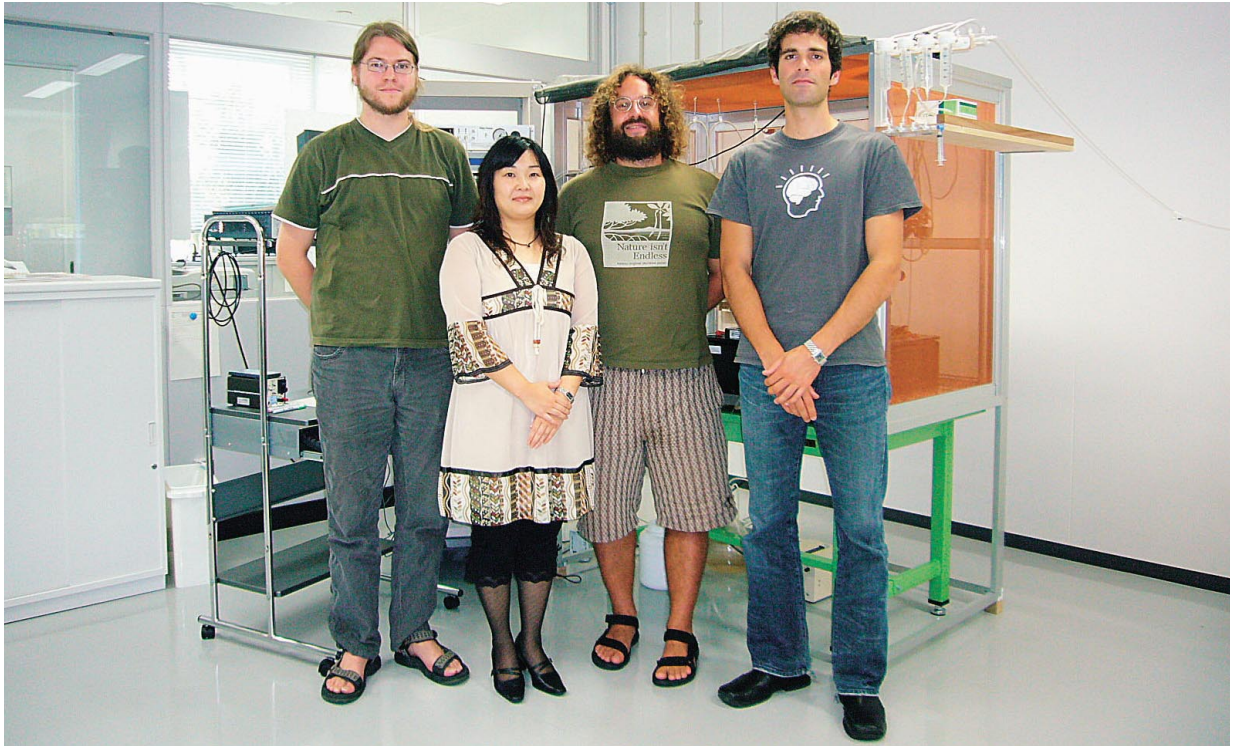


The Okinawa Institute of Science and Technology Promotion Corporation is an independent administrative institution launched in September 2005 to conduct outstanding research and to prepare for the establishment of a graduate university of science and technology in Okinawa. OIST News is a print publication intended to highlight current activities at OIST.



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Members of the Theoretical and Experimental Neurobiology Unit

Theoretical and Experimental Neurobiology Unit  
Principal Investigator: Dr. Klaus Stiefel (second from right)

The Theoretical and Experimental Neurobiology Unit, led by Dr. Klaus Stiefel, was launched in November 2006 in Uruma City. Thanks in large part to the time and effort the unit dedicated to the project in the first year, it has successfully established the necessary research infrastructure, including an in-vitro patch-clamp setup and a computational cluster. Born and raised in Austria, and educated in Austria, Germany and the U.S.A., Dr. Stiefel is fluent in German and English. He hopes to soon make Japanese his second foreign language. An avid scuba diver, Dr. Stiefel has taken a number of photos of fish in Okinawa waters, including one featured on the poster for a workshop he will co-organize in November. With *OIST News*, Dr. Stiefel talked about his background, ongoing research project and its goals.

