The NASA mission to explore the universe and search for life includes the goal of exploring the principles of biology through research in the unique natural laboratory of space. Important is the biological and physical research organizing question which asks: How does life respond to gravity and space environments? It includes four sub-questions:

1. How do space environments affect life at molecular and cellular levels?
2. How do space environments affect organisms throughout their lives?
3. How do space environments influence interactions between organisms?
4. How can life be sustained and thrive in space across generations?

Fundamental space biology is NASA’s agency-wide program for the study of fundamental biological processes through space flight as well as ground-based research that supports the NASA mission. Proposals are sought for research that:

1. Effectively make use of microgravity and other characteristics of space environments to enhance our understanding of fundamental biological processes;
2. Develop the scientific and technological foundations for a safe, productive human presence in space for extended periods and in preparation for exploration; and
3. Apply this knowledge and technology to improve our nation's competitiveness, education, and quality of life on Earth.

Ground-based and flight research is conducted on a broad spectrum of biological topics including cell and molecular biology, developmental and physiological biology, and how the space environment affects whole organisms and their interactions.
This subtopic area focuses on technologies that support the NASA Fundamental Biology Program in understanding the effects of gravity on plants and animals. The program supports investigations into the ways in which fundamental biological processes function in space, compared to their function on the ground. Given the Exploration Initiative newly assigned to NASA, this area of work and discovery is important to achieve the goals to explore the planets and allow plant, animal, and human habitation. To conduct these investigations, the program supports both ground and space flight research. The improved understanding of the role of gravity on plants requires innovative support equipment for observing, measuring, and manipulating the responses of plants to environmental variables. Areas of innovative technology development include:

- Measuring the atmospheric and radiation environment and optimizing the lighting and nutrient delivery systems for plants;
- Storage, transportation, maintenance, and *in situ* analyses of seeds and growing plants;
- Sensors with low power requirements and low mass to monitor the atmosphere and water (nutrient) environment, as well as automated control and data logging systems for the experiment containers to measure performance indicators, such as respiration (whole plant, shoot, root), evapotranspiration, photosynthesis, and other variables in plants;
- Data analysis and control;
- Modular seeding and/or planting units to minimize labor;
- Sensors for atmospheric, liquid, and solid analyses, including atmospheric and liquid contaminants, such as ethylene and other biogenic compounds, as well as analyses of hydroponic and solid media for N, P, K, Cu, Mg, and micronutrients;
- Remote sensors to identify biological stress; and
- Expert control systems for environmental chambers.

The improved understanding of the role of gravity on animals requires innovative instrumentation that tracks and analyzes from organism development, including gametogenesis through fertilization, embryonic development and maturation, through ecological system stability. Technologies may incorporate a variety of processes such as metabolism and metabolic control, through genetic expression and the control of development. Of particular interest are technologies that require minimal power and can noninvasively measure physical, chemical, metabolic, and developmental parameters. Such measurements will ultimately be made in environments at one or more of several gravity ranges, e.g., "microgravity" (0.01 to 0.00001 g), "planetary" gravity (1 g; 0.38 g or 0.12 g) or hypergravity (up to 2 g). Refined and stable measurements, however, are as important as gravity independence. Of interest are sustained instrument sensitivity, accuracy and stability, and reductions in the need for frequent measurement standardization. Parameters requiring measurement include pH, temperature, pressure, ionic strength, gas...
concentration ($O_2$, $CO_2$, $CO$, etc.), and solute concentration (e.g., $Na^+$, $K^+$, etc.). In the case of new techniques and instruments, a clear path toward miniaturization, reduction in power demands and increased space worthiness should be identified. Technologies applicable to plant, microorganism, and animal study applications include the following areas:

- Live support and energy management;
- Expert data management systems;
- Capabilities for specimen storage, manipulation and dissection;
- Video-image analysis for specimen (cell, animal, plant) health and maintenance;
- Sensors for primary environmental parameters and microbial organisms; and
- Electrophysiology sensors, biotelemetry systems and biological monitors carried on spacecraft.

