Real-Time Imaging of Nanoparticle Transcytosis in a Microfluidic Blood-Brain Barrier Model

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ANZCOP
THE AUSTRALIAN AND NEW ZEALAND
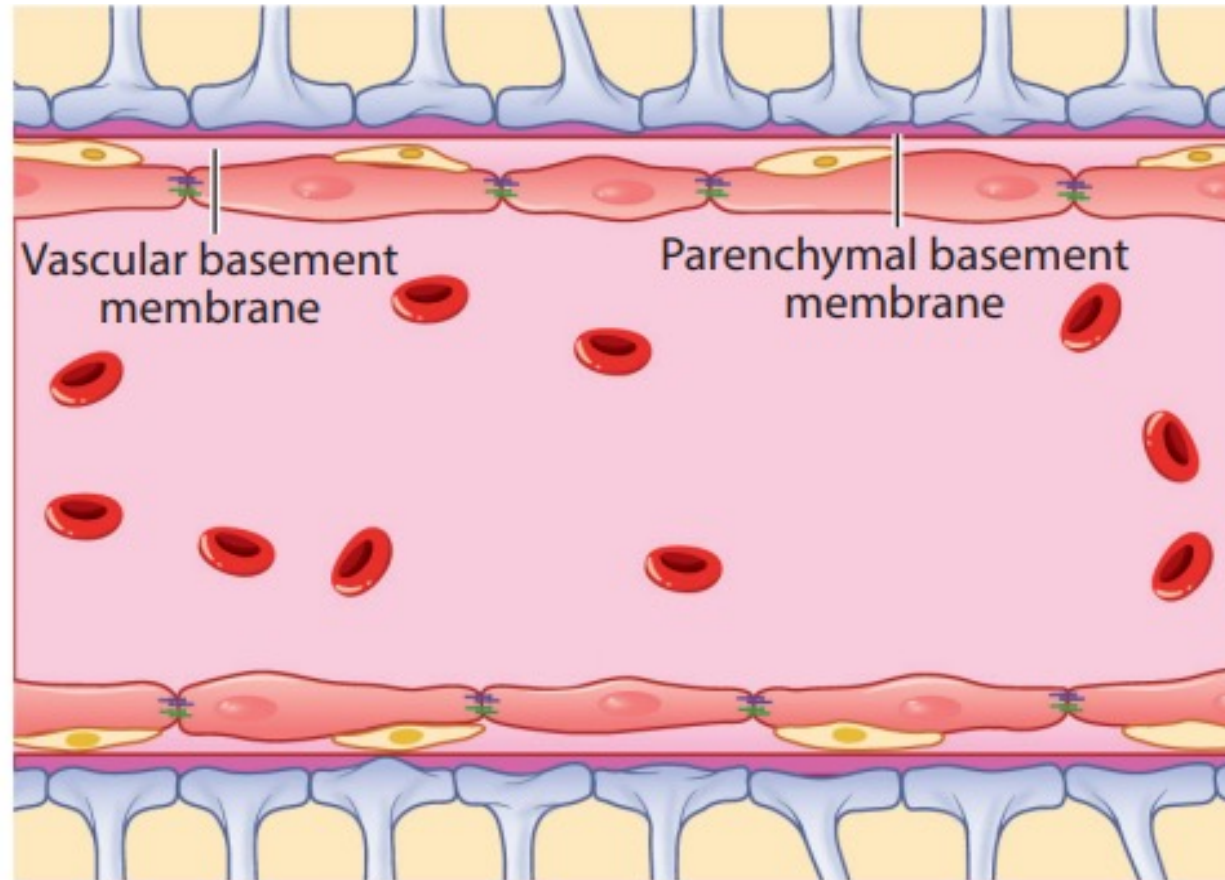CONFERENCE ON OPTICS AND PHOTONICS

WSOF
7th INTERNATIONAL WORKSHOP OF SPECIALTY
OPTICAL FIBRES AND THEIR APPLICATIONS

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CONFERENCE ON OPTOELECTRONIC AND
MICROELECTRONIC MATERIALS AND DEVICES

Background: blood-brain barrier (BBB)

The **integrity** of Blood-Brain Barrier

- **Selective permeability**

- Difficulty in drug delivery for treating mental and neurological disorders, even with the help with **nano-carriers**
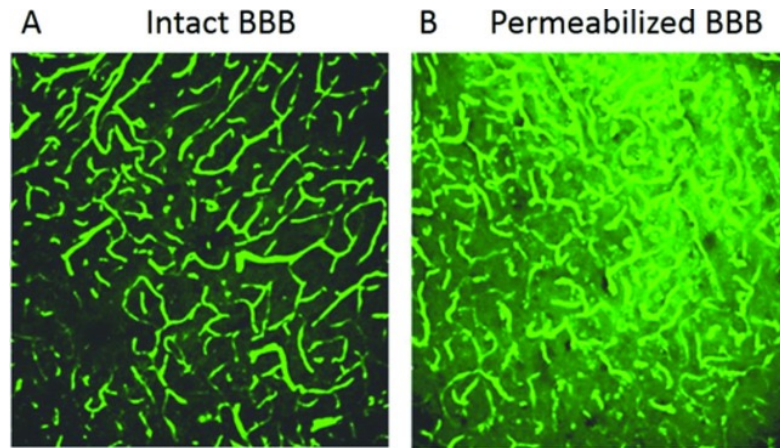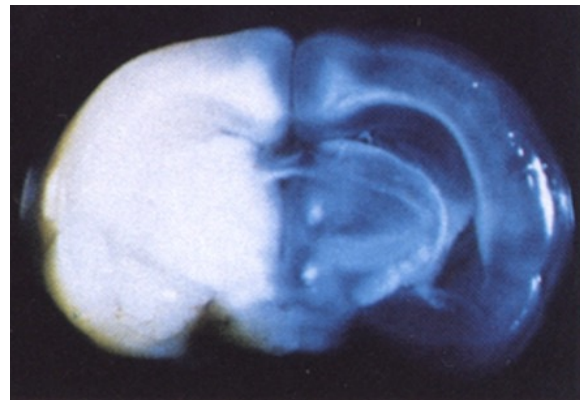
Integrity and **permeability** matters!

Background: imaging methods

- Traditional methods for observing and assessing the integrity of BBB

  - Trans-endothelial electrical resistance (TEER)

  - Magnetic resonance imaging (MRI)
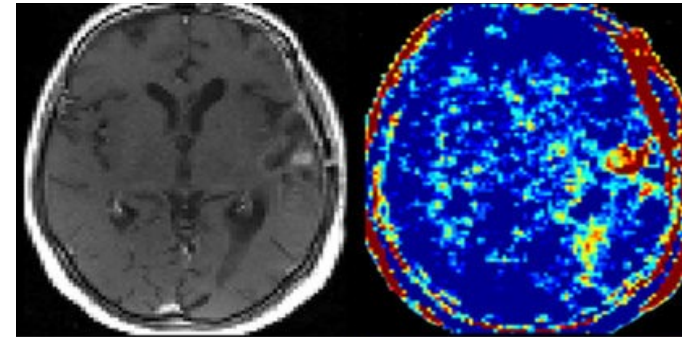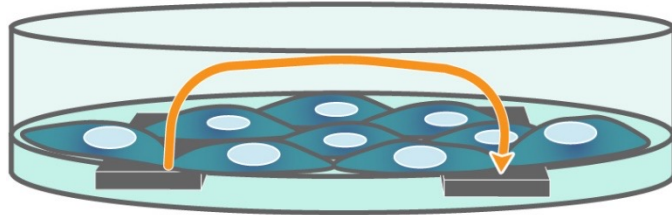
  - Organic dye: Evans blue, dextran-FITC

A   Intact BBB   B   Permeabilized BBB

Curr Protoc Neurosci. 2017, 79(1), 9-58.

