

Workshop Report

***Space Biology on the
Early International Space Station Workshop***

Held at NASA Ames Research Center
Moffett Field, CA
March 14-15, 2002

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Introduction

The Space Biology on the Early International Space Station Workshop was held at NASA Ames Research Center, Moffett Field, California, March 14-15, 2002. The purpose of the Workshop was to explore the type, scope and value of biological research enabled over the next five years given the accommodations and constraints of the Space Shuttle/Space Station system, available flight research instruments and new biotechnology assets.

The Workshop brought together scientists expert in contemporary biology research to explore new discovery areas; space flight instrument developers and technologists to examine hardware options; biotechnologists and bioinformatics specialists to investigate ways to amplify the science yield; and NASA space flight experts and program managers responsible for research implementation on the Space Shuttle/Space Station system to identify policy enablers and impediments. This "one stop shopping" approach allowed critical issues to be discussed and resolved within the workshop forum so that consensus recommendations could be implemented efficiently. The output of these deliberations is presented in this report.

The Executive Summary includes the general conclusions and recommendations that emerged from the entire workshop. The following pages summarize the presentations that were given during the event. The first day featured presentations primarily by NASA managers, committee members, investigators, and hardware developers. The second day consisted of two splinter sessions. During the first splinter session, attendees were divided into eight groups to explore science options for specific mission scenarios. Subsequent to discussion, each group presented its conclusions. Key points from each group are included in this report. During the second splinter session, each group was asked to develop a set of potential experiments. These experiment concepts appear in Appendix A. After the second splinter session, final presentations were given. Appendices B and C include the Workshop Agenda and a List of Attendees, respectively.

Executive Summary

I. Workshop Goals

The transition of the Space Shuttle (Shuttle) from research to International Space Station (ISS) construction and the current projected 6-year delay in completion and launch of ISS core elements (2002 to 2008) presents a major challenge to the vitality of the international space biology research community. These designated "core complete" elements have also been reduced in scope because of budget constraints. This caused a key research centrifuge to descope its habitat capacity (from 8 to 4). Other reductions in habitat funding allow only an incubator for small model organisms (NASA) and an insect habitat built by the Canadian Space Agency (as of this meeting). During the early Space Station period, the crew complement will be reduced by half (6 to 3) thus reducing time for support of experiments to near zero.

At the same time, three convergent technological revolutions – in biotechnology, information technologies, and miniaturized systems – have recently opened previously inaccessible domains for biological discovery in space. The resulting capability provides NASA with the means to amplify the value of a biosciences payload pound by many orders of magnitude, revealing previously unattainable biological information with unprecedented clarity and scope.

It is essential for NASA and its international partners to find innovative but effective ways to conduct high-priority, space biology research during this period of reduced resources so that the Space Station can begin to return valuable knowledge products that repay the public's investment. For this reason, the research community must remain motivated and involved in space biosciences research through frequent flight investigations. To enable these, NASA must be flexible enough to adapt its plans to work within the realities of the Space Shuttle/Space Station system and agile enough to take advantage of the opportunities offered by rapidly improving new technologies.

To explore these challenges, NASA Ames Research Center (ARC) held a workshop: "Space Biology on the Early International Space Station," on March 14–15, 2002. Sponsored by NASA's Fundamental Space Biology Program, the Workshop brought together over 100 participants including NASA managers, scientists, engineers, commercial hardware developers, international partner representatives, economists, political scientists, and policy makers.

The primary goal of the workshop was to determine what science questions and research approaches could be addressed using the current international inventory of flight and ground-based hardware and operating within projected Shuttle and ISS constraints. The Workshop was co-chaired by Nobel Laureate Dr. Baruch S. Blumberg, Director of the NASA Astrobiology Institute and Dr. Kenneth M. Baldwin, Professor of Physiology and Biophysics, University of California, Irvine, and Chair of the Biological and Physical

Research Advisory Committee (BPRAC), which provides advice to the NASA Office of Biological and Physical Research (OBPR).

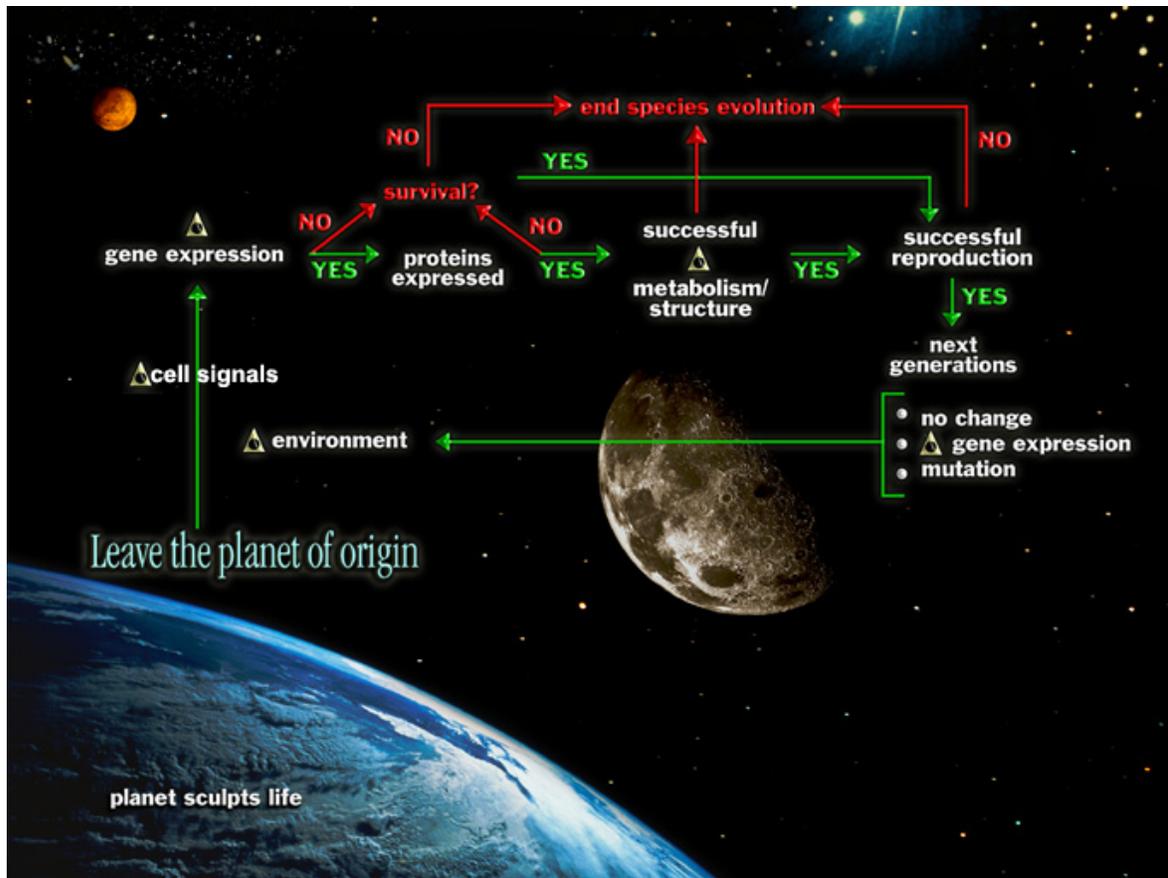


Figure 1. Schematic of how terrestrial life adapts to space. (Harper/ARC)

II. Conclusions

A. Significant Fundamental Space Biology research can be performed on the International Space Station over the next five years. ISS research limitations and constraints over the next few years make studies of vertebrate adaptation to the space environment unlikely. However, valuable, even pioneering, research can be done on the Shuttle in conjunction with the ISS by using newly available biotechnology tools, miniaturized sensor and data systems, and existing integrated hardware to support studies at the molecular, cellular, and small organism levels. This interim research will build new expertise for conduct of molecular biology studies in space to complement future more comprehensive research with higher organisms and large centrifuges on the completed ISS.

B. The space environment offers a new discovery domain for biology and astrobiology. This is the study of the only life that we know in its first generations beyond the planet of origin. The space environment is evolutionarily novel. Of all the features that changed during life's evolution on Earth, gravity was not among them. Low earth orbital space represents a three to six order of magnitude reduction in one of the fundamental organizing forces of evolution. Just as scientists seek extreme environments on Earth to discover novel biological solutions that can be applied to terrestrial problems, the space environment is an unexplored extreme environment, the extreme of very low

gravity, which offers -- at the least -- equivalent practical value. The opportunity to bring the biotech revolution to space is a historic first and may reveal features of terrestrial life that cannot be seen on Earth. It also allows us to determine whether life from Earth is biologically bound to this world and to characterize the biological costs and opportunities inherent in living beyond Earth.

