Online training and educational games for malaria diagnosis

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Compact, cost-effective and powerful microscopes can transform the way optical diagnosis is performed at the point-of-care and in future lab-on-a-chip applications.
Increasingly powerful mobile, computational, sensing devices enabled advanced micro and nano-scale sensing and diagnostic platforms.
Malaria diagnosis is a time-consuming and challenging task

Gold standard: Conventional light microscopy tested 197 million patients for malaria in 2013.

Experts diagnose ~1,000 red blood cells per sample, with ~60% false-positive rate in some developing countries.
BioGames for Crowd-sourced Tele-Pathology, Creation of Image Libraries and Improving Diagnostician Training

http://biogames.ee.ucla.edu/
BioGames for Crowd-sourced Biomedical Image Analysis and Tele-Pathology

More than 80 countries have played BioGames, with >2.6 Million cell diagnoses so far.
Each gamer is a noisy “Repeater”

Decoder: Maximum a Posteriori Probability (MAP)
Minimally trained human gamers can surpass the accuracy of computer-based image analysis

5 Initial Experiments conducted at UCLA using two methodologies

- Human gamers
- Computer-based image analysis

<table>
<thead>
<tr>
<th>Experiment</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Humans</td>
<td>Computer</td>
<td>Humans on Computer Low Confidence Cells</td>
<td>Retrained Computer</td>
<td>Overall Human</td>
</tr>
<tr>
<td># cells</td>
<td>5055</td>
<td>5055</td>
<td>459</td>
<td>5055</td>
<td>7045</td>
</tr>
<tr>
<td>Accuracy</td>
<td>99.0%</td>
<td>96.3%</td>
<td>95.4%</td>
<td>98.5%</td>
<td>98.8%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>95.1%</td>
<td>69.6%</td>
<td>97.8%</td>
<td>89.4%</td>
<td>97.8%</td>
</tr>
</tbody>
</table>

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$
Non-expert human crowd can collectively diagnose malaria infected cells

\[
\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}
\]

\[
\text{Sensitivity} = \frac{TP}{TP + FN}
\]
Crowd:

Professionals + Non-experts

(Smart and Cost-effective Telemedicine)
BioGames for Measurement of Diagnostician Accuracy and Creation of Image Libraries
Diagnosticians disagree with each other
Diagnosticians are ‘not’ self-consistent

- Digital ‘Super’ Pathologist
- Training of Experts
Digital ‘Super’ Pathologist

Agreement among cells generated using EM-based algorithm.
Using an EM-based approach, we combined the diagnoses of these experts to generate an image library of 2888 unique cells diagnosed by 9 experts.
BioGames for Improving Diagnostician Accuracy

~2850 unique cells diagnosed by 9 experts.
Positive/Questionable/Negative diagnoses.

http://biogames.ee.ucla.edu/
Review of images of misdiagnosed cells enables feedback-based education
Could this digital educational tool serve to train new diagnosticians?
Conclusion

• Platforms such as BioGames could provide crowd-sourced biomedical image-analysis services.

• Using our machine learning methodology, this platform increases in accuracy with number of gamers and cell images.

• We aim to increase our RBC image libraries with new microscopic images of thin/thick blood smears and promote the use of this digital educational tool for malaria diagnosis training.
Ozcan Research Group – Members & Funding
Thanks!
Crowd-sourcing can solve traditionally difficult and time-consuming problems

Finding Star Clusters

reCAPTCHA

EteRNA (RNA sequences)
foldit (proteins)

CUGH 2015
Appendix: Decoder Methodology

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

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

\[
z_i = \arg \max_{l \in \{0,1\}} \left[ \varphi_l + \sum_{j=0}^{M} \log p(y_i^j | x_i = l) \right], \quad \varphi \equiv \log p(x_i = l)
\]
### Appendix: UCLA Experiments

<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>
</tr>
</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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<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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<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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<tr>
<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>
</tr>
<tr>
<td>5</td>
<td>7045 test RBC images crowd-sourced to human gamers</td>
<td>20</td>
<td>1549</td>
<td>5496</td>
<td>2349</td>
<td>98.78%</td>
<td>97.81%</td>
<td>99.05%</td>
<td>96.68%</td>
<td>99.38%</td>
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