The Space Shuttle: A Platform That Expanded the Frontiers of Biology

Kenneth Souza

The Space Shuttle brought a new dimension to the study of biology in space. Prior to the shuttle, scientists relied primarily on uncrewed robotic spacecraft to investigate the risks associated with venturing into the space environment. Various biological species were flown because they were accepted as models with which to study human disease and evaluate human hazards. The results from the pioneering biological experiments aboard uncrewed robotic spacecraft not only provided confidence that humans could indeed endure the rigors of spaceflight, they also formed the foundation on which to develop risk mitigation procedures; i.e., countermeasures to the maladaptive physiological changes the human body makes to reduced gravity levels. For example, the musculoskeletal system reacts by losing mass. This may pose no hazard in space; however, on returning to Earth after long spaceflights, such a reaction could result in an increased risk of bone fractures and serious muscle atrophy.

Unfortunately, most biological research in uncrewed spacecrafts was limited to data that could only be acquired before and/or after spaceflight. With crew support of the experiments aboard the Space Shuttle and Spacelab, and with adequate animal housing and lab support equipment, scientists could train the crew to obtain multiple biospecimens during a flight, thus providing windows into the adaptation to microgravity and, for comparison, to samples obtained during readaptation to normal terrestrial conditions postflight.

With the Space Shuttle and its crews, earthbound scientists had surrogates in orbit—surrogates who could be their eyes and hands within a unique laboratory. The addition of Spacelab and Spacehab, pressurized laboratory modules located in the shuttle payload bay, brought crews and specialized laboratory equipment together, thus enabling complex interactive biological research during spaceflight. Crew members conducted state-of-the-art experiments with a variety of species and, in the case of human research, served as test subjects to provide in-flight measurements and physiological samples.

In addition to the use of biological species to evaluate human spaceflight risks, research aboard the shuttle afforded biologists an opportunity to examine the fundamental role and influence of gravity on living systems. The results of such research added new chapters to biology textbooks. Life on Earth originated and evolved in the presence of a virtually constant gravitational field, but leaving our planet of origin creates new challenges that living systems must cope with to maintain the appropriate internal environment necessary for health, performance, and survival.

How Does Gravity Affect Plants and Animals?

Throughout the course of evolution, gravity has greatly influenced the morphology, physiology, and behavior of life. For example, a support structure—i.e., the musculoskeletal system—evolved to support body mass as aquatic creatures transitioned to land. To orient and ambulate, organisms developed ways to sense the gravity vector and translate this information into a controlled response; hence, the sensory-motor system evolved. To maintain an appropriate blood supply and pressure in the various organs of the mammalian body, a robust cardiovascular system developed. Understanding how physiological systems sense, adapt, and respond to very low gravity cannot be fully achieved on the ground; it requires the use of spaceflight as a tool. Just as we need to examine the entire light spectrum to determine how the visual organs of living systems work, so too we must use the complete gravity spectrum, from hypogravity to hypergravity, to understand how gravity influences life both on and off the Earth.

Space biologists have identified and clarified the effects of spaceflight on a few representative living systems, from the cellular, tissue, and system level to the whole organism. NASA achieved many "firsts" as well as other major results that advanced our understanding of life in space and on Earth. The agency also achieved many technological advances that provided life support for the study of the various species flown.

Baruch Blumberg, MD
Nobel Prize winner in medicine, 1976.
Professor of Medicine
Fox Chase Cancer Center.
Former director of Astrobiology
Ames Research Center, California.

"The United States and other countries are committed to space travel and to furthering the human need to explore and discover. Since April 12, 1981, the shuttle has been the major portal to space for humans; its crews have built the International Space Station (ISS), a major element in the continuum that will allow humans to live and work indefinitely beyond their planet of origin. The shuttle has provided the high platform that allows observations in regions that were previously very difficult to access. This facilitates unique discoveries and reveals new mysteries that drive human curiosity.

"In the final paragraph of Origin of Species *Darwin wrote:*

> There is grandeur in this view of life, with its several powers, having been originally breathed by the Creator into a few forms or into one; and that, whilst this planet has gone circling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being evolved.

