Microfluidic Point of Care Diagnostic Device for Malaria

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Overview of Presentation

1. Background Material
    a. Types of Malaria Parasites
    b. Medical Implications
2. Existing Detection Methods
    a. Smear/Stain
    b. POC Devices
3. Product Design Specifications
4. Preliminary Designs
    a. Separation Methods
    b. Detection Methods
    c. Design Matrix
5. Future Work

Client and Advisor

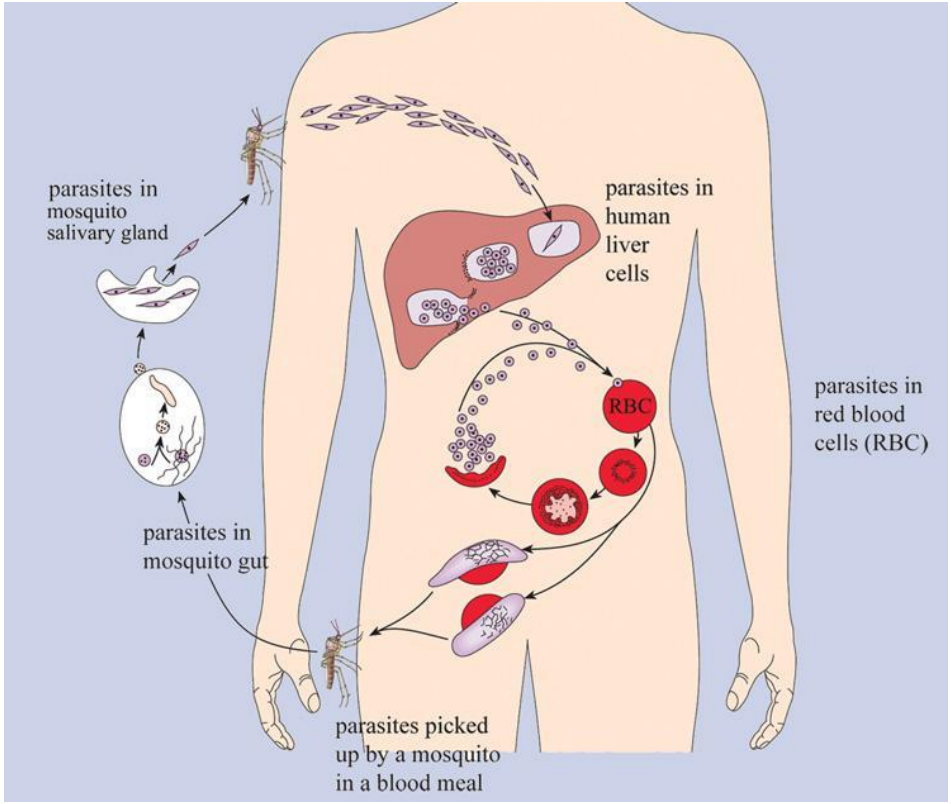
Client: Dr. Timothy Kwa, Jimma University. Jimma, Ethiopia

Advisor: Dr. John Puccinelli, University of Wisconsin - Madison, BME Department

Problem Statement

Create a microfluidic point of care (POC) testing device for diagnosing malaria in rural Ethiopia in a sensitive, cheap, and time efficient manner

Malaria Prevalence and Pathobiology



http://magazine.scientificmalaysian.com/wp-content/uploads/2016/06/life-cycle-of-malaria-plasmodium.jpg

Transmitted by Anopheles mosquitoes

Within 5 days of infection ring stage Plasmodium can be detected

214 million cases worldwide in 2015

Economic burden of $12 billion on Africa every year

A 90% effective test would save 2.2 million lives per year

iRBCs special characteristics: cell deformation, magnetism, electricity [1]

