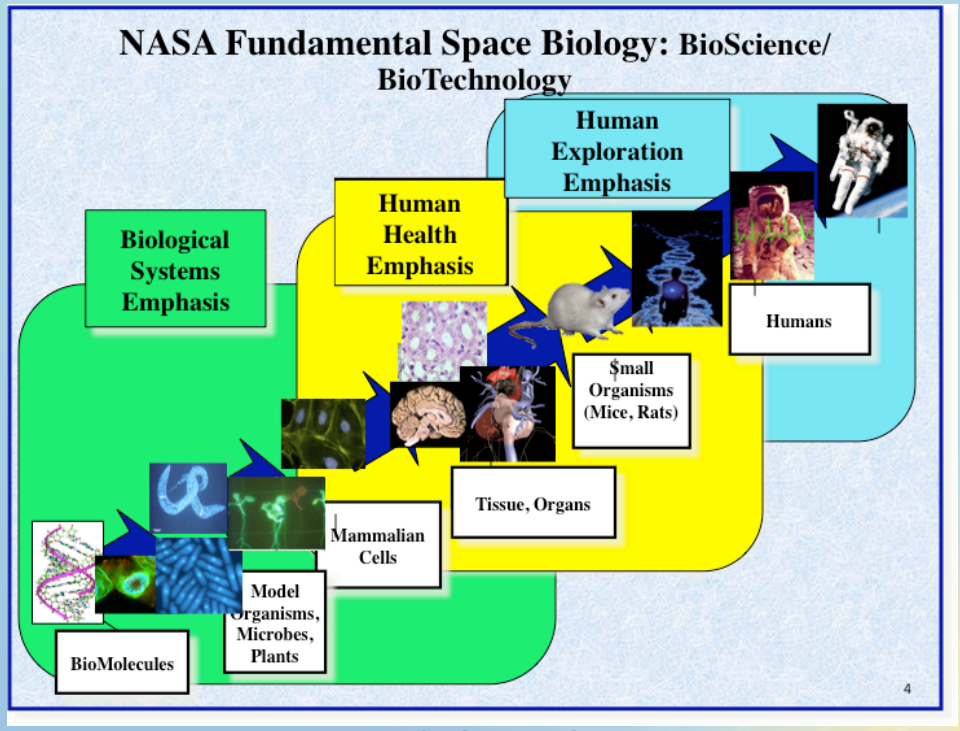
The NASA Fundamental Space Biology Science Plan 2010-2020



GOALS

- Sponsor competitively solicited FSB research to create new knowledge of how biological systems adapt to space and that can translate into Earth benefits
- Use ISS, free-flyer, ground-based analogues or other venues to conduct cutting-edge FSB research
- Maintain an internationally competitive United States FSB scientific community
- Develop cutting edge technologies to facilitate conduct of biological research in space flight
- Train and inspire the next generation of U.S. Space Biologists

The NASA Fundamental Space Biology Science Plan 2010-2020

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EXECUTIVE SUMMARY

NASA's Fundamental Space Biology Program (FSB) has been a world leader in advancing our knowledge of the role and influence of gravity on living systems. Both scientific and technological advances have been made including direct contributions to human exploration. Thousands of scientists and engineers have been educated over the four decades of NASA's FSB Program. With the new biotechnologies of the 21st century, the FSB Program is ready to spearhead new discoveries and benefits to both human exploration and humankind on Earth.

What is the science that NASA needs to do? *"An integrated multidisciplinary approach that encompasses all levels of biological organization… from molecules to cells to tissues to organs to systems to whole organisms*, a*nd employs the full range of modern experimental approaches." National Research Council, 1998. "Strategy for Space Biology and Medicine in the New Century."* This goal has been reaffirmed in many workshops: "*To investigate how organisms respond, over multiple generations, to an environment for which they have never been evolutionarily adapted." Nobel Laureate Baruch Blumberg. "Genomics on the International Space Station Workshop."*

FSB has three primary goals: 1) to effectively use microgravity and the other characteristics of the space environment to enhance our understanding of fundamental biological processes; 2) to develop the scientific and technological foundations for a safe, productive human presence in space for extended periods and in preparation for exploration; and 3) to apply this knowledge and technology to improve our nation's competitiveness, education, and the quality of life on Earth.

FSB will achieve these goals using three program elements: 1) Cell and Molecular Biology and Microbial Biology - studies of the effect of gravity and the space environment on cellular, microbial and molecular processes; 2) Organismal & Comparative Biology - studies and comparisons of responses of whole organisms and their systems; and 3) Developmental Biology – studies of how spaceflight affects reproduction, development, maturation and aging of multi-cellular organisms

This FSB Science Plan provides a roadmap for what FSB activities should be conducted and when for the 2010-2020 decade of the 21st century. The following is a summary of roadmap contents, goals and objectives. The table on page 4 is a synopsis of the major FSB activities in each of the program three elements and hardware development to be conducted over the next 10 years. The cascade indicates their priorities, and the order in which they need to be done to complete the plan.

FSB program/goals are to:

- Strive for U.S. excellence in Space Biology – Cell and Molecular, Microbiology, Plant and Animal Biology, Developmental Biology
- Contribute to basic knowledge of effect of space on living systems and maximize the probability of achieving results that can translate into Earth benefits
- Contribute to the base of knowledge that will facilitate human countermeasure development
- Optimally utilize ISS, as well as other ground and flight platforms
- Perform technology/hardware development that will enable new science
- Solicit community involvement in setting research goals and objectives

Current and future research platforms for gravity-dependent research are:

- Ground-based research will develop hypotheses for flight experiments, including hypergravity and hypogravity simulations
- Flight experiments will use the most appropriate and cost-effective platform to achieve the science results – ISS, free flyers, sub-orbital

FSB research objectives will:

- Rebuild the U.S. Space Biology user community for the next decade
- Add ISS research capabilities for whole animal and plant biology
- Maximize research capability by providing state-of-the-art automated technology and analytic capabilities wherever possible.

Current and planned FSB experiments:

- Are built on past NRC study recommendations, most notably the 1989 and 1998 NRC Space Studies Board Reports
- Roadmap will be adjusted based on the NRC Decadal Survey Report recommendations to be announced in late 2010. Decadal survey commissioned by Congress to plan Life and Physical Sciences research activities for 2010-2020.

FSB future activities will include:

- Regular NRA's to reengage the U.S. space biology community
- Preparation to implement a prioritized set of science to maximize whatever resources are available
- Work with international partners and other U.S. agencies to achieve objectives.

FSB - SPACE LIFE SCIENCES FROM MOLECULE TO ORGANISM **2010-2020 (Maximum of 4 High priorities/2yr)**

FSB Program Elements	2010-11	2012-13	2014-15	2016-17	2018-20
Research 1) Cell Biology & Microbiology; 2) Organismal & Comparative Biology; 3) Developmental Biology					
Ground Studies	NRAs	NRAs	NRAs	NRAs	NRAs
ISS Experiments	Flight NRAs		Flight NRAs		
	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments
Bion Free Flyer Exps	Bion M-2 (ILSRA ESA) AG rodents	Bion M1 Flt Experiments, rodents	Bion M2 Flt Expts; Bion M3 (ILSRA??)	Bion M3 Flt Experiments, onboard radiation	US/Russ TBD
Dragon Free Flyer or other FF Exps	Test using current experiments	TBD	TBD	TBD	TBD
Nanosat/Microsat Exs	MoO-1 and MoO-2	Flight NRA	MoO-3 and 4	Flight NRA	MoO 5 and 6
Hardware Development					
ISS Animal Habitat	Phase A/B to CDR	Flight-rated by 2013	certify habitats/ long duration missions	Use in Flight Experiments	Use in Flight Experiments
ISS Plant Habitat	Assess requirements & existing capabiilities; perform trade study; Phase A/B to CDR	Complete hardware & flight qualification begin flight application in 2013	Use in Flight Experiments	Use in Flight Experiments	Use in Flight Experiments
Glovebox	Assess requirements & existing capabiilities; perform trade study; initiate Phase A/B	Fabricate, qualify and launch to ISS	Use in Flight Experiments	Use in Flight Experiments	Use in Flight Experiments
New Hardware for Model Organisms	Qualify CCM, SLCC, ADF, and EMCS nematodes, Drosophila for ISS	Use in Flight Experiments	Use in Flight Experiments	Use in Flight Experiments	Use in Flight Experiments
Adv. Tech. Planning	Workshop - community input	Workshop -community input	Workshop	Workshop	Workshop
Adv. Tech. Development	In situ Monitoring/Analysis Instrumentation	In situ Monitoring/Analysis Instrumentation	In situ Monitoring/Analysis Instrumentation	Use in Flight Experiments	Use in Flight Experiments
STEM Activities	Integral part of grants, GSRP, Post-doc Program	Ongoing	Ongoing	Ongoing	Ongoing

NOTE: Specific priorities for each NRA will be drawn from the high priority science questions for each program element as identified in the FSB Science Plan & updated from Decadal Survey. Hardware priorities will be established consistent with what is required to support highest priority science. New advanced technologies will be determined by workshops and the science drivers as stipulated in the FSB Science Plan and NRA's and in consideration of recommendations from NASA advisory committes, e.g. the Decadal Planning Team.

Chapter 1 - Program

Introduction

For an estimated 3.8 billion years, the evolving microorganisms, plants, and animals on Earth lived and diversified in a consistent physical context of gravity, partially shielded from the magnetic fields and radiation of outer space. Trends toward more complex environmental factors, particularly the effects of other species, have exerted further pressures on the genetic complement of Earth's life forms. Currently, with an almost 4 billion year history of exposure to the Earth's environment, terrestrial life is well adapted to their home planet. The future holds the prospect of a sudden and rapid change for many Earth bound life forms—the prospect of extended travels beyond their planet of origin.

At the beginning of our ventures into space, the hazards and risks of spaceflight were unknown. Some feared that in the absence of gravity the heart would not pump properly, problems in digestion would occur, and radiation in low Earth orbit (LEO) would cause mutations and increase cancer risk. Animals and a variety of other organisms were used during the early years of spaceflight to evaluate such risks and demonstrate that spaceflight was safe for human exploration. In addition, biologists began using the unique environment of space as a tool to understand how life adapts to changes in gravity and how it responds to the hazards of space radiation. During the past 50+ years, space biologists have been able to identify and clarify many of the effects of spaceflight on representative living systems, from the cellular, tissue and system levels, to the whole organism. We've learned much about how life reacts to the challenges of spaceflight and the space environment, but many of the mechanisms living systems use to sense and react to such challenges remain unknown.

The Fundamental Space Biology Program (FSBP) grew out of NASA's Life Sciences Program of the 1960's. Initially called, Space Biology, the program was transferred to NASA Ames Research Center (ARC) from NASA Headquarters in 1996. In the years since its relocation, the program has increasingly focused on using the rapidly evolving technologies of cell and molecular biology to answer basic questions about the effects of the space environment on biological processes. The FSBP intends to learn how the changes associated with space travel will affect a diverse group of microorganisms, plants, and animals. The program focuses on the effects of gravity across the g-spectrum, i.e., from hypo- to hyper-gravity. It also covers the biological effects of modified radiation fluxes, altered magnetic fields, and the interaction of species in the unusual environments of space and spacecraft.

The Science of Fundamental Space Biology

Throughout the course of evolution, gravity has greatly influenced the morphology, physiology, and behavior of life. For example, the musculoskeletal system evolved to support body mass as aquatic animals transitioned to land. Similarly, the colonization of land by upright plants was facilitated by the production of structural reinforcement compounds such as lignin. Spaceflight experiments, capitalizing on the microgravity environment to shed light on the production of these compounds, have found that although lignin biosynthesis is decreased during spaceflight [Cowles, 1994; Sato, 1999), it is still produced in sufficient quantities to provide requisite mechanical stress responses (Kwon, 2001).

In order to orient and ambulate in their environment, organisms have developed ways to sense gravity and translate this information into a controlled response; hence the sensorimotor system evolved in animals, and analogous gravity sensing mechanisms evolved in plants. A robust cardiovascular system developed to maintain an appropriate blood supply and pressure in the various organs of the mammalian body. The development of the phloem and xylem vasculature in plants mirrors this development. Understanding how these physiological systems sense, adapt and respond to gravity cannot be fully achieved on the ground; it requires the use of spaceflight, i.e., the use of microgravity as an investigative tool. Just as one needs to examine the entire light spectrum in order to determine the capabilities and mechanisms of the visual organs, so too must we utilize the complete gravity spectrum, from hypogravity to hypergravity, to understand how gravity influences life across the gravity continuum, i.e., both on and off the Earth.

The FSBP uses model organisms (e.g., well characterized microbes, plants, insects and animals) to understand how organisms, including humans, respond to the space environment. Utilizing the new genetic tools of the 21st century, FSB scientists probe deeply into the underlying mechanisms of adaptation to the space environment in order to determine the fundamental ways life uses gravity to regulate and sustain its growth, metabolism, reproduction and development, and also how it repairs damage and protects itself from infection and disease. Such basic knowledge provides the foundation on which NASA's biomedical researchers build approaches and countermeasures to the problems confronting human exploration of space (Figure 1). In addition such knowledge has provided, and will continue to provide, benefits to the health and well being of those on the Earth.

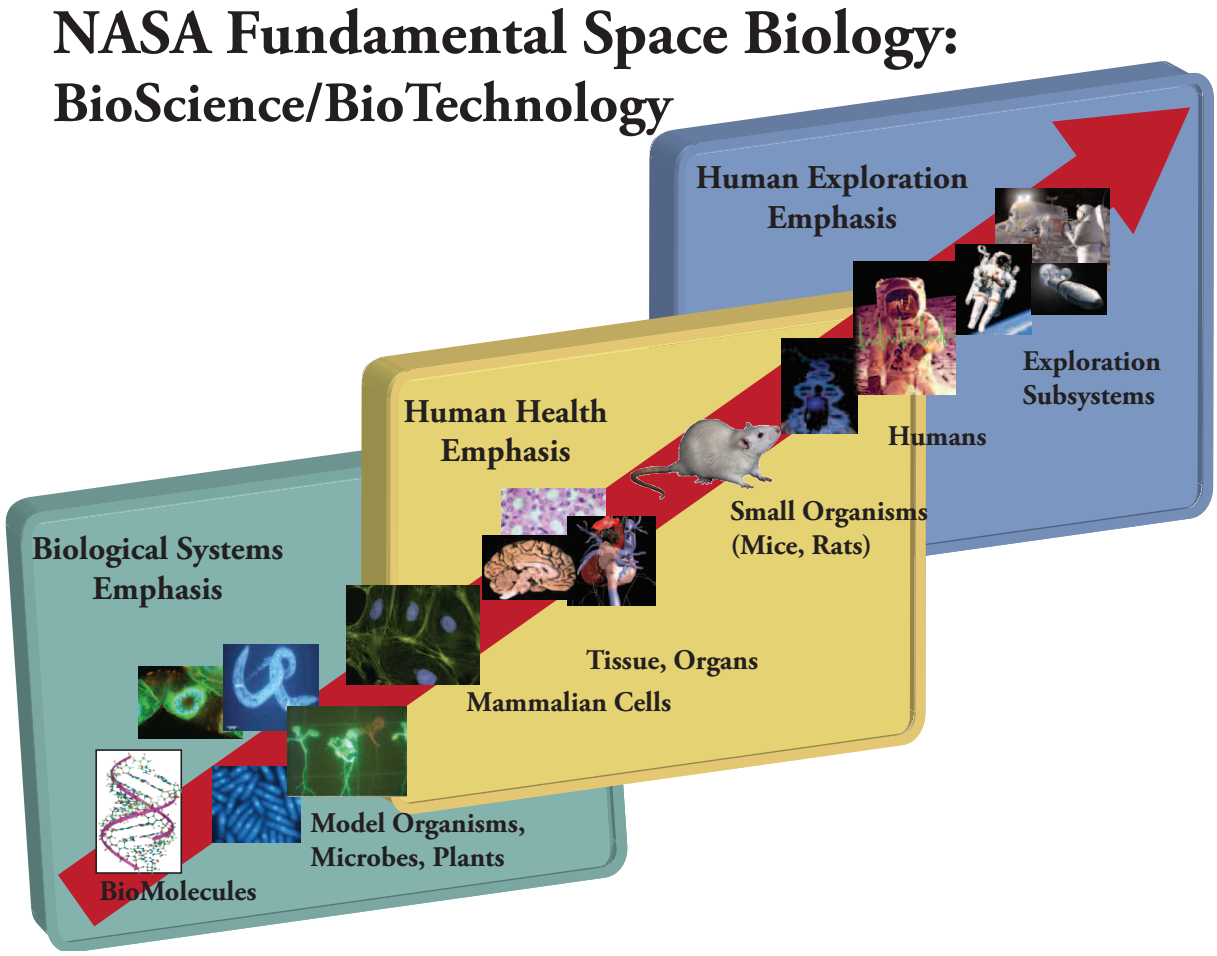


Figure 1: Fundamental biology is the foundation on which to build solutions to applied problems.