"The shuttle and the ISS now provide a means to study life and its changes without the constraints of gravity. What will be the effect of this stress never before experienced by our genome and its predecessors (unless earlier forms of our genes came to Earth through space from elsewhere) on physiology, the cell, and molecular biology? Expression of many genes is altered in the near-zero gravity; how does this conform to the understanding of the physics of gravity at molecular and atomic dimensions?

"In time, gravity at different levels, at near-zero on the ISS, at intermediate levels on the moon and Mars, and at one on Earth, can provide the venues to study biology at different scales and enlarge our understanding of the nature of life itself."

Gravity-sensing Systems—How Do Plants and Animals Know Which Way Is Down or Up?

As living systems evolved from simple unicellular microbes to complex multicellular plants and animals, they developed a variety of sensory organs that enabled them to use gravity for orientation. For example, plants developed a system of intracellular particles called statoliths that, upon seed germination, enabled them to sense the gravity vector and orient their roots down into the soil and their shoots up toward the sun. Similarly, animals developed a variety of sensory systems (e.g., the vestibular system of the mammalian inner ear) that enabled them to orient with respect to gravity, sense the body's movements, and transduce and transmit the signal to the brain where it could be used together with visual and proprioceptive inputs to inform the animal how to negotiate its environment.

STS-40 (1991) payload specialist Millie Hughes-Fulford working with the Research Animal Holding Facility.

Why Do Astronauts Get Motion Sickness in Spaceflight?

One consequence of having gravity-sensing systems is that while living in microgravity, 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 Earth. This affliction, commonly termed "space motion sickness," affects more than 80% of astronauts and cosmonauts during their first few days in orbit. Interestingly, one of the two monkeys flown in a crewed spacecraft, the Space Transportation System (STS)-51B (1985) Spacelab-3 mission, displayed symptoms resembling space motion sickness during the first few days of spaceflight.

The basic process of space motion sickness became one of the main themes of the first two dedicated space life sciences missions: STS-40 (1991) and STS-58 (1993). Scientists gained insights into space motion sickness by probing the structural changes that occur in the vestibular system of the mammalian balance organs. Using rodents, space biologists learned 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 (specialized junctions through which neurons signal to each other) between these hair cells and the vestibular nerve that occurred as the gravity signal decreased. In effect, the body tried to turn up the gain to receive the weaker gravitational signal in space. This knowledge enabled medical doctors and crew members to have a better understanding of why space motion sickness occurs.

Is Gravity Needed for Successful Reproduction?

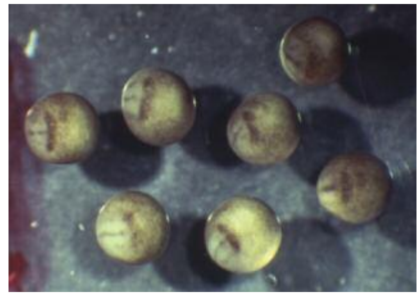
Amphibian Development

Studies of the entire life span of living systems can provide insights into the processes involved in early development and aging. The Frog Embryology Experiment flown on STS-47 (1992) 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 tadpole stage. This experiment put to rest the "gravity requirement" question that had been debated by embryologists since the late 19th century.

In Earth gravity, frog eggs, when shed, have a bipolar appearance; i.e., the spherical egg has a darkly pigmented hemisphere containing the nucleus and much of the cell machinery needed for development while the opposite, lightly pigmented hemisphere is rich in yolk that provides the energy to drive the cell machinery during early development. Shortly after being shed, the eggs can be fertilized by sperm released by an adjoining male frog. Once fertilized, a membrane lifts off the egg surface and the egg responds to gravity by orienting the dense yolk-rich hemisphere down and the darkly pigmented hemisphere up with respect to the gravity vector. This geotropic response was what spurred early embryologists to interfere with egg rotation and thereby tried to determine whether the response to gravity was required for normal development. Unfortunately, research on the ground yielded ambiguous results due primarily to the trauma imparted to the eggs by the scientists' attempts to interfere with rotation.

