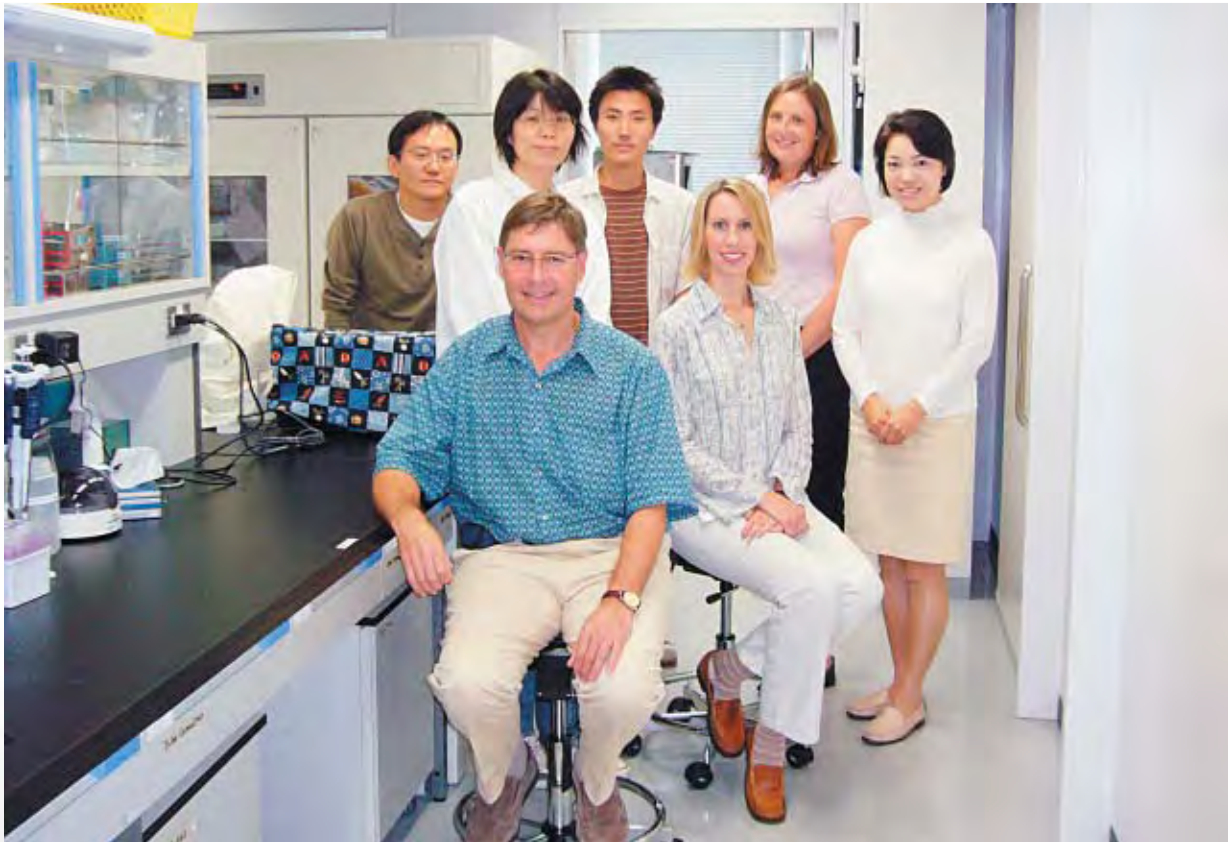


The Okinawa Institute of Science and Technology Promotion Corporation is an independent administrative institution launched in September 2005 to prepare for the establishment of a graduate university of science and technology in Okinawa. OIST News is a print publication intended to highlight current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



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Members of the Neurobiology Research Unit

Neurobiology Research Unit
Principal Investigator: Dr. Jeff Wickens (front)

The Neurobiology Research Unit, headed by Dr. Jeff Wickens, was launched in January 2007 in Uruma City. Originally from New Zealand, Dr. Wickens received a medical degree in 1982 and a Ph.D. in theoretical neurobiology in 1992, both from the University of Otago. During his 20-year tenure there in the Department of Anatomy and Structural Biology, School of Medical Sciences, Dr. Wickens was promoted to the status of Personal Professor in 2004, in recognition of his academic distinction. He has made widely recognized discoveries relating to the action of dopamine in reward-based learning, which were published in the leading international scientific journal *Nature* in September 2001.