- **Limitation**

  - Varied standards, slow procedure, resolution, sensitivity, photo-bleaching

Background: imaging methods

- **Lanthanide nanoparticle (LNP) as an imaging tool**

  ➤ Real-time

  ➤ Single pa

Probing Photon Correlation in Spontaneous Emission of Lanthanide Nanocrystals

📅 14 Dec 2022, 17:15
🕐 15m
📍 Hall C (Adelaide Convention Centre)

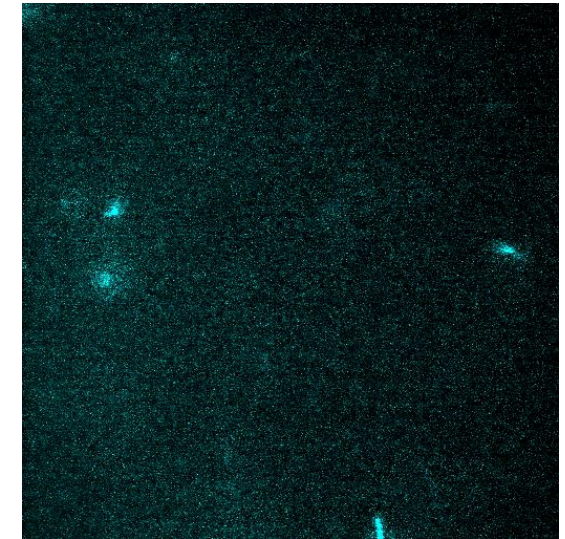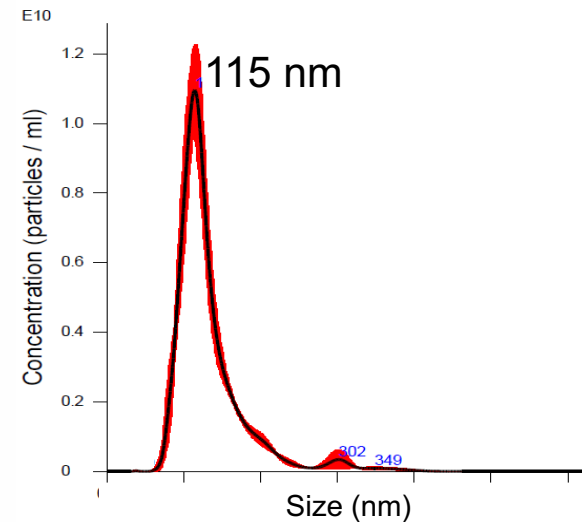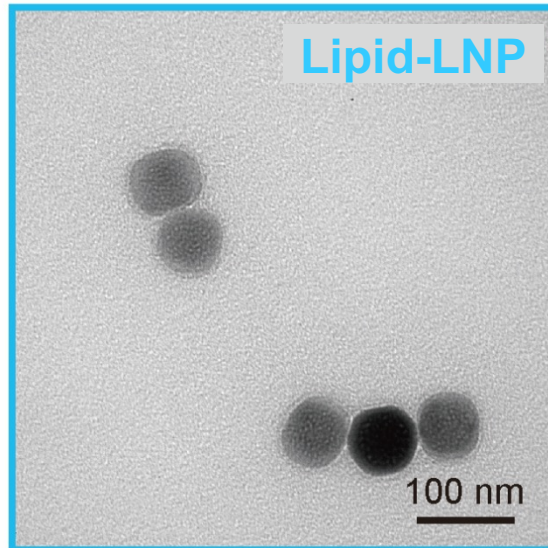Talk (preferred) ANZCOP: Nanophot... Australian and New Ze...

Speaker
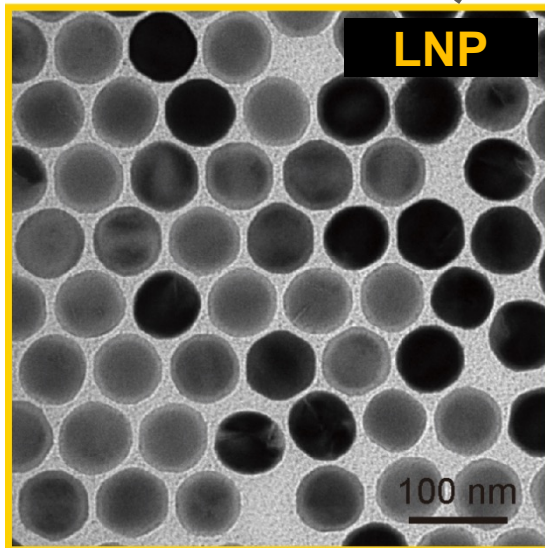
👤 Peng Ren

β-NaYbF$_4$:Tm

29–233

0, 12, 8487–8492

LNP

Lipid-LNP

100 nm

100 nm

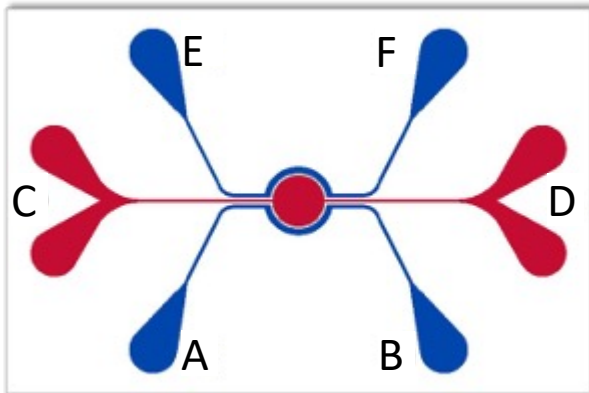115 nm
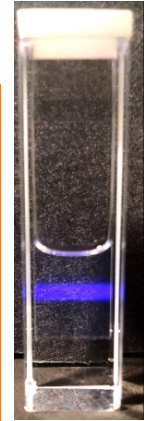
Experiment design: *in-vitro* BBB model

- BBB in microfluidic chip

Lab Chip, 2021, 21, 546-557

DAPI   Tight Junction (VE-cadherin)   Cell membrane

Apical Chamber

Basolateral Chamber

20 µm

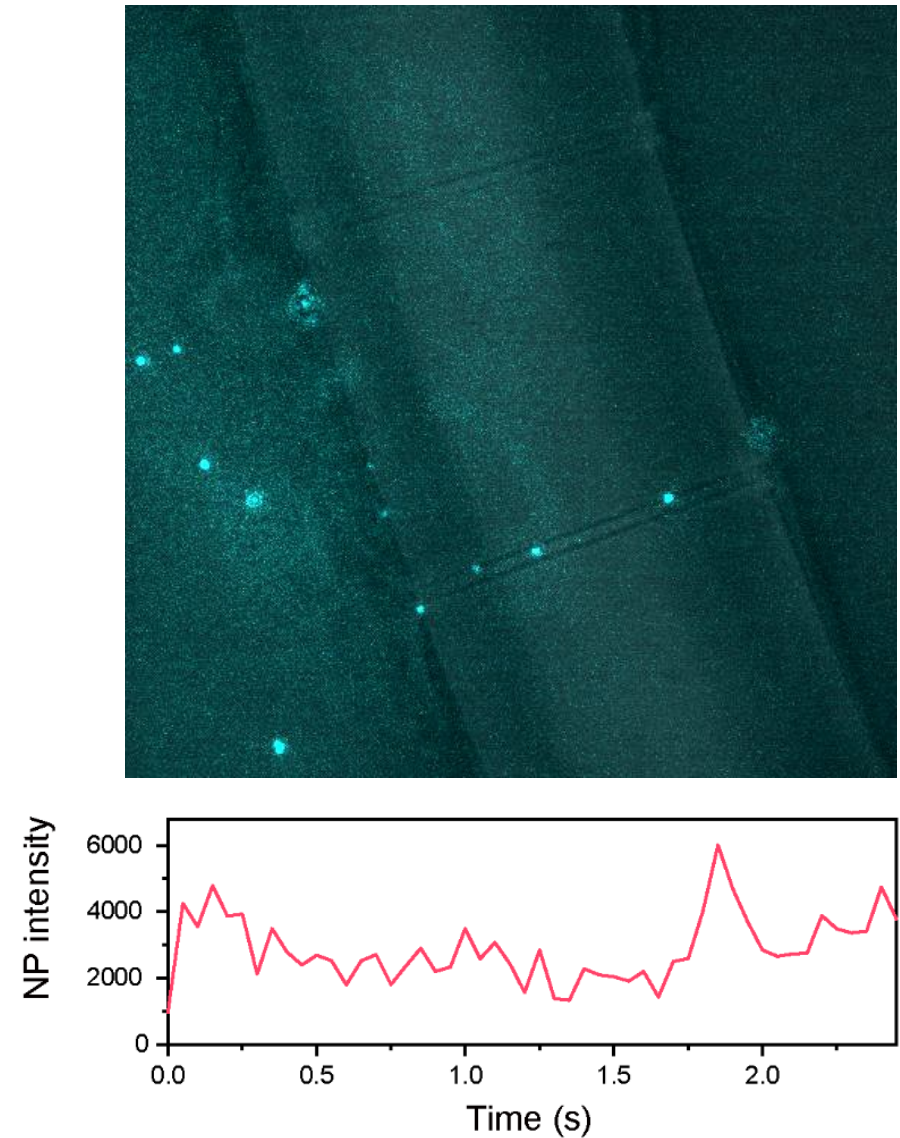Dextran-FITC (MW 10kD)

