Los Alamos NATIONAL LABORATORY ESTABLISHED 1943

2008 R&D 100 Award Winner

3D Tracking Microscope

Features

The 3D tracking microscope is the only system capable of following small (~10 nm) protein-sized objects moving through three dimensions at rates faster than many intracellular transport processes. The 3D tracking microscope can follow the transport of nanometer-sized particles at µm/second rates with a spatial accuracy of approximately 100 nm for each axis (X, Y, and Z). This enables one to follow individual protein, RNA, or DNA motion throughout the full three-dimensional volume of a cell to see where a particular biomolecule travels, the method it takes to get there, and the specific proteins it may be interacting with along the way. Conventional laser scanning confocal microscopes (LSCMs) are valuable tools for academic researchers and pharmaceutical companies, comprising a roughly 225 million$/yr market. LCSMs enable 3D rendering of cellular structure, but cannot follow individual protein motion in three dimensions. The 3D tracking microscope can do everything a conventional LSCM can do and much more. It can track single labeled molecules in three dimensions as well as render 3D images with single fluorophore sensitivity.

Applications

The 3D microscope will have a number of applications in molecular and cellular biology, where it can be used to study the transport of individual biomolecules performing their function inside living cells. This microscope will advance our understanding of disease at the molecular level by enabling researchers to follow, step by step, the transport of important signaling proteins involved in complex signal transduction cascades, such as those cascades corrupted in a number of human diseases ranging from cancer to anaphylactic shock. Some of the cellular processes that can be studied with this microscope include:

- the re-organization of molecules that takes place during cell division (mitosis)
- the transport of receptors or foreign bodies from the outside to the inside of the cell (endocytosis)
- mRNA transport from DNA to the ribosome
- diffusion and active transport of proteins from synthesis at the ribosome to their final destination in the cell
- study of the molecular response of a cell to environmental insults, pathogens, or external stimuli

Benefits

- Ability to follow small, nanometer-sized fluorescent reporters as they move through three spatial dimensions at rates faster than many intracellular transport processes
- Enables monitoring protein, DNA, or RNA interactions and transport at the single molecule level
- Data is stored as raw photons with ~50 picosecond timing resolution. This enables single molecule fluorescence lifetime measurements, which can reflect the local pH, electrostatic potential, or chemical environment.

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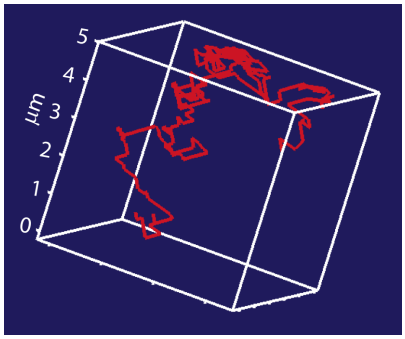

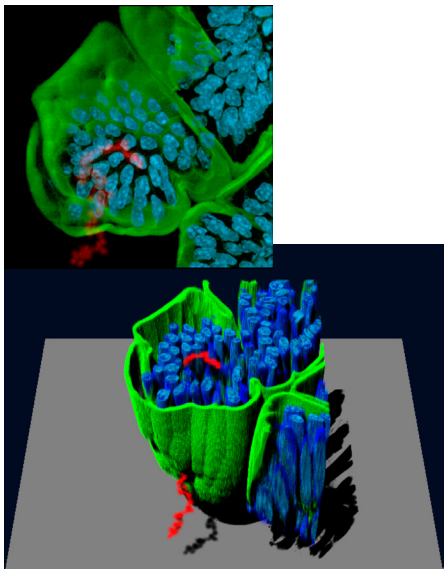

The top image shows a 3D trajectory of an individual semiconductor quantum dot followed with the 3D tracking microscope. Above is a single XY slice of a mouse intestine imaged via standard confocal microscopy. A number of XY slices taken at different Z locations in the sample were combined to form the 3D rendering shown below.

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