NSR-09-012-075

Space Biology

NATIONAL ACADEMY OF SCIENCES

Space Biology

Report of a Study Convened by the
SPACE SCIENCE BOARD
NATIONAL ACADEMY OF SCIENCES
NATIONAL RESEARCH COUNCIL

National Academy of Sciences
Washington, D.C. 1970

Foreword

This is the report of a study convened by the Space Science Board at the request of the National Aeronautics and Space Administration to "look anew at the foundations of space biology and attempt to assess the value to science of future studies in the space environment."

The Study was conducted at Crown College, University of California, Santa Cruz, during July 1969, under the chairmanship of Kenneth V. Thimann. Sixty-three scientists and technical advisors, representing the broad range of interests in biological and medical sciences, participated. In addition, the Study's Executive Committee held sessions prior to and after the main three-week study. The Study's findings and recommendations were presented to NASA management on July 23.

The Space Science Board is grateful to all who participated in this study. The Board also acknowledges with appreciation the support of the National Aeronautics and Space Administration.

Charles H. Townes, *Chairman*
Space Science Board

Preface

The Space Biology Summer Study was convened under the auspices of the Space Science Board of the National Academy of Sciences to review the program of biological investigations in the space environment and to consider these investigations within the general context of the advancement of biology as a whole. The Study was held at the University of California, Santa Cruz, July 14-25, 1969.

Particularly because the Study was to consider space biology within a general biological context, most of the participants were chosen for their research competence without special regard to their association with space biology activities, although a few did, in fact, have such a background. In addition, to take necessary advantage of space experience, the Study called on a large group of consultants who participated for periods of three to five days. Some twelve engineers were also invited as technical consultants on bioengineering problems. Finally, several officials of NASA's biology program were available throughout the Study, to provide information on the character and results of past NASA space biology activities, the nature of current efforts, and directions in their plans for the future.

The planning group early recognized that the Study's work fell into five broad areas of scientific interest. Accordingly, five panels were established, as indicated by the five subject-matter chapters of the report. A steering group coordinated these activities, while close ties were also maintained among the panels themselves.

Our grateful acknowledgments are due to many, including each of the scientific and technical consultants, the several NASA officials, and the Study members, all of whom made my task easier and pleasanter. Our thanks also go to the Space Science Board secretariat, and particularly to the Study's secretaries, Martha Mycoff of the Space Science Board and Pamela Kinnan of Santa Cruz. We are most appreciative of the many services and amenities provided by the Extension Service of the University of California, Santa Cruz, and the staff of Crown College.

Kenneth V. Thimann, *Chairman*
Space Biology Summer Study

Space Science Board

Contents

CHAPTER 1

Summary and Major Recommendations

The purpose of this Study was to take a fresh look at biological investigations in the space environment and to consider these within the general context of the advancement of biology as a whole. Thus the Study was not concerned with exobiology--living forms elsewhere in the solar system or even beyond--nor was it concerned explicitly with the medical sciences. Parts of the latter did come into our purview, not only because the spectrum of the life sciences is continuous but specifically because certain medical and physiological studies of man and other mammals, quite aside from operational and safety concerns, are intrinsically linked to the purposes of biology. Moreover, while the study was primarily addressed to biological investigations *in* the space environment, the obvious utility of vehicles circling the earth for watching and measuring biological and ecological events on the earth's surface could not be ignored, and it has become clear that such space vehicles have great potential applications and can make valuable contributions to biology generally.

Thus two of the five following chapters deal with certain medical and physiological investigations to be made in space and with earth-sensing uses of satellites, particularly with respect to animal orientation and tracking and to ecology. The three other chapters consider, respectively, biological rhythms; cells, plants, and invertebrates in space; and radiobiology.

This summary chapter attempts, first, to set forth the general biological context that dominated the study; second, to comment briefly on the work of the five panels; and, third, to summarize the main findings.

THE BIOLOGICAL CONTEXT

All life on earth has evolved under the influences of the sun's electromagnetic radiation, the earth's gravitational and magnetic fields, and perhaps other fields of force as yet unknown. Variations in these fields, regularly repeated for millenia, may have played a selective role in the evolution of the daily and monthly rhythms that so many organisms undergo. While we can experiment on the biological effects of magnetic fields here on earth, our experiments on the influence of the gravitational field are limited to increases in the field: we cannot produce extended weightlessness, although in some organisms we can compensate for it. In 1880, Darwin noted that we could not experimentally lessen the force of gravity, and he clearly envisaged the importance of sensitivity to it as a factor in biological evolution and development. Less than 100 years after Darwin, it is technically feasible to perform biological experiments in space, an environment that is free of gravitational influence, free of tidal forces and the cyclic events of celestial mechanics, and free from the earth's magnetic field. This new dimension for biological research can be significant at three levels: the intrinsic interest in how organisms react to an entirely new feature of the environment--one to which no organism in the earth's evolutionary history has been exposed; the immediate application of such knowledge to the welfare of man traveling for progressively longer periods through space; and the elucidation of the influence that gravity has exerted on the growth, development, and evolution of organisms.

Nevertheless, in space we also enter an environment in which the organism is exposed to unfamiliar and perhaps greater stresses and to types of radiation that do not penetrate the atmosphere of the earth. Since such factors may bring us into contact with biological risks not easy to foresee or assess, new, more extensive assessments of space radiation and of physiological responses to the space environment are necessary.

From the biologist's point of view, the earth can be considered one vast system whose properties dictated the nature of life that evolved on it. Six unifying principles describe the life we know:

1. The complementarity of structure and function at all levels of biological organization, from biologically active molecules to populations;
2. The organization of most living matter into cells;
3. The mechanism that provides for the continuity of genetic information;
4. Growth and development, which involve differentiation of apparently identical cells into organs comprising different cell types and exercising different functions;
5. The common biochemistry that underlies metabolic events; and
6. The evolution of organisms by the selective action of environmental factors on genetic variants occurring within a population.

These principles, not entirely independent of each other, convince the biologist that we deal with a single kind of life--that all known life can be traced back to a common origin.

Thus in one sense biology has until now been a provincial science, for we have studied one type of life in one group of environments, and our generalizations are based on this group of examples. Just as the exobiologist may have the opportunity to increase vastly our biological knowledge by discovery of an independently evolved life elsewhere, so the space biologist may increase our understanding of life by studying it in a different environment. Conversely, space vehicles, with instrumentation looking earthward, can assist in studying biological problems on the earth itself.

THE SPECIFIC APPROACHES OF THE STUDY

The task before the Study was therefore to ask: to what fields of biology, and to what general biological problems, can existing or proposed space technology make valuable contributions? We have identified five principal areas* in which we see particular interest and have treated each of them in an individual chapter of this report.

---

*Some of these have been the subject of earlier Space Science Board studies, *viz.: A Review of Space Research.* NAS-NRC Publ. 1079 (1962); *Space Research: Directions for the Future,* NAS-NRC Publ. 1403 (1966); *Physiology in the Space Environment, Vol. 1, Circulation,* NAS-NRC Publ. 1485A (1968); *Vol. 2, Respiration,* NAS-NRC Publ. 1485B (1967); and *Radiobiological Factors in Manned Space Flight,* NAS-NRC Publ. 1487 (1967).

Our working groups were composed of biologists whose interests vary widely and whose research fields lie in many different biological disciplines. The group on circadian rhythms (Chapter 2) is concerned with the periodicity of function that nearly all plants and animals display. The different hypotheses about the nature of the "clocks" that control the rhythms are particularly concerned with whether they are truly endogenous or driven by some sort of terrestrial cycles. A great many basic data have already been gathered, and reliable test organisms have been identified; the field is ready for space experiments. It is possible that eccentric earth-orbital experiments will resolve the question in favor of one of the hypotheses, but, more likely, heliocentric orbits may eventually be required to clear up the problem completely.

The biologists of this Study whose interests are at the cellular level of plants and invertebrates (Chapter 3) feel that, for the present, space-related experiments in this area can be performed most effectively on the ground. They would like to see vigorous support for ground-based research of this type, in preparation for space experimentation later. For the future, this group urges careful attention to the design of biological requirements of a manned orbiting laboratory to permit long-term biological experiments in space.

Mammalian physiologists (Chapter 4) take a different approach because they are concerned, *inter alia*, with the safety and welfare of the astronauts and because they deal with an organism--man--that is well known to us subjectively as well as objectively, having been studied more thoroughly than any other living thing. Nevertheless, many aspects of human physiology are still poorly understood, and the space environment offers an unusual opportunity to study known physiological responses under new environmental conditions. It will be difficult to use human subjects for some of the desired measurements, and subhuman primates will be the best substitute. However, we can extrapolate the data to man only with critical reservations, in part because many human responses to space conditions involve psychological factors that are difficult if not impossible to duplicate in subhumans. Extensive data of all types from man and experimental animals are needed to understand the varied effects of spaceflights.

Radiobiologists, on the other hand (Chapter 5), are able to evaluate many radiological effects of an environment by instrumentation. They have defined the radiation hazards of space; they have assessed the combined effects of a known radiation level with weightlessness and other spaceflight factors and find the interaction insignificant. They see the need for continued and improved measurement of radiation on manned and unmanned missions and for investigation of the effects of high-speed, heavy atomic nuclei which are as yet exceedingly difficult to reproduce on earth.

The Working Group on Animal Orientation and Tracking (Chapter 6) emphasizes the value of space technology in monitoring the earth's ecology and in alerting man to environmental problems. They also conclude that space technology can contribute to a fundamental component of biology: the mechanisms of animal navigation. They suggest that miniature radio transmitters be placed on animals in the wild for tracking by spacecraft. The technique should provide clues to the guides a migrating animal uses to travel thousands of miles to the same places year after year.

FINDINGS AND MAJOR RECOMMENDATIONS

The individual recommendations of the five working groups are presented in the respective chapters of this report. They are summarized below:

1. We *recommend* that a variety of ground-based studies be supported as a necessary prelude, in terms of both experimental design and scientific concepts, to subsequent experiments to be flown in space. This ground-based research must be considered a major need in the study of the effects of altered gravity, radiation, and other space-environmental factors on cells, plants, and invertebrates. Specific fields calling for ground-based research include the influence of the clinostat on structure, growth, and development; georeceptor systems of plants and animals; responses to mechanical, vibrational, and electromagnetic forces; miniaturization of transponders and other instruments; and the preservation of eggs and tissues by freezing, with subsequent thawing. Such ground-based studies represent an integral and crucial part of space biology.

2. We *recommend* that efforts be continued to obtain more physiological and behavioral data from measurements made on astronauts in flight. Data from astronauts are limited in scope and are not easy to obtain, but they are the only data directly applicable to the safety and well-being of future astronauts. If technology allows, future flights could well

include a scientist passenger* specifically to carry out this objective. If the instrumentation is sufficiently simple and reliable, and if the measurements are accepted as an integral part of the mission, the results should answer many of the pertinent questions about vertebrate physiology that cannot be answered by experiments on the ground. As the duration of manned flights progressively increases, the observations will serve to detect the first indications of any physiological or medical trouble so that appropriate steps can be taken to circumvent it.

3. We *recommend* the study of circadian rhythms in plants and animals in eccentric earth orbit and, if then necessary, in deep space removed from all terrestrial influences. An understanding of the mechanisms by which living organisms maintain a remarkably steady periodicity in function, perhaps by a "circadian clock" independent of terrestrial cycles, would be a valuable contribution to biological theory.

4. We *recommend* the future study of long-term effects of weightlessness on the early development and maturation of organisms and the subsequent changes that may occur after return to the terrestrial gravitational field. For example, small vertebrates should be raised from fertilization or birth in a spacecraft and kept there under observation until, at maturity, they are returned to earth and examined for possible modification in their microscopic and gross structure or in their chemical composition and behavior. Better than any other experiment, this will illuminate the over-all role that gravity plays in life processes. The particularly demanding controls, and the variability of biological materials, make this a difficult program that could best be carried out in a manned space laboratory; however, preliminary work of this kind could be included in a biological satellite. These studies will provide valuable information that can be obtained in no other way.