During the STS-47 flight, adult female frogs (*Xenopus laevis*) were injected with hormone to induce the shedding of eggs, followed by the addition of a sperm suspension. Half of a group of fertilized eggs were placed in special water-filled chambers and on a rotating centrifuge to provide an acceleration environment equivalent to terrestrial gravity. The other half were placed in the same type of water-filled chambers, but in a temperature-controlled incubator and were kept in a microgravity environment. Samples of developing embryos were taken during the flight to capture important developmental stages for examination postflight. Some were returned to Earth as free-swimming tadpoles. The results of the experiment ended the centuries-old debate as to whether gravity is needed for successful reproduction, and demonstrated for the first time that a vertebrate species could be fertilized and develop normally to a free-swimming stage in the virtual absence of gravity. It remains to be seen, however, whether metamorphosis, maturation, and a complete life cycle of an amphibian or other complex organisms can occur in the absence of gravity.

In summary, for the first time, a vertebrate species was fertilized and developed through to a free-swimming stage in the virtual absence of gravity.



Fertilized frog eggs (above) and free-swimming tadpoles (below).

Astronaut Mark Lee working on the Frog Embryology Experiment in the General Purpose Work Station during the STS-47 (1992) mission.

William Thornton, MD
Principal investigator for the first in-flight studies of space motion sickness on shuttle. Astronaut on STS-8 (1983) and STS-51B (1985).

Bring 'em Back Alive

The First Human Flight in Space with an Animal

"My training for the Spacelab 3 animal payload began as a toddler in North Carolina, surrounded by and growing up with a great variety of domestic and wild animals. Their humane treatment was my first lesson.

"After additional years of formal and informal education in medicine and biophysics, I used my training for research on space motion sickness. For some 18 months during the first shuttle flights, we completed human studies, which produced an array of first-time procedures in the US space program, including evoked potentials, coordination, complex reaction time, gastrointestinal activity and pressure, ambulatory blood pressure, and electrocardiograms, etc. These experiments answered some urgent operational questions and provided points of departure for the more formal studies that followed.

"Like so much of medical science, elemental knowledge of our nervous system comes from animal studies on Earth. On my first flight (STS-8 in 1983), 24 rats were flown in a research animal holding facility. But, to fly animals for study in the small, enclosed environment of the shuttle is a complex challenge that required years of preparation.

Dr. Thornton is taking care of one of the two squirrel monkeys on STS-51B.

"Finally flying on Challenger, we were able to open the cage inspection ports. All was well except for the monkey who had been a laboratory favorite (this is the animal in the photo) but who was now in deep withdrawal. He didn't eat or drink for 2 days and by the third day, dehydration was real. I used some tricks learned while feeding wild pets and he took a banana pellet and another—and more and more, then cage food.

"We returned with all animals alive and well and a great deal of experience subsequently incorporated into the shuttle legacy of astronauts and animals in space. Now, those of us who work with humans and space motion sickness have such remarkable aid as the molecular and ultra-microscopic studies from animals in Neurolab, another shuttle legacy."

Animal Development

Studies with rodents aboard the Space Shuttle identified stages of early mammalian development that are sensitive to altered gravity. They also provided insights into what might happen if humans experience abnormal gravity levels during early development. Pregnant rats on STS-66 (1994) and STS-70 (1995) showed that spaceflight resulted in striking changes in the structure of the fetal balance organ—the vestibular system. On STS-90 (1998), rat pups were launched at 8 or 14 days *postpartum*. After 16 days in microgravity, their sensorimotor functions were tested within several hours of landing; e.g., walking, and righting (rolling over). Postflight, the righting response of postnatal pups was profoundly deficient compared to ground control animals, suggesting that removal of gravitational cues during early postnatal development can significantly alter inherent patterns of behavior. In addition, neonatal animals exposed to microgravity during this Neurolab mission failed to undergo normal skeletal muscle growth and differentiation, suggesting that gravity stimuli are essential for generating the structure needed to perform basic ambulatory and righting movements when subjected, postflight, to terrestrial gravity.

The Biomass Production System installed on STS-111 (2002) carrying plants grown in the International Space Station (ISS) for return to Earth. ISS Flight Engineer Dan Bursch (pictured) conducted all of the plant experiments.

