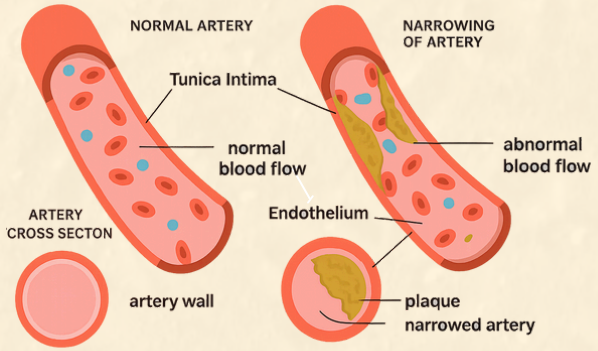
Why It Matters?

According to the WHO, cardiovascular diseases account for 32% of all global deaths. Atherosclerosis is responsible for the majority of cardiovascular-related deaths.

High levels of low-density lipoprotein (LDL, the “bad” cholesterol) seep into the vessel wall, oxidise, and trigger inflammation that builds atherosclerotic plaque and restricts blood flow.



Understanding how LDL (~25 nanometers in diameter) crosses the endothelium becomes crucial but still remains difficult to observe.

Limitations of Exisiting Methods

- Traditional microscopes:
Low resolution (diffraction limit ~200nm)
- Electron microscopy:
High resolution, but easily kills live cells
- Super-resolution methods:
Too slow for fast vesicle motion

Beyond cardiovascular diseases, F.A.S.T can track nanoscale transport in live cells, aiding research in:

- Drug Delivery
- Viral Entry
- Neurodegenerative Diseases

FAST doesn’t just observe biology
It enables proactive disease prevention.

🔎 **Scan to Explore Our Results!** 🔍

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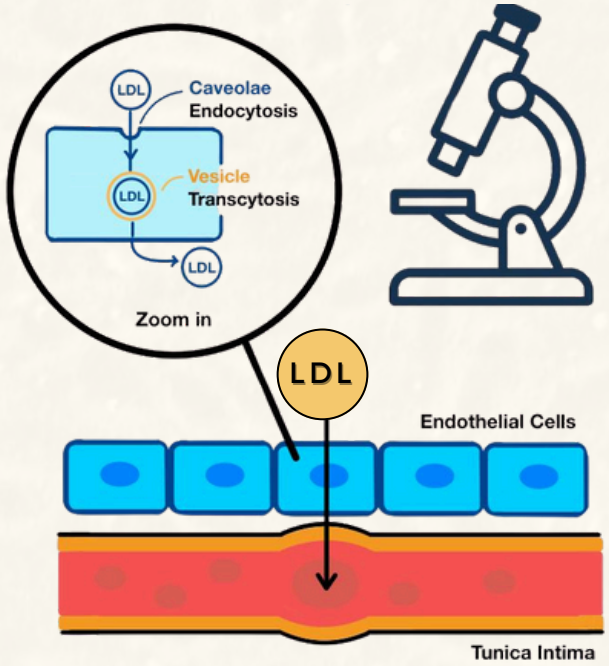
FAST

FAST AXIAL SUPER RESOLUTION TECHNIQUE



OBSERVE HOW LOW-DENSITY LIPOPROTEIN (LDL) CROSSES INTO BLOOD VESSEL WALLS — IN REAL TIME AND WITHOUT EXTRA HARDWARE.

MAROON 6

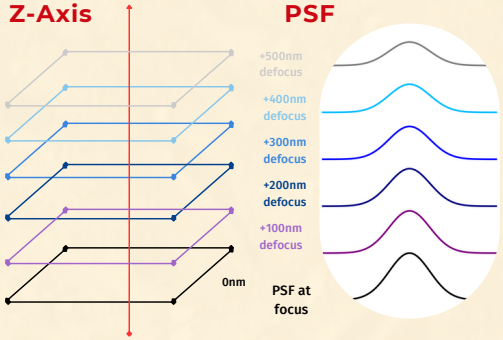
Solution: FAST

NEW APPROACH TO SUPER-RESOLUTION

To localise a particle in 3D, traditional methods have to take many scans at various focal depths. However, with FAST, axial location can be determined with a single scan. It is done by analysing the morphological change in the Point Spread Function (PSF) — how a particle's light shape distorts when out of focus.

CREATING A 3D PSF DATA LIBRARY

Using the ground-truth z-stacks, we parameterise the PSFs at known depths to build a comprehensive 3D PSF library. This bank of data allows FAST to match features from a single scan and instantly infer the particle's axial position.



FINAL WORK FLOW

Acquire time-lapse 2D images of fluorescent LDL moving through the endothelium. For each frame, FAST extracts PSFs and match them to a depth-tagged PSF library built from calibration z-stacks, so even out-of-focus particles yield precise axial positions. This reconstructs 3D LDL trajectories through the endothelium in real time.

Biological Model Preparation

To replicate biological conditions, we cultured Human Aortic Endothelial Cells (HAECs).

- HAECs seeded on biotinylated gelatin–coated glass or polymer dishes for optimal adhesion and imaging
- Quantum dots (~20 nm) and TetraSpeck™ beads (~100 nm) used as fluorescent LDL surrogates and depth-calibration markers

Confocal Imaging & Calibration

- Single slices and z-stacks acquired on a Leica SP8 confocal microscope; this provided ground truth for PSF depth variation
- Optical slices captured to assess marker intensity, spatial distribution, and compatibility with downstream analyses

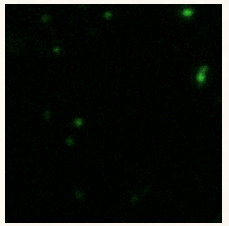
FAST Algorithm Development

A machine learning pipeline to infer particle depth from PSF shape.

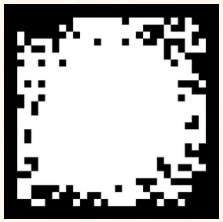
- 33 PSF shape feature parameters extracted per PSF.
- A genetic algorithm is used to optimise the weights of each parameter.
- Modular MATLAB scripts enable batch processing and flexible parameter tuning

PSF PROCESSING

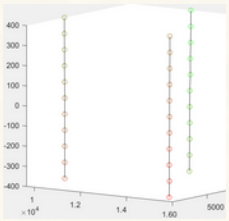
Fluorescence stacks are processed through denoising, PSF detection, and 3D localisation to determine the positions of LDL particles.



Raw Sacks

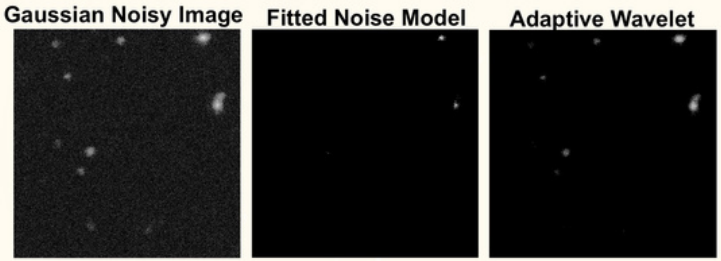


PSF extraction after denoising



Estimated location

DENOISING COMPARISON



Results

- No extra hardware needed
- Achieved 14-20 nm axial accuracy from a single 2D image.
- Denoising results of Gaussian noisy images show that our adaptive wavelet preserves key signal details while suppressing noise effectively, unlike the fitted model which oversmooths and loses information.
- Weigt of PSF feature parameter M 1(intensity spread) and M23 (radial profile) can be optimised because of their strong 1 linear relationship with depth.