5. We *recommend* continued and extended measurements of radiation dose, radiation type and quality, and depth-dose relationships, in unmanned and manned missions and, when appropriate equipment is available, of the biological effects of heavy atomic nuclei in ground-based experiments.

6. We *recommend* continued studies in spaceflight on the physiology and behavior of animals. We visualize several primate flights followed ultimately as necessary, by experiments in a manned orbiting laboratory. Many experiments can be done

---

*The Executive Committee (see page 54) *recommends* the inclusion of such a scientific passenger where possible.

on monkeys with surgically implanted probes and catheters that are not possible in man, and thus some questions about the mechanisms of response to gravity-free conditions can be investigated. Animal experiments will supplement data obtained on astronauts in flight to provide a more complete picture of man's adaptation to the space environment and an opportunity to study in depth the effects of weightlessness on vertebrates.

7. We *recommend* a program for satellite tracking of free-ranging animals. Equipment for this program can be carried by satellites serving other purposes, such as communications or Applications Technology Satellites. The goal of these studies is to understand the mechanisms by which species orient themselves and navigate.

8. We *recommend* the continued development of multispectral sensing from satellites for research on terrestrial ecology. Earth-sensing spacecraft and space photography have already demonstrated the practicality of this technique for geology, forestry, agriculture, and environmental care generally. These studies will provide a foundation for our efforts to preserve and improve the quality of our environment and to conserve natural resources.

9. We *recommend* that the National Aeronautics and Space Administration increase its efforts to develop bioinstrumentation and to make its expertise and advances in biomedical instrumentation more generally known and available to biologists.

10. We *recommend*, if the National Aeronautics and Space Administration proceeds with its plans for a manned space laboratory, the early development of scientific specifications for it by a committee convened by the National Academy of Sciences. Such a laboratory must serve physical and biological sciences as well as technology and requires very detailed planning by a multidisciplinary committee far in advance of the proposed launching.

11. We *recommend* that the National Academy of Sciences continue this Study by providing for the periodic review of programs related to each of the five major areas represented in this report and in the fields of ecology and bioengineering. It is suggested that, with the concurrence of the National Aeronautics and Space Administration, the National Academy of Sciences appoint a committee with panels in each of the above or similar areas as well as in other appropriate areas to

recommend best directions for research and to advise NASA on a continuing basis.*

The group's recommendations may also be presented more explicitly in terms of NASA programs and missions, responding thus to two critical questions: (1) What ground-based studies should NASA support in connection with NASA's space mission and subsequent spaceflight activity, and (2) what biological investigations should NASA conduct in space? This presentation takes the following form:

First, investigations calling for ground-based studies as antecedent to and contributing to subsequent spaceflight activity:

(a) Research on gravity receptors and geomorphism of cells, plants, and invertebrates (Recommendation 1, above; Recommendation 1, Chapter 3)

(b) Continued development of multispectral sensing devices for satellite application to ecological studies (Recommendation 8, above; Recommendation 1, Chapter 6)

(c) Continued development of biomedical instrumentation (Recommendation 9, above; Recommendation 2, Chapter 6)

(d) Preparation for in-flight testing of mechanisms responsible for circadian rhythms (Recommendation 1, Chapter 2)

(e) Clinostat and centrifuge experiments (Recommendation 2, Chapter 3)

(f) Development of techniques for low-temperature preservation (freeze-thaw) of living tissues (Recommendation 3, Chapter 3)

(g) Feasibility study of the potential of a geophysically isolated facility (Recommendation 4, Chapter 3)

(h) Research on biological effects of high-energy, high-Z particles (Recommendation 2, Chapter 5)

(i) Research on biological systems considered appropriate for spaceflight to assure understanding of endpoints prior to flight (Recommendations 4 and 5, Chapter 5)

(j) Microminiaturization of devices for small-animal tracking (Recommendation 2, Chapter 6)

---

*This recommendation has recently been supported in a different form by the Space Science and Technology Panel of the President's Science Advisory Committee: "We recommend that an active mechanism be utilized to broaden the participation of biomedical scientists in planned and approved manned spaceflight programs, and in the long-term biomedical studies basic to these programs."

(k) Design study for satellite instrumentation to collect data from animal-borne platforms and relay it to ground stations (Recommendation 3, Chapter 6)

Second, investigations needing unmanned earth-orbiting satellites:

(l) Test of hypotheses on circadian periodicities (Recommendation 3, above; Recommendation 1, Chapter 2)

(m) Animal tracking and ecological studies (Recommendation 7, above; Recommendations 1-6, Chapter 6)

(n) Physiological and behavioral experiments on subhuman primates in recoverable payloads (Recommendation 6, above; Recommendation 2, Chapter 4)

(o) Spaceflight effects on body composition using rats or other vertebrates in recoverable payloads (Recommendation 3, Chapter 4)

(p) Preliminary experiments on growth and maturation of animals in zero *g*, as precursor to more complete studies in a manned laboratory (Recommendation 4, Chapter 4)

Third, investigations to be done in unmanned deep-space probes:

(q) Circadian periodicities, if the question is not resolved in earth-orbital experiments (Recommendation 3, above; Recommendation 1, Chapter 2)

Fourth, investigations to be carried out on manned spaceflights:

(r) Physiological and behavioral measurements on astronauts or on scientist passengers (Recommendation 2, above; Recommendation 1, Chapter 4)

(s) Physical measurements of ambient radiation (Recommendations 1 and 2, Chapter 5)

Fifth, investigations suitable primarily for manned orbiting laboratories:

(t) Growth and maturation of organisms in zero *g* and effects on return to earth (Recommendation 4, above; Recommendation 4, Chapter 4)

(u) Physiological and behavioral experiments on subhuman vertebrates (Recommendation 6, above; Recommendation 2, Chapter 4)

CHAPTER 2

Biological Rhythms

We have a great deal to learn about biological time, for there is no element of biological organization that does not vary temporally. Some processes, such as development and aging, vary unidirectionally; many others, perhaps most, are cyclic, with periodicities that range from milliseconds to years. Among the latter are circadian* rhythms. These have been extensively studied because of their capacity to function as true "clocks" that synchronize a variety of biological processes with the solar day.

Circadian rhythms have been discovered in almost all major groups of organisms at levels from the biochemical through the behavioral. Variation in nucleic acid synthesis and function is circadian in many organisms. Circadian rhythms have been noted in organ function and in the sensitivity of organs and organ systems both to normal changes in the environment such as light and temperature and to experimental exposures such as x rays. Behavior, from simple reflexes to social interaction, has in most cases strong circadian components. These are perhaps most evident, and certainly most thoroughly studied, in systems in which periods of activity alternate with rest or sleep. An organism's ability to respond to stress depends also on circadian periodicities, as do many aspects of its function under relatively constant conditions.

Man, like other living things, is a rhythmic organism,

*The term means with period of *about a day*.

and his temporal organization is adapted to the 24-h periodicity of the terrestrial environment. His time relations, however, have become very complex through technological and cultural "advances." These create problems whose scope and resolution demand far better understanding of his circadian rhythms and clocks. The "jet disease" of air travelers and flight crews is well known; analogous pathological dysrhythmias associated with supersonic air travel, spaceflight, and space residence will present further problems. Among the more mundane problems are the effects of watch-standing in the military services and shift changes in industry. Rhythmic variations in drug effects and sensitivity to toxins will also become better understood as we develop a greater general knowledge of biorhythms.

Many economically important species of plants and animals use day length as a key source of information for control of their annual cycles, including their reproductive processes. It is now established that in many such species day length is measured by some circadian function. Insofar as we better understand the nature of circadian clocks, our ability to control or to manipulate the productivity of such species should increase, and herein lie some exciting possibilities in pest control. Lastly, orientation and navigation in many migratory species appear to involve a chronometer based on the circadian clock (see Chapter 6). Some migratory species are economically important and are coming increasingly under human management which, if it is to be intelligent, will require intimate understanding of the circadian clock and its role in navigation.

Although our ultimate understanding of periodic functions in organisms will depend largely on earth-based studies, and while immediate, spectacular benefits from space investigations of the subject seem unlikely, space experiments can make significant contribution to this field in two ways: (a) As a piece of basic knowledge, the problem of the fundamental mechanisms that generate and control circadian periodicities is of great interest and importance. This problem appears resolvable only by means of well-conceived experiments in space. A discussion of this problem and its background is given below. (b) From the standpoint of spacecraft operations, a fuller understanding of circadian periodicities is important for the health and optimal performance of astronauts and to the interpretation of many other, especially physiological, space experiments.

CONTRIBUTIONS OF PREVIOUS STUDIES

Ground-based studies over the past 20 years have produced a vast literature from which, in the present context, the following points may be extracted:

1. There are specific circadian rhythms in particular species about which enough is known so that their behavior can be specified and predicted under a wide variety of terrestrial conditions.

2. *All* circadian rhythms have certain remarkable properties in common. Among the most interesting of these are: (a) that circadian rhythms persist, in many cases indefinitely, even under laboratory conditions in which external periodicities have been nullified as much as possible; (b) that the period is about, but seldom exactly, 24 h and precise (low variance); and (c) that the period of the rhythm has a temperature coefficient close to 1.0--i.e., it is largely temperature-compensated.

No definitive in-flight experiments on circadian rhythms have as yet been performed. The few observations made to date on astronauts and on the Biosatellite monkey show only that circadian phenomena persist, or at least do not damp out immediately, in earth orbit.

UNANSWERED QUESTIONS AND POSSIBLE TESTABLE HYPOTHESES

A major question has emerged, largely as a result of the generalizations outlined in paragraph 2 above. Simply stated it is this: What drives or controls cyclic events of such remarkable and unexpected properties? Are they driven by something within the organism itself, or are they driven by, and derive their properties from, geophysical variables in the terrestrial environment? Because on the ground one cannot, *in principle*, remove an organism from the influence of all known and unknown geophysical variables, we must seek this answer in space.

Figure 1 and the discussion that follows show how flight experiments can test two hypotheses on the driving force of observed rhythms that have different properties.

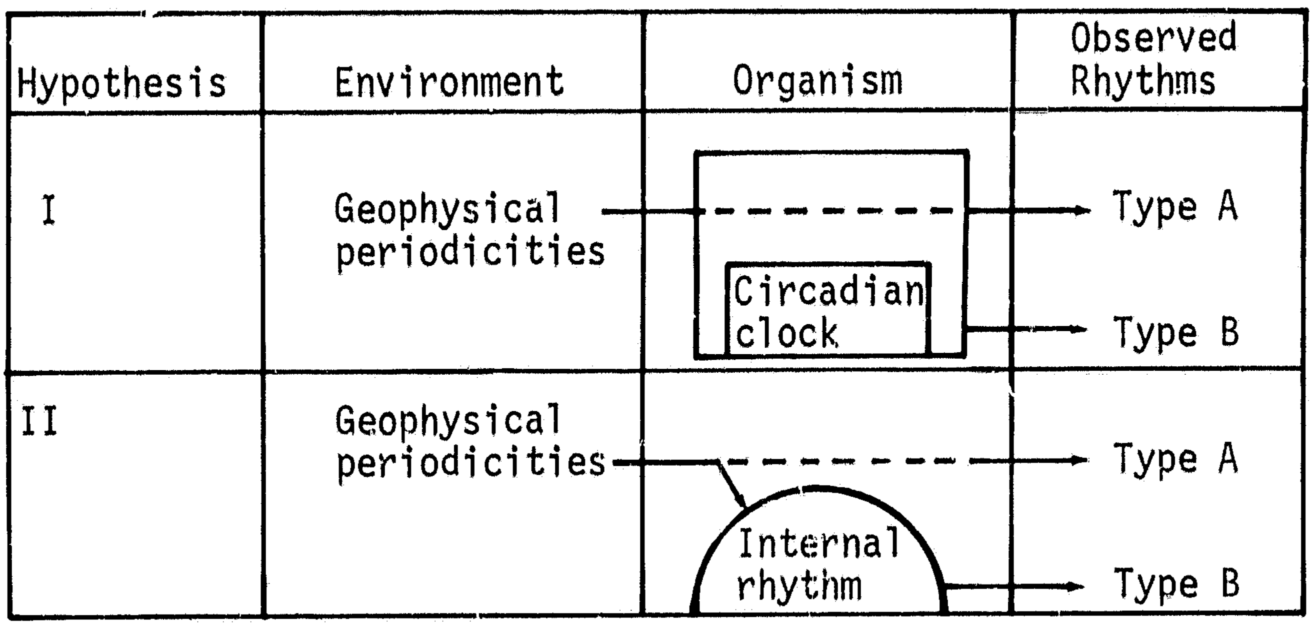

FIGURE 1 Possible alternative mechanisms responsible for observed rhythms, Types A and B.