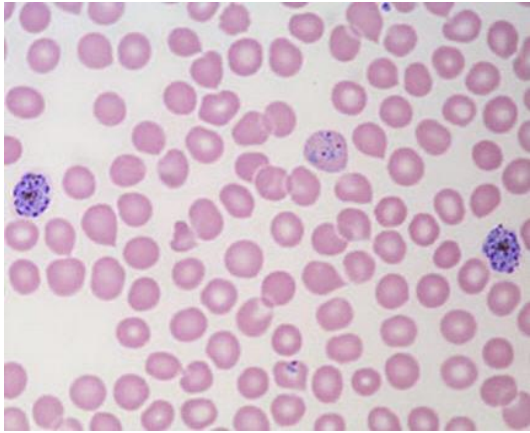
Current Diagnostic Methods

The gold standard in diagnosis is a blood smear test

- Blood stained with Romanowsky Stain highlights parasites
- No distinction between P. falciparum, P. vivax, or others
- Needs equipment and trained technicians

Rapid diagnostic tests

- $1 per test
- In a study it was found only 50% of RDT's are more than 80% accurate [2]



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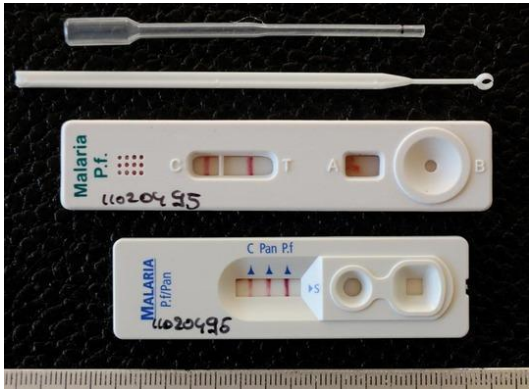
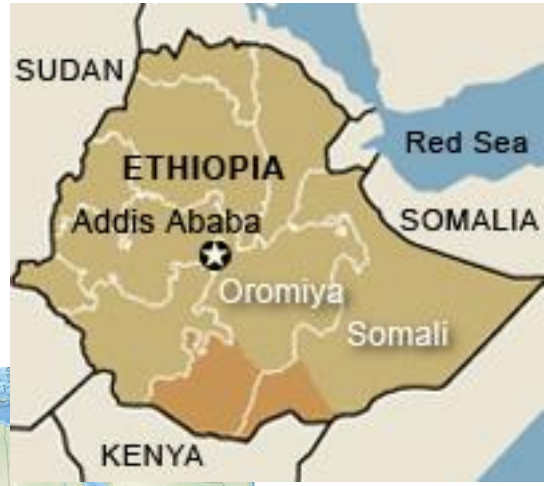


http://www.malwest.gr/Portals/0/RDT.jpg

Capabilities/Restrictions in Ethiopia

- Limited equipment/resources
- Unreliable power and internet
- Untrained laboratory personnel
- Rural locations
- Little to no laboratory infrastructure



Product Design Specifications

Accuracy > 95%

Results in < 1 hr

Battery powered (electricity unreliable)

