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Paper Session I-A - Learning about Life on Space Station

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Learning about Life on Space Station

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Abstract

The International Space Station as humanity's outpost in low Earth orbit, is an ideal platform for studying how to live in space, as well as to conduct research to learn more about life. A long-duration microgravity platform such as ISS allows the study of biological and physiological processes free of the one constant force to which they have been subjected since the origin of life on Earth: gravity. Although construction of ISS is still under way, the US Laboratory Module *Destiny* has been outfitted with its full complement of 10 research facilities, two of them dedicated to life sciences research. In the coming years, *Destiny* will be joined by the European Space Agency's *Columbus* and by Japan's *Kibo* research modules with additional facilities, and then by the Centrifuge Accommodation Module containing a centrifuge for variable gravity research. Research has been ongoing for only 2 of its planned 15 years of orbital life, so we have clearly just opened the door to learning about life on Space Station.

Introduction

The space environment offers a unique laboratory in which to study chemical, physical and biological processes. Researchers utilize the microgravity environment aboard International Space Station (ISS) to conduct experiments in physical and biological sciences that are impossible on Earth. Throughout the history of life on Earth, all organisms have been exposed to one constant factor, gravity, and therefore all their systems have adapted to it. It is a highly influential factor in many of the response mechanisms used by living organisms, and one often taken for granted. By studying a variety of organisms aboard Space Station, where the force of gravity is essentially eliminated, much can be learned about basic mechanisms of life. Experiments in which the force of gravity can be controlled will take this principle one step further.

Overview of ISS and its research facilities

The ISS has been under construction in low Earth orbit since late 1998, a process that will continue for several more years. Figure 1 depicts how ISS is expected to look in 2007, following the addition of the International Partner modules. In addition to installing the laboratory modules, much of the construction centers on providing the infrastructure to enable research, such as power generation via large solar arrays, communications for commanding of experiments and receipt of data and telemetry, and dissipation of the heat generated by the various payloads and vehicle systems. One of the first building blocks of ISS, after the initial crew quarters and solar arrays were deployed, was the US Laboratory Module *Destiny*, launched in February 2001. This cylindrical 8.5-m by 4.3-m module is the principal location for the conduct of US research, and since its launch has been progressively outfitted with 10 research racks, including two dedicated to human life sciences investigations, the Human Research

Facility (HRF) Racks 1 and 2. To date, investigations in fundamental biology have utilized racks called EXPRESS, for Expedite the Processing of Research for Space Station, for long-duration experiments and the Space Shuttle middeck for short-term investigations. Five EXPRESS racks are currently on orbit, providing support to short- or long-term payloads, typically of the Shuttle middeck locker size variety. A rack-size refrigerator-freezer, called MELFI for Minus Eighty-degree Laboratory Freezer for ISS, was recently installed in Destiny and will be used for experiments requiring cold stowage at -80^o, -22^o, or +4^{o}C.