Two sets of rhythms (A and B in Figure 1) have been observed in terrestrial organisms, and their properties are as follows. Type A: Period is exactly 24 h with no variance; period is independent of temperature; phase is fixed relative to local time. Type B: Period is circadian (*about* 24 h) with small but measurable variance; period is nearly temperature-compensated, but the temperature coefficient is not quite 1.0; phase is labile with respect to local time.

1. If, as some assume, rhythms result from direct driving by geophysical periodicities, those rhythms with Type A properties will disappear in deep space.

2. The observation of Type A rhythms has also led to the hypothesis that the geophysical periodicities that drive them also drive something (represented by the circle in Figure 1, hypothesis II) within the organism that oscillates with Type B properties, and so these geophysical periodicities are responsible for *all* observed circadian rhythms. An alternative hypothesis (I in Figure 1), possibly more widely held, asserts that the geophysical periodicities entrain an endogenous, autonomously oscillating circadian clock which can oscillate independently of geophysical periodicities to produce those properties defined as Type B. If Type B rhythms persist in space environment (where geophysical periodicities have been rigorously excluded) hypothesis I must be accepted and hypothesis II rejected.

3. It would be interesting if circadian rhythms were found to persist in deep space, but with properties different from those observed on earth. Many such variations are possible, but only one set of these has unambiguous bearing on the hypotheses outlined above. In this set, the period is circadian but with large variance; period is temperature-dependent; phase is labile. If rhythms in space have these properties, then hypothesis I must be rejected and hypothesis II accepted.

4. We consider unlikely the possibility that all rhythms will disappear in deep space, but if this should occur, it would (providing the organisms were otherwise in good condition) support hypothesis II.

PROPOSED SPACE EXPERIMENTS

The rationale of the proposed experimental program derives from the fact noted above that the period of the rhythm is temperature-compensated. The experiment should be applied commonly to several systems. ("System" as used here means test organism plus the periodic phenomena selected for observation. A single species could be common to two or more systems.) The question to be asked is: Do the characteristic features of circadian rhythms (Types A and B) persist when a system maintained in constant temperature, light, humidity, and pressure is (1) exposed to the earth's geophysical fields in highly atypical frequencies, as in an eccentric earth orbit and (2) totally removed from these fields as in a deep-space probe?

A deep-space probe ultimately is desirable because, with the possible exception of the disappearance of all rhythms when in earth orbit, no other experiment can provide an unequivocal test of the primary hypotheses. The environment provided by the earth-orbital mode is one in which almost all fixed geophysical force fields are experienced as cycles with radically changed periods and intensities as determined by the orbit of the satellite carrying the equipment. If 24-h cycles of one or more geophysical inputs are responsible for the period, stability, and temperature compensation of the free-running circadian oscillations, it is clear that these must change when the geophysical signals are provided with periods of, say, 95 min, 5 h, or 4.7 days. Not excluded, however, is the "sensing" of a real (though at present unknown) 24-h periodicity in some geophysical force field, although it seems unlikely that a system could detect such a field in the presence of odd periodicities imposed by an orbit with a period that is neither a multiple nor submultiple of 24 h.

Earth-orbital experiments should be undertaken to provide (1) a test of the possibility that gravitational fields have a major influence on circadian rhythms, as well as (2) valuable flight tests for the rhythm experiments--the measuring and control desices, and test systems--thereby leading to selection of the best experiments for deep space. Furthermore, as noted above, it is possible that circadian periodicities may disappear in earth orbit and that the arhythmia can be shown not to be the result of masking, uncoupling, or some other effect on an endogenous clock. This would reject hypothesis I and eliminate the necessity for deep-space experiments.

Requirements and Specifications for Experiments

Experiments in both the earth-orbit and deep-space flights must include at least one species assumed to have Type A properties and at least one species with assumed Type B properties under as nearly identical conditions as possible. The experimental design must be simple, and adequate replication is essential. The test systems for which technical information, engineering information, operational requirements, and resources requirements have been assembled include*:

1. Potato--respiration
2. Bean--leaf movement
3. Fiddler crab--motor activity and respiration
4. Cockroach--activity and respiration
5. *Drosophila*--eclosion
6. Pocket mouse--body temperature, heart rate, motor activity
7. C-mouse--body temperature, heart rate, motor activity

Among these test systems, *Drosophila* and cockroach offer the opportunity for a rigorous test of temperature compensation in the absence of all geophysical periodicities.

The properties of the rhythms in all these systems will need to be firmly established in ground-based experiments. The stability and precision of the period in a circadian free run are best tested in the mammal with measurements of body temperature or locomotion or both. The potato preparation does not test either hypothesis I or II but does provide the chance to

*R.C. Lindberg, "Feasibility Study for Conducting Biological Experiments Aboard a Pioneer Spacecraft," NASA CR-73178 (1968).

demonstrate that strictly "dian" periodicities (Type A properties) may disappear in deep space and be significantly altered in earth orbit.

Other fairly well-studied test systems which would require additional study before flight experiments include:

Carrot--metabolism
Euglena--phototaxis, motility
Gonyaulax--luminescence, flow and flash, photosynthesis, growth
Tenebrio larva--oxygen uptake

It appears worthwhile to encourage the development of a system involving a small poikilothermic vertebrate, such as a small lizard.

Responses to organisms to the space environment may or may not be clear-cut. Interpretation of the data will require: (1) intimate knowledge of the peculiarities of the experimental organism, derived from intensive preliminary earth-based research and (2) proof that the phenomenon is reproducible in the flight instrumentation. Because the hypotheses to be tested in some cases postulate roles for extremely subtle forces, verification of the reproducibility of an experiment in space-type hardware is an absolute requirement and must be carried out by biologists and engineers working together. Ensuring that the spacecraft and experimental hardware do not contribute a periodic input that overrides the input (or lack thereof) from the space environment will be an engineering task of first-order complexity which, in our judgment, should be undertaken first as an earth-based study. The problem also impinges on the over-all mission planning. For example, unavoidable electromagnetic fields associated with data retrieval from space might serve as an effective input; this would require that data retrieval be temporally randomized. Some ground-based experiments should also be set up in an apparatus in which the earth's magnetic field is very greatly decreased both to test the role of geomagnetism in circadian rhythms and to serve as a control for the flight experiments. Finally, data should be collected and recorded in a way that facilitates alternative schemes of data reduction and analysis.

Requirements and specifications for research on circadian periodicities in space are as variable as the number of observable systems. The common denominator is that of adequate support. Only those studies of circadian rhythmicity that require the space environment to test hypotheses should be conducted in space; some studies are by definition earth-based and should share equal attention with spaceflight experiments.

Timing of Proposed Experiments

Hardware and experiment design for the proposed experiments are at an advanced stage of development. For example, the *Drosophila*, pocket-mouse (perognathus), C-mouse, and potato plug experiments could be flown within 18 months. For these systems the bulk of the work still to be done on the ground consists of gaining experience with the experimental system in actual flight hardware. The same hardware should be flown both in the Apollo Service Module in earth orbit and, if hypothesis I is not disproved, in a Bio-pioneer in deep space.

RECOMMENDATIONS

The experiments proposed in this chapter could resolve the fundamental question on the nature of circadian clocks: Are they completely endogenous, or do they require an input from geophysical periodicities? It is extremely unlikely that this question can be answered without these critical space experiments.

Therefore, we *recommend* that NASA develop and effect a program of investigations concerning the causal nature and basic properties of circadian periodicities. These investigations should involve several test systems. Experiments with at least one species with Type A properties and at least one with Type B properties must be included in the same flight vehicle. The experiments must be as simple as possible and with adequate replication and controls. For the reasons detailed above the program should include thorough ground-based preparation, followed by a series of earth-orbital experiments, and finally, if indicated, a deep space series.

CHAPTER 3

Cells, Plants, and Invertebrates in Space

In the fields of cell, plant, and invertebrate biology, the biological questions that may best be examined with space techniques relate to the responses of organisms to gravity by their growth, form, and orientation. The approach to resolution of these problems is characterized by delicate measurements of very small forces, rigid controls, and numerous repetitions because of the variability of the organisms under study. For these reasons we are actutely aware of the constraints and limitations implicit in present space-based biological experimentation. A wide range of gravitational and vibrational forces are encountered, including acceleration forces generated at takeoff and landing and during flight-pattern corrections. Sufficient replications and controls, such as centrifuged controls in flight, may be impossible because of lack of space in the vehicle; trace contaminants in the spacecraft environment are difficult to detect or monitor and may have major effects on the experimental results. Perhaps the most serious problem is the separation of the scientist from his experiment, with associated restrictions on observation, manipulation, and experimental control. Such decisive technical obstacles in the path of flight experiments in cell, plant, and invertebrate biology lead us to conclude that at the present time scientific questions in these fields can be approached more effectively with ground-based experimentation. We believe that these questions must be studied extensively and deeply on the ground before the proper questions can be put in space.

An opportunity for experimental conditions that can circumvent many of the limitations of unmanned satellites is presented in the prospect of facilities such as manned space station or orbiting laboratory. In preparation, ground-based research on georesponses and related phenomena should be supported now to provide a rational and constructive base for good biological flight experiments.

Ground-based experiments have a different set of limitations; the principal one relates to the nature of the clinostat.* The rotation of experimental material on the horizontal clinostat does not necessarily reproduce *all* the conditions of weightlessness. This device is useful only for those physiological phenomena that have relatively long exposure thresholds (or presentation times), and when rotation of the living material can be rapid enough so that the time spent in any position does not result in an induced georesponse. The rotated material must also be small enough not to generate centrifugal forces that reach the force threshold (gravity-seconds) during rotation. Within these limitations the clinostat can be utilized to compensate for gravity.

The value of the clinostat in approximating the conditions of near weightlessness has been criticized† because it involves the equalization of the geostimulus rather than its removal. The fact remains, however, that not only is the clinostat *experimentally* capable of regulating the gravity responses of many systems, but, further, that the large majority of, and perhaps all, the morphological and physiological responses of plants flown in satellites to date have not appreciably differed from the responses of plants rotated on a clinostat.

We strongly recommend that clinostat experiments be made in all appropriate cases before establishing plans for spaceflight of plant materials. Conversely, assuming that there is a continuum of responses between zero and several *g* the centrifuge can be highly useful in analyzing gravity responses and in predicting responses to lowered gravity.

---

*The clinostat is an apparatus which by its motions modifies or equalizes directional influences, such as light or gravity, in an attached organism.

†cf., Werber, NASA contract 09-010-027 (1969).

INFLUENCE OF GRAVITATIONAL FIELD STRENGTH

Plants

Plant responses to gravity fall into two categories. The first contains all responses for which the plant, in the course of evolution, has developed specific gravity-receptor and gravity-response systems. These responses include either movement and orientation of an already formed organ in the gravitational field or polarization of a developing organ which controls its further growth and differentiation. In the second category are perturbations in the general behavior and development of plant cells and tissues.

