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Welcome to BRH

Introduction to the Biohistory Research Hall

Tokindo S. Okada
Director General

A Concert Hall for Science

My enthusiastic love for classical music has endured for more than half a century, albeit my never having received any formal education in music and my total incapability of understanding complicated music scores. On the whole, music in the original form created by composers is unapproachable for the general public. The only opportunity for most people to appreciate the beauty of music is solely provided by performers.

Likewise, science is in principle, not readily accessible to people outside the scientific community. It is clear that "performers" are equally essential to present the wonder and beauty of science. However, such talent is much more difficult to find and their professional authority much less firmly established in our society, compared to their musical counterparts. Therefore, the idea of creating a place where people could enjoy "performances" of scientific research presented through talk, art, music and contemporary auditory and visual technologies, was conceived.

I recall a statement by Dr. Maxine Singer, the President of the Carnegie Institution of Washington, at a meeting held in Japan, that "if there is a common world-wide culture, science is its name." This sentiment is the motivating force behind the creation of the Biohistory Research Hall (BRH); to promote such a "culture" which is easily accessible to the general public. My hope is that what a concert hall does for music, our Research Hall is doing for science.

Living Organisms are Full of Wonder

Undoubtedly, biology provides one of the most suitable "repertoires" for performances at the BRH, having such immense sources of wonder. The individual phenomena of each organism, from bacteria to mammals, and the inherent beauty of each species are fascinating and awe-inspring. If we could only be given more

Three main activities at BRH

Laboratory Research

(see pages 10-13 and 26-29)

At BRH, we conduct experimental research in the fields of evolutionary and developmental biology, which contribute important knowledge towards the understanding of both universal rules and diversities in the biological world.

Activities for the Public

(See pages 22-25, 30-31)

Detailed theories and results of modern biology are highly specialized, but with proper presentation, the general conclusions are often quite easy to understand and the research process itself can be fascinating even to non-specialists. At BRH, research results and scientific methods are shared with the general public through a variety of innovative presentations utilizing videos, computers, music and other forms of art media. We also organize courses for young people and provide guided laboratory tours to give people a chance to become personally involved with science.

Perspectives on an Integrated View of Life

(page 6-8, 30-31)

Based upon our understanding of life from discoveries in modern biology, scientists and researchers at BRH conduct activities to offer perspectives on an integrated view of life. In collaboration with philosophers, artists and specialists from a variety of fields, and complemented by public participation, we hope to produce new perspectives on the interrelationship of nature and humanity.

opportunities to appreciate them, these natural wonders would no doubt give much joy to mankind.

At the BRH, one of our special interests, among many others, focuses on the "changes of organisms with a lapse of time." These changes include the transformation of fertilized eggs into adults as well as those incurred during evolution over a vast span of time. Through the ongoing effort of scientists, the exciting tales of each living organism are being told in increasing detail. We refer to these historical tales as "biohistory." This way, concepts utilizing such key words as evolution, ontogeny, biodiversity, DNA, genetic code etc., can be integrated into a single historical story. The topics of our research activities are closely linked to the categories of Developmental Biology and Systematic Biology (based on DNA studies) in modern biological sciences.

BRH Campaign

The displays in the BRH are open to the public throughout the year. Our quarterly magazine, *Biohistory*, tackles diverse topics dealing with various aspects of biohistory, and is illustrated with color photographs. Our activities are conducted in collaboration with a variety of like-minded people, not only scientists, but artists, musicians, and writers, among others. Ongoing experiments in our research laboratories may be observed by visitors during "laboratory tours." We organize a "summer school" to allow children to become familiar with modern biology, i.e., how to isolate DNA. Last summer, we started a new course to provide adult amateur naturalists with an opportunity to try PCR techniques in taxonomic studies.

The BRH is, despite its modest scale, a wonderful challenge. We welcome you to enjoy science with us.

Tokindo S. Okada,
Director General of the Biohistory Research Hall (1993-present), is a Professor Emeritus of Kyoto University and Vice-President of the International Union of Biological Sciences (1991-present).
Specializing in developmental biology, he has served as President of the International Society of Developmental Biologists *(1982-86)*, and has been awarded the Harrison Prize from the Society (1989). He was Director General of the National Institute of Basic Biology (1984-89), as well as President of Okazaki National Research Institutes (1989-91). *In 1995, he received prestigious rank of* "Person with Cultural Merit" from the Japanese Goverment.
(Photo: Kenzi Akagi)

Perspectives

Biohistory

New Perspectives on the Relationship between Science and Society

Keiko Nakamura
Deputy Director General

Keiko Nakamura has been studying the relationship between biological sciences and society for over 25 years. "Biohistory," a term coined by Nakamura, refers to the creation of a comprehensive intellect based upon biology and new perspectives on the relationship between science and society.

Questions about "Life"

Everyone has questions about life, and usually they fall into one of two categories. One concerns the self, and in a slightly wider perspective, the human being. What am I? Where did we come from, and where are we going? The other relates to our interest in other living creatures around us. They fascinate us by their diversity. Most of you probably can recall a childhood memory of patiently observing ants and other insects.

Roughly speaking, questions of the former kind were systematized in the form of natural philosophy, and those of the latter in the form of natural history. Natural philosophy mainly sought universality, and natural history pursued diversity.

In Quest of Universality -Discovery of Genes in Natural Science

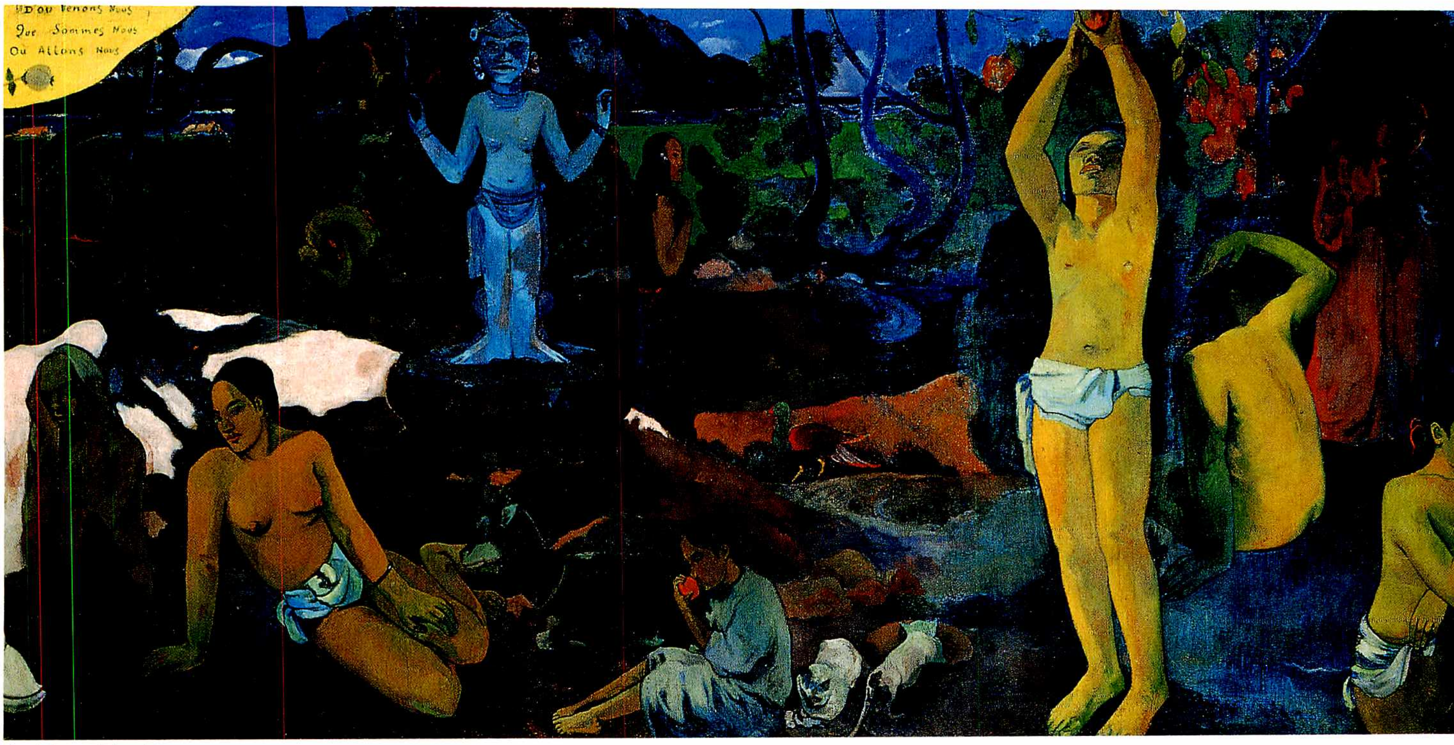
The natural science born in the 17th century introduced a strong quest for universality in natural history. This movement, which developed mainly in physics starting with Newton, began to affect biology in the 19th century. Three discoveries were largely responsible for this development in biology. One was the cell theory, which was derived from microscopic observations: it revealed that every living organism is composed of cells, and that cells are not only the units of structure, but also of function, in the organism. The second was the theory of evolution: symbolized by Darwin's "Origin of Species," which considered every organism on earth, despite astonishing variety, as descending from common ancestors. The third factor was Mendel's theory of heredity, proposing the existence of elements, afterward referred to as "genes."

In the 20th century, by the application of techniques from chemistry and physics, various substances essential for life were identified and their functions clarified. Following the discovery of enzymes (proteins), it was found that the entity of genes was DNA, which has a beautiful double helical structure. Molecular biology made astonishing progress, revealing that all organisms use DNA as genes. The transmission of genetic information from parent to offspring was explained as DNA replication. Vital processes in the body were explained as functions of proteins which were synthesized under instructions from DNA. The pursuit of universality in living organisms proceeded steadily.

Pursuit of Diversity Again - From Genes to Genomes

In the 1960s, many researchers believed that study of genes via DNA analyses would reveal every living phenomenon and allow us to understand what life is, as embodied by the saying "If you understand *Escherichia coli*, you will understand elephant."

I enjoyed molecular biology research during this time, but in the 1970s, I switched my field to that of considering the relationship between life sciences and society. I was quite fascinated by DNA research, but at the same time, I was troubled by the problem of its separation from daily life. The emergence of recombinant DNA technology made even clearer the issues to be considered. The development of this technique made it possible to study multicellular organisms. Many "wonders of living organisms" were beginning to be clarified in rapid succession, such as how cells communicate with each other to form an individual, or how the immune system is able to process such a diverse range of foreign substances. How fascinating! This was the honest feeling among researchers. The outside world of non-specialists, however, considered recombinant DNA technology as a "God-challenging technique, manipulating life." The usefulness of the technique was recognized in the form of biotechnology, but the public was unaware that many marvelous discoveries concerning "living creatures" were being made in biology by means of this technique, due to lack of communication. Society in general, regarded scientists as those who do not see living creatures as living creatures, but rather, reduce them into more inanimate



Paul Gauguin's picture, "Where do we come from? What are we? Where are we going?" (1897) These are questions which are asked by everyone, regardless of whether he/she is an artist or scientist. (Tompkins Collection, Museum of Fine Arts, Boston)

objects such as genes. It was indeed true that, due to the fascination with DNA, actual living organisms were disappearing from the minds and laboratories of many researchers. I, however, felt that one should know what life is. Therefore I searched for a way to unite the interests of researchers with those of laymen, who, I believed, both have a love for living things and curiosity to understand life.

The situation in research gradually changed during the early 80s due to new discoveries clarifying many life processes. This change can be summarized in short by saying that the interest in diversity returned. It became possible to examine complex vital processes such as immunity, development and the workings of the nervous system. As a result, we can ask such questions as to what extent, for example, the fly and mouse are identical to each other and in what ways they differ from one another. At the same time, it became clear that life cannot be reduced to genes. Therefore genetic determinism and reductionism began to disappear from the minds of molecular biologists.

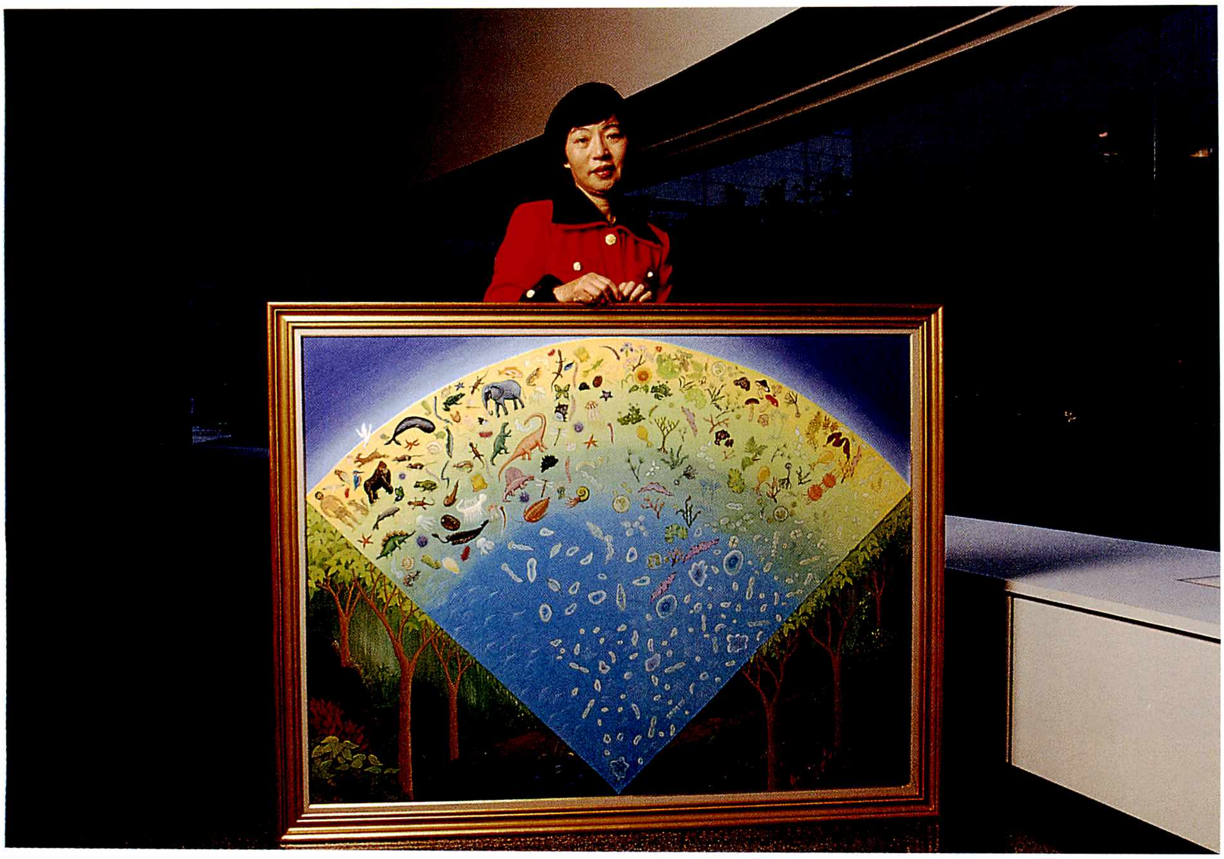
These new movements gave me a hint as to how to solve the problems of DNA research and build a new relationship between research and society. I realized that the "genome" could have a great potential to unite universality and diversity.