Plant Biology

Germination

The importance of gravity in the germination and development of plants has been observed and studied for centuries; however, it wasn't possible to unravel how a plant detects and responds to gravity until access to space was achieved. NASA had to develop specialized equipment to grow plants and study their response to gravity. The agency developed a plant growth unit to fit within a shuttle middeck locker. This unit provided light, water, and an appropriate substrate to support plant growth. On the STS-51F (1985) mission, seedlings were grown in enclosed chambers within the plant growth unit; i.e., mung beans (*Vigna radiata*), oats (*Avena sativa*), and pine (*Pinus elliotti*). Mung beans and oat seeds were planted 16 hours before launch and germination occurred in space. Pine seedlings were 4 or 10 days post-germination at launch. Although the mung bean and oat seeds germinated in orbit, root growth was somewhat disoriented and oats grew more slowly during spaceflight. In addition, the amount of lignin, a biochemical component of a plant's "skeletal" system, was significantly reduced in all three species, indicating that gravity is an important factor in lignification necessary for plant structure.


Multiple generations of plants grew in spaceflight for the first time. Examples include Apogee Wheat (top) and Brassica rapa *(bottom).*

Plant Growth

Another pioneering experiment in the study of plant responses to gravity was the Gravitational Threshold Experiment flown on the STS-42 (1992) mission. It tested plant sensitivity to altered gravitational fields during spaceflight. The Gravitational Plant Physiology Facility was built to support plant growth and stimulate plants with different levels of gravity using four centrifuge rotors contained within the facility. Two centrifuge rotors (culture rotors) were used to grow small seedlings in a 1 gravitational force (1*g*) environment (normal terrestrial level). The other two rotors provided gravity stimulations of varying strength and duration (test rotors). After stimulation on the test rotors, images of the seedling responses were captured on video recorders. This research identified for the first time the threshold stimulus for a biological response to gravity. Oat seedlings were used in the experiment and, when the seedlings reached the proper stage of growth on the 1*g* centrifuge rotor, an astronaut transferred them to the test centrifuge to expose them to a *g*-stimulus for different durations and intensities. The threshold was found to be very low—about 15 or 20 *g*-seconds; i.e., it took a force of 1*g* applied for 15 to 20 seconds to generate a plant response.

Following the pioneering plant experiments, NASA and others developed equipment with a greater range of capabilities, thus enabling more complex and sophisticated scientific experiments. This equipment included the European Space Agency's Biorack flown on Spacelabs; the Russian Svet and Lada systems flown on Mir and the International Space Station (ISS), respectively; NASA's Biomass Production System; and the European Modular Cultivation System flown on the ISS. This latter device enabled more in-depth studies of plant geotropisms than had been possible in any of the previous flight experiments with plants.

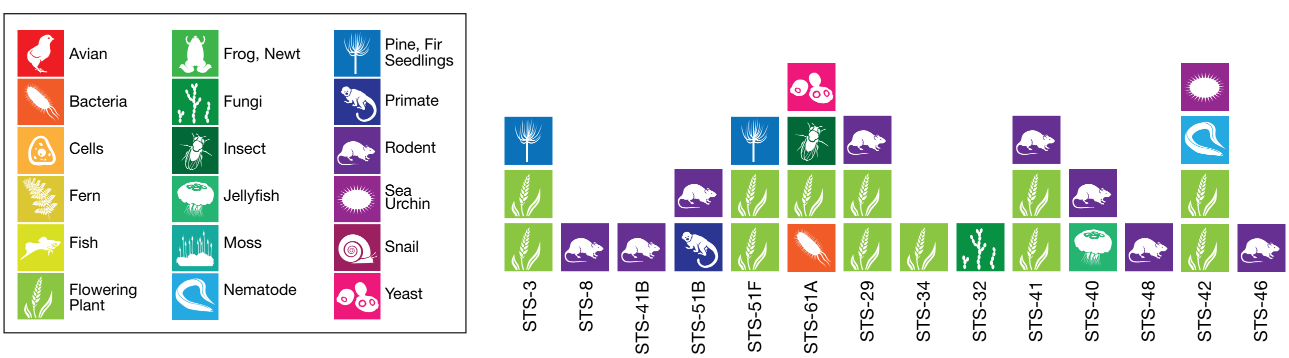
Arabidopsis ***plant. This small plant is related to cabbge and mustard and is widely used as a model for plant biology research.***

Arabidopsis seedlings were subjected to 1*g* in space on a Biorack centrifuge while a separate group was held under microgravity conditions. The experiments provided evidence that intracellular starch grains (statoliths) sediment in the presence of a gravity stimulus and influence how plants are oriented with respect to the gravity vector. Experiments within the Biomass Production System revealed much about growing plants within spaceflight hardware, particularly about plant metabolism in the absence of normal terrestrial gravity. Biomass Production System investigators concluded that plant photosynthesis and transpiration processes did not differ dramatically from those on the ground.

