# The 27th Pupil Colloquium

October 1 (Mon) to 5 (Fri), 2007

Hamanako Royal Hotel, Hamamatsu,
Shizuoka, JAPAN

Chairman: *Satoshi Ishikawa*

*Emeritus Professor, Department of Ophthalmology,*
*Kitasato University, JAPAN*

# The 27th Pupil Colloquium

## October 2 (Tuesday)

| Greeting & Meetings (1) 8:30～12:30 | Meetings (2) 14:30～17:30 | Poster (1) 17:30～18:30 |
|---|---|---|
| **Chairman** | **Chairman** | **Chairman** |
| Greg J. Siegle | Bitsios Panos | Barbara Wilhelm |
| Satoshi Ishikawa | Takashi Fujikado | Minoru Nakayama |
| Satoshi Ishikawa | Anne M. Petrock | Minoru Nakayama |
| Mari Hiraoka | Bitsios Panos | Hiroshi Mochizuki |
| Greg J. Siegle | Kenji Matsushita | Keiko Yamamoto |
| Greg J. Siegle | Takashi Fujikado | Yoshinao Nagashima |
| Wioletta Nowak | Hidenori Horie | Barbara Wilhelm |
| **Coffee** | **Coffee** | Akinori Ueno |
| **Chairman** | **Chairman** | Keiichi Tanzawa |
| Randy Kardon | Takehiko Bando | Nanae Sakakibara |
| Shiro Usui | | |
| Minoru Nakayama | Tsuyoshi Kamada | |
| Elke E. van der Meer | Ken Asakawa | |
| Shiro Usui | Hiroshi Masuda | |
| | Naotoshi Hakamata | |
| | Jumpei Matsuda | |
| | Akino Wakasugi | |

# The 27th Pupil Colloquium

## October 3 (Wednesday)

| Meetings (3)<br>8:30～12:00 | Meetings (4)<br>14:00～17:00 | Poster (2)<br>17:00～18:00 |
|---|---|---|
| **Chairman** | **Chairman** | **Chairman** |
| Helmut Wilhelm | Popat N. Patil | Fion Bremner |
| John L Barbur | Takeshi Yoshitomi | Hitoshi Ishikawa |
| Barbara Wilhelm | Merlin D. Larson | Toshio Watanabe |
| Helmut Wilhelm | Popat N. Patil | Chiharu Tamura |
| John L Barbur | Takeshi Yoshitomi | Bingjie Zhang |
| John L Barbur | **Coffee** | Mineo Takagi |
| Kamal R. Chémali | **Loewenferd Lecture** | Atsuhiko Iijima |
| Hirokatsu Takahashi | **E. Szabadi** | Rie Amano |
| Fion Bremner | **Chairman** | Toshiaki Goseki |
| **Coffee** | S.Thompson | |
| Kumiko Taira | Barbara Wilhelm | |
| Satoshi Ishikawa | | |
| Junpei Nishiyama | | |

# The 27th Pupil Colloquium

## October 4 (Thursday)

| **Meetings (5)**<br>**9:00～12:00** |
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| **Invited Lecture**<br>**Robert J. Lucas**<br>**Chairman**<br>E. Szabadi |
| **Chairman**<br>Rockefeller S.L.Young<br>Kazuhiko Ukai |
| Seiichi. Tsujimura |
| Tobias Peters |
| Eiji Kimura |
| Randy Kardon |

## Welcome Message

Welcome to the 27th International Pupil Colloquium in Hamamatsu city, and we would like to extend a warm welcome to you for being in Japan. This will be the second time to hold a colloquium in Japan since 1985. Hamamatsu is such a beautiful, as leaves begin to turn red gradually at the shore of lake called Hamanako. You will see a historic temple, some historical sites, and even hot springs around the city, which is also known for high-tech industry. We have nearly 50 abstracts from around the world prepared for this colloquium, and we feel sure that you will be satisfied as they are of high quality and multi-disciplinary. On the occasion of holding the colloquium, we have received assistance from organizations such as the Japanese Neuro-Ophthalmology Society, Japanese Ophthalmological Society, universities and laboratories. We are provided with a great amount of assistance and support, especially from Hamamatsu Photonics K.K. Although it is a short time, enjoy the colloquium and the autumn scenery of Hamanako.

Yours sincerely,

**Hitoshi Ishikawa**
The 27th Pupil Colloquium
Secretary General

**Time Table**

| | AM (8:30～12:30) | PM (14:00～18:30) | Evening |
|---|---|---|---|
| **Oct.1 (Mon)** | ------ | Registration<br>----------<br>Cocktail | |
| **Oct.2 (Tue)** | Greeting<br>Satoshi Ishikawa<br>----------<br>Meetings (1) | Meetings (2)<br>17：30～ Poster (1) | Fire work<br>Japanese drum (Wadaiko) |
| **Oct.3 (Wed)** | Meetings (3) | Loewenferd Lecture<br>E. Szabadi<br>----------<br>Meetings (4)<br>17：00～ Poster (2) | |
| **Oct.4 (Thu)** | Invited Lecture<br>Robert J. Lucas<br>----------<br>Meetings (5) | Business Meeting<br>----------<br>Tour | Banquet |
| **Oct.5 (Fri)** | Adjourn | ------ | |

## Loewenfeld Lecture

**Oct.3 (Wed) 16:00～**

Division of Psychiatry, University of Nottingham,
Queen's Medical Centre, Nottingham, NG7 2UH, UK

**E. Szabadi**

# The integrated control of arousal and pupil function: Role of the noradrenergic locus coeruleus

**Objective:** To examine (1) how manipulations known to alter LC activity affect pupillary function, (2) whether the pupillary effects of alerting and sedative drugs are consistent with predicted changes in LC activity.

