessible in Microgravity.

The Bio-Science and Engineering Program

- The results of past low-gravity investigations have already hinted to the potential for significant advances in the understanding of complex and important issues affecting biological systems.

- It has been clearly shown that the complexity of these issues requires a focused but interdisciplinary approach.

- By using both molecular-scale techniques and gravity as a controlled variable, an integrated NASA research program bringing together rigorous theoretical, computational, and experimental methodology established in the relevant disciplines will make a unique and important contribution.

Outline

- What ?
- Why ?
- How ?

What ?

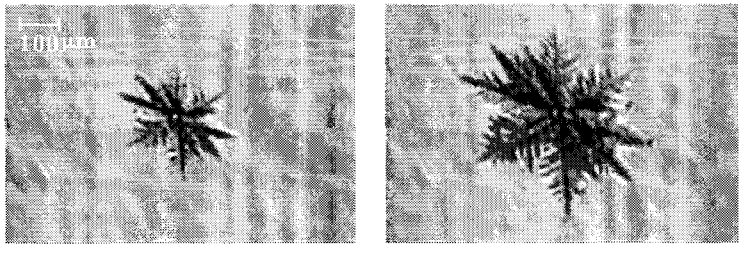
- A new cross-disciplinary scientific program bringing together physics, chemistry, biology, materials science and engineering to focus on understanding macromolecular assemblies controlling biological processes relevant to **space-based tissue engineering studies, cell biology, technologies insuring the health and safety of space flight, and the search for life in the universe**

- A program to apply newly discovered atomic and molecular-scale scientific methods and the theoretical understanding of **complex systems** to target issues associated with the molecular processes involved in the **emergence, maintenance, and evolution of living systems in space and on Earth**

- A new scientific flight program to drive the **next generation technological capabilities** needed to **fully utilize the low-gravity platforms** provided by the International Space Station and other spacecrafts

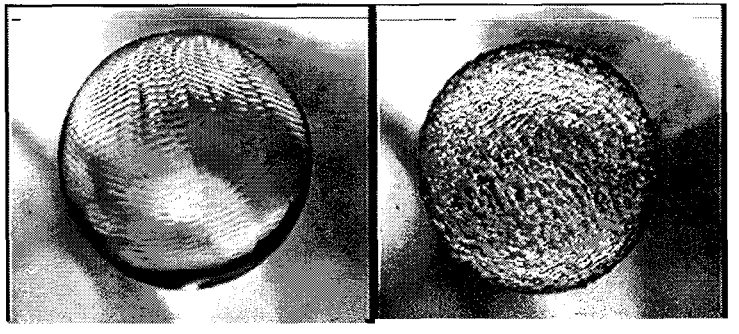
Complex Systems: From Fundamental Laws to Rich Diversity

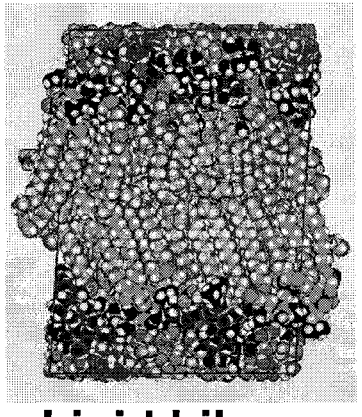
- Pattern Formation / Morphological instability in crystal growth
- Nonlinear dynamics and physiological rythms
- Macromolecular crystallization / Membrane proteins
- Self-assembling mechanisms / Mesoscale structures
- Surfactant dynamics / Complex fluids properties