C. Molecular biology research opens new and fundamentally important discovery domains, allows the use of simple organisms and available automated hardware systems, requires minimal crew time and can be implemented with modest funding.

Correlative studies involving genomic, proteomic, metabolic, and structural analyses using the simplest model organisms that pioneered the Human Genome Project will provide a wide range of new discovery opportunities for space biology research that were impossible to obtain five years ago. Hardware to support these studies is available from NASA, its international partners, NASA-sponsored Commercial Space Centers (CSC), and commercial vendors. No one group holds the full set of research instruments needed for success. Collaboration between these entities is essential to optimize access to and utilization of all hardware candidates. In addition, the biotechnology, information technology, and microminiaturization revolutions are still accelerating rapidly with new products appearing daily that further increase science yield and value. NASA must continually monitor progress in these areas and use them effectively to assure maximum value from its missions by leveraging billions of dollars of external investments. In addition, investments that increase inflight automation are strongly urged under the assumption that there will never be enough crew time.

D. Initial research objectives are to determine the basic mechanisms and metabolic pathways for microgravity and radiation effects on the molecular biology and evolution of relatively simple living systems. See Figure 1. It is now possible to determine the sequence of molecular events that underlies life's adaptation to space, readaptation to Earth, and response to countermeasures. These measurements also allow researchers to compare space results to medical, environmental, and agricultural problems on Earth and confirm or refute concepts that certain terrestrial problems can benefit from insights obtained from space research.

The approach requires phasing research to match spacecraft accommodations. The cell is the fundamental unit of life, as the atom is the fundamental unit of matter. Beginning now, when Station facilities are most constrained, productive investigations can focus on the simplest biological models and most basic measurements that will form the foundation for all space biology research. As Station facilities mature, focus will shift to increasingly complex organisms, including humans and other mammals, and increasingly sophisticated inflight measurements and postflight analyses. All information will be captured computationally and used to generate increasingly complete models of how life adapts to the evolutionarily novel environment of space. Use of inflight, built-in small centrifuges and ground hyper-g centrifuges and Rotating Wall Vessels can complement the on-orbit microgravity studies and determine which biochemical events occur directly as a result of microgravity and which occur indirectly from other environmental variables, including shear, turbulence, and radiation.

This general strategy and its mission benefits are outlined in Figure 2 and implements the National Academy of Sciences Space Studies Board (SSB) recommendation to investigate life at all levels of biological organization with all the tools of contemporary science.

E. The “new biology” allows the conduct of high-priority basic research with extensive sharing of tissues, cloning and other forms of data amplification that increase the science value of each payload pound. The ability to fly many very small organisms, use hardware with multiple experiment modules, clone DNA products, and use government and commercial bioinformatics tools for online data analysis, can provide data to share among many investigators. Through this research, NASA can add its own wing to the rapidly growing global library of bio-data. In the process there will be a biological recording for history of the transition of Earth life to space. The anticipated and actual benefits emerging from this research needs to be communicated to congress and the public so it is understandable.

F. Some small payload flight opportunities exist now and more may be available soon. It is possible that experiments proposed within two months could fly on missions of opportunity in 2003. Flight qualified cell culture hardware is immediately available for both the Shuttle middeck and the Space Station. Each instrument contains several sample containers, each of which can hold a dedicated experiment, piggyback investigations that use only part of a sample or instrument volume, or multiple partial investigations. A program analogous to the “Minuteman” approach used by NASA’s commercial program is strongly advised. Sample preservation is the biggest challenge in this scenario and workshop members strongly urge NASA to develop adequate cryopreservation techniques and recovery strategies that minimize launch and recovery artifacts. Another opportunity that begins in 2003 is the ability to fly small autonomous investigations on mini free flyer satellites in a type of “Bioexplorer” program. This can be done now during the construction phase. New flight hardware will be available in the 2004 timeframe that may accommodate additional molecular biology research requirements. An Extended Duration Orbiter, if it becomes available, would facilitate a 21-day mission and offer important opportunities for research until more resources are available on ISS.

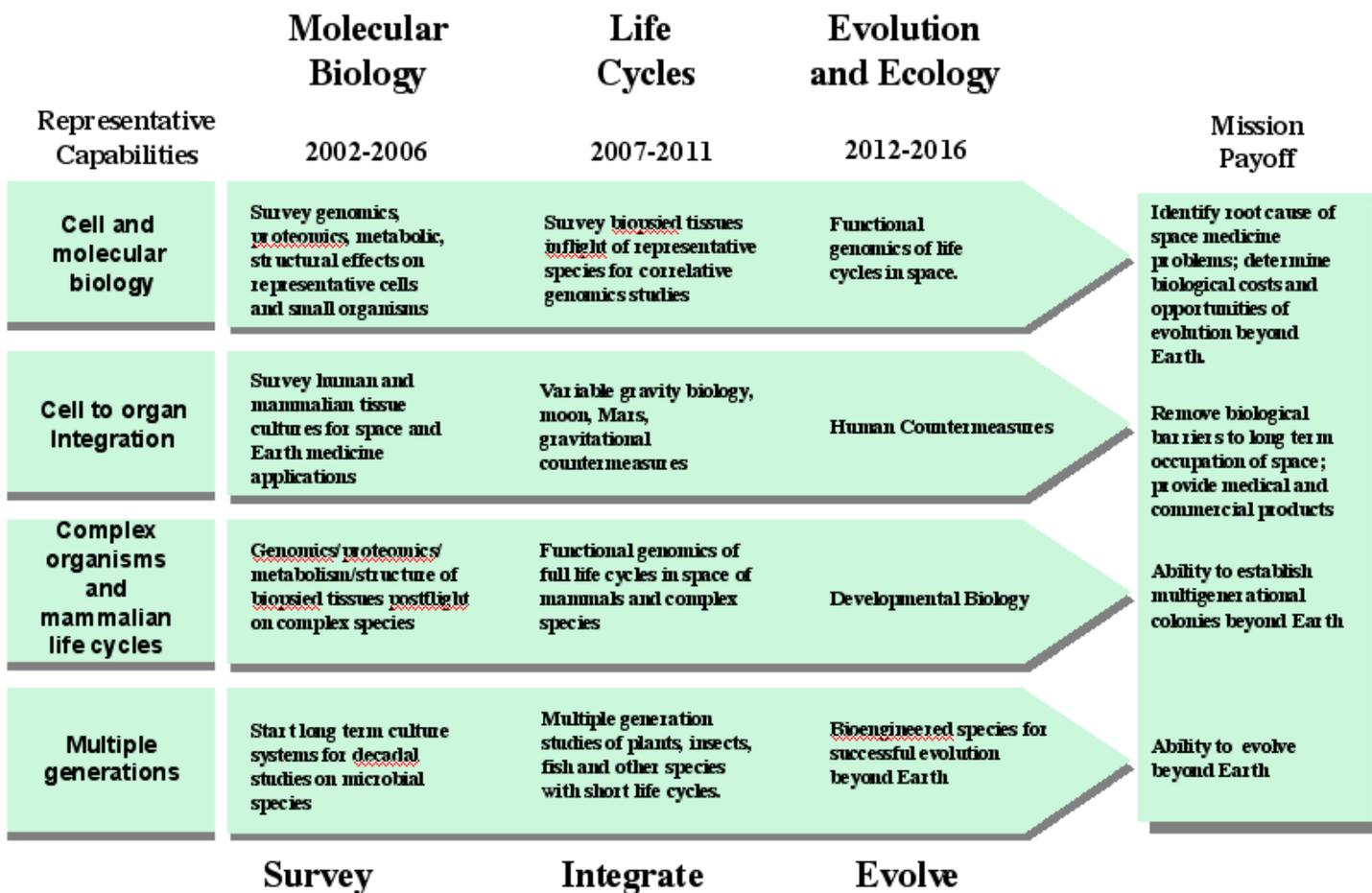


Figure 2. Phasing Strategy for Fundamental Space Biology on Space Station (Harper/ARC)

III. Recommendations

The overall strategy is to implement the following recommendation from the 1998 Space Studies Board *Strategy for Space Biology and Medicine in the Next Century*: "The present report ... calls for an integrated, multidisciplinary approach that encompasses all levels of biological organization—the molecule, the cell, the organ system, and the whole organism—and employs the full range of modern experimental approaches from molecular and cellular biology to organismic physiology."

