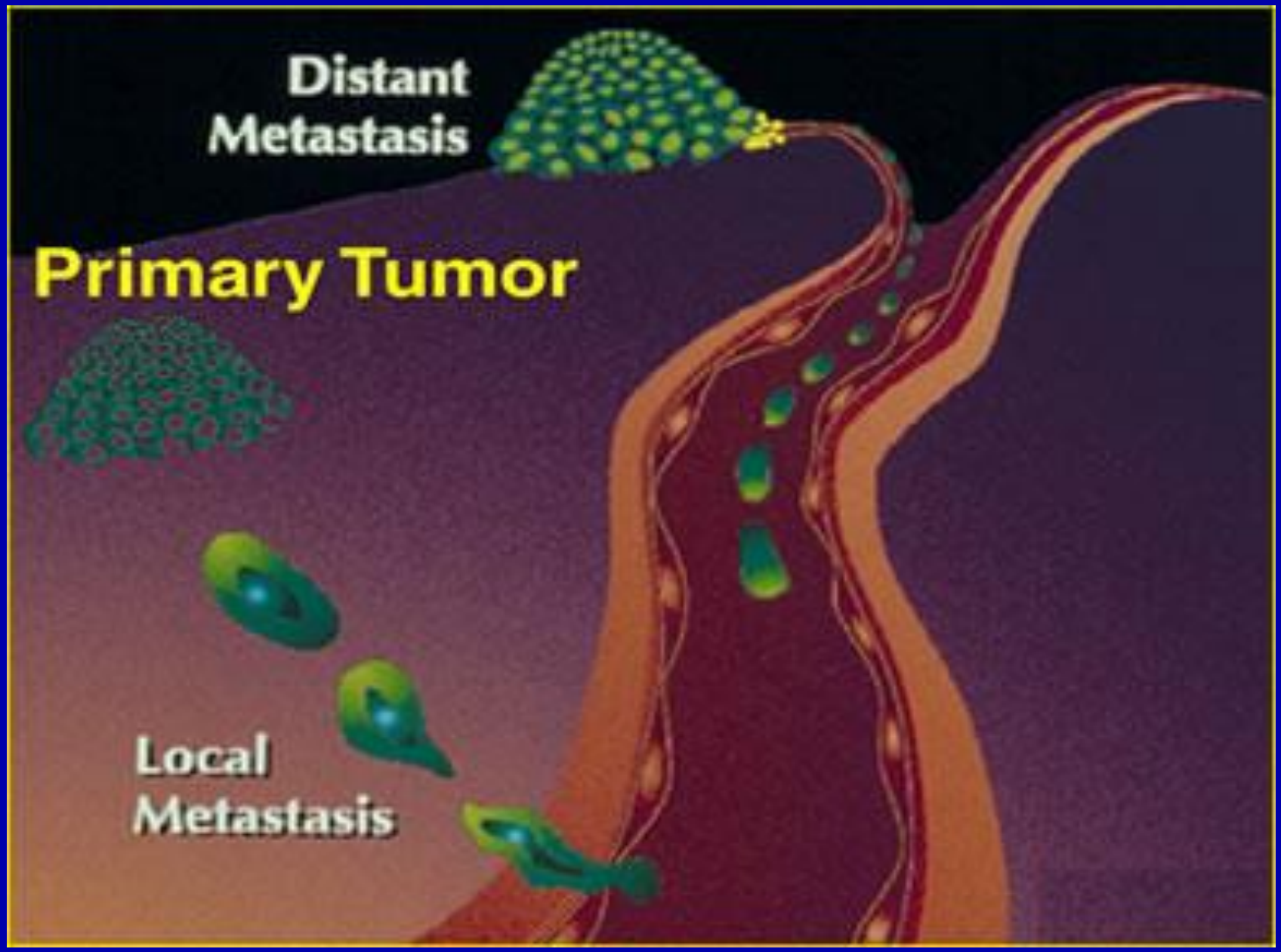
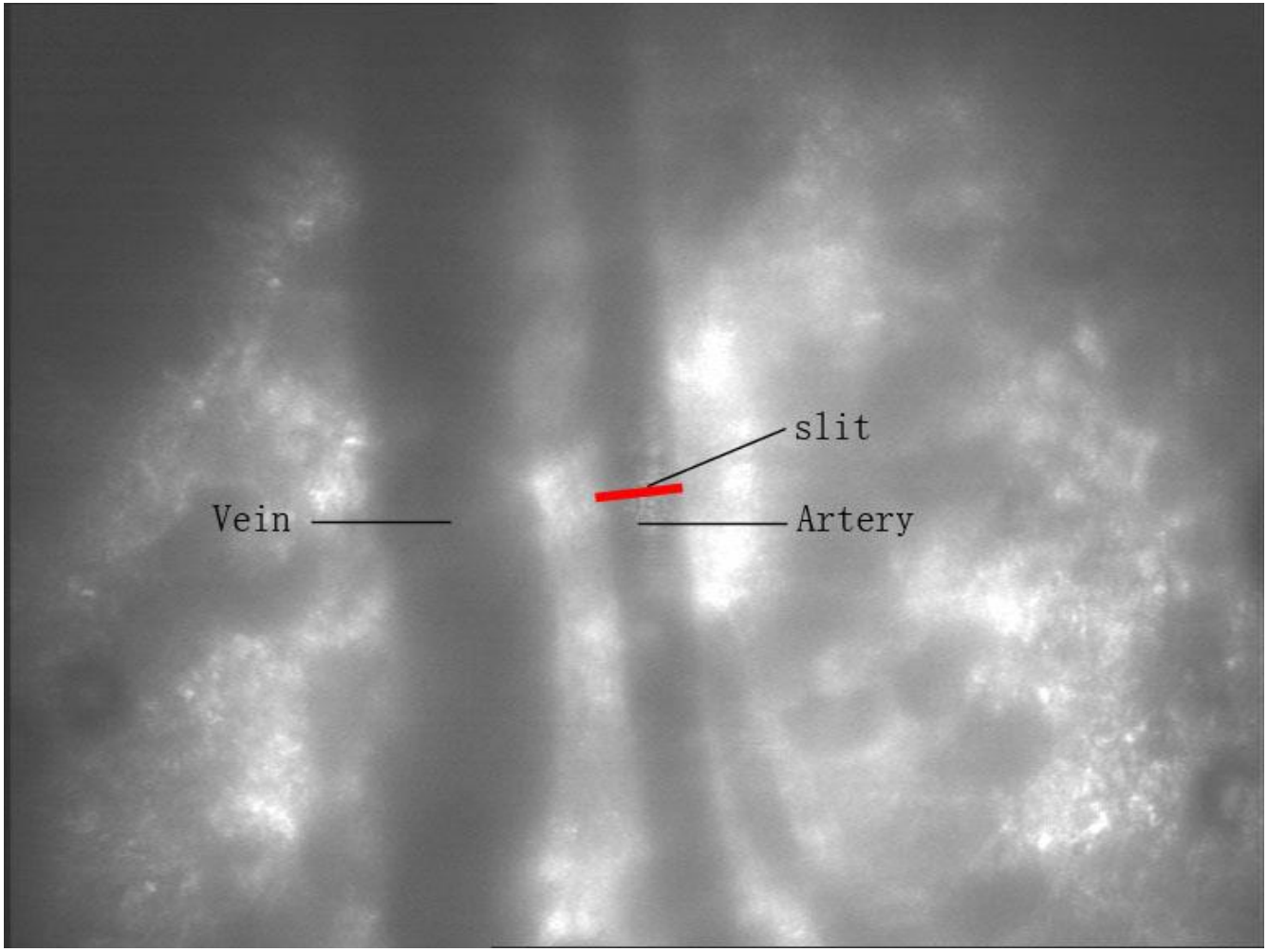
In vivo Counting and Optical Trapping Circulating Cells

Xunbin Wei, PhD

Distinghuished Professor
Med-X Research Institute & School of Biomedical Engineering
Shanghai Jiao Tong University