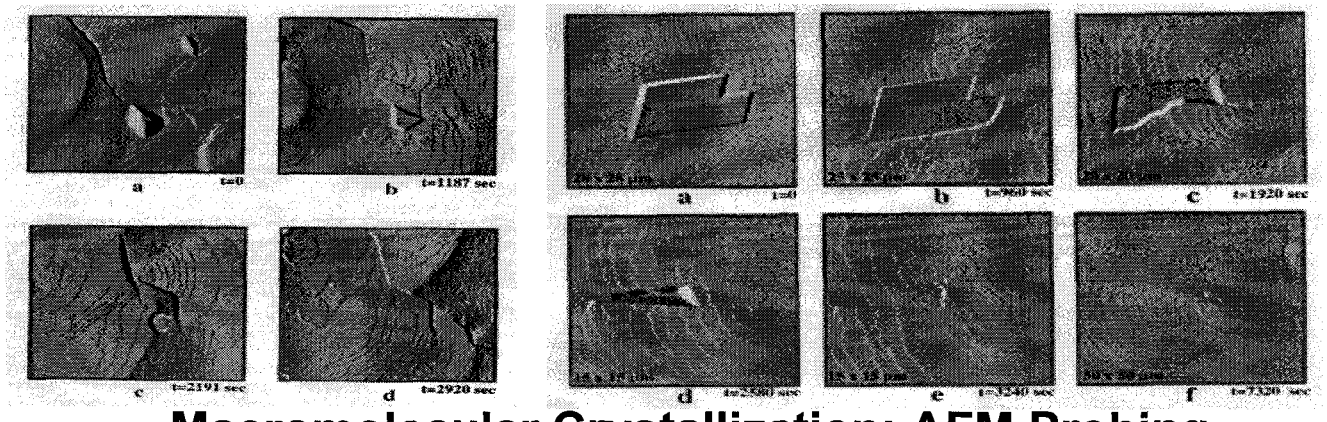
Dendritic crystal growth

Wave Turbulence





Lipid bilayer

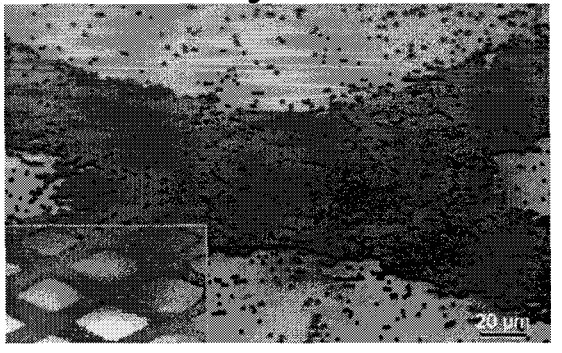


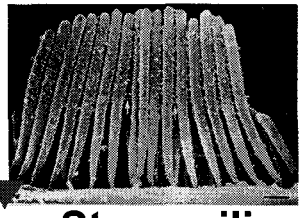
Macromolecular Crystallization: AFM Probing

Nano-technology through Biology

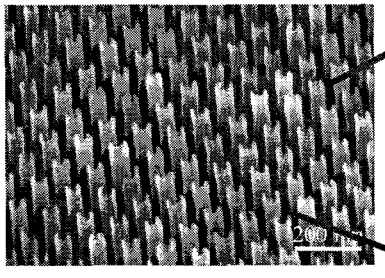
- Biology-inspired structures, properties, and functions
- Nano-scale observation, manipulation, and assembly
- Nano-micro-macro scale transition and process control development
- Macromolecular design based on biological programmed approach (DNA sequences)
- Biomaterials developed to couple biology and microelectronics