Bringing Science to Everyday Life by Bridging Universality and Diversity

The genome is "DNA in its entirety present in the nucleus of a cell" and contains all the genetic information needed to form an individual. Each human cell contains a human genome and each mouse cell a mouse genome. When I noticed these multiple aspects of genome, the thought occurred to me that it could be a powerful tool to understand life. First, "genome" has the face of universality because its DNA constituent is present in every living thing, and at the same time, it has the face of diversity because it differs from organism to organism. Second, genome can symbolize life from the levels of molecules, cells, individuals and species. The genome is made up of DNA molecules and the information contained in the genome can form cells and individuals. Moreover, genome symbolizes species.

Using the genome, we can regain a close watch on living creatures which were forgotten during the early years of DNA research. To promote research in this direction, it is necessary to clarify what the "genome" is. The genome of a given living organism is passed from its parent or parents (in the case of asexual reproduction, the genome of the parent is passed intact, and in the case of sexual reproduction, each parent contributes one half of its genome). When traced back in this manner, the origins of the genomes of all living organisms should lead back to the origin of life. When genomes are analyzed, we can reveal, for example, how humans became human and how *Escherichia coli* became *Escherichia coli*. Moreover, both similarity and difference between humans and *Escherichia coli* will be found. In this way, we will be able to see the history of life and the relationship of all living creatures on the earth.

There are two ways by which one can examine the history of life and the relationships of living creatures through genome analysis. One is to elucidate the process of evolution and the other is to examine the process of development. To examine the history of living organisms (evolution) and the process of forming individuals (development) is to see living organisms in their entirety and to pay attention to their diversity. At the same time, it places great significance on the concept of "time," which



Keiko Nakamura with the drawing "Biohistory," in which the history and diversity of life on earth are illustrated. It is an attempt to show a phylogenetic tree in an artistic way. (Original idea by Keiko Nakamura with consultation of Marina Dan, Osaka City University. Drawing by Ritsuko Hashimoto.) (Photo: Yoshiki Geka)

has largely been neglected in science that was based on reductionism and determinism. We named this field of research into the history of organisms, "biohistory." Although biohistory relies on modern biological techniques such as DNA analysis, it is not restricted to "science" in a narrow sense. In biohistory, we emphasize broad aspects of biology, such as the art contained within it. One can find many interesting "stories" of life in biology. To reconstruct these fascinating stories using research results is one of the most important activities of biohistory. Fortunately, in the front ranks of biological research, investigation into the function of genes in developmental processes (including apoptosis), cell division, signaling, etc. is becoming popular. As such studies continue to advance and to reveal the involvement of genome activity in more phenomena of life, we will get closer to the elucidation of the magnificent history of all living creatures.

What We Will Learn from Biohistory

Almost eight years have passed since we started the field of biohistory (the Biohistory Research Hall was opened in 1993). During this time, many biologists have demonstrated their support and cooperation. Strong interest was shown by specialists in other fields of science and the arts, and by the general public. Many stated "I am thinking the same thing." Biohistory is a comprehensive approach to the questions of life, such as what we are and why such diversity exists among living creatures. The constant support we have received has given us the confidence to continue pursuing the young field of biohistory.

In the society of the future, the understanding of "what is life" will become more important than ever. To ensure quality of life, we must solve many problems concerning environment, population, food, medicine, education, among others. Finding solutions will require a solid understanding of the meaning of "life."

On the basis of the results of science which originated from the dualism of Descartes and has been strictly observing the basic principles of objectivity, logic, universality, analysis and reduction, biohistory attempts to establish a way of thought that comprehends "life" in its entirety. We hope that biohistory will take root and contribute to the formation of the future society.

From our experiences over these past four years at the Biohistory Research Hall, we are convinced that biohistory has the potential to unite science and humanities, involving both academic and lay persons.

Keiko Nakamura is Deputy Director General of the Biohistory Research Hall (1993-present). She graduated from the University of Tokyo and obtained her Ph.D. in molecular biology. In 1971, she became Chief of the Laboratory for Social Life Science and in 1981, became Director of the Department of Natural and Social Environmental Science at the Mitsubishi-Kasei Institute of Life Sciences.
She became a professor at the School of Human Science, Waseda University in 1989. She was a visiting professor at the Center for the Advanced Research in Science and Technology of the University of Tokyo (1995-96), and now is at Osaka University (1996-).
She is the author of many books and also well-known for her translations of such important books as the "Double Helix" and "Molecular Biology of the Cell" into Japanese.

BRH Salon

Wonderful Mechanisms of Life

Kenichi Matsubara
Professor, Nara Institute of Science and Technology, Molecular Biology

Voyaging to Galapagos. Penetrating jungles. Diving to the bottom of the sea. Probing into a drop of water or clod of earth through a magnifying glass...These reports are always full of wonders. We find myriad forms of life everywhere. Even in the most unlikely environments, we find well-adapted inhabitants. They are very diverse, proudly displaying all the possible variations of life.

We also encounter other forms of wonders in these non-daily experiences, such as the astonishingly complex relationships between many creatures. What wonderful mechanisms for living! When we probe further, from cells to genes, we can see yet other great marvels in their structures. The fine workings and regulations. What amazes me is that all living forms strictly obey the basic forms and common functions of life,

with no exception. Like siblings from common ancestors, albeit their current widely diversified natures obtained during the course of evolution. I visualize a great stream of life, continuing without a break for 3.5 billion years since the birth of life, which has repeatedly experienced drastic changes in the global environment, successive mass extinctions, and great evolution.

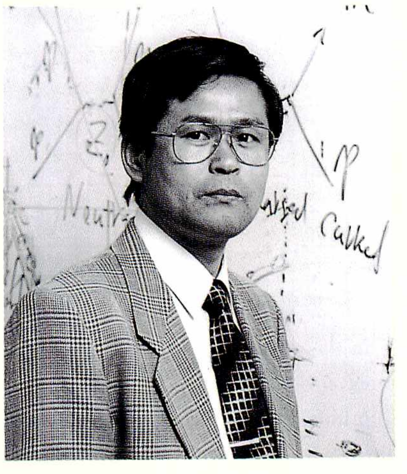
Research on the genome is now in progress. Much effort is being made to clarify how many genes are present in the human being, what they are, and how they give instructions to regulate the body. This is a quite formidable task because of the huge amount of DNA involved. The genome contains both the written instructions controlling the life of each individual, and the record of its evolutionary process to the present. We can find dead genes, traces of ad-hoc additions and modifications. We see also evidence of various viral infections that must have tormented our ancestors. Wonders related to time are now emerging with reality. "Biohistory" is indeed fascinating and enjoyable.

Into the Age of Life Sciences

Katsuhiko Sato
Professor, University of Tokyo, Cosmology

My field is cosmology, the study of how the universe was born and how it has evolved to attain its present profound configuration. The tools of our research are the physical laws that have been established by experiments here on the earth. The motion of all matter is governed by physical laws whose parameters were initially set at the birth of the universe. What we wish to understand is the actual scenario through which the universe has evolved under these physical laws.

I have a strong interest in life, because life cannot be explained in terms of "simple" laws such as those applied to the universe. We are machines working according to physical laws, but at the same time we decide our actions by our own will. This apparent contradiction, which has been in



contention since the early days of natural philosophy, has no easy answer. Our free will was attained over a long evolutionary process beginning 3.5 billion years ago with the birth of the first unicellular organisms. Now nearly one hundred million different types of organisms exist on the earth. Using basic elements from the universe such as H, C, N and O, such a diverse world of life has been created through natural selection. When we examine an individual life, we can see in its history, nature's trials and errors. As "biohistory" signifies, life cannot be understood without diversity and history.

I firmly believe that the 21st century will be the age of life sciences. The 20th century has been an age of science and technology based upon physics. Into the next century, great progress in life sciences will result in significant reforms in human society. The BRH has a very important mission; to read the stories of life, and to create a new civilization.

"I"-a Creature

Toru Nishigaki
Professor, University of Tokyo, Information Theory

I am a being, though I rarely consider this condition. I am not deploring the fact that I live like a robot being constantly urged to do trivial matters. It is not because biology was the subject I hated most in my junior high school and high school days (the pain of memorizing those strange names on the anatomical charts and taxonomic tables still lingers in my memory) and that I have been trying my best, unconsciously, to have nothing to do with any forms of life.

I think "I am living" when I put myself in the position of an outside observer to look back at myself. Can a computer do this kind of thing? When I ponder over issues such as a "machine with a mind" and "what is

information," I must also by all means face the issue of creatures. Is it true that only creatures are capable of processing information and computers technically can only manipulate symbols?

The result of this pondering is that biology is now one of the most interesting fields of learning to me, I, who study information. At BRH, we can learn about the latest topics from outstanding biologists. In the midst of these present delights, my memory of the dark and boring lessons of biology in my youth is gradually fading away.

"Biology is absolutely fascinating." To my surprise, I sometimes find myself preaching to my son. Such a haphazard and flexible creature am "I."

(Translated from *Biohistory*, No.1)

News & Views from BRH

Parallel Evolution in Radiation

A New Principle of Diversification?

How has life evolved? How has life diversified? What are species?
According to Charles Darwin's theory of Evolution, the principle of diversification of life is natural selection. But is it true that only natural selection makes new species? It may not be.
A new study on the Carabinae ground beetles by BRH has uncovered a remarkable evolutionary history.

DNA Analysis of Ground Beetles by BRH

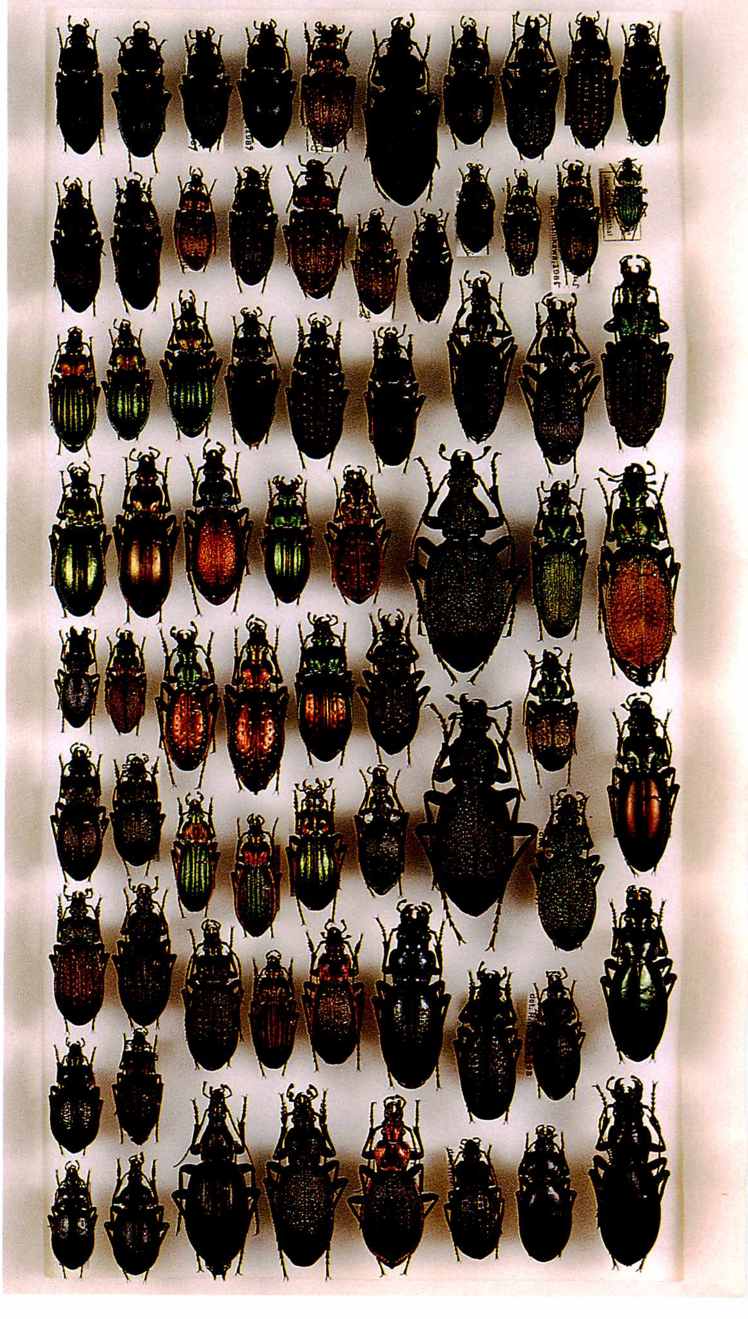
By analyzing the mitochondrial ND5 gene of ground beetles from all over Japan, the BRH research group (Zhi-Hui Su and others, headed by project leader Syozo Osawa) showed that clustering of the species in the molecular phylogenetic tree is linked to their geographic distribution, not necessarily correlating with morphological characteristics.[1] Species which are considered to be the "same" taxonomically, or members belonging to the same species-group, are scattered among more than two different clades (clade=lineage originating from a common ancester).

For example, *Ohomopterus dehaanii* is a large-sized dark blue carabid which is distributed in Chubu, Kinki, Chugoku, Shikoku and Kyushu districts. The specimens from these districts should belong to the same lineage in the phylogenetic tree if the phylogeny-based morphology is correct, but instead they radiate approximately into four independent lineages to which other smaller and morphologically different carabids belong. Taking the 9-10 million years old forewing fossil of an *Ohomopterus*-like carabid found at the Tatsumi Pass, Tottori Prefecture as the standard, it can be seen that the *O. dehaanii* of Wakayama and that of Shikoku belong to two distinct lines which diverged over several million years ago. This unusual situation is also seen in *O. yaconinus, O. japonicus and O. insulicola.*

Osawa named this phenomenon "Parallel evolution in radiation."[1] Parallel evolution is the occurrence in which organisms belonging to different lineages evolve to have similar morphological characteristics and functions. Good examples are the evolution of *Marsupialia* of the New Continent and that of *Eutheria* of the Old Continent. They have evolved into similar forms presumably resulting from the similarities in their environments and lifestyles. This type of convergence is usually explained by adaptation. Osawa, however, points out that "the present case may be better attributed to the neutral mutations of genes rather than to adaptation." The late Motoo Kimura developed a neutral

Carabinae ground beetles of the world

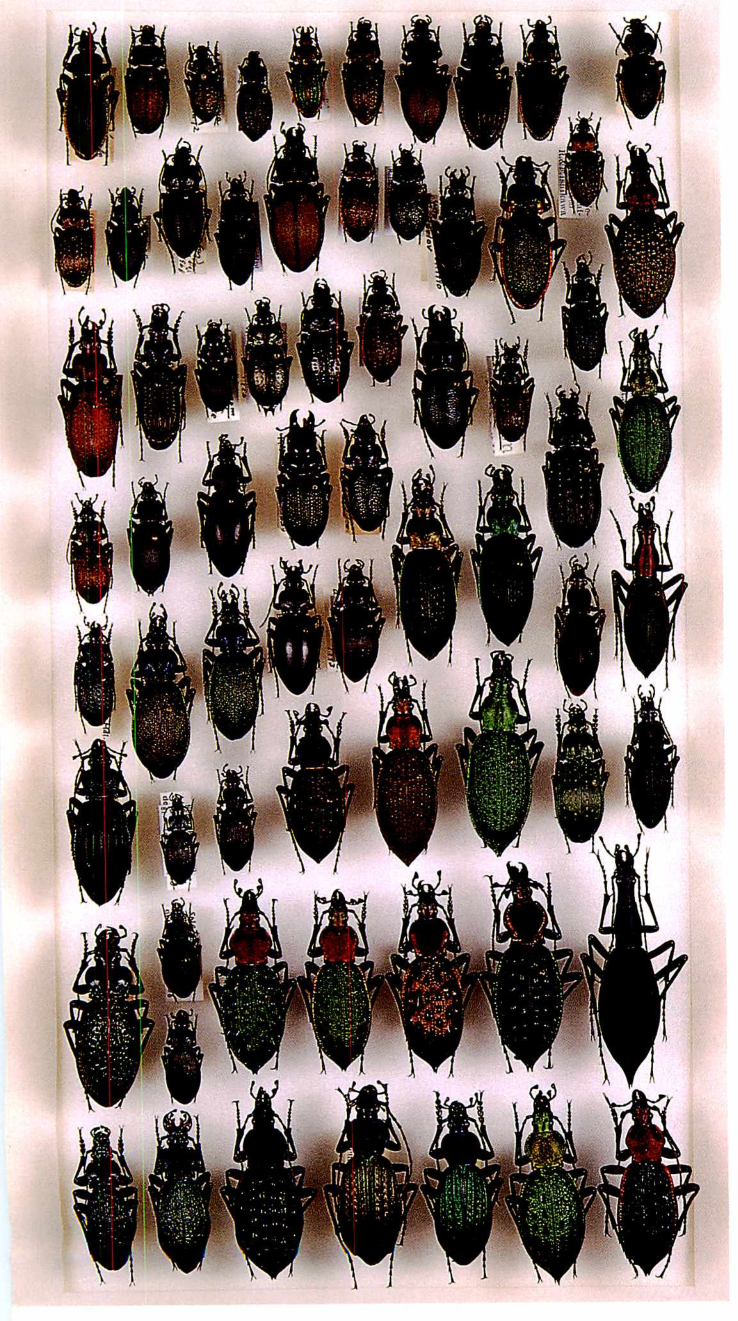
Carabinae ground beetles are found in Europe, Asia (excluding southern India), North Africa (Mediterranean side) and North America. About 700 species are known.
Left page: European species.
Chrisocarabus are iridescent beetles (center left) which are typically found in Central Europe and France. The two large beetles (center right) belong to *Procerus*, the largest-sized Carabinae species: the top one is from Caucasus, and the bottom one from Turkey.