Interested in psychology and computation, a college freshman pursues study in neuroscience

In high school, I was more interested in mathematics and physics than any other subject. When I was a first-year university student, however, I became fascinated by neuroscience after reading about artificial intelligence and studying neurobiology for the first time. I developed a passion for understanding how the brain works and found a connection between my technical interests, biology and human psychology. I have pursued this path since then. I am interested in someday having a mathematical understanding of how the brain works.

Learning from consequences

The human brain is one of the most complex systems in the known universe. It is the center of thought and emotion. It conducts and controls all of the body's activities and interprets information from each of our senses. The research focus of our unit is on the brain mechanism for learning. We are interested in physical changes that take place in the brain during learning, and how they are controlled and put to use by the rest of the brain. We are studying the basal ganglia, a part of the brain thought to play a key role in adaptive behavior through the selection of actions, goals, and strategies on the basis of previous reward-based learning.

1. Shedding light on the effects of dopamine

Our particular interest is in the cellular action of dopamine. This chemical is crucial for learning on the basis of positive reinforcement, and it is released in the brain when a reward is received or anticipated. A reward might be a food treat, but a tone, which signals a treat is about to be delivered, can also activate the dopamine cells and release dopamine. In the popular press, dopamine has been described as a type of pleasure chemical, but the subjective effects of dopamine are not so simple to explain. I would refer to it as a reinforcing chemical, one that may not necessarily produce a subjectively pleasant effect, but its importance is its effect on human behavior. For example, when you see children behaving badly, psychologists sometimes say they do it because even negative attention, like being scolded, can be reinforcing. In our research project, therefore, we are using several approaches to look at this question of what dopamine does in the brain. To investigate the effects that dopamine has on the strength of connections between nerve cells involved in behavior, we use microelectrodes to measure the changes in individual cells before and after a pulse of dopamine. The availability of two-photon microscopy allows us to use some powerful new techniques, based on the use of light, that permit measurements to be made at the level of single synaptic connections. With these methods we hope to discover the precise rules that the brain uses to rewire itself after each learning experience.

2. Finding clues for better treatment of Parkinson's disease

Dysfunction of the basal ganglia contributes to major neurological and behavioral disorders including Parkinson's disease, in which dopamine cells die off. At present, the prevailing clinical thinking is that a constant supply of dopamine is needed to treat the disease. Drugs such as L-DOPA increase the amount of dopamine that can be released from surviving dopamine cells. In our unit, however, we believe defining the timing requirements for dopamine to strengthen connections in the brain may provide a key to better treatments, because our research suggests that it might be really crucial to have pulses occurring at times when a person would be normally getting reinforcement. Replacing those pulses is becoming technically feasible, and we are now trying to determine the precise timing requirements for pulses of dopamine to bring about changes in synaptic strength.

3. Towards a better understanding of children with ADHD

My wife, Dr. Gail Tripp, is also a principal investigator at OIST, focusing on childhood behavioral disorders, most notably ADHD. She has found that children with ADHD seem to process rewards differently from other children. In most children, when rewards are delayed for some time, then the learning may be less effective. Meanwhile, children with ADHD are unusually sensitive to such delay of rewards. We think this may have a basis in the cellular mechanisms that we are studying in the Neurobiology Research Unit. One of the first joint outputs at OIST by Dr. Tripp's unit and mine is a theoretical paper in which we suggest that a deficit in the anticipatory activity of dopamine cells may explain some of the symptoms of ADHD. We believe that understanding the mechanisms in the brain that control reinforcement or behavior may lead to a better understanding of children with ADHD.



