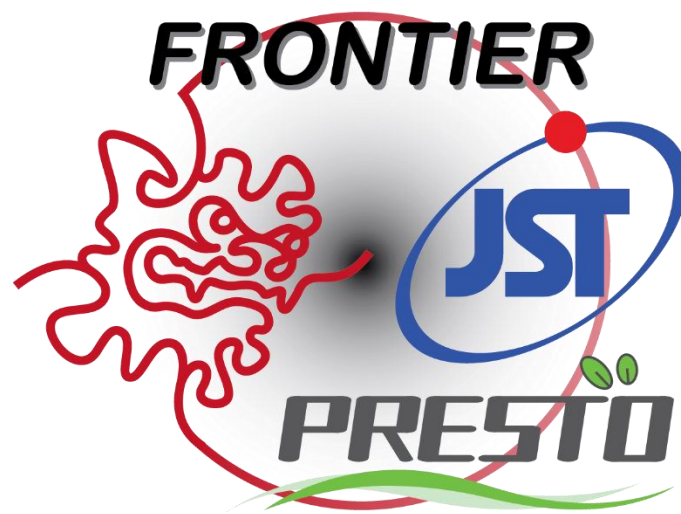


OIST-JST Presto Joint Symposium on Frontiers in Optics and Photonics



Date: 31 October, 2016 (Mon.)

Place: Room C210, Cent. Build., OIST

**Organized by Frontier-PJ, JST PRESTO, and
OIST (Quantum Dynamics Unit, Quantum
Systems Unit, Light-Matter Interactions
Unit, and Optical Neuroimaging Unit)**

Schedule

Session 0: Introduction and discussions

- 08:30-08:40 Welcome
Yuimaru Kubo, JST PRESTO & *OIST Graduate Univ.*
- 08:40-09:00 Introduction of OIST
Mary Collins, Dean of Research, *OIST Graduate Univ.*
- 09:00-09:25 JST Strategic Basic Research Programs
Sofia S. Suzuki, *JST*
- 09:25-09:45 PRESTO Frontier Project
Ken-ichi Ueda, *JST PRESTO, Univ. Electro-Comm.*

Session I: Bio-photonics

- 09:45-10:15 The light-driven ion pump proteins, microbial rhodopsins, from marine bacteria and its application to optogenetics
Keiichi Inoue, *JST PRESTO, Nagoya Inst. Tech.*
- 10:15-10:45 Imaging neuronal activity in awake mice
Bernd Kuhn, *OIST Graduate Univ.*
- 10:45-11:15 A new cancer therapy using near infrared light
Mikako Ogawa, *JST PRESTO, Hokkaido Univ.*

Session II: Quantum- and Nano-photonics

- 11:30-12:00 Feedback cooling and optical trapping of a massive pendulum for testing quantum physics at macroscopic scales
Nobuyuki Matsumoto, *JST PRESTO, Tohoku Univ.*
- 12:00-12:30 Quantum engineering of atomic systems with high fidelities
Thomas Busch, *OIST Graduate Univ.*
- 12:30-14:00 Lunch (Free for Discussions or Lab. Tour)
- 14:00-14:30 Quantum optical measurement technologies using entangled photons
Ryo Okamoto, *JST PRESTO, Kyoto Univ.*
- 14:30-15:00 Ultrathin optical fibres for studies on cold Rb atoms
Síle Nic Chormaic, *OIST Graduate Univ.*
- 15:00-15:30 Discussion & Closing

Fully-controlled photons and their proactive usage for new era creation (FRONTIER)

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Optical science has seen remarkable progress in recent years in the performance of light sources that provide new perspectives in a wide range of fields and serve as a major driving force for the development of new fields. Light is said to have essentially no intrinsic limitations. The goal of this research area is to explore boundaries by thoroughly investigating the essential character of light in all of its properties. We will conduct researches that tackle important issues in a variety of fields in an effort to tear down walls between disciplines by actively utilizing and applying these properties of light.

http://www.jst.go.jp/kisoken/presto/en/research_area/ongoing/areah27-1.html

The light-driven ion pump proteins, microbial rhodopsins, from marine bacteria and its application to optogenetics