Distant
Metastasis
Primary Tumor
Local
Metastasis


slit
Vein
Artery

In Vivo Flow Cytometry (IVFC) has realized in vivo counting

International weekly journal of science

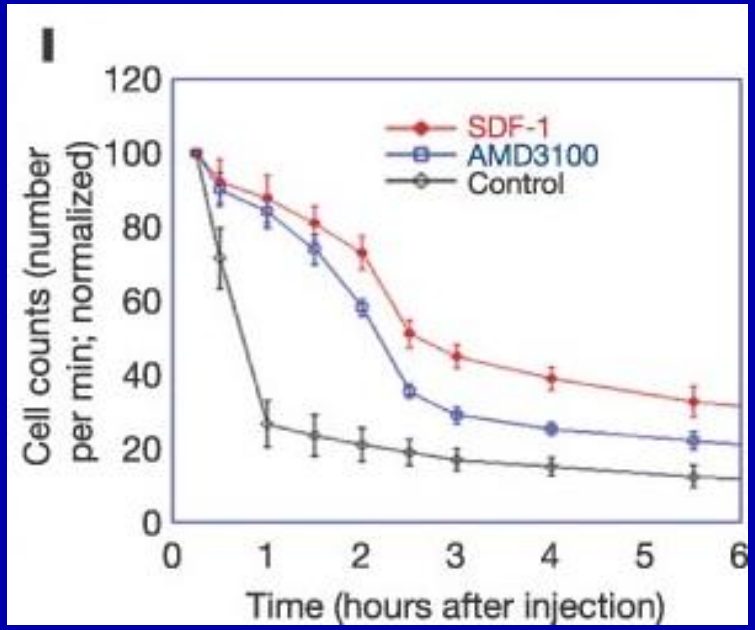
nature

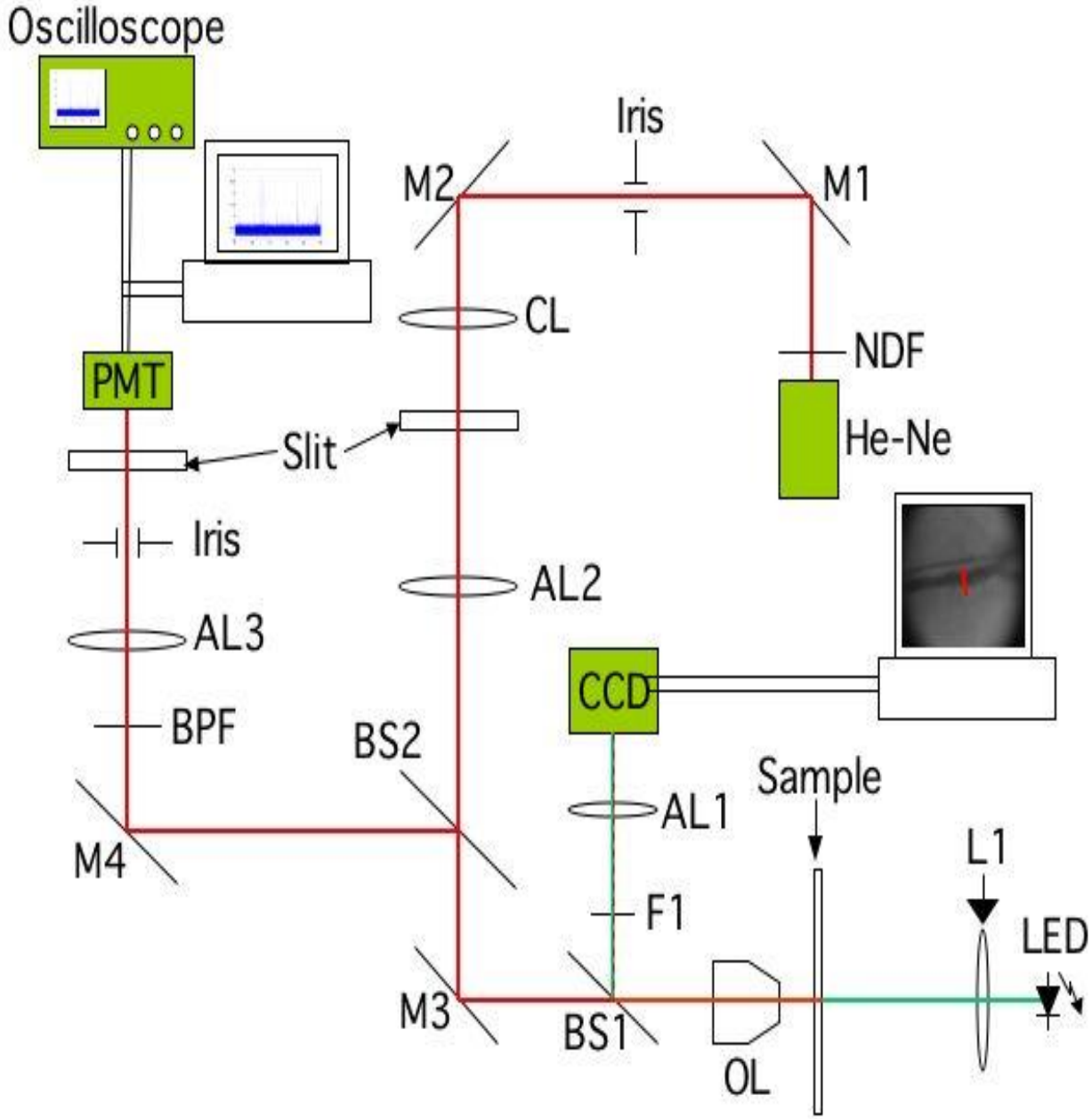
In vivo imaging of specialized bone marrow endothelial microdomains for tumour engraftment

Dorothy A. Sipkins[1,2,3], Xunbin Wei[1], Juwell W. Wu[1], Judith M. Runnels[1], Daniel Côté[1], Terry K. Means[4], Andrew D. Luster[4], David T. Scadden[2,3,5] & Charles P. Lin[1]

Reprinted from *Nature*, Volume 435, June 16, 2005

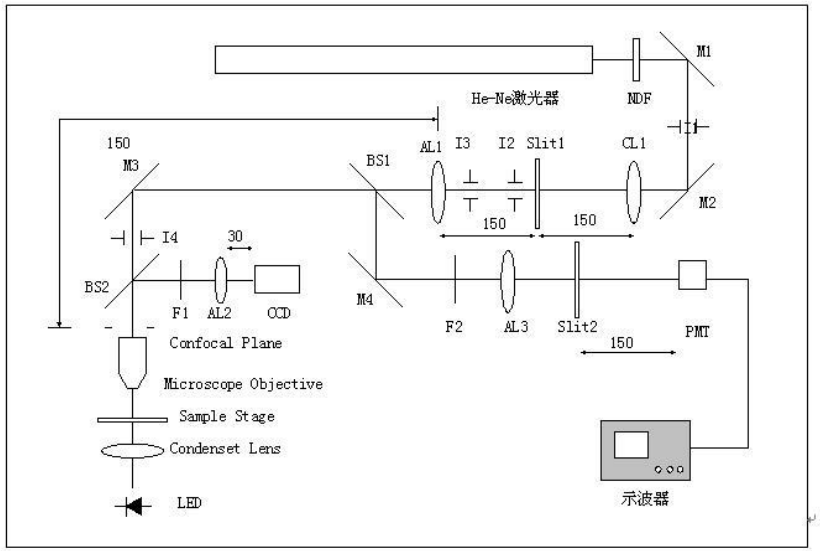
npg

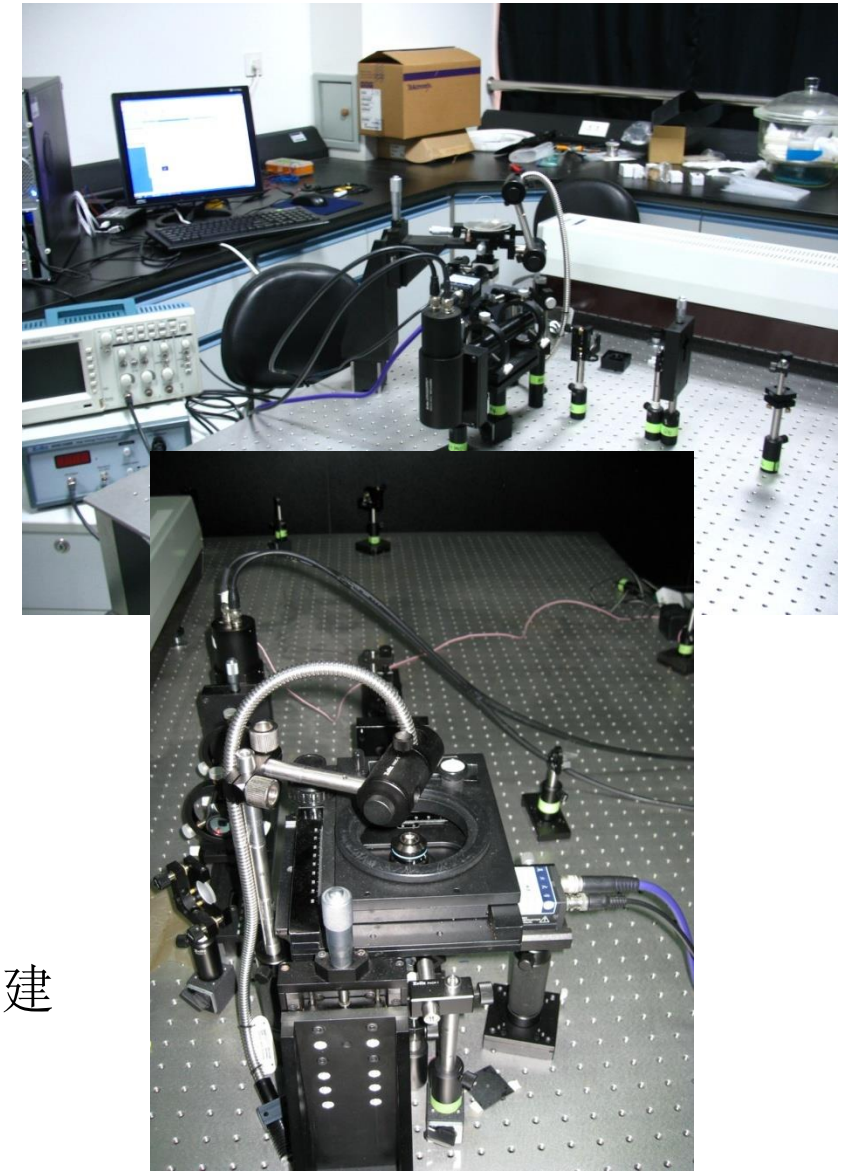



Oscilloscope
Iris
M2
M1
CL
NDF
PMT
Slit
He-Ne
Iris
AL2
AL3
CCD
BPF
BS2
Sample
AL1
M4
L1
F1
LED
M3
BS1
OL

