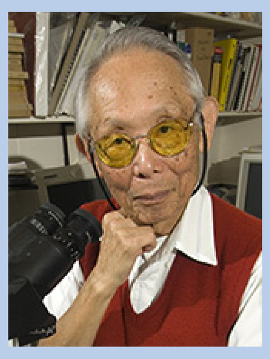


Shinya Inoué

1921 - 2019

Biography

Prof. Inoué was born Jan 5, 1921 in London. His father, Kojiro Inoué was a high-ranking diplomat who represented Japan in many countries, giving Shinya the opportunity to perfect his English. Kojiro Inoué wrote an impassioned plea to Japan's then-militaristic government to avoid the actions that led to WW II. His mother, Hideko, was highly educated and strong-willed, and became the personal interpreter of the Showa empress. He had four sisters: Sumuko, Akiko, Midori and Futaba, the last well-known as a classical pianist. He married Silvia McCandless in 1952 and had five children: Ted, John, Steve, Chris, Heather. He became a US citizen in 1989.

He attended Tokyo Metropolitan University (Rigakushi Zoology, University of Tokyo, 1944), and with one of the earliest postwar visas for Japanese, in 1948 went to Princeton University for his MA (1950) and PhD (1951). He was a member of the faculty at Dartmouth College (1959–1966) and a professor at the University of Pennsylvania (1966-1982), before joining the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts full-time in 1982.

Inoué spent the war years in Japan, finally at the Marine Biological Lab at Misaki under the mentorship of US-educated Katsuma Dan ("Katy") of Tohdai (today's University of Tokyo), who later married cell biologist Jean Clark before returning to Japan in 1934. Katy became Inoué's primary mentor and long-time collaborator.

Figure 1. Kojiro Inoué; the Showa emperor and empress looking at images at the MBL in 1975.

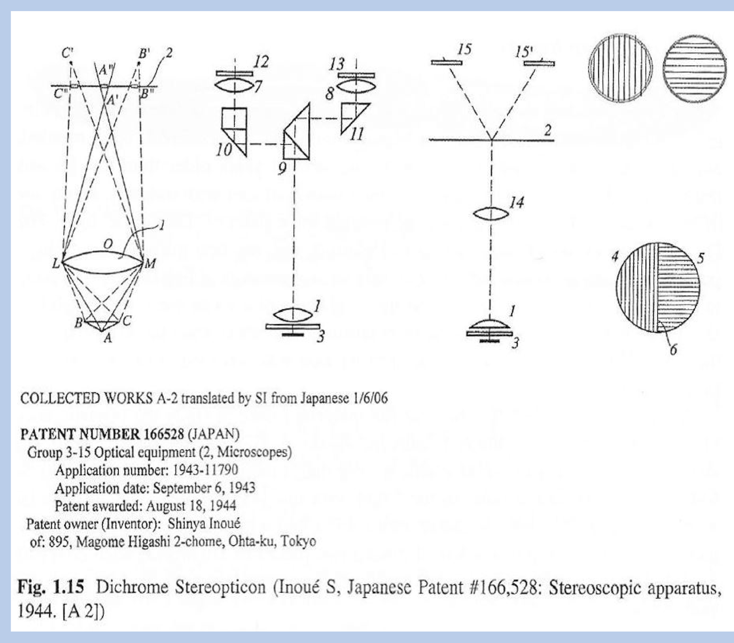


Figure 2. While at Misaki, Inoué issued his first patent (of four), which used polarization to provide stereoscopic viewing with a single objective lens.

At Misaki, Katy, whose interest was the mysterious and rarely observed (in living cells) mitotic spindle, challenged Shinya to investigate the spindle by observing its (very weak) birefringence by polarizing microscopy, citing a 1937 paper by W.J. Schmidt. This led, over time, to the development of seven "Shinya-scopes". For the first one, at Misaki, Inoué discovered that a compensator (a half-wavelength birefringent plate) was needed between the polarizer and the analyzer to improve the extinction and increase the sensitivity to birefringence. Inoué made one by thinning a sheet of mica. The need for a compensator was known by Schmidt, but Inoué re-invented it. Since the spindle birefringence was so weak, a bright light source was also needed. At Misaki, in the first of three encounters (the last in 1975 at MBL), he demonstrated the microscope to the Showa emperor (who became a published marine biologist, like his son, the Heisei Emperor, from whom Inoué later received an award).