Cell, Microbial and Molecular Biology

Cell based science in microgravity serves many areas of basic and applied research for space exploration and for Earth applications. Use of cells for investigations in microgravity carries the advantages of low mass and power, many replicates, adaptability to mission scenarios, minimum crew requirements, and amenability to real time analysis. Additionally, there are a number of analog settings that can be used to define and refine flight experiments thereby increasing the probability for a successful experiment in space.

In the past, spaceflight experiments suggested that mammalian cells respond with profound shape change, altered gene expression, diminished trans-membrane signaling, modified differentiation, increased secondary metabolism, and tissue morphogenesis. The basis of the changes may be a direct response of the cell to the change in gravity or alternatively to conditions in the cell culture environment created by microgravity. The former invokes an intrinsic response structure within the cell. The latter implicates the loss of gravity driven convection and the hydrostatic pressure

gradient, subsequent changes in mass transfer regimes and the forced shape change as etiologic to the cell response. These pose critical questions in microgravity sciences with impact on microgravity biology and on human health in space.

Knowledge of the changes in gene expression in cells facilitates understanding the basis of changes that occur at the tissue level, in organs, in systems, and ultimately the organism. This approach will support parallel investigations in human health, fundamental biology, and Earth-based biomedical research and development. Understanding the response of cells to microgravity will reveal underlying mechanisms in cell function that will increase our fundamental knowledge as well as provide unique opportunities in biotechnology and commercial developments. The observations in tissue morphogenesis reinforce the prospect for the latter.

Early studies with microbes, i.e., bacteria and fungi, showed that they reached higher population densities when grown under microgravity conditions than were obtained from cultures grown under similar conditions on the ground. Higher cell density is likely due to a more homogeneous distribution of cells in the culture medium, unlike the settling of cells that occurs on the ground. These studies also showed that spaceflight caused some bacterial species to become more resistant to common antibiotics (Klaus and Howard, 2006).

Recently, a FSB spaceflight experiment found that space-grown cultures of the pathogen *Salmonella typhimurium* were significantly more virulent than comparable cultures grown on the ground (Wilson, 2007). RNA microarray analyses revealed changes in the gene expression of over 160 gene transcripts, one of which was a cross-species conserved RNA-binding regulator protein, Hfq, which is involved in RNA transcription and has been found to play a role in microbial virulence of several pathogenic bacteria. These data suggested that Hfq can play a critical regulatory role in the spaceflight response of bacteria and the observed increased virulence, a result that has profound implications for long duration spaceflight. As astronauts and cosmonauts live for longer periods in a closed environment and use recycled water and air, there is an increased potential for microbial contamination that can impact their health, safety, and performance. Despite the lack of a demonstrable disease problem during human spaceflight to date, studies showing increased microbial virulence and increased microbial resistance to antibiotics are cause for concern. Adding to the concern are repeated reports that spaceflight suppresses immune function suggesting that disease agents may be more difficult to treat during and following long spaceflights. Space-flown plants have also shown significant levels of altered gene expression (Paul, 2005; Salmi and Roux, 2008). Also, analogous to suppressed immune function in animals, alterations in cell wall composition in plants subjected to spaceflight could result in increases in the susceptibility of plants grown in space to pathogen attack (Ryba-White, 2001).

Spaceflight has also been shown to affect a variety of mammalian cell types, e.g. bone, cartilage, and tendons, resulting in reduced matrix production or altered matrix composition (Doty, 1990 and 1992). How spaceflight affects bone cells is not

completely understood, i.e., how do cells sense and respond to changes in gravity? Some scientists suggest that certain cell types when exposed to microgravity reduce their activity or metabolism as well as the amount of new protein normally produced and enter a “resting” phase. Microgravity may affect the mature differentiated cell (final cell type for a specific organ like bone, e.g. bone cell) such that the cell generates a "signal" during spaceflight driving it to enter a “resting” phase. Another possibility is that the cell division cycle is delayed so that cells simply develop into their differentiated state more slowly than normal. A series of spaceflight experiments demonstrated that spaceflight suppresses hematopoietic differentiation of macrophages; other experiments showed that bone marrow cell differentiation in microgravity using murine primary macrophage cell cultures noted phenotypic shifts in the bone marrow cell subpopulations (Ichiki, 1996; Chapes, 1999).

Human renal cell cultures flown in space (Hammond, 1999) exhibited a genetic response to microgravity that exceeded all expectations. Based on RNA microarray analyses of spaceflight cultures compared to ground controls, more than 1,600 of 10,000 genes examined showed a change in the space-flown cells. Investigators are now beginning to focus on groups of specific genes affected by microgravity. As a spinoff of this cell biology research, a rotating wall vessel bioreactor was developed to culture cells on the ground while simulating the free fall environment that particles experience in cultures grown in microgravity. This unique bioreactor is a NASA spinoff that has yielded 25 patents, more than 20 licenses, and thousands of units that are now in research labs in universities, medical centers, commercial laboratories and the NIH (Hammond and Hammond, 2001). The technology and the research findings have become part of the testing of medicines for cancers, development of transplantable tissues and the growth of microorganisms for the development of vaccines and antibiotics.

Overarching questions that will guide FSB’s Cell, Microbial, and Molecular Biology science direction and selections during the next decade include:

- How do alterations in gravity affect:
    a. Cell and microbial replication including genetic and metabolic regulation
    b. eukaryotic cells’ ability to generate and maintain their complicated internal cyto-architecture, including the cytoskeleton, and the host of specialized membrane-bound organelles and membrane domains that are integral to the regulation of both growth and form?
    c. cell-cell interactions and communication?
    d. microbial biofilm formation and/or alter microbes’ potential for disease?
- Can microgravity be used as a tool to study and manipulate tissue morphogenesis?
- Are decreased mass transfer, or physical force changes in membranes and cell walls, the main effect of microgravity on the cell?
- Does the enhanced virulence observed with *Salmonella typhimurium* cultures flown in space occur in other species?
- Are there g-thresholds for maintaining normal cell and microbial shape and function, e.g. Will stem cells maintain pluripotency at fractional g? at hyper-g?

Organismal and Comparative Biology

As living systems evolved from simple unicellular microbes to complex multi-cellular plants and animals, they developed a variety of sensory systems that enabled them to use gravity for orientation and locomotion. For example, plants developed a system of intracellular particles called statoliths that enable them to sense the gravity vector and orient their roots down into the soil and their shoots upward toward the sun. Similarly, animals developed a variety of sensory systems, e.g. the mammalian vestibular system, enabling them to sense their body's movements and transmit signals to the brain that can be used together with visual and propioceptive inputs to inform the animal how to negotiate its environment. During the free fall that accompanies orbital spaceflight, the normal output from the vestibular system is altered leading to a confusing set of signals of the organism's position and movement. Such confusion is believed to result in symptoms not too different from the typical motion sickness experienced by seafarers on the Earth. This affliction, commonly termed, "space motion sickness" (SMS), affects about half of astronauts and cosmonauts during the first few days in orbit.

Understanding the basic process of SMS became one of the main themes of the first two dedicated space life sciences missions on the Space Shuttle (SLS-1, 1991 and SLS-2, 1993). Investigators used these missions to probe the structural changes that occur in the vestibular system, the mammalian balance organ (Ross, 1993). Using rodents, they demonstrated, for the first time, that the neural hair cells of the vestibular organ could change, relatively rapidly, to altered gravity. Such neuroplasticity was evident in the increased number of synapses between the hair cells and the vestibular nerve that occurred as the gravity signal decreased; in effect, the body tries to turn up the gain to receive the weaker gravitational signal in space.

Neuroplasticity was not the only significant benefit emanating from the science conducted on SLS-1 and SLS-2. In order to facilitate and expedite the microscopic analysis of thin sections of the vestibular organ, 3-dimensional imaging software was developed that facilitated the reconstruction of the sections to unveil the innervation pattern of the rodent's inner ear, and to do it much faster than traditional manual methods. Not only did the technology greatly accelerate analyses of electron microscopic images, it also was adapted to construct 3-D images from CAT and MRI scans of humans. Surgeons have used the resulting 3-D dynamic simulations for reconstructive breast cancer surgery, dental reconstruction, plastic surgery, brain surgery and other delicate surgeries. Such simulations enable doctors to visualize and practice procedures prior to surgery, resulting in a much shorter time for the patient to be under anesthesia and a lower risk surgery.

Studies of the effects of spaceflight on the mammalian musculoskeletal system also benefited greatly from the use of animals. During and following flights on US and Russian free flying automated biosatellites and on the Space Shuttle/Spacelabs, structural and biochemical changes were observed in muscles and bones (Grindeland, 2005; Doty, 2005). This suggested to scientists that resistive, as well as aerobic exercise, e.g. treadmill, would be needed to counteract the muscle atrophy and bone mass loss that was found to occur in humans during spaceflight. In addition, the

hypersensitivity to anesthesia experienced by monkeys following the joint US/Russian Bion 11 mission alerted flight surgeons to such a risk to astronauts and cosmonauts, potentially saving lives. Basic biological research conducted in space not only expands our knowledge of the space environment and its impact on life, it also provides the foundation on which biomedical researchers can develop and test ways to mitigate the deleterious effects of spaceflight on human physiology, behavior and performance.

Additional areas of basic biological research conducted in space includes endogenous plant movements (Johnsson et. al., 2009; Solheim et. al., 2009), phototropism (Kiss, 2009), and aspects of plant physiology relating to photosynthesis, respiration and transpiration (Tripathy, 1996; Stutte, 2005; Monje, 2005). For phototropism, investigations conducted on Earth are obfuscated by the presence of gravity and the resulting gravitropism complication. The fundamental knowledge gained through these investigations aids in our ability to better control plant use on earth in agriculture (and other) applications.

Future research on the ISS and automated free flyers offers a particularly intriguing research environment for life science experiments. Whereas the Space Shuttle and free flyer experiments were typically 2-3 weeks in duration, ISS experiments can span many months. This opens new scientific pursuits for biology as researchers will be able to investigate how microgravity affects the full life cycle and multiple generations of higher order plants and animals. When the crew is present, humans can monitor the health and well being of the experimental organisms. The crew will also provide the capability to dissect animals, pollinate plants, and perform other experimental operations and harvests on-orbit, giving investigators samples and data retrieved before the organisms undergo the environment experienced during the return from space.

The FSBP's research with plants not only advances knowledge of how plants sense and respond to changes in gravity but this information also supports NASA's Exploration Life Support (ELS) program. The ELS program anticipates that during future long duration missions, the crew will grow plants ***both*** for food and to provide positive psychological impact on crew members living in confined environments for prolonged intervals. Plants can recycle wastes, remove carbon dioxide, purify water and produce oxygen and food. Although our ability to grow plants in space has improved greatly, the fundamental processes of plant adaptations to spaceflight environments are only beginning to be understood. Already early stage vegetable production studies have been initiated on ISS (Sychev, 2007). FSB and ELS program experiments have identified several effects of spaceflight on plants that need more study before plant-based life support can become a reality. These issues relate to not only the direct effects of microgravity on plant development and physiology (FSB), but also indirect effects of space environments, including tightly closed atmospheres that can accumulate volatile organics, poor water and air movement through rooting media, elevated radiation levels, and spectral effects of electric lighting systems, to name a few (ELS). The ISS provides the opportunity to solve many of these issues, especially given the availability of new hardware that can provide more precise environmental control and sustain larger plants for multiple production cycles.

Overarching questions that will guide science direction and selection in the Organismal and Comparative Biology program element during the next decade include:

- What are the organs and systems that life uses to sense and react to gravity? How do they work? Will they function properly across the gravity continuum, i.e., hypo- through hyper-gravity levels?
- How do changes in gravity affect the regulatory mechanisms that govern alterations in the musculoskeletal system in animals and lignin formation in plants?
- Do changes in gravity affect the basic metabolic rate and metabolism of living systems? Is lifespan affected?
- Are the normal defense systems of organisms compromised at fractional or hyper-gravity, e.g. mammalian immune system, wound healing, including fracture repair?

Developmental Biology

All life has evolved under the nearly constant influence of gravity. With the advent of spaceflight, biologists can now investigate the role and influence of gravity on such basic processes as reproduction, development, maturation and aging. On several Space Shuttle missions, pregnant rodents were flown and the pups they delivered following the flights showed striking changes in the structure of the fetal balance organ within the vestibular system (Keefe, 1986, Alberts, 1986). In addition, after 16 days in microgravity neonatal rodents that were launched at both 8 and 14 days *post partum* had their sensorimotor functions tested within several hours of landing, e.g. walking, and righting (rolling over). Post-flight, the righting response of pups was profoundly deficient compared to ground control animals, suggesting that removal of gravitational cues during early post-natal development can significantly alter inherent patterns of behavior. In addition, these microgravity-exposed neonatal animals failed to undergo normal skeletal muscle growth and differentiation. This finding suggests that gravity stimuli are essential for generating the structure needed to perform basic ambulatory and righting movements when subjected post-flight to terrestrial gravity (Walton, 2005, Adams, 2000).

In another key spaceflight experiment, a frog embryology investigation demonstrated, for the first time, that gravity is not required for a vertebrate species, an amphibian, to ovulate, fertilize, achieve a normal body pattern, and mature to a free swimming stage (Souza, 1995). This experiment put to rest the "gravity requirement" controversy that had been debated by embryologists since the late 19th century. It remains to be seen, however, if a complete life cycle of a complex vertebrate can occur in the virtual absence of gravity.

Investigations of plant development in space have often reported differences attributable to the spaceflight environment. For instance, *Brassica rapa* seeds and pollen produced in microgravity were found to be physiologically younger than those produced in 1g (Kuang et. al., 2005). It was speculated that microgravity limits mixing of the gaseous microenvironments inside the closed tissues and that the resulting gas composition surrounding the seeds and pollen retards their development. Similarly,

abnormalities in the process of embryo formation and acceleration in development of the endosperm were revealed at the early stages of *B. rapa* embryogenesis in microgravity (Popova, 2009).

It has been demonstrated that secondary metabolism in plants is affected by conditions of altered gravity (both hypo- and hyper-gravity). Levels of glucosinolate production was on average 75% greater in plants grown in space than in their ground control counterparts. Similarly, the biochemical make-up of immature seeds produced during spaceflight was significantly different from the ground controls. The spaceflight environment thus influences *B. rapa* metabolite production in ways that may affect flavor and nutritional quality of potential space produce (Musgrave, 2005).

Several publications using different species in different systems have reported that plants grown under conditions of microgravity exhibit enhanced root production relative to their ground controls (Levine, 1996, 2003, 2005). Why is this? Is there a physiological basis or is it due to a spaceflight-associated artifact (e.g. more even distribution of moisture in the root zone)? One study pertinent to this question using *Arabidopsis thaliana* seedlings germinated in space found that the root cortical cells proliferated at a higher rate (Matía, 2005). In follow-up studies, Matía (2009) was able to confirm using both space-grown plants plus a Random Positioning Machine, an effective simulator of microgravity, that the number of cells per millimeter in specific cell files of the roots were higher in microgravity-grown (or simulated) samples than in the 1g control.

