Space Station Biological Research Project

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ABSTRACT

To meet NASA’s objective of using the unique aspects of the space environment to expand fundamental knowledge in the biological sciences, the Space Station Biological Research Project at Ames Research Center is developing, or providing oversight, for two major suites of hardware which will be installed on the International Space Station (ISS). The first, the Gravitational Biology Facility, consists of Habitats to support plants, rodents, cells, aquatic specimens, avian and reptilian eggs, and insects and the Habitat Holding Rack in which to house them at microgravity; the second, the Centrifuge Facility, consists of a 2.5 m diameter centrifuge that will provide acceleration levels between 0.01 g and 2.0 g and a Life Sciences Glovebox. These two facilities will support the conduct of experiments to: 1) investigate the effect of microgravity on living systems; 2) what level of gravity is required to maintain normal form and function, and 3) study the use of artificial gravity as a countermeasure to the deleterious effects of microgravity observed in the crew. Upon completion, the ISS will have three complementary laboratory modules provided by NASA, the European Space Agency and the Japanese space agency, NASA. Use of all facilities in each of the modules will be available to investigators from participating space agencies. With the advent of the ISS, space-based gravitational biology research will transition from 10-16 day short-duration Space Shuttle flights to 90-day-or-longer ISS increments.

INTRODUCTION

Throughout its evolution, life on Earth has been exposed to the constant force of gravity. It is axiomatic that gravity helped shape and continues to influence the structure and function of all living organisms. Because of its pervasive influence, understanding the effects of gravity on life is a fundamental question of substantial inherent scientific value in our quest to understand life. Knowledge of the effects of gravity on lower organisms, animals and plants, and elucidation of the basic mechanisms by which these effects occur, will be of direct benefit to understanding the impact of, and providing countermeasures to, the effects of long-term exposure of humans to the microgravity of space flight and the partial gravity of lunar and planetary bases. It will also provide the basis for the development of bioregenerative life support systems for use on human exploration missions as well as enhance the quality of life on Earth through applications in medicine, agriculture, industrial biotechnology, environmental management, and other human activities dependent on understanding our biological resources. Space flight provides the only environment where the force of gravity can be removed, or discrete levels of gravitational force between zero and 1 g can be provided, for durations required to address these critical scientific questions adequately. Space is the only environment where the effects of environmental factors, (e.g., light, temperature, nutrition) on fundamental biological processes and mechanisms can be studied in the absence of the coupled and sometimes overwhelming effects of gravity.

NASA’s Gravitational Biology Program, through implementation of the Space Station Biological Research Project (SSBRP), seeks to use the unique characteristics of the space environment, particularly microgravity, as a tool to advance knowledge in the biological sciences. In conjunction with complementary ground-based research, in-flight studies have already demonstrated that gravity plays a significant role in regulating the growth, development, and physiology of living organisms. However, limited access to space and limited flight durations have precluded detailed studies across an appropriate diversity of species with replications sufficient to characterize the effects of gravity; and little is know about the basic mechanisms by which they happen.

The SSBRP hardware developed to support gravitational biology on the International Space Station, in conjunction with other research equipment available on ISS, will focus on utilizing the unique space flight advantages provided by ISS. These include extended duration, technically advanced facilities, inflight sample preservation and analysis, sufficient sample size and replications, and variable-g capabilities. While some questions can and have been investigated on short duration flights provided by Spacelabs, biosatellites, and even sounding rockets, many questions require a long duration facility such as ISS. For example, many biological processes (e.g., organism development and multigeneration cycles, and adaptation) require extended periods of time to occur. Also, the answers to many biological questions can only be provided by extended duration experiments where the results of on-orbit observation and analysis can be used to modify parameters of ongoing or sequential follow-on experiments. Technically advanced facilities and on-orbit analysis will, for the first time, allow investigations involving key unstable biological components requiring immediate analysis, and structures, products and phenomena that are modified during reentry and return. Advanced sample preparation and preservation technology will greatly enhance science return from on-orbit experiments by increasing preservation options and variety of samples available for more sophisticated analysis on Earth.
Table I. Equipment Requirements for Life Sciences Experiments on a Space Station