Microscopy

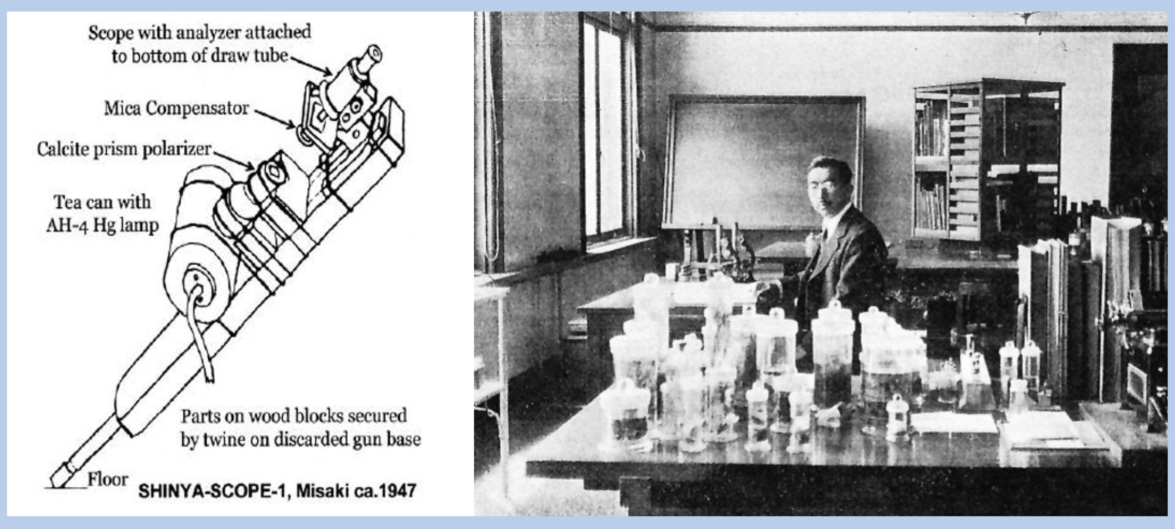


Figure 3. Shinya-scope I, along with the Showa emperor (in his imperial lab), who tried it at Misakai.