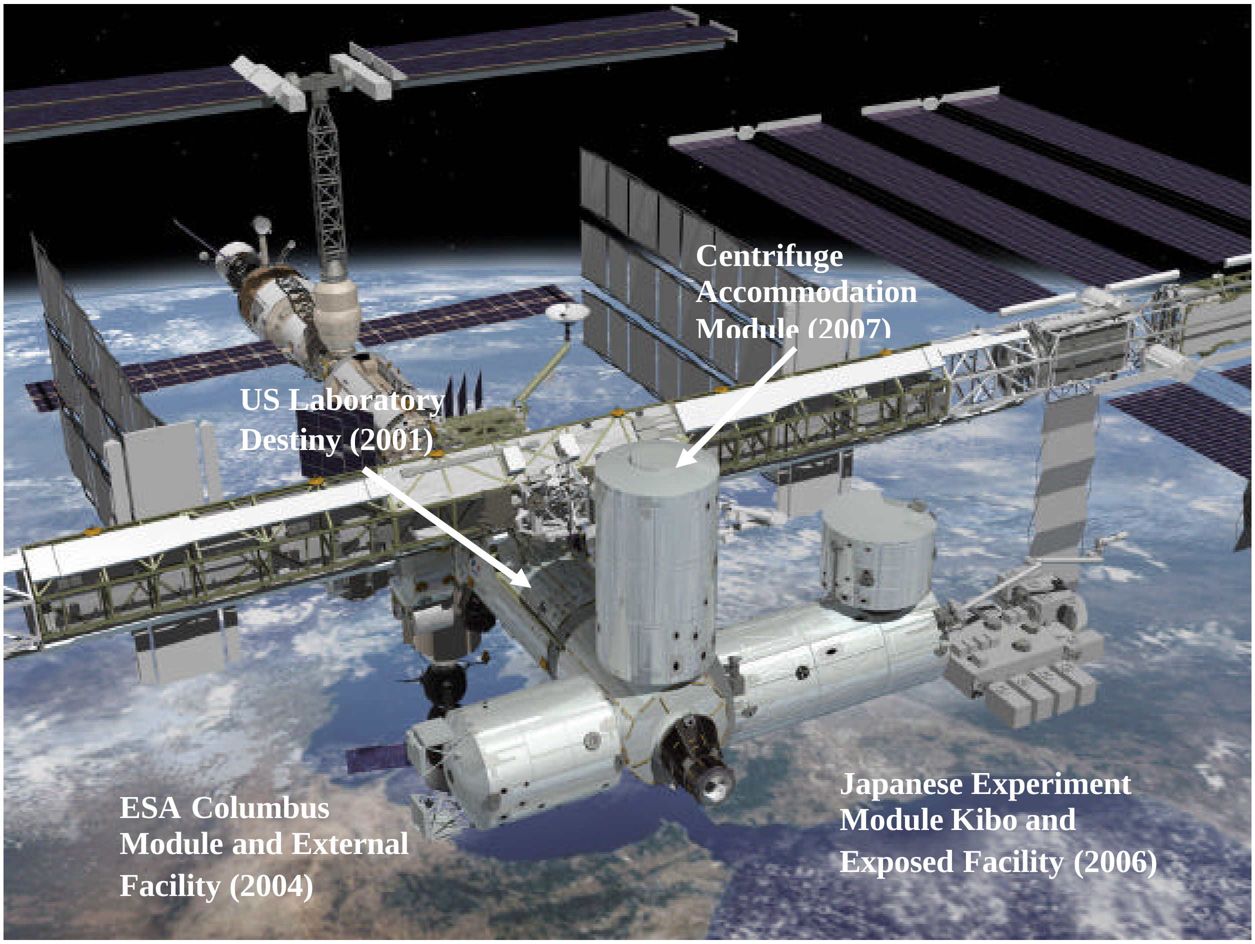

Figure 1. Artist's rendering of ISS at Assembly Complete, including International Partner modules and the Centrifuge Accommodation Module.

The European Space Agency-provided *Columbus* module is planned to be added to ISS in late 2004. It will provide the capacity for 10 new research racks. Among these, and launched with the module itself, will be Biolab and the European Physiology Modules (EPM). The Biolab facility is a modular system designed for research in regulatory mechanisms of proliferation and differentiation, the role of the cytoskeleton, mechanical loading, graviception, and mechanisms of radiation damage and repair. It can accommodate research in cell and tissue cultures, microorganisms, and small plants and animals. The EPM rack provides the infrastructure for up to eight Science Modules in a variety of life science research disciplines.

The Japanese *Kibo* module is planned to be added to ISS in 2006, providing up to 11 new rack locations. Some facilities currently in the *Destiny* module will be relocated to other partner modules, first to clear space in *Destiny* for racks that require the US module's more quiescent microgravity environment, and second to make overall placement of these racks more efficient by co-locating facilities with complementary functions. One such example is the eventual relocation of the MELFI into *Kibo*.

The Centrifuge Accommodation Module (CAM) will be added to ISS in 2007. Inside the module will be the Centrifuge Facility containing a 2.5-meter diameter centrifuge rotor. The centrifuge will be able to produce a controlled artificial gravity, allowing variable gravity studies to be carried out in a number of habitats containing various biological specimens. The module will also be able to house the habitat holding facilities and a glovebox to enable investigations requiring crew intervention.

Ultimately, up to 9 facilities, approximately one-third of all research racks, will be dedicated to studying life on Space Station, as well as supporting facilities such as the centrifuge and cold stowage units such as MELFI. Once fully assembled, ISS will indeed be an impressive research facility and a truly unique place for studying life.