Dr. Wickens at his office in Uruma City

Privilege of being able to concentrate on research

Many people have asked me why I would give up a tenured position at an established university in beautiful New Zealand, to come and work at OIST, especially since I have a young family. We have a seven-year-old son who goes to a local elementary school and a three-year-old daughter who goes to a kindergarten in Okinawa City. We are definitely pleased with our life in Okinawa, and the quality of the education available at this level. We are a little worried about how much we are asking our children to adapt, including learning a new language. We also have concerns about how their schooling will proceed in later years. But the experience they are having now is very special, and I think that they will grow up with an understanding of two cultures. I hope they will appreciate that when they are older, or at least forgive us for making this move!

I am very excited by the potential for OIST to become a leading international graduate university, and I am very pleased to be able to contribute to the realization of this remarkable vision, which I hope will bring long-term benefits to Okinawa as well as contribution to research and education internationally. For my research, there are several benefits of being at OIST. The first is the opportunity to collaborate with the excellent neuroscientists at OIST and in Japan, who enrich the work of our unit. The opportunity to host visitors and workshops also enables us to develop our international linkages and become a hub in the emerging international network of scientists connected to OIST. The second advantage is good funding for my research. This allows us to recruit excellent staff and provide good resources for their research.



Dr. Mayumi Shindou performs whole-cell recording

I have been able to recruit excellent researchers and technicians from the U.K., U.S.A., New Zealand and Japan, and have excellent administrative support. In addition to having good people, we are also able to dedicate expensive equipment to specific research projects. For example, we are able to combine two-photon microscopy with patch-clamp recording, which is possible in relatively few laboratories world wide. Third, we have the time and opportunity to think about our research. Having the time to think is the most valuable resource for scientists because our work is only as good as our ideas. Here at OIST we are challenged to do the best science we can. The freedom to concentrate on the most important scientific questions of the day is a remarkable privilege. It is quite invigorating to focus completely on the science. I hope the culture of OIST will continue to place high value on research, and protect the researchers' time so they can work creatively and achieve important scientific results.

A Promising Star

Dr. Tomomi Shindou



Dr. Shindou has played a key role in setting up the Neurobiology Research Unit ever since its launch in January 2007. Formerly a researcher at a Japanese pharmaceutical company for more than 10 years, Dr. Shindou has worked on developing a drug to treat Parkinson's disease. In the midst of his research work in 2003, Dr. Shindou came across a study by Dr. Wickens, and this led to his pursuing post-doctoral studies under Wickens. After three years in New Zealand, Dr. Shindou followed Dr. Wickens to OIST. His wife, Dr. Mayumi Shindou, a former colleague at the pharmaceutical firm and the University of Otago, was subsequently recruited to the unit by Dr Wickens.

The dopamine precursor L-DOPA has been the most commonly prescribed treatment for Parkinson's disease. However, long-term L-DOPA treatment generally leads to a decline in its effect. At the laboratory of the Japanese pharmaceutical company I used to work for, we were developing an adenosine antagonist as an alternative treatment for Parkinson's disease. I saw firsthand in mouse experiments that the new drug maintained its effectiveness without causing any apparent side-effects, such as hallucinations. But I also became aware of the need to explore dopamine. Then I encountered the work by Dr. Wickens and his colleagues at the University of Otago in September 2001 *Journal of Neurophysiology*. Their findings on inhibitory interactions between spiny projection neurons in the rat striatum had such a strong impact on me that I resigned from my company to work with Dr. Wickens. In a fortunate turn of fate, I have now followed him to Okinawa to join OIST.