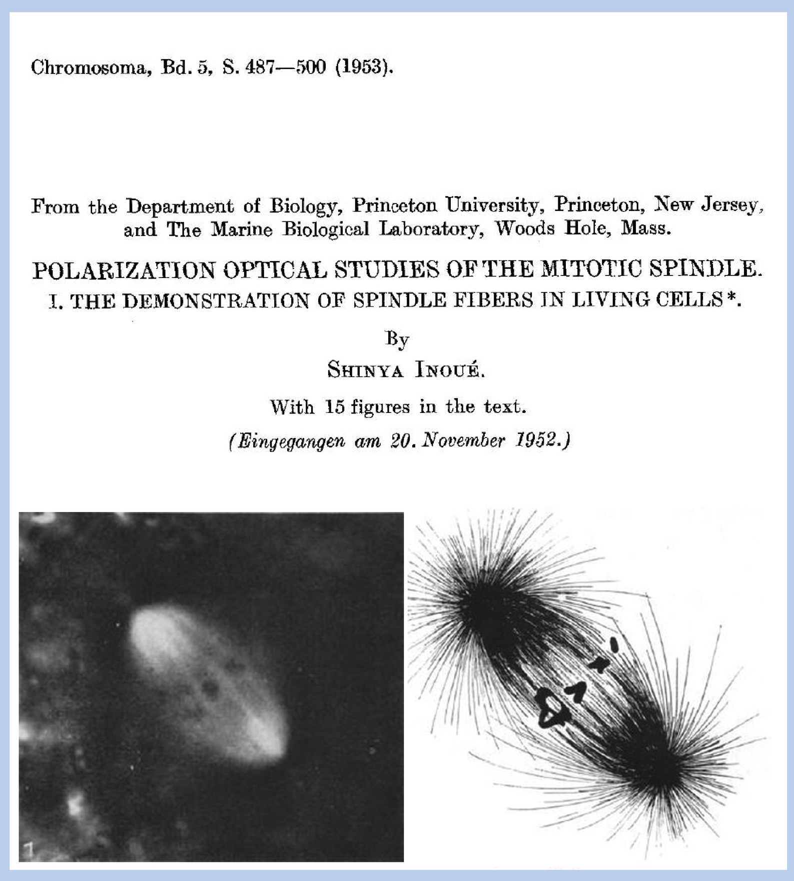
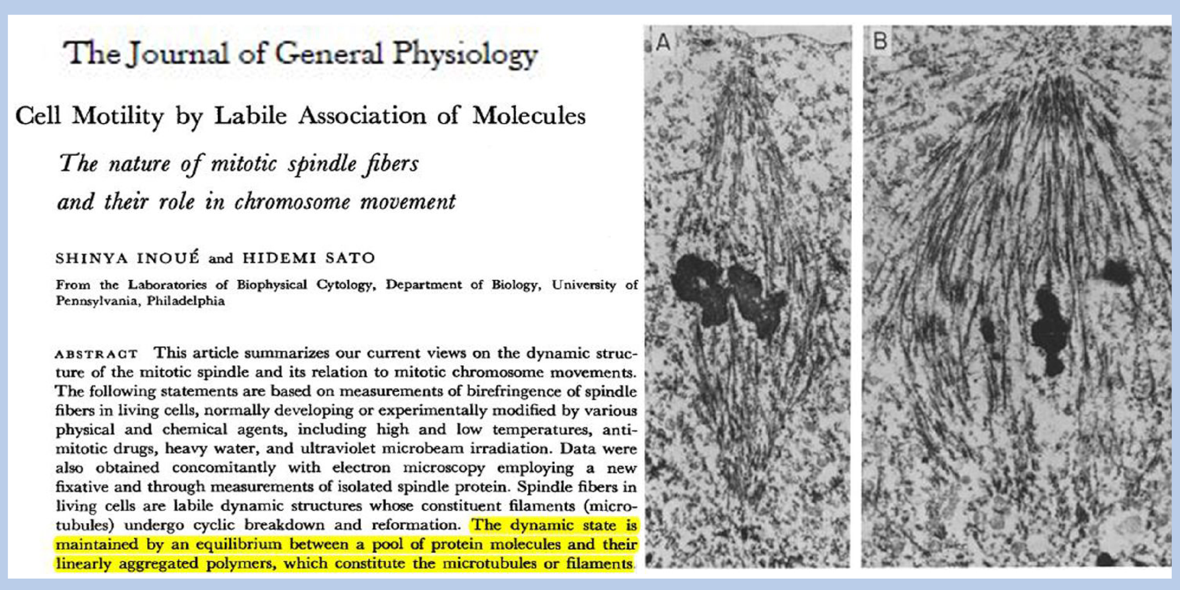


Figure 4. At graduate school at Princeton starting in 1948, he built an improved Shinya Scope that enabled him to conclusively demonstrate the reality of spindle fibers in healthy living cells (microtubules had yet to be discovered). Their existence was then controversial, because until then they were only evident in fixed and stained preparations, never in live cells, which led to the widespread belief that spindle fibers were artifacts. An example image is shown, along with Inoué's 1953 drawing. Inoue S (1953). "Polarization optical studies of the mitotic spindle 1. The demonstration of spindle fibers in living cells". Chromosoma. 5 (5): 487–500. Katy and Shinya suspected that the spindle is ubiquitous and provides motion to chromosomes by assembly and disassembly of molecules in a dynamic equilibrium with a pool of subunits. They later proved this by polarized light microscopy of living cells.