lipid-LNPs

E   F

C   D

A   B

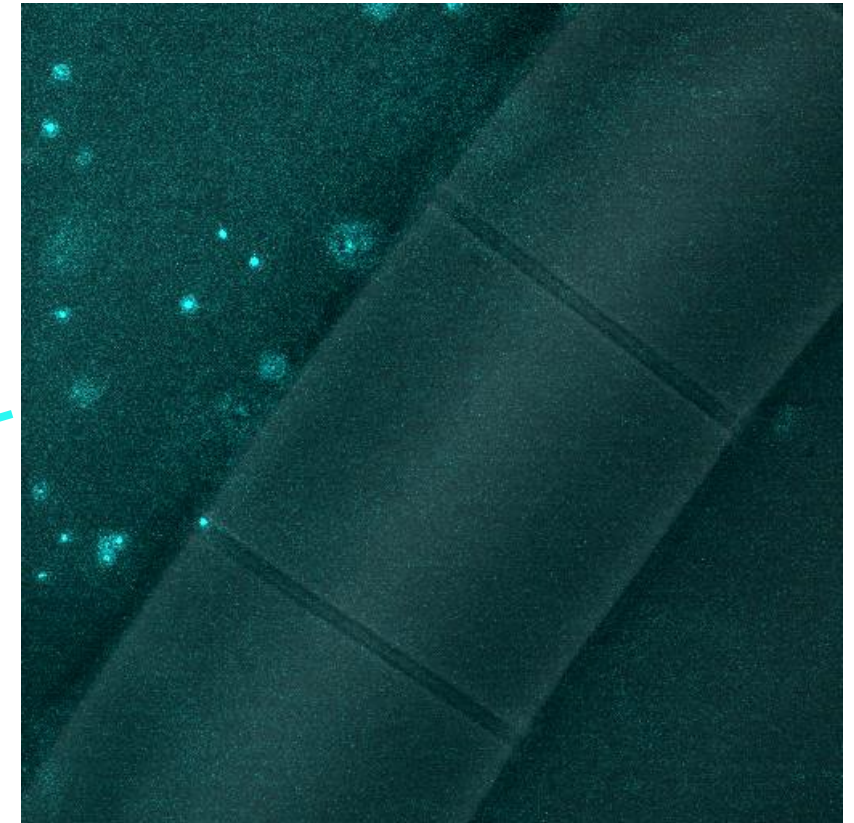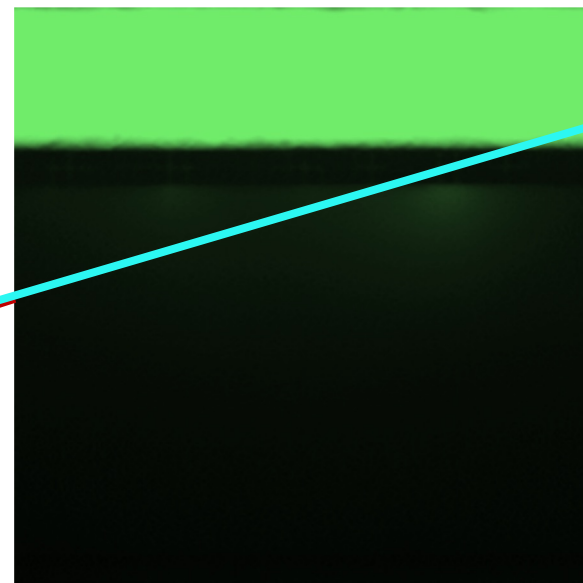*20 frames per second

