# URI MANOR

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## THE CHALLENGE

One of the key features of life is that it is *dynamic*. This is true even for relatively stable biological systems that often appear static on the surface. But if you study them at the microscopic level you will discover mind-bending levels of movement, turnover and reshaping of tiny structures driven by molecular machines. One single misstep or misplacement of a cellular structure by even just a few nanometers could cause a cell to malfunction, and the cumulative damage of such mistakes can lead to debilitating disease. For example, improper regulation of mitochondria (energy stations of the cell) leads to many aging-related disorders, including cancer and neurodegeneration. To understand how exactly these cellular dynamics are disrupted in disease, scientists must be able to see inside the cell with great precision, but current imaging methods have limitations.

## THE APPROACH

Manor develops new methods and tools for studying cellular dynamics with nanometer precision (a sheet of paper is about 100,000 nanometers thick). This includes artificial-intelligence-based computational approaches (deep learning) that integrate data from microscopes as well as sequencing data to increase image resolution, sensitivity and collection speed beyond what's possible with any other existing method. Manor also develops genetic tools that facilitate the monitoring and manipulation of cellular structures in models of neurological disorders, such as Alzheimer's and Charcot-Marie-Tooth disease.

Using these advanced technologies, Manor can capture live videos of microscopic structures, such as neuronal synapses, mitochondria, and the internal framework of the cell called the actin cytoskeleton, with unprecedented detail. This information helps researchers connect anatomy to function. Manor investigates a number of cellular structures involved in processes that, if disrupted, lead to disorders including neurodegeneration, hearing loss, cancer and metabolic disorders. His research advances scientists' understanding of these cellular processes and ultimately helps discover and create new therapies for treating these conditions.

## THE INNOVATIONS AND DISCOVERIES

- Manor developed new deep learning tools that improve the quality and amount of information that can be extracted from low-resolution microscopy images—an approach that could help democratize high-resolution microscopy and further increase the capabilities of cutting-edge microscopes.
- Manor discovered that a protein called Eps8 helps regulate the growth of microscopic "hairs" involved in hearing and is investigating viral gene therapy and small-molecule-based methods to restore both inherited and acquired hearing loss.
- Manor discovered a novel mitochondrial protein called Spire, which regulates mitochondrial division, and he created nanobody-based probes that bind to specific regions of mitochondria and the cellular cytoskeleton. Manor is studying how these cellular structures co-regulate one another in health and disease.

**For more information, please visit:**
**WWW.SALK.EDU/SCIENTIST/URI-MANOR**

BIOPHOTONICS | NEUROLOGICAL DISEASE | MITOCHONDRIA
ACTIN CYTOSKELETON | NANOBODIES | ARTIFICIAL INTELLIGENCE (AI)