Overarching questions that will guide science direction and selection in the Developmental Biology program element during the next decade include:

- How do individual eukaryotic cells carry out genetically defined programs of differentiation and development into specialized tissues and multi-cellular organisms?
- Can complex organisms, plants and animals, be grown successfully through at least two complete life cycles in altered gravity environments, hypo- and hyper-gravity? If not, why not?
- Do organisms that are raised in altered gravity environments develop normally, i.e., structurally, physiologically, behaviorally? Are reproduction, lifespan and the aging processes affected? Are changes expressed in altered g environments reversible when returned to 1g?
- Is normal terrestrial gravity required for the normal development and function of the gravity sensing organs in plants and animals, e.g., Is gravity required for the development and maintenance of the mammalian vestibular system's capability for neuroplasticity? Is a plant's gravitropic system including gravitransduction, and the translocation of the g-signal to the site of reaction?
- Are there g-thresholds for normal reproduction, development, and maturation? For example, will gravity-sensing systems develop normally at fractional gravity, (lunar? Mars?)

Mapping the Path - The Next Decade

2011-2015

FSBP research priorities for experiments on the ISS during the first five years of the decade will emphasize cell and microbiology due to the availability of a diverse array of facilities and equipment that can support cell and microbial research. Cell biologists and microbiologists will also have several opportunities during this decade to utilize Microsatellites flown by NASA's Ames Research Center. These studies will clarify how a variety of cells and microbes react to altered gravity. Experiments with microbes will provide insights into the how and why of increased microbial virulence as a result of spaceflight as well as suggest ways to mitigate such increases. Research with microbial biofilms will shed light on how bioflims form and identify materials and ways to control biofilm formation. In addition, plant and small model organisms will utilize the equipment and facilities of the US and our international partners on the ISS, including the European Modular Cultivation System that enables fractional gravity studies with small plants and other model organisms.

Development of animal and large plant habitats to support research on the ISS is a very high priority for the FSBP. The strategic use of animals will provide information at the whole system level for such important questions as the effects of microgravity on the structure and function of the sensori-motor and musculoskeletal systems, the immune system including wound healing and fracture repair. In addition, plant habitats are needed to accommodate the growth of relatively large plants for both the FSB and ELS research programs. If initiated in 2010, animal and plant habitats can be available for research on the ISS by late 2012.

Free flyers will also play a prominent part in the FSB program during this decade. In addition to the use of microsatellites for cell and microbial biology, the Russian Institute of Biomedical Problems in collaboration with NASA's FSBP, will study a variety of specimens from mice flown on the 30-day Russian Bion M-1 biosatellite mission in 2012. A second Bion mission, Bion M-2 is tentatively scheduled for 2014 and is planned to be a 45-day mission with rodents including either an onboard centrifuge for fractional gravity research or, an onboard radiation source for radiation biology studies.

2016-2020

Assuming animal habitats and a large plant habitat are developed and flown on ISS during the previous five years, animal and plant research will be emphasized during this five year period. Utilizing both biotechnology advances including the ever-increasing availability of genetically engineered organisms, the mechanisms animals and plants use to respond to gravity transitions will be unraveled at the molecular level. Long duration studies with animals, e.g. 3-6 months or more, will demonstrate the way the musculoskeletal system changes over time in microgravity as well as the impact of long duration flights on the immune system. Multiple generations of plants will be studied to both understand the long-term effects of microgravity and also to demonstrate the potential use and reliability of plants for future advanced life support systems. It is

anticipated that cooperative projects with our international partners will continue and will include research both on the ISS and free flyers. In addition, advanced technologies will continue to be developed to bring more and more capability to Microsatellite missions, perhaps including a return capability.

Core Program Elements

Ground-based and Space Research

Research on the ground will be the basis for developing and refining hypotheses to be tested in space. Proven analogs that induce biological effects similar to spaceflight will be used in conjunction with model organisms to focus on the critical overarching questions cited at the end of each of the FSB Program Elements. Research will be solicited and selected via applicable NASA policies and practices. It is anticipated that a ratio of approximately 3:1 (ground: flight studies) will be maintained for overall program balance and cost effectiveness.

Special Research and Technology Projects

New areas of research may require new equipment and/or technologies. The FSB Program will conduct regular assessments of its research needs via workshops and reports from appropriate advisory committees and/or organizations. Development of high priority equipment or technologies will be prioritized by the FSB Program and developed according to applicable NASA policies and practices. Miniaturized, highly sensitive measuring devices lead the latest wave of new tools destined to equip Fundamental Biology projects for spaceflight. These devices require cell, microbial, plant and animal model systems that will rapidly return high quality data from flight experiments, e.g. imaging, environmental, biochemical, etc. Computing capacities must accelerate to keep pace with the expanding needs for processing and analyzing the data gathered from these experiments. The FSB Program will also continue its efforts to improve the frequency and capabilities of Microsatellites

FSB Program Priorities

2011-2020

Priority	2011-2015		Priority	2016-2020
High	Cell, Microbial and Molecular Biology on ISS		High	Animal and Plant research on ISS
	Development of Plant and Animal Habitats			Cell, Microbial and Molecular Biology on ISS
	Expanded Ground Res.: Plants, Animals, Cells			Free Flyers: Bion-M3
	Free Flyers: Bion-1, Bion-M2			Microsatellites
Medium	Microsatellites		Medium	Ground & Flt Research - Developmental Biology
	Advanced Technologies for ISS and Free Flyers			Ground Research - Plants, Animals, Cells
	Ground Research - Developmental Biology			Advanced Technologies for ISS and Free Flyers
	Education and Outreach			Education and Outreach
Low	Flight Research - Developmental biology		Low	Sub-Orbital Research

References

Adams, G. F. Haddad, S. A. McCue, P. W. Bodell, M. Zeng, L Qin, A. X. Qin, and K. M. Baldwin. 2000. Effects of spaceflight and thyroid deficiency on rat hindlimb development II: expression of MHC isoforms. J. Appl. Physiol. 88:904-916.

Alberts, J.R., et al. Early Postnatal Development of Rats Exposed in Utero to Microgravity. 1986. In, Final Reports of US Monkey and Rat Experiments Flown on the Soviet Satellite Cosmos 1514. R.C. Mains and EW. Gomersall, eds. NASA TM-88223, pp. 145-188.

Chapes, S.K, S.J. Simske, A.D. Forsman, T.A. Bateman, and R.J. Zimmerman, 1999. Effects of spaceflight and IGF-1 on immune function. Adv. Space Res. 23:1955-1964.

Cowles J, LeMay R, Jahns G. 1994. Seedling growth and development on space shuttle. *Adv. Space Res*. 14:3-12.

DM Klaus, HN Howard, 2006. Antibiotic efficacy and microbial virulence during space flight. In, Trends in Biotechnology, - Elsevier

Doty, S.B., L. Vico, T. Wronski, and E. Morey-Holton, 2005. Use of Animal Models to Study Skeletal Effects of Space Flight. Adv. In Space Bio and Medicine, Vol 10:209-224. Elsevier

Doty, S.B., Morey-Holton, E.R., Durnova, G.N. and Kaplansky, A.S., 1992 Morphological studies of bone and tendon. J. Appl. Physiol. 73, 10s-13s.

Doty, S. B., Stiner, D., and Telford, W. G. The effect of spaceflight on cartilage cell cycle and differentiation. *J Gravit Physiol.* 1999, 6 (1) P89-90.

Grindeland, R.E., E.A. Ilyin, D.C. Holley and M.G. Skidmore, 2005. International Collaborations on Russian Spacecraft and the Case for Free Flyer Biosatellites, in Adv. In Space Bio and Medicine, Vol 10:41-80. Elsevier

Hammond, T.G. and J.M. Hammond. 2001. Optimized suspension culture: the rotating-wall vessel. Am. J. Physiol. Renal Physiol 281: F12-F25, 2001

Hammond, TG, FC Lewis, TJ Goodwin, RM Linnehan, DA Wolf, KP Hire, WC Campbell, E Benes, KC O'Reilly, RK Globus, and JH Kaysen. 1999. Gene Expression in Space. Nature Medicine Vol 5, No. 4, 359.

Ichiki, A., L. Gibson, T. Jago, K. Strickland, D. Johnson, R. Lange, and Z. Allebban. 1996.

Johnsson A, Solheim BG, Iversen TH. 2009. Gravity amplifies and microgravity decreases circumnutations in Arabidopsis thaliana stems: Results from a space experiment. New Phytol. 182(3):621-9.

Keefe, J.R. et al. 1986. Developmental Morphology of the Eye, Vestibular System, and the Brain in 18-day Fetal and Newborn Rats Exposed In Utero to Null Gravity During the Flight of Cosmos 1514. In, Final Reports of US Monkey and Rat Experiments Flown on the Soviet Satellite Cosmos 1514. R.C. Mains and E.W. Gomersall, eds, pp. 189-279.

Kiss JZ, Kumar P, Millar KD, Edelmann RE, Correll MJ. 2009. Operations of a spaceflight experiment to investigate plant tropisms. Adv. Space Res. 44(8): 879-86.

Kuang A, Popova A, McClure G, Musgrave ME. 2005. Dynamics of storage reserve deposition during Brassica rapa L. pollen and seed development in microgravity. Int. J. Plant Sci. 166(1):85-96.

Kwon M, Bedgar DL, Piastuch W, Davin LB, Lewis NG. 2001. Induced compression wood formation in Douglas fir (*Pseudotsuga menziesii*) in microgravity. *Phytochemistry* 57:847-857.

Levine, H.G., and A.D. Krikorian. 1996. Enhanced Root Production in *Haplopappus gracilis* Grown Under Spaceflight Conditions. *J. Gravitational Physiology* 3(1):17-27.

Levine, H.G., K. Anderson, A. Boody, D. Cox, O.A. Kuznetsov and K.H. Hasenstein. 2003. Germination and Elongation of Flax in Microgravity. Adv. Space Res. 31(10):2261-2268.

Levine HG, Piastuch WC. 2005. Growth patterns for etiolated soybeans germinated under spaceflight conditions. Adv. Space Res. 36(7):1237-43.

Matía I, González-Camacho F, Herranz R, Kiss JZ, Gasset G, van Loon JJ, Marco R, Javier Medina F. 2009. Plant cell proliferation and growth are altered by microgravity conditions in spaceflight. J. Plant Physiol. [Epub ahead of print]

Matía I, González-Camacho F, Marco R, Kiss JZ, Gasset G, Medina F-J. 2005. Nucleolar structure and proliferation activity of Arabidopsis root cells from seedlings germinated on the International Space Station. Adv. Space Res. 36(7):1244-53.

Monje O, Stutte G, Chapman D. 2005. Microgravity does not alter plant stand gas exchange of wheat at moderate light levels and saturating CO2 concentration. Planta [Epub ahead of print]
Musgrave ME, Kuang A, Tuominen LK, Levine LH, Morrow RC. 2005. Seed storage reserves and glucosinolates in Brassica rapa L. grown on the International Space Station. J. Am. Soc. Hortic. Sci. 130(6):848-56.
Paul A-L, Popp MP, Gurley WB, Guy C, Norwood KL, Ferl RJ. 2005. Arabidopsis gene expression patterns are altered during spaceflight. Adv Space Res. 36(7):1175-81.
Popova AF, Musgrave M, Kuang A. 2009. The development of embryos in Brassica rapa L. in microgravity. Cytol Genet. 43(2):89-93.
Ross, M.D. 1993. Morphological changes in rat vestibular system following weightlessness. J. Vestib. Res. 3, 241-251.
Ryba-White M, Nedukha O, Hilaire E, Guikema JA, Kordyum E, Leach JE. 2001. Growth in microgravity increases susceptibility of soybean to a fungal pathogen. *Plant Cell Physiol*. 42:657-664.
Salmi ML, Roux SJ. Gene expression changes induced by space flight in single-cells of the fern Ceratopteris richardii. 2008. Planta [Epub ahead of print]
Sato F, Takeda S, Matsushima H, Yamada Y. 1999. Cell growth and organ differentiation in cultured tobacco cells under spaceflight condition. *Biol. Sci. Space* 13:18-24.
Solheim BG, Johnsson A, Iversen TH. 2009. Ultradian rhythms in Arabidopsis thaliana leaves in microgravity. New Phytol. 183(4):1043-52.
Souza, K.A., S. Black, R. Wassersug. 1995. Amphibian development in the virtual absence of gravity. PNAS 92:1975-78.
Stutte GW, Monje O, Goins GD, Tripathy BC. 2005. Microgravity effects on thylakoid, single leaf, and whole canopy photosynthesis of dwarf wheat. Planta 14:1-11.
Sychev VN, Levinskikh MA, Gostimsky SA, Bingham GE, Podolsky IG. 2007. Spaceflight effects on consecutive generations of peas grown onboard the Russian segment of the International Space Station. Acta Astronaut. 60(4-7):426-432.
Tripathy, B.C., C.S. Brown, H.G. Levine, and A.D. Krikorian. 1996. Growth and Photosynthetic Responses of Wheat Plants Grown in Space. *Plant Physiol*. 110:801-806.
Walton, K.D., S. Harding, D. Anschel, Y.T. Harris, and R. Llinas. 2005. The effects of microgravity on the development of surface righting in rats. J. Physiol. Jun 1:565(Pt2):593-608.
Wilson, JW, et al, 2007. Space flight alters bacterial gene expression and virulence and reveals a role for global regulator Hfq. PNAS vol. 104 no. 41 16299-16304

Chapter 2 - Implementation

Introduction

To accomplish the scientific goals articulated in chapter 1 of this plan, a comprehensive ground and flight research program managed by NASA is required. The components of that program are described in this chapter. It captures how NASA engages the science community, and provides support so that world-class science is done both on the ground and in space. This chapter focuses on the specialized components of the FSB program that will support research on the ground and in microgravity.

Ground and Flight Research

The ultimate success of the FSB program relies on growing and sustaining a vibrant extramural research community, complimented with in-house science expertise to set programmatic goals and transfer knowledge to more applications- and operations-oriented NASA programs. To engage the broad science community, the FSB program funds peer-reviewed research that is performed at either NASA or investigator provided facilities. Both ground based and space based investigations are solicited and funded. Investigations may be announced through an NASA Research Announcement (NRA), International Space Life Sciences Research Announcement (ILSRA), and Stand Alone Missions of Opportunity Notice (SALMON). Technology development is a subset of research, hence technology development grants and contracts are awarded through competitive, peer-reviewed processes as well. NRA's are typically focused on either ground or flight research, but recent NRAs for ground research have also stated that experiments of sufficient merit can be considered for flight.

After grants are awarded, investigators provide regular status reports as well as a final report, and are strongly encouraged to publish. Following completion of the research, the investigator has a one year period with exclusive rights to publish their findings. After the one year period, the research data is archived and made available to the broader community.

The FSB program strives to achieve a 3:1 ratio between ground and flight research grants. NASA Ames Research Center have general oversight for cell and animal biology research, which are roughly 2/3 of the grants, and Kennedy Space Center has general oversight for plant research, which are roughly 1/3 of the grants. Ideally, the overall FSB program would have 100 active ground and flight investigations going on at one time, which was true before the original FSB program was cut in 2006. Such a program would engage thousands of researchers and students across the country, re-establishing NASA's leadership in space biology.

Ground and Flight Research Facilities

Universities and the private sector have billions of dollars invested in modern biotechnology research laboratories. The idealized FSB program will complements these capabilities by providing access to the unique environment of space to study living systems, as well as ground facilities that support such investigations. This includes:

Ground Facilities:

- Rotating and linear acceleration facilities to study the physiological and behavioral effects of hyper-gravity and acceleration
- Laboratories to support the development and performance of biological flight experiments at launch and landing sites
- Facilities that simulate the on-orbit temperature and humidity environment being seen by the payloads
- Mission operations facilities to monitor and control experiments while in space.
- Specimen and data archives that is the repository for information and tissues that are shared within the science community
- Animal care facilities to house animals for flight experiments

Flight Facilities:

- Access to microgravity via missions involving the ISS, microsatellites, and free flyers
- Habitats to sustain cells, tissues, small model organisms, rodents, and plants in microgravity (existing habitats are described in the Appendix)
- Centrifuges to provide a fractional gravity level to support lunar and Martian studies, as well as to provide an on-orbit 1-g control
- Sample retrieval and preparation equipment to capture cells and tissues on-orbit, preserve them for storage, and/or prepare them for on-orbit analysis
- In-situ analytical equipment to capture scientific data from the biospecimens while on-orbit and reducing the need for sample return
- Specimen preservation and storage equipment, including both chemical fixatives and refrigerators and freezers, to keep specimens in a condition so they can be returned to earth for study.

