

Premedical Course

Biology

Koji Takada, *Professor*

Rie Hiratsuka, *Associate Professor*

General Summary

Our research themes are as follows: (1) studies of the evaluation and mechanism of cellular phenomena associated with proteostatic disruption and (2) subcellular localization analysis of endogenous adjuvant molecules in Japanese cedar pollen.

Research Activities

Analysis of cytotoxicity and cell senescence using polyubiquitin as an index (Takada)

Two complementary proteolytic pathways of ubiquitin-proteasome system and autophagy are involved in intracellular protein homeostasis (proteostasis). Because proteasome recognizes polyubiquitin tags as degradation signals, and the autophagic pathways preferably degrade polyubiquitin-containing aggregates in a p62-dependent manner, the state in which polyubiquitin accumulates in cells indicates proteostatic disruption. We have shown that when epithelial cells are exposed to Cd and methylmercury for 48 hours, both of which are equivalent to the half-lethal concentration (LC₅₀), a marked increase in the hardly-soluble polyubiquitinated proteins precedes cell death. In the present study, to find chemicals that exhibit this type of cytotoxicity, we compare the cytotoxic events of chemicals containing metal elements (FeCl₃, CoCl₂, NiCl₂, CuCl₂, AgNO₃, ZnSO₄, and CdCl₂) in human renal proximal tubular human kidney-2 cells by using an efficient system comprised of cell culture, cytotoxicity assay, protein assay and polyubiquitin enzyme-linked immunosorbent assay. As a result, exposure to LC₅₀ levels of Co, Ag, and Zn significantly increased the cellular amounts of hardly-soluble polyubiquitin, similar to Cd, but no such phenomenon was observed upon exposure to Fe, Ni, and Cu. These results suggest that the cytotoxicity of metal ions can be classified into at least 2 types: those with or without the proteostatic disruption.

Because proteasome and autophagy activities decrease with aging (Sands *et al.*, *J. Physiol.* 595: 6383-90, 2017), senescence will affect proteostasis. In this study, we focused on the methyltransferase enzyme Su(var)3-9, Enhancer-of-zeste, and Trithorax domain-containing protein 8 (SETD8), which regulates cellular senescence (Tanaka *et al.* *Cell Reports* 18: 2148-61, 2017), and studied the effect of an SETD8 inhibitor (UNC0379) on cellular polyubiquitin levels in human epidermal keratinocyte HaCaT cells. After 6-day culturing with 10 μM UNC0379, staining of senescence-associated beta-galactosidase activity, a marker of cell senescence, was observed. The enzyme-linked immunosorbent assay-estimated polyubiquitin levels in the easily-soluble and hardly-soluble fractions prepared from the cells were significantly increased by the treatment with UNC0379. These results suggest that the cell senescence due to SETD8 suppression is accompanied by proteos-

tatic disruption.

The immunostimulatory effect of β -1,3-D-glucan contained in Japanese cedar pollen (Hiratsuka)

Many Japanese have cedar pollinosis. Under these circumstances, cedar pollen allergens have often been analyzed, but there are many unclear points regarding auxiliary substances involved in promoting allergic reactions. Therefore, we are analyzing the immunostimulatory effect of β -1,3-D-glucan (β glucan) contained in cedar pollen. As a result, the localization of β glucan in the outer wall of pollen and the germ cell wall was clarified, and the relationship with the β glucan receptor Dectin-1 is currently being analyzed.

Physics

Tsuyoshi Ueta, *Professor*

Katsumi Kasono, *Assistant Professor*

General Summary

1. We have proposed a disordered air rod photonic crystal as a model of a sponge structure inside a barb of the red-flanked bluetail and are attempting to reproduce the structural color of birds by confirming the reflection spectrum.
2. We have found that an incident electromagnetic wave is amplified resonantly within an artificially vibrating or modulating 1-dimensional photonic crystal. We are investigating the relation between the conditions of the amplification and the virtual bound states.
3. We are studying an ultrasonic lens with an adaptively deformable phononic structure constructed with microtubes into which liquid metal is injected. In this research, we are attempting to stimulate a cerebral deep part by designing a phononic lens in which a brain and the cranial bones are also taken into account as metamaterials.
4. We have been studying computational methods and algorithms for condensed matter theory. The phenomena interested in are phase transitions and critical phenomena.

