Self-imaging petri-dish and other chip-scale microscopy solutions

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Acknowledgment

Group Members:
- Guoan Zhang (microscope)
- Jian Ren (OCT)
- Sean Pang (microscope)
- Yin Min Wang (turbidity suppression)
- Seung Ah Lee (microscope)
- Chao Han (microscope)
- Mooseok Jang (turbidity suppression)
- Zheng Li (microscope)
- Benjamin Judkewitz (turbidity suppression)
- Roake Horstmeyer (turbidity suppression)
- Anne Sullivan (Lab Manager)

Funding Sources:
- DARPA, NIH, NSF, DOD,
- Industrial Collaborators

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Overhauling traditional microscopy (along the cost and efficiency axes)

Fundamental design has not changed since Galileo’s time. Its contemporaries include pendulum clock (obsolete), adding machine (obsolete), slide rule (obsolete).

Bottomline: Capitalize on mature electronic sensor techs to change microscopy.

Want:
- Cheap
- Compact
- Full field-of-view
Chip-scale microscopy

Optofluidic microscope
X Cui, C Yang et al, PNAS Vol 105, 10670 (2008)

Digital holography microscope

Self-imaging petri dish
G Zheng, S Lee, Y Antebi, M Elowitz, and C Yang; PNAS (2011)

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Recent Progress in Optofluidic Microscopy

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Optofluidic Microscopy

Optofluidic microscope

Conventional microscope

Floaters in our eyes

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CMOS sensor chip can be used to acquire direct shadow images

**Points to consider:**
1. No lenses needed = no aberrations, chromaticity
2. Requires close object proximity to chip
3. Resolution limit = 2X sensor pixel size
Another look at the problem

A stack of low-res images can be refined into a high-res image if object shifts incrementally between frames by less than pixel size.

http://www.youtube.com/watch?v=mo58SkJZFbY

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Rapid snaps or sub-pixel resolving OFM

Sub-pixel resolving OFM in action

Guoan Zheng, Seung Ah Lee, Samuel Yang and Changhuei Yang; Sub-pixel resolving optofluidic microscope for on-chip cell imaging, Lab Chip (2010)
Malaria RBC analysis

**Approaches**

Aperture  
FZPs  
Rapid snaps


L Lee, X Cui and C Yang, Biomedical Microdevices, 10.1007/s10544-009-9312-x (2009)

Aperture-based OFM

Concept:

OFM imaging geometry


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Aperture-based OFM for cell imaging

OFM

standard microscope

chlamydomonas  mulberry pollen  giardia (mature)  giardia (cyst)  microsphere

L Lee, X Cui and C Yang, Biomedical Microdevices, 10.1007/s10544-009-9312-x (2009)
Fresnel Zone Plate OFM (fluorescence)

(a) FZP array
(b) microfluidic channel
(c) filter layer
(d) CMOS sensor

Flow direction

Sean Pang, Chao Han, and Changhuei Yang; accepted (2011)

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Nuclear stained by Acridine Orange: (a-c) the fluorescence image of Acridine Orange stained HeLa cells; (e-g) the fluorescence image Qtracker labeled HeLa cells; (d,h) the fluorescence image superimposed by a bright field image acquired by conventional 20X 0.4 N.A. microscope.

Sean Pang, Chao Han, and Changhuei Yang; accepted (2011)
What is an optofluidic microscope useful for?

1. Bioscience Research
   - increase throughput by parallelizing
   - cost-effective
   **Applications:** drug screening, large ensemble experiments

2. Implantable Blood Analyzer
   - analyze blood without blood draw
   - continuous
   **Applications:** pre-symptom infection diagnosis, circulating tumor cell tracking

3. Light, Cheap and Rugged Cell Phone Microscope
   - automatic sample analysis
   - uploadable by cell phone network
   **Applications:** malaria diagnosis, water quality assessment, blood fraction analyzer
Self-imaging Petri Dish
(ePetri)
Chip-scale microscopy

Optofluidic microscope
X Cui, C Yang et al, PNAS Vol 105, 10670 (2008)

Digital holography microscope

Self-imaging petri dish

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Petri dish overview (medical)


Points to consider:
1. Needs transportation to consolidated lab.
2. Numerous back-and-forth between incubator and microscope
   - contamination risks
   - labor intensive

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**Petri dish overview (bioscience)**

**Incubator - Microscope Combination**

Points to consider:
1. $$$
2. Limited field-of-view

http://corefacilities.systemsbiology.net/imaging/microscopes/leicadmi.php
How to build a microscope out of Legos, a smartphone and a $10 sensor chip.

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011

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ePetri in action

Smartphone display

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011

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Confluent cell culture imaging

HeLa cells imaged over 6mm x5 mm area with 0.66 microns resolution.

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011)
Longitudinal study from within an incubator

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011

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Longitudinal study from within an incubator

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011

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Embryonic stem cell tracking

Guoan Zheng, Seung Ah Lee, Yaron Antebi, Michael B. Elowitz, and Changhuei Yang, PNAS October 3, 2011

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Some considerations:

- Automate and simplify petri-dish experiments by updating the technology.

- Provide imaging ability over entire sensor surface.

- Flexible platform for building lab-on-a-chip systems on top.
**Conclusion**

**Chip-scale microscopy**

- Thanks to the cellphone camera market, this is the right time.
- Disposable or recyclable.
  - biohazard considerations.
- Automatic electronic data.
  - Netflix for pathologists and biologists.
- Lower human labor cost.
- Global health considerations.