There is some urgency in implementing these investigations. Space Biology investigations on the early Space Station can and should begin now in a collaborative mode. Early Station biology studies would focus on fundamental issues and model organisms that fit within the current vehicle constraints. These foundational investigations should be completed by 2005-2006 to yield inflight resources to the more complex and medically relevant studies of mammals and to the multigenerational studies critical to understanding evolutionary processes.

Workshop recommendations were developed within four general categories: programmatic, science, technology, and societal benefits. Top-level recommendations are listed below. More detailed information is contained in the appendices.

A. Programmatic

How can NASA facilitate fundamental biology research onboard the early ISS?

1. Collaborative team research. Form voluntary cross-discipline teams to design detailed candidate experiments tailored to available hardware. These teams will consist of members of the science, engineering, and technology (hardware/software) development communities. The teams will develop near-term science for identified hardware items to ensure high-quality feasible research can be accommodated. This strategy recognizes two key workshop findings. The first is that successful space biology investigations will require sharing flight facilities across organizations. The second is that a consortia of scientists collaborating on a multi-factor attack on research problems can yield significantly higher quality and quantity of scientific information within the same manifest allocation.

2. Focused NASA Research Announcement (NRA) or Announcement of Opportunity (AO). The current NRA/AO approach, with engineering working to accommodate the proposed science, is inconsistent with the demands of the early ISS research environment. A focused AO or Dear Colleague letter will direct investigators to propose experiments that will be feasible within the capabilities of the Shuttle/ISS environment. Researchers will be encouraged to establish a cross-discipline research team to propose a series of experiments optimally configured to accomplish high-quality collaborative research and produce associated publications. Time required for processing NRAs, as currently managed, may be counter to getting early science on board ISS.

3. Biosample/data sharing and archiving. Enable and encourage organism, tissue and data sharing within and between research teams from ground-based experiments and all phases of flight experiments. As part of the experiment designs, archive biosamples and data in a manner to facilitate sharing by researchers. Use cDNA libraries to share the data within the science community and increase the science return. Utilize the bioinformatics, scientific visualization, and other computational enhancement expertise and resources within NASA, agencies that NASA collaborates with, and online systems shared by the research community. This strategy addresses the opportunity to significantly amplify the value of data obtained from a single space flight investigation and recognizes that the value of the data can increase over time if properly managed.

4. Information and tools for investigators. Conducting biological research in space is more akin to conducting field biology investigations than it is to conducting laboratory research. Further, the peculiarities of both the microgravity environment and the spacecraft demand approaches that are simply not used in any terrestrial laboratory. For these reasons, NASA should provide mentoring to assist new investigators through the complex ISS flight research process, as does the European Space Agency (ESA). For investigators to have a better understanding of the hardware available for research, NASA should collaborate with its international ISS partners to provide an online hardware catalogue profiling NASA, international partner, NASA-sponsored Centers for Commercial Development (CCDs), and commercial flight hardware vendor products. Copies of functional hardware should be made available to the research teams so that investigators can be familiar with hardware performance and organism life support capabilities in order to better propose and conduct effective experiments. This strategy was strongly endorsed by first time as well as experienced flight investigators. As part of this effort, there should be an early focus on developing a suite of common and shared procedures and tasks that will be used across all biological disciplines. This includes but is not limited to: cryopreservation, recovery from cryopreservation, sample storage on ISS, common databases for ISS that are available to the community of investigators, and state of the art approaches to the construction and performance of genomics and proteomics research in space.

5. Space Biology Research Institute. One way to establish an infrastructure to support implementation of these recommendations is to create a Fundamental Biology Research Institute, similar in concept to the Astrobiology Institute or the National Space Biomedical Research Institute, but smaller in scope. These institutes provide an essential research roadmap and science communications infrastructure that attracts high-quality university researchers and facilitates cross-disciplinary studies. A virtual institute could be established within the Fundamental Space Biology (FSB) Program Office based on a FSB web-based intranet which provides online access to information, resources similar to those provided by ESA's Virtual Campus for the ISS (<http://www.spaceflight.esa.int/file.cfm?filename=utilvirtcamp>).

B. Science

What Fundamental Space Biology science should be conducted on the Shuttle/ISS and how can it be accomplished?

1. High-priority research goals. Because the space environment (microgravity, increased radiation, closed environments) is unique for living systems, it can provide special insights into normal gene, macromolecule, cell and organism functions as well as evolutionary processes. Novel environments reveal novel biological responses. The initial focus will be on characterizing the molecular basis for life's adaptation to space. The Workshop participants recommend adding another tool to the space biology portfolio by implementing observational studies in areas newly opened by the biotechnology revolution, especially in: genomics, proteomics and molecular biology. These observational studies will be used to generate focused hypotheses to be tested in controlled experiments consistent with traditional space biology approaches. Research that can be done on early ISS should study the effects of the space environment on:

- Relatively simple organisms whose full genome is known to support future integrated studies ranging from gene expression to metabolic/structural adaptation
- Selected well-characterized organisms for special studies on aging, infectivity, immune response, disease, and high-priority space medicine topics
- Genetic changes and adaptations in organisms over multiple generations
- Cells in culture—including variable gravity effects
- Small plants to evaluate gravity sensing, long-term growth, and morphogenesis with environmental monitoring using microsensor systems

2. Science planning and design. Conduct comprehensive ground-based studies to develop and verify experiments ensuring that problems are solved before experiments fly. Experiments should be iterative: plan multiple experiment replicates over multiple flights to estimate measurement variability, solve problems, and build statistical power. Include many samples in each flight for greater statistical significance and to enable more inflight controls. Evaluate already approved experiments that no longer have a designated mission for potential accommodation on the early ISS. Develop “Minuteman” investigations, velcro science packages, and opportunistic payloads to take advantage of all flight opportunities. A number of the candidate species below can remain dormant for months before flight, can be revived inflight, and can remain fixed and chilled for weeks after experiment termination. These species, which include those that pioneered the Human Genome Project, allow maximum flexibility in manifesting. They also provide results useful to the broadest science community.

3. Candidate organisms to study. The following are the best understood organisms on Earth and are routinely used by molecular biologists to work out fundamental processes for application to more complex problems. These also provide the means to carry out the SSB recommendation to study life at all levels of biological organization: molecules to cells, cells to tissues, tissues to organs, organs to systems. On the early Space Station, small model organisms will be the focus of study. As Station facilities mature, these studies will have provided the foundation for investigations of more complex phenomena on more complex species, especially mammals.

- Human and mammalian cell and tissue cultures address space medicine issues, complexity, integration of space flight effects from cells to tissues.

- Bacteria (e.g., *E. coli*) reveal basic biochemical pathways underlying other complex cell processes
- Yeast (e.g., *Saccharomyces cerevisiae*) is often the model of choice for understanding DNA replication, transcription, RNA processing, protein function, cell division, organelle function, signal transduction
- Micro-Plants (*Arabidopsis thaliana*) address plant genetics, gene expression studies
- Nematode (*C. elegans*) are models of choice for microscopic studies of origin and lineage of cell development to study mutations
- Insects (*Drosophila melanogaster*) can be used to address multi-generation, neurobiology studies
- Humans as incubators enable investigation of flora and fauna evolution over time

C. Technology

What technology and hardware is available to support space biology on early ISS?

1. Hardware Approach. The recommended strategy includes the following:

- Use existing hardware to reduce cost and development time. Provide funding for replication of key hardware and for small but important modifications that amplify yield and quality.
- Create a cell biology suite on Space Station by combining several hardware elements: incubators, automated fixation systems, imaging systems, centrifuges, freezers, glove boxes, microscope systems. Keep hardware resident on ISS and bring up new experiments for efficiency of space, crew time requirements, and cost.
- Conduct ground baseline studies to characterize hardware performance, biocompatibility, data acquisition/processing for candidate flight systems, and establish baseline data for control variables such as launch and landing stresses. This should begin as soon as possible, ideally during the summer 2002.