Human physiology

Through the first seven long-duration Expeditions to ISS, 16 investigations in human life sciences have been completed or are still underway (Table 1). These investigations have focused on the following areas: radiation monitoring; bone demineralization; muscle deconditioning; neurosciences; cardio-vascular physiology, in particular orthostatic intolerance; pulmonary physiology; immunology; crew psychology; and regulatory physiology, in particular kidney stone formation. Nearly half of these investigations required data collection only before and after the long-duration missions. Most of the investigations that also required in-flight data collection utilized the Human Research Facility racks (Figure 2), the first of which arrived on ISS in March 2001 and the second two years later. These two racks contain multi-use facilities such as a Workstation and laptops for data handling, an Ultrasound device for imaging of internal organs, a Pulmonary Function System, a Space Linear Acceleration Mass Measurement Device for precise tracking of crewmembers' weights, and a Refrigerated Centrifuge for processing samples.

Table 1. Human life sciences investigations completed or in progress through Expedition 7. *indicates investigation continues beyond Expedition 7.

Investigation	**Investigator**	**Sponsor**	**Exp.**	**In-flight (Y/N)**	**Field of Study**
DOSMAP	G. Reitz	Germany	2	Y	Radiation
TORSO	G. Badhwar	US	2	Y	Radiation
BBND	T. Goka	Japan	2-3	Y	Radiation
BONE	T. Lang	US	2-7*	N	Bone
INTERACTIONS	N. Kanas	US	2-5, 7*	Y	Crew psychology
HREFLEX	D. Watt	Canada	2-4	Y	Neurosciences
RENAL STONE	P. Whitson	US	3-7*	Y	Regulatory physiol.
XENON1	A. Gabrielsen	Denmark	3-5	N	Cardiovascular
PUFF	J. West	US	3-6	Y	Pulmonary
EVARM	I. Thompson	Canada	4-6	Y	Radiation
BIOPSY	R. Fitts	US	5-7*	N	Muscle atrophy
MOBILITY	J. Bloomberg	US	5-7*	N	Neurosciences
MIDODRINE	J. Meck	US	5, 7*	N	Cardiovascular
EPSTEIN-BARR	R. Stowe	US	5-7*	N	Immunology
CHROMOSOME	G. Obe	Denmark	6-7*	N	Radiation
FOOT	P. Cavanagh	US	6*	Y	Neuromuscular

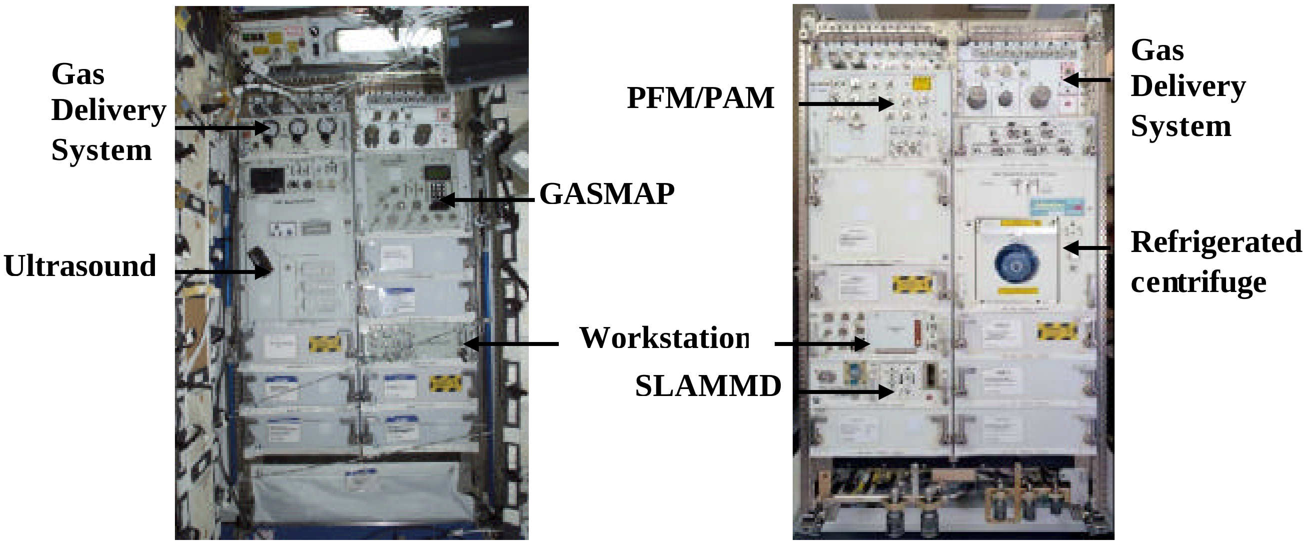

Figure 2. Human Research Facility (HRF) racks 1 (left) and 2 and their subcomponents.