In the first category, the central question is, "What is the receptor?" The following considerations suggest that extensive experimental work should be undertaken on the ground rather than in a satellite: (1) Biosatellite experiments revealed no sensible difference between the plagiotropic angles of orbiting wheat roots or pepper plants and of clinostated controls on earth; (2) georeception by the grass coleoptile, the most commonly studied system for geotropism, still needs further study on the ground; and (3) a minimum requirement for studying georeception is to establish the kinetics of the process; this has not been done and requires experiments on hundreds of plants, repeated several times each, a project not well suited to satellite experimentation. With a better understanding of gravity receptors, the possibility of good flight experiments may be more realistically assessed.

Many developmental responses are known to depend on the gravitational force vector. Both receptor and mediational mechanisms may be investigated, but because the latter will probably be easier to study and should provide clues about the nature of the former, it seems more immediately fruitful now to stimulate research on mediational mechanisms. Plants on the clinostat, continuously rotated in the gravitational field, should allow us to determine whether, for example, the evident anatomical polarization of a fern gametophyte results from migration of auxin under the influence of gravity from the upper cells to the lower ones; it is not clear that such a study could be carried out successfully in a Biosatellite. Ultimately, extended knowledge of developmental responses to gravity may permit the statement of critical hypotheses appropriate for testing in space.

The second basic category of plant responses to gravity consists of incidental effects on structures or functions that have not been evolutionarily specialized to respond to the gravitational field. Although we are not sure that metabolic effects exist, an example of a search for such an effect was provided by Biosatellite experiments in which orbited wheat seedlings were tested for differing enzyme activities. Since no really significant differences between earth-bound and orbiting plants were detected, a random search for unusual aspects of cell or plant physiology in space is not warranted. Nevertheless, to provide better evidence on which to assess the need for zero-*g* experiments, it is important to carry out ground-based experiments comparing various aspects of the metabolism and cytology of clinostated cells or tissue cultures, unicellular organisms, eggs, and zygotes with those of stationary controls. Structures as well as functions should be studied, for changes that confer increased rigidity on vertically growing plants are known to be induced or modified by the gravitational stimulus. Use of cells, as well as whole plants, in experiments of this type is important because one must distinguish between changes resulting from general effects of rotation and those caused by diffuse or continued low-level stimulation of specific receptor systems. For example, if a root or coleoptile shows a change in rates of growth and metabolism when it is rotated horizontally, is this because the axial transport of auxin is itself sensitive to gravity (even though compensated), or is the transport independent of the geosensing system? A ground-based experiment of a few weeks duration might answer this question.

Invertebrates

As with plants, the influences of gravitational acceleration on invertebrates may be considered under the two broad categories of effects mediated by (1) specialized receptors such as proprioceptors, acceleration receptors, and organs containing statoliths and (2) small shifts in the distribution of organelles or similarly nonspecific mechanisms.

In the case of orientation and geotaxis, the rapidity of the reception and responses generally limits the usefulness of the clinostat. Stimulation of an organ can often be controlled by other means without difficulty. As a result of this ease of control, knowledge of invertebrate receptors and responses to acceleration is about as well advanced as other areas of sensory and behavioral physiology, though there is much to be learned.

Questions about those effects of gravity that are not mediated through specific receptor systems (second category effects) are similar for invertebrates and plants. In both cases, our interest is focused on the behavior of cells, rather than of organs, since we need to minimize interference by specialized receptors. As with plants, flights of invertebrates in spacecraft have not as yet revealed unexpected new phenomena. While contemporary biophysical knowledge does not suggest that large or novel effects will be discovered, a careful ground-based comparison of stationary and clinostated animal material, with special emphasis on cells in culture, might establish whether this important view is correct.

INFLUENCE OF MECHANICAL STRESSES

An organism in space is subject to mechanical stresses very different from those on earth. The normal development of supportive tissues in vascular plants and invertebrates is powerfully regulated by mechanical stresses. Well-known examples are the stress-induced development of trabecular patterns in vertebrate bones and of reaction wood in trees. Specific supportive tissues are not the only ones that may be influenced, for mechanical restraints influence seeds and seedlings in many ways; for example, a pea seedling pushing through compacted soil is shorter and thicker than one growing through loose soil, and some water plants produce shorter and thicker internodes, or leaves of different geometry, if transferred from still to flowing water. Although mechanical stress of the soil medium around pea seedlings is known to provoke the biosynthesis of the powerful growth regulator, ethylene, the cellular and molecular mechanisms of response to mechanical influences are in general obscure.

Another relevant aspect of mechanical influences is the vibrational force encountered in spaceflight. Numerous cytological and genetic responses observed in some flight experiments, which have been attributed to radiation, are apparently due instead to vibration (cf. p. 38). Ultrasonic vibrations have long been known to cause intracellular damage. We believe that systematic research into the effects on organisms of mechanical forces is warranted, both to elucidate the basic mechanisms involved and to differentiate between these effects and those due to gravitational forces.

Role of Mechanical Stress in the Effects of Gravity

An effect of zero *g per se* on cellular phenomena ought to be predictable from purely physical considerations; because atomic or molecular energy levels are hardly likely to be influenced by 1-*g* fields, it is less likely that smaller gravitational forces can do so. Nevertheless, because gravity does affect cellular systems in various ways, a mechanism for this has to be envisaged.

There is a reasonable hypothesis, founded on experiment, on which to base the study of gravitational effects on the cell. According to this "mechanobiochemical" hypothesis, perturbations produced by the movement of particles in cells trigger functional changes in the cells. Sometimes the mechanism is highly specialized, as in the ear.

It would be interesting to look for effects of gravity on intracellular structures that have sufficient mass to be moved or distorted by small gravitational fields, such as the large vacuoles of plant cells. From the standpoint of space research, mechanobiochemical hypotheses offer an exceptional simplification because they point to a common basis for effects of gravity in general, for the functions of specialized organs of equilibrium in man and other animals, for the effects of vibration, and for acoustic mechanisms. All these problems merge into one--the interesting mechanisms whereby very small mechanical perturbations or shears modify the operations of cells.

In examining cell structure for the very-low-energy reactions that could respond to weak mechanical disturbances, we think that the mechanobiochemical responses of membranes (e.g., to turgor and distortion) should be studied. This promising and active field warrants increased support.

INFLUENCE OF MAGNETIC FIELDS

If, as seems possible, magnetic shielding against cosmic radiation is ultimately employed on space vehicles, it will be important to know more of the biological effects of magnetic fields. In the last five years there have been several reports of substantial and more or less mysterious effects of magnetic fields on organisms. These include modification in human circadian rhythms, magnetotropism in a higher plant, apparent severe genetic damage in a fly, the direction of a bee's orientation dance, the reported shift in the thermal death-point of a beetle, and the induction of sensations of light in man. Exploratory investigations into biological responses to magnetic fields are thus clearly warranted.

SPECIAL TOPICS

Preservation of Living Material

The development of techniques to maintain eggs and perhaps embryonic tissues viable at low temperatures is of basic importance in space biology. The possible use of these deep-frozen materials to transport organisms to or from orbiting laboratories or other planets should be worked out. It is already feasible to preserve, by freezing and thawing, blood, microorganisms, sperm, rotifers, and tardigrades.

Geophysically Isolated Facility

We suggest that NASA explore the potentialities of a geophysically isolated facility in which variations of magnetic, electrostatic, and other terrestrial influences can be minimized. The facility would have implications for general biological problems, biological rhythms, and, perhaps, human physiology as well.

Bioinstrumentation

Major contributions to biology can be made by applying advances in instrumentation, computer technology, telemetering, miniaturization, and vibration control. We believe it important that NASA continue and increase its efforts to make its expertise and facilities available to the biological community. Among the possibilities for implementing this that might be explored are: (1) extending the use of the Ames Research Center to accommodate visiting investigators, (2) contracting with a facility such as the Biological Instrumentation Advisory Center or the Jet Propulsion Laboratory to provide technical assistance to biologists, (3) establishing biomedical engineering facilities on appropriate university campuses, and (4) establishing a national biomedical engineering facility, perhaps administered jointly by several agencies.

Manned Orbiting Laboratory

On the assumption that the national space program in the 1970's will include a manned orbiting laboratory, we believe that a study of its biological uses should be undertaken promptly. We see scientific value in having a long-term orbiting laboratory for the conduct of certain biological experiments and expect it would be similarly helpful in other fields of science. It is none too early to begin asking the right questions about the orbiting laboratory, even though its use might be 6 to 10 years in the future. Accordingly, we urge that the National Academy of Sciences appoint an interdisciplinary committee to study the characteristics--scientific, technical, and administrative--of a manned orbiting laboratory as a national facility and to make recommendations thereon to NASA.

RECOMMENDATIONS

1. As a matter of general policy, we *recommend* that ground-based research on selected aspects of cell, plant, and invertebrate biology be carried out as a necessary prelude to any flight experiments. This includes research on the nature of gravity receptors, geomorphism and cellular georesponses of plants, and the georeceptor organs and cellular georesponses of plants and invertebrates. We further *recommend* research on biological responses to magnetic fields and to mechanical and vibrational forces and on cell mechanics and cell structure as altered by gravity and physical forces. Extensive knowledge of these subjects is prerequisite to the development of critical hypotheses suitable for testing under weightless conditions in space. Because the above researches have a direct bearing on future spaceflight research, they should be undertaken within the framework of the national space program.

2. We *recommend* that clinostat experiments be carried out in all appropriate cases before the plans for spaceflight of plant materials are established. Conversely, we *recommend* continued use of the centrifuge in the analysis of gravity responses and in predicting responses to lowered gravity.

3. We *recommend* support of studies on freezing and thawing of living eggs and tissues, in order to develop techniques to preserve such biological materials in a viable state at low temperatures.

4. We *recommend* that the National Aeronautics and Space Administration explore the potentialities of a geophysically

isolated facility where variations of magnetic, electrostatic, and other terrestrial influences can be minimized.

5. We *recommend* that the National Aeronautics and Space Administration continue and increase its efforts to make its expertise and facilities available to the biological community.

6. We *recommend* that the National Academy of Sciences appoint an interdisciplinary committee to develop and evaluate the scientific specification for a manned space laboratory and to make recommendations thereon to the National Aeronautics and Space Administration.

CHAPTER 4

Man and Vertebrates in Space

Space biology as related to man and vertebrates is concerned with the study of familiar terrestrial organisms exposed to the novel conditions of weightlessness and space radiation. Despite our familiarity with such organisms, there are lessons to be learned from their interaction with the space environment, and the results may expand our general knowledge.

Gravity plays an important role in the physiology of man. Countless experiments have already been performed on man's reactions to high-*g* loads and to changes in posture, and, while further ground-based experimentation may increase our knowledge somewhat, it cannot take the place of experiments on weightlessness in trial flights in space. For use on vertebrates, the clinostat introduces too many troubles of its own to substitute for a spacecraft. We therefore believe that experiments on man and vertebrates in space should continue and, in view of the direct relevance of these experiments to astronaut safety, that a reasonable fraction of the space effort should be assigned to them.

There is some urgency to further experiments on man and vertebrates, because a more thorough understanding of the responses to weightlessness may help us to predict the likelihood of satisfactory adaptation to weightlessness in flights of long duration. But since predictions are hazardous for a new environment, an exploratory approach becomes a necessity. Flights should therefore be lengthened progressively by small increments, with careful study of the astronauts to detect any cumulative physiological troubles not predicted by animal experiments.

DATA FROM MANNED FLIGHTS

Valuable physiological data on the reactions of astronauts to the space environment have already been obtained. It is of greatest importance to continue such efforts, and we may expect that securing in-flight physiological data will become progressively more feasible. Although astronauts cannot be fitted with all the probes and regional blood-flow meters than can be installed surgically in animals, many simple clinical tests can be made, and a great deal of essential information can be obtained from chemical and hormonal analysis of properly handled blood and urine samples. Likewise, it is important to know the rates of oxygen consumption and cardiac output and the volumes of air expired per minute. If the air space in the ship is small enough and the hatches are sufficiently airtight, or, conversely, if the rate and composition of outgassing are known, it may be possible to measure the oxygen consumption by recording the volumes released from a tank to replenish the cabin pressure, the CO_2 production from the volume removed by the scrubbers, and the volume of the ventilation from the small rise in pressure in the cabin caused by warming and wetting the inspired air at each inhalation. Alternatively, customary clinical methods may be adopted for these basic determinations.