IVFC Setup

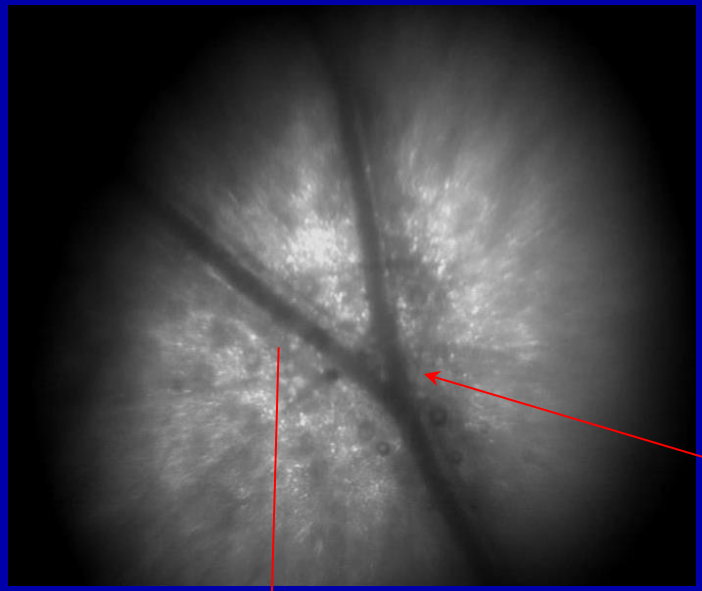
IVFC光路图

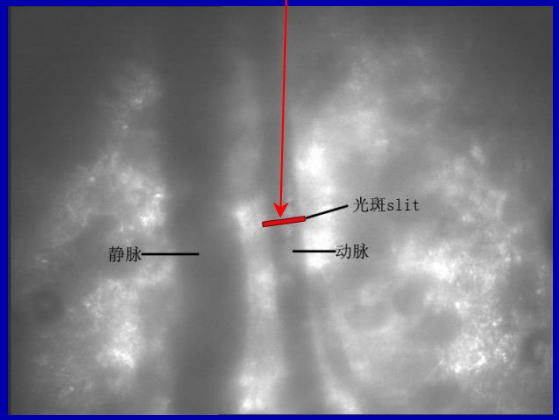


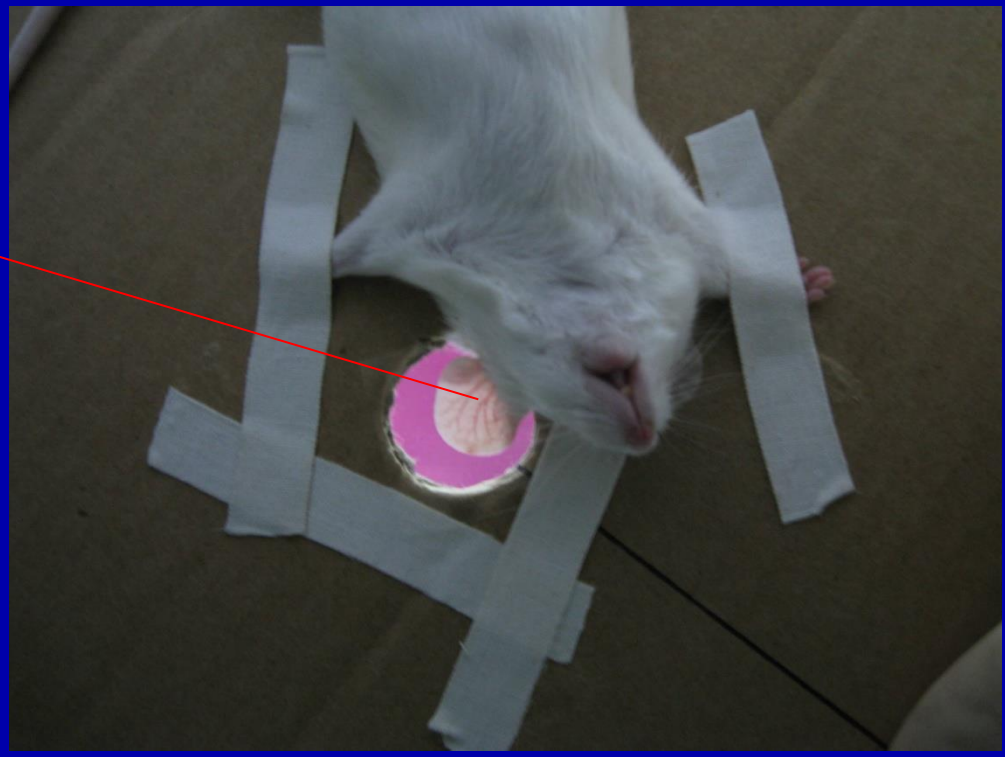


光学平台搭建

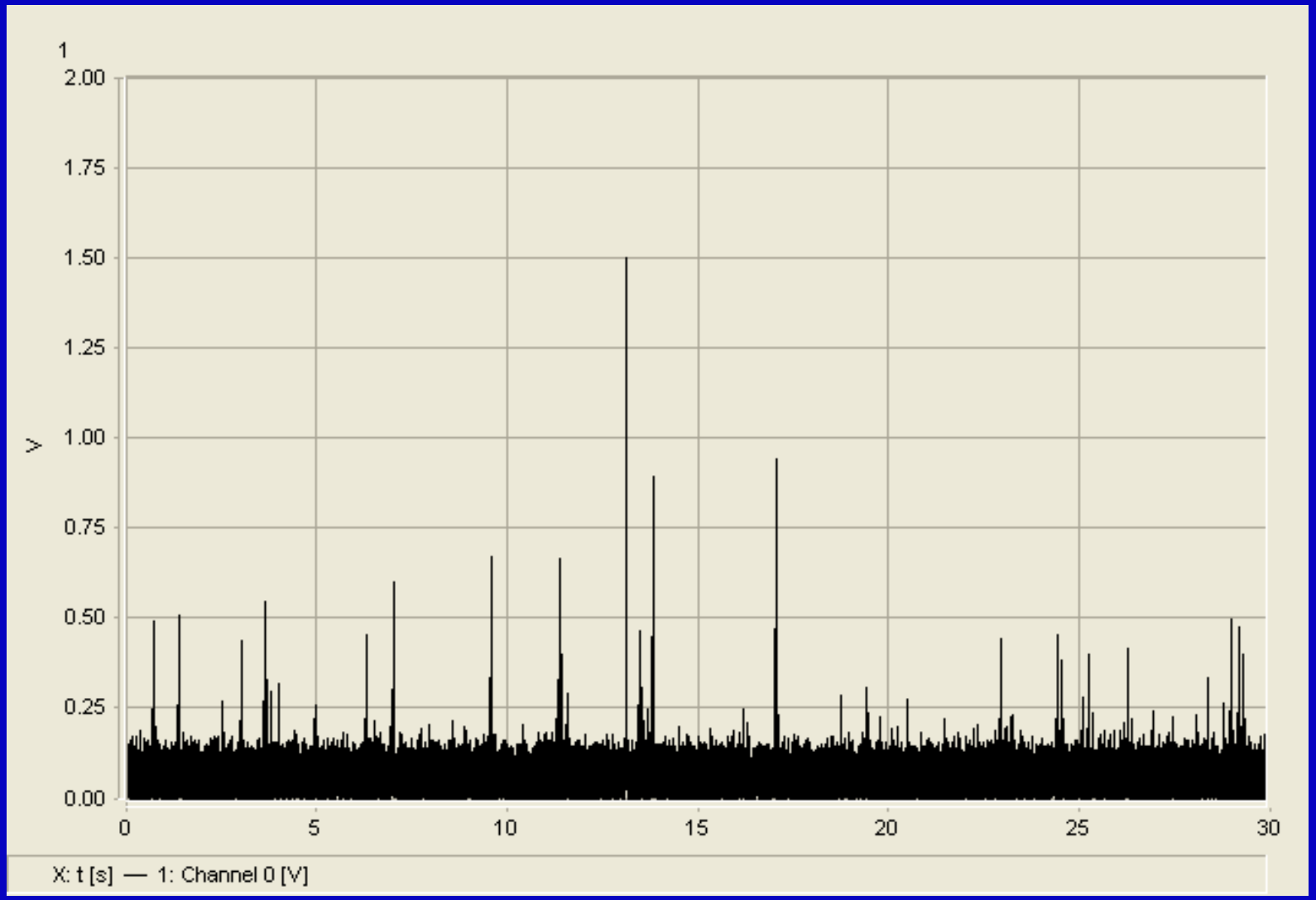
Selection of Blood Vessels



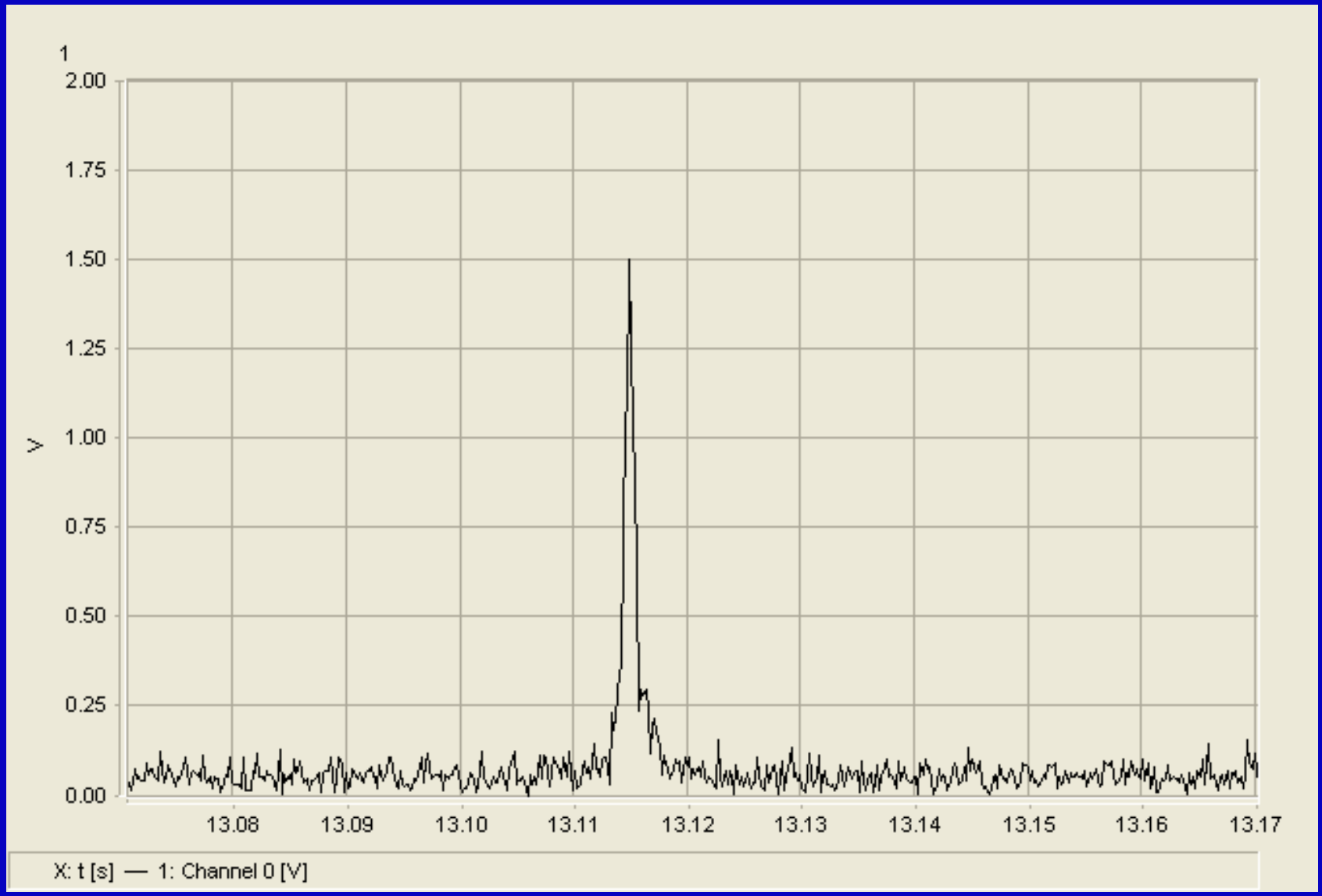




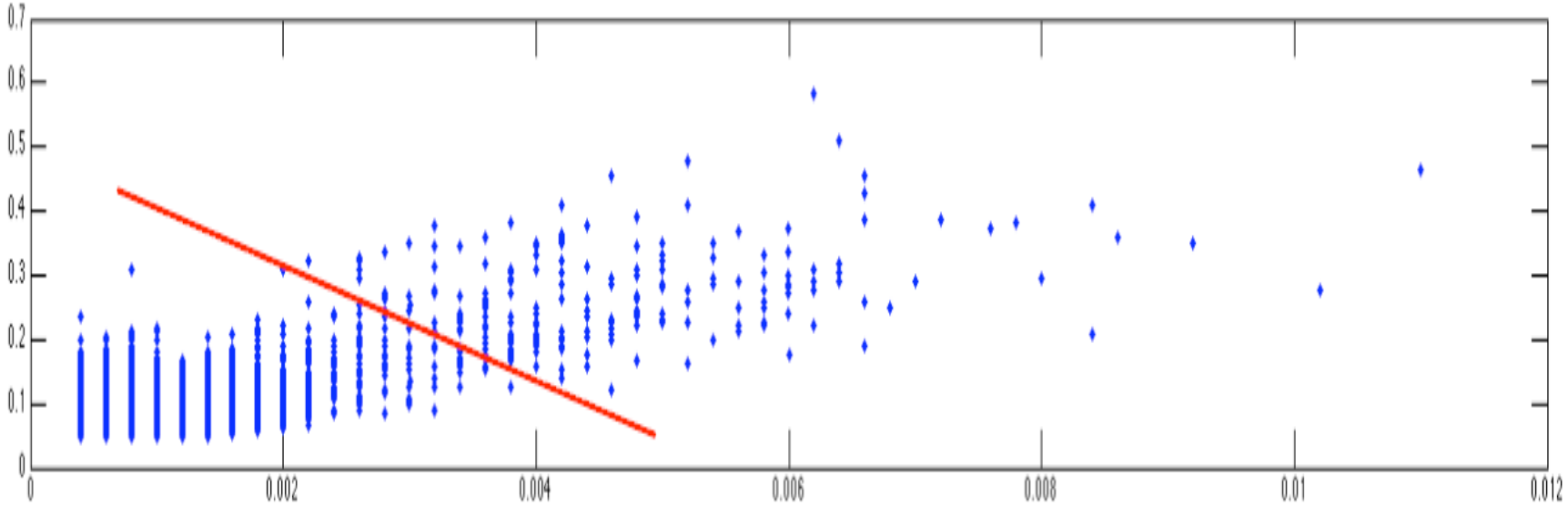
MHCC-97L Signals from IVFC in Blood Vessels after Injection