Small in size

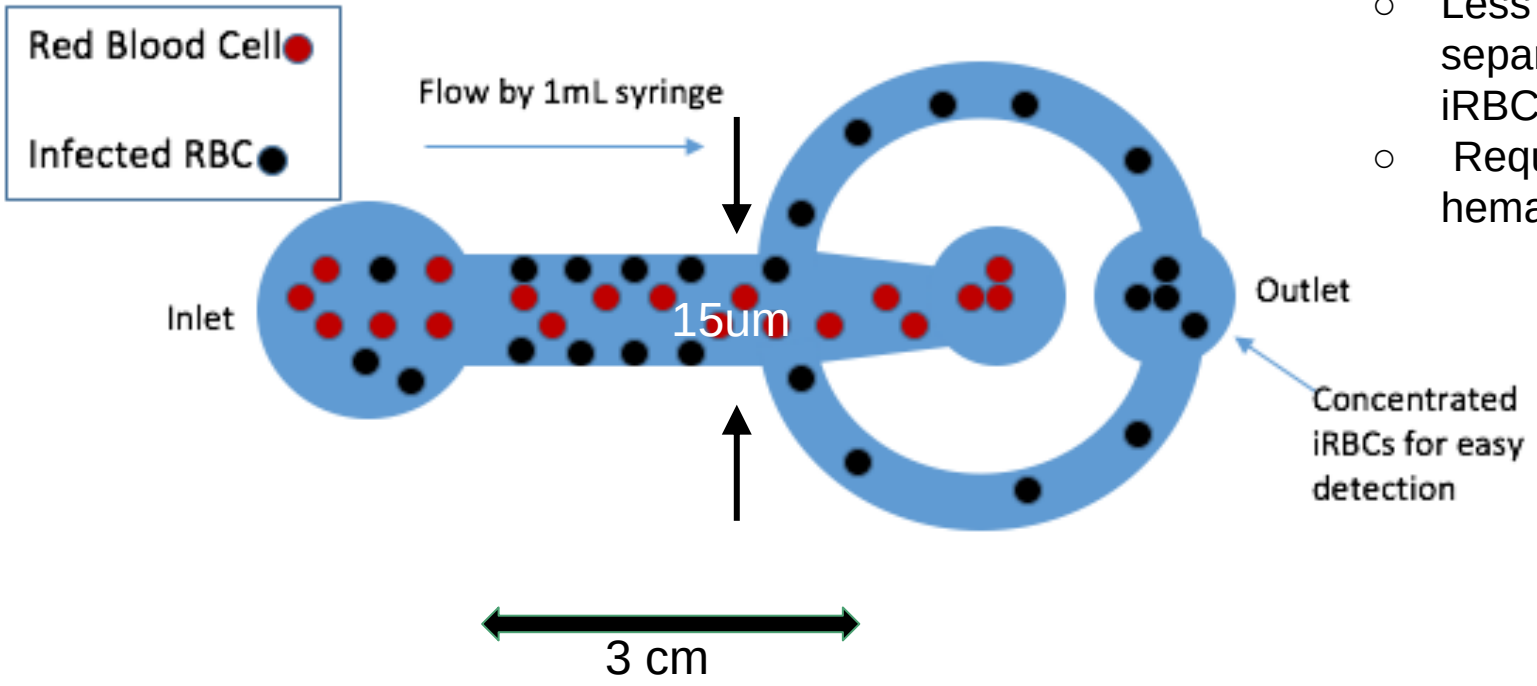
Price range: $1 - 5

Able to diagnose malaria (possibly other diseases too)