Keiichi Inoue

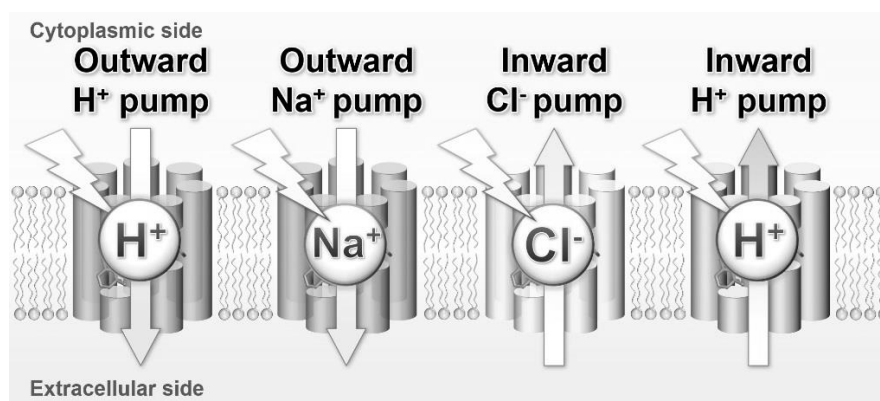
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Microbial rhodopsins are photo-receptive membrane proteins found mainly in diverse unicellular micro-organisms. They have seven-transmembrane α -helical structure and a common chromophore, all-trans retinal. Upon light absorption, the retinal isomerizes to 13-cis form leading to the expression of various biological functions. The most abundant rhodopsins are outward proton (H^+) pumps which transport H^+ from cytoplasm to outside of the cell, and bacteriorhodopsin (BR) is the first reported H^+ pump found in halophilic archaea. Following to BR, a light-driven inward Cl^- pump, halorhodopsin, was found from the same archaea. These rhodopsins are to play physiological roles of generating proton motive force (pmf) or regulating osmotic pressure in the cell by light.

While various types of H^+ pump rhodopsins were reported after BR, no light-driven pump of non-protonic cation such as Na^+ was discovered. In 2013, however, we have reported a new type of rhodopsin (KR2) in flavobacterium, *Krokinobacter eikastus*, functions as an outward light-driven Na^+ pump [1]. Whereas KR2 can transport Li^+ , H^+ is pumped in the absence of Na^+ and Li^+ or the presence of only larger cations (K^+ , Rb^+ and Cs^+). The sequence of KR2 is distinctively different from other microbial rhodopsins and it has the NDQ-motif composed of Asn112, Asp116 and Gln123 in the third helix. The spectroscopic and structural studies of KR2 revealed that the three residues of NDQ-motif play critical role for the Na^+ transport [1-3]. Upon light-activation, the all-trans retinal of KR2 isomerizes to 13-cis form. Then, a proton transfer occurs from the retinal Schiff-base to Asp116, the counterion for protonated retinal. The crystallographic analysis suggested that the protonated Asp116 changes the conformation of its side chain. The positive charge of H^+ inhibiting Na^+ transport is effectively sequestered by this movement, and the ion-transport pathway is opened between the retinal and Asp116. Then, Na^+ bounds to the site in the extracellular side of retinal from cytoplasmic side. Simultaneously, the recovery of H^+ to retinal occurs which interrupts the backflow of Na^+ and it is important for the vectorial transport. If KR2 is expressed in neuron, it efficiently inhibited neuronal firing with light [2]. This suggests KR2 can be applied to optogenetics, and the

locomotion behavior of *Caenorhabditis elegans* expressing KR2 in the neuron was inhibited upon illumination [2]. Despite of the physiological role of KR2 as Na⁺ pump, we revealed that its H⁺ transport is >1,000-times efficient than Na⁺, and new artificial K⁺ and Cs⁺ pumps were constructed based on the structural insights of KR2 [2, 5]. The unique ability of KR2 transporting various types of cations is expected to lead a new optogenetic control of diverse physiological phenomena. Following to KR2, we recently found a new class of rhodopsin, light-driven inward pump (PoXeR), from α -proteobacterium, *Parvularcula oceani* [5]. This is the first example of a light-driven pump which depolarizes membrane potential. PoXeR is expected to be a new type of optogenetic tool which suppresses neuronal cellular activity. In the presentation, the study on the ion-transport mechanism of PoXeR and the development of higher functional variants will be discussed.



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Imaging neuronal activity in awake mice

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One of the biggest mysteries is how behavior arises from neuronal activity and how sensory stimuli are represented in our brain. To shine some light on this mystery it is important to record neuronal activity on a cellular and subcellular level from many neurons, and to correlate the neuronal activity with behavior. In the Optical Neuroimaging Unit, we focus on the development and application of new methods towards this task.

