Summer School

Sustainable nanosensors for water pollution detection

“Design and Application of Paper-Based Microfluidic Analytical Devices”

Prof. Ass. Dr. **Liridon Berisha**

Department of Chemistry - FMNS, University of Prishtina

NanoAlb Unit: Electrochemical sensors and biosensors **Lab22**

Research group – Chemical sensors Lab22

Lirika Humolli

Master-st.

Prof.ass.dr.Liridon Berisha

Dr.sc.Arsim Maloku

Edita Halili

Master-st.

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Content

- Introduction
- Fabrication methods
- Design and modifications
- Detection methods
- Applications

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Our starting point!

Paper microfluidic devices - during COVID-19 pandemy

Our starting point!

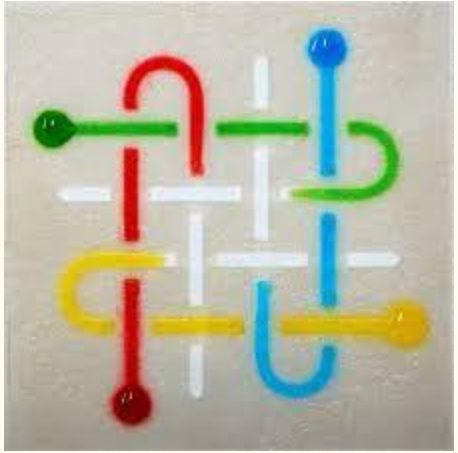
Projects:

1. Research Based Teaching – Inquiry based experiments using paper microfludiic devices – MESTI - Kosovo

2. Development of new electrochemical sensor for hydroxymethylfurural determination – NanoAlb – Academy of Science of Alabania 2022-2024

Paper microfluidic devices

- Paper based miscrofluidic devices consist of hydrophylic channels that transport fluid through medium by capilary action to the desired region.



Why paper microfluidics

- Very cheap material, widely available and easy to process;
- Capillarity absorption of aqueous solutions - transport fluid without the need for external system;
- Porosity and biocompatibility of cellulose to store reagents and biomolecules;
- Easy process combination with printing;
- Burnable, biodegradable and recyclable, easy disposal options after use
- Point of Need/Care Testing

Why paper microfluidics

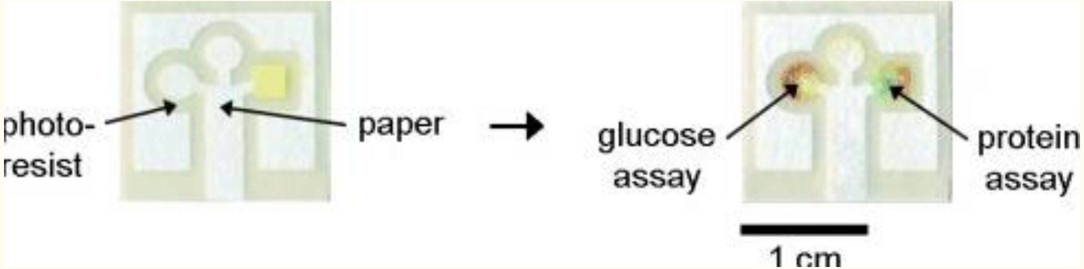
The World Health Organization (WHO) established criteria for evaluating POC

“ASSURED” to “REASSURED”

Real time conectivity
Ease of speciemen collection
Aaffordable,
Sensitive,
Specific,
User-friendly,
Rapid and robust,
Equipment-free,
Deliverable to end users”

Microfluidic paper-based analytical devices

- Microfluidic paper-based analytical devices (µPADs) -2007



- Further evolved
  - Substrate materials; Fabrication methods; Detection methods; Range of applications.

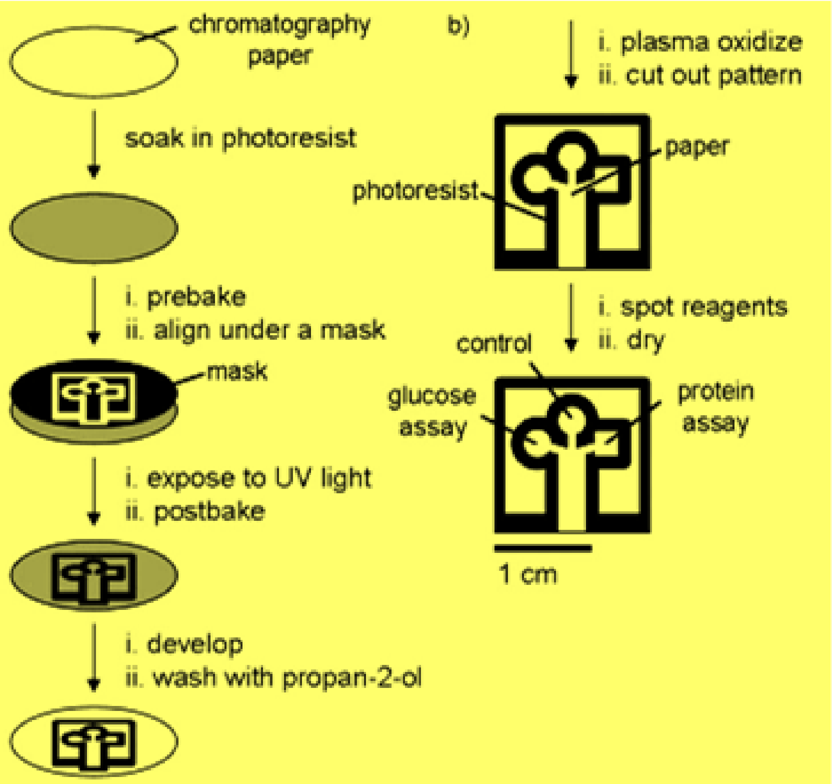
Martinez, A., Phillips, S., Butte, M. and Whitesides, G. (2007), Patterned Paper as a Platform for Inexpensive, Low-Volume, Portable Bioassays. Angewandte Chemie International Edition, 46: 1318-1320. https://doi.org/10.1002/anie.200603817

μPADs fabrication

Methods

- Photolithography
- Wax printing,
- Screen-printing
- Inkjet printing,
- Laser toner printing,
- Flexographic printing,
- PDMS printing,
- Stamping,
- Drawing,
- Inkjet etching,
- Wet etching,
- Plasma treatment,
- Spraying,
- Vapor-phase deposition.