Distinguish between 4 strain

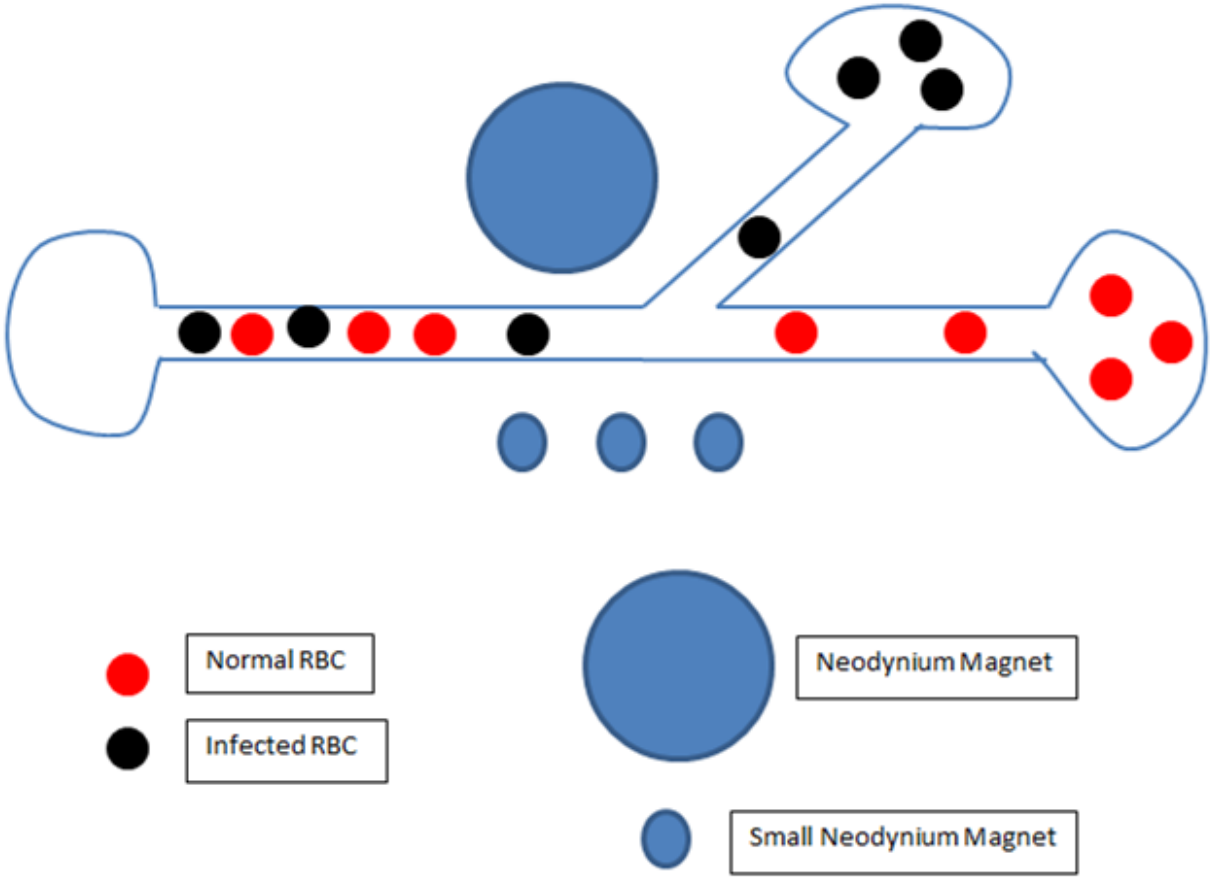
Separation 1: Cell Deformation

- Pros:
  - No additional requirements
  - Easily testable with polystyreen beads
- Cons:
  - Less effective in separating early stage iRBCs
  - Requires 40% blood hematocrit



[3]