- Centrifuge: 10^{-1} g to 1 g (or >1 g)
- General Purpose Work Station (a glovebox)
- Imaging Capability: CAT scanm Electron Magnetic Resonance, Nuclear Magnetic Resonance, etc.
- Data return to ground
- TV monitor
- Gas Analyses (gas chromatography/mass spectrometer)
- Radioisotope Measuring Capability
- Metabolic Sampling Unit and Waste Management System (urine and feces)
- High Pressure Liquid Chromatograph
- Metabolic cages to Monitor Gases, Urine and Feces
- Research Animal Holding Facility (similar to that used in Shuttle)
- Plant Growth Unit
- Freezer, Refrigerator and Clinical Centrifuge
- Incubator
- Sterilizer
- Real Time Data Processing

Inherent biological variability requires that sufficient time and sample number be provided for a response to be measurable. Our ability to clearly interpret past U.S. and international life sciences flight experiments has often been limited because there were too few replications. Hardware developed for ISS promises to provide the required time and statistically valid number of samples for clear interpretation of results. Furthermore, a continuous operating laboratory in space will allow replication of experiments and eliminate the current 2-year-plus delay required to manifest follow-up experiments. ISS facilities will permit rapid follow-up to take advantage of exciting discoveries. The breadth of habitats developed within the SSBRP provides the flexibility to allow scientists to take advantage of biological diversity and to match the question to the most appropriate biological model. The ability to use well characterized biological systems that have been used extensively for research on Earth will: (1) enhance the interpretability of results and foster a consensus in the scientific community because extensive knowledge bases already exist; (2) decrease the need for NASA-sponsored preparatory ground-based experiments; and (3) shorten the time course and reduce the cost of resolving critical life sciences questions. The diversity of habitats provided by the Gravitational Biology Facility, and the centrifuge and glovebox provided by the Centrifuge Facility, plus the human research equipment on ISS will greatly enhance the ability to conduct the kinds of interspecies comparative studies that have always been important in life sciences research.

The combination of habitats in stationary racks and on the large diameter centrifuge will provide specimens at gravitational levels from near zero to 2 g. This capability will allow gravity to be manipulated in a manner analogous to the way light intensity, temperature, nutrient levels, drug dosages, etc. have always been manipulated to elucidate the fundamental mechanisms and processes involved in the structure and function of living systems. Furthermore, it will allow us to evaluate explicitly the effect of lunar (1/6 g) and Martian (3/8 g) gravity levels on candidate organisms for bioregenerative life support systems for lunar and Martian bases. In addition, experiments with animals that serve as human surrogates or models will allow predictions of the effects of lunar, Martian and transit vehicle gravity regimes on humans.

**MERCUERIAL HISTORY OF SSBRP**

Planning for life sciences research on a space station began with a series of discipline oriented workshops during the early 1980s which resulted in a workshop and publication known as the "Fabricant Report" (Fabricant, 1983). The report summarizes the findings and recommendations from the individual working groups in the areas of: (1) Developmental Biology, Genetics and Aging, (2) Plant Physiology, (3) Cardio/Vascular and Fluid/Electrolytes, (4) Metabolism, Bone, Muscle and Immunology and the neurosciences which included one panel in (5) Neurophysiology, Vestibular and Motor Control and another in (6) Behavior and Psychopharmacology. A set of common requirements which were identified for performing experiments is shown in Table I. The report also describes of set of experiments from each of the working groups which would require a space station.

