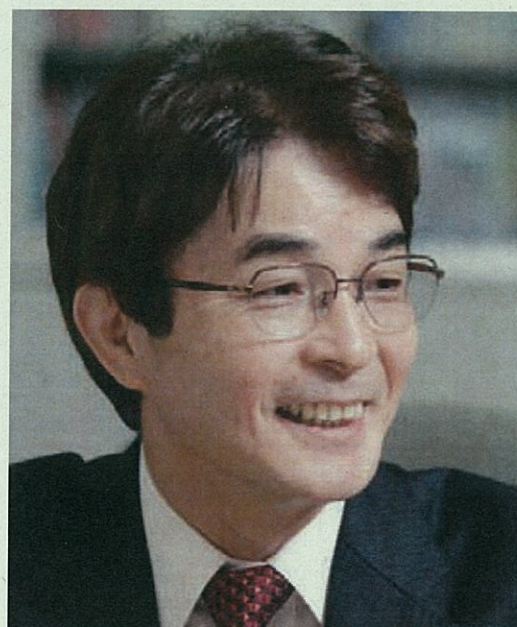


## Creating the Future



YANAGIDA Toshio

## Groundbreaking Researchers

Osaka University Professor YANAGIDA Toshio is a pioneer of single molecule imaging, a branch of bio-imaging that has led to a plethora of new techniques and technologies that have become mainstays in many biological fields. The driving force for these innovations has been his constant interest in how biological molecules, or biological machines, function in their natural environments like the human body and how this information can be applied to the design of artificial machines. The results of his research have led to significant breakthroughs that have transformed various fields and paved the way for new ones.

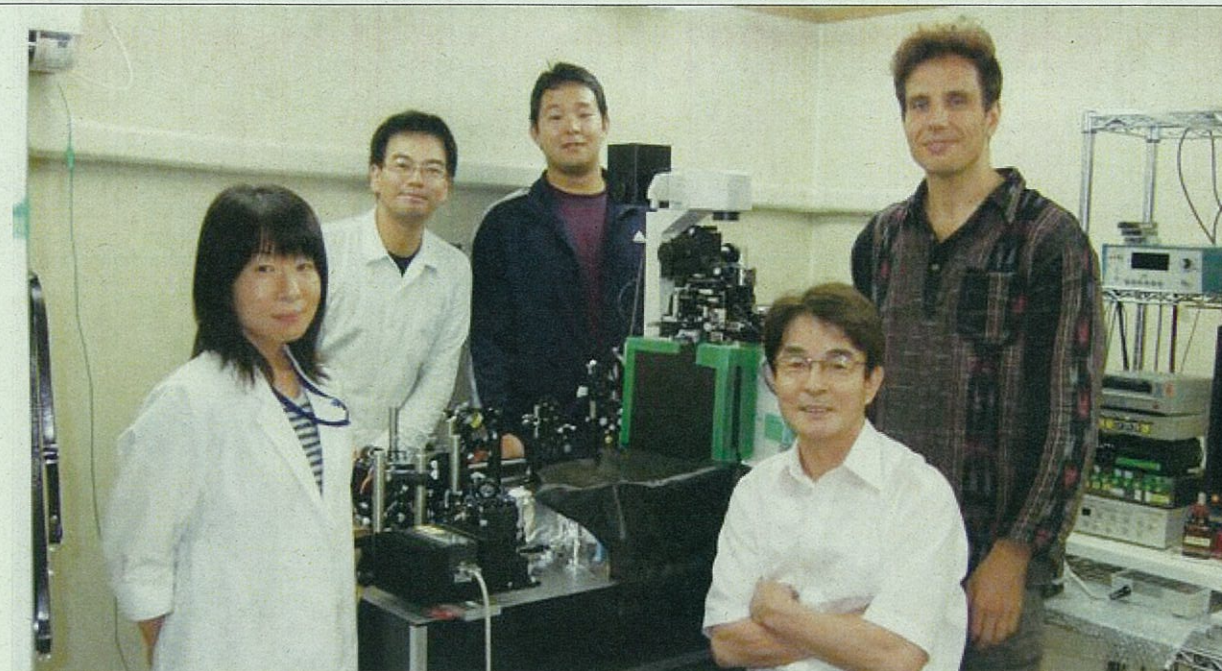
Before his work in biology, Prof. YANAGIDA was drawn to electrical engineering, which he studied at Osaka University in the 60s. Upon graduating with both his bachelors and masters, he moved to an electronics company for a year. However, Prof. YANAGIDA was dissatisfied there as he sought to apply his engineering background to a new field. This led him towards biology and his returning to Osaka University for his doctorate.

Of particular interest to him were differences between biological and artificial machines, especially in regards to energy consumption and adaptability, as biological machines are generally far more malleable to their environments and use far less energy. The first biological machine Prof. YANAGIDA investigated was

muscle, with specific focus on how the muscle molecule myosin uses ATP energy to move along actin filaments in order to generate muscle contractions.