2. Capabilities. Specific hardware capabilities needed include:

- Incubators with automated sample preservation capability and the ability to take time course measurements.
- Small, variable gravity centrifuges (1-g controls important, but fractional-g may be even more so)
- Improved preservation of specimens given current limitations of ISS: support development of freezers (-80 and -180 °C), critical for returning valid specimens; custom containers that efficiently use freezer space
- Support development of NASA Glenn Research Center (GRC) microscope for living cells
- Continuous sampling of environmental variables with download of data
- Insect habitat essential for multi-generational studies
- Modify some hardware components to increase the number of samples flown

3. Technologies. Use the following enabling technologies to support and advance space biology on ISS:

- Biotechnologies applicable to space flight such as gene expression arrays, proteomics tools, and fluorescent probes
- Advanced sample preservation for inflight sampling and transport to ground
- Miniaturized sensor systems
- For postflight data analysis and sharing, apply bioinformatics tools and develop facilities within NASA; use cDNA libraries; 3-D reconstruction for modeling and simulations; sample bank.

D. Societal Benefits

How to identify, capture, and communicate the anticipated and actual benefits from this research?

Over the past thirty years, biological responses in space have tantalized researchers with the potential to obtain important insights about aging, new pharmaceuticals, and basic biological processes. Until now, however, there was no means to confirm the promise of space biosciences research. The precision of current molecular biology techniques allows definitive comparisons between space effects and ground based biological issues and will allow researchers to validate the use of space for humanitarian benefits on Earth.

- 1. Identify benefits.** Include a category in all research proposals for anticipated benefits and assign definition of benefits task to each collaborative research team. NASA support staff will track these anticipated benefits by research topic.
- 2. Capture benefits.** Ensure that individual researchers and teams profile emerging benefits from their research beginning with ground studies. Collect benefits in a web database for use by NASA, Public Affairs, contractors and others to educate all staff and format benefits for sharing with public.
- 3. Communicate benefits.** Provide online access to benefits to NASA/contractor staff and the public. Restate on a regular basis the value of the work to the public and to congress whenever the opportunity arises. Include communicating the value in relation to the cost of doing the science as a key part of the story.

Workshop Goals

1. Define a set of specimens to be flown based on available equipment and opportunities
2. Recommend areas of research that can be pursued given above species, e.g.
 - Mechanisms of mutation
 - Cell-cell interaction
 - Cell-substrate interaction
 - Motility
 - Cell morphology
 - Development
 - Stress/stimulus response
 - Cell cycle/ growth rate

(Taken from <http://astrobiology.arc.nasa.gov/genomics/> -- the Workshop Report on *Genomics on the International Space Station* co-chaired by Nobelists Baruch Blumberg and Richard Roberts)
3. Develop a generic set of experiments which could be flown on 9-12 month centers.
4. Provide recommendations for data analyses, e.g., by:
 - Competitive peer reviewed proposals
 - Qualified in-house researchers
 - Contracts to biotech companies
5. Develop a protocol for archiving, storing and curating the data collection, including data management. Define appropriate archival storage techniques that will preserve material in condition for future studies.
6. Provide recommendations for experiment protocols examining responses of organisms at the gene level.
7. Determine if equipment and resources currently support studies of fundamental processes of DNA to RNA to protein to post translational reactions (e.g., glycosylation).
8. Determine if experiments can be structured to reflect gravity vs. other stresses, radiation, absence of magnetic field, exposure to chemicals (equipment outgassing).

Workshop Presentations

I. Thursday, March 14, 2002

A. Background

Welcome

Speaker: Dr. Henry McDonald

Center Director, NASA Ames Research Center

- Core complete stage of ISS is not satisfactory for R&D
- Conducting early science is our challenge
- Moving beyond core complete, science must be driven by early knowledge gained and potential benefits
- Many questions can be pursued at genetic and molecular levels
- ARC intends to take results of this workshop to upper level management to positively influence our future

Introduction to Space Biology Over the Next 5 years

Speaker: Dr. Maurice M. Averner

Program Manager, NASA Fundamental Space Biology Program

- We have lost many of the key elements for the Centrifuge Accommodation Module: only the Incubator is funded to completion, while the other habitats are in question
- Fundamental Space Biology looks at radiation effects and microgravity on structure, function, and evolution of living systems (from molecular biology to evolutionary biology)
- We need to come up with a rigorous research program within the constraints of ISS capabilities
- New biology provides new opportunities at the molecular and cellular level
- There is money available for modifications of existing hardware

Workshop Goals

Speaker: Dr. Baruch S. Blumberg

Director, NASA Astrobiology Institute

- International Space Station is a great achievement; construction to date has been superb and represents the most complicated project undertaken by humans
- Space biology research gives clues/insights into normal gene and cell function on Earth
- World has committed to space exploration with varying levels of support
- Space science is massive generator of new ideas driven by new access to microgravity (i.e. ISS)
- ISS is a combination of field and experimental research
- Animal experiments are difficult now, but we can do molecular biology studies
- Need to educate young scientists since they're just beginning
- Fly organisms for which we have gene sequences
- Funding cuts; focus research on what is possible and what we have available

B. NASA Advisory Committee's Key Questions and Recommendations

Biological/Physical Research Advisory Committee

Speaker: Dr. Kenneth Baldwin

University of California, Irvine

- Believes cutting edge science is not possible on the early Space Station, but would like to be proven wrong
- With Core Complete, it is suggested that we lost 80% of the science capability on ISS
- Be honest and make clear recommendations to influence the process

Committee on Space Biology and Medicine

(associated with National Academy of Sciences as advisors to NASA)

Speaker: Dr. Gerald Sonnenfeld

Morehouse School of Medicine

- Must continue to provide flight opportunities (including frequent fliers) or lose scientific communities and new researchers
- Establish ground program to define science before flight
- Ensure research is hypothesis-driven and has a clear goal to address. Don't ignore basic biological questions.

Committee on Space Biotechnology

Speaker: Dr. Lawrence DeLucas

University of Alabama

- Need to repeat experiments on multiple flights; success of crystal growth increases with additional flights
- NASA needs to continue funding for completion; budget for his experiment analysis went from \$260K to \$60K, which obliterates science results
- There is a vast array of analytical tools available to do science—NASA needs to take advantage of these
- NASA should support structural biology research; space-based crystals can help
- Microgravity produces better crystals (better protein analysis) and we have opportunities to do this now

Advisory Committee on Muscle Cell Culture in Space

Speaker: Dr. Herman Vandenburg

Brown University School of Medicine

- Centrifuge habitat slots reduced from 8 to 4 would degrade science; Committee reported that research would be scientifically invalid
- Report on readiness of biological research for ISS indicated STS research should continue
- Modifications of Shuttle hardware for use on ISS is not cost effective; use on STS and fund what's possible for ISS
- Nothing can be done on ISS that can't be done on STS; should have one dedicated space biology flight each year

ISS Utilization Advisory Sub-committee

Speaker: Dr. J. Milburn Jessup

Georgetown University Medical Center

- There is a broader research agenda than human countermeasures
- All of OBPR is being hurt so we need to strategize across OBPR to be effective
- Molecular/cellular biology is a great opportunity if we can keep it simple: how to approach methods and how to prioritize are key issues
- How to phase in capabilities? Molecular biology first, then whole organism
- Constraints are crew, power, space, lack of equipment
- Focus on what we can do

C. NASA Flight Implementation Perspectives

ISS Research—Chief Scientist Perspective

Speaker: Dr. Roger Crouch

ISS Chief Scientist, NASA Headquarters

- Constraints on ISS also include politics and budget
- The lack of a crew return vehicle, node 3, and habitat module all limit research by available crew;
- Good news is that power will increase over next 2 years
- Current research is preliminary in nature
- Each month delay in ISS costs \$100 million due to infrastructure costs, so will build as fast as possible
- 4 Shuttle and 4 Progress (Russian) flights required just for operations; if NASA cuts back to 4 flights/year, no additional research can be done
- Science is not the first priority: NASA objective is to build science capability, but first need is to show that ISS can be operated (including assoc. \$)
- Optimize research applications to ISS

Crew Interests and Opportunities —ISS Utilization Opportunities

Speaker: Dr. Yvonne Cagle

Astronaut Mission Specialist, NASA Johnson Space Center

- Current crew of 3 are often overwhelmed and timelines slip, science is compromised; as ISS grows, crew time for operations will increase
- Now doing only near-autonomous science (thus difference between ISS and free fliers is not great) until 2008
- Use ISS/Shuttle as a system to optimize science
- Extended Duration Orbiter (EDO) could really help to augment science opportunities
- 21 day dock to ISS; could provide 1000 hours of science (an additional 50 weeks of science/EDO mission)
- Must show benefits to society

JSC ISS Program

Speaker: Dr. Ned Penley

NASA Johnson Space Center

- Everything is a trade off
- EDO can only happen after 2003, would delay ISS partner modules if launched before 2005 which is a major political issue
- Get more value for EDO after 2005: this is a political issue
- If they get powered middeck lockers, they will still have periods without power
- Basically near term science opportunities faces a grim picture
- One trade-off is outfitting the ISS vs. resupplying what is already up there
- Possible additional flight in 2004

D. Available Hardware

Orbital Technologies Corporation (ORBITEC)

Speaker: Thomas Crabb

- ORBITEC has developed the Biomass Production System (BPS), a controlled environment plant growth facility with controlled temperature/humidity, fluid/gas (CO₂, O₂) monitoring, light, video, data, enabling access to plants without tools
- BPS Verification and NRA science to be completed in summer of 2002
- BPS has multiple, independently controlled small chambers that can be used for a wide variety of biological specimens such as fungi and micro-plants and organisms, by replacing growth chambers
- To develop facilities that have high reliability and low crew-time needs, it may be harder to evolve hardware from STS to ISS. Instead it may be easier and cheaper to develop hardware specifically for ISS.