### ***Nature boy becomes neuroscientist***

I have always been interested in nature. As a youth, I enjoyed playing in nature and reading about evolution. For my undergraduate degree at the University of Vienna, I pursued microbiology, the study of bacteria and viruses. During that time, I participated in a one-year exchange program at the University of California, San Diego (UCSD), from where I went on to do a research internship at the Scripps Institute of Oceanography, focusing on photosynthetic bacteria called cyanobacteria that exist numerous in the



Dr. Stiefel at his office in Uruma City

ocean. But, due to a strong neuroscience program offered by UCSD, I became interested in brain research, a field in biology I think has the most interesting open questions. I have been fascinated by this study since then.

### ***Investigating the function of individual neurons***

The goal of our research is to shed more light on the property of individual neurons by combining an experimental approach that employs whole-cell patch-clamp recordings, which allow low-noise recording of neuronal membrane voltages, and a theoretical approach that uses computer simulation. We want to find an answer to the question, "what type of computer is a neuron? "

#### **1. Study of the frontal cortex**

Animals and humans are able to do fantastic things. For

example, when a flying bird spots a fish in a river and dives into the water to catch it, the bird thinks about the speed of its dive, the size of the fish, and any move the fish makes. Many of the capabilities that animals and humans have, including the ability to react to various differences in time, depend on the capabilities of billions of neurons that exist in the brain. By looking at how precisely neurons transmit signals from one to another, our unit is investigating what individual cells in the frontal cortex contribute to the ability of the brain. The frontal cortex is a decision-making and integration area in the brain that receives inputs related to seeing and hearing, as well as inputs from motivational centers.

## 2. Relating neuronal function to morphology

After completing my Ph.D. study on synaptic plasticity in the cerebral cortex at the Max Planck Institute for Brain Research in Frankfurt, Germany, I returned to the U.S.A. to conduct post-doctoral research at the Salk Institute. There, I investigated the relationship between function and structure of dendrites using an artificial neuron. This research is what I have continued at OIST. Our unit is trying to find the best neuron to fulfill a simple function. For instance, if you want to have a car best suited to find a parking spot in city traffic, it needs to be small. If you want to win a cross-country race, then the car would be huge. Similarly, we have asked what a neuron with a specific task looks like, and how it would look if the task is more complicated or different. We have focused on dendrites, the branches that receive inputs on neurons, because they make a bigger difference in their shapes than axons, in which an active process or an enhancing signal is already present.

## 3. Combing experimental and theoretical approaches

Mathematics works with simulation aspects of our research. For electrophysiological measurements, we try to reproduce what is happening in a cell by running a computer simulation. We are looking at the effect of different neuromodulators on the precision of neural spiking. A neuromodulator is a substance that changes a basic operating mode of the brain. Computation is a tool for impossible experiments, such as eliminating all



Mr. Benjamin Torben-Nielsen, M.Sc., works on a computer

calcium channels in a cell. Additional computation also enables us to make predictions further in the future.

The problem often experienced by biologists is that there are so many components in the brain. For example, the statement, cell A activates cell B and vice versa, alone does not tell what happens in the brain. One needs to know how strongly they activate each other, how fast, and if there is any delay.

Only when all of these factors are determined, one



Dr. Stiefel stands in front of a computational cluster used by his unit

understands how they will act in concert and what kind of behavior is going to result from the system. Therefore, in order to understand what is happening in the brain, we have employed the approach of solving equations by simulating what was measured electrophysiologically.

## 4. Constructing multi-scale models of the brain

In November, I will co-organize a workshop on multi-scale phenomena, which brings biologists and mathematicians together to discuss sophisticated mathematical problems of different scales. In the ocean, there are differences between water temperatures at the surface and 30 meters below, as well as water temperatures in Okinawa and Hokkaido. The little difference and the large difference both influence fish population. Similarly, there are many levels of complexity in the brain, including a neuron which is only a tenth of a millimeter in length and composed of many membranes, individual proteins, channel proteins, etc. There are also parts of neurons, regions of the brain and the whole brain, several centimeters long. Each of these builds on lower ones and receives justifications from higher ones. They interact with each other in an interesting way. We are interested in the integration of brain function across multi-levels.