The Journal of General Physiology

Cell Motility by Labile Association of Molecules

The nature of mitotic spindle fibers and their role in chromosome movement

SHINYA INOUÉ and HIDEMI SATO

From the Laboratories of Biophysical Cytology, Department of Biology, University of Pennsylvania, Philadelphia

ABSTRACT This article summarizes our current views on the dynamic structure of the mitotic spindle and its relation to mitotic chromosome movements. The following statements are based on measurements of birefringence of spindle fibers in living cells, normally developing or experimentally modified by various physical and chemical agents, including high and low temperatures, antimitotic drugs, heavy water, and ultraviolet microbeam irradiation. Data were also obtained concomitantly with electron microscopy employing a new fixative and through measurements of isolated spindle protein. Spindle fibers in living cells are labile dynamic structures whose constituent filaments (microtubules) undergo cyclic breakdown and reformation. The dynamic state is maintained by an equilibrium between a pool of protein molecules and their linearly aggregated polymers, which constitute the microtubules or filaments

Figure 5. Later, he proposed that the force for anaphase chromosome movement was produced by the gradual disassembly of microtubules. Inoué's important contribution was the idea that spindle-fiber assembly/disassembly could produce force to move things. Inoue S, Sato H (1967). "Cell motility by labile association of molecules. The nature of mitotic spindle fibers and their role in chromosome movement". Journal of General Physiology. 50 (6): 259–292.

Figure 6. Books. Molecules and Cell Movement (with R.E. Stephens, 1975), Video Microscopy (1986), Video Microscopy: the Fundamentals (with K. Spring, 1997), Collected Works of Shinya Inoué: microscopes, living cells, and dynamic molecules (2008), Pathways of a Cell Biologist: Through Another Eye (2016).