The initial set of investigations included an international suite of radiation monitoring equipment, provided by the US, Germany and Japan, measuring various spectra of radiation in different locations inside the laboratory module. These early studies were later supplemented by experiments recording radiation inside the Extravehicular Mobility Units to characterize the radiation doses to which crewmembers are exposed during space walks, and by a biodosimetric investigation to determine chromosomal aberrations in crewmembers' lymphocytes caused by ionizing radiation.

Among the well-known deleterious effects of long-term space flight are changes in bones and muscles, and therefore this is an area of much study. Changes in bone mineral density are studied using computed tomography, ultrasound and dual-energy X-ray absorptiometry, in order to assess the locations and magnitude of demineralization as well as the effects of assorted countermeasures. Changes in muscles are evaluated at the cellular and molecular level by studying muscle samples obtained via biopsies, at structural levels by magnetic imaging and at the functional level by exercise capacities. To date, these studies have been limited mainly to data collections before and after flight, but launch of the ESA-provided Muscle Atrophy Research and Exercise System (MARES) in 2005 will allow in-flight assessments of the strength of isolated muscle groups or complete limbs. The combination of the two HRF racks, the EPM and the MARES will create an integrated suite of research hardware enabling a multitude of research capabilities heretofore impossible in the space environment.

Along with changes in the muscles themselves, changes in neuromuscular interaction are also being studied. Changes in the Hoffman Reflex, a simple neuromuscular reflex, brought about by space flight, are studied as possible contributors to observed postflight imbalance. Crewmembers' posture and locomotion after space flight are also carefully evaluated for any changes as well as speed of recovery to preflight levels. The loads, positions and muscle activity of lower extremities during long-term space flight are also under study, to investigate if reduced muscular activity contributes to observed changes in muscle mass, function and neuromuscular coordination.

One aspect of the cardiovascular deconditioning seen during space flight is orthostatic intolerance, or the inability to maintain adequate blood flow to the brain upon standing, resulting in lightheadedness and in some cases fainting. Several mechanisms have been postulated to contribute to this phenomenon, among them changes in the peripheral vasculature that make it less responsive to the stresses of changing from a supine to a standing position, since that stress would not be encountered during space flight. A study on ISS indicates that perhaps this mechanism is not as important as others, such as changes in overall blood volume. Another study is evaluating a possible pharmacologic countermeasure to orthostatic intolerance. These and other studies of the cardiovascular system during space flight have clinical applications here on Earth, since cardiovascular deconditioning is also seen in patients who are bedridden for long periods of time.

Facilities aboard ISS have allowed the first comprehensive study of human pulmonary function during long-duration space flight since the Skylab program in the mid-1970's. Changes in lung volumes, capacities and flow rates are studied at regular intervals throughout the flight to characterize changes brought about by long-term exposure to microgravity. In addition, the crewmembers are studied before and after Extra-Vehicular Activities (EVA) to monitor any possible changes, such as formation of microbubbles, that might be caused by exposure to a 100% oxygen environment at lowered pressures for up to 8 hours.

Possible changes in human immune function as a result of long-term exposure to space flight are also being investigated. This is accomplished by assessing the reactivation of Epstein-Barr virus in crewmembers, an indicator of possible immune suppression.

Various factors of space flight, such as isolation, microgravity, stresses of mission design and circadian disturbances can affect the behavior and performance of crewmembers. The cumulative effects of these stressors, as well as the additional factors present during ISS missions, such as gender and cross-cultural issues, are being studied by using standard assessment questionnaires.