If good measurements can be carried out on man in sufficient quantity, the necessity of special flights with animals will decrease. Experiments on animals will still be required, however, if we are to develop a complete understanding of physiological reactions to zero *g*.

PRIMATE EXPERIMENTS IN FLIGHT

The main problem needing further examination in primate flights is water balance and how it can be regulated under weightlessness. The most probable cause of the death of the Biosatellite III monkey appears to have been dehydration.* All the astronauts in space have lost weight, as have the Russian dogs in space. The next experiment should thus be planned not only to

---

*See, for example, W.R. Adey, A.T.K. Cockett, P.B. Mack, J.P. Meehan, and N. Pace, "Biosatellite III: Preliminary Finding," Science, *166*, 492 (1969).

solve this problem but should include as many additional experiments on the primate as can be accommodated. There are many reflex and hormonal mechanisms in the body that control blood pressure and distribute blood and water appropriately throughout the body. We know very little about how all these controls are integrated, or how the integration may be modified in a weightless condition.

In considering the final result, as, for example, a loss of weight, it might be suggested that this is not so much a danger as a beneficial adaptation to a new environment; the animal in space may need less muscle and less blood; some of this excess therefore is automatically or "wisely" eliminated. It would be reassuring to find that control systems of the body which have evolved entirely under the influence of 1 *g* can still succeed in zero *g*. Pressures, volumes, and concentrations that are normal and optimal on the ground are not necessarily optimal for space.

This, in a general way, is what can be expected to result from a primate experiment designed to study water balance and cardiovascular problems. Measurements should include arterial and venous pressures, total blood flow (by the dye dilution method) and regional blood flow (recorded by meters installed in iliac artery, carotid artery, etc.), electrocardiogram, skin temperature and body temperature, heart rate, total blood volume, plasma volume and red cell volume, total body water, extracellular water, and osmotic pressure of the blood plasma. The elaborate instrumentation required precludes carrying out all this work on man.

In the same or a later monkey flight, measurements should be made of total oxygen consumption and carbon dioxide outputs. From the volume and CO_2 concentration of air expired per minute, the alveolar CO_2 tension can be estimated. In some flights, measurements of total body weight, evaporative water loss, urine and feces output, and water and food intake should be included to obtain a total water balance. Electroencephalography, electromyography, and eye movements should also be measured on a monkey which could, as in Biosatellite III, have electrical leads implanted from other parts of the brain to permit estimates of its periods of sleep and wakefulness. Circadian rhythms should be observed and could perhaps be varied by changing the feeding program or the light-dark cycles, because the changes in such readings as gas exchange and temperature will be influenced by these rhythms.

In many ways such experiments could best be carried out in a manned orbiting laboratory, because minor corrections could then be made during the course of the experiment. Such a laboratory, however, might not be equipped for major changes in instrumentation that could become necessary. In a series of Biosatellite flights, however, new instrumentation could be prepared after each flight and tested out on the ground prior to the next flight. The results of the flight might also suggest supporting experiments which could be done on the ground to improve the focus of the subsequent flight. A Biosatellite also has the advantage that it permits the observation of the behavior of an animal completely uninfluenced by the imposed rhythm of the activities of the investigator. In the long run such preliminary Biosatellite flights might save both time and money.

METABOLISM, NUTRITION, AND BODY COMPOSITION

From the time of Lavoisier, it has been known that the caloric value of food, the amount of body-heat production, and the exchanges of oxygen, carbon dioxide, and water vapor are related by the simple laws of combustion. In recent years, more emphasis has been placed on intermediary metabolism and the energy cycle as exemplified in the production of adenosine triphosphate and creatine phosphate. The psychological factors in eating have been studied; the foodstuffs essential in nutrition have been identified. Attention has been given to the effect of many different factors such as diet, exercise, and temperature on the body composition, particularly of fat, bone, potassium, calcium, lean body mass, and extracellular fluid volume. Few of these items, however, have been studied in spaceflight, and none of them completely. From the sparse data we do have, we might infer that metabolism, nutrition, and body composition are not greatly affected by spaceflight and that pessimistic speculations are not borne out. It is possible, for example, that no change in oxygen consumption occurs other than that which would be expected from diminished activity of antigravity muscles. Yet, as suggested in Chapter 3, it is not excluded that cellular metabolism may be altered by changes in the gravitational force on cells or their organelles. This possibility can be studied by appropriate measurements in space.

Experiments on man are difficult to control. He is complex and willful. Furthermore, postflight tests are limited unless the experimental subject can be sacrificed. Animals have been successfully used in ground-based studies of the effect of diet on body composition and could likewise be used in a space experiment. On return to earth after a period in earth orbit, parts of the body would be weighed and analyzed. In these exploratory experiments the dietary preferences, body composition, and mineral and nutritional balances should be determined. Such experiments would provide a sound basis for planning further experiments for long-term manned flights.

An initial survey of metabolism requiring oxygen consumption, CO_2 output, food intake, urinary and fecal elimination, calcium balance, and nitrogen balance could be carried out on a single mammal such as a nonhuman primate. Later, body composition could be determined using a colony of rats. In each case, feeding *ad lib* should be tried, and the results of appetite and food preference noted. Regulated dietary intake could also be imposed. When these preliminary phases are complete, further detailed studies on rats could be done in a manned laboratory. The influence of circadian rhythms on the food-intake pattern should be thoroughly explored on the ground in connection with this study.

The studies suggested for a colony of rats may overlap those described for primate flights. Some analyses, however, cannot be made so easily on a single monkey whose survival and behavior during the recovery period after a spaceflight represents an important part of the experiment. With rats, using mature, nongrowing animals, a control group could be sacrificed and analyzed prior to flight, and another group analyzed in the same way after its return from flight. A third control group could be similarly studied in a ground-based simulation of the flight with the same feeding, light exposure, temperature, vibration, and acceleration. The analysis should include weights of skin, muscle, skeleton, body fat and water, bone calcium, and total body content of potassium, calcium, and perhaps other materials. Weights of different glands (adrenal, thyroid, etc.) might also be informative. The rats should be exercised during the flight, and the amount of exercise estimated from the rate of oxygen consumption and carbon dioxide output.

Experiments of this sort might tell us what types of food were optimal for use in space and how the total energy was utilized. There is some reason to believe that the body in space will contain less muscle and bone and more fat. While this study is not of the highest priority and some of the data expected might be derived from other experiments, it could well provide some valuable clues to subjects needful of further study.

VERTEBRATE DEVELOPMENT IN THE SPACE ENVIRONMENT

A study that would have great biological significance is one in which experimental animals would be reared from conception to maturation in a zero-*g* environment. Experimental and clinical studies of man and other vertebrates indicate that sensory systems (receptors and their neural connections) do not develop normally in animals raised without sensory input (e.g., visual systems of animals raised in darkness). Raising animals in the absence of gravity has become a possibility only with the development of space vehicles. If animals were allowed to develop in space from conception to maturation and then returned to earth alive, they would be of interest not only for the study of their gravity-receptor systems but also for the study of other anatomical and physiological changes. Because gravity acts directly or indirectly on so many of the body's systems, such experiments may lead to a broader range of studies than other investigations of sensory deprivation during development.

The choice of vertebrate species to be used will be of critical importance. Desirable qualities include: ease of maintenance during embryonic and neonatal phases, short period from birth to maturation, high probability of successful survival in space, highly developed gravity-sensing systems, and highly developed postural and locomotor systems. Because of the many technical difficulties that would have to be overcome to maintain experimental animals and because of the relatively long time required for maturation, the proposed experiments can best be done in a manned space laboratory. A 1-*g* centrifuge in the spacecraft would be very helpful as a control. If a suitable animal can be found that can survive in an unmanned satellite, preliminary experiments may be undertaken in preparation for more complete studies in the manned laboratory.

CENTRAL NERVOUS AND SENSORY SYSTEMS

The brain in its bony case is well protected against deformation resulting from changes in blood content or total volume, but it is not protected against changes in blood flow caused by changes in arterial and venous pressure. In this respect the absence of gravity should be, if anything, an advantage to cerebral circulation (and to blood flow elsewhere). The brain may also be affected by such factors as changes in water or plasma distribution that alter blood flow and oxygen supply to the brain.

Certain brain states potentially related to spaceflight, such as those resulting from sensory deprivation, excitement, disorientation, and severe anxiety, would be expected to affect other important physiological functions.

The marked decrease in sensory input during weightlessness is due mainly to lack of stimulation of the proprioceptive system (vestibular and kinesthetic) and to decreased stimulation of tactual and visceral receptors. This decrease may cause changes of behavior such as decreased alertness or drowsiness, fatigue, disorientation, interference with coordination, and changes in sensations such as those accompanying hunger. Although no serious disorders of these kinds have been reported in manned spaceflights to date, one would hesitate to predict that none will occur when flights are extended to 30 days, 6 months, 1 year, and longer.

Most of the behavioral changes would be best studied in man. A limited amount of information is available from astronauts' reports, but few attempts have been made to conduct controlled tests of performance of astronauts during spaceflights, and even physiological monitoring has been limited.

In the Biosatellite III flight, cortical and subcortical activities of the monkey were monitored electrophysiologically. Though full reports are not yet available, the EEG records did indicate stages of sleep and wakefulness; their value in indicating other conditions of the organism remains to be seen. Since the monkey performed reasonably well during the first five days in obtaining food rewards in the "game" that he had learned before the flight, future primate flights should be of longer duration. It is particularly desirable to monitor sleep and wakefulness cycles and to have a behavioral measure of the alertness of the animal and of his continuing ability to perform a task that involves memory and perceptual-motor skills.

RECOMMENDATIONS

The following recommendations relating to man and vertebrates in space are given in order of priority.

1. Because manned flights are apparently scheduled to continue, we *recommend* as a matter of highest priority that efforts be made to obtain as much in-flight behavioral and

physiological data as possible from the astronauts or passenger scientists. For metabolic studies, frozen samples of all urine and feces are particularly important. Measurements of oxygen consumption and CO_2 output are needed. Many such simple experiments, to provide basic behavioral and physiological data, for the welfare and safety of future astronauts can be proposed.

2. We *recommend* that several more monkey flights, with recoverable payloads, be carried out. These flights should be followed, if necessary, by primate experiments in a manned orbiting laboratory. All should be designed to obtain measurements of behavior capacities, diurnal rhythms, steroid levels, body-water balance, rates of respiration, amounts of blood pumped by the heart per minute, blood flow to different regions of the body, arterial and venous pressure, and similar quantities.

3. We *recommend* that observations using recoverable payloads be made on rats or other animals and, where possible, on man, concerning the changing composition of the body, including total weights, skeletal weight, total body fat, body water, cellular and extracellular water, calcium content and distribution, and total body potassium and sodium. So far as possible all those quantities should be related to food and water intake and total body balance.

4. We *recommend* that an experimental vertebrate be raised from conception to maturity under weightless conditions and then studied carefully after transfer to the 1-*g* environment of earth for its reactions and behavior as well as its gross and microscopic morphology.

CHAPTER 5

Radiobiology

Much of the biological experimentation carried out under the aegis of the National Aeronautics and Space Administration has dealt with the effects of ionizing radiations in space. There are two main reasons for this interest in radiobiology. The first is concern about whether there are unusual interactions between radiations and factors of the space environment, especially weightlessness. The second is the presence in space of densely ionizing cosmic radiations of high atomic number and energy. This latter type of radiation is unique to the space environment, and its biological effects are inadequately known.