10 μm
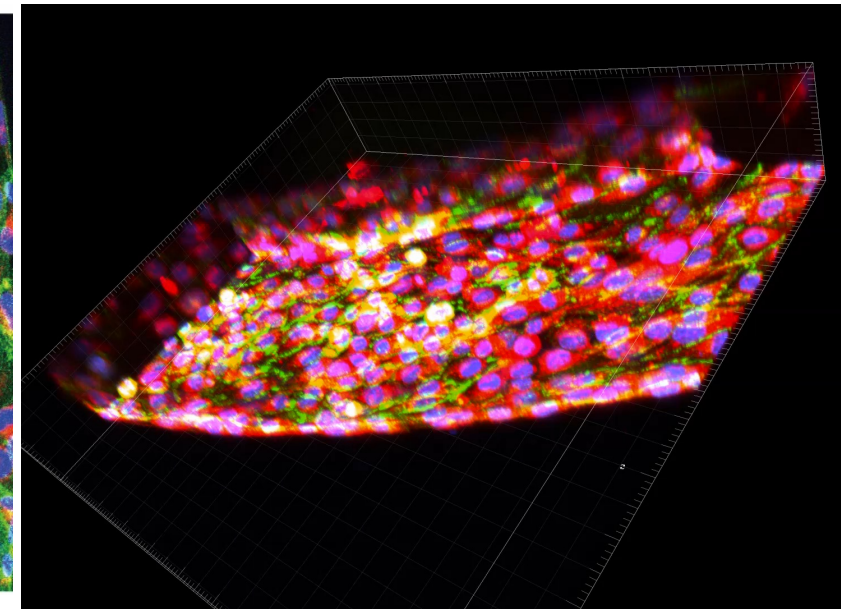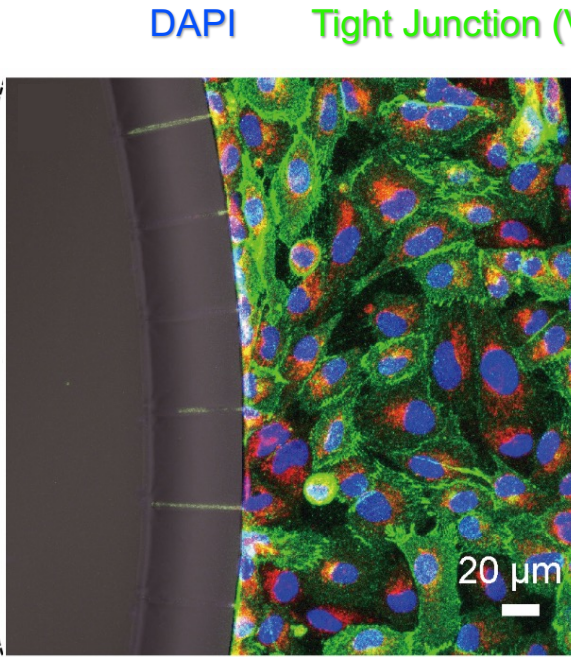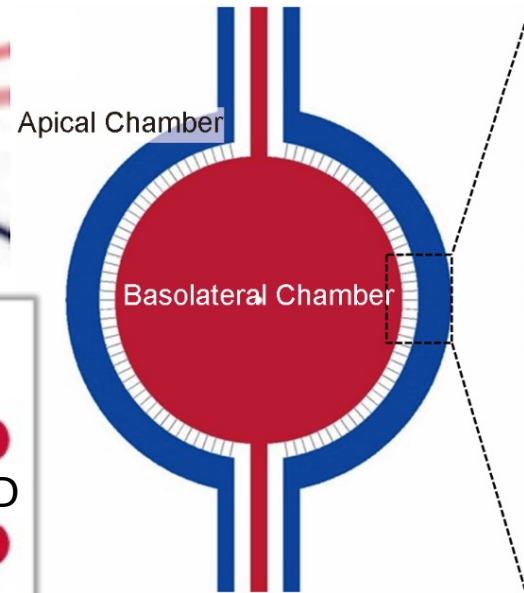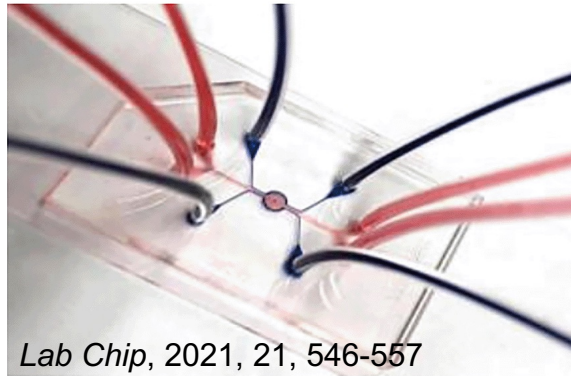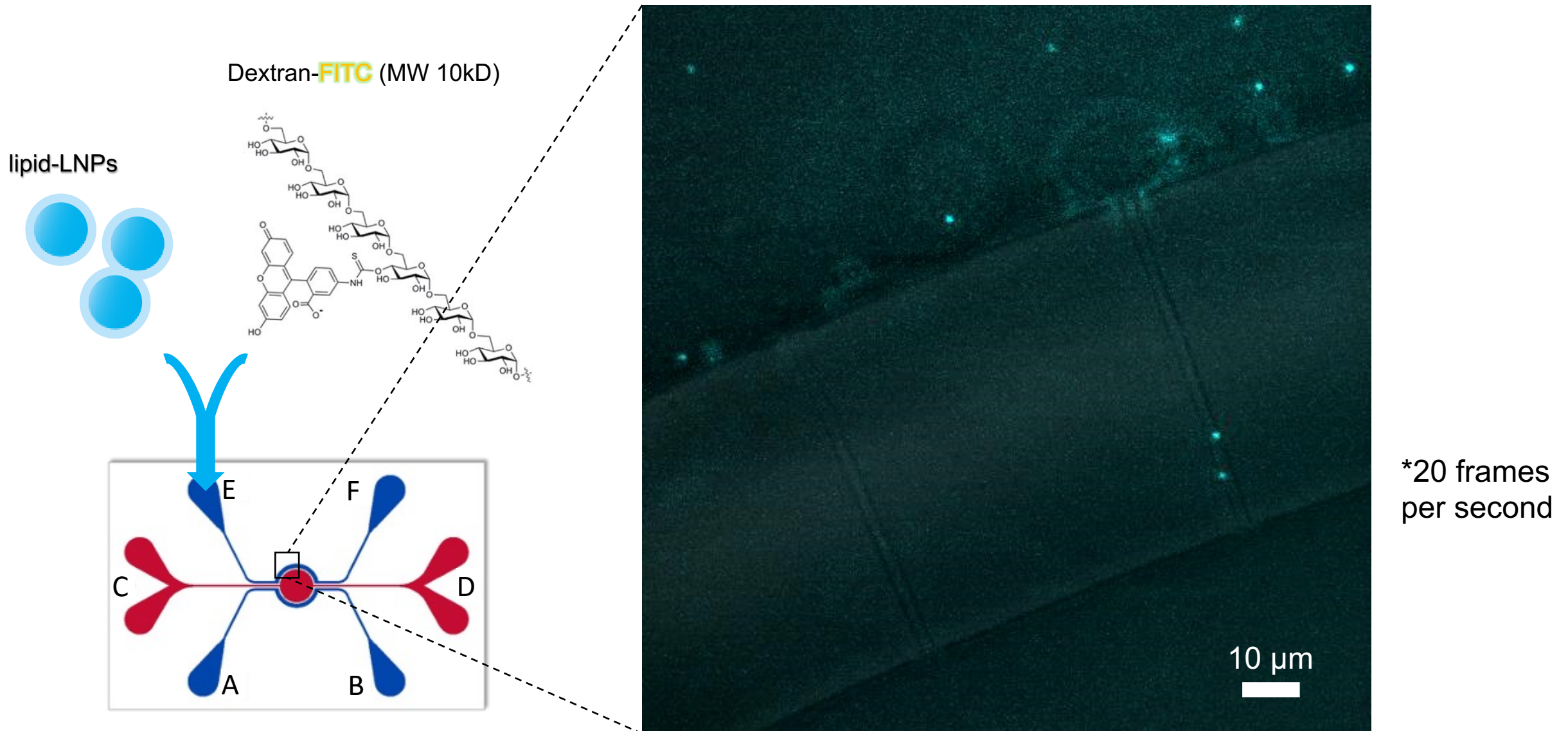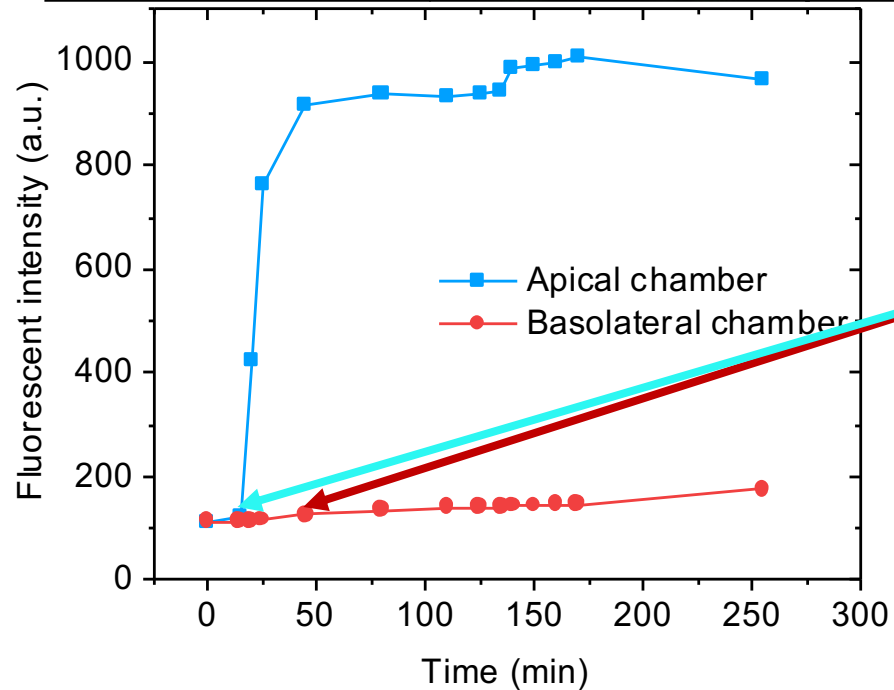