Bioserve Technologies

Speaker: Dr. Louis Stodieck

- Bioserve is a one-stop shop w/frequent access to space
- Hardware has been on STS and ISS
- Began in 1991 with space version of test tube (fluid processing apparatus)
- Commercial Generic Bioprocessing Apparatus experiment carriers (isothermal containment modules-ICMS) all middeck (fixed temps, etc) are all available for cell and molecular biology research
- Space plant growth chambers are also available
- Science/engineering need to collaborate for maximum benefit: use available hardware, share hardware space, share tissues, share data

Oceaneering

Speaker: Roy Klusendorf

- Developers of refrigerators and freezers
- Refrigerator/freezer from STS-95 available for lease
- Extended duration, ± 1 °C control

Space Hardware Optimization Technologies (SHOT)

Speaker John Vellinger

- Avian Development Facility (flew on STS-108) can be modified to support other organisms
- Advanced Separations Bioprocessing Facility (ADSEP) w/cell culture cassette is under development
- Other hardware important for cell and molecular biology research includes Thermally Controlled Facility (TCF), Advanced Avian Habitat and Avian Hatching Habitat

Wisconsin Center for Space Automation & Robotics (WCSAR)

Speaker: Dr. Weijia Zhou

- A NASA-sponsored Commercial Space Center focusing on plant biotechnology in space under Space Products Development (MSFC) and OBPR
- Core competencies are flight engineering and plant biotech
- 4 hardware elements
- 10 flights completed to date, 2 on ISS
- Commercial plant biotech facility
- WCSAR provides one stop service: payload development/integration-science design/preparation-launch support-mission operation.
- WCSAR makes direct arrangements with NASA for space flights.

NASA Glenn Research Center Microscopes

Speaker: DeVon Griffin

- Microgravity fluid physics program developed new microscope
- Light microscopy module: video, confocal, laser tweezers, oil immersion
- Confocal imaging system under development

E. Biotechnologies Applicable to Space Research

1. Analyses

Gene Expression

Speaker: Dr. Elizabeth Kerr

Affymetrix

- Human genome project stimulated gene sequencing tools
- Gene expression tools can compare disease/normal; successful treatment/not; 1-gravity/microgravity
- Identified gene expression for brain tumors with good prognosis vs. bad prognosis: expression profiles are an excellent diagnostic tool
- Spaceflight applications: adaptation, cell death, bone growth, muscle physiology, developmental biology, etc. designed to make observation and answer the question “what is the genetic mechanism behind the phenotype”

Proteomics

Speaker: Dr. Timothy Hammond

Tulane University School of Medicine

- Same revolution as genomics
- Multiple antibody gels can reveal which pathways re involved in adaptation to space
- Proteomics on a chip: purified and unpurified
- Light scattering techniques: molecular vs. abundance protein changes
- Automated 2-D gels and spot cutting: identify by GC mass spectrometry; molecular mass vs. elects change provide highly detailed response profiles
- Extremely small samples acquired and brought back from space

Fluorescent Probes

Fluorescent-Based Imaging

Speaker: Dr. Sigrid Reisch

NASA Ames Research Center

- Green fluorescent protein (GFP)
- Mutant variations of GFP, available as needed
- Can tag any protein to GFP in organism, organ, or on a protein and visualize position, distribution, quantity, movement
- Stable at 37 °C, optimized efficient in vertebrate cells, expression in cell types/organisms
- Developmental biology applications
- GFP shows in an actual gene

Fluorescent Probes in Space-based Biology

Speaker: Dr. Eduardo Almeida

NASA Ames Research Center

- We can study:
 - matrix adhesion
 - kinase activation
 - sperm/egg interaction in mouse
 - integrins expressed at cell surface
 - cell signaling/cell death/cell survival
- ISS applications
 - expert simplicity: live cell permeant 1 or 2 stage
 - visualize genetic mutation in live cells genetically encoded with GFP/DS Red with minimal crew interaction
- Hardware
- Can show characterization of any protein in cell, growth, mobility, remodeling, matrix adhesion, signaling, cell-cell interaction

2. Inflight Protocols

Sample Preservation

Speaker: Dr. Thomas Goodwin

NASA Johnson Space Center

- Science problem: no sub 0 °C storage on ISS
- MELFI (-80 °C) will go up in 2003
- Development priorities (could be developed in 30-36 months): -185 °C active; -185 °C passive; -80 °C passive

Miniature Sensors

Speaker: Dr. John Hines

AstroBionics Office, NASA Ames Research Center

- Full sensor systems are required
- Automated technologies are needed to grow, sense, image, analyze, fly biological specimens
- Need to miniaturize available ground-based systems
- Bionanosatellites/Bioexplorer I provide secondary payload opportunities with access to higher orbits than on ISS
- 2 flights/year (one-way, return, 1-G control)
- Yeast, tissue, cells, bacteria, *C. elegans*, *Drosophila* are compatible with free-flyer accommodations
- *In situ* bioanalytical systems such as rotating disk analytical system; flow cytometers are becoming available
- Automated microscopy and imaging systems are feasible
- Genomics: maskless array synthesizer and automated gene sequencing is recommended for onboard ISS work requiring sequential studies without waiting for postflight analysis

3. Postflight Data Application

Bioinformatics

Speaker: Dr. Andrew Pohorille

NASA Ames Research Center

- Bioinformatics can help design more successful flight investigations and develop better strategies when resources are constrained.
- Depth of knowledge is inversely proportional to number of genes
- Standards are important for sharing data with other researchers
- Use both for experiment planning and post-flight analysis and archiving
- Bioinformatics can provide experiment design validation before flights
- Statistical power in replicates
- Should have close collaboration between PIs and data experts
- Bioinformatics is now a standard in contemporary biology and aids in proper archiving and curating
- Conclusion: NASA needs a bioinformatics capability to maximize space research

cDNA Libraries

Speaker: Dr. Eugenia Wang

University of Louisville

- Use cDNA library to convert exhaustible resources to inexhaustible resources.
- Used cDNA library makes subtracted up regulated and down regulated dot blots

3-D Reconstruction

Speaker: Dr. Richard Boyle

NASA Ames Research Center

- Modeling and simulations—bio-visualization, imaging and simulation technology center available to amplify data yield and reveal hidden dynamic and structural information
- High resolution 3D cell imaging, structural analysis and modeling
- Enhancement and simulation of flight data
- NASA Virtual Glovebox: portable tool for working out flight protocols and simplifying procedures
- Virtual training for crew at 1G and microgravity environments via 3D modeling of NASA Virtual Glovebox under 1G and microgravity conditions

F. What Strategies Should NASA Consider...

Speaker: Ms. Lynn D. Harper

NASA Ames Research Center

- Space is evolutionarily novel and novel environments reveal novel biologies that can be applied to a number of problems.
- Use the combined biotech, infotech, and miniaturization revolutions to amplify the value of a payload pound orders of magnitude over what was previously possible and accelerate return on the taxpayers' investment.
- Use instruments and techniques from all sources – pool resources
- Develop new manifest strategies that optimize science outcomes by combining investigations synergistically and taking advantage of “nooks and crannies”.
- Use all the tools available: baseline data collection, observational science, hypothesis driven science, exploratory investigations, postflight data amplification; data mining, cloning, sample banks.
- Old data takes on new value provided it is properly managed with sample archives and bioinformatics. NASA needs to upgrade its facilities in these areas to contemporary standards.
- Phase research according to three strategies – (1) build knowledge from simplest organisms to most complex (per SSB recommendation); (2) obtain data in a correlative manner to determine cause and effect relationships (figure 1); and phase research to match Station accommodations (figure 2).