**Background:** Preganglionic neurones are under the control of preautonomic neurones located mainly in the paraventricular nucleus of the hypothalamus and the noradrenergic LC of the pons. The LC exerts an excitatory influence on the sympathetic and an inhibitory influence on the parasympathetic preganglionic neurones controlling the pupil [*1]. The LC also plays a pivotal role in the regulation of the level of arousal: it is a major wakefulness promoting nucleus contributing to cortical arousal, both directly and indirectly via the stimulation of other wakefulness promoting nuclei and inhibition of sleep promoting nuclei [*2]. As it has been shown that the fluctuations in the firing rates of LC neurones are paralleled by fluctuations in pupil diameter [*3], it is an intriguing possibility that the pupillary correlates of sedation (miosis, pupillary fatigue waves) reflect changes in LC activity.

**Methods:** A number of experiments were conducted, each including 12-20 healthy male volunteers who participated in 3-5 experimental sessions one week apart, each session being associated with the oral administration of a single treatment, one of which was always placebo. Subjects were allocated to treatments and sessions double-blind according to a balanced crossover design. Stimulant drugs included modafinil, yohimbine, reboxetine, amisulpride and pentagastrin, and sedative drugs clonidine,

diphenhydramine, pramipexole, amitriptyline and diazepam. The cold pressor test and anxiety induced by the threat of an electric shock were used to activate the LC. Tests included measures of alertness (visual analogue scales, critical flicker fusion frequency) and pupil functions (pupil diameter, light and darkness reflexes, Pupillographic Sleepiness Tests). Other autonomic functions (blood pressure, heart rate, salivation, core temperature) were also recorded. Data were analysed with ANOVA. All experiments received approval by the Medical School Ethics Committee.

**Results:** Deactivation of the LC by clonidine resulted in miosis and enhancement of the light reflex, whereas activation by yohimbine and induced anxiety evoked the opposite effects. Diazepam antagonised the inhibition of the light reflex by anxiety, but not anxiety- induced mydriasis. The cold pressor test, pentagastrin and modafinil caused mydriasis with no change in the light reflex, and this response was resistant to antagonism by diazepam. Reboxetine caused mydriasis and attenuated the light reflex. The stimulant drugs reduced and the sedative drugs increased pupillary fatigue waves. The sedative drugs had variable effects on pupil diameter: clonidine and diphenhydramine caused miosis, pramipexole caused mydriasis and amitriptyline and diazepam had no effects.

**Conclusions:** LC activation leads to an increase in sympathetic and a decrease in parasympathetic outflow to the iris. It is likely that separate groups of LC neurones are responsible for sympathetic stimulation and parasympathetic inhibition. Pupillary fatigue waves developing as a result of sedation are likely to reflect fluctuations in the firing rates of LC neurones. The variable effects of sedative drugs on pupil diameter are likely to be due to some actions of these drugs on the pupil control machinery beyond the level of the preganglionic neurones.

**References:**

*1... Szabadi E., Bradshaw C. M. (1996), *J Psychopharmacol*, 10 (Suppl. 2): 6-20

*2... Szabadi E. (2006), *Br J Clin Pharmacol*, 61: 761-766

*3... Aston-Jones G., Cohen J. D. (2005), *Annu Rev Neurosci*, 28: 403-450

## Invited Lecture

**Oct.4 (Thu) 9:00～**

University of Manchester, UK
**Robert J. Lucas**

### Using pupillometry to study inner retinal photoreception in mammals

Among the most surprising recent discoveries in vision science has been that photoreception in the mammalian retina is not restricted to rods and cones but extends to a small number of retinal ganglion cells.

These new inner retinal photoreceptors attain their photosensitivity through expression of an opsin photopigment called melanopsin.

Among the earliest indications that these photoreceptors exist came from the observation that mice lacking rods and cones retain a pupil light reflex, and since then it has become clear that pupil size is one of several behavioural and physiological systems to receive input from them.

The ease with which pupillometry experiments can be used to quantify stimulus:response relationships has lead us to use this technique extensively to probe the function and organisation of this new photoreceptor at the whole animal level.

Our pupillometry experiments have shown that ganglion cell photoreception has a spectral sensitivity function conforming to the opsin:vitamin A based template and a $\lambda_{max}$≈480nm, and that responses relying on this signal are relatively sluggish but sustained.

We have also shown that melanopsin photoreception compliments that of rods and cones by being especially active at higher irradiances.

Our ongoing experiments employ new transgenic mouse models to explore the characteristics of irradiance coding in this new photoreceptive pathway.

Among our recent findings is that in, addition to their intrinsic photosensitivity, these unusual retinal ganglion cells act as the primary site for integration of cone (and probably rod) input to the pupil light reflex.

This feature allows them to provide a reliable signal of environmental irradiance under a variety of lighting conditions.