Electrophoretic assembly of colloidal crystals

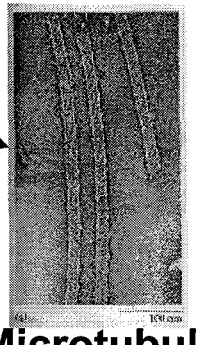




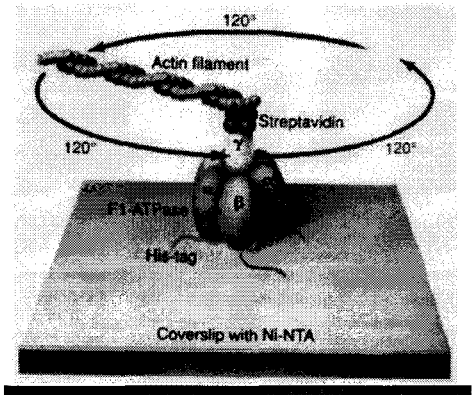
Stereocilia



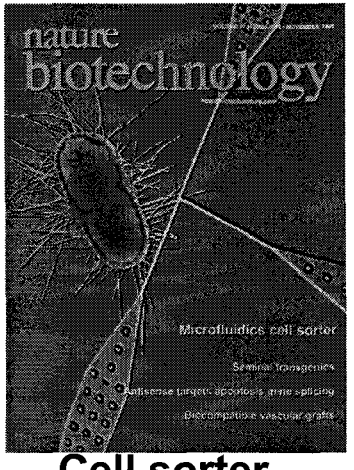
Nanotube arrays



Microtubules



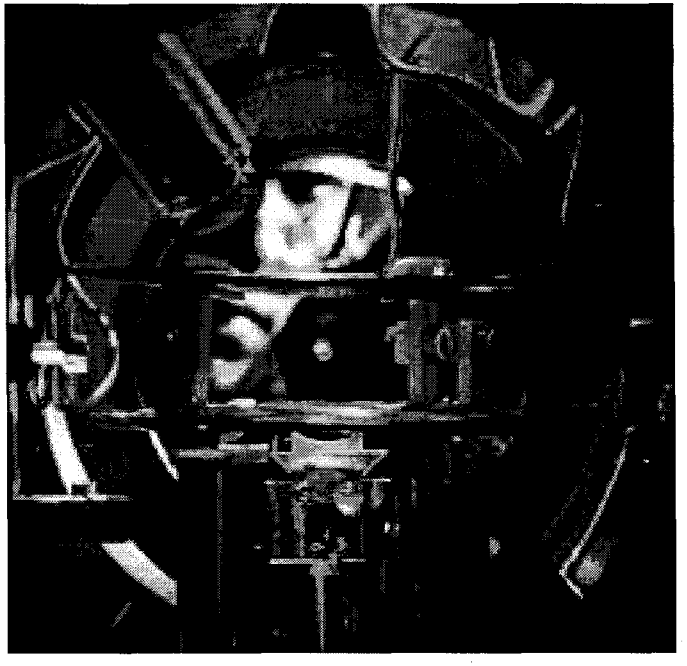
Molecular Motors



Cell sorter

Laser Tweezers

- Important new tool for molecular and cellular biology
- Allows study of biological system at single molecule and single cell level
- Can help bridge physics at atomic and molecular level, with microbiology
- Allows direct, real time observation of local dynamics
- Enables investigations with potential for new drug delivery systems (Phillips / NIST)
- Study of mechanisms for unique structures produced by RNA folding (Chu / Stanford)
- Self-assembly of phage: packaging of DNA into virus head (Tans, Smith, Bustamante)



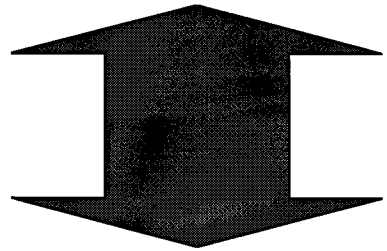
Cross-disciplinary Program

Contributing disciplines

Materials Science
Polymer engineering, Nanostructure control, Process modeling /control Crystallization processes, Biomaterials

Physics/Chemistry
Complex system physics, Protein folding modeling, Atomic / molecular tools, Self-assembly, molecular dynamics and chemistry

Engineering
Microfluidics, Transport processes, Surfactants dynamics, Rheological properties, Complex fluids



Biology Issues

Proteins function and physical structure / Chemical composition and specificity / Protein folding and chemical activity / Cell communication/ Physiological rhythms/ Molecular-scale motors / Hierarchical structures / Cellular sensors for stress, strain, and shear flow /

Why ?

•NASA has the unique opportunity to **significantly** impact scientific progress in biology and biotechnology by using its internal research expertise, its external multi-disciplinary investigators community, and its **access to space** to pursue in depth the **exciting topics revealed by low-gravity research**

- This new program will utilize the tools necessary to resolve atomic and molecular-scale processes, and it will contribute to the understanding of the **connection between the specificity of various cellular functions and the macroscopic processes in complex biological systems**

•NASA's contribution to the understanding of biological systems in space and on Earth will be significantly enhanced by establishing a new **integrated cross-disciplinary** research program that technologically connects the physical and biological sciences and uses its **unique microgravity expertise not readily available to other agencies**