One aspect of the bone demineralization discussed above is increased urinary excretion of calcium. This combined with a general dehydration in turn can lead to an increased risk of crewmembers developing certain types of kidney stones, a potentially debilitating event that could threaten a mission's success. A potential countermeasure commonly used on Earth is also being evaluated. Follow-on investigations, making use of the refrigerated centrifuge's capabilities to process samples, will define in greater detail how metabolism of calcium is changed during long-duration space flight, contributing to better understanding of both the mechanisms of bone demineralization and the susceptibility to kidney stone development.

A great deal has already been accomplished on ISS toward the goal of better understanding human adaptation to long-duration space flight. New facilities to be installed on ISS in the near future will allow even more detailed investigations to be completed, particularly using multidisciplinary approaches. Information gathered will lead to a more effective suite of coutermeasures to improve crewmembers' health and performance, as well as to better understanding of important physiological processes. Studies in fundamental biology will support this effort.

Fundamental Biology

The microgravity and other aspects of the space environment can be used to better understand fundamental biological processes that have been exposed to Earth's gravity throughout their evolutionary development. The ISS will provide for the first time a complete laboratory capable of studying appropriate sample sizes and applying scientific controls for conducting this type of research in space and for adequate periods of time. Adaptation to microgravity of a variety of biological specimens over long periods and even in some cases over multiple generations, will be studied. We will gain insight into how life adapts and perhaps even evolves in microgravity. A variety of facilities and habitats are being used or are under development to conduct the research (Table 2). In addition, large research facilities will support these habitats.

Table 2. Habitats and facilities existing or under development to support fundamental biology investigations. *indicates estimated date of first flight.

Habitat	**Purpose**	**First flight**
Advanced Animal Habitat	Rodent investigations	2007*
Aquatic Habitat	Aquatic plant and animal research	2008*
Avian Development Facility	Avian embryology and development	2001
Biomass Production System	Precursor plant growth hardware	2002
Cell Culture Module	Cell growth and development	2003
Cell Culture Unit	Cell growth and development	2005
European Modular Cultivation System	Plant biology research	2004
Incubator	Temperature controlled chamber	2005
Insect Habitat	Insect research	2005
Plant Research Unit	Large volume plant growth	2007*

To date, ISS investigations in Fundamental Biology have been modest, the program awaiting the arrival of dedicated facilities for more intensive studies. The first investigations were flown in the Avian Development Facility as a Shuttle middeck sortie in December 2001. These two investigations studied skeletal and neurovestibular development in developing Japanese quail embryos over a 12-day period of microgravity. The second Fundamental Biology project involved the Biomass Processing System (BPS), operated in an EXPRESS Rack during Expedition 4 April-June 2002 (Figure 3). One goal of BPS was to test out hardware planned for use on future plant research facilities, and successfully supported 3 cycles of growth of dwarf wheat and 2 cycles of *Brassica rapa*. A science experiment in BPS called PESTO successfully studied photosynthesis and other aspects of plant development during 3 growth cycles of dwarf wheat. In all, the BPS experience was a large step toward more complex studies of plant biology in space.

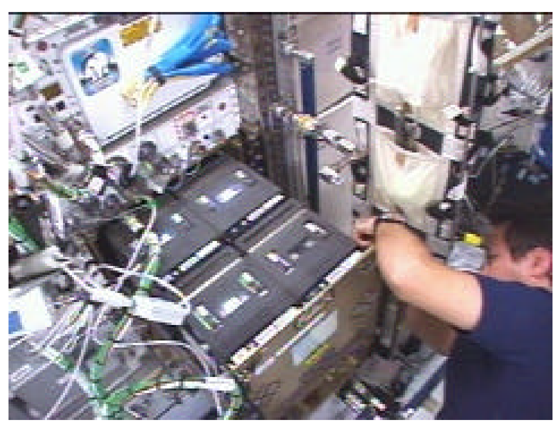

Figure 3. Expedition 4 Flight Engineer Dan Bursch pollinating *Brassica rapa* plants during BPS operations (left); BPS hardware (right), showing four growth chambers.

Upcoming investigations in 2003 will utilize the Shuttle middeck for short-duration studies. One experiment will examine how differentiation and proliferation of bone marrow macrophages may be altered in microgravity, and try to establish the molecular and biochemical basis for that process. The second experiment, using the Cell Culture Module, will evaluate whether an insulin-like growth factor can attenuate muscle atrophy in tissue cultured skeletal muscles. Each experiment will last approximately 12 days.