As the scientific community was being asked to define the uses of a space station, early feasibility studies were funded by NASA Ames Research Center. These studies were to define the engineering feasibility of building such a laboratory for space and to identify new technologies which would be required to implement it. This effort culminated in the establishment in 1984 of the Centrifuge Facility Project at NASA Ames Research Center to develop a life science research facility for a space station. Early activities of the Centrifuge Facility Project focused on the definition of requirements and
Table II. Chronology of Space Station Biological Research Project

1984 Centrifuge Facility Project established
- Centrifuge Requirements Workshop
- Establishment of Science Working Group
- Science requirements for: Centrifuge, Glovebox, Primate, Rodent and Plant Habitats
- Hardware feasibility studies with industry

1992 Gravitational Biology Facility established
- Establishment of Science Working Group
- Identified habitats to support cell and developmental biology and plant biology
- Defined requirements for: Cell, small Plant, Insect, Aquatic, Egg, and Mouse Development Habitats

1994 Centrifuge Facility and Gravitational Biology Facility Projects merged into Space Station Biological Research Project

1996 Development and funding of Space Station Biological Research Project transferred from Life Sciences Division at NASA Headquarters to the Space Station Project Office at Johnson Space Center

reference experiments for plant, small primate, and weanling through adult rat habitats, a Life Sciences Glovebox, and the large diameter centrifuge (Johnson et al., 1989; Smith et al., 1992 ) and (2) more detailed engineering analyses by NASA Ames Research Center (Synnestvedt, 1991) and two major aerospace contractors, Lockheed Missiles and Space Company, Inc. and McDonnell Douglas Space Systems Company. This activity resulted in a Request for Proposals in 1991 to build the centrifuge, glovebox, plant and rodent habitats. Proposals were received and evaluated from the two contractors, but the contract was never awarded, primarily because of restructuring of the Space Station Program and the uncertainty of where the hardware would be installed on the ISS.

In 1992 an independent project known as the Gravitational Biology Facility was established with the objective of developing habitats to support cell and developmental biology and plant biology. Following a major review by Ames Research Center management and by NASA Headquarters in 1994, the two projects were consolidated into a single project, the Space Station Biological Research Project. Hardware was reallocated between the two Facilities with the Centrifuge Facility retaining responsibility for development of the host systems, i.e., the Habitat Holding Racks, the 2.5 m diameter centrifuge and the glovebox; and the Gravitational Biology Program focusing on the development of the specimen habitats, including the plant and rodent habitat defined by the Centrifuge Facility. A second Request for Proposals was released to industry in 1994 but limited to the development of the 2.5 m diameter centrifuge and the glovebox. Proposals were received and evaluated. However, this procurement was also canceled.

Negotiations were initiated with the Japanese space agency, NASDA, to provide this hardware as an offset for the cost of launching NASA ISS hardware, i.e., the Japanese Experiment Module (JEM) and logistics module. This approach reduces the transfer of Japanese currency to the United States and reduces Space Station Program expenditures in the near term where budgets are severely constrained. Development of the habitats was pursued via in-house development, extensions of existing Small Business and Innovative Research contracts and open competition. In addition two habitats--the aquatic and insect habitats--will be provided by international partners in the ISS program. A brief chronological history and list of accomplishments of the two projects is in Table II.

Both the Centrifuge Facility and the Gravitational Biology Facility Projects held a series of workshops to define the general requirements for the centrifuge, the glovebox and the environmental and operational requirements for each of the habitat types. These requirements have been documented in the Level II Science and Technical Requirements Document (ARC/BRP-40002). The Level II Science and Technical Requirements Document defines the requirements as specified by an independent group of science advisors as well as Project Positions which reflect what it is felt is technically and economically feasible at this point in the development of the hardware. The Project Positions have been agreed to by the science advisors during subsequent meetings and form the basis of the engineering specifications to which the habitats will be built. A brief description of the pieces of...
hardware which comprise the Space Station Biological Research Project is given below.