Our animal model system is the mouse and for detecting the brain activity we use optical methods. To allow imaging of the brain we replace a small area of the skull by a glass cover slip which acts as a chronic cranial window to the brain. To convert the neuronal activity to an optical signal we use specifically designed genetically encoded calcium indicators which are based on the green fluorescent protein from jelly fish. The gene of this indicator is inserted into a viral vector nowadays regularly used for gene therapy. We inject the viral vector into the mouse brain before mounting the chronic cranial window. The indicator gene is under the control of specific regulatory sequences so that the indicators are only expressed in specific cell types. About 2 weeks after the injection of the viral vector into the brain the targeted neurons will start to fluoresce. To detect this fluorescence, we build two-photon microscopes which are specifically optimized for in vivo imaging. This microscopy technique allows us to three-dimensionally reconstruct neurons in the living mouse with a resolution of about 1 μm . The 2-photon imaging technique is limited to about 1 mm imaging depth. For this reason, we focus our research on cerebral or cerebellar cortex. 2-photon microscopy and the genetically encoded calcium indicators also allow us to record movies of the brain activity. During imaging the mice have to be head-fixed. To avoid unnecessary stress, the mouse is mounted on a treadmill to allow for running. In some of our projects we use virtual reality systems to give sensory feedback in response to running. For example, we increase sound intensity if the mouse runs toward a virtual sound source. So, even with being head fixed the mouse can perform behavioral tasks like decision making. The combination of these techniques allow us to study neuronal activity patterns of more than 600 somata of neurons or thousands of neuronal compartments simultaneously and to correlate the neuronal activity with behavior. With this data we can try to decode the neuronal activity patterns by machine learning algorithms and predict future behavior by analyzing current neuronal activity.

A new cancer therapy using near infrared light

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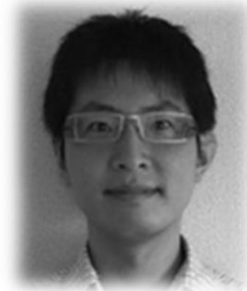
Near infrared photoimmunotherapy (NIR-PIT) is a new method of treating cancers by exposing them to an antibody-photosensitizer conjugate (APC) consisting of an antibody directed at a cell surface antigen overexpressed on the plasma membrane and a photo-activated silica-phthalocyanine (IRDye700DX: IR700) dye. The APC binds to cells expressing antigen and after NIR light exposure (690 nm), induces highly selective cancer cell death with immediately adjacent non-target expressing cells suffering no toxic effects. A phase I study of an antibody conjugate consisting of cetuximab (anti-HER1 antibody) linked to IR700, for the treatment of inoperable head and neck cancers is ongoing in USA (NCT02422979). However, the mechanism for killing the cells are not elucidated yet. To make the more potent and effective drug for PIT, it is necessary to know the mechanism.

In this study, we have investigated dynamic morphological changes after NIR-PIT using three-dimensional dynamic low coherence quantitative phase microscopy (3D LC-QPM), which is based on light scattering at the lipid bilayer. Additionally, cell membrane permeability was studied using various sized molecules. Also, we have shown that NIR-PIT rapidly induces the cardinal signs of immunogenic cell death, and that NIR-PIT-killed tumor cells induce the maturation of dendritic cells (DCs). Photochemical analysis is now ongoing.

Feedback cooling and optical trapping of a massive pendulum for testing quantum physics at macroscopic scales

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Is it possible to put a massive object into quantum superposed states? In terms of quantum physics the answer is “YES”, because quantum physics is a valid theory even at macroscopic scales. However, macroscopic objects are never found in a linear superposition of position states. This contradiction is related to the well-known measurement problem, which possibly implies that the breakdown of superposition and the quantum-to-classical transition are involved with fundamental gravitational effects. In opt-mechanical systems like gravitational-wave detectors, we focus on the realization of the ground state of a suspended mirror with the aim of testing quantum mechanics at macroscopic scales. To test quantum physics with a massive object, we try to cool a ‘pendulum’ mode of a mg-scale suspended mirror down to its ground state and preserve the state over one mechanical period. The suspended mirror is a part of an optical cavity, which is pumped by a continuous-wave optical laser. Reflected lights from the cavity is measured to extract information about the pendulum’s displacement. The displacement signal is electrically filtered and negatively fed back to a part of cavity’s mirrors, resulting in cooling of the pendulum mode. The cavity is detuned from its resonance so that the pendulum is optically trapped. Since each photon of the laser is too hot to be thermally excited even at room temperature, optical trapping reduces the number of quanta in the mode so that thermal decoherence is mitigated, i.e., oscillation number in the ground state is enhanced. To reach the ground state and preserve the state over one mechanical period, we try to: (i) make an optical cavity with intra-cavity laser power over than about 10 W; (ii) realize optical trapping, which enhances the resonant frequency of the pendulum to 1 kHz; (iii) make a suspended mirror with a mechanical quality factor over 10^7 ; and (iv) develop a displacement sensor with spatial resolution about 10^{-18} m/sqrt(Hz) @1 kHz. We have already met the demands given in (i) and (ii), which are often limited by instability of the cavity. Demand (iii) is partially satisfied, and demand (iv) can be satisfied by laser frequency stabilization.