The launch of the unit meant starting from scratch, including setting up equipment and ordering supplies. But I actually found this job highly satisfactory because I had the same experience during my undergraduate years and at the pharmaceutical firm. Unlike my previous research environment in New Zealand, here I can communicate in Japanese, my mother tongue, and this has also made my work easier at OIST. The current focus of the unit is on the functions of the striatum in the basal ganglia. We are using mouse brain slices to record single-neuron electrical activity in the brain. This way, we are investigating the action of dopamine on the neural networks most involved in reward-based learning and movement. I would like to elucidate such physiological roles of dopamine and contribute to high-level research of the Neurobiology Research Unit.

Okinawa visit by BOG co-chair Dr. Torsten Wiesel

On October 15, Dr. Torsten Wiesel, a co-chair of the OIST Board of Governors and the winner of the Nobel Prize in physiology and medicine in 1981, met with Okinawa Governor Hirokazu Nakaima, and gave lectures at Okinawa Prefectural Naha Senior High School in Naha City as well as Okinawa Prefectural Nanbu Medical Center and Children's Medical Center in Haeburu Town. In the meeting with Governor Nakaima at the prefectural government office, Dr. Wiesel emphasized the need to exercise patience in building a world-class graduate university of science and technology. Governor Nakaima expressed his gratitude that many distinguished researchers from all over the world have come to assist OIST.



Dr. Wiesel (left) and Okinawa Governor Nakaima discuss OIST through an interpreter

In the lecture at Naha Senior High School, which marked the 60th anniversary of its founding this year, Dr. Wiesel addressed the entire school of about 1,400 students. He explained how visual information is processed in the brain, the very research that won him the Nobel Prize. In a lively



The entire school filled the gymnasium

Q&A session that followed his lecture, one of the students asked Dr. Wiesel why people learn. Dr. Wiesel answered that human beings have the curiosity to find out about things they do not know, and that strong curiosity nurtures scientists. At the Nanbu Medical Center and Children's Medical Center, Dr. Wiesel gave a similar presentation, but this time, to an audience of doctors, nurses and hospital staff. He encouraged the medical practitioners to go back to school to learn about state-of-the-art medicine and apply it to a clinical field of their specialty.



Dr. Wiesel receives a question from one of the students through an interpreter

Dr. Torsten Wiesel

Born in Sweden in 1924. After receiving his M.D. from the Karolinska Institute in 1954, Dr. Wiesel held academic positions at the Johns Hopkins School of Medicine and Harvard Medical School, where he became chairman of the department of neurobiology in 1973. In 1983, Dr. Wiesel joined The Rockefeller University and served as president for seven years until 1998. Dr. Wiesel has been secretary-general of the International Human Frontier Science Program Organization since 2000 and a BOG member of OIST since 2002. He is the 1981 Nobel Laureate in Physiology or Medicine.



Dr. Wiesel takes a question from one of the hospital staff

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 an interview with one of the speakers, Dr. Asha Gopinathan of GenSci-e-Tech in India, who visited OIST in September.



Dr. Asha Gopinathan,
Consultant, GenSci-e-Tech

Dr. Asha Gopinathan of GenSci-e-Tech in Kerala, India, visited OIST in early September to give two seminars hosted by the Theoretical and Experimental Neurobiology Unit led by Dr. Klaus Stiefel. In her first seminar, she talked about the role of the dendrite – how it converts synaptic input to neuronal output, with a focus on numerical analysis of the cable equation. For her second seminar, Dr. Gopinathan chose an entirely different topic: The issue of women in science, technology, engineering and math. By showing global data to back her point, Dr. Gopinathan presented reasons behind the glass ceiling preventing women from reaching positions of leadership and power, including a perceived gender bias and the disadvantage they find themselves in after temporarily taking time off from work to raise families. Finally, she discussed the situation surrounding female scientists in India, where their numbers remain very low even at world renowned institutions. With OIST News, Dr. Gopinathan shared her upbringing, career, and what can be done to remedy the situation.