In Vivo Signal of DiD-Labeled MHCC-97L Cell (Balb/c Mouse)



PCA Analysis



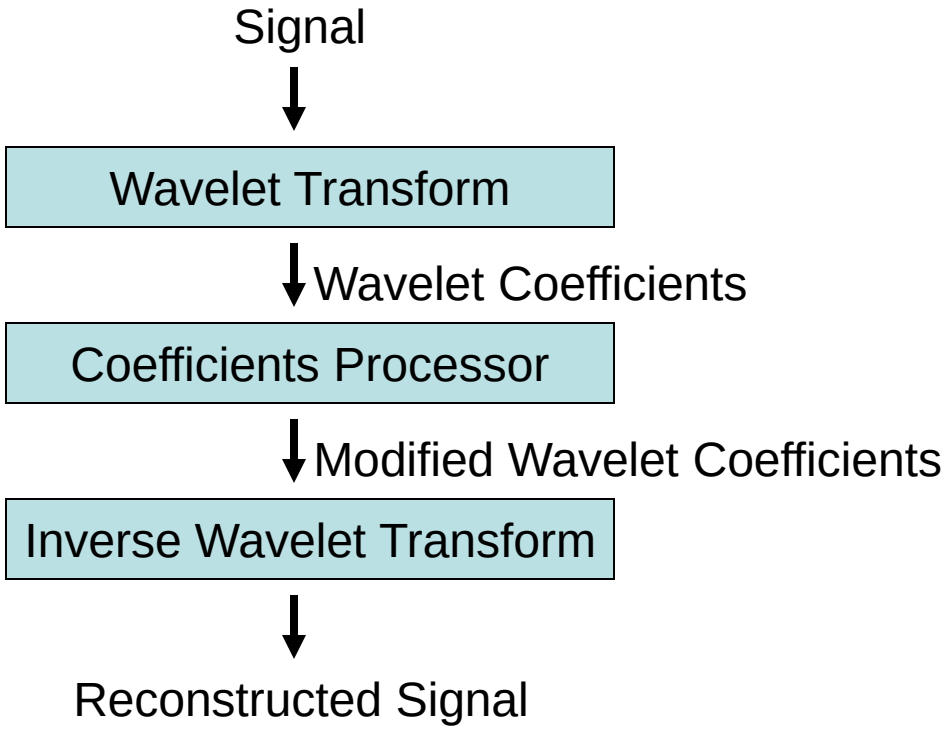
- Perform bi-clustering in width-vs.-height feature space
- Eventually supported by pure-noise control data set
- Problem: Requires user interaction, parameter-tuning, control data dependent...