Multiple Generations of Growth—Fresh Foods

The early shuttle experiments with plants focused on basic questions about gravity-plant interactions. The scientific results as well as the knowledge gained in the design and fabrication of plant growth habitats greatly contributed to the development of the next generation of growth chambers. Russian investigators from the Institute of Biomedical Problems, Moscow, with support of US scientists and engineers, provided the equipment necessary to achieve multiple generations of plants in space. Multiple generations of wheat and mustard species were obtained during spaceflight on Mir and the ISS. In addition, a variety of edible vegetables were grown during spaceflight, demonstrating that plants can be used to provide fresh food supplements for future long-duration space exploration missions.

Space Biology Payloads



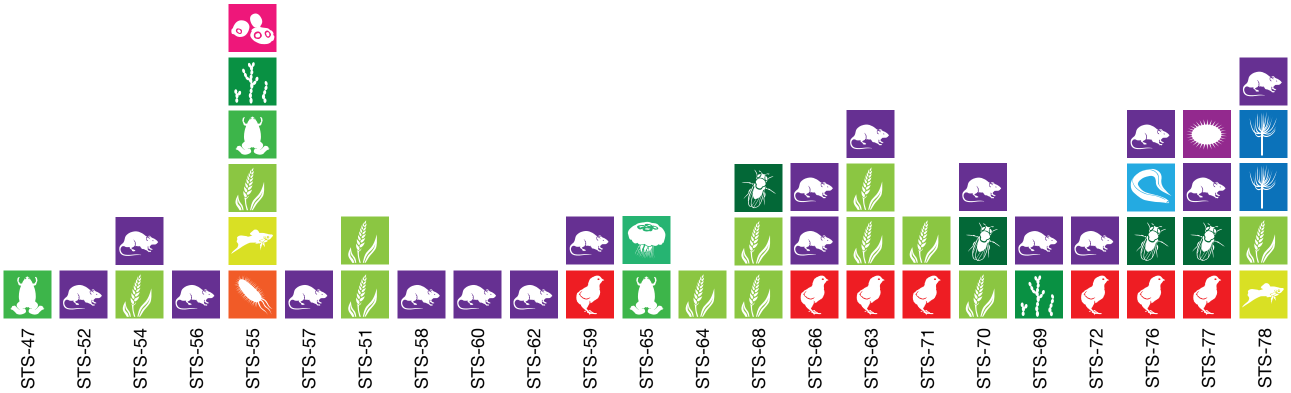
Bacteria More Dangerous in Space Environment

As reported by Cheryl Nickerson, the interplay between the human immune system and the invading microorganism determines whether infection and disease occur. Factors that diminish immune capability or increase the virulence of the microorganism will greatly increase the likelihood of disease.

To gain insight to this issue, investigators compared responses of the food-borne bacterial pathogen *Salmonella typhimurium*, grown in the microgravity of spaceflight, to otherwise identical ground-based control cultures. Interestingly, they found that the spaceflight environment profoundly changed the gene expression and virulence characteristics (disease-causing potential) of the pathogen in novel ways that are not observed when growing the cells with traditional culture methods. This work also identified a “master molecular switch” that appears to regulate many of the central responses of *Salmonella* to the spaceflight environment.

On both the STS-115 (2006) and the STS-123 (2008) shuttle missions, scientists investigated the spaceflight response of *Salmonella* grown in various growth media containing different concentrations of five critical ions. The effects of media ion composition on the disease-causing potential of *Salmonella* were dramatic. Flight cultures grown in media containing lower levels of the ions displayed a significant increase in virulence as compared to ground control cultures, whereas flight cultures grown in higher ion levels did not show an increase in virulence. The wealth of knowledge gained from these *Salmonella* gene expression and virulence studies provides unique insight into both the prevention of infectious disease during a spaceflight mission and the development of vaccines and therapeutics against infectious agents on Earth.

Astronaut Heidemarie Stefanyshyn-Piper, in the middeck of the Space Shuttle Atlantis, activates the MICROBE experiment, which investigated changes to Salmonella *virulence after growth in space.*



Why Do Astronauts Get Weak Muscles and Bones?