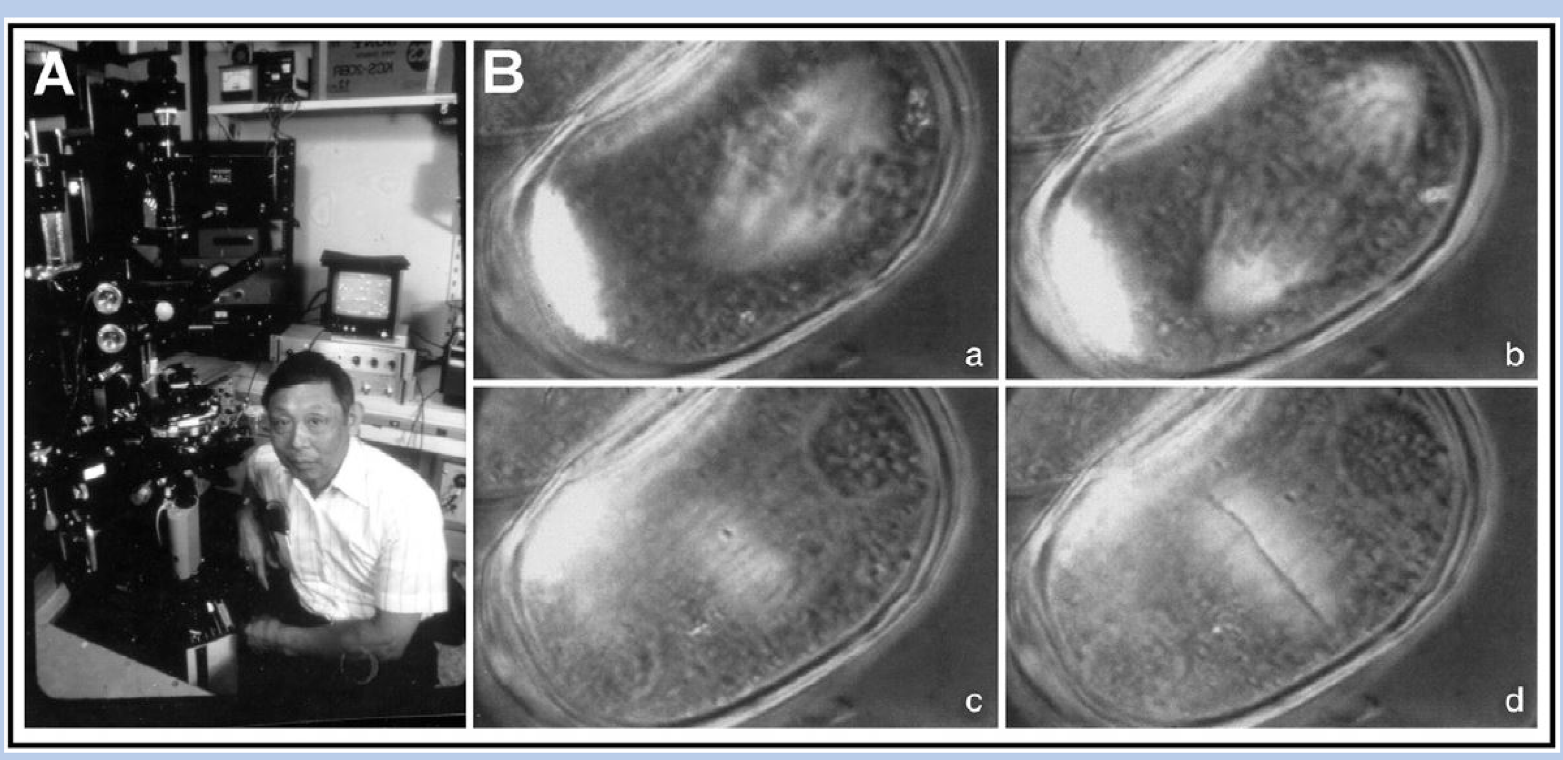


Figure 7. The combination of video with the light microscope in the late 1970s to early 1980s opened up a completely new world. The finest details could be seen only after such improvements.