Wavelet-based Denoising

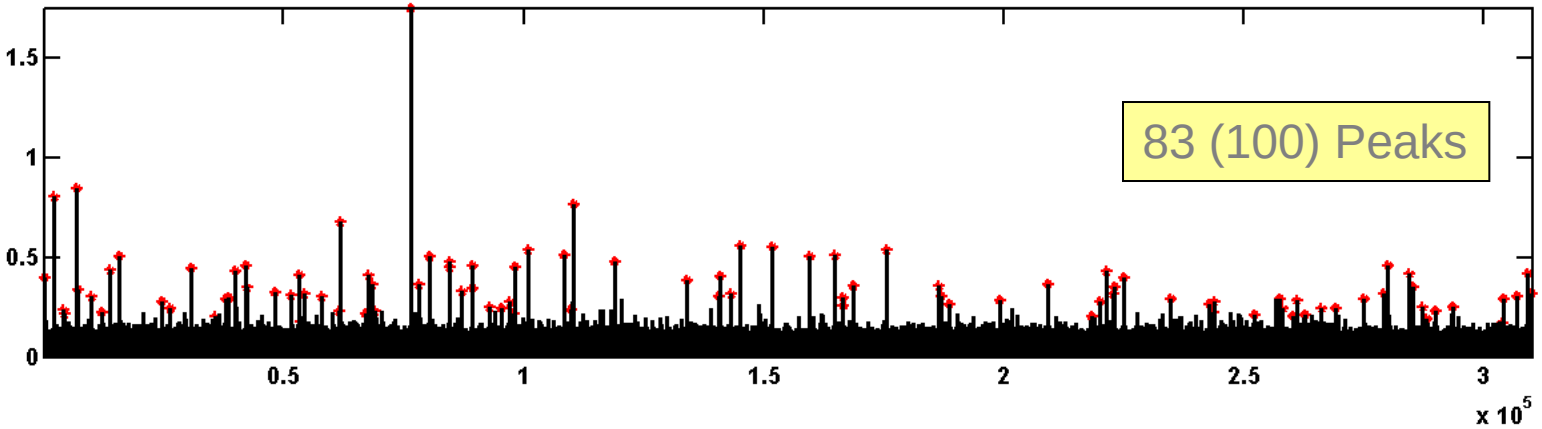
- Wavelets?
  - …are hierarchical (nested) basis functions
    - wavelike oscillating functions that are localized in time
    - finite ("compact") support
  - …are used to decompose signals into coefficients that give frequency and temporal information
  - …can approximate anything well (discontinuity, non-periodicity)
  - …can approximate a function with few coefficients facilitating compression, storage, transmission
  - …are fast to compute ➔ convert n-sample function in $O(n)$ (single level) or $O(n \log n)$ (multilevel) time

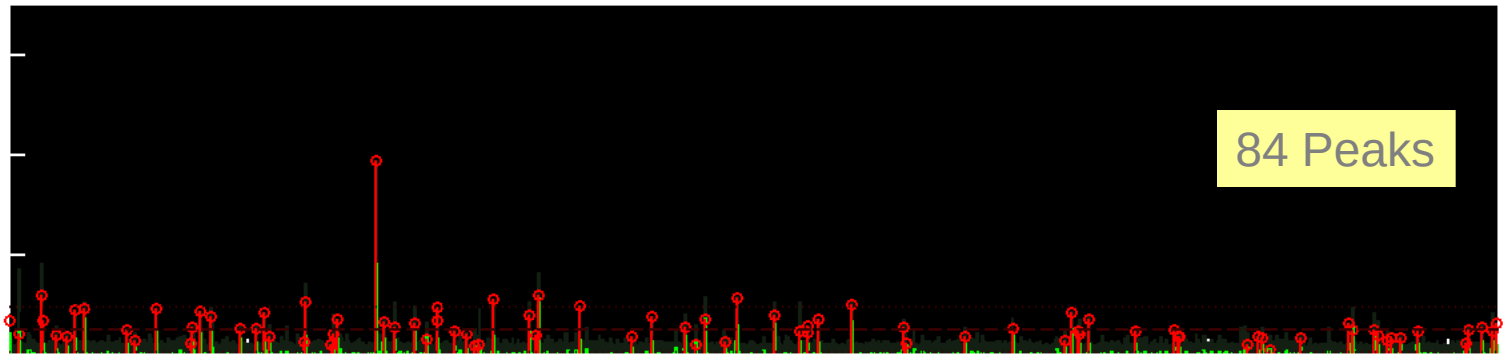
Wavelet-based Denoising

- General wavelet-based processing



Expert-annotated vs. automatically classified peaks





•Li Y, *Wei X, etal. Cytometry Part A*, 79A: 848–854, 2011.

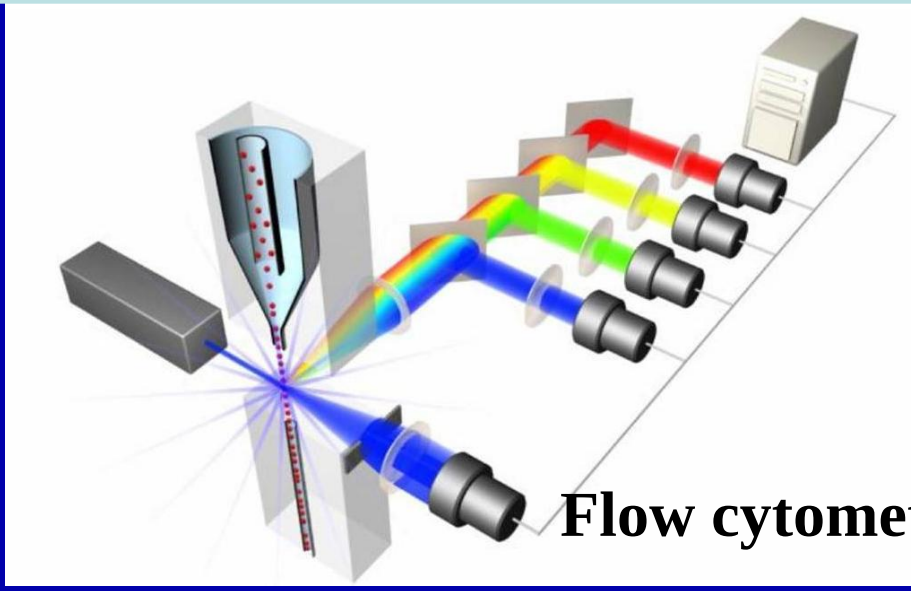
Challenge for CTCs detection

- Current technologies

-- (In vitro)Flow Cytometry（**popular**）

-- Confocal/two-photon microscopy

-- Regular fluorescence microscopy



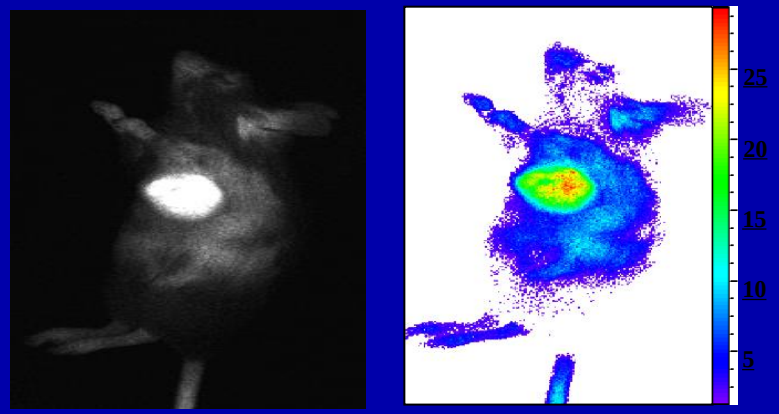
- Limitations

-- No dynamic monitoring

-- Not real time/quantitative

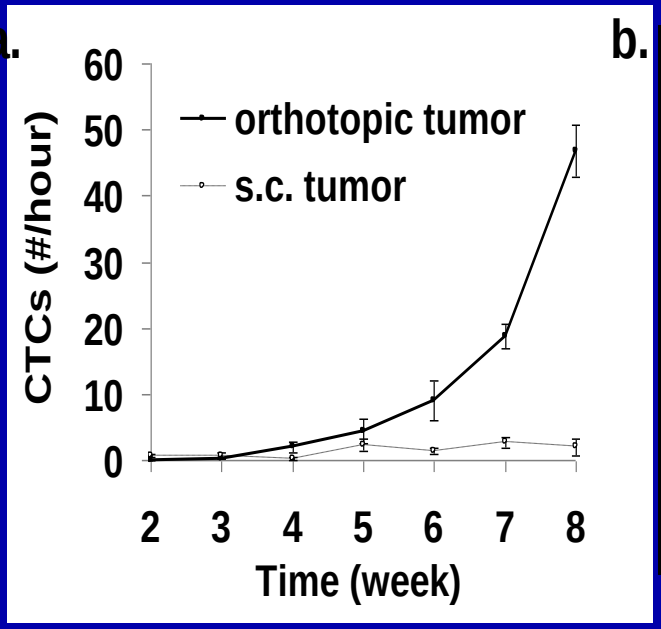
-- Low sensitivity（ **no early detection** ）