II. Friday, March 15, 2001

A. Conducting Research on the International Space Station between 2002 and 2007

Lessons from the Past

Speaker: Dr. Gary C. Jahns

Deputy for Flight Programs, Fundamental Space Biology Program Office

- Avoid repeating mistakes of the past
 - Lack of duplication
 - Proper ground controls
- Not requiring power up will be an advantage
- Need to balance good science with the constraints
- Need to reprioritize science
- ~17 US PIs and ~7 International PIs have gone through the review process
- Some of these cannot fly given current constraints so there are still some openings for the right kind of experiments
- No power up experiments can get power perhaps several days after launch

Cell Research

Speaker: Dr. Neal N. Pellis

Director, Cell Research, NASA Johnson Space Center

- Did extensive tour on Mir to understand long-duration operations
- Advocating cell research in space because it is manageable and achievable.
- Cellular research can answer a lot of key questions
 - Adaptive responses
 - Phenotypic and genotypic changes
 - Metabolic and replication changes
- Applies to FSB, Bioastro, Astrobio, Cellular Biotech programs
- Fits Administrator direction to focus on outcome rather than throughput
- Current Research Strategy requires frozen cultures to be launched in passive freezers, thawed, put in incubator, fixed, refrigerator/freezer, brought back to Earth for post-flight analysis; this requires 2 lockers and 4 hours/week crew time. Better automation would be helpful
- Early phase research should show logical extension to higher models
- Research should fit NASA mission
- Maximize throughput, emphasize outcomes
- Target commercialization and applications
- Need fractional gravity controls as well as 1G
- Need two lockers
- Reliability of the equipment right now does not let us put automated science on unmanned platforms.

B. Splinter Sessions

1. A.M Session – These sessions demonstrated that pioneering work could be done during early Space Station even under severe constraints. Participants identified classes of investigations that could be done with existing hardware under the most constrained conditions when no power was available on the Shuttle during the transfer of biological samples from Earth to Space Station (no power up). Other participants identified investigations enabled by powered lockers during transfer from Earth to the Space Station (power up).

Group 1—Existing hardware, no power up

Lead: Dr. Roger Crouch

NASA Headquarters

- Science recommendations:
 - Study the effects of space flight on relatively simple, well-characterized organisms (Bacteria, yeast, nematodes, *Drosophila*, plant cells)
 - Maximize science return by having multiple PIs share hardware and data
 - All flight qualified preservation techniques and fixatives are available
- Hardware requirements for doing solid science:
 - -80° and -185°C freezers
 - Imaging: video, stills, fluorescence
 - Inflight gravitational controls

Group 2—No power up

Lead: Dr. Gerald Sonnenfeld

Morehouse School of Medicine

Proposed experiments, assuming dewars for up/down transport

- Bacterial phage
 - Send up frozen, incubate on orbit, freeze, and return for analysis
 - Requires one hour crew time and existing hardware with minor modifications
- Mammalian development
 - Send up frozen sperm and egg, fertilize on orbit, freeze, and return
- Self-contained life support system
 - Use cells or plants taken up and down at ambient temperatures
- Long-term cell culture
 - Send up and down frozen and leave on ISS for an extended period
- Crew as transport mechanism
 - Look at changes in viruses commonly resident in humans, how they evolve and reactivate in space
 - Take samples from crew on orbit and freeze for return
- Seeds
 - Incubate/germinate on orbit, freeze, and return for genomic analysis

Group 3—No power up

Lead: Dr. Timothy Hammond

Tulane University School of Medicine

- Science recommendations:
 - Use quiescent organisms in an iterative series of studies to establish variability, fine tune protocols, and increase N
 - Controls (ground and inflight): shear, coriolis, radiation, gas
 - All fixatives available
- Hardware recommendations:
 - Battery in the Multi-Purpose Logistics Module and Get Away Special packs offer flight possibilities
 - PIs need non-flight-certified copies of hardware for use in the lab
- NASA recommendations:
 - Fund PIs early so they can do good preparatory ground-based work
 - More focused, mature NRAs will result from providing better information on flight hardware and on the flight experiment process
 - Need NASA support for use of commercial hardware

Group 4—Power up for mammalian cells

Lead: Mr. John Hines

NASA Ames Research Center

- Science recommendations:
 - Use cells (bone, muscle, renal, immune, developmental) to study gene expression and gravitational signaling
 - Need controls and sampling at every mission phase and every experiment transition point
 - N of at least six
 - Should generate cDNA cell libraries to increase science return
- Hardware recommendations:
 - BIOPAK and Simplex are the available hardware items that meet most science requirements and mission constraints

Group 5—Power up Mammalian

Lead: Dr. Joshua Zimmerberg

National Institutes of Health

- Scientific Recommendations:
 - Should look across species, kingdoms, generations
 - The most important issues: effect on space environment on cells in culture; effects of space environment on genetics and adaptations in the organism
 - Re-associate Biological and Medical Sciences research
 - Gravitational work done on Earth
 - ISS cell research should focus on model systems to maximize research options
 - Effect of space on the immune system important
- Investigator interactions:
 - Investigators should conduct experiments in consortium style environment
 - Experiments should promote the sharing of tissue, data
 - Hardware should be developed and tested by groups
 - Sensors should be added to existing hardware to increase functionality
 - Should develop a Station planning group
- NASA Recommendations:
 - A user manual should be developed for investigators in a community language that everyone could use and understand
 - Accurate reporting of experimental parameters is essential
- Technical Recommendations:
 - Need to focus on current resources to have an impact
 - Variable Gravity Centrifuge
 - Freezers as proposed.
 - Glenn Research Center microscope for living cells
 - Hood space for handling
 - Better preservation options
 - Hardware website which has updated information from all international space agencies
 - Continual sampling of environmental variables
 - Gene experiments by GFP
 - Growth of cells and organisms in the same container
 - Establish a bioinformatics facility for data archiving and sharing

Group 6—Power Up

Lead: Dr. Eduardo Almeida

NASA Ames Research Center

- NASA Recommendations:
 - ISS research should take the multi-investigator analysis approach by opening research up to the scientific community through NASA facilitated competitive flight opportunities and grants.
 - NASA provides the flight hardware, transportation and ISS space.
 - The research opportunities on the ISS would be advertised by NASA and RFPs sent to researchers.
 - Researchers would be given the hardware specifications and would write proposals based on available hardware and station resources.
 - This would decrease the overall time investment a researcher would have to commit to an ISS project and would encourage new research.
- Science Recommendations:
 - Experiments should use arrays of a large number of small model species and readily available genetic and genomic tools, such as the GFP (Green Florescence Protein) genetic marker, for conducting large scale research
- Example Experiment:
 - Subject: Transgenic Expression of GFP-Fruit Fly in Micro-gravity
 - Organism: Fruit Fly (*Drosophila melanogaster*) has a history of microgravity research and the genetic effects of gravity on earth has been studied.
 - Hardware: Bioserve CGBA, CSA-2004/s (insect habitat), SHOT Egg Incubator
 - Methods: Samples would be stored in stasis at 11 °C on earth until launch. Once in orbit the specimens would be activated by increase of temperature to 25 °C. Using the Glenn Microscope, the GFP expression patterns could be observed and recorded in the ISS. At the end of the experiment, the specimens would be returned to 11 °C and transported back to ground for ground based genetic testing and storage.

Group 7—Problem Solving

Lead: Mr. Gregory Schmidt

NASA Ames Research Center

- Goals:
 - Implement science asap and enable more rapid technology transfer to flight
 - We have taken some first steps by making a list of available hardware (in workshop folders), this was done a year ago by Dr. Rita Briggs and will be updated and put on the web.
- Impediments: (problems)
 - The NRA process as currently implement is too general and unfocused
 - The experiment development/analysis process is too lengthy
 - The flight opportunities are limited by funding, space and crew time
- Opportunities: (solutions)
 - The 2004 Manifest should be complete in the next 6 months.
 - Low power experiments proposed within the next 2 months might be able to fly in 2003
- Actions:
 - Conduct this 2002 ISS workshop (completed)
 - Form voluntary groups to draft mission definitions.
 - Pre-select Hardware to be used in missions.
 - Release focused NRA or AO driven by experiment definitions and resource availability. Use the model that ARC developed for tissue sharing
 - Archive all flight experiment materials (sample tissue, DNA, cDNA libraries) for later use by the international research community.