### *Bringing experiences to OIST*

The good thing about the American research system is, at least in a place like the Salk Institute, people are really open. If you have a question, you can talk to world-class scientists without having to worry too much about hierarchy. Also, the interactions among researchers from different local



Seminar by Dr. Stiefel at the University of the Ryukyus in October 2007

universities and research institutions are very active. The intellectually-thriving, very positive research environment I experienced there is what I would like to help create at OIST.

From a research aspect, I feel fortunate to receive good funding. To my knowledge, our unit is among the first ones in the world to use a field-programmable gate array (FPGA), a piece of reconfigurable hardware, to implement the dynamic patch-clamp recording technique. We are still a small unit, but I hope to add more members. Since we are conducting purely basic science, our research is unlikely to directly impact the treatment of ailments associated with the brain. It will, however, help researchers studying psychiatric diseases understand about the brain mechanism. I hope our research will contribute to the study of brain disorders such as schizophrenia.

The good funding also allows us to invite scientists from all over the world. Last year alone, I co-organized four workshops and hosted seven seminars. The workshops, such as the Okinawa Computational Neuroscience Course (OCNC), provide student participants with opportunities to talk to some of the leaders in the field. Even though Okinawa is a bit isolated, we feel part of the worldwide scientific community because of our ability to host visitors and these workshops.

At the new OIST campus, preparation is underway to develop scientific computing facilities, including a high-performance computing (HPC) center that is 70 times bigger than the computing facility of our unit. The HPC center will shorten simulation time tremendously, taking only about one hour to finish what it currently takes us three days. Realizing a mistake after one month of simulation is crucial, so I hope our scientific productivity will go up.



Poster artwork by Dr. Stiefel for the workshop on multi-scale phenomena in biology he will co-organize on November 4-6, 2008 in Okinawa. The poster features a photograph of a spadefish, taken by Dr. Stiefel, at Cape Maeda.

More about the workshop can be found at <http://www.irp.oist.jp/tenu/multi.html>

## A Promising Star

### Mr. Maxence Le Vasseur, M.Sc.



Mr. Le Vasseur joined OIST in March 2007, shortly after the launch of the Theoretical and Experimental Neurobiology Unit. A native of Quebec Province in Canada, Mr. Le Vasseur studied biomedical sciences for his bachelor's degree and obtained a master's degree in neuroscience at the University of Montreal. Inspired by the ongoing research at OIST, Mr. Le Vasseur has decided to pursue a doctoral degree starting this fall. With a few months remaining until his departure, Mr. Le Vasseur talked about his role in the unit and future aspirations.

I came to Okinawa in the summer of 2006 following my girlfriend from home. She was starting postdoctoral research at the University of the Ryukyus, where I also ended up taking Japanese classes. A few months later, I was recruited to the Theoretical and Experimental Neurobiology Unit after applying for a position that surprisingly matched my research background.

In the unit, I use whole-cell patch-clamp techniques to record single neuron electrical activity in brain slices from mouse prefrontal cortex. We investigate the influence of different neuromodulators on diverse signal processing properties in neurons such as spiking precision and reliability. Although a lot of research has taken place on the effect of individual neuromodulators, there is no well-established study investigating the effect of neuromodulator interactions on signal processing. We aim to unravel this question by testing how serotonin, dopamine and acetylcholine, individually or in combination, modulate the spiking properties of neurons when applied at different concentrations. Preliminary results suggest that combinations of these neuromodulators modulate the neuronal properties in a way not directly predictable from the effects observed when the neuro-modulators are applied separately.

Working at OIST has been a stimulating experience and I am thrilled to start my Ph.D. with all the knowledge and experience I have gained here. The average length for a doctoral program in Canada is about three to four years and I would absolutely consider coming back to OIST afterward.