Some of these research and support facilities have been fully developed and are operational, some exist but need to be upgraded, and others do not exist and need to be developed. Figure 1 describes the relative priorities for implementation for each of the science areas identified in chapter 1. Prioritization was based on scientific urgency, the status of the current facilities supporting each science area, and a projected ramp up of program budget. For example, cell biology has been and will continue to be important. There are a number of excellent systems to support cell biology in space, so there is not much emphasis placed on developing brand new cell biology hardware. What is lacking, however, are the U.S. facilities to do long duration plant and rodent research. So in the near term, the program will emphasize the development of plant and rodent habitats to operate onboard ISS, while maintaining a strong cell science program.

This plan assumes that NASA provides adequate logistics to and from the ISS. With the Space Shuttle nearing retirement, FSB recognizes the need to maximize science while minimizing how much has to be launched to and returned from ISS. Much of the microgravity research will be done onboard ISS, but microsatellites and free flyers will also be critical. Free flyers, such as the Russian Foton and Bion, offer the advantage of scientific and cost sharing with Russian collaborators. The microsatellites (50-100 kg payloads) and nanosatellites (less than 50 kg payloads) can be developed relatively cheaply and quickly, and fly beyond the Low Earth Orbit of ISS. Because free flyers and microsatellites can go beyond LEO and without the same safety concerns as human-crewed missions, a wider range of radiation biology experiments can be flown. NASA anticipates Bion missions in 2012, 2014, and 2016. A nanosatellite or microsatellite launch is anticipated once or twice a year starting in 2009 (Pharmasat was launched on May 19th, 2009).

Program Elements	2010-11	2012-13	2014-15	2016-17	2018-20
Cell Biology & Microbiology					
Ground Studies	Ground NRA: Cell Biology & Microbiology	Ground NRA: Cell Biology & Microbiology	Ground NRA: Cell Biology & Microbiology	Ground NRA: Cell Biology & Microbiology	Ground NRA: Cell Biology & Microbiology
ISS Experiments	Flight NRA: Cell Biology & Microbiology		Flight NRA: Cell Biology and Microbiology		
	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments
Bion Free Flyer Exps	See Organismal & Comp Bio.	Bion M1 Flt Experiments	See Organismal & Comp Bio.	Bion M3 Flt Experiments	US/Russ TBD
Dragon Free Flyer and other FF Exps	TBD	TBD	TBD	TBD	TBD
Nanosat/Microsat Exs	MoO-1 and MoO-2	Flight NRA	MoO-3 and 4	Flight NRA	MoO 5 and 6
Organismal & Comparative Biology					
Ground Studies	Ground NRA: Animal & Plant Biology	Ground NRA: Animal & Plant Biology	Ground NRA: Animal & Plant Biology	Ground NRA: Animal & Plant Biology	Ground NRA: Animal & Plant Biology
ISS Experiments	Flight NRA: Animal & Plant Biology		Flight NRA: Long Duration Animal & Plant		
	Flight Experiments	Flight Experiments	Flight Experiments	Long Duration Animal & Plant Flight Expts	Long Duration Animal &Plant Flight Expts
Bion Free Flyer Exps	Bion M-2 (ILSRA ESA) Artificial Gravity, rodents	Bion M1 Flt Experiments, rodents	Bion M2 Flt Expts; Bion M3 (ILSRA??)	Bion M3 Flt Experiments, onboard radiation	US/Russ TBD
Dragon Free Flyer and other FF Exps	TBD	TBD	TBD	TBD	TBD
Nanosat/Microsat Exs	MoO-1 and MoO-2	NRA: See Cell Biology and Micro	MoO-3 and 4	NRA: See Cell Biology and Micro	MoO 5 and 6
Developmental Biology					
Ground Studies	Ground NRA: Dev Biology	Ground NRA: Dev Biology	Ground NRA: Dev Biology	Ground NRA: Dev Biology	Ground NRA: Dev Biology
ISS Experiments	Flight NRA: Dev Biology		Flight NRA: Dev. Bioiogy		
	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments	Flight Experiments
Bion Free Flyer Exps	N/A	Bion M1 Flt Experiments	See Organismal & Comp Bio.	Bion M3 Flt Experiments	US/Russ TBD
Dragon Free Flyer and other FF Exps	TBD	TBD	TBD	TBD	TBD
Nanosat/Microsat Exs	MoO-1 and MoO-2	See Cell Biology and Micro	MoO-3 and 4	See Cell Biology and Micro	MoO 5 and 6
Hardware Development					
ISS Animal Habitat	Phase A/B to CDR	Flt-rated by 2013	upgrade or duplicate habitats for long duration missions	Flight application	Flight Application
ISS Plant Habitat	Assess requirements and existing capabiilities; perform trade study; initiate Phase A/B to CDR	Complete hardware and flight qualification begin flight application in 2013	Flight Applications	Flight Applications	Flight Applications
Glovebox	Assess requirements and existing capabiilities; perform trade study; initiate Phase A/B if funds available	Fabricate, qualify and launch to ISS	Flight Appliations	Flight Appliations	Flight Appliations
New Hardware for Model Organisms	Qualify CCM, SLCC, ADF, and EMCS nematodes, Drosophila for ISS	ongoing	ongoing	ongoing	ongoing
Adv. Tech. Planning	Workshop - define requirements and priorities	Workshop - update requirements and priorities	Workshop	Workshop	Workshop
Adv. Tech. Development	Instrumentation for In situ Monitoring & Analysis	Instrumentation for In situ Monitoring & Analysis	Instrumentation for In situ Monitoring & Analysis	Instrumentation for In situ Monitoring & Analysis	Instrumentation for In situ Monitoring & Analysis
STEM Activities					
K-12	TBD	TBD	TBD	TBD	TBD
Undergrad	TBD	TBD	TBD	TBD	TBD
Graduate	TBD	TBD	TBD	TBD	TBD
Post-Doc	TBD	TBD	TBD	TBD	TBD
Faculty	TBD	TBD	TBD	TBD	TBD

New Activity: Highest Priority/2y block; max of 4
Ongoing High Priority Activity
Medium Priority

NOTE: **Specific priorities for each NRA will be drawn from the high priority science questions for each program element as identified in the FSB Science Plan. Hardware priorities will be set to be consistent with what is required to support high priority science. New advanced technologies will be determined by workshops and the science drivers as stipulated in the FSB Science Plan and NRA's and in consideration of recommendations from NASA advisory committes, e.g. the Decadal Planning Team.**

Figure 1

Science and Payload Operations

Over the course of 5 decades and the performance of hundreds of successful missions in space, NASA has developed a core competency in developing non-human biological science payloads. This expertise is vital in helping scientists shape the science they want to do in the challenging environment of space. Helping scientists achieve their science objectives is the #1 goal for NASA's science and payload operations staff. To do so, they help investigators by:

- streamlining and simplifying experiments to maximize their feasibility given the constraints of limited crew time, power, payload mass, etc.;
- adapting experiments to work with existing systems as well as developing new systems to support the science;
- making experiments safe so they don't endanger the crew or the vehicle;
- physically and analytically integrating the payload into the rest of the space vehicle or laboratory;
- monitoring experiments on-orbit and providing real-time data and command capability to the PI;
- supporting pre-launch and post-landing operations on the ground.

The process used for science award, development, and execution is depicted in Figure 2.

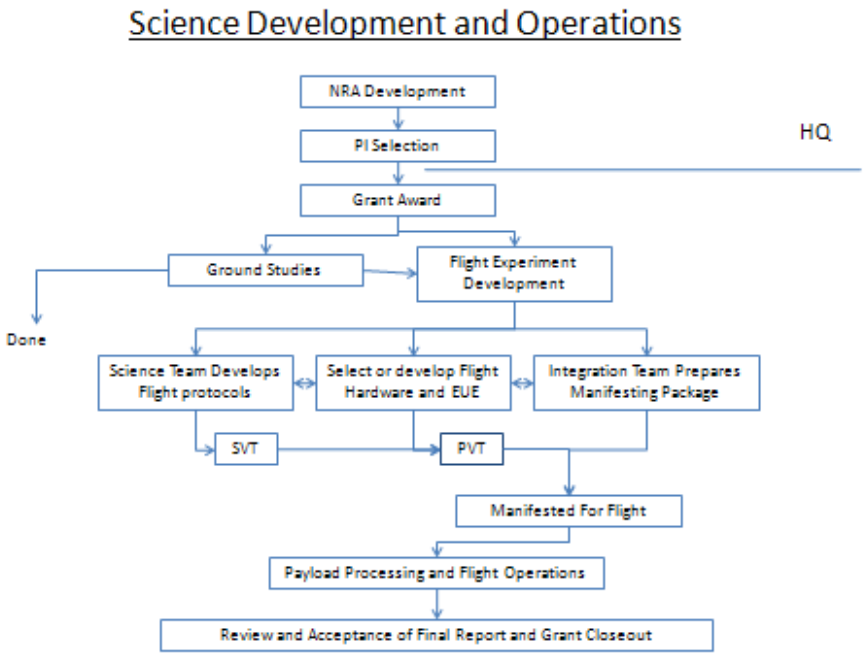


FIGURE 2.

Technology Development

Fundamental Space Biology both generates and relies upon advanced technology. Recent advances in biotechnology have given scientists great insights into the genomic and proteinomic phenomena that drive biological systems. Instruments and techniques to analyze genetics and molecular chemistry are relatively common in ground laboratories, but the capability to do such research in space is still in the developmental stage. Over the next 10 years, the FSB program will pursue multiple waves of biotechnology development to expand the research capabilities in space and resolve the technical challenges associated with exploration. Discoveries resulting from the biological research can also drive technology development. Such has been true in the past. FSB experiments have provided the knowledge that has fueled current biomedical countermeasures for the crew, as well as benefits to the general public (please see chapter 3 of this plan for more information about Earth benefits).

Relationship to Other Programs

The FSB program complements the applied biomedical research that is the focus of the Human Research Program, the commercial research that is funded by private industry, and space research done by other government agencies such as the National Institutes of Health and the U.S. Department of Agriculture, as well as research done by the International Partners. In the latter arena, there are several government agencies with strong research capabilities and diverse science objectives, but none of them are committed to the long-term goal of the exploration of space that is uniquely NASA's.

Each of these programs has its own unique ground and flight research capabilities that are leveraged by FSB. Similarly, FSB's existing facilities and expertise are used by organizations inside and outside of NASA. The FSB program has a long history of collaborating with these other programs, both in terms of joint missions, shared facilities, and collaborative science investigations. As we look ahead, we anticipate that partnerships will become strategically more important as the science interests are vast while the budgetary and flight resources (e.g., crew time, launch upmass) are limited.

A robust FSB program will provide the infrastructure to accelerate research by the private sector and other U.S. government agencies. Currently, both groups have not been able to take full advantage of ISS National Laboratory because of the paucity of US facilities to do biological research in LEO. Indeed, ESA and JAXA have their own dedicated racks for fundamental biology research, but the US does not. There are also multiple US racks dedicated to physical sciences research, and this plan describes the development of a similar capability for FSB. Once these on-orbit facilities are established, it will be much easier and cost effective for the private sector and other government agencies to do biological research in space.

Program Summary

NASA's full commitment to the FSB program will lead to a vibrant biological research program onboard ISS, Bion, microsats, and hundreds of labs around the country. Such a program will be closely connected with related research programs, inside and outside of NASA, to do extensive ground and spaceflight research. Investments must be made in the near term to upgrade the FSB research facilities, in particular, the facilities to support biological research in space. In parallel, the pool of investigators must be grown, and their experiments matured from ground to flight, so that the goals identified in chapter one can be addressed. Experiments in space will answer questions about how the basic biology of living systems are affected by long term spaceflight. At the same time, new phenomena will be discovered and new research questions will be generated. The exact pace of progress and scope of the program will be determined by funding. When fully mature, this program requires funding at the $100M a year level, but can be scaled up or down depending on the funding profile that is established.

Chapter 3 - Benefits

The substantial benefits resulting from NASA-sponsored Fundamental Space Biology research flow directly from the pursuit of its three Program goals. University and NASA researchers, collaborators from non-FSB NASA centers, other federal agencies, the commercial sector, and several international partners have collaborated to produce these benefits. The FSB Program has always been a broad, networked community, which is one of its strengths.

- Discover the effects of microgravity and other unique characteristics of the space environment on fundamental biological processes by bringing the genomics revolution to space.
- Develop the scientific and technological foundations to allow a safer, more productive human presence in space to further space exploration
- Design solicitations and experiments to maximize the applicability of this new knowledge and technology to improve the nation's competitiveness, educational prowess, and the quality of life on Earth.

To appreciate the true significance of FSB Program accomplishments it is important to define space biology research, since its scope and rationale for conduct by NASA is sometimes misunderstood. These accomplishments have significance in many ways, but we organize them here by the three FSB goal categories above (Discover, Develop and Apply) to emphasize a major value area. Specific benefits are profiled by their research Question, Result and Significance, to assist comparability.

What is Space Biology?

The only life we have yet encountered in the universe is life on Earth. Every known living thing evolved under the common influence of Earth's gravity, atmosphere, and radiation. Space exploration, defined as missions conducted to pursue new discoveries, new development and new applications beyond Earth, can be accomplished in different ways by people traveling on spacecraft, or by robot surrogates monitored by people. FSB conducts research to optimize the value of the human exploration component by all practical means.

Transport of an Earth-based human organism to space requires provision of an artificial environment sufficient to support and sustain life both there and back and as in the case, for example, of the International Space Station (ISS), while living in space. This requires knowing the limits of human adaptation to the quality of the artificial environment we are able to provide. For long-duration and/or long-distance exploration leading to habitation or even future colonization beyond the ISS, we need to better understand the environmental conditions and technologies that will allow humans to perform productive work and hopefully to thrive. To optimize human health and safety, we transport other organisms beyond Earth and by studying their adaptive capacity, better understand the ability of humans to live with minimum effective gravity or on

worlds with other gravity levels. Humans, of course, carry their own biota with them and these become part of the new ecosystems created in closed space environments.

These challenges are the purview of space biology and we have discovered that humans, plants and animals undergo many changes associated with living in microgravity or other levels of gravity. We have discovered aspects of livings things buried in their genetic code that can only be observed away from Earth's environment.

Highlights From 30 Years of FSB Research

Using a range of standard model organisms for research, gravity's effects on many physiological and biological systems have been identified and the underlying mechanisms clarified. We've determined the importance of the environmental changes within spacecraft and discovered how amazingly adaptable and "plastic" biological systems can be. We know that gravity affects life at the cellular and sub-cellular levels. Great progress has been made in determining gravity-related molecular responses in cells, plants, and animals (e.g. signal transduction, stretch receptors, cytoskeleton changes). A recent profound finding with major implications indicates that gravity has effects on life at its most fundamental level - the gene itself. We've seen that the absence of the single force that's shaped life for its entire existence on Earth - gravity - has significant effects on life, and at all levels.

The tools for solving the most fundamental problems in biology - from the biotechnology, information technology and miniaturization revolutions - are only becoming available now. FSB is leveraging upon enormous investments in R&D in the pharmaceutical and biotechnology industries, and in essence is bringing the Human Genome Project to space. The quantity of information being brought in through biotechnology - DNA chips being only one example - would have overwhelmed older computers and IT systems, but new, high-speed computers are able to provide the analyses to reveal the biology of spaceflight.