Right page: Asian species. Beetles from China and Siberia (tundra and steppe areas) are shown in the top left. Those with small lumps on their backs belong to *Coptolabrus*. *Damaster blaptoides* (second row from the bottom, right) easily recognized by their black color and long necks, are endemic to Japan. (Photo: Susumu Yamaguchi)

theory of molecular evolution. He proposed accidental drifts of neutral changes of genes as being the main motive force of species diversification rather than natural selection.[2] Osawa argues, "If some master genes which control the expression of multiple genes to manifest certain morphological characteristics mutated neutrally independent of natural selection in each respective area, carabids morphologically indistinguishable from each other would have evolved in parallel."

He named such neutral and discontinuous changes in morphology "type-switching." A very similar phenomenon of parallel evolution in radiation is known in the case of the neotropical *Heliconius* butterflies of South America. Specimens which appear to belong to one morphological species were found to radiate into several distinct lines, based upon phylogenetic analysis using mitochondrial genes (Brower, 1994).[3] In that region, drastic climatic changes during the glacial period produced many geographically isolated areas, where similar, if not identical, wing-color patterns seem to have evolved independently. The well-studied differentiation of the ejaculatory bulb of the fruit fly, Drosophila, is a very similar phenomenon, in which an identical organ evolves in different lineages (Throckmorton, 1965).[4]



One might argue that the results on the Ohmopterus mitochondrial phylogeny may be brought about by participation of ancestral polymorphism and random lineage sorting or of hybrid individuals. Evidence has been obtained against these possibilities for the observed distribution of mitochondrial DNA haplotypes. The most plausible explanation of the results is that parallel evolution took place in different lineages during radiation.

Parallel Evolution and Diversification of Organisms

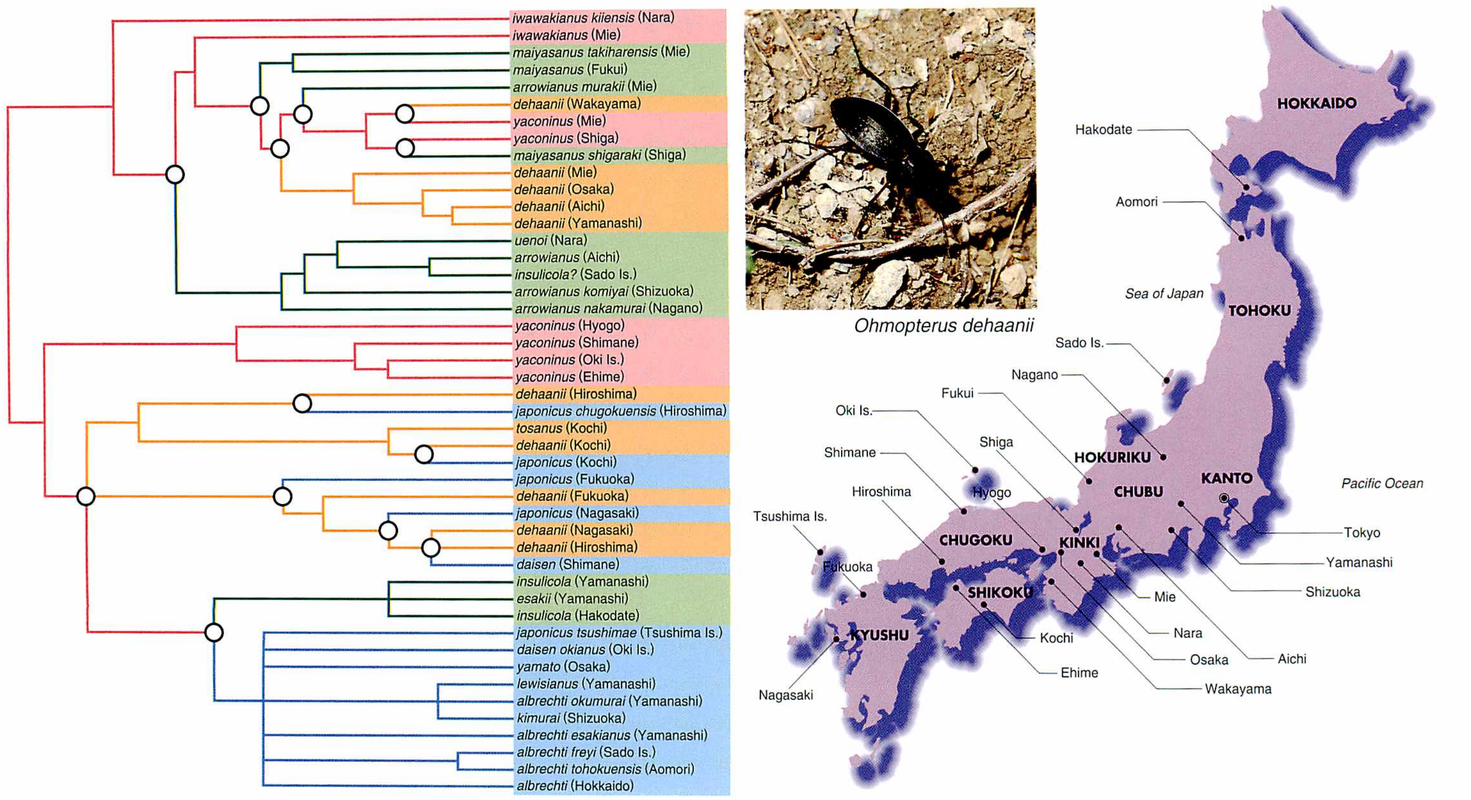
Dramatic periods of the explosive diversification of organisms are known in the history of evolution; such as the big explosion of life in the Cambrian period (500 million years ago), the diversification of Insecta (300-400 million years ago), and the diversification of Mammalia after the end of the dinosaurian period (60 million years ago). Douglas Erwin of Smithsonian Institution found that a single tree in a tropical rain forest was inhabited by about 600 species of arthropods, mainly insects. From this, he deduced that there could be as many as 30 million species of tropical arthropods, since there are an estimated 50,000 species of tropical trees (1982).[5] Osawa believes that the explosive diversification and concentration of species in limited areas such as tropical forests "may be more rationally explained by neutral type-switching rather than Darwinian natural selection."

The idea of "parallel evolution in radiation" was first suggested by Osamu Tominaga, an amateur entomologist and co-worker of the present project. He organized the Kinki Study Group of the Carabinae more than 20 years ago, and since then has made precise distribution maps of the Carabinae in the Kinki district. While investigating the distribution of *O.dehaanii*, he found strange blank areas. He explains, "If we assume that *O.dehaanii* evolved from a certain single lineage and evenly dispersed, the presence of such blank areas can not be explained even taking the changes in geohistory into consideration. If, however, identical forms were to have independently evolved in the respective areas, as observed in the phylogenetic tree drawn from mitochondrial DNA analysis, these blank areas are easily explained."

Role of Neutral Mutations

Does the type-switching hypothesis really suggest a possibility that neutral mutations of genes might have been the cause of the phenotypic changes which spread into the population without natural selection?

Takashi Miyata (a molecular evolutionist at Kyoto University) examined many kinds of genes and reached a surprising conclusion that many neutral changes must have



Type switching and parallel evolution in radiation.

A molecular phylogenetic tree constructed from mitochondrial ND5 gene sequences. Species which were considered to be the same from morphological analysis are found to be dispersed into various distantly related lineages by the DNA analysis. During diversification they are believed to have undergone rapid changes in morphology by type switching (marked by circles) many times. Since a variety of type switching combinations are possible, this flow shows just one possible case.
yellow = *dehaanii* type
red = *yaconinus* type
blue = *japonicus* type
green=*insulicola* type
(Photo: Hirotaka Matsuka)

occurred at the molecular level in the Cambrian explosion. Miyata suggests that when the pressure of natural selection slackened during this period, mutations which otherwise would have been harmful and selected out, became neutral. Thus morphological diversification of organisms was accelerated (1994).[6] Osawa suggests that the parallel radiation of *Ohomopterus* is an example of the scenario of "accumulation of neutral variations→diversification in morphology" and that such parallel radiation occurs commonly in evolution regardless of the presence or absence of natural selection.

The *Ohomopterus* have chitin pieces (copulatory organs) in the male genitalia which are characteristic to each "species group." Females are provided with a corresponding vaginal appendix (Ishikawa, 1973).[7] This combination demonstrates a clear example of reproductive isolation through a lock-and-key mechanism. There have been many observations of attempted copulation between carabids possessing such different reproductive organs where either the female died due to vaginal bleeding or the male copulatory piece was broken (Sota & Kubota, 1995).[8] Using these copulatory pieces as markers, Ryosuke Ishikawa classified *Ohomopterus* into five species groups including two groups of triangular types, one peach stone type, and another hook type. Then he considered these copulatory pieces as deriving from an ancestral form, which evolved orthogenetically from a smaller (and simpler) form into larger (and more elaborate) forms. However, the present analysis by the BRH group based upon mitochondrial gene sequences, does not support his idea. *Ohomopterus* having copulatory pieces of different types appear within the same lineage in our phylogenetic tree.

Experiments on the butterfly *Maniola jurtina* show that these lock-and-key mechanisms of the copulatory organs are not necessarily functional (Gourson, 1993).[9] According to Gourson, some parts of the copulatory organs which are used by taxonomists to identify the species do not, in fact, participate in copulation. A study using carabid-beetles shows that the "lock-and-key" does not necessarily function perfectly (Sota & Kubota, 1995).[8] Gourson (1993)[9] pointed out that the morphological changes in copulatory organs may be caused not only by natural selection, but involve neutral differentiation as well.

Tadashi Komatsu of Hokkaido University (insect systematics) examined these two alternatives. He selected eight features of the copulatory organs and ten features in the overall morphology. Then he examined the variance and correlation within individual groups and intergroups of *Aphrophora intermedia* collected from seven areas in Sapporo city.[10] He also compared the same characteristics of *Aphrophora intermedia* with its four closely related species. Contrary to the traditional view, variances in genital features within populations were found to be much larger than those in non-genital features. Furthermore, there is a large among-population variance in genital characteristics. These results suggest that stochastic processes (random genetic drift, etc.) should have significantly affected the differentiation of male-genital morphology among species as well as within species. From this study, Komatsu concludes "at least in some insect groups, the traditional view of genitalia having such an important function that their morphology should remain invariable under strong natural selection was not supported."

The idea of "developmental constraints" exists, even in orthodox Darwinism (Alberch, 1982;[11] Maynard Smith et al., 1985[12]). These constraints are defined as biases on the production of variant phenotypes or limitations on phenotypic variability caused by the structure, character, composition, or dynamics of the developmental system. Alberch argues in the paper, Developmental constraints in evolutionary processes, "Neo-Darwinian theory in evolution based on natural selection can predict what is more likely to survive once it has appeared, but it cannot address the question of what is more likely to be generated. Developmental constraints defined the potential pathway of transformation and impose an additional deterministic component on evolutionary processes." If these constraints which work in different evolutionary lineages are removed independently in the respective lineages, and result in the emergence of some identical features, does this not look like parallel evolution in radiation by type-switching?

The type-switching hypothesis has been welcomed by researchers outside experimental biology. One group includes the structuralists, who assert that all possible forms are structured *a priori* in a group of organisms; organisms can diversify only within a range which the "structure" provides. They argue that parallel evolution in radiation may be explained by parallel manifestation of hidden, but pre-existing, characteristics in related species.

Atsuhiro Sibatani, one of the pioneers of structuralism, attributes the explosive diversification of cichlids in Lake Victoria to a type-switching-like inherent force. Lake Victoria, together with its satellite lakes, harbours roughly 200 endemic forms of cichlid fishes, whose morphology is extensively varied. Yet the lake system is less than a million years old. Based on phylogenetic analyses using mitochondrial genes, several authors suggested that the diversification took place within the past 200,000 years from one ancestral species in the lake (Meyer, Willson et al, 1990[13] Avise, 1990[14]).

Another well known feature of these fish is that similar morphologies are found among species in different lakes. Recently Kocher and others analysed the mitochondrial DNA from six pairs of morphologically similar cichlids from Lakes Tanganyika and Malawi and found that these fish originated from separate ancestral species.[15] Such a rapid parallel diversification is hard to attribute to natural selection alone.

Importance of Natural Selection

Is it then really difficult for natural selection to explain rapid morphological changes and explosive diversification of species? Recent studies of finches by Mr. & Mrs. Grant of Princeton University in the Galapagos Islands, where Darwin was firmly convinced of evolution of organisms, show that natural selection does change morphology very quickly. These small birds, which look like Java sparrows, have beaks whose diverse shapes correspond to their eating habits. It was calculated that one species can evolve into a different one within about one hundred years if natural disasters such as drought occur frequently. They suggest that recombinations of genes occurr through crosses, and the resulting hybrids that fit themselves to the environment lead to the emergence of a new species. (*The Beak of the Finch*, Weiner, 1994[16]) However, even through the work of the Grants, the emergence of a new species by natural selection has not yet been completely confirmed. Presumably, evolution is a great complex drama, in which many factors, including Darwinian natural selection and neutral type-switching, have been operating together.

According to the molecular phylogenetic studies on the Carabinae ground beetles by the BRH group, the following facts have been finally revealed. "An apparent morphological continuity does not necessarily indicate a continuity in evolution. Therefore even if two specimens have similar morphologies, their time of divergence is not necessarily recent." In short, we conclude that "so-called morphological species do not necessarily belong to a single phylogenetic line."

Taxonomically, it has been believed that each cross in the phylogenetic tree signifies a splitting of the species. The finding of parallel evolution in radiation in ground beetles suggests that this traditional view is invalid and that we should carefully rethink what "the species" is.