## PI Lectures

Researchers of OIST have given a number of lectures to local schoolchildren as part of an effort to raise their interest in science and to promote the graduate university project. This spring, three Principal Investigators, Dr. Ichiro Masai of the Developmental Neurobiology Unit, Dr. Mary Ann Price of the Developmental Signalling Unit, and Dr. Gordon Arbuthnott of the Brain Mechanisms for Behaviour Unit, each gave a lecture at a local school to talk about their background and research.

### Using genes to investigate the mechanisms of developmental biology

Dr. Ichiro Masai of the Developmental Neurobiology Unit

February 25, 2008 at Yamada Junior High School in Onna Village

In his first lecture to schoolchildren since joining OIST in October 2006, Dr. Masai first talked to the entire school of approximately 60 students about his academic background, saying that he had first learned in a university biology class that genes determine the formation of multi-cellular organisms of living creatures. Dr. Masai said his desire to investigate this mysterious mechanism has led him to pursue biology. Explaining that the human body consists of hundreds of cell types, all originating from the fertilized egg, Dr. Masai told the students that developmental biology is the study of the process by which a single fertilized egg develops into different parts in our body. He said the whole mechanism behind the process has yet to be revealed, adding that his unit aims to elucidate the mechanisms that control cell fate decisions and tissue pattern formation by using zebrafish. He further explained that the unit is investigating whether genes regulate neuronal development by focusing on mutants showing defects in retinal development of zebrafish.



Dr. Masai



Dr. Masai takes a question from one of the students

Using an analogy of mountain-climbing, Dr. Masai concluded his lecture by saying that in order for scientists to conduct research, one must first choose a mountain (research theme) and a course to climb (research strategy), while also obtaining funding (research funding). He said the next state would be to arrange climbing gear (procurement of research equipment and goods), and to form a climbing party (training of research staff and formation of a unit), after which an actual climb (experiments) begins. He noted that it is also important to summarize the climb afterwards (research results to be disseminated in various forms including presentation at society meetings and publication in journals) to complete the research.

### Why I became a scientist

Dr. Mary Ann Price of the Developmental Signalling Unit

February 29, 2008 at Afuso Junior High School in Onna Village

Dr. Price began her lecture by passing out several samples of live *Drosophila* to a curious audience of about 60 students, explaining that although all of the samples are biologically categorized as *Drosophila*, their fly wings are not identical, and that the wings actually have different numbers of veins because of their patterning during development. Saying that her unit is using *Drosophila* as a model system, Dr. Price explained that the major interest of her research is the mechanisms cells use to decode



Dr. Price

extracellular signals during development. She added that inherited developmental disorders in humans result in such forms as skin cancer and polydactyly, a term used to describe having extra fingers and toes.

For the remainder of her lecture, Dr. Price talked about her youth, surprising the students that she was born in Zama City, Kanagawa Prefecture, and spent four years in Okinawa with her family from 1984. An avid athlete whose first love was mathematics, Dr. Price said she was immensely inspired by her biology teacher in the U.S.A., as the enthusiastic teacher taught a young Dr. Price the pleasure of studying science. Showing the students an old photo of a DNA model she once made in school using gumdrops, Dr. Price said she had once thought of becoming a high school science teacher. She continued, however, that she decided to become a scientist after conducting a project on the structure of a stable form of sulfuric acid.

Dr. Price said the project, which she worked on during the third and fourth year of her undergraduate study, made her realize the excitement of finding the first answer in the world to a question. Dr. Price said she has pursued research since then.



Students take a close look at a *Drosophila* sample

## Brain Mechanism for Behaviour

Dr. Gordon Arbuthnott of the Brain Mechanism for Behaviour Unit

March 12, 2008 at the Senior High School affiliated with Showa Pharmaceutical University in Urasoe City

In a lecture that fell on this year's Brain Awareness week, Dr. Arbuthnott talked to a group of about 80 students, who are planning to pursue either medical science or pharmacy in a university. Originally from Scotland, Dr. Arbuthnott humorously began the talk by showing a photo of the traditional Scottish uniform as worn by his grandfather, a former captain in the Gordon Highlanders, and a map of Scotland with a town's name, Arbuthnott.