Habitat Holding Rack (HHR)

A key component of SSBRP is the Habitat Holding Rack (HHR) which provides structural support for habitats in microgravity. It provides power distribution from the ISS to the habitats, heat rejection (avionics air, low or moderate cooling loop), and data/video management and interface to the ISS data system for data transmission to the ground and command functions.

Life Sciences Glovebox

The Life Sciences Glovebox (LSGB) plays a central role in the operations of the centrifuge and habitats. It provides an isolated work volume for operations such as dissection and tissue fixation, sampling, and video or videomicroscopy. One of the key requirements is to support two operators simultaneously.

Centrifuge

The Centrifuge is a 2.5 m diameter rotating system that provides the same resources (power, heat rejection, and data/video) that the HHRs provide while accelerating the habitats. It can accommodate up to 8 habitats and will provide 0.01 g to 2 g. The centrifuge will be mounted in the end of the Centrifuge Accommodation Module since that location maximizes the diameter and minimizes the rotational effects on the specimens. The centrifuge will provide two different gravity levels simultaneously by locating habitats at two different radii.

Cell Culture Unit (CCU)

The Cell Culture Unit (CCU) is designed to support experiments with animal and plant cells, microbes, tissue cultures, and potentially non-feeding small aquatic specimens for up to 30 days. Culture size is planned to be 3 to 30 ml in volume, with 8 to 24 individual specimen chambers. The CCU will provide fresh nutrient media and manage waste products. Temperature control will be provided over a range of 15° to 39° C, with the option to refrigerate the samples either prior to or following an experiment. Automatic sampling will be possible, as will the ability to add fixatives into the individual cultures. The CCU will fit in the HHR and on the centrifuge.

Aquatic Habitat (AH)

Aquatic vertebrates such as fish and amphibians, as well as aquatic plants and invertebrates may be accommodated within the AH. Features of the AH include a water quality management system for fresh water organisms. Oxygen will be maintained at 60-95% saturation (at STP) and pH will be maintained between 6.7 and 7.5. Food will be provided to larval stage animals, and nutrients to all other plants and animals. The programmed temperature range will be between 14° and 30° C. The AH will be able to operate for up 90 days and accommodate all life stages of development for species such as zebrafish. Specimens will be accessible through all life stages for manipulation, fixation or videography.

Plant Research Unit (PRU)

The Plant Research Unit (PRU) is designed to support long duration studies of plants with a height of up to 38 cm and will fit in the HHR and on the centrifuge. It provides nutrient delivery, CO₂ control over the range of 350 ppm to 2000 ppm, and up to 600 μmole/cm²/s PAR. Fluorescent illumination is baseline but the capability exists to provide LEDs as experiment unique equipment for photobiology experiments. The growing area of 550 cm² can either be a single chamber or be segregated into smaller chambers. The capability to sample the atmosphere, nutrient solution and individual plants will be provided. Video imaging is possible during both the light and dark cycle.

Advanced Animal Habitat - Centrifuge/Mouse Development Insert

The AAH-C will support rats and mice from weanling to adult and, using the Mouse Development Insert, mice through birth and nursing. Up to 6 rats and 12 mice may be group housed per habitat or the habitat can be subdivided to provide individually housed animals. Food and water will be provided ad lib; temperature will be maintained and monitored between 18° and 27°C. Video monitoring is also provided. The AAH-C will fit in the HHR and on the centrifuge.

Insect Habitat

The Insect Habitat will support investigations in developmental biology, gerontology, evolutionary biology and behavioral biology using insects. Initial emphasis will be on Drosophila, but other species will also be accommodated. The top level hardware requirements are to maintain temperature between 4° and 40°C, maintain humidity between 20% and 95% (RH), provide a programmable lighting source and supply nutrients and media for adult maintenance and larval development. A key requirement of the Insect Habitat is to provide separation of at least three generations of Drosophila. Specimen collection, preservation, and storage of all developmental stages is also planned, as is the capability for video monitoring. This habitat contains its own centrifuge so it will be used only in the HHR.
Egg Incubator