A. Discover

1) First Vertebrate Fertilization and Development Achieved in Micro-g: *A definitive study of the role of gravity in reproduction and development was conducted on an international STS/Spacelab mission.* It was clearly shown that gravity was not required for frog ovulation, fertilization, embryo development, and maturation to the free-swimming stage. This research answered the classic "gravity requirement" question in the negative as debated by embryologists for over 100 years and proposed for study in space by several committees of the National Academy of Sciences.
PI: K. Souza, ***Mission:*** STS-47/SL-J

2) Vestibular System Shows Amazing Adaptability to Gravity Changes: *The number of nerve connections between hair cells of the inner-ear and the brain increased dramatically in micro-g and decreased shortly after return to Earth, in rodent subjects.* This "neuroplasticity" measured for the first time in a gravity-sensing organ overturned the text-book concept that peripheral nerves don't change structurally over time. This

result has significant implications for human adaptability to the micro-g of space and variable gravity environments on other planets. The new basic knowledge of how information is processed by gravity sensors and the brain could improve our understanding and treatment of Earth-based problems such as; Meniere's disease, vertigo, imbalance and similar disorders.
PI: Ross, M.D., ***Mission:*** STS-40/SLS-1; STS-58/SLS-2

3) Cellular Cytoskeleton Found is a Key to Mechanical Sensing: *The "Tensegrity" theory's prediction that cell surface receptors (e.g. integrins) function as mechanoreceptors has now been validated and provides an explanation for how living cells physically and biochemically can respond to external mechanical stress, such as gravitational loading/unloading.* The FSB Program funded the ground-based research of Donald Ingber who coined the "tensegrity" term with a view that changes in a cells shape due to external loading can change the internal protein-based architectural structure and the biochemical signaling and gene activation that can have broad effects on cell function. Ingber, who gave birth to this exciting and expanding field acknowledges that his "work [was] made possible in part by funding…from the Space Biology Program at NASA….[They] gave me a chance when no others would do so by funding my first grant proposal." This research could show how gravity can influence an organisms cell dynamics and help identify countermeasures to certain untoward effects in living systems, including humans.
PI: D. Ingber, ***Mission:*** Ground-based

B. Develop

1) Mysterious Cause of Space Anemia Discovered: *This pioneering study using rodents as subjects on a USSR Biosatellite flight was driven by observations of astronaut anemia (red cell depletion) of unknown cause observed in the SkyLab crew.* The first observation of programmed death of newly formed red blood cells was confirmed from immediate postflight measurements and was subsequently validated in human subjects. Identification of this effect (termed "apoptosis") solved the riddle of how you can have fewer circulating red blood cells while the formation of new and destruction of older red cells doesn't change. This is a classic example of the major value of animal space research for human space exploration applications.
PI: H. Leon, ***Mission:*** Cosmos 782/Bion 3

2) 30 Years of Cosmos Biosatellite (Bion) Research with the USSR/Russia: *NASA FSB forged a deep and broad collaborative relationship with the Russian Institute for Medical and Biological Problems (IMBP) after they invited NASA to join their international Cosmos Biosatellite Program (Bion).* Beginning with Bion 3 (Cosmos 782) in 1975 and continuing for eight missions through Bion 10 (Cosmos 2229), NASA flew experiments on USSR biosatellites as an invited guest of the Russian Space Agency (until collapse of the Soviet Union) and the Institute of Biomedical Problems, Moscow. NASA provided flight and ground hardware and expendables that were used cooperatively by U.S. and Russian investigators and also shared use of Russian research habitats. For the 1996 Bion 11 mission that carried non-human primates in addition to simpler organisms, NASA and the Russian Space Agency negotiated a

contract whereby NASA received 50% of the science payload. For each of these Bion missions, U.S. and Russian scientists shared all cooperative science results and regularly published joint articles on their results.

Planning is underway for a revival of this collaboration on a 30-day Bion M1 mission in 2012 that would conduct space biology and biomedical research on rodents with an emphasis on studying adaptation to spaceflight and readaptation to Earth. PIs will have an opportunity to propose to a Biospecimen Sharing Program (BSP) utilizing rodent biosamples which will accommodate a broad, lower-cost research endeavor.

Over 250 peer reviewed scientific publications resulted from US participation in the nine cooperative Bion missions. The scientific findings not only advanced our basic understanding of how life senses and adapts to changes in gravity but also laid the foundation and provided guidance for the design, development and implementation of biomedical and artificial gravity countermeasures that could mitigate several adverse effects of spaceflight on human physiology.
PIs*:* Hundreds, ***Missions:*** Bion Mission Reports, and Bion Experiment Summaries in online "Life into Space" references (this chapter)

3) Major Space-related Muscle/Bone Revelations Emerge from Micro-g Simulation Model: T*he FSB Program funded a NASA PI to develop and validate a rodent model that has allowed scientists to simulate microgravity by decreased mechanical loading on Earth and thus begin to probe molecular mechanisms associated with variable loading of the musculoskeletal system*. Highlights from hundreds of research studies conducted by NASA PIs, NASA-sponsored PIs and other investigators world-wide with decreased loading have shown that:

- Changes in adult animals are specific to muscles and bones associated with maintenance of posture and movement against a load.
- In growing animals, certain muscles and bones stop growing at their normal rate while others actually lose mass.
- The specific changes found in the ground-based rodent unloading model are similar to those noted during spaceflight.
- Decreased synthesis of new tissues is as important as the destruction of existing bone/muscle mass.
- Muscle physiology experiments showed that resistive exercise provides a better countermeasure to muscle atrophy than the aerobic treadmill. Resistive exercise was adopted by the crew health program but the treadmill is also used since surface impact is good for bone loading and aerobics has cardiovascular benefits.

These advances will allow more logical countermeasures for solving space-related adaptation that makes return to Earth rather difficult. The model is also being used to test the hypothesis that development of reflexes associated with posture and balance require mechanical loading at certain critical periods during maturation of newborn animals.
PI: Holton, E., Baldwin, K., Riley, D. and others ***Mission:*** Flight and Ground-based

C. Apply

1) Pioneering Studies in Biovisualization: *Space research by a NASA PI on cell-level vestibular adaptation to variable gravity, required development of custom 3-D software and related analysis tools (see B. 1-b, above) to visually reconstruct tissues from slide sections.* This major FSB innovation and resulting technology transfer has become common practice for reconstructive surgery, breast cancer surgery, dental reconstruction, plastic surgery, brain surgery and other complex procedures requiring 3-dimensional dynamic simulations.
PI: Ross, M. ***Mission:*** Ground-based data analysis

2) Space Biosensor & Biotelemetry Technology: Applications to Medicine & Surgery: *NASA's need for advanced biosensor and biotelemetry technology (wireless bio-data communications) to remotely monitor subjects has direct application to Earth-based medicine and surgery.* Ideally, research subjects in long-duration studies, including small animal models like rodents, are unrestrained to fully reflect the impact of microgravity and other aspects of the spaceflight environment on their behavior and physiology. The FSB Program established a Sensors 2000 Project in the 1990s and a FSB Advanced Technology Project after 2000 to stimulate innovative biosensor and biotelemetry research for both human and animal subjects. In addition to developing new miniaturized biophysical, bioelectrical, and biochemical sensors, they were integrated with battery-powered or inductively coupled implantable biotelemetry systems to support freely moving subjects.

Continuous, data acquisition and improved measurement capabilities combined with the ease and flexibility offered by automated, wireless, and portable instruments and data systems, has transformed ambulatory medicine and intensive care facilities in hospitals, world-wide. This has lowered health care staff costs and sped return of patients to their homes where telemedicine (remote monitoring of patients via advanced biosensors, intelligent systems and broad-band networks) is increasingly utilized. A specific FSB-sponsored telemedicine application was with the Fetal Treatment Center (FTC) at the University of California at San Francisco. Miniaturized implantable biotelemetry was adapted to continuously monitor fetal patients after extra-uterine surgery to repair congenital defects. The monitor was designed to be implanted subcutaneously in the mother over the uterus to provide early-warning via telecommunications of premature labor that would allow quick removal of the fetus via ceasarian surgery since it could not survive a vaginal delivery.
PI: Hines, J. ***Mission:*** Bion Flights and Ground-based

Benefit Profiles

A. Shuttle Laboratory Research (plus related Ground-based studies)

1) Vibration is Protective of Bone Loss During Simulated Microgravity

***Question*:** Could mild vibrations applied via the feet lessen bone loss typically seen in a rodents experiencing unloading to simulate microgravity?

Results: Scientists showed mild vibrations prevent bone loss that normally occurs in hind-limb suspended rats, a ground based animal model of unloading. The technique works by stimulating the bones' stress response. A team of researchers, at the SUNY-Stony Brook, discovered that normally active animals exposed to 10 minutes per day of low-magnitude, high frequency vibrations experienced increased bone formation when compared to a control group. In addition, when animals, prevented from regular, weight-bearing activity, were exposed to 10 minutes of vibrations per day (during normal weight-bearing), bone formation remained at near-normal levels. Animals not exposed to the treatment, but who participated in 10 minutes of weight-bearing activity each day, still exhibited signs of significant bone loss.
Significance: While these preliminary animal results are encouraging, a full clinical study would be needed to demonstrate the effectiveness of using vibrations to recover bone mass and architecture in people with osteoporosis or lessen the bone loss observed regularly in astronauts during long duration space flight.
PI: Rubin, C., ***Mission:*** Ground-based

2) Microbial Drug Resistance and Virulence Changes in Microgravity

Question: Spaceflight research has demonstrated that microgravity significantly changes gene expression and virulence potential in Salmonella typhimurium, a very common disease producing organism in humans that is present in crewed spacecraft and ubiquitous on Earth. Would repeating the earlier microgravity studies using various growth media and ions as variables influence the virulence as has been seen in ground studies.
Results: Changes in gene expression and protein synthesis were found with increased virulence seen in rich media. When this media was augmented with custom ions the increased virulence was prevented.
Significance: Results suggest that this experiment model in which ions can control spaceflight associated virulence holds great promise for reducing the associated risk to crew health during spaceflight and could be exploited on Earth to combat infectious diseases.
PI: Wilson, Nickerson ***Mission:*** STS-123

B. ISS Laboratory Research

1) Advanced Astroculture

Question: The model organism, Arabidopsis thaliana, a small flowering plant, was successfully grown to the seed stage (a first) and harvested during earlier ISS inflight research studies. The Wisconsin Center for Space Automation and Robotics (WCSAR) proposed to use their updated Advanced Astroculture Apparatus in an attempt to grow a second generation of plants from those flown seeds. This multigeneration experiment had never been conducted in space.
Results: This attempt successfully grew a second generation of plants in space using space-germinated seeds while on the ISS. These observations and accompany analysis of the plants and seeds suggest that there were significant benefits to the longer duration microgravity than possible during Shuttle missions.

Significance: This initial development of an automated habitat for conducting multigenerational growth of a non-food crop paves the way for multigenerational research including gene expression, and the development of a variety of food crops and improved crop development in space. A successful study on the ISS was also conducted using soybeans that produced viable seeds.
PI: Zhou, Weijia ***Mission:*** ISS Expeditions 2,4,5

2) Signal Transduction and Gravi-sensing Threshold in Human Lymphocytes

Question: Will human T-lymphocytes flown on the ISS (an ESA PI) after transport by the Russian Soyuz show an altered genetic expression of Interleukin-2 and/or its receptor and is there a gravity threshold of 0.6 g above which this effect is not seen. Are the gravity effects direct (gravitational force acting in cell structures) or indirect (acting on the cell environment). Immune suppression of T-cell response to a simulated infectious agent (mitogen) inflight suggests the above hypotheses which need to be tested.
Results: Preliminary results suggest that the above hypotheses are real and that the gravity effect is direct due to its impact on the cellular endoskeleton.
Significance: Understanding of the mechanisms whereby the immune response in humans is drastically curtailed via such studies provides the potential to develop a countermeasure to this effect both in space and on Earth where immune suppression is a major medical problem.
PI: Walther, I, Cogoli, A., Hughes-Fulford, M., ***Mission:*** ISS – Expedition 14, Sept 2006

C. Free-Flyer Research

1) Russian Foton Free-Flyers

NASA FSB participation in the Foton-M2 (May 2005, 16 day) and the Foton M3 (September 2007, 12 day) missions (basically duplicate missions) continued, at a lower-level, the interaction with Russia after suspension of the Bion Program (see 2-b above for Bion-M1). The Foton spacecraft is similar to Bion, but it utilizes solar cells instead of a fuel cell for power and can thus support longer duration research. Discussions of potential options for future collaborative rodent research have occurred since such studies are unlikely to be accommodated on the ISS in the near-term. The focus was on the M2 and M3 missions was on the use of lower-level organisms including: newts (tissue regeneration), bacteria (genetic changes), snails (neural responses to gravity) and geckos (cell, tissue, structural changes).

Significance: Spaceflight enhanced cell proliferation in the amphibious newt, unlike in mammals. The proliferation may be due to the evolutionary changes newts made in adapting to neutrally buoyant conditions in an aquatic environment. Hypothetically, in an aquatic environment the neutral buoyancy unloading, of the animal's musculoskeletal system, would mimic the unloading that occurs in microgravity. This hypothesis can be tested and if correct, the response of the aquatic newt with the terrestrial gecko could provide a model for determining the genetic and biochemical pathways governing

muscle and bone growth and regulation. These missions provided new insights into the effects of microgravity on the process of sensing and adapting to changes in gravity. Using the snail, an organism that has a neurosensory system similar to humans, gene expression studies showed that a peptide found in the gravity receptor organ was up-regulated during the spaceflight. This suggests that in microgravity, an organism's ability to sense the weak gravity signal may increase. In engineering terms, the animal is turning up the gain to get better reception. The M3 mission incorporated several US-proposed scientific enhancements to the M2 experiments that provided increased science return. Also, the FSB Flight Systems and ARC science team developed add-on boxes to the newt/gecko habitats that included a battery-powered video camera for inflight recording, a solid-state video recorder, infrared LEDs for continuous lighting, and a pump to provide an optimal water supply. Such augmentations of Russian habitat systems by FSB based on their use over repeated missions, have been a staple feature of this fruitful collaboration.
PIs: Various, NASA ARC/Montana State Univ., ***Missions:*** Foton-M2 and M3 (reflight)

2) NanoSats

A more recent FSB collaboration with "free-flyers" is the NASA ARC-developed NanoSat or Micro/Nano Spacecraft Program (http://mstl.atl.calpoly.edu/~bklofas/Presentations/DevelopersWorkshop2008/session6/5 - NASA_Ames-John_Hines.pdf). These are developed within the ARC Small Spacecraft Division under management of its Chief Technologist, John Hines, who was the founder and manager of the ARC-based Sensors 2000 and Advanced Technology for FSB Projects (see 3-b, above). The NanoSats are based on emerging, advanced technology, often of commercial origin, and leveraged as an example from the highly-successful CubeSat Project (see References). Lower-cost, flexible access to space launch as secondary payloads with data downlinks are key features of FSB-related payloads such as GeneSat 1,2
http://space.skyrocket.de/index_frame.htm?http://space.skyrocket.de/doc_sdat/genesat-1.htm and PharmaSat.
http://space.skyrocket.de/index_frame.htm?http://space.skyrocket.de/doc_sdat/genesat-1.htm
Significance: The NanoSat Program has developed advanced technologies for research such as integrated sensor/measurement systems on a disk, digital microscopes, integrated biofluidic systems for experiment processing and has developed complete free-flying spacecraft with solar power panels and complete data and communication systems. These revolutionary capabilites provide a whole new opportunity for testing and validating innovative technology but also provide new ways to conduct research that supports space biology and a wide range of other research disciplines. It also opens the door to STEM-focused hands-on research and development opportunities for college students.
PI: Various, ***Missions:*** GeneSat, PhamaSat, more

Technology Spin-offs

1) Surgical Software: Developed by a NASA PI to facilitate postflight reconstruction

and visualization of the body's balance organ in the inner ear, the software is now being used by surgeons to plan and implement 3-D reconstructions of a wide range of patient defects or injuries. The software won a NASA "Software of the Year" award, and is being used in hospitals around the world. Using this software, the surgeon can re-create the 3D anatomy from 2D medical images, develop a computer-generated model, and evaluate through simulation alternative surgical options to optimally benefit the patient. The first test of the software application with human patients was by a NASA Ames-Stanford team that utilized the virtual reality computer tools to support complex facial reconstructive surgery.
Significance: As a follow-on the team has used these simulation tools for space life sciences applications including: development of complex procedures in an ISS glove box; interactive procedural training incorporating problem solving scenarios; enhanced interactions between the principal investigator and an astronaut using distributed internet connections; teleoperations; and complex human-computer interactions for surgery on soft and hard tissues. Thus these major Earth benefits came full-circle back to NASA FSB after refinement in the medical research community.