Dr. Arbuthnott

On his research at OIST, Dr. Arbuthnott said his unit is investigating how the brain controls movement in order to understand the parts of brains that control behaviour. In an experiment that caught the students by surprise, Dr. Arbuthnott asked them to stand up and lean against the nearest wall. As the students found themselves able to lift the foot near the wall, but unable to do so when trying to lift



Students try an experiment

the other foot, Dr. Arbuthnott explained that the difficulty is similar to what is experienced by people diagnosed with Parkinson's disease. Introducing the students to his past and ongoing research on the disease,

which focuses on the role of dopamine in a rat's behaviour, Dr. Arbuthnott explained that even though the dopamine precursor L-DOPA helps treat Parkinson's disease, it still remains unknown how L-DOPA works in the brain.

Saying that one of the students might one day find the answer to the question, Dr. Arbuthnott concluded his lecture by stressing the importance of basic science in developing treatment for patients. He added that having curiosity and questions is the key to becoming a scientist.

### Student interviews

*"It was my first time to listen to a lecture by a foreign researcher. Dr. Arbuthnott told us about his research in a very interesting way, using experiments. I also learned about the current activities of OIST toward the opening of the graduate university."* Ms. Yuko Oshiro Second-year student

*"I had never seriously thought about studying the brain since I have been interested in becoming a pharmacist. Dr. Arbuthnott's lecture, however, has generated my interest in brain research."* Mr. Shota Fukushima Second-year student

*"The lecture gave me an opportunity to learn about the brain and neurons, which I have yet to study in a biology class. It was very interesting and easy to understand."*

Ms. Hanae Henzan First-year student

*"I learned that basic scientific research including experiments with rats is important to find a treatment for a disease. The experiment allowed me to put myself in the shoes of a Parkinson's patient. The lecture was very useful for me to determine a future academic course."*

Ms. Kyoka Shiroma First-year student



Dr. Arbuthnott listens to a student during a Q&A session

*"I had heard of OIST as a research institution with world-class scientists. Contrary to my impression of them, Dr. Arbuthnott was very friendly and his talk was very easy to understand. It was very refreshing to listen to a lecture by a foreign speaker."*

Mr. Shota Nagahama Second-year student

## International Workshops and Seminars

OIST has been hosting international workshops and seminars to enhance cooperation with research institutions at home and abroad. These workshops and seminars also help introduce the vision of establishing a graduate university in Okinawa to the worldwide scientific community. Below is a list of workshops and seminars that took place between March and May, 2008

### March 3 Seminar at the Research Laboratory "Specialized Synapses in the Eye and Ear"

Speaker: Dr. Henrique von Gersdorff, RIKEN Harima Institute SPring-8 Center  
Organizer: Dr. Tomoyuki Takahashi, OIST

### March 6 Seminar at the Research Laboratory "Shortest Computer Programs: Life outside the Effective Universe"

Speaker: Dr. Jason Teutsch of RAND Corporation  
Organizer: Dr. Robert Sinclair, OIST

### March 8-11 Workshop on Systems Biology of MAPK pathways at the Seaside House

Co-organizer: Dr. Hiroaki Kitano, OIST

### March 12-25 KNU-OIST Workshop on Stem Cell Biology and Neuroscience at Kyungpook National University in South Korea

Speakers: Dr. Kenji Doya, Dr. Shogo Endo, Dr. Mary Ann Price, Dr. Jeff Wickens

### March 14 Seminar at the Research Laboratory "Parallel Simulation of Large Neuronal Networks on Clusters of Multiprocessor Computer"

Speaker: Dr. Hans Plesser, Norwegian University of Life Sciences  
Organizer: Dr. Erik De Schutter, OIST

### March 18 Seminar at the Research Laboratory "Global organization of cerebral cortical networks: Topology, layout, development and function"

Speaker: Dr. Claus C. Hilgetag, Jacobs University  
Organizer: Dr. Robert Sinclair, OIST