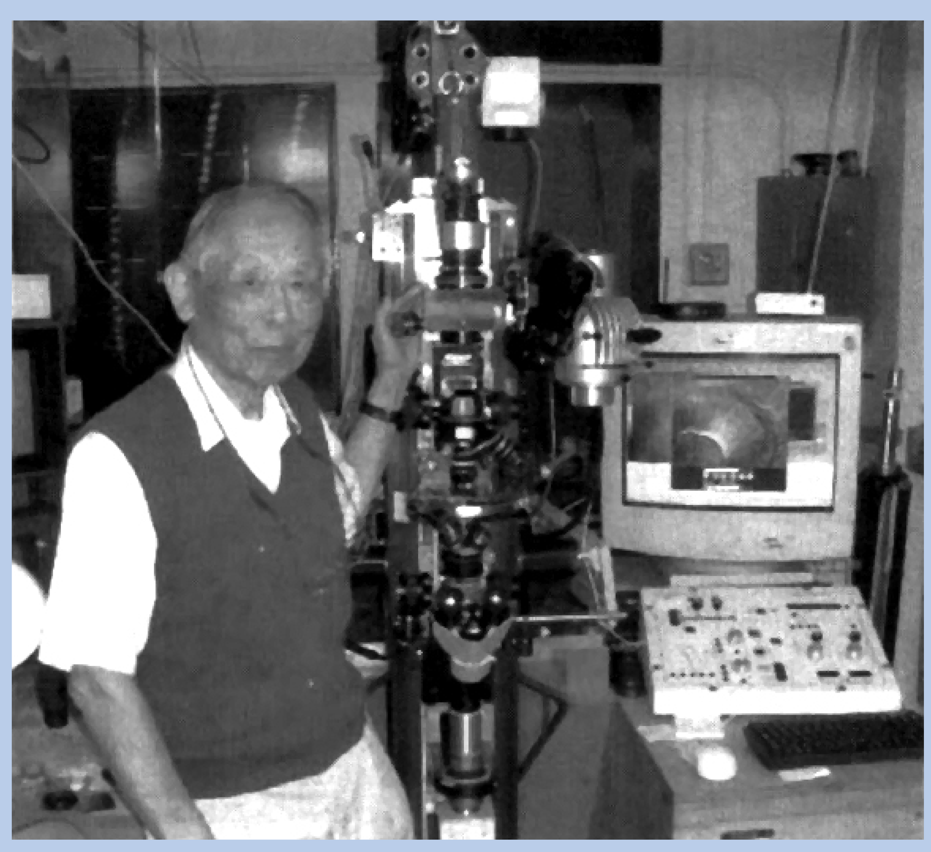


Figure 8. Shinya-scope 7 incorporated many refinements, made over the years in a series of Shinya-scopes (which provided both sensitivity to weak birefringence and high resolution), and also took advantage of video microscopy and image-processsing, developed from the impetus of the courses given by Robert and Nina Allen and Shinya Inoué at MBL, which was furthered by son Ted's development of the first computer-based digital image acquisition/analysis system (CIS) designed, with Inoué's constant input, specifically for research biologists (it was later marketed by and known as MetaMorph). In addition, Shinya-scope 7 included computer control of the microscope, making its use more efficient and intuitive.

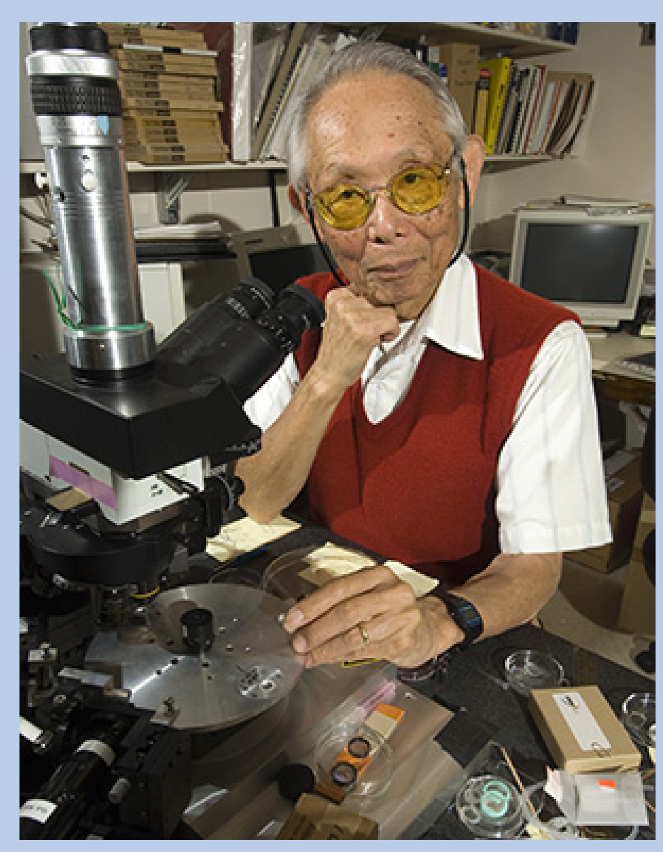


Figure 9. Finally, a centrifuge microscope was developed, which had two specimen chambers and provided high-resolution imaging of weak birefringence. Centrifugation helped remove birefringent particles that obscured the spindles in images of some cells.

Honors

Honors (of many) include:

- Guggenheim Fellowship, 1970
- Distinguished Scientist at MBL, the laboratory's highest honor (1986).
- Rosenstiel Award (1987).
- The E.B. Wilson Award from the American Society for Cell Biology (1992).
- United States National Academy of Sciences (elected 1993)