2) Nutrient Film Technique for Hydroponic Crops: NASA FSB researchers based at KSC were the first to research Nutrient Film Techniques (NFT) to automate hydroponic systems for application to in-space plant production. In doing so they first demonstrated *on a production scale* NFT-based hydroponics to grow potato tubers.
Significance: This approach is now utilized for the production of "seed" potatoes to propagate disease-free planting stock. Several potato seed growers as well as large corporations (e.g., Frito Lay) are using hydroponic production techniques developed by NASA for producing improved seed potatoes.
PI: Wheeler, Ray, ***Mission:*** Ground-based

Outreach Projects

The FSB Program has had an active outreach effort, funded and coordinated at both NASA ARC and KSC. Its web site, "Web of Life", is online within the NASA Exploration Science Mission Directorate (ESMD) at http://weboflife.nasa.gov. Web of Life is tasked by ESMD with imparting the relevancy and results of NASA-sponsored research via the Internet. By doing so, NASA improves scientific and technical literacy, contributes to academic excellence, and helps ensure the availability and quality of a new American workforce. Because of the general accessibility of the Web of Life content it supports both education and public outreach by "bringing space to the classroom" and profiling the "benefits of space research for applications to space exploration and life on Earth".

FSB Program outreach projects are carried out by the ARC and KSC organizations profiled below.

- NASA ARC: Biosciences Division, at http://spacebiosciences.arc.nasa.gov/ supports NASA's space exploration objectives by providing bioscience knowledge, engineering innovations and operations capabilities to extend the human presence beyond Earth. It includes three Branches for Bioengineering, Radiation & Space Biotechnologies, and Flight Systems Implementation.

- NASA KSC: Life Sciences Services Contract (LSSC) at http://www.lssc.nasa.gov/ supports Life Sciences Research, Ecological Programs and Health and Fitness projects. NASA's LSSC supports nearly all life sciences experiments, regardless of origin, that have been launched into low-Earth orbit from Kennedy Space Center, for more than 80 scientific missions and including more than 150 life science experiments. The LSSC has developed and demonstrated new technologies with life science applications, including; sensors, low-energy lighting systems, waste treatment systems, and advanced hydroponic systems.

- Several project examples are profiled below along with their significance.

1) SpaceBio.net: The FSB Program and the American Society for Gravitational & Space Biology jointly-sponsored and developed a college level web site beginning in 1997 to provide online education resources for teachers and students in space biology. "Space Biology: An Education Resource" used "spacebio.net" for its original url, but it is currently located at http://www.mainsgate.com/spacebio/index.html. It was last funded by FSB in 2005 but it is hoped that NASA-related student-users can be solicited as part of NASA's increased emphasis in supporting STEM education, to help update its links and, with mentor oversight, its content.
***Significance**:* The site received several awards from independent science web evaluators including the NASA Astrobiology Program ("excellence in information and education"), the National Science Teachers Association SciLinks Program ("meets our rigorous standards"), and the scholarly publisher,Thomson ISI (for its "authority, accuracy and currency"). At NASA's request, SpaceBio.net was evaluated by a panel of college science educators and given a recommendation for continued support.

2) Spaceflight and Life Sciences Training Program: The Spaceflight and Life Sciences Training Program (SLSTP) was developed as "an investment in tomorrow". It was designed as an intense, STEM-focused, academically challenging, six-week summer program at the KSC for college students interested in learning how to successfully design and conduct biological research and operations in space and to assess the environmental impacts of a launch site. The SLSTP was sponsored and implemented by NASA, the KSC Life Science Services Contract, NASA's SLSTP Academic Partner Alliance (NSAPA) and the USDA. NSAPA included Tuskegee University, South Mountain Community College, and Dine' College. Student projects ranged from "Plant Health and Evaluations for Earth and Space Applications" (http://weboflife.nasa.gov/slstp/mc.htm) to "Gene Analyses of Arabidopsis After Exposure to Stresses Associated with Spaceflight Environments" (http://weboflife.nasa.gov/slstp/kristen.htm). The last class was held in 2004.
Significance: The Program received several awards for its education innovations and its hundreds of graduates were the source of several recruits to NASA's space life sciences research endeavors.

3) Online Space Biology Course: A college level comprehensive set of online lectures and accompanying slides was developed by Dr. Chris Brown, a FSB-sponsored PI.

Brown utilized funding from FSB Program Outreach, the Kenan Institute, and the NASA Specialized Center of Research and Training in Gravitational Biology for which he served as Director. IT expertise to develop this product was provided by the North Carolina State University Department of Communication Services and the Distance Education & Learning Technology Applications Department. This course (http://www.cals.ncsu.edu/plantbiology/spacebiology/index.html) provides an overview of the biology of plants, animals and humans as related to gravity and the spaceflight environment. Students will become familiar with: experimental approaches to gravitational and space biology; mechanisms for observed spaceflight effects on living systems; current and past research results in gravitational and space biology; and the role that space science plays in society.
Significance: This is the only college-level course that exists to convey the breadth and depth of space biology. It is team-taught to ensure the quality of its content and to provide a broad view of the field.

4) Flies in Space Site: (http://quest.nasa.gov/projects/flies/index.html) A complete online teaching unit for middle school students was developed by FSB that is focused on one of the best known model organisms used for genomic-based research, the fruit fly (Drosophia melanogaster). The reasons for studying the fruit fly in space, the similarity of its immune response to humans, its anatomy, behavior and life cycles are all available for student exploration. Also, an experiment is described that students can conduct themselves in the classroom that will provide a hands-on experience of how research is conducted. Students therefore are introduced to the benefits of studying simpler model organisms for the value they provide in better understanding more complex organisms than ourselves.
Significance: This education unit for 5^{th}-8^{th} grade students is based on national education standards and provides a window into STEM-focused basic biology research as well as space biosciences research which makes it especially valuable to both teachers and students.

References

American Society for Gravitational & Space Biology, online at http://www.asgsb.org.

CubeSat Program web site coordinated by San Luis Obispo and Stanford Universities at http://www.cubesat.org/

GeneSat 1,2 http://space.skyrocket.de/index_frame.htm?http://space.skyrocket.de/doc_sdat/genesat-1.htm

Hertzfeld, Henry, "Measuring the Economic Returns from Successful NASA Life Sciences Technology Transfer", The Journal of Technology Transfer, Vol. 27, No. 4, December 2002, see at http://www.springerlink.com/content/mx377r26428538p8/

Hines, J., Technologies for Space Biology: New Horizons, presentation to Space Biology for Engineers, NASA Ames Research Center, online at http://www.dsls.usra.edu/biologycourse/workbook/Unit1.6.pdf

Ingbar, D, "Cellular Basis of Mechanotransduction", Biol. Bull. 194: 323-327. (June, 1998), online at http://www.biolbull.org/cgi/reprint/194/3/323.pdf and http://weboflife.nasa.gov/currentResearch/currentResearchBiologyGravity/skeleton.htm

Leon, H.A. et al.: "Alterations in Erythrocyte Survival Parameters in Rats After 19.5 Days Aboard Cosmos 782". Aviation, Space, and Environmental Medicine, vol. 49, 1978, pp. 66-69

Lomax, Terri, Fundamental Space Biology: Accomplishments Report, 2000-2002, 2004, online at http://www.nasa.gov/pdf/185052main_FSB2000-2002REPORT.pdf

PharmaSat. http://space.skyrocket.de/index_frame.htm?http://space.skyrocket.de/doc_sdat/genesat-1.htm

Ross, M., "Bioinformatics May Forever Change Medicine", in Innovation: Aerospace Technology, Vol 7, No. 5, Sept/Oct 1999. See online at http://ipp.nasa.gov/innovation/Innovation_75/bio.htm

Ross, M.D., "Synaptic Changes in Rat Maculae in Space and Medical Imaging: the Link", Otolaryngol. Head Neck Surg. 1998 Mar;118(3 Pt 2):S25-8

Rubin, C. et al: (1999) Expression of novel gene products upregulated by disuse is normalized by an osteogenic mechanical stimulus: NASA Space Biology Program; Biomedical Investigators' Workshop, Jan. 11-13, League City, Texas.

Souza, Kenneth, Robert Hogan, and Rodney Ballard, eds. Life into Space: Space Life Sciences Experiments. NASA Ames Research Center 1965-1990. Washington DC: National Aeronautics and Space Administration, 1995. NASA Reference Publication-1372. Online at http://lis.arc.nasa.gov/lis/index.html

Souza, Kenneth, Guy Etheridge, and Paul X. Callahan, eds. Life into Space: Space Life Sciences Experiments. Ames Research Center, Kennedy Space Center, 1991-1998. Washington DC: National Aeronautics and Space Administration, 2000. NASA Special Publication 2000-534. Online at http://lis.arc.nasa.gov/lis/index.html

Souza, Kenneth, ed. Life into Space: Space Life Sciences Experiments. Ames Research Center, 1996-2003. Partial online version contains experiments, hardware and publications only. See at http://lis.arc.nasa.gov/lis/index.html

Souza, K.A. et al., "Amphibian Development in the Virtual Absence of Gravity". Proceedings of the National Academy of Sciences United States of America, vol. 92(6), 1995, pp. 1975–1978.

Walther, I, Cogoli, A., Hughes-Fulford, M., "Influence of the effects of microgravity on function and activation of human T-cells" results summary online at http://www.spacebiol.ethz.ch/missions/leukin

Wheeler, R., et al, "Potato Growth and Yield Using Nutrient Film Technique" online at http://www.springerlink.com/content/h3v126671765t380/

Wilson, J.W., C.A. Nickerson, et al: "Media Ion Composition Controls Regulatory and Virulence Response of Salmonella in Spaceflight", http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0003923

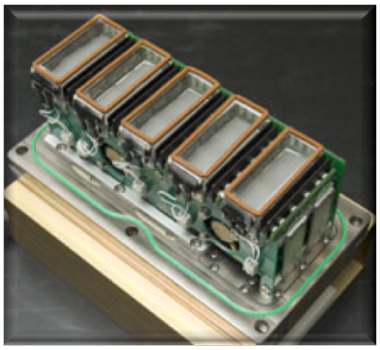
Zhou, W., Advanced Astroculture Plant Growth Unit: Capabilities and Performance", 35th Annual International Conference on Environment Systems, Rome, Italy, July 2005. Experiment summary online at http://www.nasa.gov/mission_pages/station/science/experiments/ADVASC.html#publications

Appendix 1

Fundamental Space Biology (FSB) Flight Hardware

Available for use on ISS

European Modular Cultivation System (EMCS)



The EMCS is an experiment facility for biological investigations under microgravity. It shall allow for cultivation, stimulation and crew assisted operation of biological experiments under well controlled conditions. Depending on the experiment specific hardware, it can be adapted to different applications e.g. to (larger) plants and invertebrates. The EMCS experiments use Experiment Containers (EC) and Experiment Unique Equipment (EUE) which are inside the EC.

The Plant Growth EC's have been designed to support experiments using small plants such as Arabidopsis.

Each EC has an internal volume of 60 x 60 x 160 mm with a transparent cover and up to 8 of these EC's can be integrated into the EMCS. The EC's work with the EMCS to provide lighting, water, environmental control and monitoring, video, and digital still image capture.

Single Loop Cell Culture (SLCC)

The SLCC consists of individual, self-contained, spaceflight cell culture systems with capabilities for automated growth initiation, feeding, sub-culturing and sampling. The cells are grown and contained within a rigid cell specimen chamber (CSC). Bladder tanks provide flush and media fluid. SLCC uses active perfusion flow to provide nutrients and gas exchange, and to dilute waste products by expelling depleted media fluid into a waste bladder tank. The cells can be grown quiescently, or

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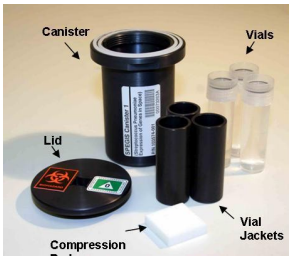
suspended using magnetically coupled stirrers.

Each system contains a cell specimen chamber and six removable sample/inoculation containers. The removable containers provide the capability to take cell samples at multiple time points that can be stabilized on-orbit for post-flight genetic or morphological analysis and for analyses of the effects of microgravity.

Microbial Cryogenic Canister Assemblies

The Microbial Cryogenic Canisters provide containment for microbial experiments. The canisters containing the Cryovials can be stored in temperature controlled environments during ascent, on-orbit, and descent.

The Microbial Cryogenic Canister Assemblies consist of an aluminum canister. Each Canister contains three 8 ml polypropylene vials. The vials are inserted into vial jackets to improve contact and enhance thermal transfer. The compression pad eliminates space between the vials and canister lid.



The unit can be used at ambient temperatures or on-orbit in an incubator.

Biological Research in Canisters (BRIC)

The Biological Research in Canisters (BRIC) is an anodized-aluminum cylinder used to provide passive stowage for investigations studying the effects of space flight on small specimens. The BRIC have supported a wide variety of research on many Space Shuttle missions and has multiple configurations.

- The BRIC-60 can hold a maximum of twelve, 60 mm petri dishes (total of 24 per full canister) or thirteen Teflon tubes (total of 26 per full canister) can be placed inside each canister chamber. No power is required.

- The BRIC-100 can accommodate nine polycarbonate 100 mm petri plates. The bottom and top lids of each canister have twenty-five 0.5 mm holes and a Teflon membrane (pore size 0.5 micrometers). Two

septa are located in the lid to allow gas sampling. Underneath this lid, the semi-permeable membrane is attached and supported by an anodized-aluminum ring. The ring and membrane assembly are supported by five stainless steel screws. If gas exchange is not required, the semi-permeable membrane and capture ring can be replaced by an aluminum capture plate to provide a closed experimental environment. The petri plates inside the canister are held in place by a petri dish cage insert.

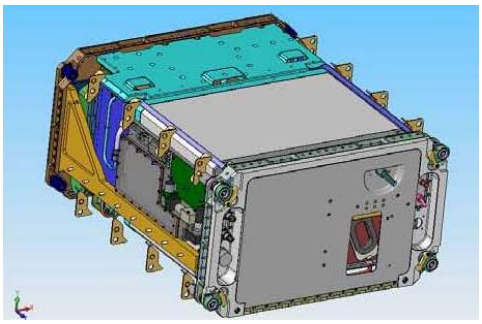
- The BRIC-100VC canister can accommodate standard 100 mm laboratory petri plates. The BRIC-100VC canister provides containment and structural support for the specimens and their associated hardware. The lid of the canister uses a toggle switch and O-ring assembly which allows quick sealing and removal of the lid. The bottom of the canister has sufficient storage space for passive temperature and relative humidity recorders.

- The BRIC-LED can utilize a complement set of hardware, the Petri Dish Fixation Unit (PDFU). The PDFU is a specialized holder for a standard 60 mm petri dish which delivers fixative to the sample within the petri dish. The PDFU is inserted into the BRIC-LED. Each BRIC-LED can house six PDFUs. Electrical requirements are 6 watts. The lid of each BRIC-LED is secured using ten screws, and includes a silicone gasket to provide a seal between the lid and the base. Six holes are present in the lid of the BRIC-LED for insertion of a PDFU actuator attachment which allows fixation of the specimens. Each of the holes is sealed using a silicone septum. The lid of each BRIC-LED also houses a circuit board which contains red surface mount LEDs (6 per BRIC) for specimen illumination; switches (6 per BRIC) for controlling on/off status of red LEDs; and green surface mount LEDs (6 per BRIC) for verification of the on/off status of the red LEDs. Each red LED is located on the bottom of the circuit board, with a corresponding green LED located on top of the lid. The green LEDs provide the crew with a method of verifying red LED illumination/operations. Each red LED provides a wavelength of 640 - 660 nm red light to the samples located inside the canister via a Pyrex light pipe. The switches are located on the top of the circuit board to

switch the LEDs on or off at the appropriate time. An additional orange LED is located on top of the circuit board to indicate that power is being properly supplied to the canister?s circuitry. A custom stowage tray is used to house the BRIC-LED canisters and power distribution box. The tray is made of anodized aluminum and contains a power connector to allow Orbiter power connection to the locker before flight. An enclosed fan prevents samples from reaching extreme temperatures.