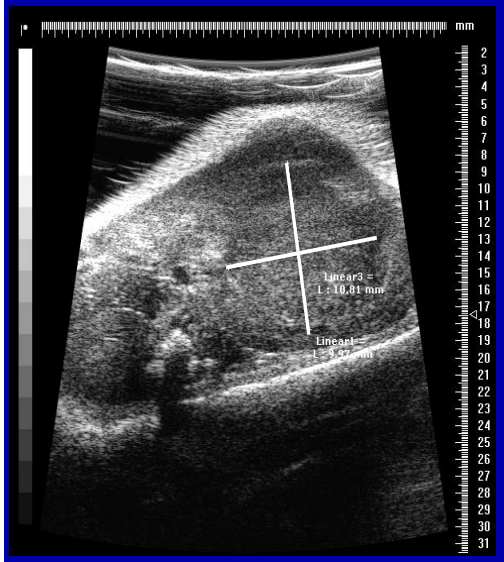
-- depends on blood drawing

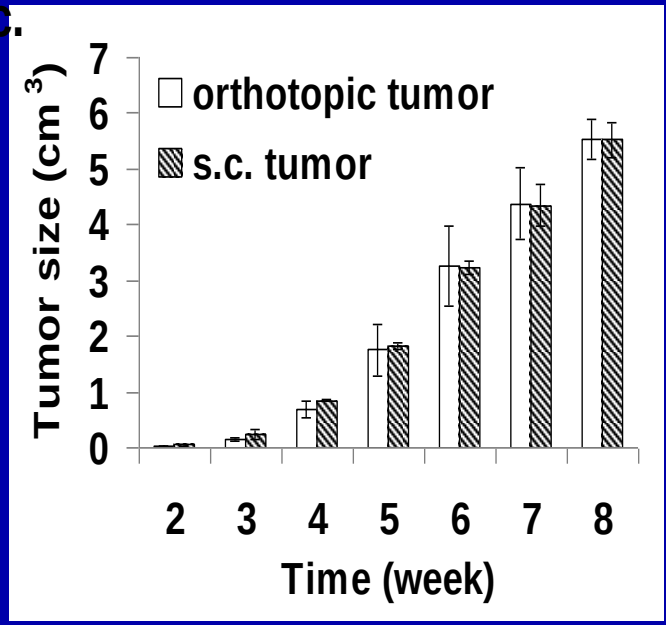


Optical molecular imaging can not analyze blood components

CTCs dynamics in s.c. and orthotopic metastatic liver tumor model



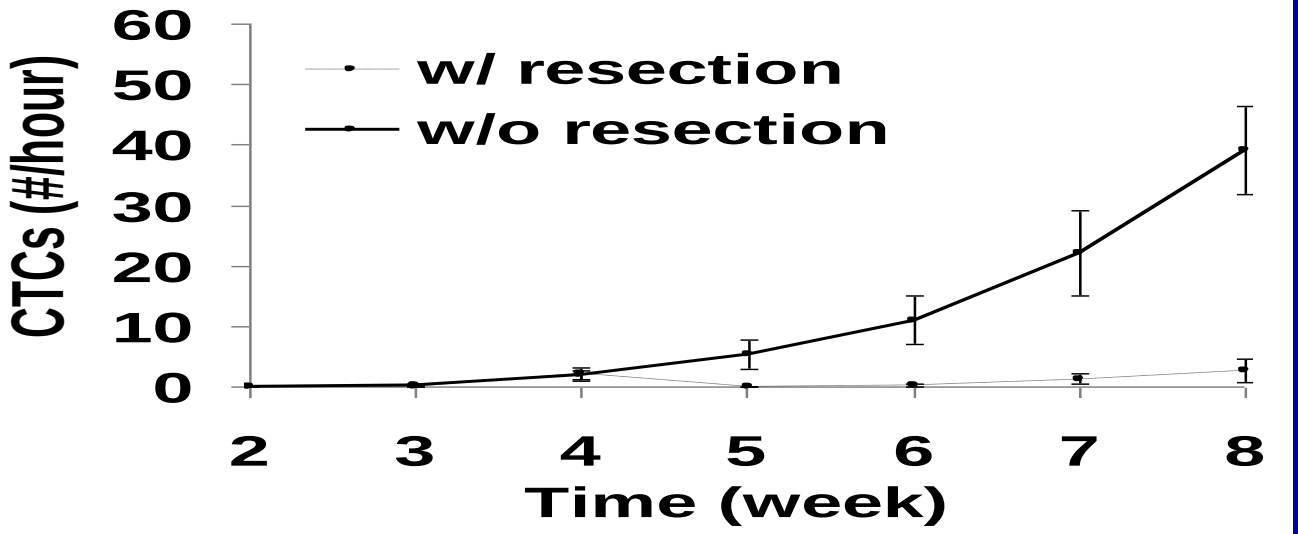




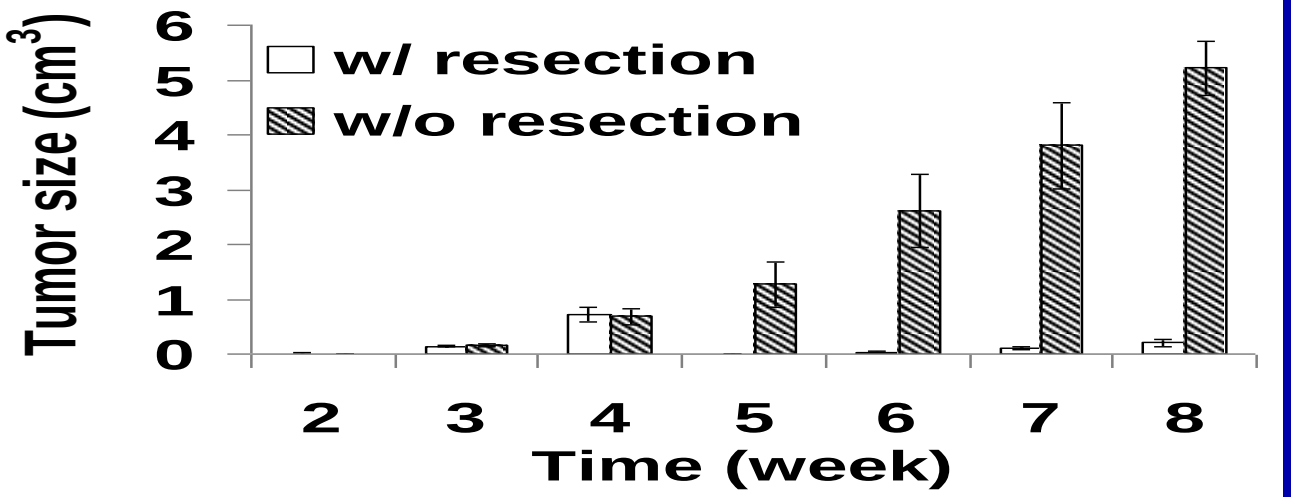
•Fan Z, Wei X, *et al. Cancer Research, 2012.*

Depletion of CTCs by surgical treatment

a.

