Mobile Imaging, Sensing and Diagnostics

Aydogan Ozcan, Ph.D.
Electrical Engineering Department & Bioengineering Department &
California NanoSystems Institute

University of California, Los Angeles (UCLA)

ozcan@ucla.edu

http://www.innovate.ee.ucla.edu/
Digital Diagnosis

Aydogan Ozcan, Ph.D.
UCLA

ozcan@ucla.edu
http://www.innovate.ee.ucla.edu/

2016
A different view of the Moore’s Law

Mega-pixel Count on Mobile Phone Cameras vs. Transistor Count in CPUs
Cell phones are now everywhere: A great potential for Telemedicine needs

World Bank
- >7 billion cell phones are being used worldwide.
- ~15 billion cell phones have been sold so far.
- >75% are in developing countries. (International Telecommunication Union)
Providing a new platform for telemedicine
Providing a new platform for telemedicine
Providing a new platform for telemedicine

E. coli sensor

Allergen detector

Heavy metal detector

Chlorophyll Measurement

Diagnostic test reader (HIV, malaria, etc.)

Blood Analyzer
The μ-Internet

Big Data

New opportunities in micro-analysis, medical diagnostics and epidemiology
Providing a new platform for telemedicine

**LUCAS:** Lensfree (On-Chip Imaging)
Compact, Cost-effective
High-throughput
Highly sensitive (Incoherent Holography)
Tolerant to Misalignments

**LUCAS:** Lensless, Ultra wide-field Cell monitoring Array platform based on Shadow imaging
Imaging of shadows

Cell Shadows imaged using lensfree on-chip imaging

$H < 1-2 \text{ µm} \rightarrow$ contact on-chip imaging

$H \sim 10 - 1,000 \text{ µm} \rightarrow$ holographic on-chip imaging
Cell Density: 102K [Cells/μL]
Lensfree imaging of histopathology slides

Breast Cancer Tissue
LUCAS (NA=0.65)

10 µm

2.5 radians

Plasmodium falciparum

5 Megapixel CMOS imager
Lensfree imaging of histopathology slides
Abnormal Pap Smear

Lensfree reconstructed amplitude

Microscope 40X 0.75NA
A different view of the Moore's Law

Mega-pixel Count on Mobile Phone Cameras vs. Transistor Count in CPUs
Imaging and Sizing of Single DNA Molecules on a Mobile-Phone

ACS Nano, 2014
Quantification of Giardia lamblia cysts using mobile-phone based fluorescent microscopy and machine learning

Lab Chip, 2015
Cellphone-Based Hand-Held Micro-Plate Reader for Point-of-Care ELISA Testing

ACS Nano
2015
Colorimetric Plate Reader for ELISA

ELISA Image Selection:
Select Image: 111014d_highres.png
Moderate Image: 111014m_highres.png
Bright Image: 111014b_highres.png

ELISA Input Parameters:
Measles
Calibration: 0.28
Columns: 6 ~ 9

ELISA qualitative
Measles: cols 6-9, 16N, 0E, 16N
Mumps: cols 10-12, 9P, 0E, 15N
Process Time: 2014/11/26 7:52pm

ELISA quantitative
Measles: cols 6-9, 16N, 0E, 16N
Mumps: cols 10-12, 9P, 0E, 15N
Process Time: 2014/11/26 7:52pm
Mumps Measles HSV 1 HSV 2

**Analysis Type**
- Curve Fitting
- M.L

**Specificity**
- Mumps: 92.70% ± 0.49%
- Measles: 97.37% ± 2.63%
- HSV 1: 92.09% ± 0.77%
- HSV 2: 94.56% ± 3.43%

**Sensitivity**
- Mumps: 100.00% ± 0.00%
- Measles: 98.39% ± 0.42%
- HSV 1: 99.47% ± 0.59%
- HSV 2: 97.32% ± 0.32%

**Agreement**
- Mumps: 97.21% ± 0.41%
- Measles: 99.61% ± 0.39%
- HSV 1: 96.08% ± 0.32%
- HSV 2: 98.56% ± 0.53%

ACS Nano 2015
Providing a new platform for telemedicine

- **E. coli sensor**
- **Allergen detector**
- **Heavy metal detector**
- **Diagnostic test reader (HIV, malaria, etc.)**
- **Blood Analyzer**
- **Google Glass based Diagnostics**
The μ-Internet

Big Data
- An opportunity or a challenge?
Imaging technologies experience an exponential growth, but human experts and diagnosticians do NOT!
Diagnosis of Malaria using Crowd-Sourced Games

http://biogames.ee.ucla.edu/
Diagnosis of Malaria using Crowd-Sourced Games

More than 80 countries are playing BioGames, with >3 Million cell diagnoses so far.
Each gamer is a “Repeater”