Muscles

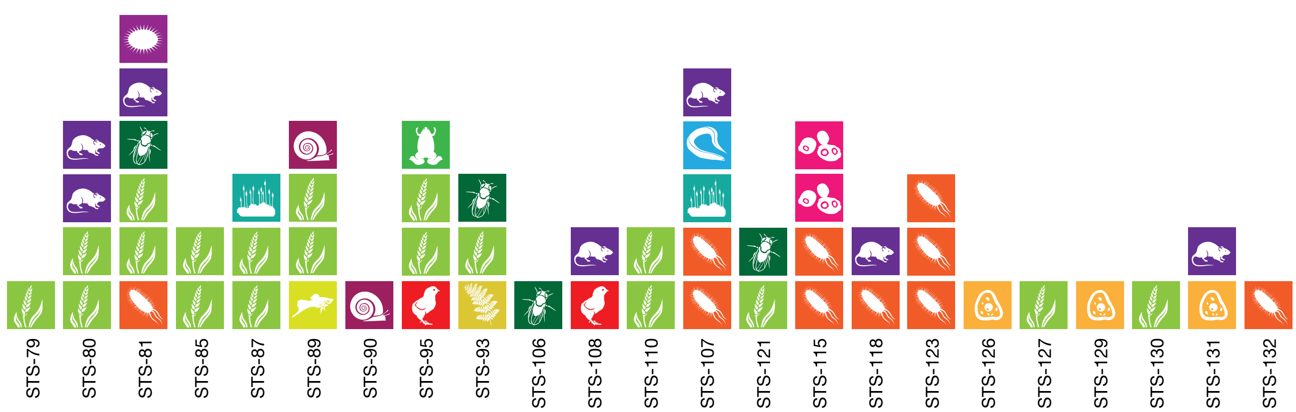
The Space Transportation System (STS)-58 (1993) mission opened a new window on how weightlessness affects muscle structure and function. Previously, scientists knew that skeletal unloading (lack of gravity) resulted in the atrophy of muscle fibers. Until this flight, all of the skeletal muscles studied were obtained from humans or rats postflight, several hours after readapting to terrestrial gravity. Consequently, distinguishing the structural and biochemical changes made in response to microgravity from changes readapting to Earth postflight was very difficult. During the STS-58 mission, crew members obtained tissue samples from animals and processed these samples for detailed structural and biochemical analyses postflight, thus avoiding the effects of re-entry and readapting to Earth's gravity. Danny Riley of Wisconsin Medical College summed up how sampling in flight changed his understanding. "When we looked at muscle samples that we obtained from previous missions, we saw muscle atrophy and muscle lesions, small tears. Samples taken from rats during and following the STS-58 flight enabled us to determine that the atrophy was clearly a response to microgravity while the muscle lesions were a result of re-entry and readaptation stresses," Riley said.

For the STS-58 mission, muscle physiologists examined the contractile properties of rat muscles and demonstrated large changes that correlated well with the biochemical and morphological changes they had previously observed. As Ken Baldwin of the University of California at Irvine stated, "The uniqueness of performing spaceflight studies aboard STS-58 using the rodent model was that we discovered marked remodeling of both structure and function of skeletal muscle occurring after such a short duration in space. The results enabled scientists to better predict what could happen to humans if countermeasures (i.e., exercise) were not instituted early on in long-duration space missions."

The fundamental research with animals aboard the shuttle Spacelabs contributed markedly to the current understanding of the effects of spaceflight on skeletal muscle. The results laid the foundation for defining optimal countermeasures that minimize the atrophy that occurs in the human response to microgravity.

Bones

Skeletal bone, much like skeletal muscle, atrophies when unloaded. Bone mass loss as a consequence of skeletal unloading during spaceflight is a well-established risk for long-term human space exploration. A great deal of the insight into "why" and "how" bone mass loss occurs in flight resulted from research with rodents both on board the US Space Shuttle and the Russian Bion biosatellites. Such research revealed that bone formation becomes uncoupled from resorption (process of minerals leaving the bone) and normal bone mineral homeostasis is compromised. Consistent with several previous studies, results from the Physiological Systems Experiments series of payloads (STS-41 [1990], STS-52 [1992], STS-57 [1993], and STS-62 [1994]) showed that bone formation in the weight-bearing bones of male rats was inhibited by short-term spaceflight. Radial bone growth in the humerus (long bone in the arm or forelimb that runs from the shoulder to the elbow) was also decreased, though no changes in longitudinal bone growth in the tibia (shin bone in leg) were detected. These effects were associated with a decrease in the number and activity of bone-forming cells (osteoblasts). Results of experiments on board STS-58 and STS-78 (1996) provided further