It was around this time that the Huxley model for muscle contractions was published, a model that is still apt to this day. However, this and most other muscle models apply to muscle fibres, which contain innumerable myosin molecules meaning that the models describe not an individual myosin molecule but rather the behaviour of these molecules in an ensemble. Prof. YANAGIDA, on the other hand, was more interested in how a single myosin molecule operates in isolation. But this required the ability to directly observe single molecules, which has been the impetus for his pioneering work in the field of bio-imaging.

The potential of his research was recognized by the Japanese government, who in 1992 funded the ERATO project and announced Prof. YANAGIDA as director. In 1995, ERATO researchers successfully observed fluorescently dyed single molecules, including myosin, in an aqueous environment. This allowed researchers for the first time to observe functioning single molecules, and therefore meant researchers could now observe single molecule dynamics. With regards to muscle, the techniques used enabled direct observation of single molecule



Prof. YANAGIDA before one of his imaging systems with present and past lab members.

myosin ATP energy consumption and, when combined with nanometry techniques also developed from the ERATO project, how myosin converts this energy into the mechanical movement needed for muscle contraction. This technique proved crucial for identifying an underlying distinction between biological and artificial machines: biological machines are efficiently stochastic. In other words, unlike artificial machines, which are deterministic, biological machines innately use probability in their movement, that is Brownian motion.

The combination of single molecule imaging with nanometry has been instrumental in revealing numerous biological mechanisms and dynamics that before were simply unattainable. These include various enzyme kinetics, DNA transcription, single ion channel activity, cell signalling and signal transduction. Overall, the techniques fostered by Prof. YANAGIDA and his teams have become essential to such biological studies.

Overall, his research has attracted international attention from both leading scientists and the general public. He is regularly invited to a diverse number of conferences including those focusing on engineering, optics, muscle, and chemistry, a recipient of numerous awards, and is often consulted by government officials on science policy. Yet perhaps his proudest accomplishment is that his laboratories consistently churn out scientists who are now scattered throughout the world running their own research groups in almost all basic science fields due to the versatile nature of the skills and techniques one learns in his labs.

## The Yuragi Project

Having realized that the adaptability and low energy demands of biological machines is in part because the mechanisms they use embrace rather than resist the inherent uncertainty in Brownian motion has given researchers a whole new perspective on a myriad of biological systems including neuroscience and cell-cell communication, which operate similarly. More importantly, understanding biological machines offers the potential for improving artificial ones, as these same mechanisms are now being applied to information systems and robotics, which is the heart of the Yuragi Project. Yuragi is a Japanese word that can be loosely translated into adaptable. As energy policy comes more

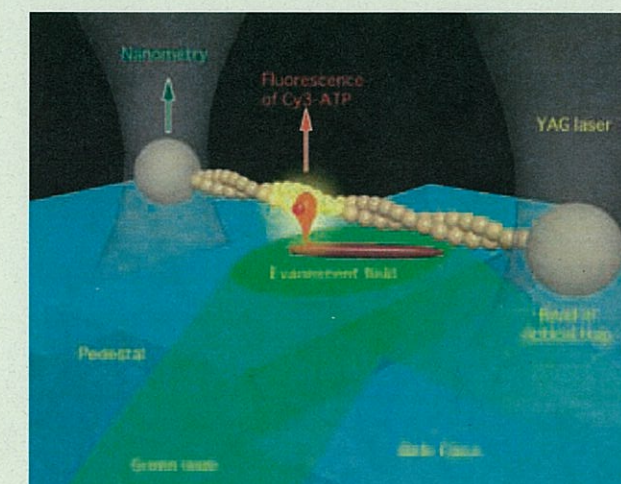


Fig. legend  
Simultaneous Measurement of Individual ATPase and Mechanical Reactions of Single One-Headed Myosin Molecules

to the forefront, there will be a growing need for more energy efficient machines. The Yuragi project aims to contribute to solving this problem by designing artificial machines that employ the energy efficient mechanisms used by biological ones.

## REFERENCES

- (1) H.E. Huxley "The mechanism of muscular contraction." Science 164,1356-1365 (1969)
- (2) A.F. Huxley, R.M. Simmons. "Proposed mechanism of force generation in striated muscle." Nature, 233, 533-538 (1971)
- (3) T. Funatsu, Y. Harada, M. Tokunaga, K. Saito, T. Yanagida, "Imaging of single fluorescent molecules and individual ATP turnovers by single myosin molecules in aqueous solution", Nature, 374, 555-559 (1995)
- (4) K. Kitamura, M. Tokunaga, A. H. Iwane, T. Yanagida, "A single myosin head moves along an actin filament with regular steps of ~5.3nm", Nature, 397, 129-134 (1999)
- (5) Edited by T. Yanagida and Y. Ishii "Single Molecule Dynamics in Life Science" WILEY-VCH Verlag GmbH & Co. KGaA (2005)