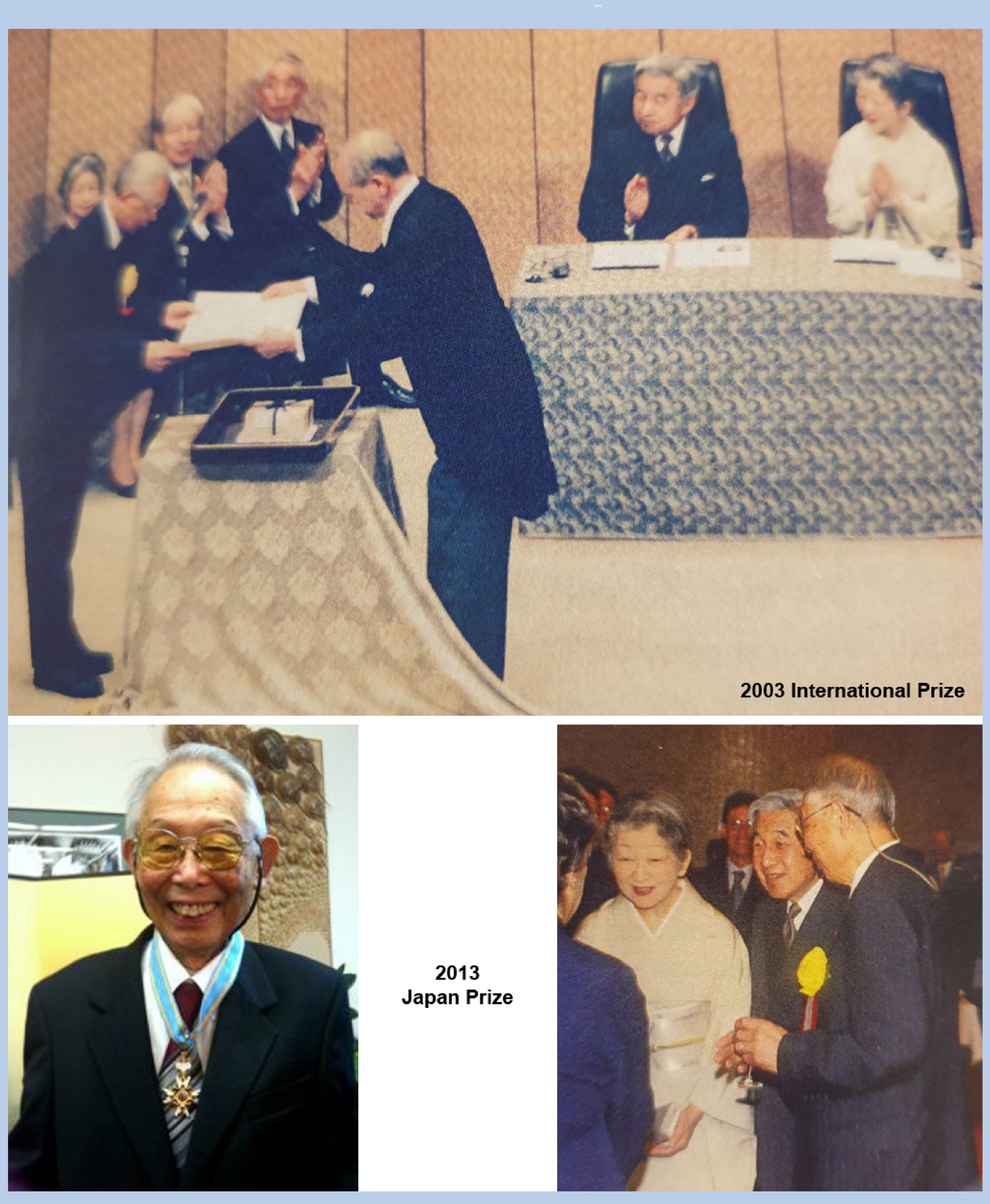


Figure 10. Awarding of the 2003 International prize; the 2013 prize and at a reception with the Heisei emperor (also a published scientist) at the awarding.

Honors

- The Distinguished Scientist Award from the Microscopy Society of America (1995).
- Ernst Abbe award, New York Microscopical Society (1997)
- The International Prize for Biology from the Japan Society for the Promotion of Science (2003).
- The Order of the Sacred Treasure, Gold Rays with Neck Ribbon Award from the Government of Japan (2013).

Publications

Primary Publications: 126.

Acknowledgements

Obituaries from the MBL and Wikipedia; Shinya Inoué's monograph "Pathways of a Cell Biologist"; a remembrance by Greenfield (Kip) Sluder; the Journals *Journal of Cell Biology*, and *Cell*; oral history (Feb 26,27 1999) by Sondra Schlesinger.