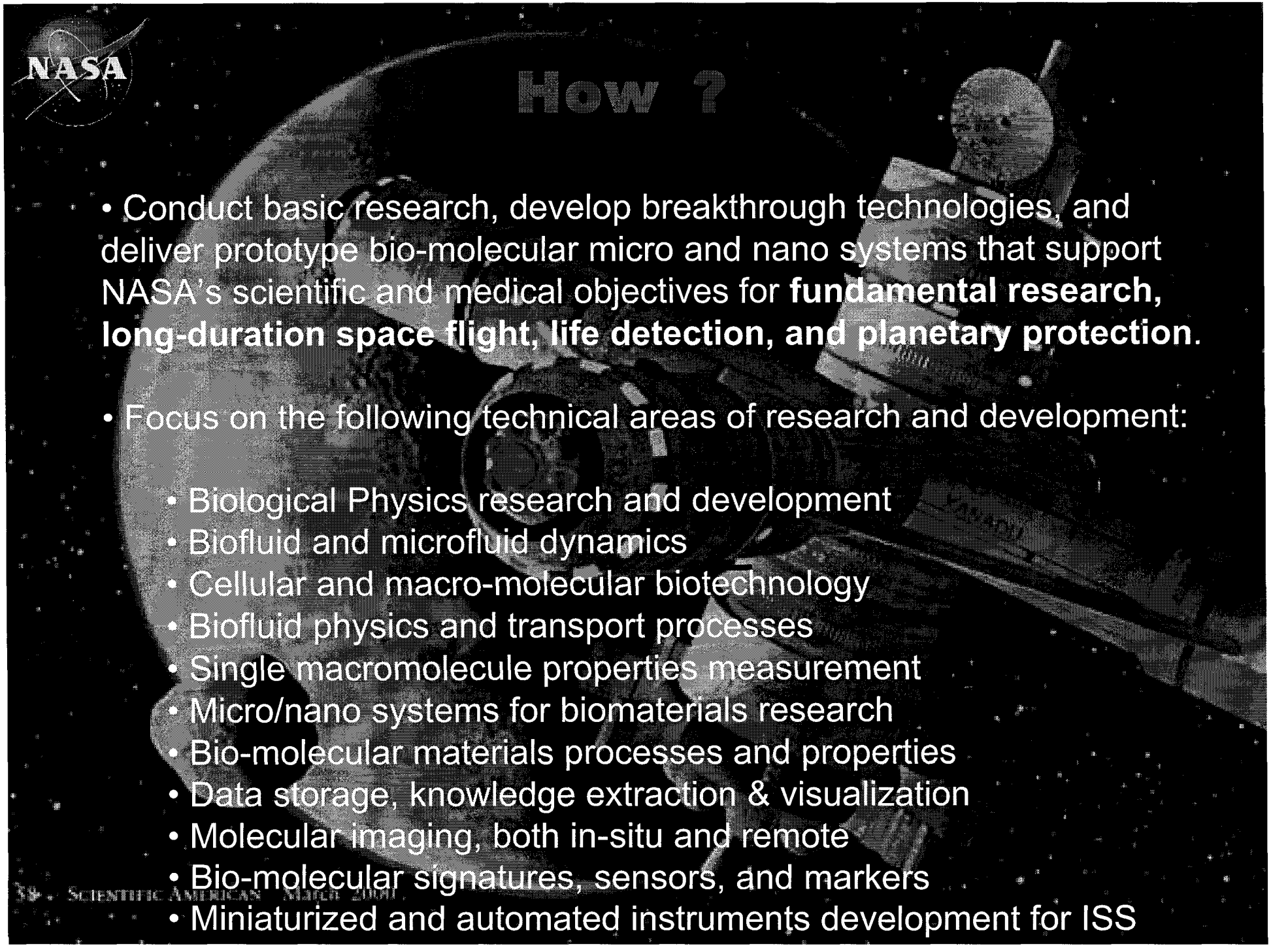
Bio-Science and Engineering Research
Rationale for a NASA New Initiative

- To initiate a new Bio-Science and Engineering cutting-edge research program at a productive and sustainable level, and to contribute to NASA's thrusts in Astrobiology, Fundamental Biology, Crew Health and Safety, Planetary Protection, and Spacecraft Systems, by carrying out fundamental research.

- To initiate the development of next-generation scientific tools and technology to enable new ISS science and applications experiments.

- To fully utilize the NASA physical sciences and engineering capabilities to enhance the Agency's biological and biomedical research.

- To reinforce the agency's commitment to provide rigorous foundations for **directed,** higher Technology Readiness Level NASA development efforts in collaboration with other US agencies and the private sector


NASA
How ?
• Conduct basic research, develop breakthrough technologies, and deliver prototype bio-molecular micro and nano systems that support NASA's scientific and medical objectives for **fundamental research, long-duration space flight, life detection, and planetary protection**.
• Focus on the following technical areas of research and development:
• Biological Physics research and development
• Biofluid and microfluid dynamics
• Cellular and macro-molecular biotechnology
• Biofluid physics and transport processes
• Single macromolecule properties measurement
• Micro/nano systems for biomaterials research
• Bio-molecular materials processes and properties
• Data storage, knowledge extraction & visualization
• Molecular imaging, both in-situ and remote
• Bio-molecular signatures, sensors, and markers
• Miniaturized and automated instruments development for ISS

Bio-Science and Engineering Research

- Program with funding authority at NASA HQ Code UG and Program includes three parts:
  1. Biomolecular Physics and Chemistry program
  2. Bio-Science and Engineering Institute
  3. Coordinated research with Cellular and Macromolecular Biotechnology, Fundamental Biology, Biomedical Research and Countermeasures, Advanced Human Support Technology, and Astrobiology programs

- Associated NRAs issued from NASA HQ. Selection authority at NASA HQ

- Interface to other Government Agencies for future partnerships

- Collaborative agreements with private sector companies as technology affiliates of the program

- Program element functions implemented at NASA centers: JPL, ARC, JSC, GRC, MSFC: