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Trends in Research on the Utilization of Microgravity — Competition and Collaboration between Research in Space and Research on the Ground —

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1 Introduction

The Former Soviet Union launched Sputnik 1, the world's first space satellite, in 1957. Sputnik 2, launched in the same year, carried a female dog making possible the first animal experiment in space. This dog became the first orbital animal and made a pioneering contribution to the life sciences in space. Since then, the special characteristics of space, such as strong radiation and high vacuum, have been gradually revealed by space exploration using many satellites. In particular, scientific experiments that proactively utilize the long-term microgravity environment in satellites are being carried out.

It is more than 20 years since Japan started experiments utilizing the space environment, and a great deal of new fundamental knowledge has been obtained. The next step is the implementation of industrial applications and utilization for consumer products including using microgravity to produce products with nonconventional functions and to develop new pharmaceuticals. Using the U.S.A. and Russian modules on the International Space Station (ISS), Japanese scientists have conducted space experiments including the development of original techniques such as the creation of high-quality protein crystals and three-dimensional photonic crystals. It may even be possible in the future to continuously manufacture products in space. Furthermore, it is anticipated that the operation of the Japanese experiment module (JEM), "KIBO," on the ISS will allow the full-scale utilization of the space environment by Japan. However, it is expected to take a few more years to complete this experimental module. Until then, it is necessary to move on from the creation of high-quality protein crystals and three-dimensional photonic crystals, and make the most of all possible experimental opportunities to explore new subjects such as the creation of high-value-added materials.

This article describes the major topics of experiments using a microgravity environment, outlines the experimental opportunities, and introduces the applications that are likely to advance in the future. Experiments that utilize a microgravity environment (scientific elucidation of phenomena that depend on gravitational acceleration) must be promoted using not only ISS/KIBO but also various other means both in space and on the ground.

2 Microgravity environment and subjects of experiment

On the ground, all objects and their inner structures are governed by universal gravitation, the attraction force between the object and center of the earth. The magnitude of gravitational acceleration that is the source of gravitation is defined as "1 G," which is about 9.8 m/s^2. However, in a satellite orbiting the earth, the gravitation is reduced to the quite minute level of 1 $\mu G = 10^{-6}$ G (0.000001 G) because the gravity of the earth exerted on the satellite and the centrifugal force balance out. Also, in a freely falling capsule, objects float in the air. Such a condition is called a microgravity environment, and microgravity experiments are conducted in this special environment.

The microgravity experiments that have been conducted by various countries are mostly related to life and materials sciences. The accomplishments and lessons learned from the experiments in space are summarized in the report[1] published by the Japan Aerospace Exploration Agency (JAXA) in March 2005. This report also provides information on the researchers, and the purpose and results of experiments for each subject.

2-1 Life science experiments

According to the Sectoral Classification Table[2] of Japan Science and Technology Agency (JST), life science is classified into seven groups: (i) biological science, (ii) biochemistry, (iii) breeding and quarantine of organisms, (iv) fermentation engineering and utilization of microorganisms, (v) pharmaceutical science, (vi) medical science, and (vii) bioengineering. Microgravity experiments have been conducted for (i), (ii), (iii), and (vi).

(i) Biological science

Biological science is further divided into genetics, cytology, microbiology, botany, zoology, ecology, radiobiology, etc. In these fields, the following experiments are being conducted.

- Experiments on cell culture (differentiation of stem cells, three-dimensional cell culture, and exhaustive analysis of gravity-sensitive genes)
- Experiments on plants (completion of life cycle, experiments on gravitational tropism)
- Environmental Control and Life Support System (ECLSS) (establishment of circulatory system of living organisms, assessment of microbial safety)
- Experiments on small animals (effects on reproduction, bones, and muscles of amphibians, fish, and mice; experiments on the effects of radiation)

(ii) Biochemistry

Experiments on the growth of high-quality proteins and enzyme crystals.

(iii) Breeding of organisms

Plant seeds and animal sperm are carried on the craft for use in the space environment where microgravity and strong radiation act simultaneously to improve varieties of organisms.

(iv) Space medical science

Using astronauts as the test subjects, changes in the functioning of various parts of the human body in space and measures to be taken in preparation for the return to earth have been the subject of a wide range of experiments that have contributed to the development of space medical science.

2-2 Materials science experiments

Materials science experiments include crystal growth, fluid physics, and combustion. Special experimental apparatus has been used for each experiment. It may be possible in the future for researchers to routinely use a microgravity environment to create high-quality, sophisticated nanomaterials.

(1) Crystal growth

Studies on the formation of high-quality single crystals and elucidation of the mechanism of crystal growth are being conducted using special devices such as those for crystal growth from solutions. Effectiveness of the application of microgravity environment has been confirmed not only for the precipitation of crystals from solutions but also for the uniform mixing of several materials. At present, the space experiment on the growth of three-dimensional photonic crystals, which started in December 2005, is the focus of attention[3].

(2) Fluid physics

Although convection caused by differences in temperature and specific gravity does not occur in a microgravity environment, convection caused by the difference in surface tension due to temperature difference becomes apparent. This phenomenon is called Marangoni convection. Experiments that use Marangoni convection, the effect of which cannot be separately studied on the ground, and other experiments such as phase changes between a gas and a liquid are being performed.

(3) Combustion

Combustion conditions are different in a

Space medical science

(1) Developments in research on the effects of the space environment on the human body

When the ISS is completed, Japanese astronauts will stay there for a lengthy period of about six months. In addition, opportunities for commercial space trips are increasing and it will not be long before ordinary people can travel into space. To carry out these activities safely, the effects of space on the human body are being studied.

- (i) Bones: Bone mass decreases after a long period of space flight. Ways of avoiding this phenomenon include exercise and drugs to prevent osteoporosis.
- (ii) Muscle: Since astronauts do not carry heavy objects in space and can make movements without the restriction of body weight, it is thought that muscle strength decreases after a long period of space flight.
- (iii) Circulatory system: In a space flight of extended duration, cardiorespiratory function is depressed. Red blood cell mass decreases, blood and lymph fluid shift to the upper half of the body and excretion of urine is promoted resulting in decrease of body fluid by about 2 litters. For this reason, sports drinks or similar fluids are taken just before returning to the ground to supplement body fluid.
- (iv) Sensory organs: Some people suffer from space sickness even during space flights of short duration. Space sickness causes stomach discomfort, vomiting, and dizziness. While there are various theories for the mechanism of such symptoms, the generally accepted theory is that the eyes and ears give different information on the sense of the vertical, thus confusing the senses.
- (v) Mental health: A prolonged stay in the closed environment of a spacecraft causes astronauts to suffer from the same kind of mental stress as experienced by Antarctic exploration team members and submarine crews. To cope with such a situation, astronauts are selected who can endure long periods in a closed environment and are trained on the ground to enhance their stress tolerance. Furthermore, while on the spacecraft, they are supported by communication from earth.

(2) Health management in space

If an astronaut suddenly gets sick on the spacecraft, other astronauts on the craft do not always have sufficient medical knowledge and onboard medical instruments are not always adequate. The environment is very poor for telemedicine services due to the limited capacity for transmission of communications between the spacecraft and the ground. Therefore, health management of astronauts is an important issue for the prevention and early detection of disease.

Furthermore, nutrition and metabolism are taken into account in the development of easy-to-eat space foods to maintain the health of astronauts. On the July 2005 space shuttle mission, aggregated instant noodles were adopted as the space food. In the Chinese manned space flight in October 2005, Chinese foods using costly foodstuffs were added to the space foods.

(3) Training in preparation for the return from space

On the former Soviet Union space station, astronauts performed indoor exercises on the spacecraft to maintain their physical capability in preparation for the return to earth. If space flight is continued for a long period without performing such exercises, astronauts may not be able to stand on their own, break bones by careless movements, or damage muscles on their return to earth.

microgravity environment from those observed on the ground. For example, it is known that a flame has a spherical shape in a microgravity environment. Experiments are being carried out in which flame propagation is observed while part of the fuel is nebulized.

(4) Measurements of thermophysical properties, etc.

It is possible to conduct high-temperature melts without using containers in a microgravity environment, and thermal conductivities of semiconductors and molten metals and diffusion constants have been measured. These experiments have not only provided the data on the physical properties required for crystal growth, but have also contributed to the creation of a new technology field called “supercooled high-temperature melt.” Crystal growth that prevents contamination from containers is also drawing attention.

3 Methods for creating a microgravity environment

Methods for creating a microgravity environment include: drop test facilities, aircraft, small rockets, recoverable satellites, space shuttles, and the International Space Station. Figure 1 shows the levels and time range of microgravity for these methods.

3-1 Drop test facility

A drop test facility is where a test device is placed in a falling capsule, which falls freely in a tower or vertical mineshaft. A microgravity environment is created in the capsule for a very short time until the capsule reaches the brake at the bottom. Since the testing time is very short, this method cannot be universally applied. However, the drop test provides the safest, simplest, and least expensive method for obtaining a microgravity environment. The level of microgravity is relatively high and testing is reproducible. Whereas major drop test facilities in the U.S.A. and Europe are owned by public institutions, such facilities in Japan are operated by private companies.

The drop test facility in Toki City, Gifu Prefecture, is owned by the Micro-Gravity Laboratory of Japan (MGLAB)[4]. The testing facility is in one of the vertical mineshafts of the Tono Mine owned by the Japan Atomic Energy Agency. A capsule is dropped freely in the vacuum tube provided in the 150 m mineshaft. The upper 100 m is for the free falling area and the lower 50 m is the braking area, which uses rubber. The vacuum in the tube is maintained at about 4 Pa to prevent deterioration of the microgravity level due to air resistance. A microgravity level of about 10^{-5} G is reached for 4.5 seconds. To use the facility, experimental modules must be designed to fit in the cylindrical space of the capsule of 720 mm D × 885 mm

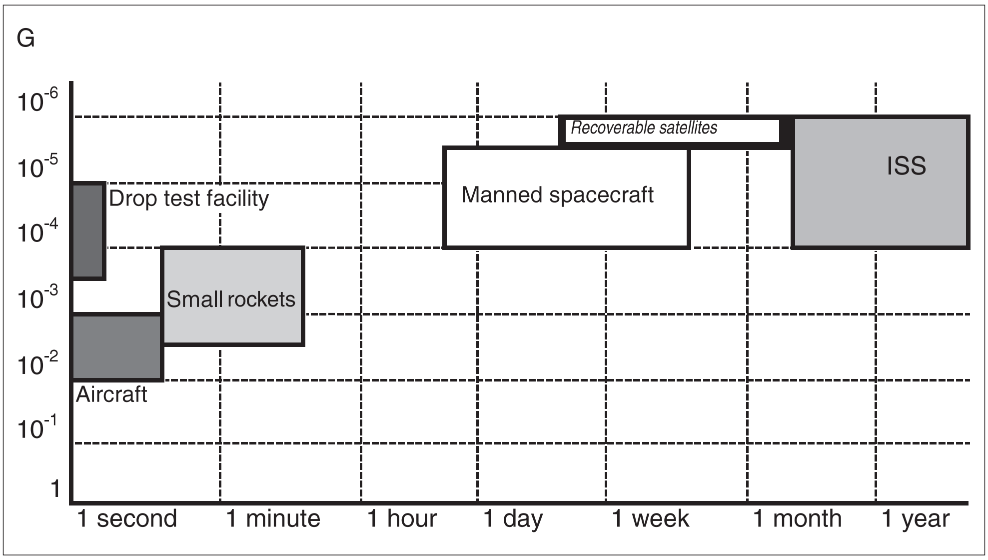


Figure 1 : Microgravity level and period of microgravity by experimental method

H. Currently, 300 to 400 drop experiments are conducted annually. Since the start of operation in 1995, the total number of drop experiments has exceeded 6,000. Most of the experiments are for fundamental studies, which are performed mainly by national and public universities and public institutions aided by the Proposals for the ground-based Facilities program of JAXA. Experiments include fluid experiments, combustion experiments, materials testing, life science experiments as well as technical verification tests of newly developed apparatus for space use. The demonstration of the sampling system using metal projectiles shot by the asteroid exploration spacecraft “Hayabusa” was made using this MGLAB.

In Europe, the Center of Applied Space Technology and Microgravity (ZARM) at the University of Bremen in Germany has a 146 m drop tower and carries out all the drop experiments for European Space Agency (ESA) and European countries. In the U.S.A., the National Aeronautics and Space Administration (NASA) has a 145 m drop tower in the Glenn Research Center (GRC), and in China, the National Microgravity Laboratory of Chinese Academy of Sciences (NMLC) in Zhongguancun, Beijing, has a 110 m drop tower.

3-2 Parabolic flight by aircraft

Microgravity experiments using aircraft are being performed by public institutions and private companies in the U.S.A., Europe, and Japan. It is significant that manned experiments on the ground can only be conducted by this method. In Japan, Diamond Air Service (DAS)[5], located in Toyoyama-cho, Aichi Prefecture, provides a regular service using aircraft such as the Gulfstream-II (Figure 2) and MU-300 in which a parabolic flight path creates microgravity conditions for about 20 seconds. For example, DAS is planning to perform simple experimental flights in April 2006. In these flights, microgravity experiments can be carried out for 100 seconds (20 seconds × 5 times / 1 flight) with an approximate cost of ¥300,000 to ¥400,000 per person. The level of microgravity of about 10^{-2} G is inferior to that of a drop test facility. On the one hand, it is possible to carry relatively large experiment modules because the fuselage is large, however, the person on board is exposed to the physical strain caused by the acceleration of gravity reaching between 1.5 and 2 G before and after the microgravity period.

Figure 2 : Gulfstream-II of DAS (total length: about 24 m)

In the U.S.A., NASA owns a DC-9 in order to provide a service for scientists from various countries wanting to conduct experiments using the space shuttle. A private company, Zero-G, carries out business including a microgravity experience for the general public.

In Europe, the Centre National d’Etudes Spatiales (CNES) and other institutions have carried out microgravity experiments using the Caravelle aircraft since 1988 and the Airbus 0G (A300-0G) since 1997.

3-3 Small rockets

Ballistic flight of a small rocket has been frequently used in the past in Japan to achieve a microgravity environment, and it may also be used in the future using new rockets. When using a small rocket to achieve a microgravity environment, it is necessary to take into account the acceleration at the launching, the deceleration on recovery, as well as the impact. Although the microgravity environment lasts only several minutes, various types of microgravity experiments, mainly in materials science, can be performed. In Europe, Germany and Sweden, microgravity experiments are carried out using small rockets independently.

In Japan, the former National Space Development Agency of Japan (present JAXA) performed seven microgravity experiments using TR-IA rockets between 1991 and 1998. After launching, the rocket entered ballistic flight at an altitude of 100 km where the air resistance drastically decreases. At an altitude of about 270 km, a fairly good microgravity environment of 10^{-4} G was obtained for about six minutes until the rocket again reached the altitude of 100 km. The experiments were mainly in materials science including (i) crystal growth from solution, (ii) colloidal crystals, (iii) fluid physics, (iv) boiling tests, (v) creation of semiconductor materials, (vi) diffusion tests, and (vii) combustion tests.

Currently in Japan, the Hokkaido Aerospace Science and Technology Incubation Center (HASTIC), a specified nonprofit organization (NPO), is improving the performance of the CAMUI hybrid rocket, which uses solid fuel and liquid oxidizing agent as the propellant so that microgravity experiments can be provided[6]. The aim is to obtain a microgravity environment for about three minutes at an altitude of 110 km. Combustion tests are being repeated at the HASTIC Akabira Center located in Akabira City, Hokkaido.

In Europe, Germany has conducted microgravity experiments using the Texus rocket since 1977 and the Maxus rocket since 1991. Since 1987, Sweden has performed 10 microgravity experiments for the European Space Agency using the MASER rocket, and intends to continue the tests.

3-4 Recoverable satellites

The above-mentioned experiments conducted near the ground can provide a microgravity environment from several seconds to several minutes. If unmanned experiments are performed in a satellite and the satellite returns to the earth without any problems, microgravity environments can be provided for dramatically longer periods. Depending on the size of the satellite and the existence of solar battery panels, experiments can be conducted throughout the duration of the whole orbital flight of several days, several months, or even more than one year. It is also possible to conduct multiple experiments simultaneously. Microgravity experiments using such recoverable satellites are being performed by Japan, China, Europe, and Russia and it is expected that these satellites will also be utilized in the future. Japan has launched recoverable satellites such as the Space Flyer Unit (SFU) and EXPRESS for space experiments and space observation, and the Unmanned Space Experiment Recovery System (USERS) is the next generation system. Figure 3 shows the appearance of USERS and the concept of the capsule separation.

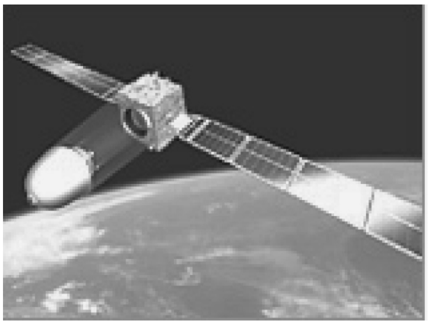


Figure 3 : USERS satellite

The USERS is being developed by the Institute for Unmanned Space Experiment Free Flyer (USEF) as a project started in 1995, sponsored by the Ministry of Economy, Trade and Industry and the New Energy and Industrial Technology Development Organization (NEDO). The purpose of the project is to develop a system that returns to the ground by itself after performing experiments in space for a long period of time. The first system was launched into orbit by H-IIA F3 on September 10, 2002, and performed an experiment on the production of superconducting material under good microgravity conditions for about six months. It returned to the earth by controlling and adjusting its reentry path and landed in the water at the planned point, offshore east of Ogasawara on May 30, 2003, bringing back the results of the space experiments without any problems. This success demonstrated that the heat protection technology required for atmospheric reentry and the trajectory control technology necessary for returning to a planned point in the sea have been established, confirming that the unmanned experimental system is suitable for practical use. The Users Guide[7] for this system has now been published to promote the utilization of USERS. However, no launch is scheduled at present. It is difficult to launch the second flight based on the private sector projects unless the government becomes the anchor tenant and underwrites a definite number of experiments.

3-5 Manned spacecraft (space shuttle, etc.)

The U.S.A. space shuttle had been launched a total of 114 times by the end of 2005. The major missions of space shuttles are to put satellites into orbit, perform space experiments, and construct the ISS. Table 1 shows the breakdown of the missions.

Of the 114 shuttle flights, missions primarily for space experiments include: USML and USMP of the U.S.A. for microgravity experiments; D-1 and D-2 of Germany; International Microgravity Laboratories IML-1, IML-2, and Neurolab; and the First Material Processing Test (FMPT, "FUWATTO '92") of Japan. In the ISS construction missions, which are being sent almost continuously, small-scale experiments were recently performed by students utilizing surplus space and weight.

In the FMPT, which was the first thorough Japanese space experiment, 34 of 43 experiments were from Japan, 2 were collaborations between Japan and the U.S.A., and 7 were from the U.S.A. Japan prepared 21 kinds of experimental apparatus, and astronaut Mamoru Mori managed the experiments as a payload specialist (PS). In the space shuttle, a microgravity environment is continuously maintained for a maximum period of two weeks allowing a range of simultaneous experiments to be managed by the space shuttle crew. However, the U.S.A. is caught between the construction of the International Space Station that will provide long-term space experiments, and the retirement of the space shuttle in only five years resulting in decreased flight opportunities. There is little room for setting up a mission aimed mainly at space experiments using the space shuttle.

In China, a rack for experiments was installed neighbor to the astronaut's seat in the Chinese independent spacecraft "Shenzhou-5" (2003) and "Shenzhou-6" (2005) to carry out microgravity experiments.

Table 1 : Breakdown of major space shuttle missions

Mission		Number
Primarily ejecting, recovery, or repair of satellites		45
Primarily space experiments	Primarily life science	15
	Primarily materials science	7
	Primarily earth observation and astronomic observation	8
Primarily transportation of parts and supply materials for the ISS (including Shuttle-Mir Mission)		27
Others (test flight, unknown mission, etc.)		10
Failure (accident)		2

3-6 International Space Station (ISS)

(1) Recent situation of the ISS

The space station is a facility for continuous manned space flight over an extended period of time and functions as a routine space laboratory or space factory. However, on previous space stations, such as Mir of the former Soviet Union and Skylab of the U.S.A., the majority of missions were on medical research into the effects of long-term space travel, astronautic observations, earth observations, and reconnaissance, and the proportion of microgravity experiments was relatively small.

The International Space Station Program was advocated by President Reagan of the U.S.A. in 1984, and started in 1985 with the participation of Europe, Canada, and Japan. Initially, construction was scheduled to start in the early 1990s and be completed in the 20th century. However, the construction work has been slowed by space shuttle accidents etc., and completion is expected to be delayed by more than 10 years.

In 1993, Russia joined the ISS Program and "Zarya" (=Dawn, built by Russia and owned by U.S.A.), a control module that has the same function as the Russian space station "Mir," was launched in November 1998. After that, the Russian service module, "Zvezda" (=Star), the American experiment module, "Destiny," and the Canadian robot arm were attached in July 2000, February 2001, and April 2001, respectively. Now the initial ISS system has been completed that enables two astronauts to stay aboard all the time. Figure 4 shows the appearance of the ISS as of 2005.

Figure 4 : Appearance of the ISS as of 2005

At present, two astronauts, one from the U.S.A. and one from Russia, are always on the ISS and data on space medicine related to long stays in space, which the U.S.A. has not undertaken in the past, is being recorded and space experiments by participant countries are being conducted.

In the future, the European experiment module, “Columbus,” and a Japanese experiment module, “KIBO,” are scheduled to be attached; in the Heads of Agency (HOA) meeting held on March 2, 2006, it was agreed to launch the space shuttle 18 times (including two reserves) by 2010. “KIBO” is scheduled to be sent three times in the eighth, ninth, and twelfth launch. According to the agreement of the HOA in March 2006, it is possible that “KIBO” will be launched in FY2007 although a definite time has not been decided yet. The key to the success of this project is whether or not the resurgent second “KIBO” is successfully launched in July 2006. Space experiments will move into full swing when all the experimental modules of the U.S.A., Europe, Japan, and Russia start operation with astronauts, including Japanese astronauts, present on the station all the time.

(2) Access to the ISS

The transportation of crews and supply materials to the ISS are solely dealt with by the Russian spacecraft Soyuz (accommodating three astronauts) and the Progress resupply vehicle.

Russia sent the spacecraft Soyuz to the space station Mir in April 2000 for the last transfer of crew, and since October of the same year, Soyuz has been launched solely to transport the replacement crews to the ISS every April and October. Since it takes about eight days to take over the job, opportunities are offered to civilian travelers to make use of the spare seat in the Soyuz spacecraft and experience short-term space travel to the ISS. It is possible for a Japanese traveler to ride on the craft in October 2006.

With regard to materials supply, Progress has been launched 25 times in the period of nearly six years from February 2000 to December 2005, and the reliable Russian transportation capability is widely appreciated by the international partners of ISS.

4 Trends in research on the application of microgravity - High-quality protein crystals growth

4-1 Overview of research on protein

To maintain life, living beings have vital functions such as food digestion, energy supply, nervous transmission, and the capacity for immune response. It is said that these functions rely upon more than 20,000 different proteins. The kinds and functions of proteins are determined by the arrangement of amino acids and the steric structure of the protein. Establishing databases for protein structures and functions will allow both qualitative and quantitative understanding of complex vital phenomena. Furthermore, understanding the structures and functions of target proteins permits rational and effective design of therapeutic medicines. Attempts to apply drug discovery and personalized medicine to innovative technologies for prevention, diagnosis, and treatment of diseases and the development of new foods through the analyses of the structure and functions of proteins are being made by universities, research institutes, and private companies.

To conduct research on protein structures, it is necessary to prepare samples for analysis by separating the target proteins. Although samples prepared on the ground have been mainly used in research on protein engineering, it is quite difficult to obtain high-quality samples. In one case, a researcher could obtain only one crystal in the first five years of research.

It was planned to prepare crystals utilizing microgravity in space in the early days of space experiments and the technology has been available for more than 20 years. Among the microgravity experiments that have been performed, high-quality protein crystals growth is one of the best developed technologies so far. In the spacecraft, where the gravity of the earth and the centrifugal force balance out, the gravity is around 10^{-6} G so that the convection caused by the difference in density of the solvent does not occur in the neighborhood of the protein crystal, providing a uniform growth rate of the crystal and reducing the crystal defects. At the same time, the number of nucleations of crystals is suppressed resulting in a smaller number of larger-sized crystals.

The Japan Aerospace Exploration Agency (JAXA) has performed a series of space experiments, including several experiments that utilized the shuttle and those of the "High-quality Protein Crystallization Project" conducted on the ISS, in order to obtain protein crystal samples, and reached a stage in which the creation of high-quality protein crystals became possible in space. The results are published in "Progress and Problems in High-Quality Protein Crystal Growth Technology Using Microgravity Environment"[8].

In Europe and the U.S.A., however, in addition to the skepticism about the sense of obtaining high-quality crystals from space experiments, experimental results were lost due to an in-flight disintegration of the space shuttle, and the space experiments on the preparation of protein crystals have made little progress.

4-2 Structural analysis of proteins

X-ray diffraction is often used for the determination of protein structure, and requires that the protein must first be crystallized. Furthermore, it is desirable to use larger crystals. The RIKEN Harima Institute located at the Japan Synchrotron Radiation Research Institute (JASRI) in Sayo-cho, Hyogo Prefecture, has established an experimental automated system that enables the acquisition of several tens of high-precision structural images daily from small crystals using the large-scale synchrotron radiation facility JASRI SPring-8.

The RIKEN Yokohama Institute has developed a method for structural analysis of relatively small protein samples (with a molecular weight of 60,000 or less) prepared on the ground without crystallization, using a Nuclear Magnetic Resonance (NMR) apparatus.

With regard to magnetized proteins, the National Institute of Advanced Industrial Science and Technology (AIST) and National Institute for Materials Science (NIMS) are attempting to prepare high-quality crystals in a pseudo-microgravity environment created by magnetic levitation using superconducting magnets.

In the future, it may be possible to conduct x-ray spectroscopic analysis of proteins of large molecular weight using an X-ray Free-Electron Laser (X-FEL) that provides a peak radiance 100 million times stronger than that of the SPring-8. Such a device is expected to be available in 2010 at the earliest. At present, it is difficult to predict whether or not the preparation of protein crystals in space will still be required when the X-FEL is operational. It will be appropriate to determine the optimum methodology from a comparison of ground-based and space-based techniques.

4-3 Four issues concerning protein crystal growth in the space environment

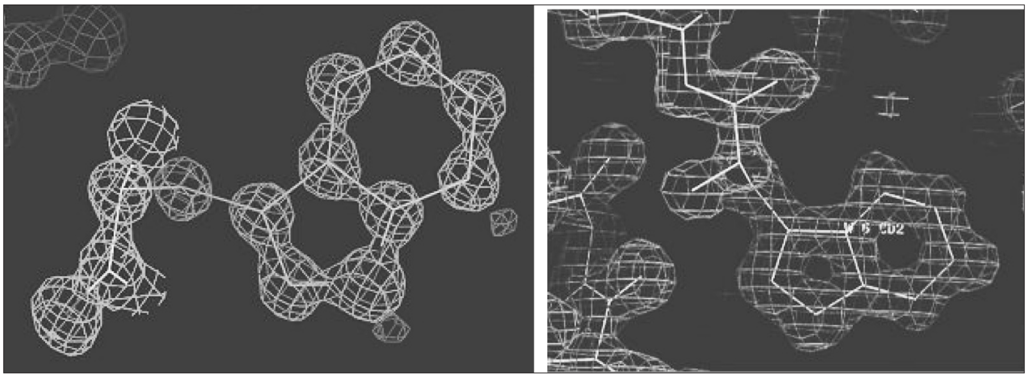
Issues to be resolved for achieving protein crystal growth in space are: (i) achieving a higher quality that cannot be achieved on the ground, (ii) cost reduction, (iii) reduction of turnaround time (time required for the results to be returned to the researcher), (iv) improvement of support systems. The present status and future targets for resolving these issues are as follows:

(1) Method for the quality evaluation of protein crystals

The quality of protein crystals is expressed as the resolution of the crystal structure. The resolution is expressed in angstroms (Å, 0.1 nanometer); the smaller the value, the higher the resolution and the higher the quality of the crystal. For example, when the resolution is about 2 Å, the structure of the side chain can be accurately determined, and when it is 1 Å, even a hydrogen atom can be identified. To compare the quality of a crystal prepared in space with one prepared on the ground, a check test was performed using alpha amylase and lysozyme. Using the 12B2 beam line of SPring-8, the X-ray diffraction of the alpha amylase crystallized in space had a resolution of 0.89 Å. This value represents the highest resolution that had ever been obtained. However, the resolution of a crystal of alpha amylase prepared on the ground was 1.12 Å. Figure 5 shows the electron density maps of these crystals. For the lysozyme crystal, the resolution of a crystal prepared in space was

Preparation of single crystals of diamagnetic proteins on the ground

Depending on the type of protein, crystallization may take from several days to several weeks. However, crystals can be formed in reduced gravity, but not necessarily microgravity, environments. For example, diamagnetic proteins such as fructose bisphosphatase and lysozyme can be crystallized under the low gravity (about 0.7 G) obtainable with a strong magnetic field. In collaborative research between the National Institute for Materials Science (NIMS) and Hiroshima University, high-quality crystals of diamagnetic protein were successfully formed in a pseudo-microgravity environment (about 10-3 G) created by a strong magnetic field of about 10 tesla using superconducting magnets. NASA has succeeded in creating a pseudo-microgravity environment on the ground using laboratory equipment of the rotating vessel type. These are examples of low gravity and pseudo-microgravity environments that can be achieved and maintained for long periods relatively easily on the ground.



Left: prepared in space, Right: prepared on the ground. See the color photo on the front cover. (Obtained on SPring-8 BL-12B2)

Figure 5 : Electron density maps of alpha amylase crystals

0.88 Å while that of a crystal prepared on the ground was 1.08 Å.

In some cases, the resolution of about 3 Å for a crystal prepared on the ground can be improved to about 1.5 Å with ingenuity and trial and error. However, it is quite difficult to obtain a crystal with a resolution better than 1 Å (<1 Å). The European researcher who succeeded in obtaining an image with a resolution in the order of 0.6 Å, which is thought to be the best in the world, has a very high expectation for the quality of protein crystals prepared in space. He once commented that he would like to take every opportunity available to prepare crystals in the space environment, e.g., using Japanese apparatus if possible, paying a fee, regardless of the cost, time, and limitation of launch opportunities. It is also necessary to assess what kinds of protein samples should be sent into space and the timing necessary to obtain effective results taking into account cost and restrictions on availability.

(2) Reduction in the cost of growing protein crystals

It was confirmed by space experiments conducted on the ISS from 2003 to 2005 that high-quality protein crystals can be created in a long-term microgravity environment. The noteworthy technologies that have been developed in the above-mentioned experiments are as follows.

(i) Temperature control: It is important to maintain the ambient temperature of the apparatus at 20°C. In the initial experiments, some crystals that had been created after considerable effort melted due to an increase in temperature in the spacecraft. To keep the temperature at a constant 20°C, an alkane with a melting point of 21°C

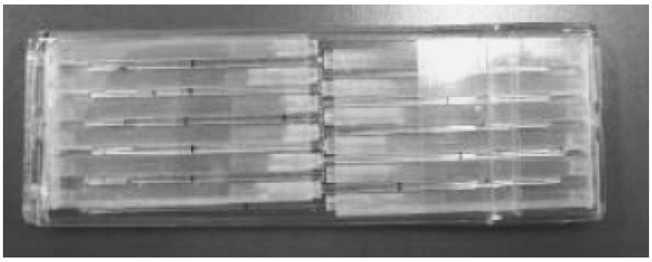


Figure 6 : Appearance of the JAXA Crystallization Box (JCB)

Table 2 : Major previous experiments related to proteins

Month and year	Spacecraft	Country	Contents and number of experiments
1983 ~ 2002	Space shuttle	U.S.A.	Insulin separation, etc., 54 cases
1983 ~ 2002	Space shuttle	Europe	13 cases
1992.1	Space shuttle	International	IML-1
1992.9	Space shuttle	Japan	FMPT (enzymes, etc.)
1993~ 2000	Space shuttle	U.S.A., etc.	SPACEHAB (private sector)
2003.1 Failure to return	Space shuttle (STS-107)	Japan	Enzymes, pathogenic proteins, animal lectins, etc., 10 cases
2003.2~ 2006.4	ISS Destiny/Zvezda	Japan	High-quality protein crystal growth project (conducted 6 times)

(heptadecane) was placed with the sample in a vacuum insulator, and the internal temperature of the Soyuz carrying the crystals back to the earth was decreased. These methods established a fail-safe technology for preparing high-quality protein crystals at a constant temperature and bringing them safely back to the earth.

(ii) Improving the apparatus for preparing protein crystals: The apparatus for the preparation of protein crystals, the “GCB” (Granada Crystallization Box) that was jointly developed by the European Space Agency (ESA) and the University of Granada in Spain, had defects such as solution leakage. JAXA eliminated these defects by using a gel tube (GT) method to guarantee crystal growth. The improved apparatus is called the GCB-GT.

Furthermore, JAXA developed apparatus for preparing protein crystals called the “JCB” (JAXA Crystallization Box) that allows about a 10 times higher packaging density than the GCB. Figure 6 shows the appearance of the JCB. While the GCB-GT uses six glass capillaries for only one kind of protein, JCB is equipped with 12 glass capillaries allowing a maximum of 12 different kinds of proteins or 12 different testing conditions. This improvement contributes to a reduction in the cost of crystal growth.

On December 22, 2005, Japanese protein preparation experimental apparatus was launched to the ISS in its 400km orbit on the Russian resupply craft, Progress, and experiments were performed for three month on the Russian service module “Zvezda” until the apparatus was brought back on the Soyuz spacecraft on April 9, 2006. This experiment was the last stage of the development by Japan of high-quality protein crystal preparation technology. In this experiment, 42 kinds of proteins were launched in a set of apparatus consisting of 11 JCBs and 34 GCB-GTs. In the future, it is hoped to increase the opportunities for low-cost experiments by adopting JCBs so that private companies and foreign researchers can easily utilize the space environment for experiments.

(3) Reduction of turnaround time for protein crystal preparation

Some of the experiments that have been performed by various countries relating to proteins are shown in Table 2.

In the past, the U.S.A. and Europe took a lead in space experiments related to proteins and Japan tried to catch up.

Of the experiments shown in Table 2, the separation of insulin differs from crystal growth and aims to separate high purity insulin for production. It is unlikely that insulin will be produced in space because of the quality and cost. However, crystal growth of proteins has potential because it is difficult to prepare them on the ground. An obstacle to the impetus for these experiments is the length of time it takes for the finished crystals to be returned to the researcher.

According to the staff in charge of the space shuttle payload at the NASA Johnson Space Center, although it took 44 months in the initial stage of the protein crystal growth experiments from shipment of samples to the space shuttle to receipt of samples by the researcher, the time has now been reduced to 14 months. For experiments that use the Russian module, the total time required for sample shipment, the space flight period, and return to the researcher has been reduced to about 7 months. However, many researchers are very keen for an even shorter turnaround time for the preparation of crystals in space.

In order to shorten the turnaround time, it is necessary to increase the frequency of access to the ISS and select the timing of launches so that the samples are recovered more frequently. After the space shuttle is retired and to avoid delays, it will become necessary for international cooperation to establish appropriate transportation schedules using the Japanese H-II transfer vehicle (HTV), the European automated transfer vehicle (ATV), and the new U.S.A. and Russian transportation systems. It is desirable to reduce the total time required for transportation and experiments to three to four months.

(4) Improvement of support systems

In Japan's "High-quality Protein Crystallization Project," the Japan Space Forum (JSF) has been commissioned by JAXA to support researchers by preparing apparatus, and the mounting and recovery of samples.

In space experiments, as in any other research activity, the development of experimental equipment is the means by which data is obtained and functions confirmed rather than the research itself. However, since data cannot be obtained without the development of experimental methods, part of the funding and human resources are naturally allocated to the development of experimental equipment and implementation of experiments. Not all the scientists and researchers who are going to perform experiments in life science and materials science are good at developing experimental apparatus and implementing experiments in the microgravity environment; and it is necessary to improve the comprehensive support system for such scientist and researchers. Therefore, from a long-term perspective, it is necessary for space-related organizations like JAXA, which play such a role, to secure research support personnel and accumulate know-how about testing and the development of experimental equipment.

4-4 Plan for commercial protein crystal growth

It is fairly clear that high-quality protein crystals that cannot be created on the ground can be created in the microgravity environment of space. Since the difficulty of preparation of high-quality samples is the bottleneck in protein research, the microgravity environment in space is likely to be utilized frequently as a means of removing this bottleneck.

Taking this into account, JAXA, which has developed crystal growth apparatus for proteins such as JCB, is planning to transfer these technologies to private-sector institutions from 2006. When this plan is achieved, it is expected that the growth of high-quality protein crystals will be carried out continuously on the ISS.

According to the previous plan, "KIBO" was supposed to be almost completed in 2006, making it possible to start full-scale experiments. However, it will take two or three more years to complete "KIBO" due to the delay in the flight schedule caused by the space shuttle accident. In this time, demonstration in space must be brought forward as far as possible by finding any available opportunities to use the microgravity environment. It is expected that crystal growth will be performed on a large scale using Japan's dedicated experimental rack after "KIBO" is completed around 2007.

In the U.S.A., Dr. DeLucas of the University of Alabama at Birmingham (UAB), who traveled on board the space shuttle STS-50 as a payload specialist, conducted protein crystal growth experiments using the U.S. module, "Destiny." Since the space shuttle is not operating regularly, it is proving difficult to recover these experimental samples.

The important points in the promotion of commercial growth of protein crystals are: (i) high quality, (ii) low cost, (iii) shorter turnaround time (or timely provision of samples to researchers), and (iv) support systems. By the time the ISS is in full use, all of these four factors must be improved.

5 Opportunities for manufacture of products in the microgravity environment

5-1 Utilization of existing ISS modules

Because the ISS participating countries have agreed to allow private visitors to stay on the orbital space station, it has become possible for private citizens to travel on board the Soyuz spacecraft and stay on the ISS for about a week. There is a plan for a Japanese person, who is currently on a training course, to travel on the spacecraft in October 2006. Assuming that this person does travel on board the spacecraft as part of the Space Open Lab[9], JAXA is inviting applications for scientific experiments, applied experiments, educational experiments, and cultural experiments to be conducted by the passenger on the spacecraft. Costs for the experimental equipment and loading of the samples are to be borne by the applicants.

5-2 Microgravity experiments using Japanese experiment module "KIBO"

The protein crystal growth experiments, currently performed on a limited scale in the Russian module etc., will be expanded when "KIBO" is completed. It will be possible to prepare experimental samples as well as carry out pilot production of raw materials for pharmaceuticals.

For Japan to fully utilize the space environment on the ISS, the parts of "KIBO," which are waiting to be launched, must be launched and assembled in orbit so that the Japanese space laboratory can be constructed.

It is planned to mount the following experimental equipment on "KIBO" in the initial stage[10].

(i) Experiments in life science: protein crystal growth apparatus, cell culture equipment, a clean bench, and a refrigerator,

(ii) Experiments in materials science: temperature gradient furnace, experimental equipment for fluid physics, and equipment for observing the crystal growth solution.

These instruments are integrated into the international standard payload rack (ISPR), and will be launched and stored in the pressurized storage room before the main unit is launched. After the main unit of "KIBO" is attached to the station, these instruments will be transferred to the pressurized section so that experiments can be performed. After the process is started, it will also be possible to exchange racks as required. The development of experimental equipment and determination of research topics are inseparable so both must be considered together. Since the number of ISPRs that can be loaded is limited, it must be noted that experiments being conducted at any particular time will not necessarily continue forever.

5-3 Opportunities other than the ISS

Future opportunities for the utilization of the microgravity environment are not limited to the ISS.

(i) USERS satellites can be used for long-term microgravity experiments when human support is not required. However, the flexibility of launch and recovery schedules for USERS satellites are limited by various setting-up difficulties.

(ii) When human support is required during the experiment, experiments can be performed rapidly for short durations using an aircraft as described in Section 3-2.

(iii) When developing various types of experimental equipment to be carried by the ISS, recoverable satellites, or aircraft, the drop test described in Section 3-1 provides the simplest microgravity environment for the confirmation of structures and performance or rough estimation of various parameters. Drop tests will remain an effective method for carrying out microgravity experiments in the future.

(iv) When the enhanced hybrid rocket, as described in Section 3-3, is completed, a microgravity environment that lasts longer than that possible in aircraft will become available. In Hokkaido, the Hokkaido University and HASTIC are conducting combustion tests at the Akabira Center to develop a hybrid rocket.