### B2.02 Biological Instrumentation

**Lead Center:** ARC

**Participating Center(s):** JPL

The Fundamental Biology (FB) Program is the Agency lead for biological research and biological instrumentation and technology development, and focuses on research designed to develop our understanding of the role of gravity in the evolution, development, and function of biological processes. Increasingly, the research thrusts are directed at incorporating the most advanced technologies from the fields of cell and molecular biology, genomics, and biotechnology, to provide researchers with the most up-to-date methods to conduct their biological research. For these requirements, the capability to perform autonomous, *in situ* acquisition, and preparation and analysis of samples to determine the presence and composition of biological components is a highly desired objective. As the size of flight payloads becomes increasingly smaller, and information technologies permit smarter and more independent payload and device control and management, the realization of completely autonomous *in situ* biological laboratories (ISBL) on spacecraft platforms and planetary surfaces will become more desirable.

Biological and biomolecular, microbiological, and genomic research is enabling unprecedented insight into the structure and function of cells, organisms, and subcellular components and elements, and a window into the inner workings and machinations of living things. Techniques and technologies, which have evolved from the microelectronics and biological revolutions, have permitted the emergence of a new class of instruments and devices. Many devices, techniques, and products are now available or emerging, which allow measurement, imaging, analysis, and interpretation of the biological composition at the molecular level, and which permit determination of DNA/RNA and other analytes of interest. Advances in information systems and technologies, and bioinformatics, provide the capability to understand, simulate, and interpret the large amounts of complex data being made available from these biological-physical hybrid systems. These synergistic relationships are facilitating the development of revolutionary technologies in many areas.
Biological instrumentation technologies to support FB objectives are grouped into the solicited categories below.

**Biological Sample Management and Handling:**

- Technologies for remote, automated biosample and biospecimen collection, handling, preservation/fixation, and processing; and
- Modular, embeddable systems and subsystems capable of supporting a variety of tissue, liquid, and/or cellular specimens, from a wide range of biological subjects, including cells, nematodes, plants, fish, avians, mice, rats, and humans.

**In situ Measurement and Control:**

- Technology development for sensors, signal processors, biotelemetry systems, sample management and handling systems, and other instruments and platforms for real-time monitoring and characterization of biological and physiological phenomena.

**Genomics Technologies:**

- Technologies to enhance and augment research in genomics, proteomics, cell and molecular biology, including molecular and nanotechnologies, cDNA arrays, gene array technologies, and cell culture and related habitat systems.

**Bio-Imaging Systems:**

- Advanced, real-time capabilities for visualization, imaging, and optical characterization of biological systems. Technologies include multidimensional fluorescent microscopy, spectroscopy systems, and multi- and hyperspectral imaging.

**Biological Information Processing**

- Capability for automated acquisition, processing, analysis, communication, and archival and retrieval of biological data, and interface and transfer to advanced bioinformatics and biocomputation systems.

**Integrated Biological Research Systems and Subsystems**

- Integrated, experiment- and subject-specific biolaboratory modules and systems, providing complete flight prototype capability to support the above five categories.
B2.03 Understanding and Utilizing Gravitational Effects on Molecular Biology and for Medical Applications

Lead Center: JSC

Participating Center(s): ARC

Microgravity allows unique studies of the effects of gravitational effects on cell and tissue development and behavior. These studies use novel and advanced technologies to culture and nurture cells and tissues. Additionally, the ability to manipulate and/or exploit the form and function of living cells and tissues has significant potential to enhance the quality of life on Earth and in space through novel products and services, as well as through new science knowledge generated and communicated. This capability may lead to new products and services for medicine and biology. Current space research includes the development of space bioreactors for culturing fragile cells, which has applications in biomedical and cancer research; tissue engineering systems which take advantage of microgravity to grow 3-D tissue constructs; testing the effectiveness of drugs and biomodulators on growth and physiology of normal and transformed cells, and methods for measuring specific cellular and systemic immune functions of persons under physiological stress. Biotechnology research systems also are being developed for microgravity research on the International Space Station and future space-based laboratories. Studies of this nature are critical to our understanding of how the space environment affects astronaut health, and for maintaining a healthy environment for astronauts during missions of exploration.