Quantum engineering of atomic systems with high fidelities

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Spatial Adiabatic Passage is a technique with which the centre of mass of single particles can be moved between different trapping sites with high fidelity. It is an analog to the well-known STIRAP process for electronic systems, but allows for a larger number of controllable degrees of freedom. It is therefore a versatile and flexible approach to creating and controlling quantum states.

Among the additional degrees of freedom are access to higher dimensionalities, the possibility to create and control finite (angular) momentum states, the presence of interactions in many particle systems and the ability to add additional external fields. Here we will discuss all of these and show that they allow to extend the range of quantum states that can be accessed significantly.

While adiabatic techniques allow to obtain high fidelities and are robust against noise and errors, their adiabatic nature of it is often considered to be an obstacle, as it prevents experimental implementation. For spatial adiabatic passage, however, we will show that a shortcut to adiabaticity exists, which can be experimentally implemented with minimal experimental complexity.

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Quantum optical measurement technologies using entangled photons

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Optical measurement techniques have been widely applied to many fields. Recently, the news of the first detection of gravitational waves traveled around the world. In the experiment, the interferometric measurement with laser light enabled to detect the incredibly small fluctuation of space ($\sim 10^{-21}$ m). In medical field, optical coherence tomography which is based on low coherence interferometry is used to take cross-section pictures of retina. In near-future, a laser-sensing system called LIDAR may put the autonomous vehicles to practical use.

However, light has limits and weaknesses for optical measurement: standard quantum limit caused by the particle feature of light, diffraction limit caused by the wave feature of light and spread of the optical pulse by spectral dispersion. Recently, it has been found that these problems could be overcome using quantum light which is impossible to be described by classical electromagnetism. One of the candidates for such quantum light is “entangled light” which has quantum correlation between spatially separated two systems.

So far, various measurement techniques utilizing entangled photons have been proposed and demonstrated. For example, we experimentally realized an interferometer beating standard quantum limit with four photon entangled state [1, 2]. We also found that the depth-resolution of differential interference microscope could be improved by using two photon entangled state [3]. In this talk, we will introduce some latest quantum optical measurement technologies with our experiments.

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Ultrathin optical fibres for studies on cold Rb atoms

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Optical nanofibres (ONFs) have recently emerged as very useful tools for probing and trapping cold atoms, due to the functionality of such fibres in the development of atom-photon hybrid quantum systems. For example, ONFs have been shown to be highly efficient tools for demonstrating nonlinear optics phenomena in atomic media [1, 2]. This arises from the very high evanescent field intensities that can be achieved due to the very tight light confinement within very small mode areas over the length of the nanofibre. Exploiting this phenomenon, we have studied quantum interference effects using an optical nanofibre surrounded by cold 87Rb atoms via 2-photon processes at 780 nm and 776 nm. We have observed frequency up-conversion for a 776 nm probe power as low as 200 pW, asymmetric Autler-Townes (A-T) splitting for 20 nW of 780 nm coupling power, and EIT. These power levels are several orders of magnitude lower than those used in free space experiments and provide an all-optical switching technique at the few-photon level.

We also present our recent progress towards ONF-based atom trapping schemes [3,4], which rely on engineering the optical nanofibres by (i) selection of the taper profile to enable higher order mode propagation [3], or (ii) through focused ion beam milling [4] of nanostructures in the nanofibre. In one study we consider modal interference in few-mode ONFs in order to generate optical potentials around the fibre. In another experiment, we have considered atom trapping by removing the central part of the ONF, thereby creating a slot region rendering the system equivalent to two parallel optical waveguides. This increases the coupling interaction between the fibre-guided modes and atoms near the fibre surface and can also be extended to submicron scale colloidal particle trapping. Early tests using test beads instead of atomic systems will also be presented.

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