Decoder: Maximum a Posteriori Probability (MAP)
Decoding of Diagnosis

\[ p(x_i = x^* | \mathcal{Y}_i) = \frac{p(\mathcal{Y}_i|x_i = x^*) \cdot p(x_i = x^*)}{p(\mathcal{Y}_i)} \]

\[ = \prod_{j=0}^{M} p(y_i^j|x_i = x^*) \cdot \frac{p(x_i = x^*)}{\sum_{l=0}^{1} \left[ p(x_i = l) \prod_{k=0}^{M} p(y_i^k|x_i = l) \right]} \]

\[ \log p(x_i = x^* | \mathcal{Y}_i) = \sum_{j=0}^{M} \log p(y_i^j|x_i = x^*) + \log p(x_i = x^*) \]

\[ - \log \left[ \sum_{l=0}^{1} p(x_i = l) \prod_{k=0}^{M} p(y_i^k|x_i = l) \right] \]

\[ z_i = \arg \max_{l \in \{0, 1\}} \left[ \varphi_l + \sum_{j=0}^{M} \log p(y_i^j|x_i = l) \right], \quad \varphi \equiv \log p(x_i = l) \]
### Non-expert human crowd can collectively diagnose malaria infected cells

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Description of Test Images</th>
<th>Gamers</th>
<th>Positive RBCs</th>
<th>Negative RBCs</th>
<th>Control Images</th>
<th>Accuracy</th>
<th>SE</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>5055 test RBC images crowd-sourced to human gamers</td>
<td>19</td>
<td>471</td>
<td>4584</td>
<td>1266</td>
<td>99.01%</td>
<td>95.12%</td>
<td>99.41%</td>
<td>94.32%</td>
<td>99.50%</td>
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<tr>
<td>2</td>
<td>5055 test RBC images presented to a boosted set of classifiers, trained on 1266 RBC images</td>
<td>NA</td>
<td>471</td>
<td>4584</td>
<td>1266 (Training Images)</td>
<td>96.26%</td>
<td>69.64%</td>
<td>99.00%</td>
<td>87.70%</td>
<td>96.95%</td>
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<tr>
<td>3</td>
<td>459 low-confidence test images taken from the results of experiment 2</td>
<td>27</td>
<td>274</td>
<td>185</td>
<td>1266</td>
<td>95.42%</td>
<td>97.81%</td>
<td>91.89%</td>
<td>94.70%</td>
<td>96.59%</td>
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<td>4</td>
<td>Hybrid diagnosis results using experiments 2 &amp; 3</td>
<td>27</td>
<td>471</td>
<td>4584</td>
<td>1266</td>
<td>98.50%</td>
<td>89.38%</td>
<td>99.43%</td>
<td>94.18%</td>
<td>98.91%</td>
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<td>7045 test RBC images crowd-sourced to human gamers</td>
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<td>1549</td>
<td>5496</td>
<td>2349</td>
<td>98.78%</td>
<td>97.81%</td>
<td>99.05%</td>
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<td>99.38%</td>
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</table>
Non-expert human crowd can collectively diagnose malaria infected cells

<table>
<thead>
<tr>
<th>Term</th>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Accuracy</td>
<td>ACC</td>
<td>$\frac{TP + TN}{TP + TN + FP + FN}$</td>
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<tr>
<td>Sensitivity or True Positive Rate</td>
<td>SE or TPR</td>
<td>$\frac{TP}{TP + FN}$</td>
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</table>
Experts disagree with each other
Experts are ‘not’ self-consistent
Digital ‘Super’ Pathologist & Training of experts

Average Accuracy of Experts

- Digital ‘Super’ Pathologist
- Training of Experts
Big Data Management: Crowd + Machine

Crowd: Professionals + Non-experts (Smart and Cost-effective Telemedicine)
Distributed Medical Image Analysis and Diagnosis through Crowd-Sourced Games
Training on Malaria Diagnosis

Score: 30
False positives: 5
False negatives: 67
False questionables: 1

Username:

Leaderboard
Submit Score

False Positives
False Negatives
False Questionables

Next

http://biogames.ee.ucla.edu/
BioGames @ Korea reached >1600 middle school students
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Online educational content maintains student interest and trains students about global health topics.

8 sessions: Video Lecture & Quiz followed by BioGames malaria training session

91% satisfied with the program
98% want to participate in future programs
BioGames @ Korea reached >1600 middle school students

<table>
<thead>
<tr>
<th>Rank</th>
<th>Username</th>
<th>Score</th>
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http://biogames.ee.ee.ucla.edu/
Distributed Medical Image Analysis and Diagnosis through Crowd-Sourced Games

http://biogames.ee.ucla.edu/
You can move from cell level diagnosis to slide level diagnosis

Figure 9. ROC curves for smear-level diagnosis. A) parasitemia $\xi = 0.5\%$. B) parasitem $\xi = 1\%$.
doi:10.1371/journal.pone.0046192.g009

Optimize diagnosis time based on the statistics of the individual diagnostician