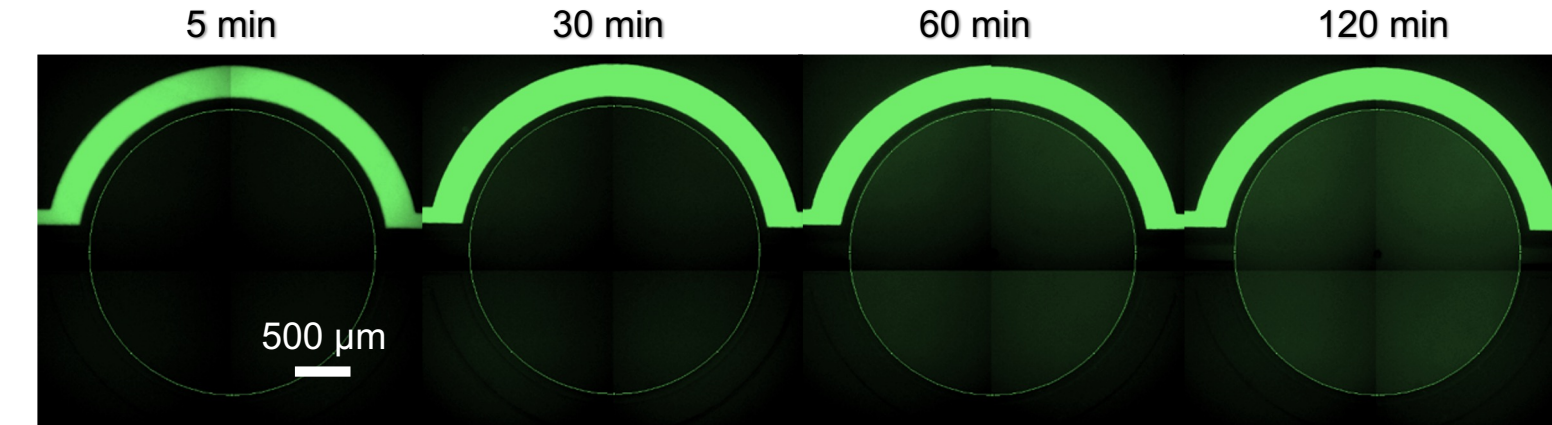
Single nanoparticle sensitivity
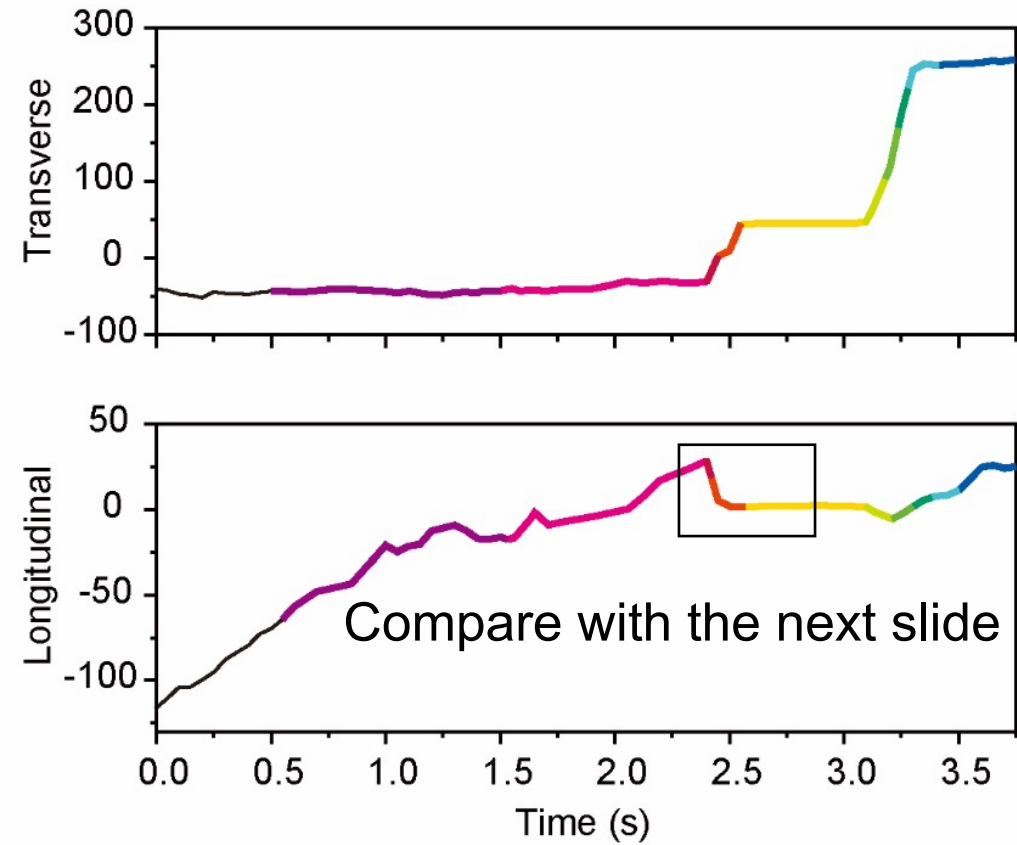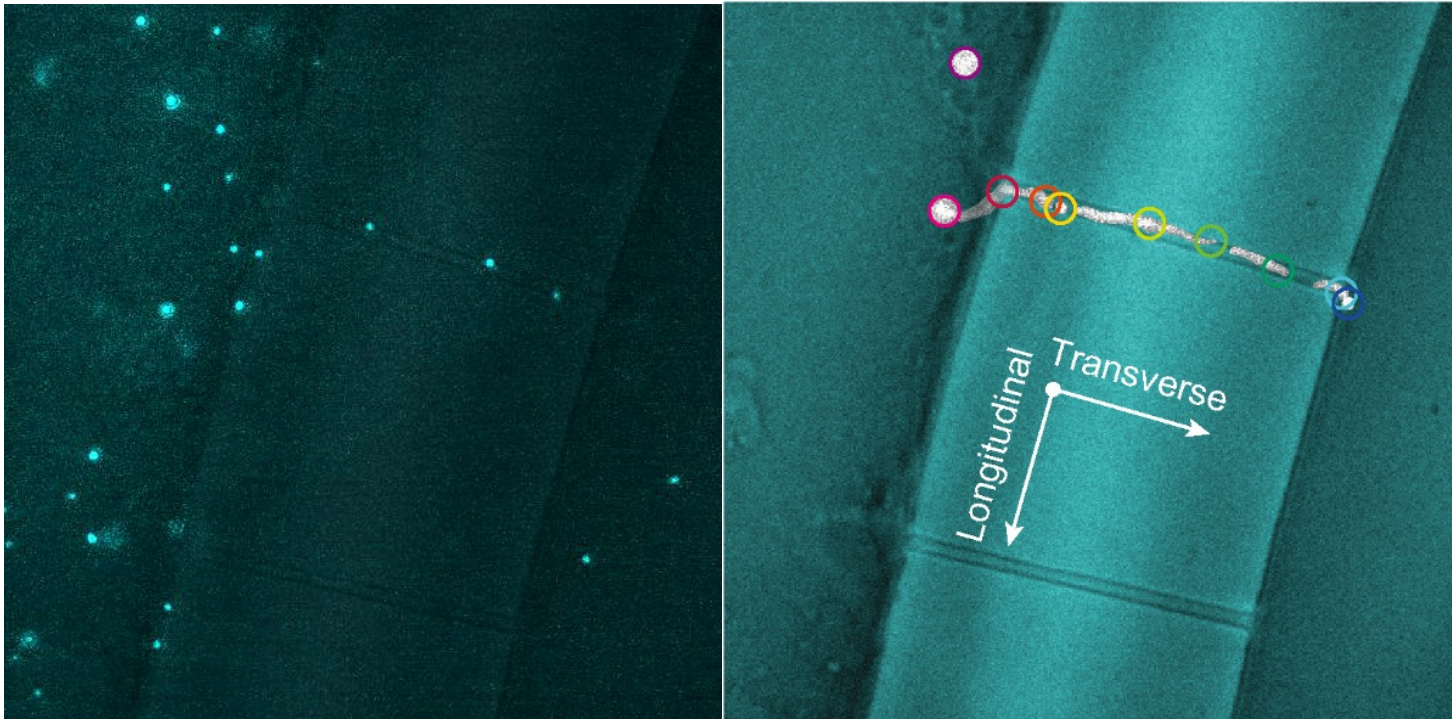
- *ex-vivo*
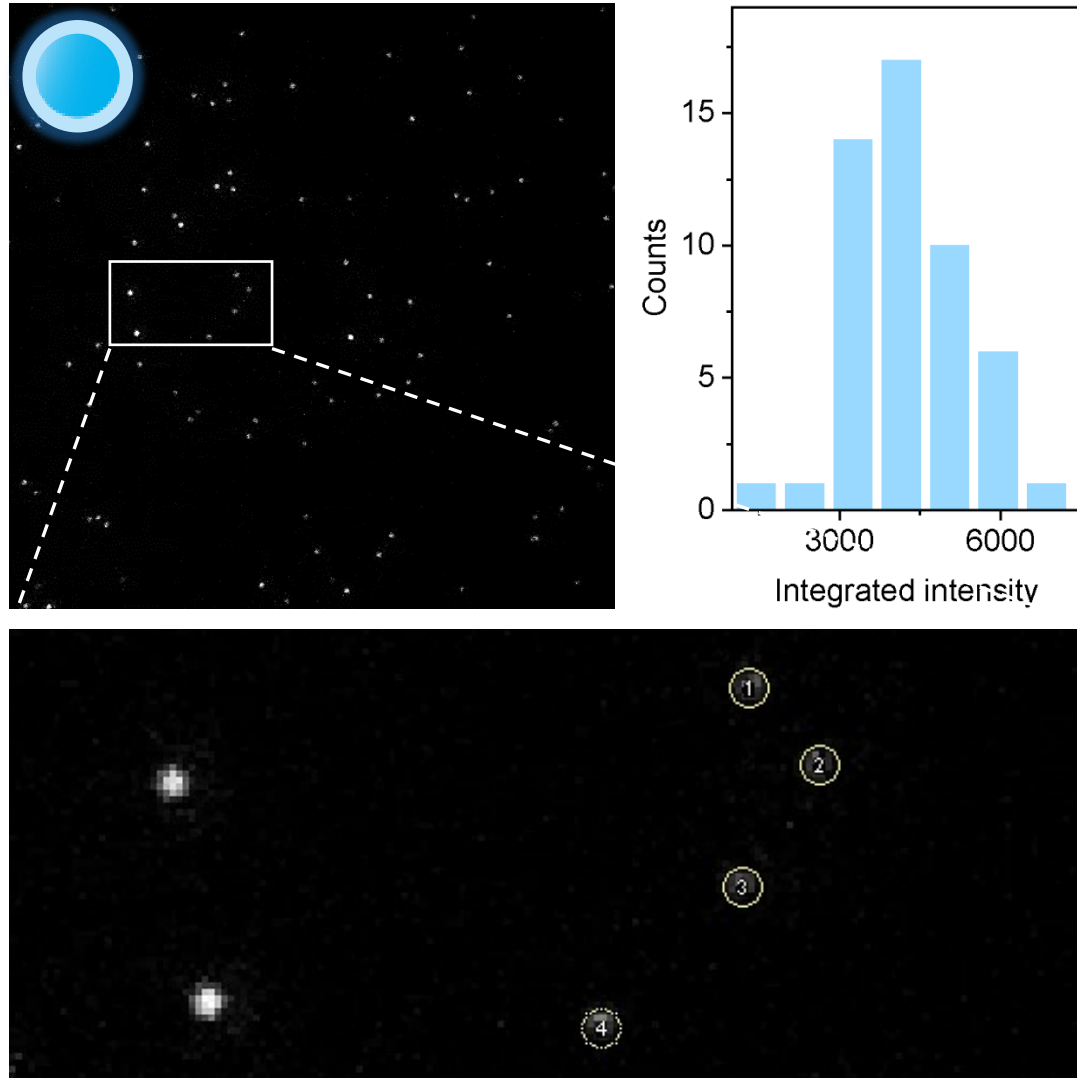
- *in-vitro*