The Egg Incubator is designed to support development of avian and perhaps reptilian eggs through all stages of development up to hatching, but not including hatching. The incubator will house up to 48 small eggs, such as quail, or 24 large eggs, such as chicken. Temperature will be maintained between 26° and 40°C, with the capability to chill the eggs to between 10° and 18°C prior to and following experiment operations. Humidity is controlled to between 50% to 70% for avian eggs (100% humidity is required for reptilian eggs). Automatic fixation, as well as turning of the eggs is provided. The current concept of the Egg Incubator incorporates an internal centrifuge, so it is not necessary for the Egg Incubator to be placed on the 2.5 m diameter centrifuge.

Laboratory Support Equipment

Small laboratory equipment which will be used to support microgravity and life sciences experiments is designated Laboratory Support Equipment. The items which the SSBRP is responsible for developing are: a small mass measurement device, a dissecting microscope, a compound microscope, a passive dosimeter, a refrigerated centrifuge, and an incubator. Functional requirements for these items were collected from potential users within the microgravity and life sciences community. Responsibility for developing the remaining laboratory support equipment was given to Microgravity Sciences.

In addition to the hardware elements listed above, the Space Station Biological Research Project is responsible for the development of the ground facilities required to support on-going operations. This includes developing an expanded operations and data communication center to provide interfaces between Ames Research Center and the Payloads Operations Center located at Marshall Space Flight Center which will communicate with the orbiting Station, data distribution to Principal Investigators at their home institutions, and archiving of engineering and scientific data.

CURRENT STATUS

The specifications and development schedule for the hardware to be developed by the Space Station Biological Research Facility (SSBRP) for Life Science research on Space Station are a complex synthesis of requirements from several groups: science objectives of the Life Sciences Division at NASA Headquarters (Code UL), science requirements from the user community, accommodation capabilities of the ISS, operational requirements from the astronaut office, feasibility analysis by industry, and budgetary constraints of the Space Station Program office as illustrated in Figure 1.

A complete set of requirements for accomplishment of the SSBRP mission objectives has been developed over the years and is under configuration control. In
addition the project had developed, and projected up through mid-2006, a complete set of plans which fit within the ISS master schedule (with the first Habitat Holding Rack launched in late 1999) and project funding guidelines.

However, ISS Program cost and schedule problems continue to affect the SSBRP and all of the other Station Payloads, e.g., those being developed for human life sciences and microgravity sciences. As noted earlier in this paper, negotiations are currently underway with NASA for development of the centrifuge and glovebox (and the module in which they will be housed on the ISS, the Centrifuge Accommodation Module). These negotiations may require compromises on some of the current technical requirements and/or schedule. At the direction of the Space Station Program Office, the Project is also studying means of reducing the costs for the remaining hardware. The primary constraint is funding through the middle of 2002. The approach being studied is to develop the simpler habitats first and to spread out the development and fabrication of the more complex (and more expensive) habitats, thus reducing the pre-2003 funding requirements. The first Habitat Holding Rack is now scheduled to be launched in late 2001, Table III. Unfortunately, we believe that further slips in schedule will probably occur as the ISS deals with the inevitable problems which come with a development of this magnitude and complexity. It is expected that research in the first rack will be with the Cell Culture Unit and the Incubator. This approach helps meet the project funding constraints and falls within the resource constraints (primarily power and crew time) of the ISS prior to 2003.

Questions which could be addressed and suggested experiments for early science were presented in an earlier publication. (Johnson, Hargens and Wade, 1996). Another option strongly supported by the SSBRP Science Working Group is to use the modified Animal Enclosure Module from the Neurolab Shuttle mission and the prototype hardware for the plant habitat and egg incubator during the Assembly Phase of the Space Station to provide continuity with animal, plant and avian development experiments conducted on the Shuttle and Russian Mir space station.