(v) When the experimental process, such as the growth of single crystals of silicone, is completed in a microgravity environment of short duration, a mass production system can be established by installing a drop tower in the production line. In the Microgravity Utilization Laboratory of Kyosemi Corporation located in Eniwa City, Hokkaido, a new drop tube has been installed to establish a mass production system for high-value-added spherical solar cells[11].

In research on such subjects as high-quality protein crystal growth, where full-scale space experiments are carried out on the ISS, drop test facilities and aircraft were frequently used for the confirmation of functions in the initial stages when the experimental equipment was developed. In view of the fact that tremendous amounts of research work are required in preparation for space experiments, it is desirable that microgravity experiments are more easily performed on a wider range of subjects.

6 To enhance the status of Japan as a science and technology oriented nation through research on the application of microgravity

In research on microgravity, there is competition or trade-off in quality and cost between space experiments and alternative methods on the ground. This means that space is not the only available means of carrying out microgravity experiments. Sometimes, achievements in space may be enhanced by combination with the results obtained by experiments on the ground. In order to prepare the best possible samples for protein research, it is important to retain competition between experiments in space and on the ground to raise the level of research through creative ingenuity and hard work.

By the time “KIBO” is completed, ending the initial training and beginning the new stage of research in space experimental technology, it will be necessary for Japan to strengthen its competence in space experiments with a long-term perspective, not only for proteins but also for other fields, taking into consideration proposals for new experimental topics, research and development of instruments required for the implementation of experiments, and the application of results.

The desirable focus of various sectors are summarized below.

(1) Promotion of research on microgravity leading up to the full-scale operation of “KIBO”

Because the resumption and full-scale use of the space shuttle is foreseeable and the long-awaited “KIBO” may be launched in FY2007, utilization of the microgravity environment in space that has been at a standstill is approaching a new stage. The types of experiments to be performed on “KIBO” must be carefully selected and refined by repeated preliminary experiments on the ground with regard to the development of experimental equipment and the application of results. Currently, universities and private companies are using drop test facilities and aircraft to improve equipment and conduct experiments to obtain new information. Researchers are keenly committed to the utilization of an experimental environment that cannot normally be obtained on the ground. However, in Japan at the moment, facilities are not fully utilized due to the national budget system and insufficient public subsidies. With the recognition that research on microgravity is not just for the utilization of the space station but also to carry out valuable experiments on the acceleration of gravity, every existing opportunity for experiments must be utilized to promote research on microgravity.

(2) Promotion of industrial applications of microgravity

As a result of space experiments that have been conducted for over 20 years, materials and products that cannot be obtained under normal gravity on the ground are now being produced. The current period is a period of preparation for the full-fledged utilization of the space environment by Japan. It is expected that the current stage will progress in a step-by-step fashion to the next stage where both industrial and consumer applications will begin with microgravity applied in a wider range of uses.

Experiments specifically attracting interest are:

(i) High-quality protein and three-dimensional photonic crystal growth on the ISS.
(ii) Long-term space experiments using USERS satellites of USEF.
(iii) Application of drop test facilities, aircraft, and small-scale rockets on the ground.

Proactive participation of public institutions and private companies in the preparation of materials and developmental experiments must be promoted taking into consideration the required level of microgravity, cost, accessibility to facilities, and availability of public support.

As a matter of course, in order to achieve full-scale industrial and consumer applications, progress in technical development from an overall perspective of utilizing the space environment is required, including the operation of "KIBO" and HTV supply craft for the space station. With regard to basic studies for creating new seeds for industrial applications, there are research areas in which not only space experiments but also experiments on the ground are effective. It is necessary to continue to provide opportunities of microgravity experiments for such areas.

(3) Other possible benefits

Since Japan intends to become a science and technology oriented nation, it is important to nurture human resources in science and technology, but it is difficult to obtain new knowledge without developing new experimental methods. The experience of the step-by-step process of developing an idea, the performance of experiments, through to research application utilizing the special environment of microgravity (including experience in a parabolic flight) would be a valuable method for training people in science and technology. It would also assist young researchers develop the basic technical capabilities necessary for a range of future applications. It is recommended that a strategy for training young people is established by fully utilizing opportunities for microgravity experiments on the ground and unmanned satellites.

In the face of serious concerns about the rapidly aging population and a very low birthrate, it is timely to consider how people can feel happier in their lives. In a company that began the production of space application equipment, jobs related to space applications were given to employees in addition to their conventional jobs. Following success in the new jobs related to the space applications, the morale of employees was greatly strengthened. The slogan, "a science and technology oriented nation," achieves nothing by itself. It is the spontaneous activities of individuals and private companies that create values.

Prior to the routine operation of full-scale space experiments, creative ingenuity in research and development, including activities in the preparatory stages, will lead to the awakening of public pride in Japan's science and technology.

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Abbreviations

- *DAS* Diamond Air Service
- *ECLSS* Environmental Control and Life Support System
- *FMPT* First Material Processing Test
- *GCB-GT* Granada Crystallization Box-Gel Tube Method (improved GCB)
- *HASTIC* Hokkaido Aerospace Science and Technology Incubation Center (nonprofit organization)
- *HOA* Heads of Agency
- *ISPR* International Standard Payload Rack
- *ISS* International Space Station
- *JASRI* Japan Synchrotron Radiation Research Institute
- *JCB* JAXA Crystallization Box
- *JEM* Japanese Experiment Module
- *JSF* Japan Space Forum
- *MGLAB* Micro-Gravity Laboratory of Japan
- *NMLC* National Microgravity Laboratory, Chinese Academy of Science
- *S* Starboard
- *UAB* University of Alabama at Birmingham
- *USEF* Institute for Unmanned Space Experiment Free Flyer
- *USERS* Unmanned Space Experiment Recovery System
- *USML* United States Microgravity Laboratory
- *USMP* United States Microgravity Payload
- *X-FEL* X-ray Free-Electron Laser
- *ZARM* Zentrum für angewandte Raumfahrttechnologie und Mikrogravitation (Center of Applied Space Technology and Microgravity) (University of Bremen)

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