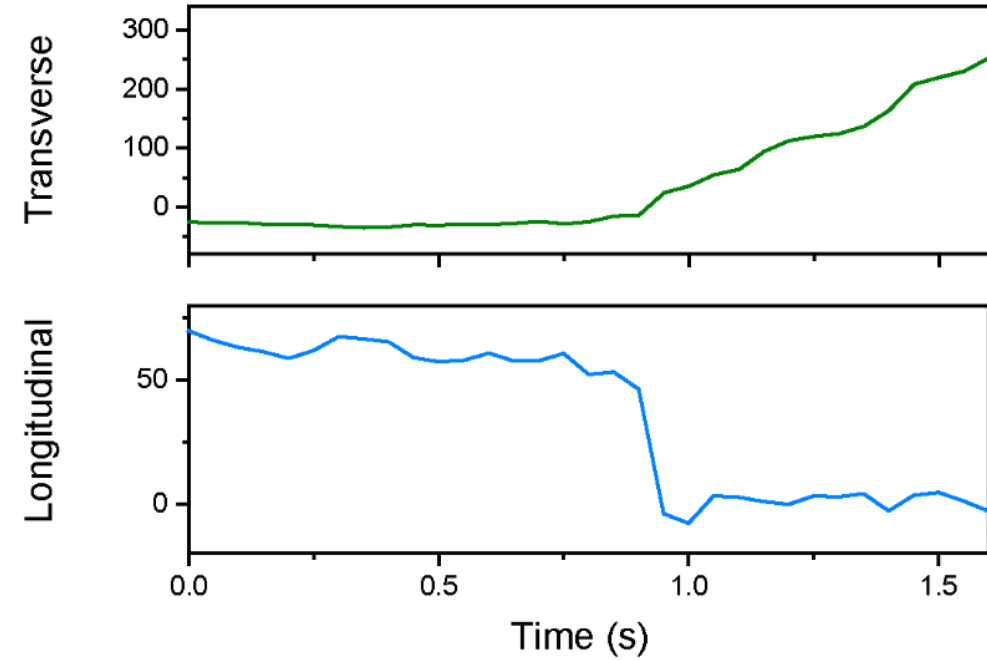# Compare with traditional dextran-FITC method