Ohomopterus is endemic to Japan and its radiation is calculated to have started about 10 million years ago, concordant with the time of the separation of the Japanese Archipelago from the continent as estimated by recent geological studies. The study of finches shows that their evolution was closely related to natural phenomena such as droughts and floods on the Galapagos. Evolution may now be understood in relation to dynamic global changes. Evolutionary biology based on substantial evidence is progressing very rapidly all over the world and we have begun to map the relationships between genetic changes and morphological effects. Contrary to Carl Popper's famous view that the study of "evolution" is not a science because it could not be verified, evolution has become real science 150 years after Charles Darwin wrote *The Origin of Species*.

(Kazuyuki Mogi/Former editor of *Biohistory*. Present Address : Seitoku University)

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Human Network

Collaborations

The Biohistory Research Hall, where science meets art and where scientists meet people.

The exhibition hall seen through the glass balls in one of Junko Mada's art works. (Photo: Naruaki Onishi)

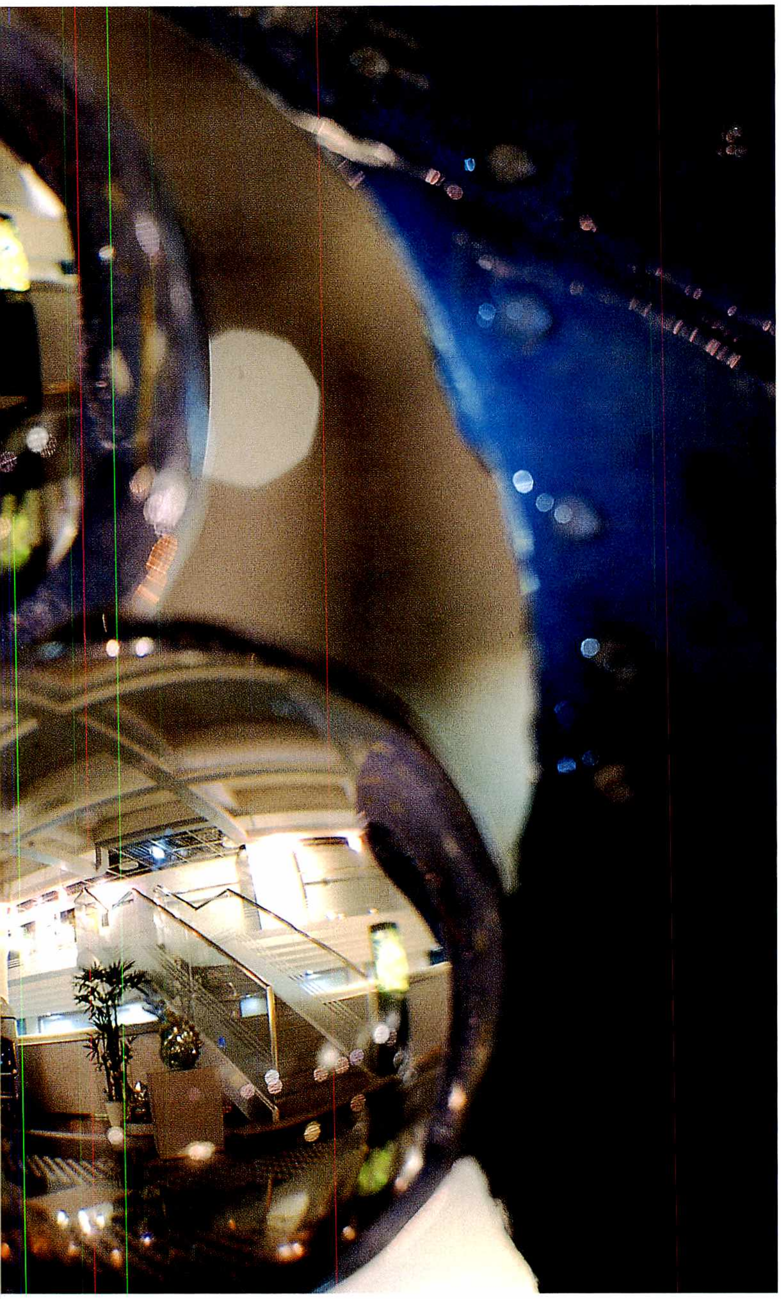
To perform a variety of activities at the BRH, it is important to collaborate with people in different fields. Over the past four years we have had the honor of working with many people outstanding in their field.

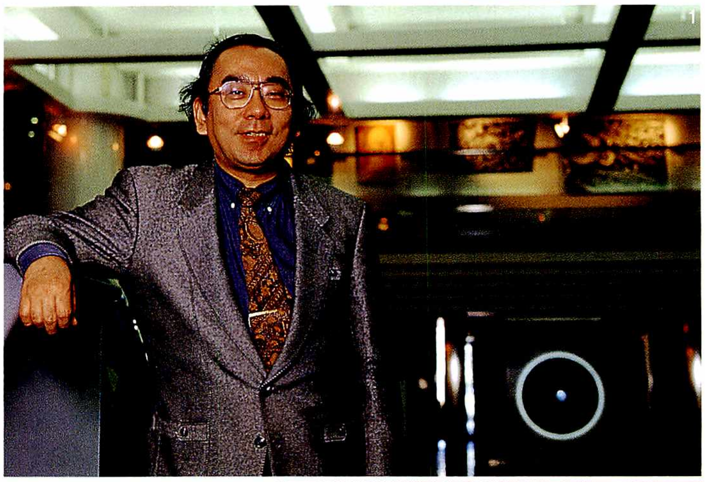
First, many scientists both in and outside Japan have continued to offer their generous assistance for the publication of our journal and organization of our exhibitions. One example was the photo exhibition of "The Cell," for which ten biologists in the fields of cell and developmental biology kindly contributed photographs. Dr. Nobutaka Hirokawa (University of Tokyo) generously let us use many of his photographs including those of kinesin motor proteins. We also regularly ask scientists to describe their research in our quarterly journal *Biohistory* to allow non-specialists better access to the forefront of research progress. Many foreign researchers kindly spared time for interviews or discussions.

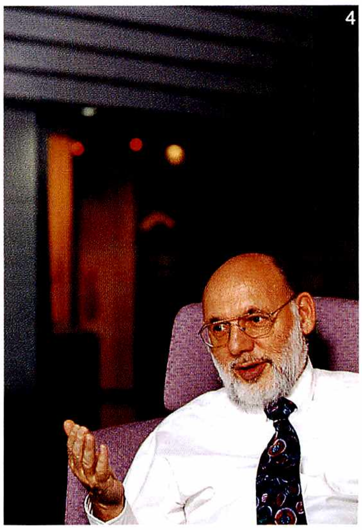
Our research project on the evolution of Carabinae ground beetles (p.10-13) is a fine example of collaboration between professional biologists and amateur beetle enthusiasts who often have a remarkable depth of knowledge on the insects. We organized a network through which we could exchange ideas and research results. It was these amateurs (though they are professional in terms of their enthusiasm and knowledge on the beetles) who went out in the field to collect insects from all over Japan.

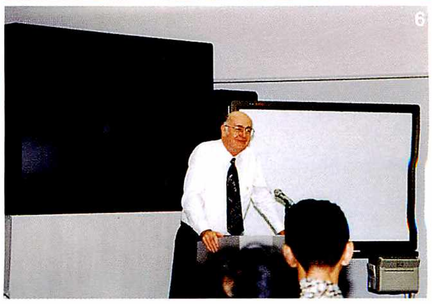
Many people outside biology also participated in our activities in a variety of ways: Artists, graphic designers, musicians, and researchers in diverse fields, including social sciences and literature. Artists contributed their work for display in our exhibition hall. Korean artist Jae Eun Choi's work using butterflies gives a fresh welcome to our visitors. Junko Mada made several artistic objects inspired by animals. Masashi Kimura, a scientific illustrator trained at the Smithsonian Institution was in charge of designing many of our displays in the exhibition hall. We also collaborated with the Kyoto Symphony Orchestra (conductor: Michiyoshi Inoue) to perform "science opera" in April, 1995 (p.22-23). More performances with them are planned in 1997. Other people contributed articles and essays to *Biohistory*.

In the following pages (p.16-23), you will find some examples of our cooperative interaction.









1. Nobutaka Hirokawa of the University of Tokyo at "The Cell" exhibition. The round black object is an art work by Jae Eun Choi, "Moment and Life," which is installed in the exhibition hall entrance of the Biohistory Research Hall. A butterfly that was placed inside can be seen through a magnifying lens in the center.

Many scientists from abroad helped us.

2. Cornelia I. Bargmann (University of California, San Francisco, USA)
3. Nicole Le Douarin (CNRS, Institute of Cellular and Molecular Embryology, France)
4. Walter J. Gehring (University of Basel, Switzerland)
5. Simon Conway Morris (University of Cambridge, UK)
6. James D. Ebert (Former President of the Carnegie Institution of Washington, USA)

(Photo 1, 4: Yoshiki Geka)

Gallery

Ground and Underground

Relation between Me and Life

Jae Eun Choi

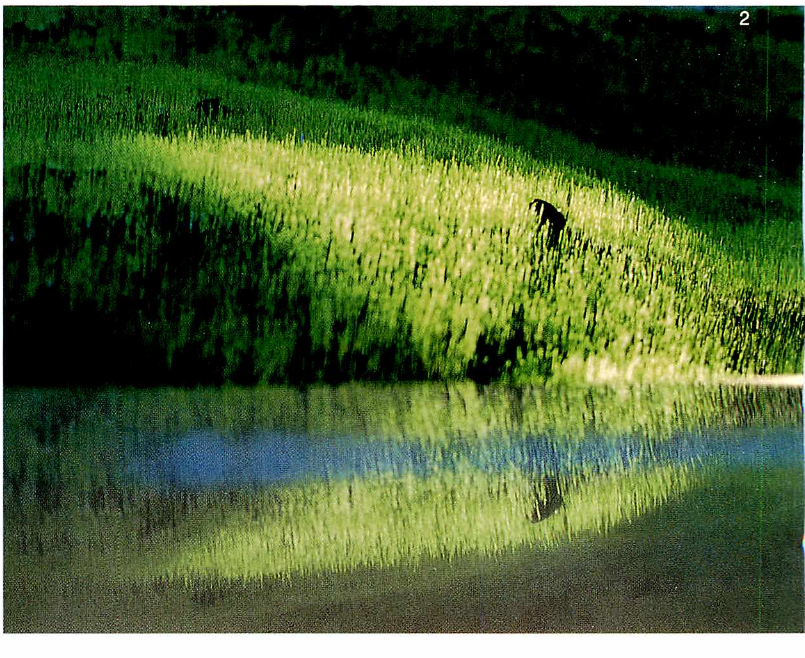
Jae Eun Choi is an internationally reknowned artist.
Originally from Korea, she has been actively working in Japan, Korea and other countries.
Many of her creations are related to the processes of life.
Here, she talks about her works and her relationship with nature.

I was born in Seoul, Korea. When I was 23 years old, I came to Japan and became fascinated by the world of *Ikebana* (flower arrangement), and the following year, I began studying it at the Sogetsu School. I held a strong interest in such an aesthetic in which forms of life are cut off and artistically arranged, and the resulting works transmitted as forms. Cutting means termination of life, but in the world of *Ikebana*, it creates a new life. Dying is, in fact, a new birth. This intrigued me very much.

In 1985, my exhibition entitled "Earth" was held at the Sogetsu Plaza in Tokyo. Thirteen tons of black soil were brought into a terraced garden (designed by Isamu Noguchi). Then I sowed seeds of *Kinuitoso*, a very thin plant which grows very quickly. Within two weeks, the first shoots appeared and they grew to a height of about 11 centimeters. The black soil transformed into a carpet of green grass. The degree of the growth of the grass and the direction of light, depending on the time, exhibited the very diverse colors of the garden; black, red, green. From these changes one could feel time. It was the theme of this work. *Kinuitoso* was the plant I found in my search for the saddest plant in the world. The weaker the appearance, the stronger the life. Don't you agree?

The next year, I started a new project, The World Underground Project, which involved taking sheets of a special paper, developed by Mr. Heizaburo Iwano of Fukui Prefecture, and burying them in ten different countries, including Japan, Korea, Italy, and Kenya. Three to four years later the sheets were retrieved, and when exposed to air, the corrosive changes due to bacteria could be seen. From them, I created an art work.

For me, the underground or earth signifies "pure nature." It is the unity of matter, time, and space. It is the place of birth and generation. As long as we humans are present on the earth, the destruction of nature cannot be avoided. Therefore I think of the ground as a man-made place. The relationship between ground and underground is my eternal theme. To me, the ground (above) and underground (beneath) despite their dichotic nature, complement one another; like plus and minus, surface and



1,2. "Earth" 1985. Stone sculpture garden by Isamu Noguchi, Sogetsu Plaza, Sogetsu Kaikan, Tokyo. Architect: Kenzo Tange.

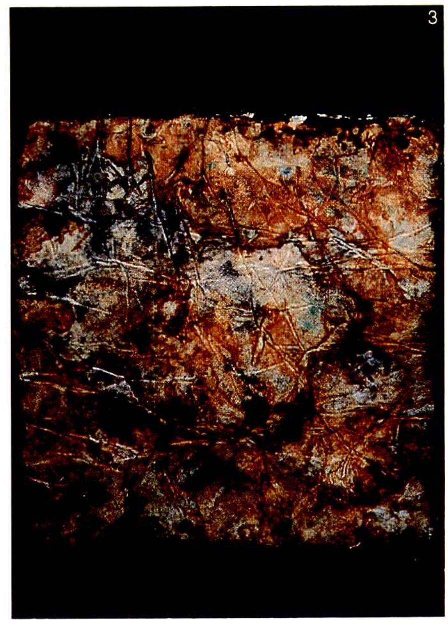
interior, and light and shadow.

Every time I look at the changes in the paper that was recovered from the ground, I am deeply moved. It is indeed a wonderful thing if I can create my works of beauty and at the same time, ponder on such diverse aspects as the potential of the earth as a place of generation and birth, and the numbers and types of bacteria which contributed to the changes on my buried pieces of paper.

Bacteria themselves were the tools for my expression. I wished to know what shapes and forms those bacteria, that produced the beauty of my works had. Several years ago, I paid a visit to Dr. Masao Karube at the Research Center for Advanced Science and Technology of the University of Tokyo. I had no previous acquaintance with him, but he was kind enough to show me samples of soil from various countries through a microscope. It was fascinating. The world which is visible to our naked eye is so very limited. What we can not see is infinite.