INTERACTION BETWEEN RADIATION AND SPACE FACTORS

Although the space environment differs from that on earth, the differences are not so extreme as to lead most radiobiologists to expect strikingly different effects of radiations in space. Nevertheless, because some preliminary observations indicated that there might be a marked synergism between radiation and spaceflight factors in the production of biological damage, there has been considerable concern about radiation hazards in spaceflight. Furthermore, if such marked interactions were real, they would be of great theoretical importance to radiobiology.

In 1963, a Space Science Board Panel on Radiation Biology concluded that it was "barely conceivable" that radiations whose effects were well known under terrestrial conditions could have unsuspected biological effects when combined with the unusual features of the space environment. The panel recommended that a few simple but discriminating experiments be performed, not in an expectation of striking fundamental findings but as insurance against the remote possibility that the negative expectations were wrong. Since that time, two series of radiobiological experiments have been flown, one in the manned Gemini program and the other in the Biosatellite program.

These experiments were well designed. They made use of well-known biological systems with a sufficient number of individuals in each experiment to provide for statistical precision of the results. The systems were exposed to known quantities and qualities of radiation, and efforts were made to provide adequate controls. Well-defined effects were examined whose dose-effect kinetics were well understood. Furthermore, the systems were sensitive to radiation so that the observed endpoint would occur at a frequency that would allow statistical precision in the analysis.

The populations of cells studied were homogeneous in respect to their response to radiation. This is an important consideration because various cell types and various stages within the cell cycle not only show differential sensitivities to radiation *per se*, but they also can show a differential delay in mitosis and progression through the cell cycle. As a result, cells more sensitive to radiation might be sampled and compared with a less sensitive group of cells in the control experiments, which would lead to the spurious recording of an effect.

The experiments included entire dose curves. The importance of this in testing for possible synergistic effects cannot be overemphasized. The shape of the dose curve *must* be known, because many of the effects of radiation do not increase in a simple linear fashion with dose. If the observed effect increases at a greater rate than the first power of the radiation dose, any slight increment in "dose" caused by another factor could result in a large increase in the effect recorded. The magnitude of the change of response or effect would depend on the shape of the dose curves and the position on them at which the measurements were being made. A large change in effect would not necessarily indicate synergism.

The experiments carried out in the Gemini series were performed on such well-known genetic systems as the induction of chromosome aberrations in both human lymphocytes and *Neurospora* spores (manifested as irreparable mutations) and also on point (reparable) mutations and survival in *Neurospora conidia.* Neither experiment showed significant, repeatable interaction between radiation and spaceflight factors. The results obtained in the space environment were essentially the same as on the ground. The second Gemini flight did not confirm the anomalous result obtained in the first Gemini experiment on human lymphocytes, in which one-hit (and therefore relatively insensitive) chromosome aberrations seemed to increase in the space environment, whereas the far more sensitive two-hit aberrations did not. In the second flight, the yields of both the two-hit and one-hit phenomena were not significantly different from those obtained on the ground.

The *Neurospora* experiments employed both wet and dry spores. The experiments with wet spores seemed to show that, if anything, there was less of an effect of radiation under spaceflight conditions than on the ground--i.e., the dose-response curve of the mutations observed in space was somewhat lower than that obtained in ground controls. For dry spores, however, the space and ground curves are superimposable. The experimenter believes that the different effects observed in wet spores reflect physiological differences in the spores resulting from the higher cabin temperatures during the first day of the mission rather than from antagonism between radiation and some spaceflight factor.

At the same time that these experiments were planned and performed, similar experiments were proceeding for the Biosatellite program. Biosatellite II contained another *Neurospora* experiment and an experiment designed to test the effects of radiation on various genetic phenomena in the wasp *Habrobracon;* both included entire dose-response curves. Several additional radiobiological experiments were flown on Biosatellite II, but because of the limitation of space aboard the vehicle they had to be restricted to single doses. The two experiments that included entire dose-response curves showed no major differences between the effects obtained in the space environment and on earth, which confirmed the results obtained in the Gemini program.

The experiments using single dose points are less informative both because of the single doses and because some of them made use of equivocal biological endpoints. These results fall into three classes: those showing no spaceflight effect, those suggesting an interaction (synergism or antagonism) between a spaceflight parameter and the deliberate radiation exposure, and those suggesting an effect of the spaceflight profile alone in producing biological damage. The second group is of radiobiological interest; the third of more general interest.

In early reports of the Biosatellite experiments, comparisons of results on flight material and ground controls suggested synergism (or, in a few cases, antagonism) for several endpoints. More recently, however, additional ground-control experiments have been carried out in which the actual flight satellite was used or in which the biological material was subjected to a simulation of the vibration profile for the Biosatellite mission. Many of the differences attributed earlier to weightlessness were shown to have been generated by vibration instead. Others turned out to be peculiar to the flight vehicle itself. It should be noted that, because simulations of actual mission acceleration and vibration profiles are at best imperfect, failure of the Biosatellite vibration-control experiment to demonstrate a vibration component in some cases does not completely rule out such an origin. Nevertheless, we are left with a group of results from Biosatellite II which, on the basis of present data, *could* possibly be caused by interactions between spaceflight and radiation.

For the most part, however, the biological systems that provide evidence for such interactions are those that are least well understood. Thus, experiments in which larval *Drosophila* were flown and irradiated showed an increased yield of sex-linked recessive lethal mutations, X-Y chromosome exchanges, and chromosome breakage. Experiments on the much better understood adult *Drosophila* system, however, showed no such synergism for sex-linked recessive lethals, translocations, or mutations at four specific autosomal loci. There were, however, significantly more thoracic deformations than in flies hatching from eggs laid by the irradiated ground-control; but mating tests showed that the deformation must have been developmental rather than genetic. Its mechanism of production is poorly understood. In the *Habrobracon* experiments, the apparent synergism between radiation and spaceflight depended on decreased hatchability of the eggs that had been in meiotic metaphase or prophase during the flight. The decrease in hatchability is thought to be caused by increase in chromosomal nondisjunction. The better understood endpoints of recessive and dominant lethal mutation and of translocation production, however, showed no interaction.

In the *Tribolium* experiment pupae were flown, and wing abnormalities (in the treated animals) and dominant lethality (among F_1) were used as endpoints. The yields of both in the material irradiated in flight were greater than those in the irradiated ground-controls. We believe that these results are equivocal, however. Because pupae were irradiated, the endpoints examined were removed by many cell generations from the events of flight and irradiation, thus complicating the interpretation. Furthermore, there is little reason to think that the wing abnormalities were genetic rather than developmental. The frequency of the wing deformities induced by a given radiation dose varied greatly with time and reached higher levels in some ground experiments than in the flight animals. Finally, the animals in the experiments had been irradiated prior to flight, putting them on a steep portion of the dose-response curve, so that small changes in dose (or presumably in other factors) would lead to large changes in the frequency of the effect and would not necessarily indicate synergism.

In the *Tradescantia* experiments several of the endpoints yielded evidence for synergism, but a number of other did not. As in the insect experiments, those failing to show synergism were the better understood phenomena. Thus no synergistic effect was found in production of chromosomal aberrations or of pink or colorless mutations in somatic cells of either petals or stamen hairs. The mechanisms leading to the phenomena that did show synergism--stamen hair stunting, disturbed mitosis, and pollen abortion--are much less well understood. The positive results may well prove to be sensitive to factors influencing cell division or cell population dynamics in general.

In addition to a possible synergistic effect, the *Habrobracon* experiment showed an antagonistic interaction between the spaceflight environment and radiation. The endpoint used was female fecundity, which is poorly understood and subject to perturbations because of metabolic effects on the duration of the various parts of the cell cycle and on egg development. The investigator himself attributes the antagonistic effect on female fecundity to such an inhibition of cell division.

Thus, the analyses of the radiobiological data from Biosatellite II and Gemini, when considered as a whole, lead us to conclude that there are few, if any, repeatable, statistically significant results that indicate a synergism between radiation and spaceflight. If such interactions do exist, they are of very small magnitude and of little practical importance.

SPACEFLIGHT EFFECTS

Exposure of biological materials to the spaceflight environment in the radiobiological experiments did, however, demonstrate several unexpected effects, the mechanisms of which are not yet understood. Some of these effects were genetic. Three translocations were induced in *Drosophila* sperm in flight without irradiation and two were induced by vibration alone on the ground. Because spontaneous translocations are virtually nonexistent in *Drosophila* sperm this is a significant effect. Similarly, sex-linked recessive lethals in *Habrobracon* were induced both on the ground, by vibration alone, and in flight without deliberate irradiation. Vibration alone also induced pollen abortion and color mutations in stamen hair cells in *Tradescantia*.

Some of the effects were cytological. For instance, in *Tradescantia* it was found that mitosis was disturbed in both root-tip cells and microspores. In this case (and also in the stamen hair stunting in *Tradescantia*) the effects did not seem to have been induced by vibration because the ground-vibration experiments, although not perfect duplications of the actual flight-vibration profile, did fail to produce the effects. Qualitatively similar cytological effects were reported earlier by Soviet investigators.

Two of the organisms flown on the Biosatellite yielded evidence of an effect of spaceflight on chromosome nondisjunction. Increases were reported in brains of unirradiated *Drosophila* larvae and also in oogonia and oocytes of *Drosophila* adult females. Hatchability of eggs laid by *Habrobracon* females during the first few days after flight was significantly reduced, and, from the type of death observed, it was concluded that most of the embryo death was caused by chromosomal nondisjunction. Again, the nondisjunction results are in qualitative agreement with the results of earlier Soviet experiments with *Drosophila* oogonia and oocytes.

Although such spaceflight effects on cell division and chromosome segregation are not themselves effects of radiation, it seems likely that at least some of the indications of synergism between radiation and spaceflight could be explained by an influence on cell division and cell population dynamics. This is particularly likely for some of the endpoints that are removed by many cell divisions from the original events incurred during irradiation and spaceflight.

It should also be noted that such effects are by no means universal. Many of the systems flown on Biosatellite II failed to show such effects. Furthermore, preflight and postflight cytogenetic analyses on peripheral leukocytes from Gemini and Apollo astronauts have failed to show any effects that could be attributed to spaceflight *per se*.

Although the evidence is good that these effects of the spaceflight environment by itself are real, the difficulty and complexity involved in isolating the variables and in repeating, directing, and quantifying the stimuli are so great that we believe that this line of study should not be pursued further in spaceflight experiments until its complexities have been thoroughly studied in earth laboratories.

RADIOBIOLOGY OF SPACE RADIATIONS

Ambient Radiations

Ambient radiations in space, including those produced during periods of increased solar activity, consist almost entirely of electrons and protons. In the sense that the dose-effect relationships for these radiations have been well studied in the laboratory, no significant gaps in their radiation biology exist. The types and degree of hazard can be predicted adequately from physical measurements of the types and amounts of radiation present. Additional studies in flight of the biological effects of ambient radiations do not now appear necessary, but further physical data are required on total dose, radiation types and quality (LET* spectra), and depth-dose characteristics. Particular efforts should be made to measure and characterize the radiations emitted by the sun during periods of increased solar activity.

Galactic Radiations

Particles of high atomic number, Z, and high energy, E (HZE particles†), are currently unique to the space environment.

---

*LET, linear energy transfer. The rate of energy transfer and absorption in tissue expressed in keV/μm is numerically equal to rate of energy loss (REL), or dE/dx, but differs conceptually in that it refers to energy absorbed rather than that emitted.

†Arbitrarily defined here as those particles with a rate of energy loss (REL) in tissue of about 2000 keV/μm or greater, corresponding, for instance, to a Z of 18 (argon), E = 500 MeV/nucleon; Z of 26 (iron), E = 800 MeV/nucleon; Z of 35 (krypton), E = 1.58 GeV/nucleon; or any Z > 34, entire range of E.

HZE particles, of Z extending as high as 90 or greater, are observed in relatively small numbers in space. These stripped heavy nuclei can penetrate tens of centimeters into tissue, and energy is deposited at very high densities in the track core. These two properties combined suggest the possibility of biological or radiobiological effects, not documented to date, at the level of the cell, the organ, and the entire mammal.