- BBB model integrity monitoring

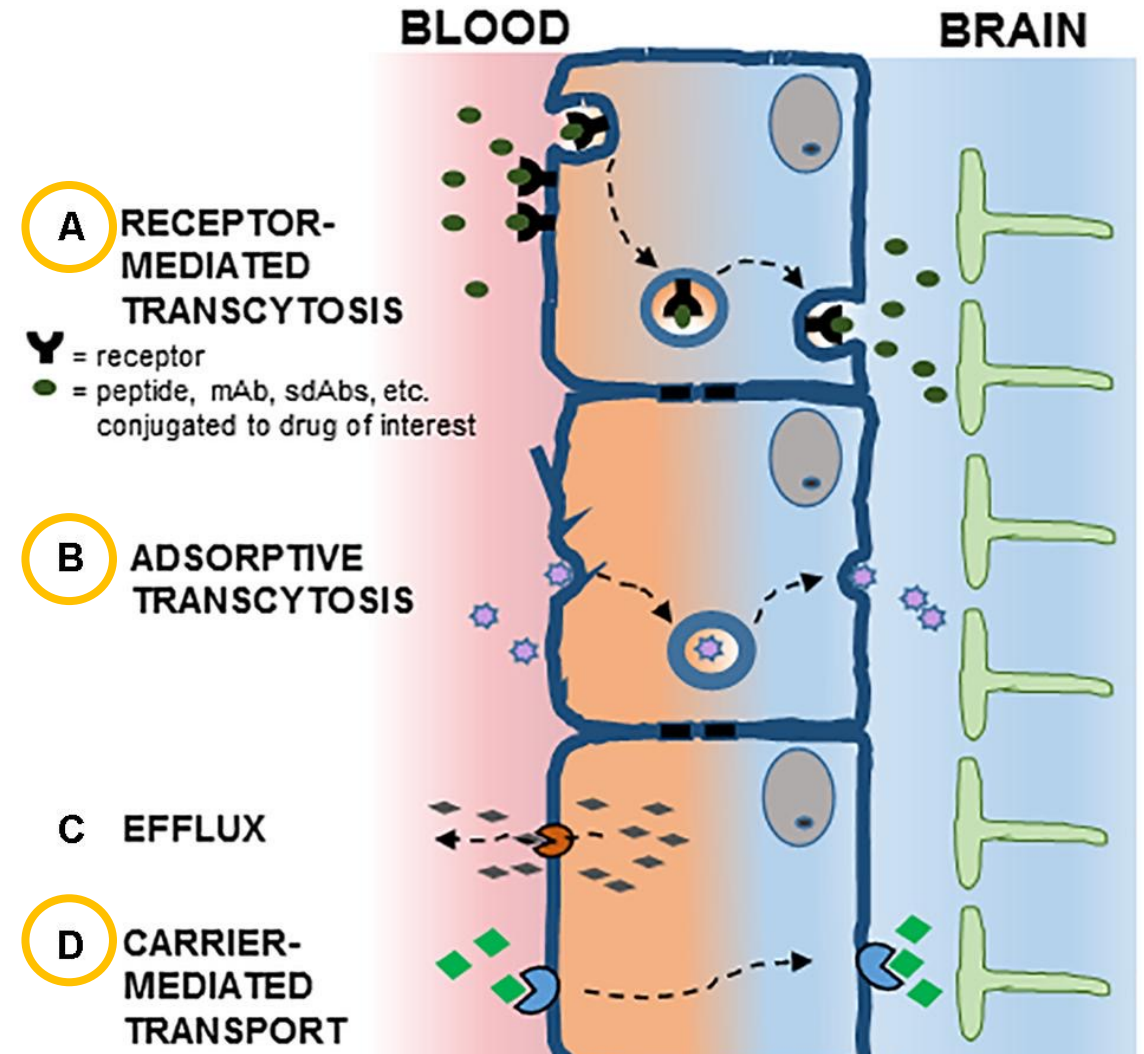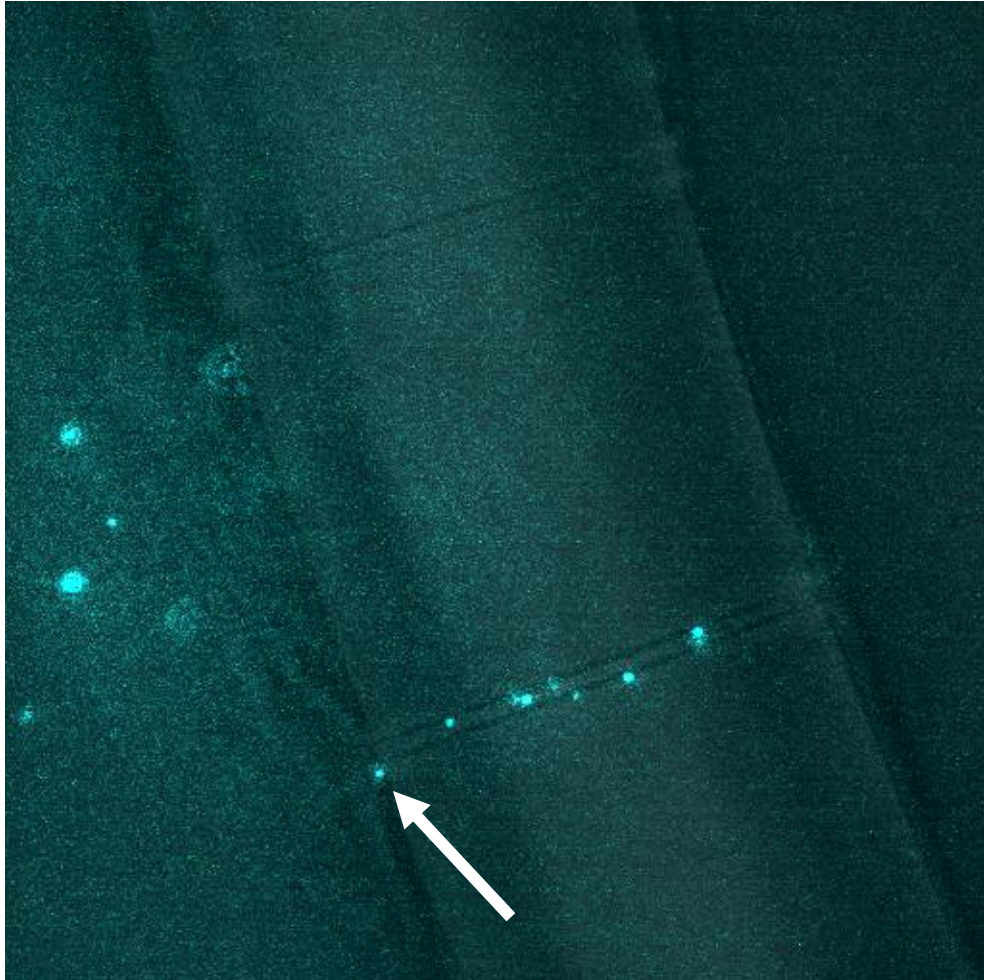- LNP **movement** trajectory extracted