When Dr. Karube told me that nowadays artists and scientists work together, it impressed me deeply. I have had the opportunity of attending the BRH salon twice. The scientists that I met there seem to have such a realistic view of life that I do not know how science could be related to my works. In spite of this, I wish to have as many opportunities as possible of attending the salon.
(Translated from *Biohistory*, No.1)

The World Underground Project, which began in 1986, is still ongoing today with different methods of expression.
In recent years, Ms. Choi has been assisted by Dr. Eiichi Tamiya of the Japan Advanced Institute of Science and Technology.
In 1994, she embarked on a new work, "Chaos," in which small pieces of the paper that had been buried were further cultured and then photographed by electron microscopy to reveal the patterns of the bacteria responsible for the original designs.
In 1995, she represented Japan at the Venice Biennale with her new work "Micro-Macro" in which the microscope-magnified images of the bacteria on the sheets of paper were shown, along with video images of the bacteria in motion.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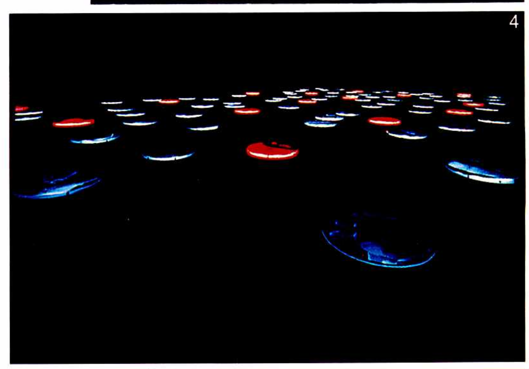
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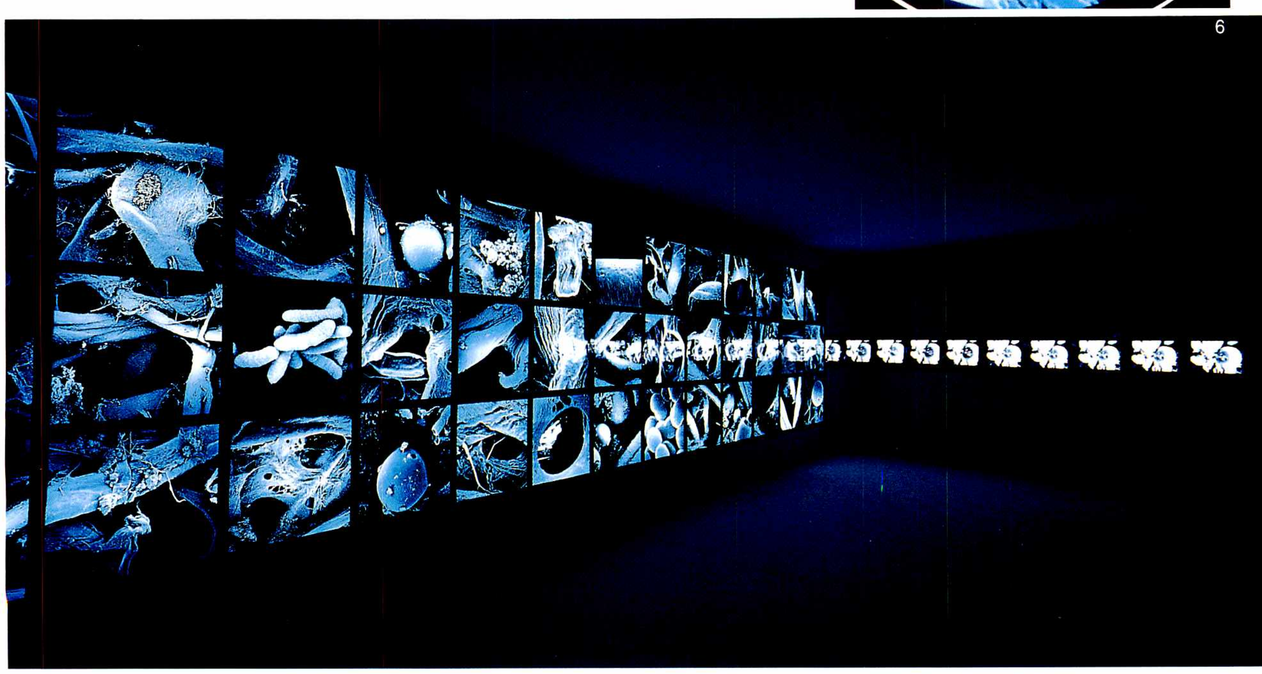
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3. "World Underground Project" 1986- . Kyong-Ju, Korea: in 1986; out 1990. medium: Buried Japanese paper etc.

4,5. "Chaos" 1994. The Sogetsu Art Museum, Tokyo. Diameter: 58 cm. Height: 90 cm. Medium: drum, water, heat, film, buried paper (World Underground Project, Gifu pref., Japan 1991-1994).

6. "Micro-Macro" 1995. Japan pavilion, Venice Biennale, Venice Italy. Installation, Area 250m². medium: acryl sheets, film, TV monitor, LD, neon light.
(Photo1:Shigeo Anzai, 3~6:Shigeo Muto)

Science Topics

Looking at Membrane Proteins through an Electron Beam

Yoshinori Fujiyoshi
Professor, Faculty of Science,
Kyoto Universitiy

You may have been intrigued by the wonder of the double helical structure of DNA. Proteins, which are as important to organisms as DNA, have fine and elaborate structures. At the microscopic level, they appear quite beautiful, like works of art. The most advanced electron microscope can now reveal the virtual images of proteins at a resolution of 3/10,000,000millimeters.

"Seeing is believing." There is some truth in this old proverb stressing that human cognition relies mainly on vision. This applies also to understanding the function of proteins, which are central to life, by "looking" at their detailed structures.

The foundations of crystallography, which examines molecular structure, were laid out by W. H. Bragg and his son, W. L. Bragg in1912. Among some of the methodologies in crystallography, X-ray crystallography has progressed considerably so that in recent years, new information regarding protein structure has accumulated rapidly. However, the structures of membrane proteins, which are essential for exchange of information and energy between cells and their environment, have eluded analysis. These membrane proteins posed a problem for X-ray crystallography due to the difficulty in obtaining large crystals.

Theoretically, it had been speculated for some time that electron diffraction, 10,000 times more powerful than X-ray diffraction, could be applied to analyze protein structure at the atomic level from membranous arrays of just one molecule in thickness (50Å). If achievable, one might then imagine electron crystallography, as a replacement for X-ray crystallography. But in 1973, when I first began to study electron microscopy, it was uncertain whether indeed atoms could be visualized by electron microscopy.

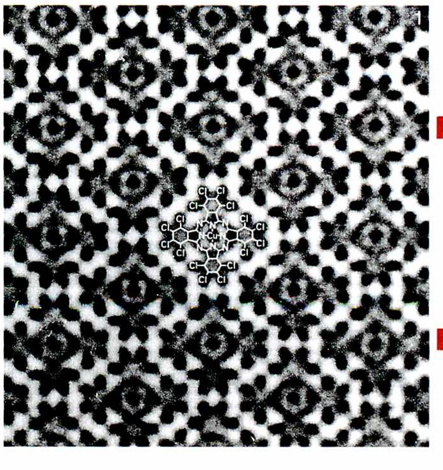
Therefore even after 15 years, I still remember clearly the knee-shaking sensation upon seeing our first successful photographs of the molecular structure of chlorinated copper phthalocyanine crystals allowing individual atoms to be distinguished (photo 1). This experiment convinced me of electron microscopy's tremendous potential for structural analysis with atomic resolution. However, we encountered difficulty when adapting this method to analyze organic molecules, as they were too fragile to withstand the electron beam.

In 1980, we came up with more effective equipment which required only a minimal dose of electron beam for taking images of radiation-sensitive specimens. Unfortunately, this alone was yet insufficient to preserve the integrity of our specimens. We concluded that to maintain the intact molecular structure under a minimal dose of electron beam, the specimens must be kept at an extremely low temperature close to absolute zero (-273.16℃). The difficulty that remained was to develop a microscope stage for holding the specimens, which would resist against the vibrations caused by the coolant.

In collaboration with Dr. Hideo Yamagishi at Kyoto University and JEOL Ltd., we began in 1983 to develop an electron microscope that could be used at a very low temperature. During this time, I also happened to meet Dr. Takao Mizusaki during a nursery school excursion to which I accompanied my daughter. Fortuitously, it turned out that Dr. Mizusaki was a specialist in low temperature physics at Kyoto University, and without his valuable advice, all of our efforts would have yet been in vain. Over the next eleven years, we were able to develop three prototypes, each of which cost several million U.S. dollars. Finally, we succeeded in reducing the damage to our protein specimens by more than an order of magnitude with the latest version which was able to achieve a 2Å resolution at 1.5K (-271.7℃).

1. Image of chlorinated copper phthalocyanine crystal molecules as seen through an electron microscope. This historical photograph proved for the first time that individual atoms could be distinguished by use of electron beams.

2. A schematic three-dimensional structure of the broad bean antenna chlorophyll-binding protein. The helical region of the protein is represented by the purple ribbon, green - chlorophyll a; light green - chlorophyll b; yellow - lutein.



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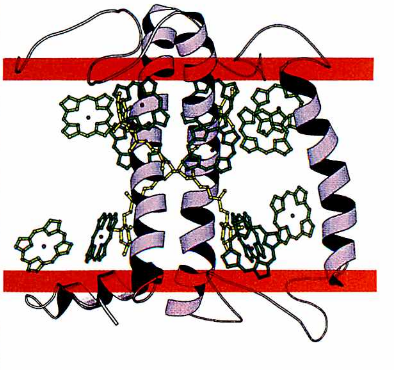

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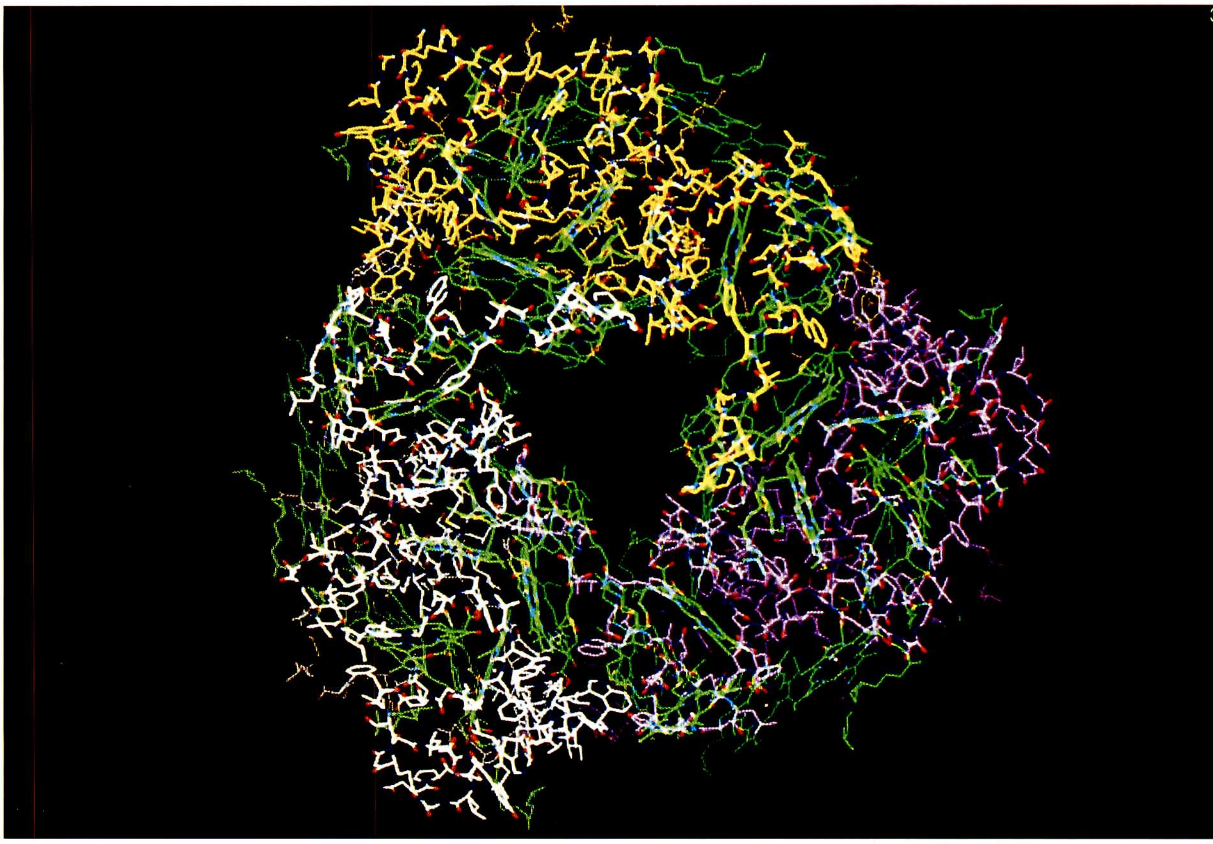
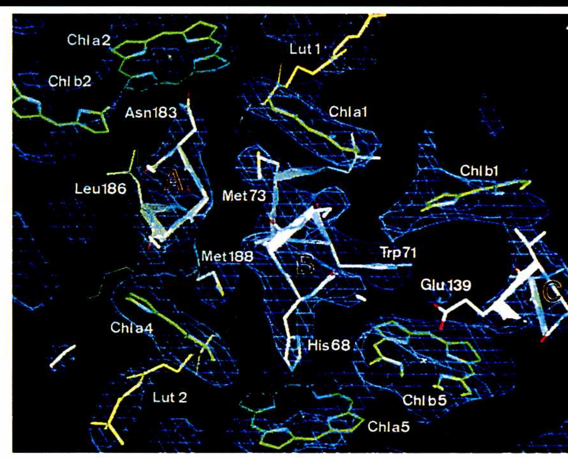


3. Three molecules of the antenna protein are arranged to form a compact trimeric structure.
4. A computerized electron density map showing the arrangement of amino acids down to the level of their atoms (*Nature*, vol 367, p. 616, 1994).



However, this was just the first step. Only two-dimensional information can be obtained from a single electron microscopic image. To obtain three-dimensional structural data, images from a series of more than 200 tilted specimens must be processed to produce a computerized electron density map, based on the electron crystallography technique developed by R. Henderson et al. In accordance with the protein's amino acid sequence, this information then allows us to determine the coordinates of individual atoms to reconstruct a stereo view of the protein.

Finally, we had all the tools we needed to proceed. Our first breakthrough came with the analysis of the antenna chlorophyll-binding protein from soybean chloroplast membranes in collaboration with W. Kuhlbrandt and P. N. Wang. This protein, which plays a central role in the light-harvesting step of photosynthesis, is tightly arranged as a trimer within the chloroplast membrane. Our results allowed us to visualize the actual arrangement of the individual chlorophyll moieties within the trimeric complex down to the atomic level. Consequently, we discovered that the antenna protein coordinates two different types of chlorophylls (a and b) and an accessory pigment, lutein, in order to transmit light energy with minimal loss. Furthermore, this configuration appears to protect chlorophyll a from oxidative degradation during photosynthesis.

Almost twenty years have passed since I started working with the electron beam. Our progress during these years have at last enabled us to analyze the three-dimensional structure of proteins at the atomic level, by means of electron microscopy. At present though, it still takes us over two years to determine each new structure. However, what I do anticipate in the near future, are further improvements which would allow consecutive analyses, enabling the determination of dynamic four-dimensional structures of membrane proteins.

(Translated from *Biohistory*, No.6)

Essay

Basho's Crow and Mandelbrot

My View on the Issue of Flock of Crows vs. a Crow

Soichi Furuta

"Quoi? Quoi? Quoi?" "Rien"
Le Corbeau: Renard, *Histories Naturelles*

The "Study of the Coastline" by Benoit Mandelbrot* is a beautiful poem. It is more inspiring to me than any one of the modern poetry. He wrote in his *Fractal Geometry* as follows: The finer the scale of observation is, the more jagged the coastline: It becomes monstrous, and its length is extraordinarily long when measured by any method. All in all, it would be appropriate to consider that the length of the coastline is infinite. This may be summed up, in essence, that reducing the field of observation leads to infinity. Since then I have been possessed with this concept. It has become the beautiful key to my cosmology.