In the absence of nuclear interactions, the particle loses energy by interaction with electrons. The rate of energy loss depends on Z and velocity and extends as high as 15 MeV/μm or greater. The track of the particle can be divided arbitrarily into a "core" and a peripheral region. The core is variously estimated as 10 to 50 A or more in diameter; the periphery is due to delta rays and has a diameter in emulsion as great as 0.1 mm or more (very high Z, sensitive film). At least half of the total energy is absorbed in the core; absorption falls off extremely rapidly as a function of lateral distance. Because of this marked nonuniformity of dose deposition along the track of HZE particles, magnitudes calculated for absorbed dose depend heavily on the values used for energy distribution and the dimensions of the biological target. Thus, calculations of dose and conventional dose-effect relationships are of little value in estimating the expected amount of cell killing. Although nuclear interactions occur frequently along the path of HZE particles with the production of "stars" or "showers" of secondary radiation, nevertheless the hazard from these interactions is considered small compared with cell damage in cells traversed by the primary particle.

Although HZE particles strike the body surface randomly in terms of location and angle of incidence, the interaction of a single particle with cells is ordered and is confined to the column of cells within or immediately adjacent to the path of the particle. As will be shown below, the cross section for cell inactivation in the track core may be effectively that of the cell diameter; thus, in the path a column of cells, at least one cell diameter in width will almost certainly be inactivated. Effects on cells not traversed by the particle and irradiated only by delta rays are probably negligible.

Although the usual dosimetric parameters such as absorbed dose and LET can be utilized to some extent in assessing the amount of cell injury and death along the path of the individual particles, neither these parameters nor the quality factor and dose equivalent in rem is useful in characterizing the radiation field or the over-all probability of its effect or in comparing the estimated hazard with that from ambient or ordinary laboratory radiations.

No direct information on cellular effects of HZE particles is available from laboratory experimentation, but data obtained with the High Energy Linear Accelerator (HILAC) using particles of low-to-intermediate Z and E and thin-layer cellular systems offer some guidance. The inactivation cross section for proliferating T1 human kidney cells is commensurate with the area of the cell nucleus at LET values of approximately 1 MeV/μm and above. These data indicate clearly that in proliferating mammalian cells the passage of a single particle of $\gtrsim$ MeV/μm will inactivate that cell with a probability of $\sim$ 1.0.

The above considerations apply directly only to dividing cells, the criterion of survival being the ability to produce progeny (colonies). They do not necessarily apply to nonproliferating cells in the adult mammalian body, for which the criterion of effect is inactivation, i.e., inability of the cell to perform its special function. Such cells are in general more resistant to radiation. Their dose-effect curves for conventional irradiation are poorly known, but they appear to exhibit a sizable "threshold," with doses of many hundreds to a few thousands of rads being required for 50 percent inactivation. Thus the difference in sensitivity to conventional radiation between neural cells in the brain and dividing mammalian cells in tissue culture is likely to be a factor of 10 or more. No direct information on the effects of HZE particles on normally nonproliferating mammalian cells is available, but several bits of data, taken collectively, suggest that the interaction of a track core with any part of the cross section of any cell, dividing or nondividing, will inactivate that cell.

Studies on the effects of single long-range (several centimeter) HZE particles at the level of the organ or entire mammal have not been possible in the laboratory; some data are available from balloon flights at northern latitudes and from laboratory efforts to simulate HZE tracks by means of microbeams of light nuclei. Efforts also have been made to observe histological damage from HZE particles in the brain and to correlate such damage with the expected tracks of these particles as determined from film emulsions fixed in a known position relative to the animal. However, experimental problems and internal inconsistencies in the data do not allow firm conclusions to be drawn.

The principal effect studied in the balloon flights has been production of gray hairs in black mice, and the data are consistent with the thesis that cosmic-ray particles inactivate melanin-producing cells in the hair follicle, and that this leads to the appearance of nonpigmented (gray) hairs.

Microbeam experiments have directed x-ray and deuteron beams on the skin (hair follicles) and brain. Hair graying was ascribed to a direct "hit" on and inactivation of the pigment cells of the hair follicle. Histological lesions were found in the mouse brain that conformed to the path of the microbeam; the damage was considerably less than that from wide-field irradiation. No behavioral or other effects of the microlesions in the brain were observed. However, the total number of tracks per brain was small, and specific procedures to detect possible changes in behavior or performance were not employed.

All the above data are consistent with the expectation that the principal hazard from HZE particles is at the organ level and derives from inactivated cells located in columns along the particle paths. The problem is essentially that of a "microbullet" that might destroy a column of cells, one cell width in diameter. No significant damage would be expected in renewal tissues such as the bone marrow, bowel epithelium, and testis, where inactivated cells are quickly replaced. Graying of the hair, discussed above, is not considered to be a hazard. The principal hazard would be expected in nonrenewing vital tissues, such as the central nervous system structures, in which a reduction in the number of functional cells by some small fraction might lead to functional impairment. Greatest concern would be for the loss of neurons. The severity of the hazard would depend on the fraction of permanently inactivated cells in an organ. This can be estimated primarily from the number of particles of a given Z, their E and range, and the appropriate inactivation cross sections for cells.

We do not have enough data to calculate the fraction of cells that would be destroyed in this manner, nor can we state what effects on organ function, if any, will result from the inactivation of, say, 1 percent of the cells in an organ. One might conjecture, from the known redundancies in central nervous tissues and from the small number of functional effects following deliberate or accidental cell or tissue destroying procedures such as surgery, needle probes, or some bullet wounds that the likelihood of serious effects would be small. Nevertheless, experiments are indicated.

RECOMMENDATIONS

1. Much of the interest in a possible synergism between ionizing radiation and spaceflight factors was founded on a

concern over whether radiation hazards to flight crews could be estimated on the basis of terrestrial radiobiological experience. The fact that flight experiments carried out to date have not produced convincing evidence of any important interaction between radiation and spaceflight increases our confidence that radiation hazards to men in space can be adequately estimated from physical dose information. Just as for estimates of radiation exposures in the terrestrial environment, however, it is impossible to overemphasize the importance of prompt and adequate physical dose measurements. In the absence of information on dose, dose rate, penetrating power, and quality factor, one can only assume the worst possible case, thus basing practical decisions on what might well prove to be gross overestimates of biological damage.

Since radiation hazards from electrons, protons, and other light atomic nuclei can be adequately predicted from terrestrial radiobiological experience if sufficient dosimetric information is available, we therefore *recommend* that additional in-flight measurements be made of total dose, radiation types and quality, and depth-dose characteristics of the spaceflight environment. We further *recommend* that the National Aeronautics and Space Administration continue to make every effort to assure that complete physical dosimetry is carried out on every manned mission so that estimates of radiobiological effects on crew health and performance can be made in the event of a solar flare during a mission. Such estimates could form a major basis for command decisions if a flare were to occur. In this connection, we *recommend* that NASA give consideration to the possibility of frozen storage of viable bone-marrow samples from individual astronauts for therapeutic use, should they receive large radiation doses from solar-flare events. It is quite well established that in cases of acute, whole-body exposures of from 400 to 1000 R, autologous bone marrow may save the life of the exposed individual.

2. Information now available on the fluxes and energies of heavy atomic nuclei (galactic cosmic rays) and on their biological effects is insufficient to allow adequate evaluation of the hazard they present for long-duration manned spaceflight. We *recommend* further investigation of this problem with both additional physical measurements in space and ground-based radiobiological experimentation.

3. Radiobiological experiments carried out on Gemini flights and in Biosatellite II have shown that, for well-defined genetic endpoints, there is no significant synergism between radiation and the spaceflight environment. The question of whether space factors modify radiobiological principles as we know them has been answered in the negative. In this context the experimental program has been successful. We conclude that further flight experiments on such factors are not necessary.

4. Several less well-understood endpoints gave evidence in flight experiments of biological damage induced by the spaceflight environment alone. At present, the use of such perturbations to extend basic knowledge of biological systems seems to us limited. We *recommend* that these phenomena not be studied in spaceflight experiments until the complications involved in isolating the variables and repeating, directing, and quantifying the stimuli have been thoroughly studied in ground laboratories.

5. Several of the radiobiological experiments flown in the space program were excellently designed to give unequivocal information about the point being studied. Some were not. We *recommend* that, in the design of future experiments, particular attention be given to those criteria that would ensure that the biological system used is well understood and lends itself to a proper understanding and analysis of end effects.

CHAPTER 6

Animal Orientation and Tracking

The greatest contributions of satellites to biology in the next ten years may well come from their use in the study of our own planet. The powerful on-board sensing techniques currently being developed by the National Aeronautics and Space Administration and others enable satellites to monitor continuously, on a global scale when necessary and with increasingly finer resolution, a wide range of interesting aspects of our environment. For example, the multispectral sensing techniques already in use measure the phenology of vegetation, atmospheric turbidity, crop and forest production (and disease), oceanic productivity, surface water and rainfall effects, and a host of other variables.* These data are integrated by the systems ecologists with the use of computers, into models that describe, interpret, and predict changes in the complex interactions that make up our global ecosystem. When sufficient information is available from closely distributed locations, systems ecologists can also contribute much to the understanding of local environmental problems. Multispectral sensing from satellites can thus be expected to make major contributions to the analysis of pollution, conservation, and productivity problems.

Satellites can also contribute to our understanding of processes on earth through radiotelemetry. This is the topic that

---

*See Philip Johnson, ed., *Remote Sensing in Ecology* (University of Georgia Press, Athens, 1969).

we develop in this chapter, using the particular case of maintaining contact with free-ranging animals in order to acquire information about their methods of orientation, behavior, energy expenditure, physiology, and responses to environmental conditions. The plan, in brief, is to equip animals with a device that transmits signals whenever it is interrogated by a satellite. The signals would convey information about the position, physiological state, and environment of the animal. The satellite would receive these data, process them as necessary, and transmit the information to ground stations where the analysis would be completed.

THE PROBLEM OF ANIMAL ORIENTATION

The study of animal travel, particularly long-distance migration and homing, has been of interest to scientists since Aristotle's experiments with marked swallows. Many types of animals make pinpoint landfalls after long journeys over or in the ocean, where to humans no obvious landmarks exist. These adaptations for navigation rank among the most striking products of animal evolution. We still know astonishingly little, however, about the mechanisms that drive such animals to travel and to select particular routes, the guidance systems they utilize, the physiological hardships they encounter, the energy they expend, or the precise environments through which they move.

Numerous hypotheses have been proposed to explain the navigational ability of animals. Visual features of the local landscape are probably important cues for many species; others probably use the sun and the stars to determine direction. But such a compass sense has limited value unless the animal also determines the direction of its destination. This requires navigational ability and information about actual position relative to that of the goal. Several hypotheses assume that animals use both celestial and geophysical coordinates in migration and homing, others that they navigate by reverse displacement, but empirical support for any of these assumptions is meager.

Radar studies of bird migration show that oriented flights commonly occur under heavily overcast conditions when celestial cues are unavailable. To explain these phenomena other hypotheses invoke geomagnetic cues, wind direction, the Coriolis force, and inertial navigation mechanisms. To account for the directed open-ocean movements of aquatic organisms, other hypotheses invoke currents, heat gradients, olfaction, and acoustical cues.

To determine which of so many potential cues are in fact used in homing and migratory navigation, detailed knowledge of what animals actually do, and what they encounter in their travels, is required. Yet no one to date has ever obtained a complete, detailed record of the exact route traversed by any individual migrant. This lack of information is a major obstacle in developing an acceptable animal navigation theory. It could be corrected by obtaining position-and-behavior data through the use of orbiting and geostationary satellites. Satellite technology developed for other purposes, if modified and expanded for biological research, could answer important questions about free-living animals on land, in the sea, and in the air.