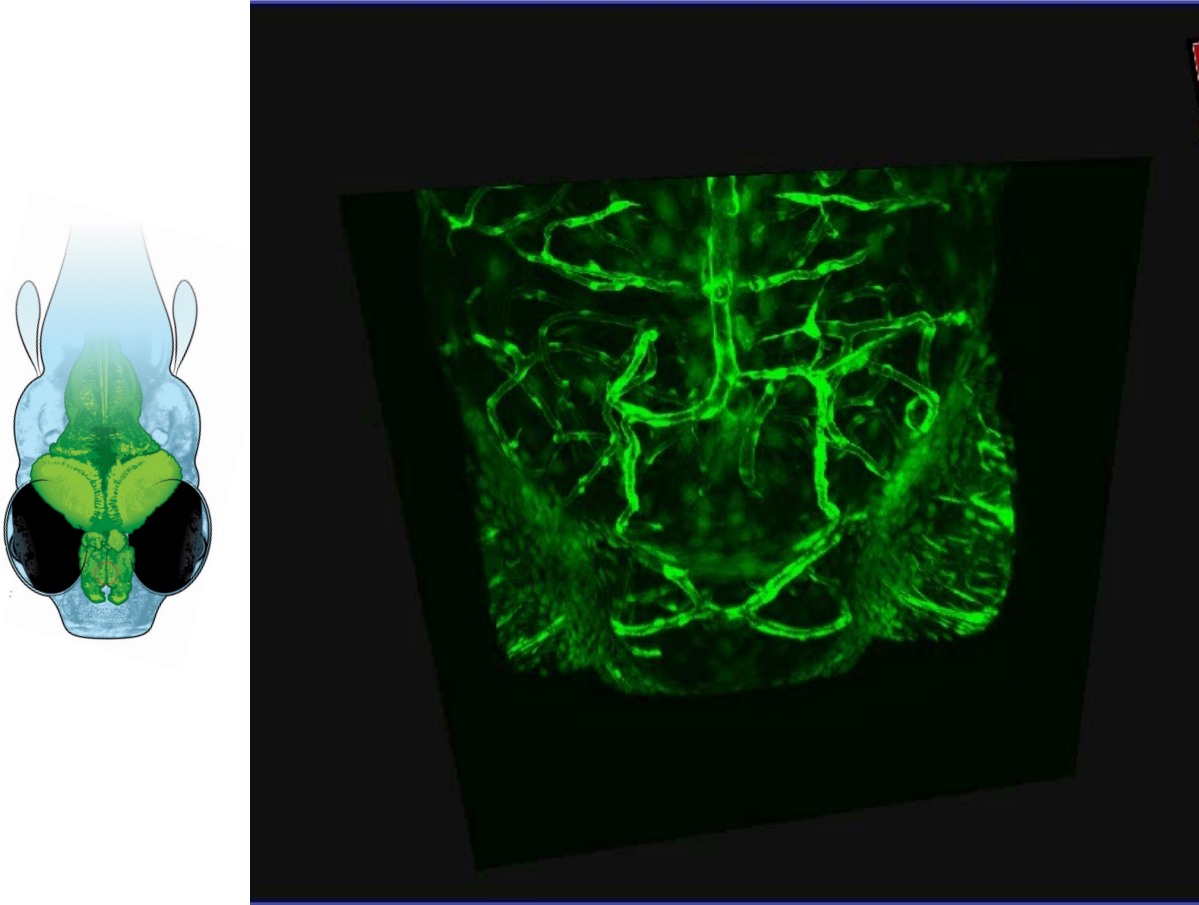Compare with the next slide

- **movement patterns** and **transport pathways**

Trajectory Analysis

- **movement patterns** and **transport pathways**

In-vivo imaging

- Blood vessels in zebrafish brain

- Live imaging of LNPs in zebrafish brain

Illustration by Chris Philpot
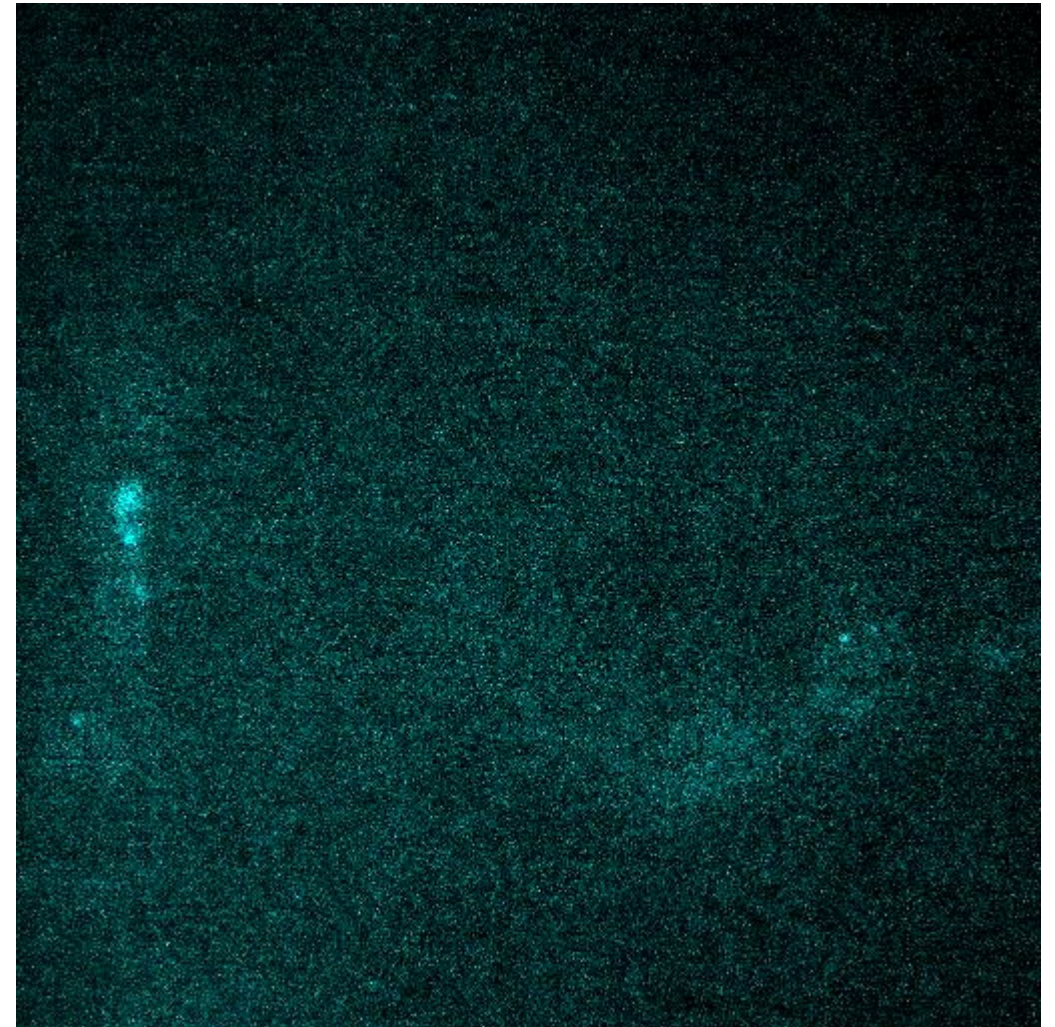
Summary and scope

- **Methodology capability and achievements**

  ✓ Video rate imaging of single nanoparticle penetration process

  ✓ BBB model integrity monitoring

  ✓ Trajectory analysis and statistics comparing between conditions enabled

- **Nanoparticle penetration pathways**

  ❑ Inhibitors for suppression of different receptors

  ❑ Co-staining of endocytic vesicles

  ❑ Surface modified LNPs

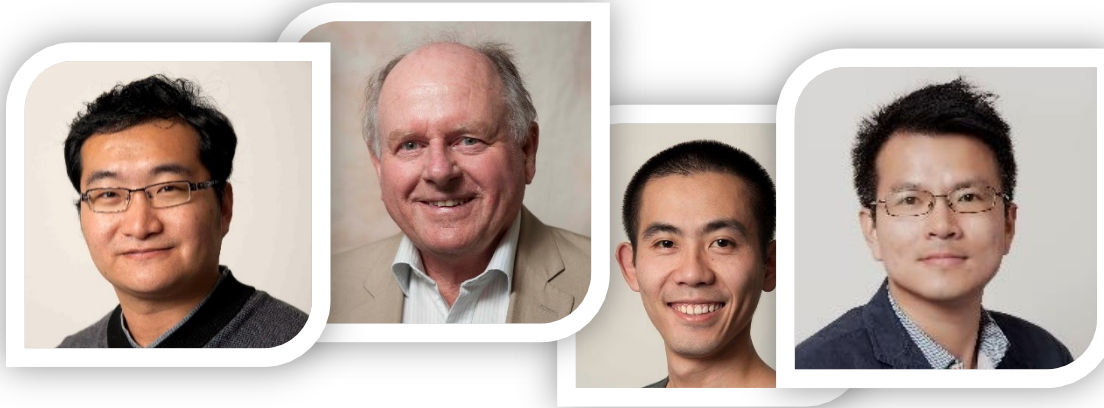- ***In-vivo* zebrafish model**

Acknowledgment

MQ School of Engineering:

- Dr. Yiqing Lu
- Professor Jim Piper
- Dr. Xianlin Zheng
- Dr. Jun Zhang

MQ Medical School:

- A/Professor Bingyang SHi
- Dr. Guoying Wang
- Dr. Jia Li

Thank **you** for your attention!