Specific areas of interest are:

- New methods for culturing mammalian cells in bioreactors, including advanced bioreactor design and support systems; microprocessor controllers; and miniature sensors for measurement of pH, oxygen, carbon-dioxide, glucose, glutamine, and metabolites. Neural fuzzy logic network systems for the control of mammalian cell culture systems. Methods to minimize biofilm formation on fluid-handling components, sensors and bioreactors. Spectroscopic and biochemical analysis of biofilm formed in bioreactors. Micro-scale bioreactors for biomonitoring of radiation and other external stressors.

- Technologies that allow automated biosampling and bio-specimen collection, handling, preservation/fixation, and processing in cellular systems. Methods for separation and purification of living cells, proteins, and biomaterials, especially those using electrokinetic or magnetic fields that obviate thermal convection and sedimentation, enhance phase partitioning, or use laser light and other force fields to manipulate target cells or biomaterials.

- Techniques or apparatus for macro-molecular assembly of biological membranes, biopolymers, and molecular bio-processing systems; bio-compatible materials, devices, and sensors for implantable medical applications including molecular diagnostics, in vivo physiological monitoring and microprocessor control of prosthetic devices.

- Methods and apparatus that allow microscopic imaging including hyperspectral fluorescent, scattering and absorption imaging, and biophysical measurements of cell functions; effects of electric or magnetic fields, photoactivation, and testing of drugs or biocompatible polymers on live tissues. Integrated instrumentation for separation and purification of RNA, DNA, and proteins from cells and tissues.

- Quantitative applications of molecular biology, fluorescence imaging and flow cytometry, and new methods for measurement of cell metabolism, cytogenetics, immune cell functions, DNA, RNA, oligonucleotides, intracellular proteins, secretory products, and cytokine or other cell surface receptors. Small scale mass
spectrometers. Means to enhance and augment genomics/proteomics techniques, including molecular and nano-scale tools. Development of novel fluorophores that tag proteins mediating cellular function, particularly those that can be excited using solid-state lasers.

- Micro-encapsulation of drugs, radiocontrast agents, crystals, and development of novel drug delivery systems wherein immiscible liquid interactions, electrostatic coating methods, and drug release kinetics from microcapsules or liposomes can be altered under microgravity to better understand and improve manufacturing processes on Earth.

- Miniature bioprocessing systems that allow for precise control of multiple environmental parameters such as low level fluid shear, thermal, pH, conductivity, external electromagnetic fields, and narrow-band light for fluorescence or photoactivation of biological systems.

- Novel low temperature sample storage methods (-80°C and -180°C) and biological sample preservation methods. Methods to reduce launch/return mass of biological samples and support reagents.

- DNA template for molecular wiring that permits macro- to nanoscale connectivity. Nanoscale electronics based on self-assembling protein-based molecular structures.

- Computer models and software that better handle large numbers of coupled reactions in cell science systems.

- Tools and techniques to study mechanical properties of the cell: subcellular rheology, cell adhesion, affect of shear flow, affects of direct mechanical perturbation. Tools and techniques to facilitate multiple simultaneous probing and analyzing of a cell or sub-cellular region (examples include atomic force microscope coupled with microelectrode or micro-Raman, Optical trap)

- Nanosensors for sub-cellular measurements: ultra-microelectrodes with less than 1µ diameter including cladding, nanoparticle reporters that provide spectroscopic information, and other novel intracellular sensor devices to provide spectroscopic data on intracellular processes.