The ESA-built European Modular Cultivation System (EMCS) will be launched in 2004 and operated in an EXPRESS Rack in *Destiny* for two years. The EMCS facility is dedicated to experiments on plants, in particular multi-generation studies and investigations on early development and growth, and on signal perception and transduction.

Two Habitat Holding Racks (HHR) are being developed and will be installed on ISS in the next few years, the first to be located in the *Columbus* module in 2005. These racks will host a variety of habitats, providing the required support services such as mechanical interfaces, power, thermal control, data, video and command and control functions.

The Life Sciences Glovebox (LSG) is under development by the Japanese Space Agency NASDA. Once installed on ISS in 2006, it will provide a sealed work area providing bioisolation waste control, and in which crewmembers will perform investigations in cell, insect, aquatic, plant and animal developmental biology. Various habitats will be attached to the LSG during experiment operations to prevent any exchange of biological materials between the cabin and the LSG and between the LSG and the habitats. The LSG will have a working volume of approximately 0.5 m^3, and it will be able to control temperatures to +/- 1^o in the 18-27^o range.

The arrival of the CAM (Figure 4) in 2007 will herald a new age in gravity-dependent research. The 2.5-m centrifuge, under development by NASDA, will be able to produce a controlled artificial gravity from 0.01 g to 2 g, allowing variable gravity studies to be carried out in a number of habitats containing various plant and animal species. The module will also be able to house a Habitat Holding Rack and its Habitats and any required stowage. The LSG will also be relocated to the CAM to enable those investigations that require crew interaction.

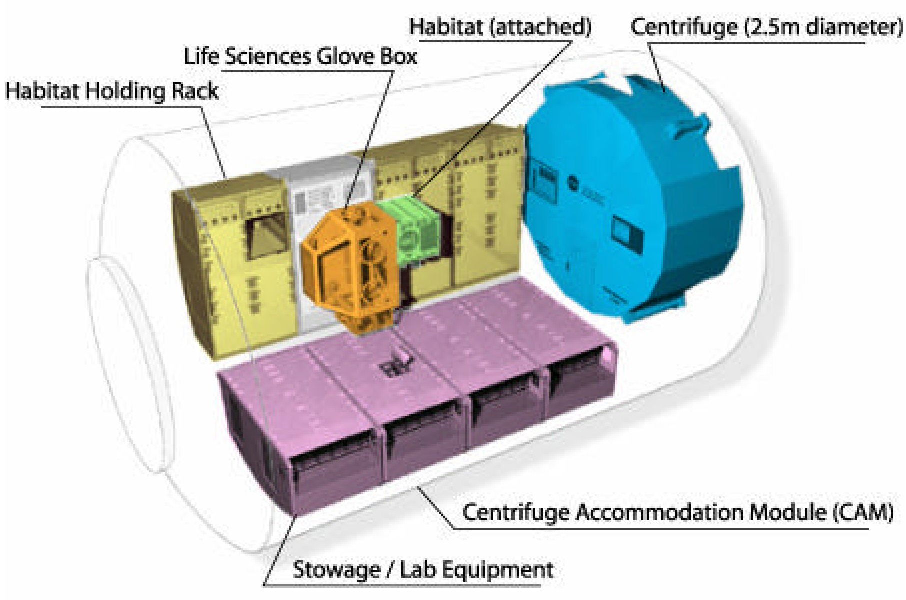

Figure 4. Diagram of Centrifuge Accommodation Module, showing 2.5-m centrifuge rotor facility, Habitat Holding Rack and habitats and Life Sciences Glovebox.

Studies in Fundamental Biology in the ISS Program have been limited in number to date, awaiting the arrival of dedicated facilities for more comprehensive investigations. But the investigations flown already have added valuable information on avian embryology in microgravity as well as learning how to successfully grow repeated cycles of plants. In the years to come, the effects of microgravity will be studied on a broader range of biological samples, with facilities uniquely designed for those experiments.

Summary

The ISS provides an opportunity to study life on Earth in the unique environment of microgravity. This is an evolutionary process as the complex is assembled, with newly-arriving components expanding the research capability. And for the first time, a space-based laboratory will be available to study various physiological processes across different species and over long periods of time. It will be possible to see how various organisms adapt to microgravity and perhaps even document how some species evolve to thrive in this novel environment.