Consider, as an example, the breeding congresses of animals on tiny oceanic islands. The Atlantic green turtle migrates 1300 miles from the coast of Brazil across the apparently featureless ocean to make a landfall on Ascension Island, five miles in diameter. Though much as been learned about the sensory capabilities of these turtles and about the cues used by hatchlings to locate the sea, massive efforts employing both aerial-visual observations and ground-based radiotelemetering have failed to track them in the open ocean for more than a few miles. Do they mass somewhere along the Brazilian coast before departing for Ascension? What specific routes do they follow? Do they travel in large groups? Are ocean currents cues for orientation? Does travel continue at night? Does their orientation become more accurate as they approach the Island? Do any turtles miss the landfall, and, if so, do they manage to reorient and reach Ascension? Some of these questions could be answered by data from a radiopackage towed by the animal providing information (in response to satellite interrogation) on the turtle's position, velocity, heading, physiological condition, and environment. Such information would not only be basic to animal navigation theory but also to our efforts to protect this endangered and economically important species.

Another example is the Golden Plover, a 150-gram shorebird that breeds in the Arctic tundra and migrates 5000-6000 miles to winter in central and southern South America. Spotty evidence suggests that adult and young plovers migrate at different times and follow different routes to their winter quarters, the adults on an over-ocean voyage (possibly 3000 miles nonstop), the young over land. Satellite tracking of this species would provide an excellent opportunity to study a highly evolved migratory phenomenon. What are the actual routes followed? Do the young in fact migrate along a different path, and, if so, are inexperienced birds less accurate navigators than the adults? Does this give any indication of the method of information transfer--inherited, imprinted, or acquired? Is migration affected by long periods of overcast? How do nocturnal movements compare with daytime travels? How do the birds cope with the shift in the trade winds from Westerlies to Easterlies as they proceed southward?

There is little hope that ground-based tracking systems can provide the necessary data about these long-distance travelers, yet these are the very species that have evolved the most highly developed physiological and navigational capabilities and therefore hold the most interest and promise for experimenters. Even the age-old problem of homing in pigeons has not yet been solved. Pigeons lend themselves readily to experimentation, and this field is, with the possible exception of bee orientation, methodologically the best advanced and may be considered the closest to solution. Nevertheless, the difficulty of keeping precise track of the low-flying birds by airplane or ground tracking has thus far prevented sufficiently useful accounts of their homing behavior.

Attempts to answer the questions posed by these feats of animal navagation require action along two different lines. The first, as just described, is systematically to collect descriptive data on specific migratory tracks. Such data will eliminate certain hypotheses. The second approach is to test hypotheses and models experimentally. This can be done, for instance, by tracking animals that have been displaced in time or space or both, with or without artificial modification of their sensory capabilities. The potentialities of satellite tracking thus include not only descriptive, correlative, data-gathering studies but the testing of specific hypotheses as well.

A successful tracking program could yield further valuable results. As man's impact on his environment grows increasingly disruptive, the opportunity for scientific study of wild animals in their natural habitat recedes or, as in the case of the passenger pigeon, disappears forever. It is, fortunately, not yet too late to perform studies on some species. Moreover, many of the animals to be tracked are, or have been, important sources of human food. When they range between breeding and feeding grounds separated by vast expanses of intervening territory, detailed knowledge of the routes and schedules of their migrations is essential for their protection and management. While the research proposed here is aimed mainly at answering scientific questions, the same data would also provide a better basis for stewardship of our diminishing wildlife resources, both through the results of the research itself and the technology developed to carry it out.

The studies could enhance our understanding of the vector transfer of disease via migratory and nomadic animals, by revealing potential routes of transport that may otherwise escape attention.

For many years some investigators have studied the navigation systems of animals because the results of their research might eventually find practical applications: if an unknown sensory modality or environmental cue is indeed responsible, the discovery could be put to use for the benefit of man.

Finally, major technical advances must be made before all the species of interest can be studied. Such advances in electronic miniaturization would undoubtedly find wide application in aviation, medicine, and other fields.

TECHNICAL REQUIREMENTS

To perform the experiments outlined will require, first, a satellite instrumented to query the animal-borne transmitter, receive signals from it, and transmit the data to ground stations for analysis. We are assured that existing capabilities can satisfy these requirements.

As for the animal-borne transmitters, or "platforms," further miniaturization is necessary in most cases. If the estimate that platform weight should not exceed 5 percent of animal weight is correct, platforms weighing about 0.5-g for a very small migrating bird, 50-g for a racoon or rabbit, and 500-g for a small deer will have to be developed. Platforms are already available to study animals as large as elk, and some of the biological programs need not await these developments.

Opinions vary on the feasibility of reducing platform weight to the few-gram or fractional-gram levels suitable for the smallest animals of interest. Though we are not prepared to say whether one opinion or the other is correct, we note that certain engineers,* with quite limited resources, have produced tracking-telemetry systems that approach the necessary weights. A 40-g thrush wearing a 2.2-g transmitter with a 25-mile range has recently been tracked 7-10 h over 150 miles by vehicle. A 15-g unit having a 100-mile range and 5-h lifetime also exists; its range might be just enough to contact an orbiting satellite. In any event, this is existing technology; further power-cell miniaturization may be expected to increase the range or lifetime of transmitters, and perhaps the rapidly

*Howard A. Baldwin, Sensory Systems Laboratory, Tucson, Arizona, and W. W. Cochran, Illinois Natural History Survey, Champaign-Urbana.

expanding transponder technology will at some future time remove the power source from the platform altogether. Whether such developments take place, satellite tracking of many animals seems technically feasible at the present time.

The sensors to be carried by animals in these experiments are of three types: those that establish the geographical position of the platform, those that sense the physical characteristics of the environment, and those that monitor the physiological state of the animal. Available sensors would permit reasonably accurate measurements of at least some parameters in all these categories. Among needed developments and refinements, however, are sensors to permit the study of the physiology of traveling animals, both because of the intrinsic interest of such measures and because they would supplement and help to interpret orientation and navigation performance. Some features that might ultimately be monitored are body temperature, metabolic rates, circulatory, respiratory, and motor activity, and even blood chemistry. Suitable sensors for many of these measurements are already available, but further miniaturization of most of them will be necessary before they can be applied in long-range monitoring, especially when the studies involve small animals.

Consideration also should be given to tracking by aircraft rather than by satellite. Aircraft tracking in conjunction with satellite observations might greatly improve the quality of the data in particular cases, and aircraft should of course be used if they can accomplish a given task more efficiently, as, perhaps, in tracking for short times over small distances. In the absence of platforms of a size suitable for small birds, visual tracking from airplanes, stationary and moving balloons, and by radar may be helpful even though, as noted above, the success of these methods has been limited in the best-studied case--the pigeon. The availability for this purpose of research aircraft and other facilities to biologists with well-planned experiments is very desirable.

RECOMMENDATIONS

1. Because space techniques seem readily applicable to ecological problems we *recommend* that a panel composed of experts in the various branches of ecology and in the use and capabilities of multispectral sensing devices be convened to carry out an evaluation in depth of this promising application.

2. We *recommend* developmental work aimed at extreme miniaturization of electronic devices, or platforms, to be mounted on free-ranging animals to fix geographical position, monitor relevant aspects of the environment, determine the physiological state of the animal, and relay this information on demand.

3. We *recommend* that a design study be initiated for satellite instrumentation to establish and maintain contact with the animal-borne platforms in order to collect information from the platform sensors and relay it to ground centers for analysis.

4. We *recommend* that specifications be developed for a general support system for the biological studies, consisting of a network of monitoring stations to receive telemetered data from satellites and receiving and transfer centers to process such data and transmit them to investigators. In this connection, we suggest that the National Aeronautics and Space Administration tracking radar capability and other ground-based facilities be made increasingly available for biological tracking and monitoring, not only to supplement satellite-based studies but also to support those not requiring satellite surveillance.

5. We *recommend* that an organization such as the Smithsonian Institution or the National Science Foundation's proposed National Institute of Ecology be encouraged to develop a coordinating mechanism for dissemination of information on technological advances, changing requirements, and opportunities for biological tracking research.

We see no useful purpose in recommending a rigid schedule for developments in satellite-tracking investigations. The priority of experiments and technological developments will be largely established by the investigators who propose the research. One early need, however, is for studies of migratory animals that appear to be in danger of extinction or of extirpation from large sections of their ranges. The blue whale is such an animal.

6. Because successful tracking of animals carries with it the danger of improper exploitation of valuable species, we *recommend* that the National Academy of Sciences examine this matter and take appropriate preventive steps with both the U.S. Government and the International Council of Scientific Unions.

Study Participants

* Kenneth V. Thimann, *Chairman*
Provost, Crown College, University of California, Santa Cruz

Harry Beevers
  University of California, Santa Cruz
M. A. Bender
  Oak Ridge National Laboratory
*L. R. Blinks
  University of California, Santa Cruz
Victor P. Bond
  Brookhaven National Laboratory
H. A. Borthwick
  U.S. Department of Agriculture (ret.)
Frank A. Brown, Jr.
  Northwestern University
Warren L. Butler
  University of California, San Diego
A. F. Carr
  University of Florida
Arthur B. DuBois
  University of Pennsylvania
Stephen T. Emlen
  Cornell University
*Donald S. Farner
  University of Washington
*Wallace O. Fenn
  University of Rochester
*Robert Galambos
  University of California, San Diego
*David R. Goddard
  University of Pennsylvania
*H. K. Hartline
  Rockefeller University
Alexander Hollaender
  Oak Ridge National Laboratory
Lionel F. Jaffe
  Purdue University
*Harold P. Klein
  NASA, Ames Research Center
*Henry Koffler
  Purdue University
A. Carl Leopold
  Purdue University
Daniel Mazia
  University of California, Berkeley
Michael Menaker
  University of Texas
William D. Neff
  Indiana University
Barbara G. Pickard
  Washington University
*Colin S. Pittendrigh
  Stanford University
Klaus Schmidt-Koenig
  Duke University
*Wolf Vishniac
  University of Rochester
*Sheldon Wolff
  University of California, San Francisco
Raymond E. Zirkle
  University of Chicago

Frank G. Favorite, *Study Director*
Space Science Board

*Executive Committee

SCIENTIFIC CONSULTANTS AND TECHNICAL ADVISORS

Frank C. Bellrose
  Illinois State Natural History Survey
Allan H. Brown
  University of Pennsylvania
Robert N. Colwell
  University of California, Berkeley
Herbert L. Eaker
  NASA, Goddard Space Flight Center
Larry J. Early
  Wallops Station
David D. Few
  NASA, Ames Research Center
Alfred H. Gaehler
  NASA, Ames Research Center
Sidney R. Galler
  The Smithsonian Institution
Loyal G. Goff
  NASA Headquarters
Solon A. Gordon
  Argonne National Laboratory
Eberhart Gwinner
  University of Washington
Franz Halberg
  University of Minnesota
William J. Hamilton III
  University of California, Davis
D. Mark Hegsted
  Harvard University
John D. Hilchey
  NASA, Marshall Space Flight Center
Dale W. Jenkins
  NASA Headquarters
Jerry Johnson
  NASA, Marshall Space Flight Center
Adelbert L. Lavery
  NASA, Electronics Research Center
Robert A. Lavond
  NASA, Ames Research Center
R. G. Lindberg
  Northrop Corporation
Dan L. Lindsley
  University of California, San Diego
Everett E. Maynard
  NASA, Ames Research Center
Nello Pace
  University of California, Berkeley
Bruce W. Pince
  Space Defense Corporation
Grover C. Pitts
  University of Virginia
Orr E. Reynolds
  NASA Headquarters
Arnold H. Sparrow
  Brookhaven National Laboratory
Nelson T. Spratt
  University of Minnesota
Beatrice M. Sweeney
  University of California, Santa Barbara
Thor Tendeland
  NASA, Ames Research Center
John W. Tremor
  NASA, Ames Research Center
Charles A. Wilson
  NASA, Ames Research Center