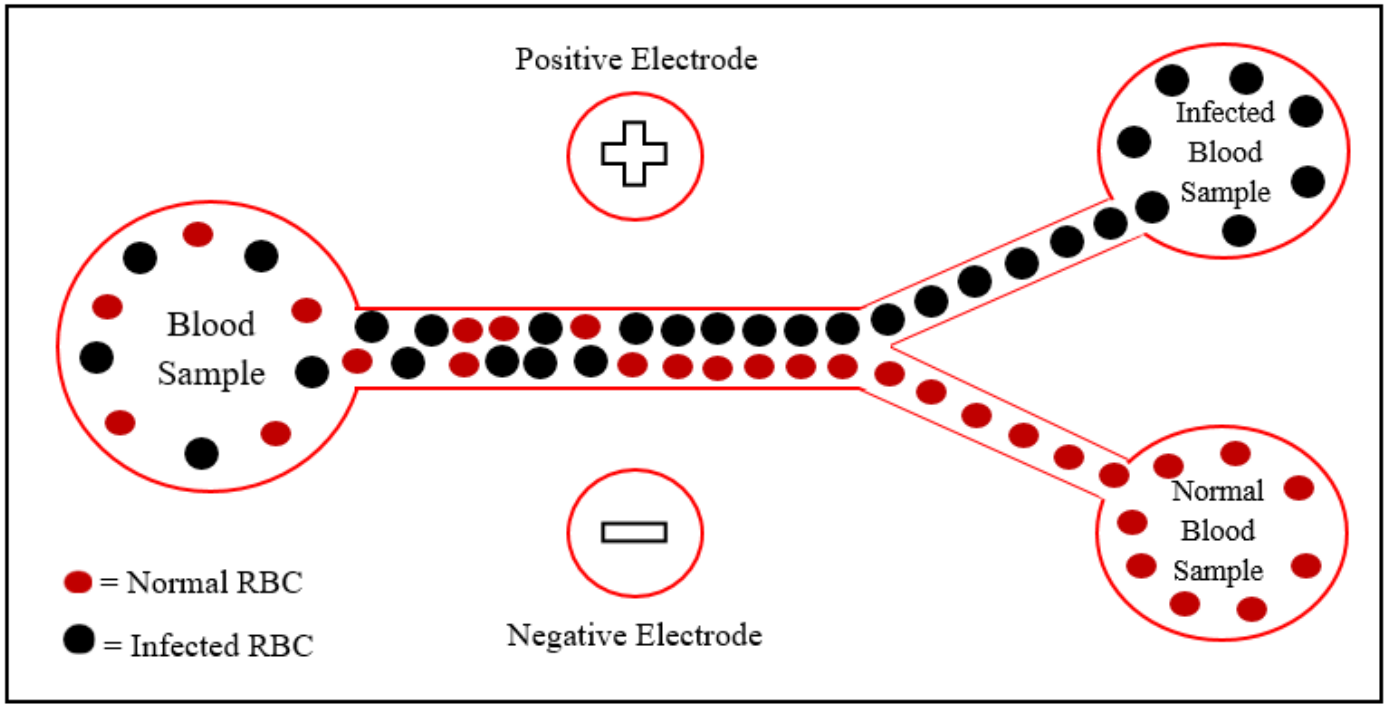
Separation 2: Magnetism



- Pros:
  - Hemozoin produced at all life stages
  - Fast detection
  - Detect a minimal amount of iRBCs
- Cons:
  - Intensely complicated magnetic field equations
  - Requires extra fabrication

[4],[5]

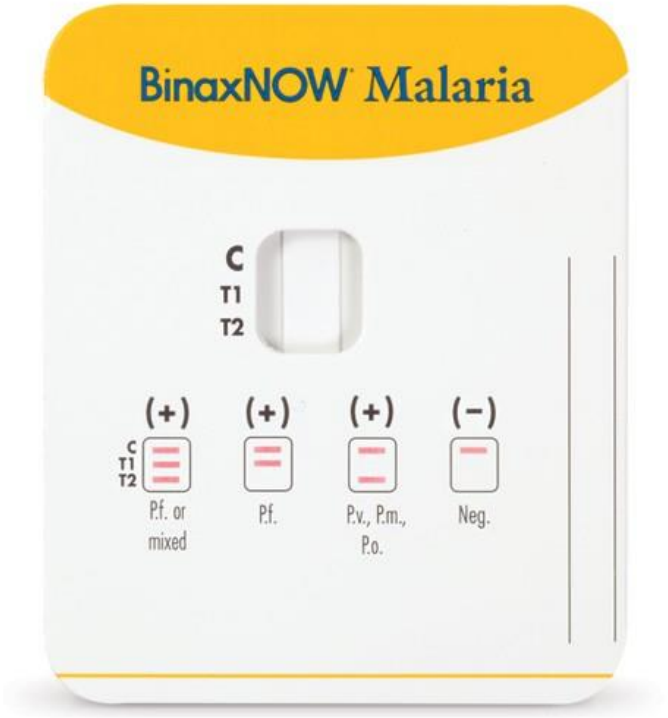
Separation 3: Electrical



- Pros:
  - High specificity
  - iRBCs very sensitive to + charges (Conductivity)
- Cons:
  - Electrical difficulties for POC
  - High cost due to batteries