### March 19 Seminar at the Research Laboratory "A Diamond Twin - An application of discrete geometric analysis"

Speaker: Professor Toshikazu Sunada, Meiji University  
Organizer: Dr. Robert Sinclair, OIST

# New Research Units at OIST

June 20, 2008

07

## Marine Genomics Unit (established in April 2008)



Principal Investigator  
Dr. Noriyuki Satoh

The Marine Genomics Unit, led by Dr. Noriyuki Satoh, aims to elucidate the gene regulatory networks in development, evolution, and environment, mainly using a marine invertebrate chordate, *Ciona intestinalis*. After receiving a Ph.D. from the University of Tokyo in 1974, Dr. Satoh taught at Kyoto University's Department of Zoology as a lecturer and as an associate professor, before becoming a professor in 1994. Currently the president of the Zoological Society of Japan, Dr. Satoh served as an editor-in-chief of *Zoological Science* (1997-1999) as well as an editor of *Development Genes and Evolution* since 1994. In 2005, Dr. Satoh became the first Japanese scientist to receive an Alexander Kowalevsky medal, awarded to scientists for their achievements in comparative and evolutionary embryology.

## Physics and Biology Unit (established in April 2008)



Principal Investigator  
Dr. Jonathan Miller

Dr. Jonathan Miller, head of the Physics and Biology Unit, received a Ph.D. in biology (experimental) from the University of Cambridge in 1988 and a Ph.D. in physics (theoretical) from the California Institute of Technology in 1991. After holding research positions in the U.S.A. at AT&T Bell Labs, the University of Chicago, NEC Research Institute, and Princeton University, he served as an assistant professor at Baylor College of Medicine in Houston, Texas prior to joining OIST. Dr. Miller's current research focuses on quantitative comparative genomics: the inference of the action of selection on the sequence of a gene from its evolutionary history. Dr. Miller is widely known for his discovery of the first "zinc finger" in Sir Aaron Klug's laboratory, and subsequently for contributions to condensed matter physics and most recently to the interface of physics, biology, and medicine.

### March 25 Seminar at the Research Laboratory "Neuro-dynamical model framework for nicotine addiction"

Speaker: Dr. Boris Gutkin, ENS-Paris  
Organizer: Dr. Klaus Stiefel, OIST

### March 27 Seminar at the Research Laboratory "The thermodynamic formalism: from the statistical mechanics of spin systems to applications in evolutionary biology"

Speaker: Professor Dieter Mayer, Clausthal Technical University  
Organizer: Dr. Robert Sinclair, OIST

### March 28 Seminar at the Research Laboratory "A Coupled Oscillator Approach to Network and Single Cell Activity"

Speaker: Dr. Boris Gutkin, ENS-Paris  
Organizer: Dr. Klaus Stiefel, OIST

### March 31 Seminar at the Research Laboratory "Visual processing and short term synaptic depression"

Speaker: Dr. Mark van Rossum of the University of Edinburgh  
Organizer: Dr. Erik De Schutter, OIST

### April 6-10 International Workshop on Cell Regulations in Division and Arrest Under Stress at the Seaside House Organizer: Dr. Mitsuhiro Yanagida

### April 18 Seminar at the Research Laboratory "Extracellular nucleotides regulate two different micro-gial functions, i.e., phagocytosis and chemotaxis"

Speaker: Dr. Schuichi Koizumi, University of Yamanashi  
Organizer: Dr. Jeff Wickens

### April 18 OIST-IRP Internal Seminar at the Research Laboratory "Some experiments that suggest a surprising source of the therapeutic effect of deep brain stimulation"

Speaker: Dr. Gordon Arbuthnott, OIST

### April 18 OIST-IRP Internal Seminar at the Research Laboratory "Introduction of the Single Neuron Computation Unit"

Speaker: Dr. Klaus Stiefel, OIST

### April 25 Seminar at the Research Laboratory "Feedback learning in ADHD - Can reward resolve the problem?"

Speaker: Dr. Marjolein Luman, Free University  
Organizer: Dr. Gail Tripp

### May 9 OIST-IRP Internal Seminar at the Research Laboratory "Synaptic Plasticity in the Corticostriatal System"

Speaker: Cathy Vickers, OIST

### May 9 OIST-IRP Internal Seminar at the Research Laboratory "Analysis of zebrafish mutants showing defects in photo-receptor development and maintenance"