There the time-honored cosmology of the East unites remarkably with that of the West. Let us suppose that Mandelbrot was born 300 years ago and came to Japan, and that there he happened to meet Basho,* an itinerant poet, and traveled the *Narrow Road to the Deep North* with him as a fellow traveler. It gives me a thrill of pleasure to imagine how these two extraordinary men, being possessed with macroscopic and microscopic objects, would make marvelous travels. Basho, an eternal wanderer, might have anticipated the "fractal theory" of Mandelbrot and have gone on a journey to his infinite coastline. Basho composed a famous haiku (or a failure?) in 1681:

Kareedani Karasuno Tomaritaruya Akinokure
(On the withered branch/Has a crow alighted /Nightfall in autumn)

There is a variant of this haiku, which was composed in 1689:

Kareedani Karasuno Tomarikeri Akinokure
(On the withered branch/A crow has alighted /Nightfall in autumn)

Today, the latter haiku is more widely known. Opinions of the haiku world and lovers of Basho vary in the appraisal of this haiku. They are roughly divided into a group rating it as a fine piece and a group rating it as a dull one. I myself belong to the latter rather than the former.

Now, I would like to narrow down my theme for this essay to "whether Basho treated "crow" as singular or plural." Most of the readers would say, "It is a silly question. No doubt only one crow." It is common knowledge that in Zen expression "only one" crow should alight on a withered branch. Many years have passed since people in general, including myself, were brainwashed to accept the conventional subject of Chinese painting "withered branch and a winter crow." This is well illustrated by the fact that in the translations of this haiku of Basho into many languages including English, nine out of ten translations opted for "a crow."

An extraordinary event occurred in 1974, which seemed to destroy this generally accepted idea from its very basis. Mr. Rihei Okada, a leading student in the graphology of Basho's legends written on *sumie*, or ink drawings, published in *Renga Haikai Kenkyu* Vol. 46 a scroll of which sumie and haiku were attributed to Basho.(photo on the right page) The drawing and the writing took the believers of "withered branch and a winter crow" by surprise. Since then the work has been known as *Kareeda karasu, Kasayadori* (Withered branch and crows/taking shelter under a hat from rain). The drawing shows seven crows perching on withered branches with scarlet-tinged ivy. Above them, to my surprise, a flock of twenty crows are flying around. I saw this work for the first time in the full color photograph reported by Mr. Okada in *Bessatsu Taiyo* published at the end of 1976. It was indeed a shock "like being bewitched by a fox." I immediately showed the work to my esteemed friend Dr. Donald Keene, a great authority on Japanese literature who specializes in Basho. Even the erudite Dr. Keene moaned. Both I and Dr. Keene belonged to the adherents of "single crow." By the way, his translation into English was:

On the withered branch/A crow has alighted... /Nightfall in autumn.

According to an essay, *Drawing of Crow*, by Mr. Tsutomu Ogata (*Yusei* Vol.2, 1987), many scholars, one after another, are

A typical legend symbolizing one crow (1692 or 1693) written by Basho on a drawing by his student, Kyoroku Morikawa. It is known as an excellent example depicting the charm of the refined simplicity of Basho. (Property of Idemitsu Art Museum).

The legend (written in 1615) reported in 1974 by Mr. Rihei Okada, a researcher of Basho. It was used as the basis for the "flock of crows" theory. The haiku "*Yonifuruwa Sarani Sougino Yadorikana*" (Rain reminds me of the hardship of life, I am now sheltering under a small hat and my life is much harder than that of Sougi) was written on a background of a winter scene. Although it has the sign and seal of "*Hakusendo Bashoou*," the general view now is that the style of the drawing suggests the work of a professional artist rather than Basho. (Private collection)

arguing about the development of a state of Basho's haiku on the basis of the picture of a flock of crows. It is the occurrence of a group for "a flock of crows" versus the group for "a crow." Mr. Ogata presented his doubt, in his essay, about the assumption by Mr. Rihei Okada and other disputants that the legend on this scroll was written by Basho himself. Mr. Ogata stands on the side of a negative theory that the legend was not written by Basho himself.

My point, however, lies somewhere else. I would like to elaborate on my opinion from the macroscopic and microscopic viewpoints of Basho mentioned at the beginning of this article. In short, both the disputants for one crow and those for a flock of crows are but a mob like a flock of crows.

Araumiya Sadoni Yokotau Amanogawa

(A surging sea.../Reaching over Sado Isle/The Galaxy)

Akebonoya shirauo Shirokikoto Issun

(Dawn twilight/Whiteness of a whitefish/an inch long)

Both the Milky Way of the cosmic scale in the former and the tiny icefish of the latter show, to the eyes of Basho traveling along the coast, the state that "everything in the universe is self-content". Seen in the phase of eternity, they are one and the same. Basho, who saw multitude in solitude, and solitude in multitude, was a clairvoyant having both ocellar and ommateal eyes. He developed a state of poetic mind wherein foulness and purity, such as excrements, stars and flowers, are all compatible to each other. What he felt by intuition at the core of this unconventional scene with a flock of cawing crows might be the sound of solitude; a solitude to be felt in a multitude after the manner of Baudelaire.

Now let us examine the main issue. First, let us forget about the issue of whether the scroll with a legend was directly written by Basho. Then, let us focus on how his imaging process developed when he happened to see a scene with a flock of crows like detail A. (1) His macroscopic eyes would view the entirety of detail A. (2) He then would move his viewpoint to detail B and notice solitary crows on withered branches (in four circles). (3) Then his eyes by intuition would converge on the solitary image of a crow perching on the higher branch, zoom up and stop at the detail C. (The readers will now see how close detail C is to the conventional "withered branch and a winter crow." The three legends written by Basho and the legend jointly written by Basho and Kyoroku all belong to this group.) While Basho was staring at the solitary image of the crow dressed in black, his microscopic eyes would begin to work. Along the contour line of the crow, his eyes would rotate dizzily, and eventually Basho and the black point would merge together, finally entering the delightful part of fractallization. The minuter they become, the vaguer and obscurer the contour lines become. It would expand to become a coastline infinitely stretching far beyond. Basho eventually would see himself traveling along the coastline. Mandelbrot would appear and totter to Basho. They would happen to meet each other on a dune. Mandelbrot would speak to Basho. "Even if you travel far beyond, you would only see the infinite." Basho would respond, "I am in a hurry... We should write down the objects we grasped through the illumination of insight before they disappear from our image." (*Sanzoshi**) Mandelbrot would say, "I do not understand at all. By the way, let me ask about the issue of the crow, is it one crow or seven crows?" Basho would respond, "Everything in the universe is self-content. One is seven, and seven is one..."

(Translated from *Biohistory*, No. 3)

*Benoit Mandelbrot (1924-) : American mathematician born in Poland and raised in Paris who is well known for his "Fractal theory."

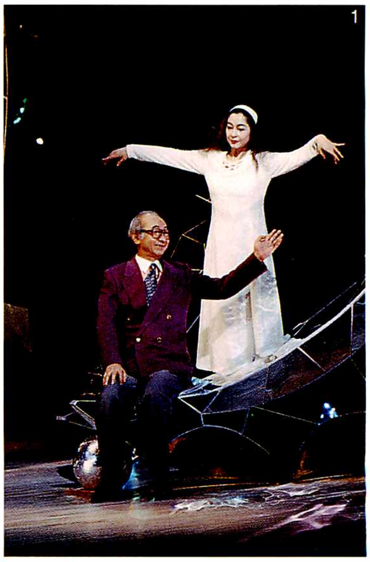
*Basho Matsuo (1644-1694) : Japanese poet who established a new style of "haiku" poems (Haiku is a Japanese seventeen-syllable poem).

**Sanzoshi* : A book by Doho Hattori on Basho's haikus published in 1776.

Soichi Furuta: Born in the USA in 1927. Graduated from the Department of Literature, Matsumoto Junior College, Japan, and the Department of Art, UCLA. His self-selected collection of English poems, *Montefeltro The Hawk Nose* was nominated for the Pulitzer Prize in 1989. Currently, *Adjunct Professor of* Literature, St. Andrews College, NC. He lives in New York.

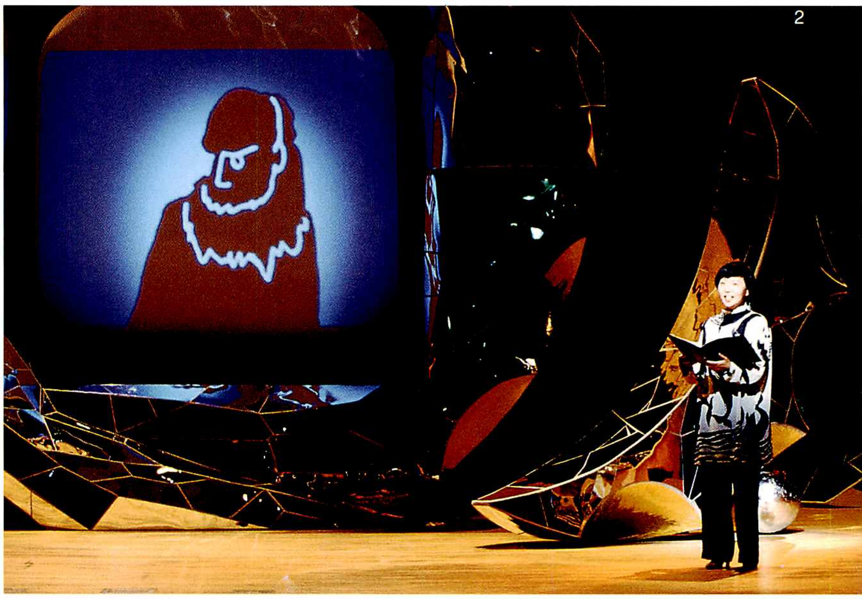
Performance

"Science Opera"



1

What is a "Science Opera"?
It is an innovative way of presenting science, created by the BRH.
To learn more about it, please read on!



2

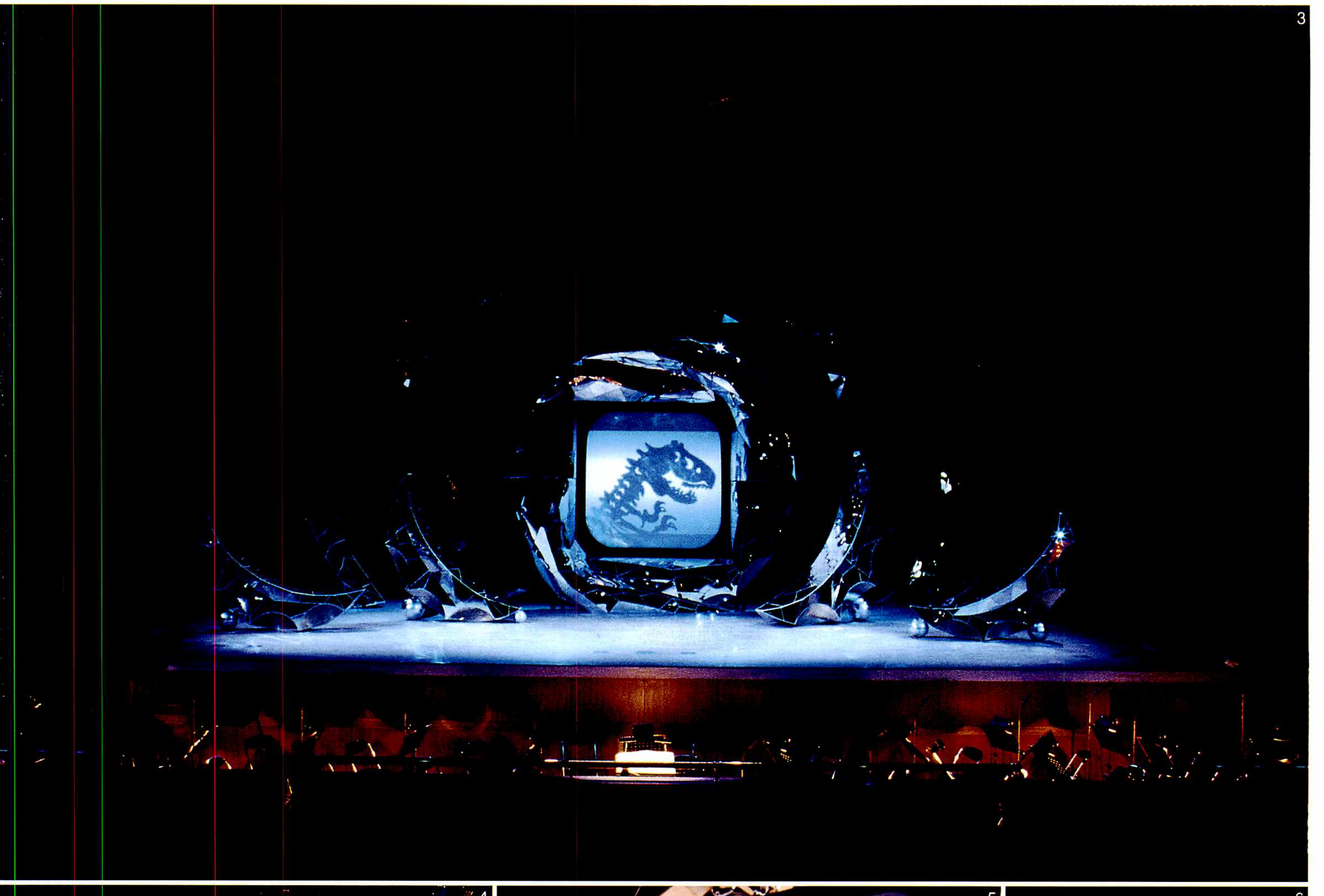
While the opening of Haydn's symphony *The Clock* was being played solemnly, Tokindo Okada, the director of BRH appeared on the stage, wearing an Agnes B T-shirt featuring a design of a newt. An image of a newt was projected onto a large amorphous, Gaudi-style object on the stage. The newt possesses the amazing ability of regeneration: if the lens is removed from the eye, a new lens can be formed from the pigment cells of the retina. Transdifferentiation was the theme of Okada's work as a developmental biologist. He is also an enthusiastic lover of music, with a particularly deep attachment for Haydn. A curious combination of a scientific story of the regenerating power of the newt and the music of Haydn. Thus the curtains rose on the BRH's first performance of a "science opera."

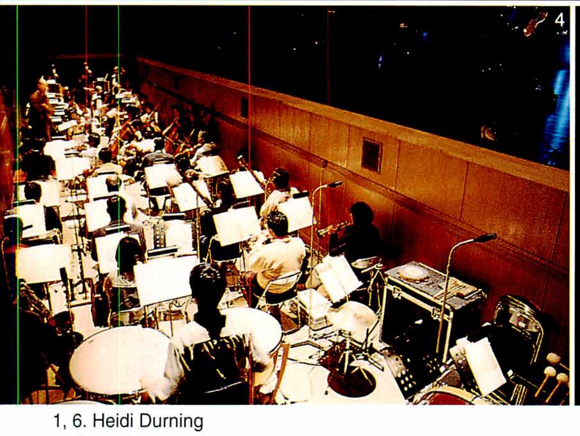
The date was April 5, 1995 and the location was Takatsuki Modern Theatre, Takatsuki City, Osaka Pref. This day was to become a memorable one for the BRH. The theatre with 500 seats was almost full, and the opera began smoothly with Okada's attention-holding narrative of the history of regeneration. During the interludes of this first part, the dances of various creatures were skillfully performed by dancer, Heidi S. Durning. Part 1 concluded with Haydn's Drum-Roll.

After the intermission, the spotlight shifted to Keiko Nakamura, the deputy director of BRH, who recited a biohistory version of *Peter and the Wolf*. This well-known story by S. Prokofiev was newly adapted to tell the story of evolution, with the role of Peter substituted by Time, the wolf replaced by a dinosaur, and the grandfather by Darwin. The story began with, "Five hundred million years had passed since the creation of the earth. Time awakened ...." Bacteria, Darwin, and the dinosaur were represented by flutes, bassoon, and horns, respectively. Time is played by a string ensemble. This new version of *Peter and the Wolf* received much applause and was praised as a "very unique and splendid story of evolution."