Aspired by a female principal, a Delhi schoolgirl dreams of becoming a scientist

My parents always encouraged me and my sister to have a career. We went to a girls-only school in Delhi, where my principal became a source of inspiration. She exposed us to the various professions girls could hold, such as judges, doctors, scientists and diplomats. I became interested in becoming a scientist, probably because I excelled in math and science. I went to the Indian Institute of Technology (IIT) in Delhi for my undergraduate degree in Chemistry. After working in Professor M.K. Chandrasekharan's lab on bat brains for a semester in 1982, I pursued graduate studies in neurobiology in the United States where I worked in several laboratories including the HHMI laboratory of Professor Paul Adams.

Importance of networking among female scientists

Since returning home from the United States in 2000, I have not been able to find a tenured job. Meanwhile, I

have collaborated with various researchers, including Professor Joseph Mathew of the Department of Aerospace Engineering at the Indian Institute of Science in Bangalore. I am currently based in Trivandrum, the capital of Kerala, located at the South Western tip of India. With the growth of information technology, young people are lured away from a career in research in India even though new institutions are cropping up in the country. Women are still unrepresented in the field of science. In 2005, I attended the triennial International Conference of Women Engineers and Scientists in South Korea and saw firsthand the importance of networking among women. I would like to see a similar network develop in India so that female scientists and engineers will be able to share their expertise, experience and difficulties facing them as professionals, mothers, wives, and caregivers of the elderly.

Contact: dendron.15@gmail.com

August
6**Seminar** at the Initial Research Project Laboratory
"Bayesian Inference Using Spiking Neurons"Speaker: Dr Mike Paulin, Department of Zoology and Centre for Neuroscience, University of Otago
Organizer: Dr. Jeff Wickens, OISTAugust
24**Learning & Memory Seminar**
at the Initial Research Project Laboratory
"Regulation of Socio-Sexual and Emotional Behavior by Estrogen-Related Genes"Speaker: Professor Sonoko Ogawa, Laboratory of Behavioral Neuroendocrinology, University of Tsukuba
Organizer: Dr. Shogo Endo, OISTAugust
27**Seminar** at the Initial Research Project Laboratory
"From decision making to addiction: implications of new neurophysiological observations in hippocampus and striatum"Speaker: Dr. A. David Redish, Department of Neuroscience University of Minnesota
Organizer: Dr. Kenji Doya, OIST

Seminar by Dr. David Redish of the Department of Neuroscience, University of Minnesota, on August 27.

September
4**Seminar** at the Research Laboratory
"From Knot Theory to Molecular Biology"Speaker: Dr. Nafaa Chbili, Department of Mathematics, Korea Advanced Institute of Science and Technology
Organizer: Dr. Robert Sinclair, OISTSeptember
5**Seminars** at the Initial Research Project Laboratory
"Dendritic dynamics" and "Pathways to power and leadership"Speaker: Dr. Asha Gopinathan, GenSci-e-tech
Organizer: Dr. Klaus Stiefel, OISTSeptember
12**Seminar** at the Initial Research Project Laboratory
"Functional Interpretations of Adult Neurogenesis in the Dentate Gyrus"Speaker: Dr. Peter Appleby, Institute for Theoretical Biology
Organizer: Dr. Klaus Stiefel, OISTOctober
18**Seminar** at the Initial Research Project Laboratory
"Modeling Evolving Multiple Compartment EGFR Networks with the Multinomial Tau Leaping Algorithm"

Speaker: Dr. Michel Francois Pettigrew, Scientific Analyst, ScienceOps

November
8-10**OIST-Salk joint neuroscience workshop**
at the Salk Institute for Biological Studies

Participants from OIST: Dr. Robert Baughman, Dr. Erik De Schutter, Dr. Kenji Doya and Dr. Klaus Stiefel

