MUKUND THATTAI

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Mukund Thattai is a biological physicist and professor at the National Centre for Biological Sciences (NCBS) of the Tata Institute of Fundamental Research in Bangalore. In 2004, Prof. Thattai obtained his Ph.D. from the Massachusetts Institute of Technology. He joined NCBS in the same year.

Thattai helped establish the Simons Centre for the Study of Living Machines at NCBS. Under his leadership, it has emerged as one of the important centers internationally for work at the interface of biology and physics. He was instrumental in setting up the ICTP-ICTS Winter School on Quantitative Systems Biology as well as the Simons-NCBS Monsoon School on the Physics of Life, which for over a decade have attracted hundreds of ambitious students and postdocs to this interdisciplinary area. In all these ways, Prof. Thattai has helped nurture a new generation of computational biologists and put India on the map in a rapidly growing and exciting field. Mukund Thattai has guided three Masters-by-Research and nine Ph.D. students, who have gone on to become group leaders, physician scientists, and industry researchers internationally, including at EMBL Heidelberg, the University of Warwick, and Brown University.

PHYSICAL SCIENCES

The Infosys Prize 2023 in Physical Sciences is awarded to Prof. Mukund Thattai in recognition of his groundbreaking contributions to evolutionary cell biology. He has explored the origins of endomembrane organelles, shedding new light on how they emerged from ancient, primordial cells.

SCOPE AND IMPACT OF WORK

One of biology's central mysteries is how a modern-day cell with its complex network of organelles evolved from a primitive, or archaeal, cell that had none of these structures. Data has emerged suggesting that the symbiosis of bacteria and archaeal cells led to a "proto-eukaryote", a prototype for a modern-day cell, but one that lacked internal membranes or endomembranes. Cells as we know them today harbor an array of membrane-bound compartments, called organelles, that work collaboratively to ferry cargo into, around and out of the cell. How did so many kinds of organelles emerge and how did they form networks amongst themselves as we see in modern cells?

Prof. Mukund Thattai's work combines molecular biophysics with DNA sequence information to metaphorically go back, deep in time, to reconstruct a physical picture of how new organelles evolved. He pinpointed that the evolution of vesicle trafficking proteins can lead to the emergence of new endomembrane organelles. Injecting ideas from statistical physics and information theory into rich bioinformatics, he has studied how organelle networks within cells evolved. Thattai showed that the unique organization within the Golgi was an inevitable consequence of the basic flows of vesicle traffic within the cell.

CITATION BY THE JURY

The Infosys Prize 2023 in Physical Sciences is awarded to Prof. Mukund Thattai for his work that has expanded our understanding of one of biology's central mysteries: the emergence of complex cells. Prof. Thattai has studied a problem lying at the crossroads of cell biology and evolution using powerful tools from physics and computer science. His groundbreaking contributions include his work on the emergence of eukaryotes from prokaryotic ancestors, the origin of hallmark eukaryotic traits such as mitochondria and the vesicle trafficking system, and the evolution and function of the Golgi apparatus.

Your efforts to understand how organelle networks arose and evolved from primitive cells that had no organelles, have seeded a new area in evolutionary cell biology. Your findings related to how the organization of organelle networks came to be, by considering them as natural information processing systems, are both pioneering and profound. We have recognized these brilliant achievements with the Infosys Prize. Congratulations Mukund Thattai!

Shrinivas Kulkarni

EXPLORING THE PHYSICS OF LIFE

Living organisms are built from molecules that obey the laws of physics, so it is inevitable that the threads of biological and physical research often intertwine. Ever since the light microscopes of Antonie van Leeuwenhoek and Robert Hooke uncovered the cellular basis of life in the 1600s, instruments based on physical principles have revealed how cells are organized at the smallest scales. In the early 1900s J. C. Bose conducted pioneering electrical recordings on plant cells. In the 1950s George Palade studied the architecture of animal cells using the electron microscope and discovered the ribosome. In the same period X-ray crystallography allowed Linus Pauling and G. N. Ramachandran to solve protein structures and led Watson and Crick to discover the DNA double helix.

Ideas from physics have also stimulated the formulation of biological principles. Physicists such as Max Delbruck and Seymour Benzer, deeply influenced by Erwin Schrödinger's 1944 book *What is life?* helped establish the field of molecular biology. Their work contributed to the discovery of the genetic code. Importantly, this has not been a one-way street. Physicists and engineers have always been inspired by the amazing things cells can do at the smallest scales. Richard Feynman's 1959 lecture "There's plenty of room at the bottom", considered to be the start of nanotechnology, was influenced by his explorations of biology in Delbruck's laboratory.

The molecular biology revolution has generated a "parts list" of the biomolecules that underpin life. Yet, we still know very little about how cells actually work. The question of how random interactions between biomolecules could lead to such precise cellular architecture and dynamics is what attracted Prof. Mukund Thattai, originally trained as a physicist, to the life sciences. Thattai studies one of the central mysteries of biology—the question of how complex eukaryotic cells emerged from simpler prokaryotic ancestors.

There are three distinct types of cellular life on Earth—prokaryotic bacteria and archaea, lacking nuclei; and nucleated eukaryotic cells, including those that make up plants and animals. Originally there were only prokaryotes. Eukaryotes arose about two billion years ago, from within a symbiotic population of bacteria and archaea. The bacteria eventually took up residence within the archaea, becoming what we now call mitochondria. These ancient hybrid cells were the first eukaryotes.

Present-day eukaryotes use an active transport network to move material around the cell. Small carriers called vesicles move molecules between large membrane-enclosed compartments called organelles, just as trucks ferry specific cargo between warehouses in a city. Prokaryotic cells don't have such a transport system. Thattai pioneered the application of tools from physics and computer science to study how biomolecular interactions generate this cell-scale transport network. He has combined biophysical models with genome sequence information to 'go back in time', probing how vesicles and organelles may have arisen in the earliest eukaryotes.

Mukund Thattai's discoveries provide a quantitative foundation for the emerging field of evolutionary cell biology and have contributed to our understanding of the diversity of cellular life.