Research Activities

1. We consider amplification of an incident electromagnetic wave within a photonic crystal, which is made by stacking dielectric plates arranged in parallel with equi-intervals. We have confirmed that an incident electromagnetic wave is resonantly amplified when the dielectric constants of the plates are artificially modulated in time and space.
2. We propose a computational method of the most suitable initial structure for topology optimization and show the resulting structure (acoustic lens). To generate the phononic structure with multiple focuses, we employ a holographic technique with which a suitable phononic lens is obtained as low-valued domains of the interference pattern between radiative waves from all of the focal points within the skull and a reference wave, namely a plane wave. The phononic structure is the same as the so-called Fresnel zone plate. The

effect of scattering by the skull on the phononic structure will be discussed.

3. The optimized lens constructed by arranging point-like scatterers on a lattice has been designed in terms of the concept of the Fresnel lens. The arrangement of the scatterers has been optimized so that the wave intensity vanishes at any point except the focal point within the object domain and to make the wave intensity convex around the focal point. We have confirmed that the optimized lens focuses an incident plane wave sharply on the focal point, whereas the wave intensity at the points except the focal point is constant and small enough.

4. We have made Monte Carlo simulations to study systems with phase transitions. Multi-grid cluster update simulations are used to study q -state ferromagnetic Potts models on square lattices. We calculated the relaxation times of order parameters and energy.

Publications

Dincel O, Ueta T, Kameoka J. Acoustic Driven Microbubble Motor Device. *Sensors & Actuators A: Physical*. 2019; **295**: 343-347. doi: 10.1016/j.sna.2019.05.013.

Itoga H, Morikawa R, Ueta T, Miyakawa T, Natsume Y, Takasu M. Effect of particles with repulsive interactions enclosed in both rigid spherical shells and flexible fluid vesicles studied by Monte Carlo simulation. *Phys Rev E*. 2019 Apr; **99**(4-1): 042418. doi: 10.1103/PhysRevE.99.042418. PMID: 31108718.

Chemistry

Takashi Okano, *Professor*

Naruyoshi Komiya, *Associate Professor*

General Summary

The research of this laboratory is focused on synthesis-oriented organic chemistry, including the synthesis of bioactive compounds and fluorine-containing materials, and the development of novel functional organic/organometallic compounds for fine organic synthesis.

Research Activities

Conformation analysis of anti-gauche transformation of butane

The anti-gauche conformational energy change of butane was reanalyzed with the second-order Møller-Plesset method and the large basis functions because of the differences (2.5-3.8 kJ/mol) among organic chemistry textbooks. The calculated energy difference between anti conformation and gauche conformers was 2.3 kJ/mol. This smaller difference is due to the additional van der Waals interaction between the methyl groups.

Phosphorescent molecules that resist concentration quenching in the solution state

The first phosphorescent molecules that do not exhibit concentration quenching in the homogeneous solution state throughout the entire range of concentrations were discovered in this study. A series of newly designed polymethylene-vaulted trans-bis[2-

(iminomethyl)imidazolato]platinum(II) complexes was prepared by treating $[\text{PtCl}_2(\text{CH}_3\text{CN})_2]$ with the corresponding imino ligands. The trans coordination and vaulted structures of the complexes have been unequivocally established from X-ray diffraction studies. When the concentration of a clear homogeneous solution of the complexes in organic solvents increases from the diluted to the saturated state, the emission intensity and quantum efficiency increase continuously without concentration quenching at the ambient temperature. The present concentration-driven emission enhancement is observed more intensely in a solution of a racemic mixture in comparison to that of the optically pure solution.

Publications

Le NH, Inoue R, Kawamorita S, Komiya N, Naota T. Phosphorescent Molecules That Resist Concentration Quenching in the Solution State: Concentration-Driven Emission Enhancement of Vaulted *trans*-Bis[2-(iminomethyl)imidazolato]platinum(II) Complexes. *Inorg Chem.* 2019 Jul 15; **58**(14): 9076-9084. doi: 10.1021/acs.inorgchem.9b00608. Epub 2019 Jun 24. PMID: 31247829.

Social Science (Law)

Ryuichi Ozawa, *Professor*

General Summary

Problems of Constitutional Law in present-day Japan

Research Activities

Professor Ozawa published articles and books cited in Japanese Research Activities 2019.

Human Science

Kazushi Misaki, *Professor*

General Summary

The study of Western philosophy and ethics

Research Activities

Origin of the ego: The intersubjective approach to the subject

Descartes' "cogito," the ego as a subject of thought, is still a popular and paradigmatic image for the human subject: to be a mature human means that one can think indepen-

dently and autonomously and can act according to one's own beliefs.