evidence of changes at both the structural and the gene expression levels associated with spaceflight-induced bone loss. Alterations also occurred in bone mineral distribution, ultrastructure and geometry, and mechanical properties as well as in site and gene-specific decreases in expression of bone matrix proteins (structural proteins with minerals attached). Taken together, these results suggest that significant tissue-specific alterations at the structural and molecular levels accompany bone loss in microgravity.

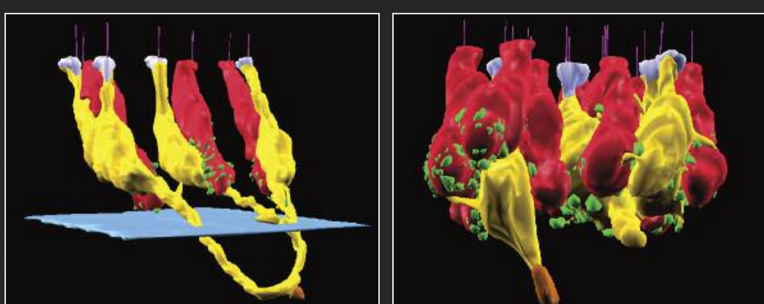
At the cellular level, spaceflight was also shown to affect bone, cartilage, and tendons, resulting in reduced matrix production or altered matrix composition.

How do bone 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. This microgravity effect could be due to a direct effect on the mature differentiated cell (final cell type for a specific organ like bone; e.g., osteoblast) so that the cell generates some “signal” during spaceflight, thus driving the cell 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 experiments was flown on STS-118 (2007) and STS-126 (2008) that studied bone marrow cell (the progenitors of bone cells) population changes in microgravity

New Technology for Three-dimensional Imaging

Surgical planning using 3-D virtual imaging software. Dr. Stephen Schendel, Stanford University.

Rodent inner-ear hair cells are almost identical to human inner-ear hair cells. These cells are important for the vestibular system. Space biological research contributed novel technologies for diagnostic medicine on Earth. NASA developed three-dimensional (3-D) imaging software to facilitate and expedite the microscopic analysis of thin sections of the body’s balance organ—the vestibular system of the inner ear. The software enabled reconstruction of the innervation pattern of the rodent’s inner ear much faster than traditional manual methods. Not only did the technology greatly accelerate the analyses of electron microscopic images, it also was adapted to construct 3-D images from computerized axial tomography (CAT) and magnetic resonance imaging (MRI) scans of humans, providing surgeons with 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.



3-D reconstructions of rodent inner-ear hair cells using Ross software.

using mouse primary white blood cell (macrophage) cultures, respectively. The mouse study identified phenotypic (any observable characteristic or trait of an organism, such as its structure or function) shifts in the bone marrow cell subpopulations, including a subpopulation of macrophages.

On STS-95 (1998) scientists placed bone cartilage cells into cartridges carried in a special cell culture device built by the Walter Reed Army Institute for Research, Washington, D.C. Samples of these cells were collected on Flight Days 2, 4, 7, and 9. The media in which the cells grew were also collected on the same days, and the conversion of glucose to lactate in the media—a sign of metabolic activity—was determined postflight. Following flight, these cells were analyzed for their state of differentiation and parameters showing the cell cycle activity. The results strongly indicated that these cells were affected by flight. Flight cells were metabolically less active and produced fewer matrix components (necessary for structure) than the cells grown on the ground. In contrast to this, the flight cells showed a greater content of cyclins (proteins related to different stages of the cell cycle), suggesting that these cells were undergoing more proliferation (producing more cells) than their ground control counterparts. Exposure to spaceflight also resulted in cartilage cells undergoing more cell division, less cell differentiation (maturation), and less metabolic activity compared to ground controls. This is the first time that cell cultures flown in space were shown to exhibit alterations in their normal cell cycles.

Do Cells Grow Differently in Spaceflight and Affect Crew Health?