The concept of a "science opera" was first conceived by Kazuyuki Mogi, the former chief of the SICP (the Department of Science Communication and Production) division. Together with Keiko Nakamura, he remodeled the story of *Peter and the Wolf* into a very artistic interpretation of evolution. Wagner created the concept of "music drama" as a new genre that unites music and drama. With "science opera," Mogi sought to unite science with art. His idea was to "reinstate inspiration" in science, as he believes that "Science will meet with rejection when it is transmitted as pure knowledge. Science should start with inspiration, as does music, art, literature."

The performance of the "science opera" was realized through the cooperative effort of all the staff of BRH. With a limited budget, the capable members of the SICP division efficiently carried out the many tasks required, from negotiations for stage settings and coordinating arrangements with the Kyoto Symphony Orchestra (under the baton of conductor Michiyoshi Inoue) to even dramatic





1, 6. Heidi Durning performs her creative dances.
2. Keiko Nakamura's narration of *Peter and the Wolf* against a background projection of Darwin.
3. The stage setting designed by Junko Mada.
4. Kyoto Symphony Orchestra. Comments from many members were that "with the new story, the music sounds different."
5. Tokindo Okada discusses Haydn's music.
7. The finale. From the left, conductor Michiyoshi Inoue, Okada, Nakamura and Heidi Durning.
(4, 7: *during rehearsal*)
Photo: Yoshiki Geka

presentation and stage management.

The BRH received a special award in 1995, at the "Tokyo Creation Grand Awards" sponsored by the Tokyo Fashion Association. The recognition was given for "biohistory," the concept created by Keiko Nakamura, and for BRH's ability to incorporate the efforts of its two divisions, laboratory research and SICP, to attain such a successful program. The production of this "science opera" no doubt contributed significantly towards the acquisition of the award. The performance was telecast nationwide by NHK satellite broadcasting on April 29,1995.

Reports from BRH

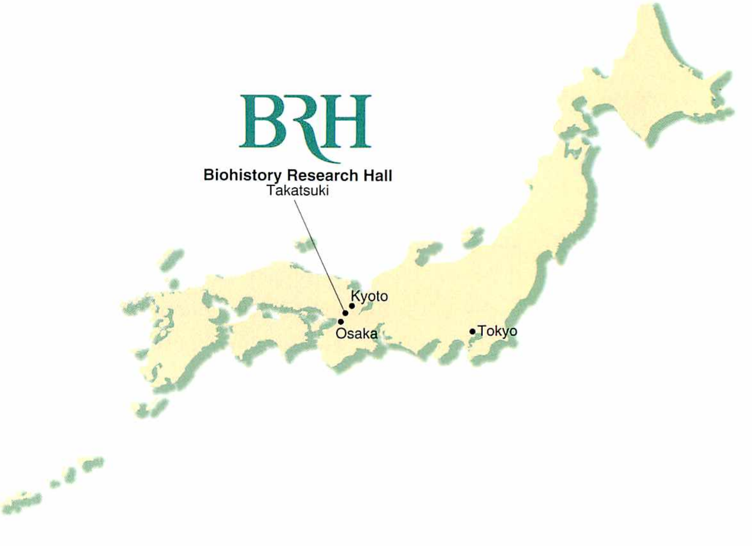
Our Departments

Photo: Kenzi Akagi

The Biohistory Research Hall is located in Takatsuki city between Osaka and Kyoto. It takes only 15 to 20 minutes by train from either of these two cities. The BRH is within easy reach of the Kansai International Airport. Situated on 1,320 square meters, the BRH occupies a spacious four-story building, housing an exhibition hall and gallery, a lecture hall, research laboratories and other facilities. The exhibition hall and gallery are open to the public five days a week throughout the year.

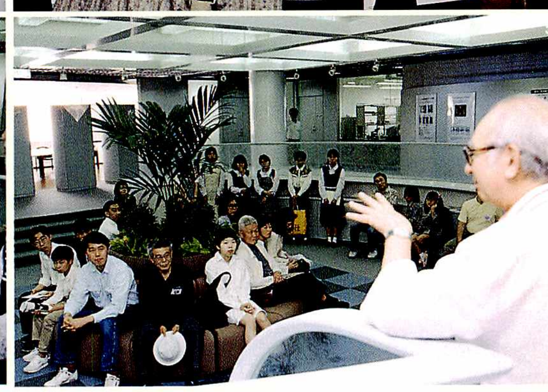
The Biohistory Research Hall has three departments, the Department of Laboratory Research, the Department of Science Communication and Production (SICP) and the Department of administration.

In the organization and carrying out of our activities, we particularly emphasize the importance of collaboration among staff members. Our "Laboratory tours" are organized jointly by the department of Laboratory Research and SICP. Laboratory research staff participate in the designing of exhibitions, and members of the SICP join in with laboratory scientists for seminars and discussions.



Laboratory Tour at BRH

At BRH, we organize "lab" tours several times a year. Our laboratory research staff guide visitors through their laboratories and explain the purpose of their research and the methods by which they conduct their experiments.



1. "Ribs form from this region," explains Aoyama in his discussion about the development of a chicken embryo.

2,3. "How beautiful they are!" Looking at chicken embryos in which the bones have been specifically stained blue.

4. "These are the algae I am using in my experiments." Yasuko Ishimaru explains in front of her laboratory. She was a postdoc in Ohama's laboratory for two years and is now at the Rockefeller University, USA.

5. The Director, Dr. Okada, welcomes visitors to the BRH.
(Photo:Yoshiki Geka)

A brief history of the BRH

1989············Keiko Nakamura proposed the concept of "biohistory."

1992············The first issue of the journal *Biohistory* was published, and a multi-method presentation was held in Tokyo.

1993············The exhibition hall was opened to the public in November.

1994············A special exhibition *Insects in Amber:Time Capsules from the Past* opened.

1995············The first "Science Opera" was performed in Takatsuki, Osaka. A special exhibition *The Cell:Motor Proteins and Cytoskeletons* opened.

1996············New findings of DNA analysis were displayed in the Hall of Evolution.
The BRH became affiliated with the Graduate School of Osaka University and has started to accept students from the University.

1997············"Science on Music" was performed in Tokyo in March.
A special exhibition *The Flower Biohistory* opens in April.

Lab Report 1

Mechanisms of Pattern Formation and Morphogenesis in a Butterfly Wing

Akihiro Yoshida
Ph. D. Senior Researcher
Eriko Takayama
Predoctoral Fellow
Mayumi Motoyama
Research Assistant

Patterns and forms of multicellular organisms are created via cell differentiation, changes in cell shape, cell movement, and cell death in both temporally and spatially defined manners. A lepidopteran wing is a good model for studies on pattern formation and morphogenesis since it is a simple two-dimensional system, consisting of a flat monolayer of epidermal cells. Using a wing of a cabbage butterfly, *Pieris rapae*, we are studying the following three subjects:

1) Scale arrangement formation. Scales, each of which are differentiated from a single epidermal cell, are arranged in a regular manner in the adult wing. This cellular arrangement develops from the homogenous cell population in the pupa through cell differentiation, cell shape change, and cell rearrangement. We are analyzing the underlying mechanisms involved in this process, both experimentally and theoretically.

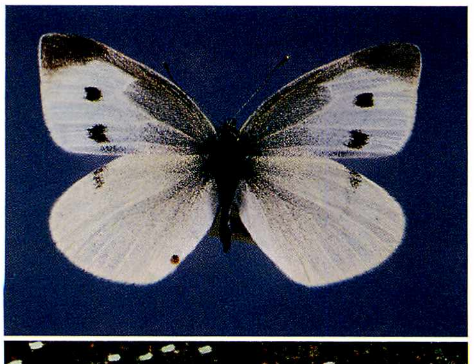
2) Degeneration of the marginal area. The outline of the adult wing (which gives the butterfly its beautiful distinctive shape) is formed by degeneration along the margin of the early pupal wing, involving extensive cell death. This cell death shares some common characteristics with apoptosis in vertebrates. Concomitantly, a morphological change takes place in the region of differentiation. We are studying the possibility that the change occurring in the differentiation region may result in efficient degeneration along the wing margin, in other words, total cooperation in the whole organism may occur during the partial degeneration.

3) Color pattern formation. The color pattern of the *Pieris* wing is basically composed of black and white scales; the former synthesizes a black pigment, melanin, while the latter produces a white pigment, pterine. We are studying the developmental mechanism of this simple color pattern, focusing in particular, on the cellular responses which are elicited by the administration of local perturbations in the pupal wing.

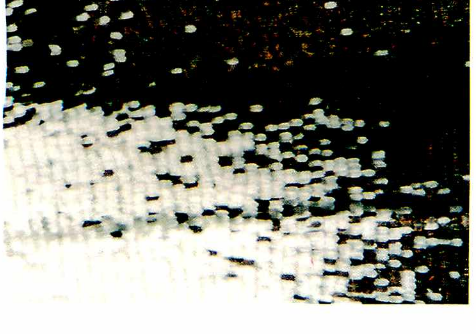
Kodama, R., Yoshida, A. and Mitsui, T. (1995)
Programmed cell death at the periphery of the pupal wing of the butterfly, *Pieris rapae*. *Roux's Arch. Dev. Biol.,* 204: 418-426.

Yoshida, A., Motoyama, M., Kosaku, A. and Miyamoto, K.(1996). Nanoprotuberance array in the transparent wing of a hawkmoth, *Cephonodes hylas. Zool. Sci.* 13: 525-526 .

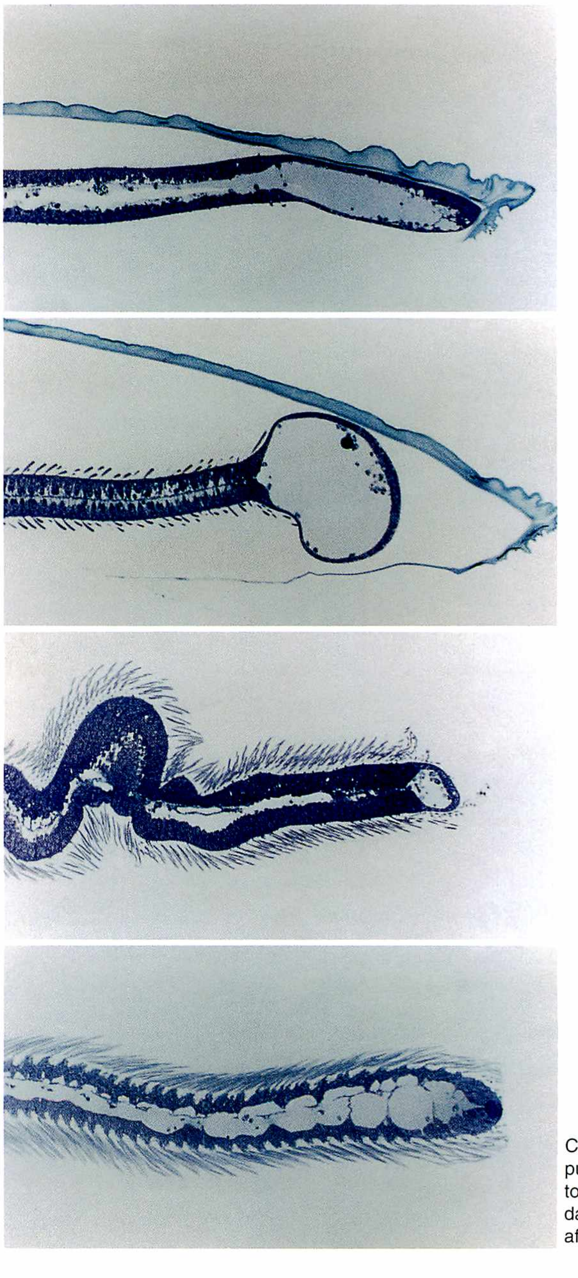
Takayama, E. and Yoshida, A.
Color pattern formation on the wing of the butterfly *Pieris rapae.* 1. Cautery induced alteration of scale color and delay of arrangement formation. *Develop. Growth & Differ* in press.



A cabbage butterfly, *Pieris rapae.*



A black spot in the *Pieris* wing. The color pattern is composed of black and white scales. Scales present anteroposterior rows arranged periodically in the proximodistal direction, irrespective of the color pattern.

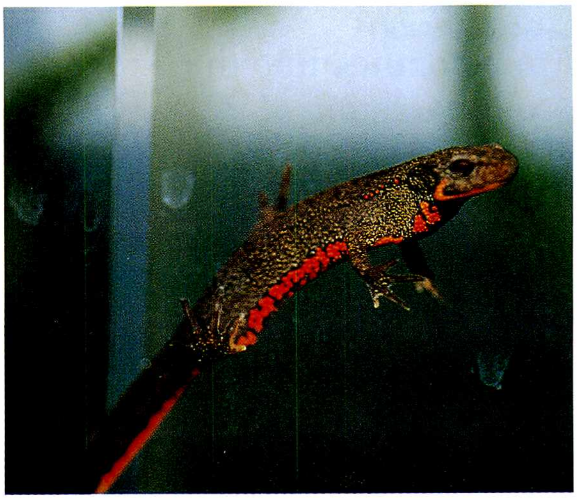


Cross-sections of the pupal wing (from the top) at 3 days, 3.5 days, 4 days, 4.5 days after pupation.

Lab Report 2

Non Lens Member of the Vertebrate Beta/Gamma Crystallin Superfamily is Exclusively Expressed in the Epidermis

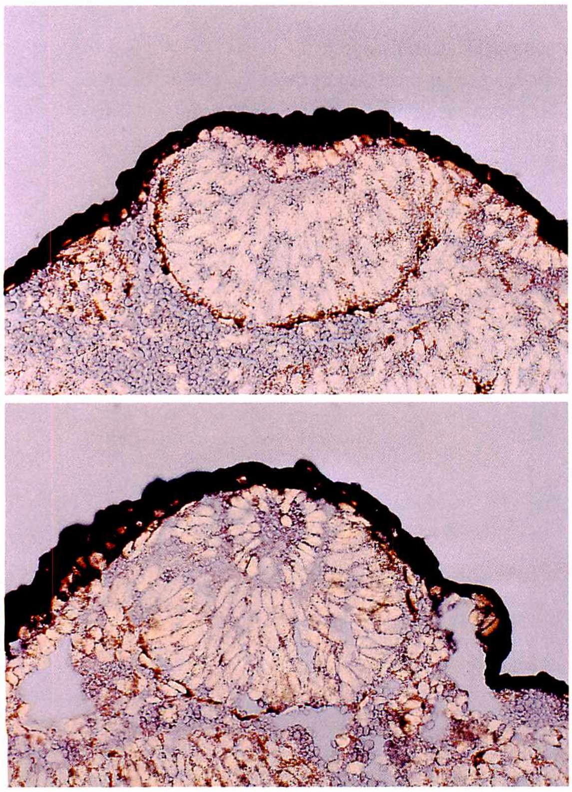
Tadashi Choku Takahashi
Ph. D. Senior Researcher
Nobuhiko Mizuno
Ph. D. Postdoctoral Fellow
Hiroyuki Sasakura
Graduate Student, Osaka University



The lateral view of the Japanese newt, *Cynops pyrrhogaster*, characterized by its typical red belly.

Our studies focus on the differentiation of the lens of the vertebrate eye. Lens develops from the epidermal ectoderm adjacent to the developing retinal primordium, the eye cup. Classical studies showed that lens development is fundamentally dependent on the presence of an eye cup. This mode of dependent differentiation was called "lens induction" by the eye cup. How and what interactions between the embryonic regions decide the developmental fate of the lens epidermis?