Advanced Biological Research System (ABRS)

The Advanced Biological Research System (ABRS) is a single middeck locker replacement facility. As a middeck locker replacement, the ABRS is compatible with both the Space Shuttle and the ISS EXPRESS racks. While in the middeck, ABRS is a rear-breathing, powered locker that can be used as a primary facility or as an up and down specimen transportation device. In EXPRESS, the ABRS is a subrack facility payload that takes advantage of both rear air breathing and also intercooling via the moderate temperature loop (MTL). Sensor data and images are conveyed via Ethernet through the EXPRESS rack to the ground. ABRS may be commanded either from the ground or by the crew using an EXPRESS laptop. The current operating scenario includes a low-power ascent mode in the middeck and permanent residence of the ABRS facility on the ISS.



Each ABRS Environmental Research Chamber (ERC) can independently provide the following services:

- Temperature control to 8 degrees C below ambient
- PAR of 50-300 micromol/m2/sec illumination
- Continuous ethylene removal to below 25 parts per billion (ppb)
- Controllable atmospheric carbon dioxide (CO2) level
- Continuous removal of volatile organic compounds (VOCs)
- Relative humidity control between 60-90%

- Generic chamber imaging from three cameras
- Generically supports experiment unique equipment (EUE) including a Green Fluorescent Protein (GFP) imager

Passive Dosimeter System (PDS)

The Passive Dosimeter System (PDS) hardware consists of two kinds of radiation dosimeters and an electronic "reader." The “reader” and one of the dosimeters are currently on orbit and available for use.

The PDS consists of two kinds of dosimeters and a reader. One of the radiation dosimeters is a thermoluminescent detector, or TLD. These detectors are used to measure incident ionizing radiation (protons, neutrons, electrons, heavy charged particles, gamma and x-rays). Each TLD, which resembles a fat fountain pen, contains calcium sulfate crystals inside an evacuated glass bulb. These crystals absorb energy from incident ionizing radiation (protons, neutrons, electrons, heavy charged particles, gamma and x-rays) as the radiation passes through them. This process results in a steady increase in the energy level of the electrons in the crystal.

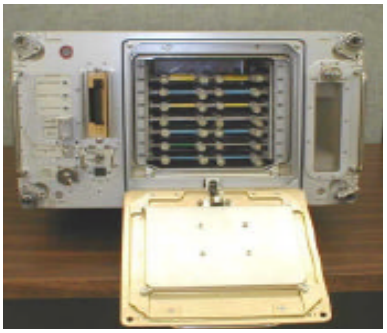
The other type of dosimeter is a set of Plastic Nuclear Track Detectors (PNTDs). The PNTDs are thin sheets of plastic, similar to the material used for some eyeglass lenses. As heavy charged ions pass through the PNTDs, the surface becomes pitted with tiny craters. When the PNTDs are subsequently returned to Earth, the plastic is etched to enlarge the craters. Then the craters are counted and their shapes and sizes are analyzed using a microscope. This information is used to improve the accuracy of the radiation dose the TLDs have recorded and to improve the estimate of the biological effects of the radiation.

The TLDs and the reader used to anneal the TLDs prior to use are currently in stowage on the ISS. The PNTDs need to be launched in support of each individual experiment.

Biotechnology Specimen Temperature Controller (BSTC)

The Biotechnology Specimen Temperature Controller (BSTC) provides a platform for the Cellular Biotechnology Operations Science System (CBOSS) investigations to study basic cell to cell interactions, in a microgravity environment and the formation of functional cell aggregates.

BSTC is a self-contained apparatus designed to allow multiple experiments studying various cells types to operate simultaneously. It is a multi-component cell incubator intended to grow three-dimensional clusters of cells in microgravity. BSTC contains one large chamber which can house 32



stationary tissue culture modules (TCMs) at temperatures between 4 degrees C - 50 degrees C (39.2 degrees - 122 degrees F). The TCMs are clear Teflon bags that hold approximately 30 milliliters (1 oz) of growth media. BSTC can also be reconfigured to include a gas purge system, carbon dioxide monitoring (provided by the front display), and an Ethernet connection to the ISS computer via the EXPRESS Rack. BSTC is equipped with systems and temperature monitors that are able to detect conditions inside its chambers.

Certified for Shuttle Operations

The hardware listed in this section has been certified and flown on the Shuttle. Additional work to upgrade and/or certify the hardware is required for use on the ISS.

Animal Enclosure Module (AEM)

The AEM hardware is used for experiments which study the influence of microgravity on rodent physiology and anatomy. Research conducted with the AEM is an analog to the human research program which has the objective are to extend the human presence safely beyond low Earth orbit. Animal research is a key component of solving critical human health and performance problems resulting from long-duration missions in space

The AEM is a self-contained habitat that provides its occupants with living space, food, water, ventilation, and lighting. Its internal waste management system guarantees that animals are isolated from their waste by-products and that these by-products and food crumbs do not escape into the open middeck where the crew is living..

The AEM supports up to five adult rats or eight adult mice and fits inside a standard middeck locker with a modified locker door. It is composed of a stainless steel grid cage module, fan blowers, a layered filter system, interior lamps, food bars and a water unit. Total animal floor space, with water box installed, is 645 cm2. A removable divider plate provides two separate animal holding areas (if required). The AEM remains in the stowage locker during launch and landing. On orbit the AEM may be removed from the locker and the interior viewed or photographed through the clear Lexan cover over the cage; the AEM  must be pulled out of the locker approximately three quarters of its depth for observation of the rodents. Temperatures inside the AEM can be recorded with a data logger and the data is read out and provided to investigators postflight. A main breaker protects and distributes power to fan and lighting subsystems. Additional circuit breakers independently protect lights and fans in diagonally opposed corners to assure light and air circulation on each side of the AEM should one breaker fail. The AEM can be moved into the Orbiter approximately twelve hours before launch and removed approximately one hour after landing.

Cabin air is exchanged with the AEM through a filter system. Four fan blowers, operated by a switch on the front panel, create a slight negative pressure inside the cage, causing an air sweep to pull animal waste products into a collection filter. Cabin air is drawn through the front panel inlet slots, then along the side plenum walls, to be directed though the inlet filter located at the rear of the AEM, into the animal habitat. High efficiency particulate air (HEPA) filters (electrostatic and phosphoric acid treated fiberglass pads) prevent any microbiological escape into the cabin atmosphere. Treated charcoal, within the unit, confines animal odors within

the closed system. After exiting the habitat through the exhaust filter, located at the front of the unit between the rodent cage and fans, the filtered air is drawn through the fans into the cabin and directed by the air deflector.

The four internal lamps provide an average of 14 lux illumination and are controlled by an automatic timer to provide a programmable lighting cycle for the AEM. The lamps are mounted two to a side in the rear corners of the AEM, between the animal habitat and inlet filter, and are covered with a clear cap to protect each lamp from animal debris. The timing of the day/night sequence can be selected, and is typically set to a 12/12-hour day/night cycle.

The AEM has a 1,500 and 2,000 cm3 capacity automatic watering unit that utilizes four "Lixit Drinking Valves" and two flexible plastic (polyvinylchloride) bladders for water storage. Sufficient water pressure is maintained via compression springs. Water consumption can be monitored in flight by observation of water levels via a Lexan window on the top of the water box. Rodent food bars are attached to up to four slide-in food bar plates inside the rodent cage. The food, a sterilized laboratory formula, is molded into rectangular bars (approximately 1.8 x 1 x 8 inches) accessible to the animals at all times during the mission.

Appendix 2

Planned Payloads

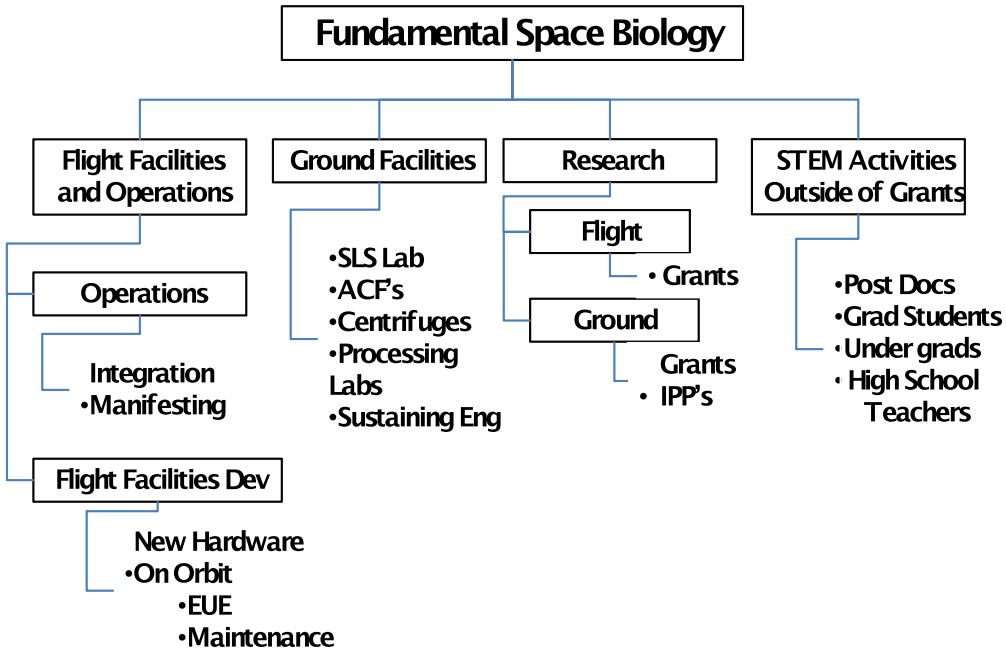
Payload	Investigation title	Investigator	Research Objectives	Hardware	Projected Flight Ascent	Projected Flight Descent
MDS Biospecimen Sharing Program	Effect of Space Flight Conditions on Immune System Parameters Effects of long-duration spaceflight on the circadian and metabolic systems of mice Effects of Microgravity on Heart Mass and Extracellular Matrix Cellular/molecular causes of skeletal deterioration in mice exposed to long duration microgravity Synaptic plasticity in hair cells of utricular macula	Shi UMD New Jersey: Fuller UC Davis Delp University of FL Bateman Clemson University Boyle	Shi: The overall objective is to examine the effect of spaceflight on changes in lymphocyte number and on the stress response in wild type and osteoblast stimulating factor-1 transgenic mice. Fuller: To understand the effects of long-duration microgravity exposure on the regulation of circadian rhythms and metabolism in mice. Delp: Determine whether microgravity induces cardiac atrophy in mice and whether microgravity alters cardiac extracellular matrix protein concentration and composition. Bateman: Examine the functional skeletal deterioration and cellular/moleular causes in mice exposed to long duration microgravity exposure and the potential bernefits of transgenic osf-1 expression in mitigating the expected osteopenia. Boyle: Identify the morphological changes that occur in the synaptic organization of the vestibular hair cells of the utricular otolith organ as	**ASI Mouse Drawer System**	**STS-128/17A 8/28/09**	**STS-129/ULF-3 11/12/09**
SPEGIS-2	Streptococcus Gene Expression in Space	Niesel University of Texas Medical Branch	SPEGI-2 is a follow-on to the first S. pneumoniae virulence study that was conducted on STS-118 and on the Microbial Drug Resistance and Virulence study conducted on STS-123. SPEGIS II builds on the virulence molecular and biochemical findings of the first experiment.	**BioServe GAPS**	**STS-129 / ULF3 Nov. 2009**	**STS-129 / ULF 3**
Tropi II	EMCS-TROPI 2 (European Modular Cultivation System - Gravitropism)	Kiss PI: Miami University	The TROPI 1 experiment was performed on the ISS in late 2006. Video data collection was compromised due to software problems and neither video nor RNA data from fractional g levels were obtained. The reflight of the TROPI experiment provides an opportunity to collect video and RNA data from two experiment runs at four g levels; micro-g to 1.0g. The purpose of this research is to understand the mechanisms of gravitropism and phototropism in Arabidopsis thaliana seedlings. Two experiment runs will be performed in ESA's EMCS facility on ISS. Seedling images will be collected during the runs on orbit and frozen samples will be	**EMCS ECs and Seed cassettes**	**STS-130 / 20A Feb. 2010**	**STS-131 / 19A Mar. 2010**
Padiac	Sensitivity modulation of different T-cells activation pathways by microgravity'	Hughes-Fulford Northern CA Institute of Research and Education,	International collaboration between Dr. Millie Hughes-Fulford, and ESA Principal Investigator Isabelle Walther. The Leukin experiment was performed on Soyuz 13S in Sept. 2006. Cells were only incubated for 1.5 hours. Leukin will refly as PADIAC for the critical 4 hour incubation timepoint .Experiment is designed to determine the effect of microgravity on lymphocyte activation. To study the regulation of lymphocyte activation especially at the level of the cytokines IL-2, IL-1 and their receptors.	**ESA Cell culture hardware**	**Soyuz 22S Apr. 2010**	**Soyuz 21S May 2010**
Mouse Immunology	Mouse Antigen-Specific CD4+ T Cell Priming and Memory Response during Spaceflight	Hughes-Fulford Northern CA Institute of Research and Education	Determine whether antigen-specific CD4+ T cell priming in vivo is inhibited or dysfunctional during spaceflight. Determine whether antigen-specific CD4+ memory T cells are maintained normally during spaceflight and able to mount robust secondary responses.	**AEM**	**STS-131 / 19A Mar. 2010**	**STS-131 / 19A Mar. 2010**

Planned Payloads

Payload	Investigation title	Investigator	Research Objectives	Hardware	Projected Flight Ascent	Projected Flight Descent
STL	Stem Cells/Role of Artificial g in Promoting Tissue Regenerative Matrix-Integrin-Kinase Cell Signaling	Almeida NASA ARC	Investigate cell differentiation and embryonic development. Embryoids display all of the major differentiation processes for tissue and organ development and is an important model system for studying cellular and molecular developmental and regeneration pathways	**STL CCM Rails**	**STS-131 / 19A Mar. 2010**	**STS-131 / 19A Mar. 2010**
STL	Micro/RNA Binding Proteins as Evolutionarily Conserved Cellular S/F Response Mechanisms	NIckerson ARizona State University	Determine if RNA binding regulatory proteins and their small RNA binding counterparts are key to a common conserved cellular spaceflight response mechanism and if the response can be manipulated by environmental ion levels.	**STL CCM Rails**	**STS-131 / 19A Mar. 2010**	**STS-131 / 19A Mar. 2010**
Micro 2	Micro/Gravity Effects on Quorum Sensing and Biofilm Formation	Collins Rennsselar Polytechnic Institute (RPI)	Examine the influence of mutations affecting cell/cell communication and motility on biofilm formation; identify changes in gene expression and signal transduction related to quorum sensing, biofilm.	**CGBA**	**ULF4 May 20010**	**ULF4 May 2010**
Mouse Immunology 2	Effect of Space Flight on Innate Immunity to Respiratory Viral Infections	Garofalo University of Texas Medical Branch	Using the mouse experimental model this experiment will continue the investigation of the effects of micro gravity on immune function. In microgravity, astronauts experience changes in immune function. These studies will help determine the biological and/or biomedical significance of spaceflight induced changes in immune responses.	**AEM**	**ULF5 Sep 2010**	**ULF5 Sep 2010**
Seed Growth 1 (formerly ATRIP)		TBD; to be selected from NASA Research Announcement NNH09ZTT002N NRA Research Opportunities for Flight Experiments in Space Life Sciences, proposals due September 14, 2009	TBD Pi to be selected	**EMCS ECs and Seed cassettes**	**ULF6 July 2010**	**SpaceX CRS1 Dec 2010**
Micro 3		TBD: to be selected from Physiology NRA	TBD PI to be selected	**GAP / CGBA**	**Space X CRS1 Dec 2010**	**Space X CRS Dec 2010**
Seed Growth 2		TBD; to be selected from NASA Research Announcement NNH09ZTT002N NRA Research Opportunities for Flight Experiments in Space Life Sciences, proposals due September 14, 2009	TBD PI to be selected	**EMCS ECs and Seed cassettes**	**49 P April, 2011**	**TBD**