In modern philosophy this image of the ego has been attacked from various positions. From one such position, an intersubjective approach criticizes Descartes' cogito as an isolated subject and maintains that an ego can be a subject only in intersubjective relations. Through the recognition of the other, one can become and can be a subject. Studies by Donald Winnicott show how important the relationship of the baby with his mother is at the first stage of the ego. George Herbert Mead considers the development of the ego as a process of "ideal role-taking of others." The goal of this development is a subject that can think from the universal point of view, as Descartes imagined.

Learn from experiences in Auschwitz

From another respect, the "inhuman" situations in the Auschwitz concentration camp showed various elements needed to be "human." From the experiences in Auschwitz written about by Viktor Frankl we can learn the "human conditions" that in ordinary life remain unconscious but essential.

Japanese

Ikuko Noro, *Professor*

General Summary

A study of the review conversation in the closing psychotherapy session.

Research Activities

The characteristics, contents, and expressions of the review conversation in the closing psychotherapy session by an expert therapist was examined by applying the Roter Interaction Analysis System (RIAS), a quantitative method to analyze medical communication.

The study was presented at the 20th annual meeting of the Japanese Federation for Psychotherapy held in Yokohama on May 11, 2019.

Mathematics

Katsuya Yokoi, *Professor*

Yasuko Hasegawa, *Assistant Professor*

General Summary

- I. To study dimension theory and topological dynamics
- II. Applications of automorphic forms to number theory

Research Activities

I. We studied omega-limit sets, (strong) chain recurrent sets on topological dynamics, Conley index theory, and Lusternik-Schnirelmann category.

II. Many analytical properties of a real analytic Siegel-Eisenstein series, which is one of several variable automorphic forms, have been studied for a long time. We were able to prove some analytical properties of certain Dirichlet series through the relation of the Siegel-Eisenstein series to the Dirichlet series.

Publications

Yokoi K. Lusternik-Schnirelmann category based on the discrete Conley index theory. *Glasgow Mathematical Journal*. 2019; **61**(3): 693-704. doi: 10.1017/S0017089518000447.

English

Alan Hauk, *Professor*

Tetsuro Fujii, *Professor*

General Summary

Medical English education and materials development (Hauk)

English Language communication and education: material analysis and development (Fujii)

Hauk has been developing in-house medical English teaching materials for use in a new English program for 2nd-, 3rd-, and 4th-year English classes. The materials emphasize learning medical vocabulary in context and cyclical learning as a way to improve students' understanding and retention of class contents. In addition, the materials are designed to connect to what the students are studying in medical classes to make them more relevant and to improve students' motivation to learn English. Hauk has also been active as an editorial committee member of the *Journal of Medical English Education*, reviewing manuscripts submitted for publication.

Fujii joined a project team to compile English textbooks for high school English classes: *English Communication I, II, and III*. Along with compiling the textbooks, Fujii has been writing their exercise materials and teacher's manuals. In addition, Fujii has been studying how teaching materials influence learner motivation and language development.

Research Activities

Hauk researched what overseas medical students are learning in standard medical textbooks to make materials for teaching medical English in the university. Also, research was conducted in how to improve understanding and retention of study materials by students. The goal is to produce a textbook for medical English that will meet the students' needs in the future as physicians in the global medical community.

Fujii analyzed and collected authentic English materials to meet the level and the needs of high-school textbooks based on current teaching methods, theories, and research findings on learning English as a foreign language. These materials were used to compile textbooks following the revised teaching guidelines issued by the Ministry of Education, Culture, Sports, Science and Technology. The new textbook series will be published in 2020. In addition, Fujii studied bible verses as materials to learn English and published *Eigo de Ajiwau Seisho no Kotoba (Appreciating Bible Verses in English)*. Tokyo: Inochi No Kotoba Sha; 2019).

First Foreign Languages

Katsumi Suzuki, *Professor*

General Summary

German contemporary literature

Research Activities

My research topic is the modern German literature of nonnative writers in German-speaking areas.

I am working with the novels of Sherko Fatah. His father is Kurdish-Iraqi, and his mother is Polish-German. In fact, he is a native writer with the background as an immigrant. His heroines are always playing their part in Germany, as well as in the Middle East, mainly in Iraq. What is offered to him in the creative work as subjects, is the fatherland of his father. He writes his work in his mother tongue. I have already written and published an essay about the relationship between the fatherland and his mother tongue in his novels.