

6. Oktober 2022

## **2022 Heinrich Wieland Prize: Watching molecules at work – from the cell level to the organ level**

**Xiaowei Zhuang of Harvard University in Cambridge, USA, will receive the 2022 Heinrich Wieland Prize of the Boehringer Ingelheim Foundation worth 100,000 euros on 6 October 2022 for making seminal discoveries in cell and neurobiology with the ingenious imaging technologies she developed. Thanks to her work, we can observe how structures about 100 atoms wide do their work in human cells and get clear snapshots of the activity of 10,000 genes within one cell at the same time. Over the past 16 years, Zhuang, as well as scientists worldwide, have gained valuable insights into complex biological processes using STORM, her super-resolution method, and MERFISH, her genome-scale imaging method.**

Professor Zhuang's invention, STORM – short for STochastic Optical Reconstruction Microscopy – is one of the first imaging technologies to overcome the physical boundary (diffraction limit) of resolution in light microscopy. While some other imaging methods can achieve much higher resolutions, many technologies, such as electron microscopy, do not work with intact living cells. Previously, light microscopy only allowed us to see down to about 200 nanometres – about the size of the flu virus, or a fifth of a micrometre. But STORM achieves a resolution that is more than an order of magnitude better, going down to less than 10 nm. This is about 100 atoms wide, or the size of an average protein. It thus enables us to observe single proteins performing their job within the crowded environment of intact, living cells.

A most exciting discovery in super-resolution microscopy

“What makes Xiaowei Zhuang's achievements so exceptional is that she has not only invented these technologies but also applied them to make discoveries in cell biology and neurobiology that will change the textbooks,” says F.-Ulrich Hartl, chair of the international board of scientists that selects the Heinrich Wieland laureates. “She has, for example, discovered a new part of the cell skeleton in nerve cells. No one had expected it to be there, although we now know that it is found in the brains of organisms as diverse as worms and humans.” The cage-like structure helps to keep nerve cells and especially their long projections in shape. It is also essential for signalling in brain cells. “This striking structure is for sure one of the most exciting discoveries to come out of super-resolution microscopy so far,” adds Hartl.

While STORM focuses on relatively few different molecules at a time, Zhuang's recently developed method known as MERFISH – Multiplexed Error-Robust Fluorescence In Situ Hybridization – allows the imaging of more than 10,000 different genes simultaneously in single cells, enabling gene expression profiling of millions of individual cells in tissues.

Using MERFISH, Zhuang has identified hundreds of new types of cells in the brain, by distinguishing their characteristic patterns of gene activity. She has used this spatial genomics approach to generate high-resolution cell atlases of the brain, determine the spatial organizations and functional roles of different types of cells, and reveal striking differences between the brains of mice and humans.

Both STORM and MERFISH are invaluable to the scientific community and are already widely used in academic and commercial laboratories worldwide.

MERFISH, for example, is one of the key technologies behind the Human Cell Atlas, a worldwide initiative to map all the cells in the human body and characterize them on a molecular basis to understand human health, as well as diagnose, monitor, and treat disease.

About her work, Xiaowei Zhuang says: “Seeing is believing. It is such a thrill looking at the beautiful images of molecules in cells and cells in tissues generated by STORM and MERFISH. When these images revealed something totally new, the feeling is even more remarkable!”

Xiaowei Zhuang will be presented with the Heinrich Wieland Prize during a festive ceremony following a scientific symposium at Nymphenburg Palace in Munich on 6 October 2022.

“Her discoveries enable us to much better understand how cells and organisms function in health and what goes wrong in disease,” says Christoph Boehringer, chairman of the Executive Committee of the Boehringer Ingelheim Foundation. “We are also sure that the fantastic tools Zhuang has given the research community will enable many more exciting discoveries, by her and other scientists worldwide”.

#### **Professor Xiaowei Zhuang – the award winner**

Xiaowei Zhuang studied physics at the University of Science and Technology of China in Hefei and obtained her PhD at the University of California at Berkeley in 1996. After postdoctoral research in biophysics at Stanford University, she joined the faculty at Harvard University in 2001 and was selected to be a Howard Hughes Medical Institute (HHMI) investigator in 2005. Since 2006, she has been a full professor at Harvard, where she is now the David B. Arnold Professor of Science. She is a member of several academies, among them the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences. She has received numerous awards, including a MacArthur Fellowship, the Heineken Prize for Biochemistry and Biophysics, the Breakthrough Prize in Life Sciences, the Vilcek Prize in Biomedical Science, and the FNIH Lurie Prize in Biomedical Sciences.

#### **Heinrich Wieland Prize – the award**

This international award honours outstanding research on biologically active molecules and systems in the fields of chemistry, biochemistry, and physiology, as well as their clinical importance. The 100,000-euro prize is named after Nobel Laureate Heinrich Otto Wieland (1877–1957) and has been awarded annually since 1964. Among the awardees – selected by a scientific Board of Trustees – are four subsequent Nobel Laureates. Since 2011, the prize has been endowed by the Boehringer Ingelheim Foundation.

[www.heinrich-wieland-prize.de](http://www.heinrich-wieland-prize.de)

#### **Boehringer Ingelheim Foundation – the donor**

The Boehringer Ingelheim Foundation is an independent, non-profit organization that is committed to the promotion of the medical, biological, chemical, and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931–1991), a member of the shareholder family of the Boehringer Ingelheim company. Through its funding programmes Plus 3, Exploration Grants, and Rise up!, the

Foundation supports excellent scientists during critical stages of their careers. It also endows the international Heinrich Wieland Prize, as well as awards for up-and-coming scientists in Germany. In addition, the Foundation funds institutional projects in Germany, such as the Institute of Molecular Biology (IMB), the department of life sciences at the University of Mainz, and the European Molecular Biology Laboratory (EMBL) in Heidelberg.

[www.boehringer-ingelheim-stiftung.de/en](http://www.boehringer-ingelheim-stiftung.de/en)

**Images:**

Portrait: Prof. Xiaowei Zhuang, receives the 2022 Heinrich Wieland Prize 2022 for inventing the super-resolution methods STORM and MERFISH and her groundbreaking results gained with them.

3D STORM image: 3D STORM (above) imaging of actin molecules in axons of nerve cells revealed a new part of the cell skeleton not visible in conventional (below) light microscopy.

Copyright for both images: X. Zhuang laboratory, HHMI, Harvard University

Images can also be downloaded at [www.heinrich-wieland-prize.de](http://www.heinrich-wieland-prize.de).

For higher resolution, please contact us, details below.

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