Group 8—Societal Implications

Lead: Mr. James Pagliasotti

JMP Associates

- Heartened to see an interest in returning value back to the tax payer
- The public wants to understand what NASA does for them and has a general need for such information
- Since the moon landing in 1969 the public has spent 500 billion dollars. There is a need for the funders to justify the money being spent. This is done by demonstrating the effects NASA research has had on the worlds major concerns. (world hunger, world health, national security, etc.)
- General societal implications should be integrated into NASA thinking
 - A way to bring the information or relevance of NASA research to the world is via the Internet. The public expects information about the NASA research being funded.
 - Promote public awareness by providing information on what to expect from the research, what has been observed and what the public should find valuable
 - Managers should build in a rewards system for researchers who succeed at promoting NASA outreach
- NASA Biology can be successful within the government by:
 - Instituting a well-managed program
 - Supporting research and development and minimizing costs of infrastructure
 - Outsourcing for commercial solutions whenever possible
 - Repeatedly explaining objectives
 - Building e-information systems to facilitate public awareness
- The goal of outreach is to be able to explain to your children what NASA does without confusion.

P.M. Session

Bioinformatics

Speaker: Dr. Steve Zornetzer

NASA Ames Research Center

- NASA and Science Recommendations
 - Bioinformatics research will require a large initial investment in computer hardware and software
 - ISS experiments should be designed around community standards and use available resources from other research institutions; examples include Stanford's gene-chip array database and array data standards.
 - Bioinformatics support will be ground based through the core complete phase of ISS development.
 - NASA's research program should have two strong areas: image processing; regulatory networks
 - NASA bioinformatics should develop a core competency not a core facility

- Core Complete Phase
 - How much of the research budget are we willing to devote to establish a bioinformatics facility?
 - There is a need to develop a ground-based repository for genomic and genetic data before building the facility.
 - Space Station bioinformatics should focus on the reuse and publication of the data from the ISS.
 - The data should be shared after a grace period, which would allow researchers enough time to use and publish their results.
- Program Complete Phase
 - The ground-based system will be fully operational with additional in-flight data collection and possibly analysis.
 - The in-flight system would run experiments, collect data, make experimental decisions and relay data to ground based storage/research facilities.
 - Future bioinformatics hardware would ideally include voice recognition programs, which could save crew time and effort.
 - Eventually the project could develop into a PI-in-a-Box, a fully automated system for conducting experiments on the ISS without crew supervision.

Technology

Speaker: Mr. John Hines

NASA Ames Research Center

- The ideal system capabilities: modular, reconfigurable, upgradable
- Technologies should support the following: **grow** (including fixation/freezing), **sense** (including sample management), **image** (microscopy, cytometry, spectroscopy, etc.), **analyze** (data acquisition, analysis, processing, communication), and **fly** (support all platforms)
- Technology development approach:
 - Technology development and demonstration on the ground, on Bion, and freefliers; use a biotech consortium to integrate components and maximize benefits of the biotech revolution
 - Port technologies to STS and ISS
 - Develop new platforms
- This approach will occur over a 2-year development cycle
- A directed effort is required to move technology from development to use as rapidly as possible.

Summary

Speaker: Dr. Kenneth Baldwin

University of California, Irvine

- Is now convinced that exciting work can be done during the early Space Station
- This work doesn't replace the important space biology research planned for core complete, but it does amplify its value and is complementary in nature
- Don't settle for simple science
- Look at the model of NAI and NSBRI
 - Virtual institutes
 - Explore creating a Fundamental Space Biology Research Institute spanning the gravitational continuum

Speaker: Dr. Baruch Blumberg

NASA Ames Research Center

- ISS is more like a field station than a remote laboratory. Science adapts to realities and generates problems to be studied.
- Human Genome Project began with negative reviews from the science community, but they provided input and it became a great success.
- Use both observational and hypothesis driven research
- Focus near term activities on what can be learned within the constraints

Closing

Speaker: Ms. Bonnie Dalton

NASA Ames Research Center

- Life Sciences/Fundamental Space Biology needs to hold this sort of meeting annually
- Intend to take results to the Biological/Physical Research Advisory Committee

Appendix A: Candidate Investigations under Early Space Station Constraints

IA — Title: Investigative Study on Mammalian Fertilization in Space

Purpose: Demonstrate that mammalian fertilization and early development can occur in space

Rationale: Establish feasibility for critical early development beyond Earth (fundamental science, fertilization of mammal is key issue for human expansion, insights may be useful for developmental biology)

Proposed species: Mouse

Transport to Station: LN2

Requirements on Station:

- Incubators
- 2-hours crew time

Transportation from ISS: LN2

Preservatives: Freeze and/or Fix

IB — Title: Investigative Study on Growth, Nucleic Acids, Gene Expression, and Protein Structure in Bacteria and Phage in Space

Purpose: Characterize adaptation to space flight conditions

Rationale: Space flight has been shown to alter bacterial and viral replication and growth (basic science of very small organisms with space and Earth medicine applications)

Proposed species: *E. coli*, phage MS 2

Transport to Station: LN2

Requirements on Station:

- Culture facilities
- <1-hour crew time

Transportation from ISS: LN2

Preservatives: Freeze

IIA — Title: Investigative Study on Self-Contained Ecosystem

Purpose: Examine communal interactions in space

Rationale: Discover how space flight alters interspecies interactions (basic science on extraterrestrial ecology issues important for long duration space flight)

Proposed species: Bacteria, aquatic plants

Transport to Station: Stowage

Requirements on Station: Place to place ecosystem

Transportation from ISS: Stowage

Preservatives: Freeze

IIB — Title: Investigative Study of Seed Germination and Growth in Space

Purpose: To monitor stress responses of *Arabidopsis*

Rationale: Use existing hardware systems to gather data that describes the response of plants to space flight (basic science, plant based life support issue)

Proposed species: *Arabidopsis*

Transport to Station: As stowage; “plant in bag” format

Requirements on Station: 2 hours crew time to freeze samples

Transportation from ISS: LN2

Preservatives: Freeze

IIIA — Title: Investigatory Study of Viral Expression (in Space) during Space Flight

Purpose: To determine the effects of space flight on the genome and structure of latent human viruses carried by the crew

Rationale: To discover whether space flight alters the frequency and expression of latent virus, including gene array analysis (basic science and space medicine issue)

Proposed species: Crew members with EB (Epstein Barr Virus) or CMV (Cytomeaglovirus) or HSV (herpes simplex virus)

Transport to Station: Not required, sampling of crew will take place during mission (assume also pre/post mission)

Requirements on Station: 2 hours crew time to swab and freeze samples

Transportation from ISS: LN2

Preservatives: Freeze

IV A & B — Title: Investigative Study of the Bacterial Response to Space Flight

Purpose: To monitor stress responses of bacteria to living in the space environment

Rationale: Use minimal crew time to gather data on changes in gene expression related to adaptation to space (basic science of simplest organisms, also important for space and earth medicine)

Proposed species: various bacteria, such as *Pseudomonas*, *Serratia*

Transport to Station: LN2

Requirements on Station: 2 hours crew time to thaw and refreeze samples

Transportation from ISS: LN2

Preservatives: Freeze

VA — (Shuttle Experiment--regular or EDO) — Title: Small animal experiments – mice

[NOTE: The group strongly supported the NRC report on Readiness Issues related to research in the biological and physical sciences on the ISS (2001) – NASA should provide ANNUAL shuttle flights devoted to science until assembly complete under Rev. F.]

Purpose: Analysis of animal tissues and microbes (multigenerational and mutational) using modern bio-technological techniques (microarrays, chips, etc.) to survey for changes in response to space flight. (This addresses the SSB recommendation)

Proposed species: Normal as well as transgenic animals (e.g., fully humorized immune system mice) -- 1000's of other possibilities

Transport to Station: powered Animal Enclosure Modules (AEMs)

Requirement on Shuttle: Crew activity mandatory—"monitor"

Equipment: Storage, freezer space, utilize new noninvasive technology for studies, in situ blood flow visualization, glucose levels, etc.

