In vivo Counting and Optical Trapping Circulating Cells

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Primary Tumor

Distant Metastasis

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

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

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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 \(\Rightarrow\) convert \(n\)-sample function in \(O(n)\) (single level) or \(O(n \log n)\) (multilevel) time
Wavelet-based Denoising

- General wavelet-based processing

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Signal
↓
Wavelet Transform
↓
Wavelet Coefficients

Coefficients Processor
↓
Modified Wavelet Coefficients

Inverse Wavelet Transform
↓
Reconstructed Signal
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Expert-annotated vs. automatically classified peaks

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 cannot analyze blood components.
CTCs dynamics in s.c. and orthotopic metastatic liver tumor model

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

focusing lens

$P_{\text{tot, bead}}$

$P_{2, \text{bead}}$

$P_{1, \text{bead}}$
Trapping single RBCs \textit{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)
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