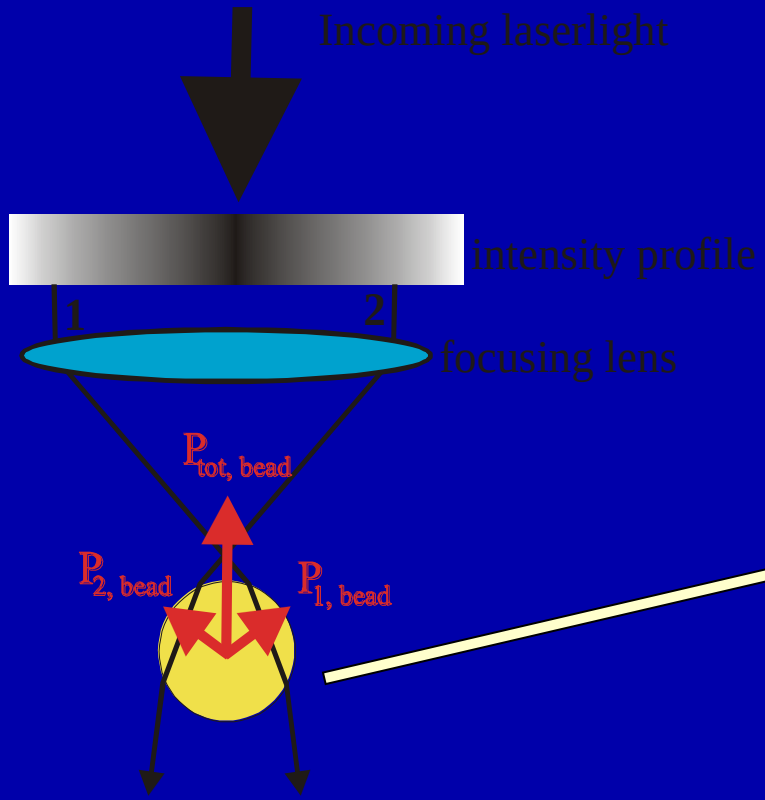


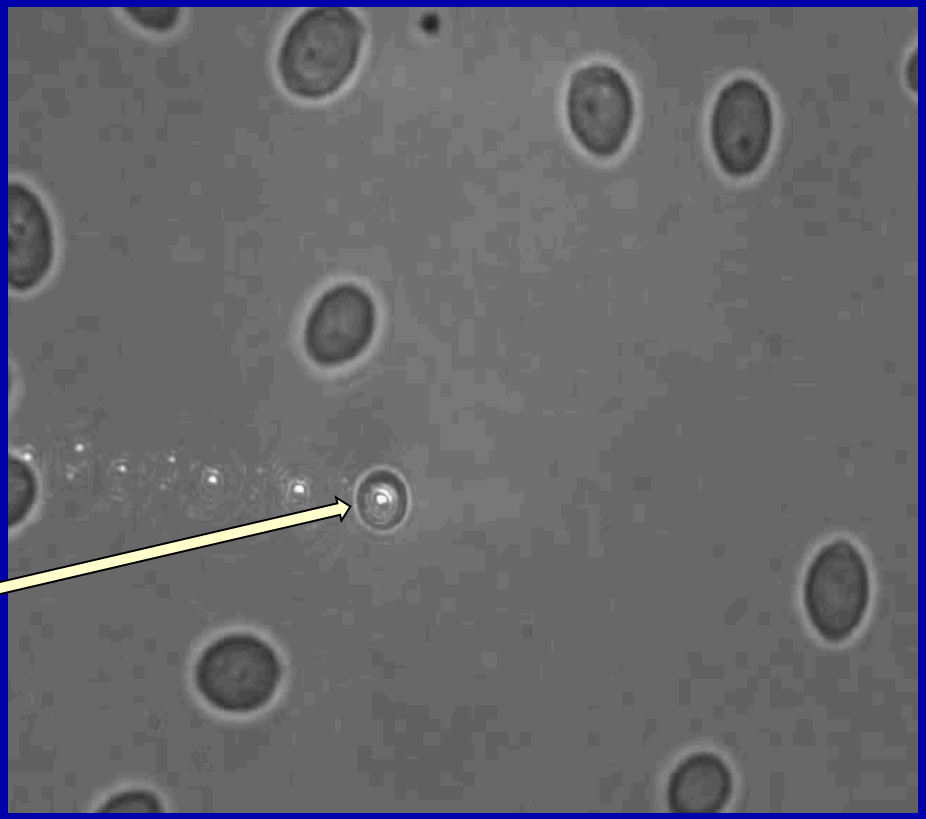
b.



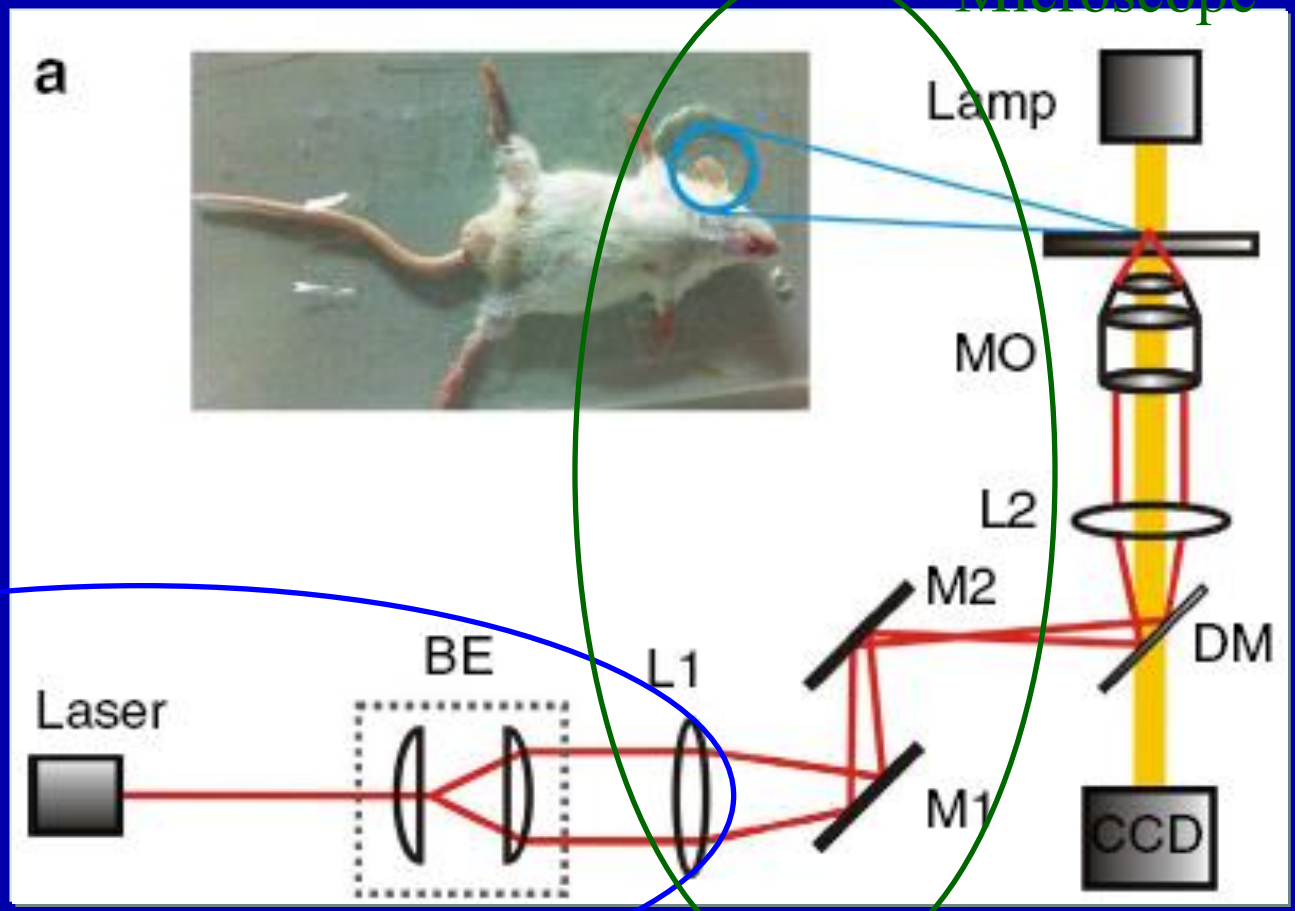
In Vivo Trapping of Cells ?

- Although there are numerous reports on manipulation of microscopic objects at cellular level, techniques of trapping and manipulating the cells within living animals have not been established

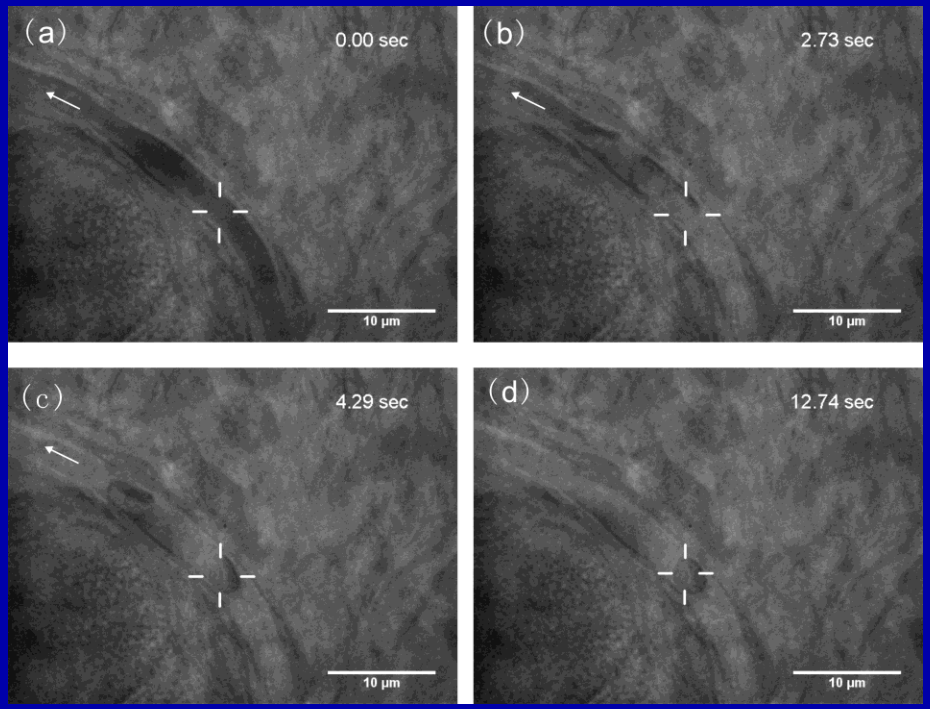

Incoming laserlight
intensity profile
1
2
focusing lens
P tot, bead
P 2, bead
P 1, bead