Cell and Molecular Biology

A large number of experiments with microorganisms were flown. Nearly all revealed that higher populations of cells are obtained from cultures grown under microgravity conditions than are obtained in cultures grown statically on the ground, possibly due to a more homogeneous distribution of cells. Recent studies of microbial cultures grown in space resulted in a substantial increase in virulence in the space-grown cultures when used postflight to infect mice.

The response of terrestrial life to microgravity at the molecular level is reflected in the response of many of an organism's genes when gravity is significantly reduced in the environment. Human renal (kidney) cell cultures flown on the Space Transportation System (STS)-90 (1998) mission exhibited a genetic response to microgravity that exceeded all expectations. More than 1,600 of the 10,000 genes examined in the renal cells showed a change in expression (i.e., increased or decreased production of the protein products of the genes) as a result of spaceflight. Armed with these results, investigators are now focusing on specific groups of genes and their functions to try and unravel why certain genes and metabolic pathways may be amplified or reduced due to a change in gravity.

Human renal cortical cell culture grown on STS-90 (1998).

Summary

The Space Shuttle's unique capabilities, coupled with the unbounded curiosity, energy, and creativity of scientists and engineers, enabled huge leaps in our knowledge of how biological species, including humans, react and adapt to the near weightlessness of orbital spaceflight. Over the past 3 decades, space biologists demonstrated that gravity, and the lack thereof, affects life at cellular and molecular levels. They determined how amazingly durable and plastic biological systems can be when confronted with a strange new environment like space. Even in the Columbia Space Transportation System (STS)-107 (2003) tragedy, the survival of the small soil nematode worms and the mosses on board was an extremely stunning example of plant and microbial responses and resiliency to severe stress.

Over the past 4 decades of space biology research, our textbooks were rewritten, whole new areas of study were created, new technologies were developed for the benefit of science and society, and thousands of new

Microgravity—A Tool to Provide New Targets for Vaccine Design

The use of spaceflight as a tool for new discoveries has piqued the interest of scientists and engineers for decades. Relatively recently, spaceflight also gained the attention of commercial entities that seek to use the unique environment of space to provide opportunities for new product design and development.

For example, Astrogenetix, Inc. was formed by Astrotech Corporation, Austin, Texas, to commercialize biotechnology products processed in the unique environment of microgravity. Astrogenetix developed capabilities to offer a turnkey platform for preflight sample preparation, flight hardware, mission planning and operations, crew training, and certification processes needed within the highly regulated and complex environment of human spaceflight.

Astrogenetix's primary research mission is to discover therapeutically relevant and commercially viable biomarkers—substances used as indicators of biologic states—in the microgravity environment of space. By applying a biotechnology model to this unique discovery process, the company finds novel biomarkers that may not be identifiable via terrestrial experimentation. Through this method, Astrogenetix expects to shorten the drug development time frame and guide relevant therapeutics agents (or diagnostics) into the clinical trial process more quickly and cost-effectively.

Astronaut John Phillips activating a Fluid Processing Apparatus containing tubes of microorganisms on STS-119 (2009).

Specifically, Astrogenetix used assays of bacterial virulence in the microscopic worm *Caenorhabditis elegans.* Bacteria, worms, and growth media were launched separated in different chambers of the Fluid Processing Apparatus, which was developed by Bioserve Space Technologies, Boulder, Colorado. Astronauts hand-cranked the hardware twice, first to initiate the experiment by mixing bacteria, worms, and growth media and at a later scheduled time to add fixative to halt the process. This was the first direct assay of bacterial virulence in space without the effects of re-entry into Earth's atmosphere and delays due to offloading the experiment from the Space Shuttle. This experimental model identified single gene deletions of both *Salmonella sp* and *Methicillin-resistant Staphylococcus aureus* for potential acceleration of vaccine-based applications. The investigative team included Timothy Hammond, Patricia Allen, Jeanne Becker, and Louis Stodiek.

scientists and engineers were educated and trained. In the words of Nobel Prize-winner Baruch Blumberg, "Like the pioneering voyages of the early European explorers to the New World, Darwin's voyages of scientific discovery, and the historic lunar missions by the Apollo astronauts, the Space Shuttle expanded the boundaries of biology, providing insights into the role and influence of gravity on living systems."