Appendix 3

Work Breakdown Structure for the Optimal Utilization Program



Appendix 4

NASA Biological Payloads in Space, 1965-2010*

Mission	**Launch Date**	***Payload***	***No. of Expts.***	**Organisms** *(see legend)*
Gemini 3	03/16/65	Sea Urchin Experiment	1	35
Gemini 8	03/16/66	Frog Egg Package	1	18
Gemini 12	11/11/66	Frog Egg Package	1	18
Biosatellite I	12/14/66	Experiments Capsule	14	18, 24, 29, 30, 31, 44, 50, 56, 57, 59, 61, 65
Biosatellite II	09/07/67	Experiments Capsule	14	18, 24, 29, 30, 31, 44, 50, 56, 57, 59, 61, 65
Biosatellite III	06/28/69	Primates Experiment Capsule	7	6
OFO-A	11/09/70	Frog Otolith Experiment Package (FOEP)	3	1
Apollo 17	12/17/72	Biological Cosmic Ray Experiment (BIOCORE)	6	10
Skylab 3	07/28/73	Circadian Periodicity Experiment Package (CPE)	2	10
Cosmos 782	11/25/75	Bion 3	18	**13**, 15, 24, 37
Cosmos 936	08/03/77	Bion 4	8	**13**, 24
Cosmos 1129	09/25/79	Bion 5	19	**13**, 20, 37
STS-3	03/22/82	Office of Space Science 1 (OSS-1)	1	36, 48, 52
STS-8	08/30/83	Student Shuttle Involvement Program (SSIP)	1	**13**
Cosmos 1514	12/14/83	Bion 6	5	7, **13**, 21
STS-10	02/03/84	Student Shuttle Involvement Program (SSIP)	1	**13**
STS-51B	04/28/85	Spacelab 3 (SL-3)	30	5, 8, **13**
Cosmos 1667	07/10/85	Bion 7	1	7
STS-51F	07/29/85	Spacelab 2 (SL-2)	1	36, 48, 51
Cosmos 1887	09/29/87	Bion 8	33	**13**
STS-29	13/13/89	Chromosome and Plant Cell Division 1 (CHROMEX-1)	1	40, 43
		Student Shuttle Involvement Program (SSIP)	2	**13**
Cosmos 2044	09/15/89	Bion 9	48	7, **13**
STS-34	10/18/89	Growth Hormone Concentration & Distribution (GHCD)	1	38
STS-32	01/10/90	Characterization of Neurospora Circadian Rhythm (CNCR)	1	65
STS-41	10/01/90	Chromosome and Plant Cell Division 2 (CHROMEX-2)	1	40, 43
		Physiological Systems Experiment 1 (PSE.01)	1	**13**
STS-40	06/05/91	Spacelab Life Sciences 1 (SLS-1)	32	**13**, 25
STS-48	09/12/91	Physiological/Anatomical Rodent Experiment 1 (PARE.01)	1	**13**
STS-42	01/22/92	International Microgravity Laboratory 1 (IML-1)	4	26, 48, 56, 70
STS-46	07/31/92	Pituitary Growth Hormone Cell Function (PHCF)	4	68
STS-47	09/12/92	Spacelab J (SL-J)	2	3, 5, 17
STS-52	10/22/92	Physiological Systems Experiment 2 (PSE.02)	1	**13**
Cosmos 2229	12/29/92	Bion 10	12	7
STS-54	01/13/93	Chromosome and Plant Cell Division 3 (CHROMEX-3)	1	46
		Physiological/Anatomical Rodent Experiment 2 (PARE.02)	1	**13**
STS-56	04/08/93	Physiological/Anatomical Rodent Experiment 3 (PARE.03)	1	**13**
		Space Tissue Loss 3A (STL-3A)	1	21
STS-57	06/21/93	Physiological Systems Experiment 3 (PSE.03)	1	**13**
STS-51	09/12/93	Chromosome and Plant Cell Division 4 (CHROMEX-4)	3	46, 56
STS-58	10/18/93	Spacelab Life Sciences 2 (SLS-2)	28	**13**
STS-60	02/03/94	Immune System Experiment (IMMUNE.1)	1	**13**
STS-62	03/04/94	Physiological Systems Experiment 4 (PSE.04)	2	**13**
STS-59	04/09/94	National Institutes of Health Cells 1 (NIH.C1)	3	63, 68
STS-65	07/08/94	International Microgravity Laboratory 2 (IML-2)	3	19, 25
STS-64	09/09/94	Biological Research in Canisters 2 (BRIC-2)	1	49
STS-68	09/30/94	Biological Research in Canisters 1 (BRIC-1)	2	33
		Chromosome and Plant Cell Division 5 (CHROMEX-5)	1	46, 53
STS-66	11/03/94	National Institutes of Health Cells 2 (NIH.C2)	2	63, 67
		National Institutes of Health Rodents 1 (NIH.R1)	13	**13**
STS-63	02/03/95	Biological Research in Canisters 3 (BRIC-3)	1	53
		Chromosome and Plant Cell Division 6 (CHROMEX-6)	1	56
		Immune System Experiment 2 (IMMUNE.2)	1	**13**
		National Institutes of Health Cells 3 (NIH.C3)	3	63, 68

Soyuz 70	03/15/95	Incubator 1	9	20
STS-71	06/27/95	Incubator 2	9	20
		Greenhouse 1	1	56
STS-70	07/13/95	Biological Research in Canisters 4 (BRIC-4)	1	32
		Biological Research in Canisters 5 (BRIC-5)	1	40
		National Institutes of Health Rodents 2 (NIH.R2)	5	**13**
STS-69	09/07/95	Biological Research in Canisters 6 (BRIC-6)	1	65
		National Institutes of Health Cells 4 (NIH.C4)	2	64, 68
STS-72	01/11/96	National Institutes of Health Cells 5 (NIH.C5)	2	63
		National Institutes of Health Rodents 3 (NIH.R3)	2	**13**
STS-76	03/22/96	Biorack 1	3	26, 64, 67
		Incubator 3	9	20
		Environmental Radiation Measurements on Mir 1	1	N/A
STS-77	05/19/96	Aquatic Research Facility (ARF)	1	34
		Biological Research in Canisters 7 (BRIC-7)	1	32
		Immune System Experiment 3 (IMMUNE.3)	1	**13**
		National Institutes of Health Cells 7 (NIH.C7)	2	63
STS-78	06/20/96	Biological Research in Canisters 8 (BRIC-8)	1	40
		Life and Microgravity Spacelab (LMS)	3	**13**, 15, 42, 51
STS-79	09/16/96	Greenhouse 2	1	56
		Environmental Radiation Measurements on Mir 2	1	N/A
STS-80	11/19/96	Biological Research in Canisters 9 (BRIC-9)	1	54, 55
		National Institutes of Health Cells 6 (NIH.C6)	2	64, 67
		National Institutes of Health Rodents 4 (NIH.R4)	1	**13**
Bion 11	12/24/96	Bion 11	15	7
STS-81	01/12/97	Biorack 2	5	46, 58, 64, 67, 70
		Effective Dose Measurements during EVA 1	1	N/A
		Environmental Radiation Measurements on Mir 3	1	N/A
STS-84	05/15/97	Biorack 3	4	46, 64, 67, 69
		Effects of Gravity on Circadian Rhythmicity	1	22
		Greenhouse 3	1	47
		Effective Dose Measurements during EVA 2	1	N/A
		Environmental Radiation Measurements on Mir 4	1	N/A
STS-85	08/07/97	Biological Research in Canisters 10 (BRIC-10)	1	54, 55
STS-86	09/25/97	Active Dosimetry of Charged Particles	1	N/A
		Environmental Radiation Measurements on Mir 5	1	N/A
STS-87	11/19/97	Collaborative Ukranian Experiment (CUE)	11	47, 53, 66
STS-89	01/22/98	Closed Equilibrated Biological Aquatic System (CEBAS)	2	2, 27, 45
		Microgravity Plant Nutrient Experiment (MPNE)	1	56
STS-90	04/17/98	Neurolab	15	2, **9**, 13, 14, 23, 27
STS-95	10/29/98	Biological Research in Canisters 13 (BRIC-13)	1	49
		Biological Research in Canisters PEG/C (BRIC-PEG/C)	1	39
		National Institutes of Health Cells 8 (NIH.C8)	1	63
		Vestibular Function Experiment Unit (VFEU)	1	14
STS-93	07/23/99	Biological Research in Canisters 11 (BRIC-11)	1	46
		Biological Research in Canisters 12 (BRIC-12)	1	41
		National Institutes of Health Biology 1 (NIH.B1)	1	24
		Plant Growth Investigations in Microgravity 1 (PGIM-1)	1	46
STS-106	09/08/00	National Institutes of Health Biology 1 (NIH.B1)	2	24
STS-108	12/05/01	Avian Development Facility	2	20
STS-110	04/08/02	Photosynthesis Experiment and System Testing Operation (PESTO)	1	47, 56
STS-107	01/16/03	Biological Research in Canisters 14 (BRIC-14)	2	66
		Fundamental Rodent Experiments Supporting Health 2 (FRESH-02)	3	13
		Biopack	2	58, 64
Progress 13P	01/29/04	Yeast Group Activation Pack 1 (Yeast GAP-1)	1	71
Soyuz 8	04/18/04	First International *Caenorhabditis elegans* Experiment (ICE-First)	1	26
M2	05/31/05	Foton	4	4, 12, 28, 62
STS-121	07/04/06	Phototropism (TROPI)	1	46
		Fungal Immunity (FIT)	1	31
STS-115	09/09/06	Microbial Gene Expression and Virulence (Microbe)	1	60, 61, 72
21P	09/18/06	Role of Interleukin-2 Receptor in Signal Transduction and Gravisensing Threshold in Lymphocytes (Leukin)	1	64

STS-118	08/08/07	Commercial Biomedical Testing Module-2 (CBTM)	1	9
		Streptococcus Pneumoniae Expression of Genes in Space (SPEGIS)	1	73
M3	09/14/07	Foton	4	28, 12, 59, 60, 74, 75, 79
STS-123	03/11/08	Microbial Gene Expression and Virulence (Microbe)	1	60, 61, 72
		Streptococcus Pneumoniae Expression of Genes in Space (SPEGIS)	1	73
		Bacterial Physiology and Virulence	1	60
		Drug Resistance and Virulence (MDRV)	1	71
STS-126	11/14/08	Differentiation of Bone Marrow Macrophages in Space (BONEMAC)	1	77
STS-129	11/16/09	Streptococcus Pneumoniae Gene Expression and Virulence (SPEGIS reflight)	1	73
STS-130	02/08/10	Phototropism (TROPI-2)	1	46
STS-131	04/05/10	Mouse Immunology-1	1	9
		Space Tissue Loss (STL)	2	61, 76, 78
STS-132	05/14/10	Gravitational Effects on Biofilm Formation During Spaceflight (Micro-2)	1	60, 76
STS-134	09/18/10	Mouse Immunology-2	1	9

** This table lists payloads managed through NASA Ames Research Center and Kennedy Space Center, therefore some commercial biological experiments are not included. International experiments flown on US spacecraft and US experiments flown on Russian spacecraft are included. Experiment abstracts and associated publications for the majority of the payloads listed here are available in the* Life into Space *volumes at http://lifesci.arc.nasa.gov/lis_home.*

LEGEND

Organisms Flown

Vertebrates: Adults or Juveniles

1 Bullfrog (*Rana catesbeiana*)
2 Fish, swordtail (*Xiphophorus hellerii*)
3 Frog, African clawed (*Xenopus laevis*)
4 Gecko, Mediterranean house (*Hemidactylus turcicuse*)
5 Human (*Homo sapien*)
6 Monkey, pigtail (*Macaca nemestrina*)
7 Monkey, rhesus (*Macaca mulatta*)
8 Monkey, squirrel (*Saimiri sciureus*)
9 Mouse, house (*Mus musculus*)
10 Mouse, pocket (*Perognathus longimembris*)
11 Newt, Japanese red-bellied (*Cynops pyrrhogaster*)
12 Newt, Spanish ribbed (*Pleurodeles waltl*)
13 Rat, Norway (*Rattus norvegicus*)
14 Toadfish, oyster (*Opsanus tau*)
79 Gecko, thick-toed (Pachydactylus turneri)

Vertebrates: Embryonic Forms

15 Fish, killifish/mummichog (*Fundulus heteroclitus*) roe
16 Fish, medaka (*Oryzias latipes*) egg
17 Frog, African clawed (*Xenopus laevis*)
18 Frog, northern leopard (*Rana pipiens*) egg
19 Newt, Japanese red-bellied (*Cynops pyrrhogaster*) egg
20 Quail, Japanese (*Coturnix coturnix japonica*) egg
21 Rat, Norway (*Rattus norvegicus*)

Invertebrates: Adults or Juveniles

22 Beetle, black-bodied (*Trigonoscelis gigas*)
23 Cricket (*Acheta domesticus*)
24 Fruit fly (*Drosophila melanogaster*)
25 Jellyfish, moon (*Aurelia aurita*)
26 Nematode (*Caenorhabditis elegans*)
27 Snail, bloodfluke planorb (*Biomphalaria glabrata*)
28 Snail, striped Roman (*Helix lucorum)*
29 Wasp, parasitic (*Habrobracon juglandis*)

Invertebrates: Embryonic Forms

30 Beetle, confused flour (*Tribolium confusum*) pupa
31 Fruit fly (*Drosophila melanogaster*) larva
32 Hornworm, tobacco (*Manduca sexta*) pupa
33 Moth, gypsy (*Lymantria dispar*) egg
34 Sea urchin, painted (*Lytechinus pictus*) egg and embryo
35 Sea urchin, purple-spined (*Arbacia punctulata*) egg

Plants

36 Bean, mung (*Vigna radiata*) seedling
37 Carrot, wild (*Daucus carota*) tissue and/or cell

Cell Cultures and Unicellular Forms

57 Amoeba (*Pelomyxa carolinensis*)
58 Bacteria (*Burkholderia cepacia*)

38	Corn (*Zea mays*) seedling
39	Cucumber (*Cucumis sativus*) seedling
40	Daylily (*Hemerocallis*) shoot
41	Fern, triangle waterfern (*Ceratopteris richardii*) spore cell
42	Fir, Douglas (*Pseudotsuga menziesii*) seedlings
43	Flowering, yellow daisy (*Haplopappus gracilis*) shoot
44	Flowering, spiderwort (*Tradescantia*) plant
45	Hornwort/Hornweed (*Ceratophyllum deresum*)
46	Mouse-ear cress (*Arabidopsis thaliana*)
47	Mustard, field (*Brassica rapa*)
48	Oat (*Avena sativa*) seedling
49	Orchardgrass (*Dactylis glomerata*)
50	Pepper, cayenne (*Capsicum annuum*) plant
51	Pine, Loblolly (Pinus taeda) seedlings
52	Pine, slash (*Pinus elliotti*) seedling
53	Soybean (*Glycine max*) seed
54	Tobacco (*Nicotiana tabacum*) seedling
55	Tomato (*Lycopersicon esculentum*) seedling
56	Wheat (*Triticum aestivum*) seed and seedling
59	Bacteria (*Escherichia coli*)
60	Bacteria (*Pseudomonas aeruginosa*)
61	Bacteria (*Salmonella typhimurium*)
62	Bacteria (*Streptomyces lividans 66*)
63	Chicken (*Galus galus*)
64	Human (*Homo sapien*)
65	Mold, bread (*Neurospora crassa*)
66	Moss, ceratodon (*Ceratodon purpureus*)
67	Mouse, house (*Mus musculus*)
68	Rat, Norway (*Rattus norvegicus*)
69	Sea urchin, painted (*Lytechinus pictus*) sperm
70	Sea urchin, purple (*Strongylocentrotus pupuratus*) sperm
71	Yeast (*Saccharomyces cerevisiae*)
72	Fungus (Candida Albicans)
73	Bacteria (Streptococus pneumoniae)
74	Fungus (Aspergillus niger)
75	Bacteria (Lactobacillus casei)
76	Bacteria (Staphylococcus aureus)
77	Mouse (C57BL/6J)
78	Stem Cells (mouse)