November
14**Seminar** at the Initial Research Project Laboratory
"Cell cycle regulation of organelle biogenesis in fission yeast: the role of the cytoskeleton and dynamin-related proteins"Speaker: Professor Jeremy Hyams, Institute of Molecular Biosciences, Massey University
Organizer: Dr. Mitsuhiro Yanagida, OISTNovember
16**Seminar** at the Initial Research Project Laboratory
"Neuropeptides in Nematodes: The Ascaris Nervous System - a Simple Nervous System"Speaker: Professor Antony O. W. Sretton, Department of Zoology, University of Wisconsin- Madison
Organizer: Dr. Robert Sinclair, OISTNovember
19**Seminar** at the Initial Research Project Laboratory
"Designing Higher Performance Neural Prosthetic Systems"Speaker: Dr. Byron Yu, postdoctoral research fellow at the Department of Electrical Engineering & Neurosciences Program, Stanford University, as well as the Gatsby Computational Neuroscience Unit, University College London
Organizer: Dr. Kenji Doya, OISTNovember
21**Seminar** at the Initial Research Project Laboratory
"Formation of the capping complex at the pointed end of the actin filament"Speaker: Dr. Alla Kostyukova, Robert Wood Johnson Medical School, University of Medicine & Dentistry of New Jersey
Organizer: Dr. Fadel Samatey, OISTNovember
21**Seminars** at the Initial Research Project Laboratory
"The role of neuronal synchrony for coding information in visual cortex" and "The associative mechanisms of grapheme-color synaesthesia"Speaker: Dr. Danko Nikolic of Max-Planck Institute for Brain Research
Organizer: Dr. Klaus Stiefel, OIST

OIST celebrates 2nd anniversary



President Brenner and Minister Kishida

OIST celebrated the 2nd anniversary of the launch of the corporation in September 2005 with a reception at Manza Hotel in Onna Village on September 3. Among the distinguished guests was State Minister for Okinawa and Northern Territories Affairs, Science and Technology Policy Fumio Kishida, who also met with OIST President Dr. Sydney Brenner prior to the reception. Dr. Brenner announced that Dr. Robert Baughman, Associate Director for Technology Development, Office of the Director NIH/NINDS (National Institute of Health/National Institute of Neurological Disorders and Stroke) and Senior Advisor to the President at OIST at the time of the reception, will assume the post of Vice President and Executive Director on September 30, 2007.

Visit by Singaporean Health Minister Khaw

Mr. Khaw Boon Wan, the Minister for Health of the Republic of Singapore, and his delegation visited OIST on August 31. At the Research Laboratory in Uruma City, Dr. Mitsuhiro Yanagida of the G0 Cell Unit and Dr. Jeff Wickens of the Neurobiology Research Unit each took the minister on a tour of their units. Mr. Khaw then visited the Okinawa Health Biotechnology Research and Development Center in Uruma City, as well as the main campus site in Onna Village, where he was briefed by OIST staff on the main campus construction. Mr. Khaw commented afterward that he was very impressed with the ongoing research activities and the large number of young researchers at OIST.



Dr. Wickens shows Minister Khaw a microscopic photo



Dr. Yanagida (left) briefs Minister Khaw about his research

Dr. Doya wins prizes

Dr. Kenji Doya, who heads the Neural Computational Unit, was awarded the 21st Tsukahara Nakaakira Memorial Award given by the Brain Science Foundation at a ceremony on September 10 in Yokohama. This year, Dr. Doya also won the 3rd JSPS Prize, given by the Japan Society for the Promotion of Science.

OIST Main Campus Update

On October 20, construction workers drilled through the final wall of soil to join a vertical elevator shaft of the Center Building in the Lab Zone and an 80-meter tunnel that link the Lab Zone and the Village Zone. The extent of progress on the construction can be viewed on our Website, along with the latest activities at OIST. <http://www.oist.jp>



A view of the tunnel from the elevator shaft

OIST News No. 3

December 1, 2007

Published by Okinawa Institute of Science and Technology Promotion Corporation

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