INTERNATIONAL COLLABORATION ON ISS

Past successes in the Spacelab, COSMOS and Shuttle/Mir programs have clearly demonstrated the value of international cooperation in space flight through collaboration on experiments, exchange of data, and sharing of hardware. The international partners of the International Space Station (ESA, NASA/CSA, and NASA) have agreed to implement a similar approach loosely based on the Spacelab model for integrating life science activities and thus maximizing the scientific return for each participant.

Each of the Life Sciences organizations from the participating agencies would directly fund scientific investigations on the ISS. For the United States, NASA Headquarters would release an annual solicitation for researchers to propose ground-based and flight experiments through the NASA Research Announcement (NRA) process. The proposed schedule would be to release the NRA at the beginning of the calendar year, to convene peer review panels mid-year, and to award grants to successful investigators in the fall of that same year. For the ISS, the international partners have agreed to coordinate the solicitation and selection process to allow for a more efficient use of limited ISS research resources beginning with the 1997 cycle. The agreed upon process is:

1. Each agency will issue its own solicitation based on internal science priorities. The release of the solicitation would be synchronized with release of the other agencies’ solicitations. Each of the solicitations would contain standard elements, e.g., a section on the integrated selection process itself, descriptions of flight elements (supplied by each developing organization), a standardized set of forms and instructions, an international flight hardware catalog, and descriptions of research and support facilities available to researchers.

2. Proposals will be submitted to the respective sponsoring agency and screened at the discretion of the agency. Candidates would then be forwarded to a Central Review Coordinator.

3. A consolidated international peer review panel will evaluate the proposals with each participating agency designating a panel member.

4. After proposals are scored for scientific merit, they will be evaluated for engineering and cost management feasibility against known hardware capabilities/limitations by the agency developing or operating those facilities. The agencies would then prepare a final candidate list based upon the scientific peer and engineering feasibility reviews.

5. All of the participating agencies will meet to review the final candidate list and to select the investigators and experiments jointly. Any conflict would be resolved and overlapping investigations would be consolidated. Selection rationale by the participating agencies will be based upon programmatic priorities of that specific agency.

A partial list of hardware which has been developed or will be developed by the international partners is

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<th>Table III. Launch Dates for NASA Developed Life Sciences Payloads</th>
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<tr>
<td>Habitat Holding Rack #1 2001</td>
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<td>Glovebox 2002</td>
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<td>Habitat Holding Rack #2 2002</td>
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<td>Centrifuge 2003</td>
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Table IV. Partial List of Hardware Developed by the International Partners

Existing:

- CEBAS
- BOTEX
- VFEU
- IBIS

NIZEMI
ARF
FERTILE

Planned:

- Cell Biology Experiment Facility
- Clean Bench
- Modular Cultivation System
- Biolab

shown in Table IV. For a description of the hardware capabilities, consult the hardware catalogue being published in conjunction with the release of the 1997 NRA.

SUMMARY

Although the development of the Space Station Biological Research Project for the International Space Station has suffered numerous delays and a reduction in budget, the science requirements developed in conjunction with the science community and the engineering specifications based on those requirements are well established and provide a firm basis on which to proceed. The hardware being developed by NASA and the international partners for life sciences research on the International Space Station will expand the general knowledge of the role gravity has played in the evolution of life on Earth. Inclusion of the large diameter centrifuge and smaller centrifuges on orbit will allow investigators to study the gravity spectrum between microgravity and 1 g. One can begin to understand how living systems interact with, and adapt to, changes in gravity as well as explore the efficacy of centrifugation as a biomedical countermeasure. Collaboration among the international partners on ISS will provide investigators access to all available life sciences facilities and hardware. Through the use of a diverse and complementary set of hardware, investigators will be able to design experiments creatively to use microgravity as a research tool to comprehend biological process in space and on Earth more fully.

REFERENCES

Fabricant, Jill D. 1983. *Life Sciences Experiments for a Space Station*, University of Texas Medical Branch, Galveston, Texas.