VB (90 days) — Experiment Title: Humans as Incubator

Purpose: Multiple generations/mutational studies

Utilize new drug screening technologies based on microarray chips in space

Look at proteomics in human –is drug metabolism altered, human cells (stain, muscle biology, blood smears)

Look at proteomics in human (microbial species)

Rationale: basic science with space and earth medicine applications

Proposed species: Controls = ground control astronauts

- Virtual reality technology or internal controls, use archived samples also

Requirements on Shuttle: crew, power

- Equipment –crew serum sampling equipment, storage of samples

Transportation from Station: utilize new technology e.g., in situ for visualizing blood flow, glucose levels

Preservatives: fix, cool

Other: Immunization in space – follow response e.g., skin antigen response

VI (Serves as ISS or 16-20 Day experiment) — Title: Effect of spaceflight on gene expression on (small whole organisms of interest. E.g., yeast, bacteria, nematode, flies, *Arabidopsis*)

Purpose: To study relatively simple and well characterized organisms that hold implications for more complex system and their response to spaceflight environment

Rationale: To provide insights into molecular mechanisms of adaptations to microgravity (These are the pioneer species of the Human Genome Project and offer basic science insights into key cellular processes with broad applications to space and earth medicine and commerce)

Proposed species: Yeast (*S. cerevisiae*), bacteria (*E. coli*, *Salmonella*) or *C. elegans*, *Drosophila melanogaster*, *Arabidopsis thaliana*, cell cultures of aquatic, reptilian, and plants

Transport to Station:

- Unpowered – ambient
- Unpowered – passive carrier
- Unpowered – battery, if available

Requirements on Station: STP

- Unpowered – connect power
- Crew time – contingency only, e.g., use of fully automated system

Transportation from Station: No power, but some may require “first off” status

Preservatives: All flight approved, e.g., RNA Later, Trizol, formaldehyde, ethanol

Other:

- -80 to -180 °C capability
- Imaging – video, still, fluorescent
- O₂, pH monitoring sensors
- on orbit 1xg & fractional g

VIIA&B — Title: *Drosophila Melanogaster* Experiments on ISS with Existing Hardware

Two experimental protocols can be conducted with **existing flight hardware** using *Drosophila melanogaster* (fruit fly) specimens. These experiments are designed to minimize or altogether eliminate the use of crew time.

These experiments can be done as a **consortium** where **several PIs** can propose to use their favorite genetic strains (e.g. different mutant lines, different GFP transgenic lines, different genetically marked balancers to track filial generations etc)

Protocol 1:

This proposal assumes that power is available for the payload on its way to ISS.

Purpose: (a) Use different **GFP fusion lines** (these are abundantly available in the *Drosophila* field) to look at neuronal, tracheal, muscular and other changes during **development in microgravity**. Several compartments are available in the hardware for accommodating multiple specimen types. (b) Use **wild type or mutant strains** to analyze **proteomics and gene expression (using microarrays)** changes resulting from microgravity. (c) Examine **aging and mutagenesis** effects of microgravity on samples that are returned to Earth. How all of these goals can be achieved concurrently in one experiment will be described on the next page.

Use **hardware like BioServe's Commercial Generic Bioprocessing Apparatus (CGBA)** where different compartments can be programmed to hold different temperatures at different time points. These parameters can be preprogrammed and no crew time is necessary. If hardware such as **SHOT's Avian Development Facility (ADF)** is used, different specimen lines can also be sent to ISS, but crew will have to remove containers and freeze or cool different samples at different times. This may require slight hardware modifications. CGBA has no centrifuge for on board 1g controls, while the ADF has the capability to centrifuge samples. The merits of each hardware piece can be decided based on the specifics of the experimental requirements.

- **Hold embryos or larvae at 11.5 °C** (stasis temperature) till the experiment is ready to be initiated on station
- **Raise the temperature to 25 °C or 18 °C** (if one wants to lengthen the development time for any reason) **to initiate** the experiment.

The Insect Habitat that is currently under development will be able to carry out all these functions effectively and will also be able to separate the individual generations (there can be 8-9 generations of fruit flies developing in a 3 month increment). However, as this

exercise was aimed at using existing hardware and conducting early experiments with minimal crew time usage, this is being suggested as an alternative plan.

Protocol 2:

Using **Bio explorer-type hardware** a much **simpler protocol** can be implemented that **captures a subset of the goals** from the previous experiment. In this example, no samples would need to be returned to Earth. Therefore, even a free-flyer type of platform would be sufficient. No crew time would be necessary if some of the described functions are automated.

- Send the GFP embryos and/or larvae in stasis at 11.5 °C (as described for the previous experiment). Use the consortium approach of several PIs proposing to use different GFP lines in this experiment as well.
- Initiate the experiment at 25 °C or 18 °C depending on the desired length of time for development
- Get images from a fluorescence microscope to visualize the localization of the GFP protein fusion. Analyze the data on Earth to assess the developmental changes undergone by the specimens in space in a variety of different tissue and organ systems as determined by the different GFP lines used.

The Bio explorer hardware developers are working on a fluorescence capability for their microscope, I was told, and that would fit into this plan. Also, temperature maintenance capabilities, other than 30 °C, is being considered for the hardware and that would broaden the science scope for the hardware as illustrated in this experiment.

VIII A (Shuttle) — Experiment Title: Gene expression patterns in the early stages of microgravity

Purpose: Compare gene expression alteration in microgravity to identify signaling pathways and genes sensitive to gravity

Rationale: Muscle atrophy is a key issue in microgravity. This research addresses how microgravity is sensed at the single cell level, focuses future studies on identified pathways in the developing rat or mouse and is useful in developing countermeasures.

Approach: Review ground vs. flight cultures and compare microgravity and use of 1G centrifuge; also have launch vibration control

Transport to Station: Use mature cultures in bio-reactor

Requirements on Station: Sample culture for RNA at hourly intervals as indicated by literature. Add Triazol to cultures

Transportation from Station: -20 °C or -180 °C frozen

Preservatives: Freeze in Triazol at -20 °C

Other: Use gene chips for experiment analyses

VIII B (ISS) — Experiment Title: Gene expression patterns during long term adaptation to microgravity

Purpose: Compare gene expression alteration in microgravity to identify signaling pathways and genes sensitive to gravity m- examining at weekly intervals to 30 days.

Rationale: Muscle atrophy occurs in microgravity and determine how microgravity is sensed and transduced at single cell level – compare 1G onboard centrifuged samples; also perform IGF-1 administration

Transport to Station: Use mature cultures in bio-reactor

Requirements on Station: Sample culture for RNA at weekly intervals

Transportation from Station: -20 °C or -180 °C frozen

Preservatives: mRNA Triazol for gene chip analyses
Fix cultures also for morphology and 2D gel analysis for proteins

AGENDA (continued)

SPACE BIOLOGY ON THE EARLY INTERNATIONAL SPACE STATION

1:00 **Biotechnologies Applicable to Space Research**

Analyses:

Gene Expression	-E. Kerr, Affymetrix
Proteomics	-T. Hammond, Tulane
Fluorescent Probes	-E. Almeida, ARC
	-S. Reinsch, ARC

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Inflight Protocols

Sample Preservation	-T. Goodwin, JSC
Miniature Sensors	-J. Hines, ARC
JSC – ISS Issues	-N. Penley, JSC

Post-flight Data Application

Bioinformatics	- A. Pohorille, ARC
cDNA Library	- E. Wang, Louisville
3-D Reconstruction	- R. Boyle, ARC

4:00 **What Strategies should NASA Consider for Understanding the Response of Life to Space Over the Next 5 Years? Key questions and techniques.**

General Discussion
Ms. Lynn D. Harper, Lead, Integrative Studies

6:00 **Working Social hour and buffet 240A**

Building 244 Centrifuge Accommodations Module Mockup Tour
Building 240A Flight Hardware Display

AGENDA (continued)

SPACE BIOLOGY ON THE EARLY INTERNATIONAL SPACE STATION

- 2:45-3:45 **Discipline Working Groups**
 Science Strategies: Species Size, Complexity, Multigeneration,
 Developmental Biology, Comparative Biology, Evolutionary, Studies
 Relevant to Space and Earth Medicine

 Implementation Approaches: Pros and Cons among Competitive Peer
 Reviewed Studies, Focused Research, Systems Biology, Opportunistic
 Research, Observational Science, Hypothesis Driven Research

 International Space Station Constraints and Hardware Problem Solving:
 Flexibility in Station Accommodations and Constraints, Solutions from
 Advanced Technologies to meet Highest Priority Science needs

 Value to Science and Society
- 3:45-4:00 **Break**
- 4:00-4:30 **Summary** Drs. Blumberg and Baldwin

 What will this Body of Work Teach Us? What is its Value to Science and
 Society?

Appendix C: List of Attendees

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