Speaker: Yuko Nishiwaki, OIST

### May 13 Protein 3D Structure Visualization and Structural Bioinformatics Workshop at the Research Laboratory

Lecturer: Dr. Eric Martz, University of Massachusetts

Organizer: Dr. Fadel Samatey

### May 14 Seminar at the Seaside House "Models of synaptic plasticity and their computational consequences"

Speaker: Professor Thomas Trappenberg, Dalhousie University  
Organizer: Dr. Erik De Schutter, OIST

### May 26 Biology, Levels and Learning Seminar Series at OITC "Part I: Introduction"

Speaker: Dr. Tony Bell, Salk Institute  
Organizer: Dr. Klaus Stiefel, OIST

### May 28 Seminar at the Research Laboratory "Focal stimulation of single presynaptic boutons on rat CA3 hippocampal neurons"

Speaker: Dr. Elena Kondratskaya, Trinity College Dublin  
Organizer: Dr. Klaus Stiefel, OIST

### May 28 Biology, Levels and Learning Seminar Series at OITC "Part II: Basics of Learning Theory"

Speaker: Dr. Tony Bell, Salk Institute  
Organizer: Dr. Klaus Stiefel, OIST

## OIST Career Seminar

On May 17, OIST held a career seminar, inviting approximately 30 students living in Okinawa and mainland Japan. In the event that began with opening remarks by Executive Director Dr. Robert Baughman in the Seminar Room of the Seaside House, a summary introduction of OIST was delivered, followed by a presentation by administrative staff on their work and job qualifications. In the afternoon, the students were taken on a tour of the Seaside House and the main campus site in Onna Village, before visiting the Research Laboratory in Uruma City. In their visit to research units, the participants had an opportunity to listen to the Principal Investigators speak about their research. At the end of the day, the participants commented that the event served as a great opportunity to see world-class science firsthand and to learn about various administrative positions in detail. Some undergraduate students considering pursuing a graduate study also expressed their eagerness to acquire the necessary skills to apply for a position at OIST.



Participants listen to presentations by OIST staff



Participants visit the campus construction site

## Visit by Vice Minister Yoshio Nakagawa

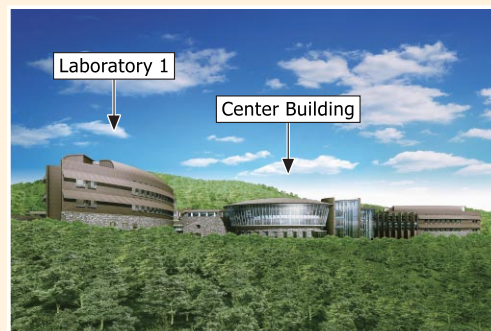
Mr. Yoshio Nakagawa, Senior Vice-Minister for Okinawa and Northern Territories Affairs, Science and Technology Policy, visited the Seaside House and the main campus construction site on May 15. Mr. Nakagawa, who once toured various renowned research institutions overseas, expressed his gratitude to Executive Director Dr. Robert Baughman that many distinguished scientists from all over the world have come to assist OIST. Mr. Nakagawa also pledged continued cooperation from the Japanese government to establish a graduate university of science and technology in Okinawa. Referring to the scarcity of natural resources and land in Japan, the vice minister said education and personnel training is indispensable for the nation to maintain global competitiveness. He added that the graduate university project is particularly important from this standpoint.



Vice Minister Nakagawa (center) receives a briefing on the campus construction by OIST staff

## Main Campus Update

Construction of Laboratory 1 and the Center Building commenced in March toward the initial use of the main campus buildings in FY2009. The extent of progress on the construction can be viewed on our Website, along with the latest activities at OIST. <http://www.oist.jp>



(CG-image)

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