We have identified an epidermal differentiation-specific protein, EP37, and its gene, *ep*37, from the developing ectoderm of the Japanese newt, *Cynops pyrrhogaster*. The onset of *ep*37 expression throughout the entire epidermal ectoderm was found to coincide with the time when the neural ectoderm starts to differentiate. Our recent investigations, however, demonstrate that expression of *ep*37 was inhibited specifically within the lens epidermis during the time of lens development, while its continuous expression could be observed in other epidermal tissue including the regions overlying the lens tissue.



Photographs of in situ hybridization experiments to demonstrate *ep*37 expression in the eye region of the developing newt at tail-bud stages, showing that the lens placode (above) and lens vesicle (right) do not express *ep*37, while the epidermis, the developmental source of lens tissue, strongly expresses the gene.

Lens is characterized by the presence of highly specific proteins called crystallins, which can be classified into several subfamilies such as α, β, γ-crystallins, etc. Interestingly, detailed analysis of the amino acid sequence deduced from the EP37 cDNA revealed that EP37 is evolutionally related to the beta/gamma crystallins. We now believe that the EP37 may be one of the key molecules for studying the fundamental cues in lens development. Why and how does the lens epidermis cease to express EP37? How did crystallins become historically employed as structural proteins of the lens? Further study of EP37, not only from the level of gene expression regulation, but also from an evolutional point of view (eg. homologue studies) will bring us helpful hints to better understand these questions.

Takabatake, T., Takahashi, T. C. and Takeshima, K. (1992)
Cloning of an epidermis-specific *Cynops* cDNA from neurula library. *Devlop. Growth & Differ.*, 34, 277-283.

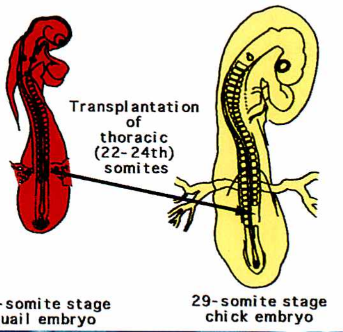
Takahashi, T. C. and Takeshima, K. (1995)
Expression of the epidermis-specific gene *ep*37 before and after metamorphosis of the Japanese newt, *Cynops pyrrhogaster*. *Zool. Sci.*,12, 333-336.

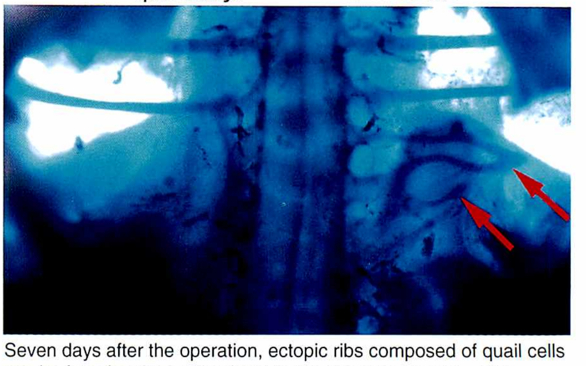
Ogawa, M., Takabatake, T., Takahashi, T. C. and Takeshima, K. (1997)
Metamorphic change in EP37 expression: members of the $\beta\gamma$-crystallin superfamily in newt. *Development Genes and Evolution* 206, in press.

Lab Report 3

From Somites into the Axial Skeleton

Hirohiko Aoyama
Ph, D. Senior Researcher
Kaichiro Sawada
Ph. D. Postdoctoral Fellow
Noriko Kato
Graduate Student, Osaka University
Yurie Hirosaki
Research Assistant





Seven days after the operation, ectopic ribs composed of quail cells can be found at the lumbar level in the chimeric embryo. This demonstrated that the transplanted region had been already determined to form skeleton possessing region-specific morphology.

The axial skeleton is derived from somites, which are the first segmental structures to appear during vertebrate development. How does each segmental unit develop? How do the somites regionally differentiate to form various types of vertebrae and ribs along the rostro-caudal axis?

One of our projects concerns the tissue interaction during the morphogenesis of the axial skeleton. Although a somite is destined to form certain types of skeletal elements , it requires interactions with other tissues to manifest its own morphogenetic ability. For example, if somites are temporarily cut off from the influence of the axial tissue, neural tube and notochord, by placing a piece of aluminum foil between them, the proximal part of the ribs tends to be lost.

We are further studying the tissue interaction between two derivatives of the somite, the dermomyotome and the sclerotome. We wished to determine whether the sclerotome, by itself, has the ability to direct its own morphogenesis independent of any influence from the dermomyotome. We address this question by means of heterotopical transplantation of isolated sclerotome and dermomyotome between chick and quail embryos.

Another project is on the study of regionalization during axial skeletal development along the rostro-caudal axis. Labeling of cells through the injection of a fluorescent dye (DiI), enabled us to trace the origin of thoracic somites back to the segmental plate and primitive streak. When we transplanted the prospective thoracic somitic region of the segmental plate, even transplants from the caudal-most portion gave rise to the thoracic vertebrae and ribs, suggesting that the presomitic mesoderm is already determined to form thoracic skeleton prior to or while passing through the primitive streak.

Aoyama, H. and Asamoto, K. (1988)
Determination of somite cells: independence of cell differentiation and morphogenesis. *Development*, 104, 15-28.

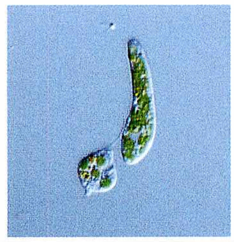
Aoyama, H. (1993)
Developmental plasticity of the prospective dermomyotome and the prospective sclerotome region of an avian somite. *Develop. Growth & Differ.* 35, 507-519.

Heterotopic transplantation of thoracic somites showing their ability to generate thoracic skeleton.
(left) Two day old chick embryo (29-somite stage) in which three lumbar somites were removed. Three thoracic somites isolated from a quail embryo at the 24-somite stage were put by the chicken embryo.
(right) After the transplantation.

Lab Report 4

Phylogenetic Analysis of an "Evolutionary Chimera": a Protozoan which Acquired Chloroplast from Symbiotic Algae

Takeshi Ohama
Ph. D. Senior Researcher
Yuji Inagaki
Ph. D. Postdoctoral Fellow
Megumi Ehara
Graduate Student, Osaka University
Hideko Tanaka
Research Assistant



(Photo)
Euglena gracilis, possessing both the abilities of photosynthesis and of taking on various forms due to its lack of a rigid cell wall.

Molecular evidence has clearly shown that mitochondria and photosynthetic plastids were once free-living bacteria which were acquired symbiotically by eukaryotic organisms early in their evolution. Such a "whole organism capture" seems to be a favorite trick for acquisition of a new set of profitable functions. This method has been used, not only during the very early stages of eukaryotic evolution, but many times ever since.

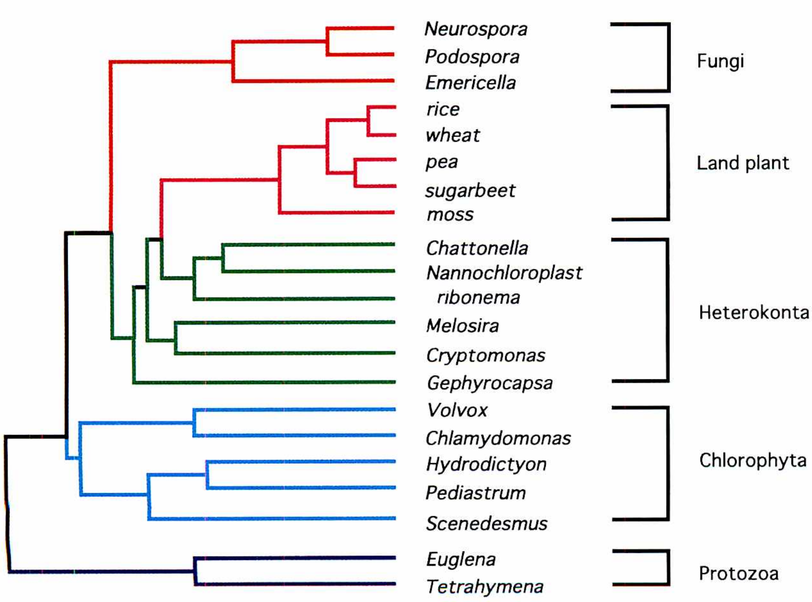
Existence of "Evolutionary Chimera," protozoan which contain chloroplasts acquired from symbiotic algae, has been suggested mainly based upon the electron microscopic analysis of chloroplasts. Like land plants, green- and red-algae possess chloroplasts surrounded by two membranes, while other algae have chloroplasts surrounded by three or four membranes. This observation has promoted speculation that some chloroplasts might have descended from endosymbiotic algae.

Circumstantial evidence also exists in support of the possibility that some algae may also be evolutionary chimeras. For example, wild type *Euglena gracilis* possess chloroplasts with a triple envelope, but strains that have lost their photosynthetic capacity (easily obtainable by UV- or antibiotic-treatments) still have the ability to grow efficiently in sugar-containing media, even in the dark. This is easily understandable if we suppose *E. gracilis* to be an originally heterotrophic organism (protozoa) that has recently "captured" chloroplasts. However, there is yet no conclusive data to prove this.

How can we reveal incidents that happened in the past? Molecular phylogenetic analyses might be the key. We have already obtained some preliminary results through our comparison of phylogenetic trees based on the mitochondrial COXI gene with those based on chloroplast genes. The mitochondrial COXI-based tree suggested that euglenophytes are closely related to protozoa. In contrast, euglenophytes have been shown to occupy a position very close to green algae in chloroplast-based phylogenetic trees. This discrepancy in the phylogenetic position of *E. gracilis,* which seems dependent on the genes used in constructing the trees, can be readily resolved if the chloroplast genes are assumed to have been acquired from green-algae.

We are in the process of constructing a molecular phylogenetic tree based on the mitochondrial COXI gene which will cover various species of algae. Comparison of trees based on different genes located in chromosome, mitochondria, and chloroplast will help in uncovering how many organisms have acquired chloroplasts through symbiosis with algae.

Ishimaru, Y., Ohama, T., Kawatsu, Y., Nakamura, K. and Osawa, S. (1996)
UAG is a sense codon in several chlorophycean mitochondria. *Current Genetics*, 30, 29-33.



Phylogenetic tree constructed by one of mitochondrial genes *COXI*

Lab Report 5

Evolution of Carabinae Ground Beetles Based on Mitochondorial Gene ND5 Sequences

Zhi-Hui Su
Ph. D. Researcher
Choong-Gon Kim
Ph. D. Postdoctoral Fellow
Syozo Osawa
Ph. D. Executive Researcher

Su, Z.-H., Ohama, T., Okada, T. S., Nakamura, K., Ishikawa, R. and Osawa, S. (1996)
Phyologenetic Relationships and Evolution of the Japanese Carabinae Ground Beetles Based on Mitochondrial ND5 Gene Sequences. *J. Mol. Evol.*, 42, 124-129.

Su, Z.-H., Tominaga, O., Ohama, T., Kajiwara, E., Ishikawa, R., Okada, T. S., Nakamura, K. and Osawa, S. (1996)
Parallel Evolution in Radiation of *Ohmopterus* Ground Beetles Inferred from Mitochondrial ND5 Gene Sequences. *J. Mol. Evol.*, 43, 662-671.

(The research group for the phylogenetic analysis of ground beetles had been working within Ohama's group, but became an independent group from April 1997. See details of research in page 10-13)

Report from SICP

Communicating the Wonder of the Natural World – From DNA to butterflies

Department of Science Communication and Production (SICP)
Keiko Nakamura Ph. D. Director
Kazuto Kato Ph. D. Associate Director
Akiko Takagi Staff, Editorial Direction
Shuya Tanimoto Staff, Art Direction
Mitsuko Kudo M. Sc. Research Staff
Yasuko Noumi Assistant
Sachiko Mitsuishi Graduate Student, Osaka University

Oh! I have never seen so many stick insects!
They are remarkable!
How did their shape evolve?
(Comments by visitors at the exhibition of "Stick insects from around the world")

How beautiful these ground beetles are!
They shine like jewels!
(In the exhibition room of the evolution of ground beetles)

The natural world is full of wonder. It does not matter whether you are a professor of biology or a six-year old child. Looking at the remarkable shapes of stick insects or the beautiful patterns of butterfly wings, everyone instantly feels the intricate workings of nature. To do so is instinctive, one does not need much knowledge from biology textbooks.

Then, why not the same inspiration from DNA, proteins or cells? The double helical structure of DNA is quite well known for its beautiful structure. Cells seen through microscopes are often so beautiful that they appear as works of art. Developing embryos of animals never fail to fascinate observers with their beauty.

How can we impress people with the wonder of the natural world at all levels, from molecules to cells to organisms? How can we present science, usually thought of as being hard to understand, in a manner that can convey to people its truly enjoyable character? It is probably not good tactics to try to explain all the details of research, and risk overwhelming people with too many facts. Rather, we should choose good examples to illustrate the wonderful workings and stories of life processes.

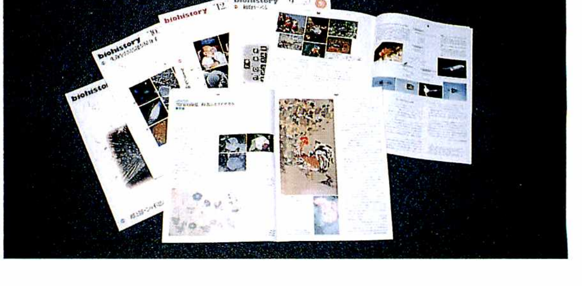
When organizing our activities, we always ask: How can we be scientific, artistic, and at the same time entertaining? To do this, we try to combine a variety of disciplines such as art, music, poetry and literature with science. We believe that science should give the same joy and wonder as these various activities. So, by combining many of them together, we can create a new way of presenting science.

One of our exhibitions at the BRH featured fossilized insects in amber. Visitors were first invited to look at the beautiful amber and examine the insects within. Then we explained what could be learned about the evolution of insects and other animals from these amber specimens. Finally, we showed them how to extract and analyze DNA from the insects embedded in the amber using the PCR method. In this way, visitors were not forced to understand all the explanations, but they could enjoy part or all of the exhibition depending on their interests and background knowledge.

Showing stick insects and ground beetles (currently on display at the BRH) is also a good way to introduce visitors to the marvels of the natural world. In the room containing the exhibit of the evolution of ground beetles, we present the ground beetles along with the results of their DNA analysis (from the BRH lab) in a beautifully displayed setting.

In our exhibition of "The Cell" (October 1995-March 1997), we asked ten biologists in the fields of cell and developmental biology to contribute their photographs of cells. We enlarged these photographs onto huge panels (many larger than one square meter) and arranged them to obtain the atmosphere of an art exhibition. Although not all visitors understood the details of the scientific content, most were impressed by the beauty of the cells. In particular, many artists and designers expressed strong interest in the microscopic world. They did not have much knowledge of cell biology, yet they were instantly captivated by the beauty of the cells. Even those biologists who use cells as everyday tools in their studies were deeply impressed by the beautiful photographs.

Of course, organizing exhibitions is only one of many ways to present science. We publish the quarterly journal *Biohistory*, organize talks by scientists in a wide range of fields, produce videos and other audiovisual products and welcome visitors to the BRH. The "science opera" was one



Our quarterly journal *Biohistory*, a 32-page full color publication. It is distributed to more than 3000 readers all over Japan, including public libraries and universities and other schools.