[6]

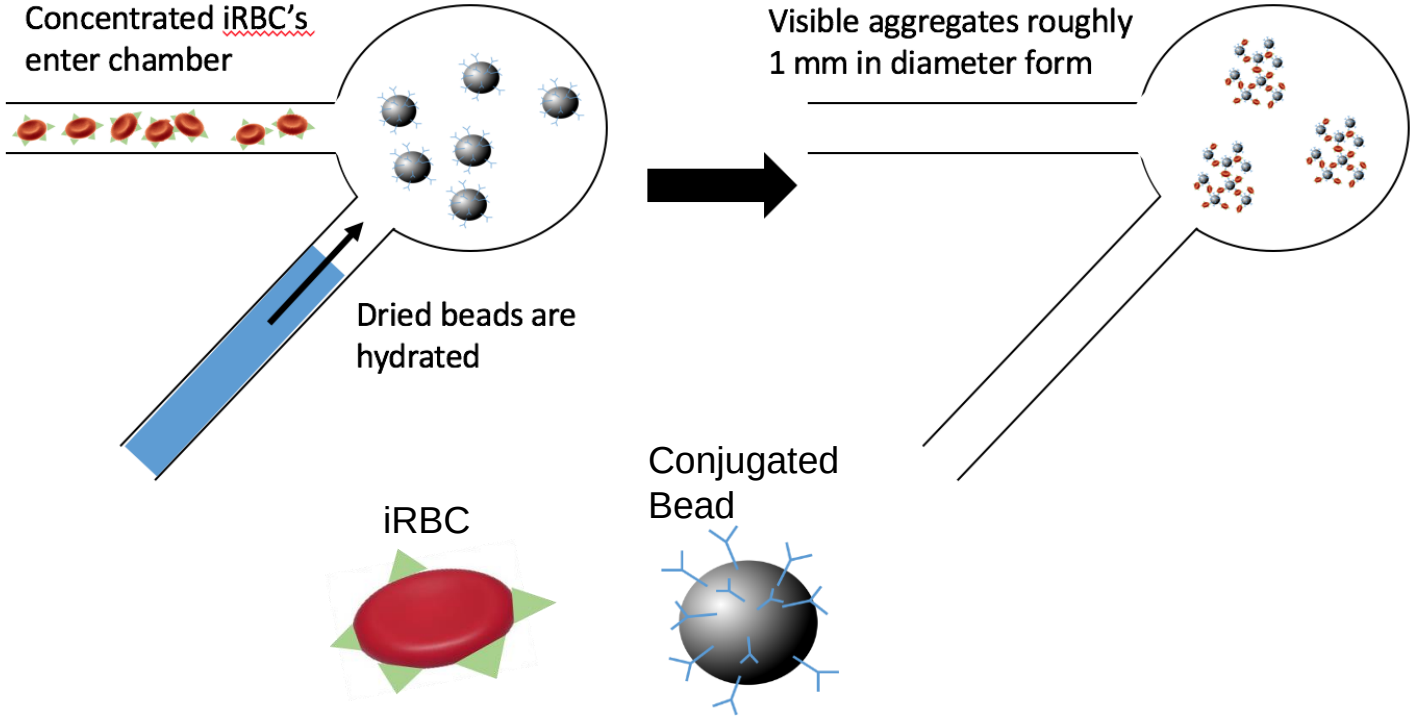
Detection 1: BinaxNOW



- Pros
  - 15 minutes
  - Small blood volume
  - Easy to interpret
  - Sensitivity > 93.5% for all 4 strands
- Cons
  - Needs parasite levels > 5,000 parasites/uL
  - Very expensive, around $40 each for a pack of 12

[6]

Detection 2: Polystyrene Beads



Pros:

- Two minute diagnosis
- 2 uL of blood

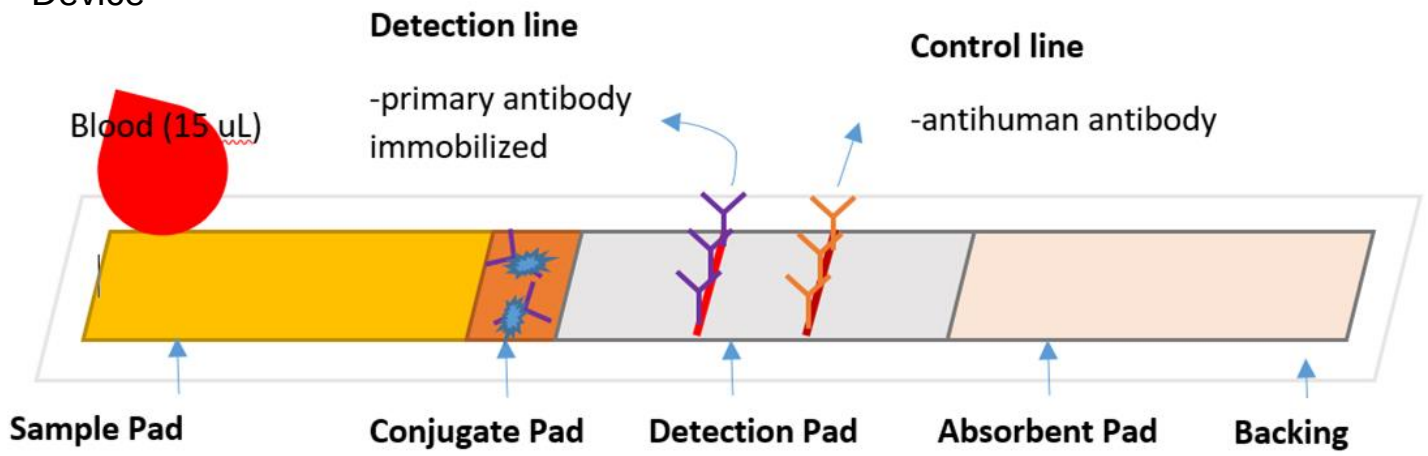
Cons:

- Testing for multiple strains would be cumbersome
- ~80% specific

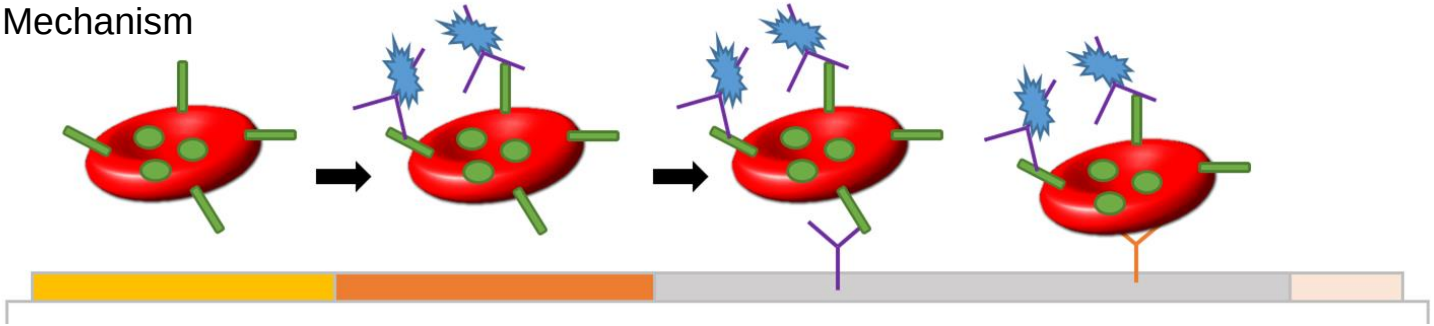
[2]

Detection 3: Gold Nanoparticles

Device



Mechanism



Pros:

- Demonstrated Method
- Low detection time
- High accuracy
- Species Specific

Cons:

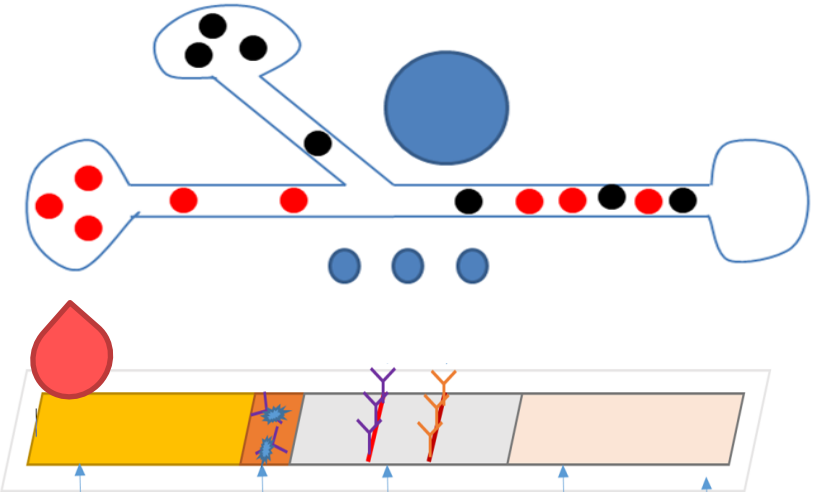
- Expensive without mass production
- Possible fabrication difficulties

[6]

Design			*Separation*				*Detection*					
Criteria (weight)	Cell Deformation		Magnetic Separation		Electric Separation		BinaxNOW		PS Beads		GNPs	
Sensitivity (25)	3	15	5	25	4	20	5	25	4	20	5	25
Equipment Free/Usable in Field/Intuitive (20)	5	20	4	16	3	12	3	12	4	16	5	20
Userfriendly (20)	5	20	5	20	3	12	4	16	4	16	5	20
Time (10)	2	4	4	8	4	8	4	8	5	10	4	8
Cost (10)	5	10	4	8	3	6	1	2	5	10	3	6
Ease of Fabrication (10)	4	8	4	8	3	6	5	10	3	6	2	4
Versatility (type of Malaria or other diseases) (5)	4	4	2	2	2	2	3	3	1	1	5	5
Total	81		**87**		66		76		79		**88**	

Future Work

- Combine both the separation and detection methods
- Determine optimal fabrication techniques
- Develop prototype
- Testing methods
- Challenges
  - Placement of magnet(s) calculations
  - Biological testing difficulties
  - Costs on individual scale



Questions?

References

[1] WHO, "Malaria," in *World Health Organization*, World Health Organization, 2016. [Online]. Available: http://www.who.int/malaria/en/. Accessed: Oct. 11, 2016.

[2] D. Polpanich et al. "Detection of malaria infection via latex agglutination assay," *Analytical chemistry.*, vol. 79, no. 12, pp. 4690–5, May 2007. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/17511424. Accessed: Oct. 11, 2016.

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[4] A. Trafton and M. N. Office, "A new way to diagnose malaria," MIT News, 2014. [Online]. Available: http://news.mit.edu/2014/new-method-diagnose-malaria-0831. Accessed: Oct. 11, 2016.

[5] W. K. Peng, L. Chen, and J. Han, "Development of miniaturized, portable magnetic resonance relaxometry system for point-of-care medical diagnosis," *Review of Scientific Instruments*, vol. 83, no. 9, p. 95115, Sep. 2012. [Online]. Available: http://scitation.aip.org/content/aip/journal/rsi/83/9/10.1063/1.4754296. Accessed: Oct. 14, 2016.

[6] A. Tay, A. Pavesi, S. R. Yazdi, C. T. Lim, and M. E. Warkiani, "Advances in microfluidics in combating infectious diseases," *Biotechnology Advances*, vol. 34, no. 4, pp. 404–421, Jul. 2016.