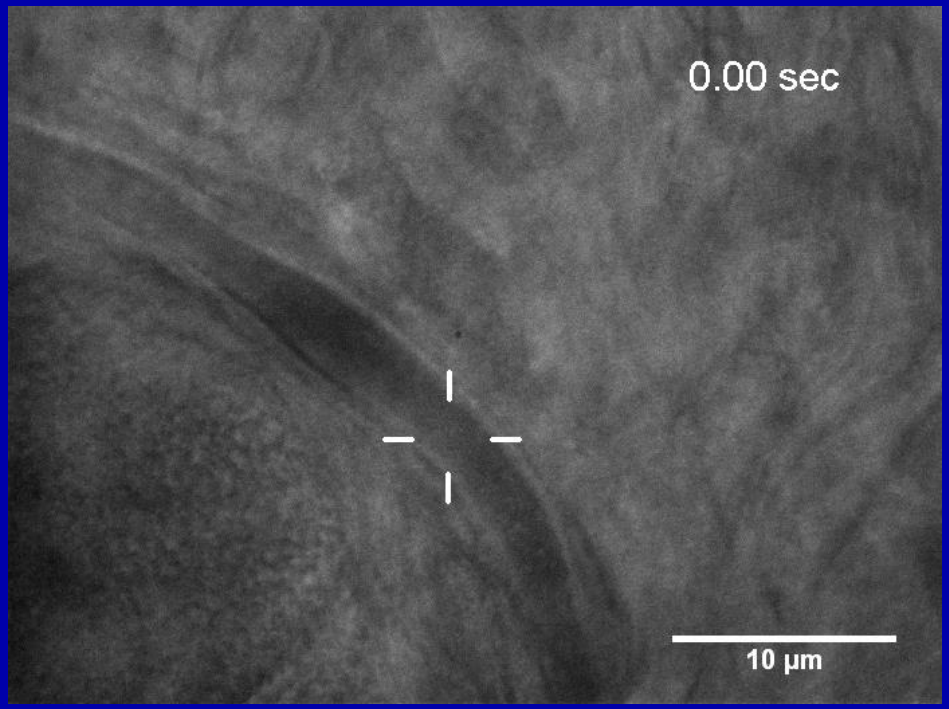


Trapping single RBCs *in vivo*

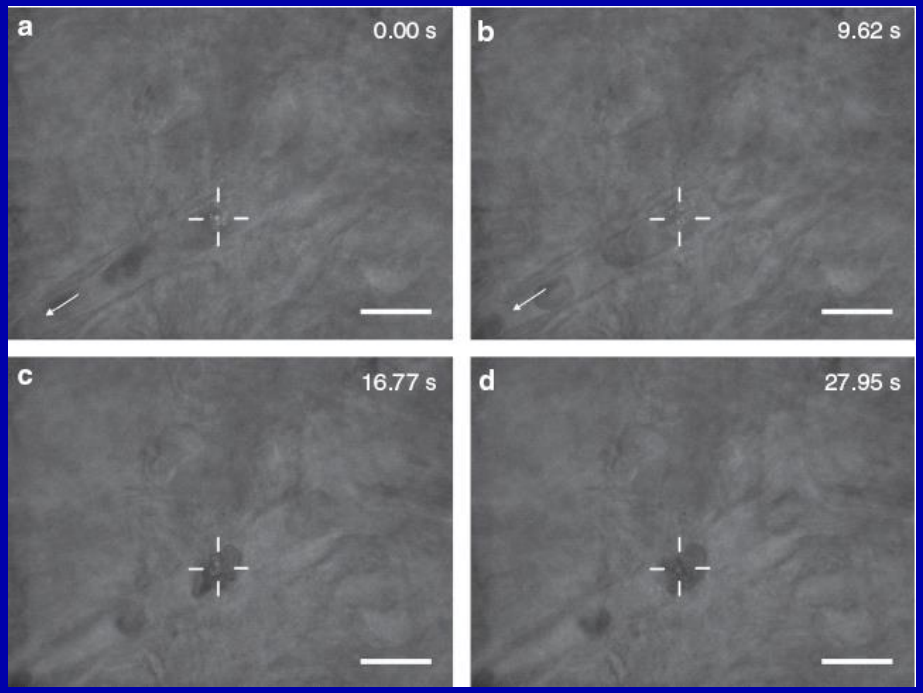


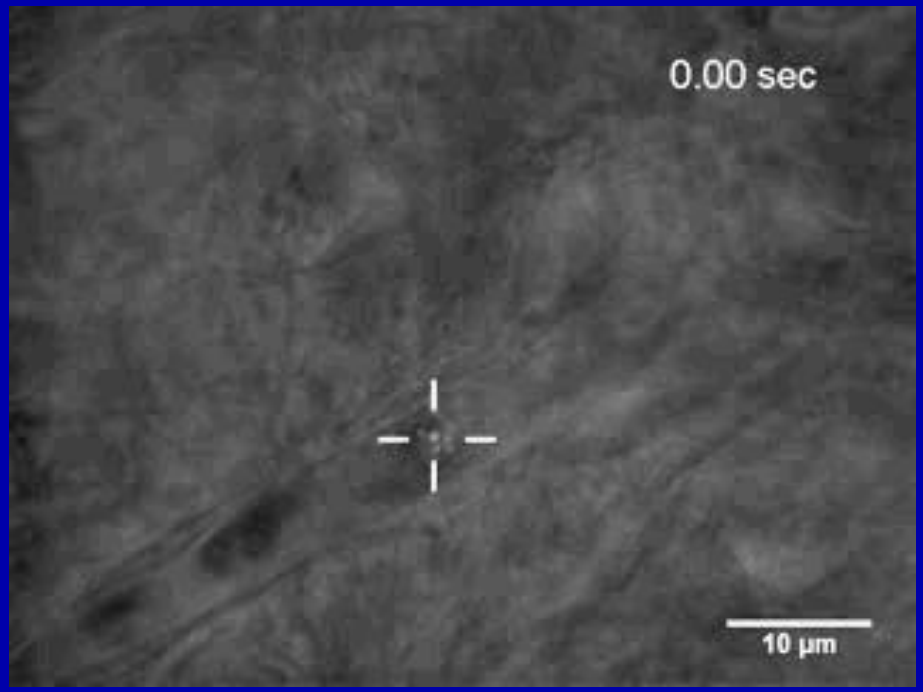
Trapping single RBC in a living mouse





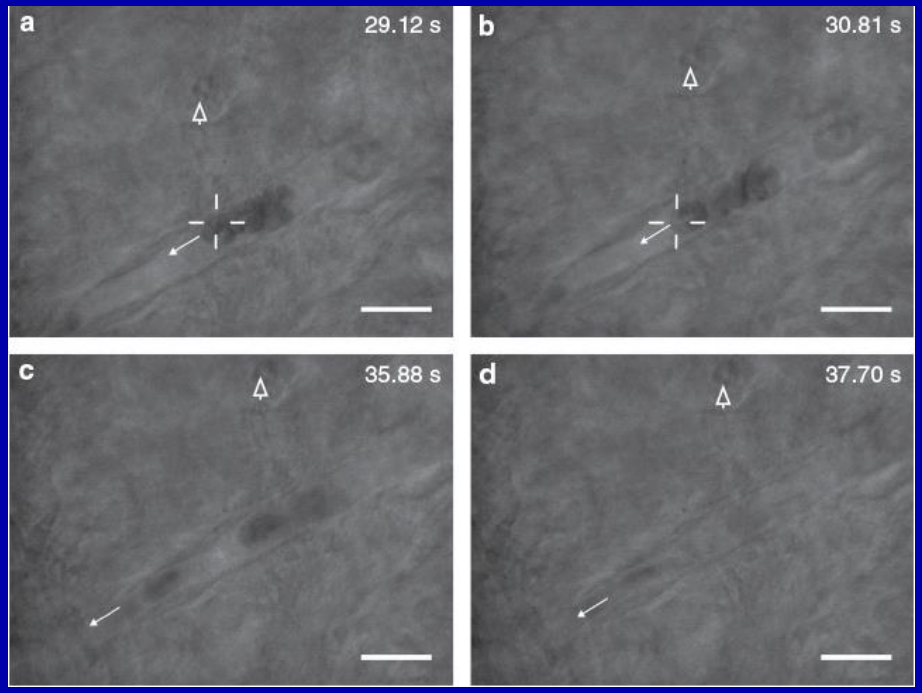
Optical trapping of RBCs leads to capillary blockage





Zhong M, Wei X, *et al., Nature Communications*
(April 23, 2013; Featured in Medical Research: Clearing blocked capillaries with light)

Optical tweezers clear clogged capillary



Zhong M, Wei X, *et al., Nature Communications*
(April 23, 2013; Featured in Medical Research: Clearing blocked capillaries with light)

ACKNOWLEWDGEMENTS

Charles P. Lin, Harvard Medical School

Axel Mosig, Shanghai Institutes for Biological Sciences

Jan Zhou, Fudan Medical School and Zhongshan Hospital

973 (2011CB910400)

China National Key Projects for Infectious Disease (2008ZX10002-021)