μPADs fabrication



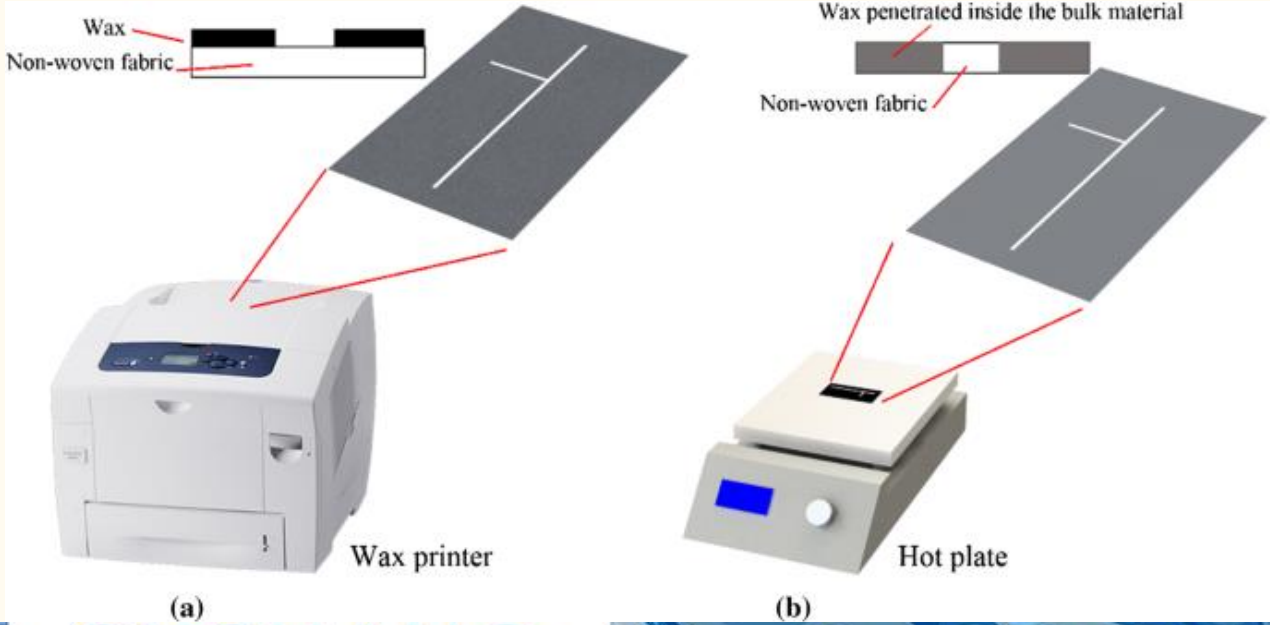
Photolithography

- **Advantages:** Convenient, useful, high resolution;
- **Disadvantages:** Expensive chemicals and equipment, multiple steps, time consuming, reduced paper flexibility

µPADs fabrication

Wax printing

- **Advantages:** high throughput, low cost, simple fabrication
- **Disadvantages:** wax printer, resolution is limited and influenced by the melting of the wax



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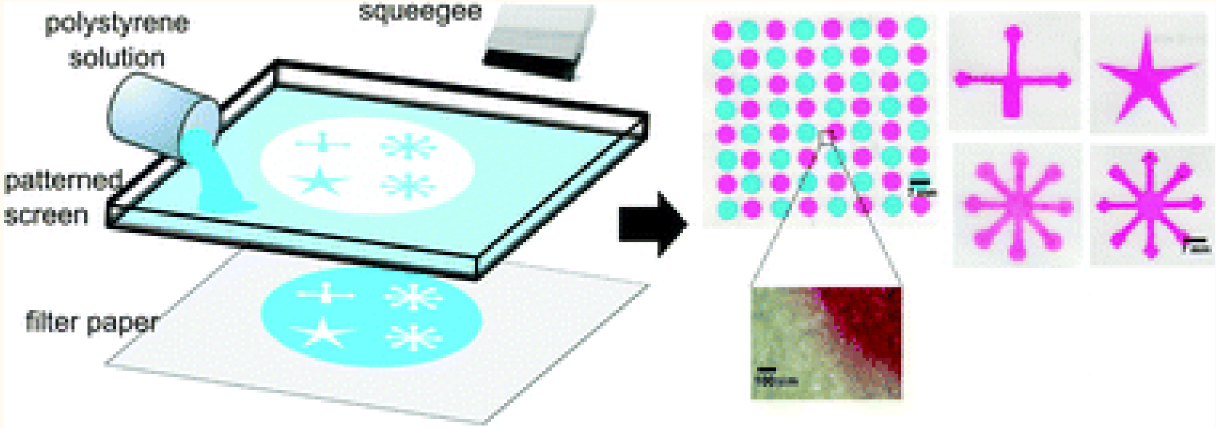
µPADs fabrication

Screen printing

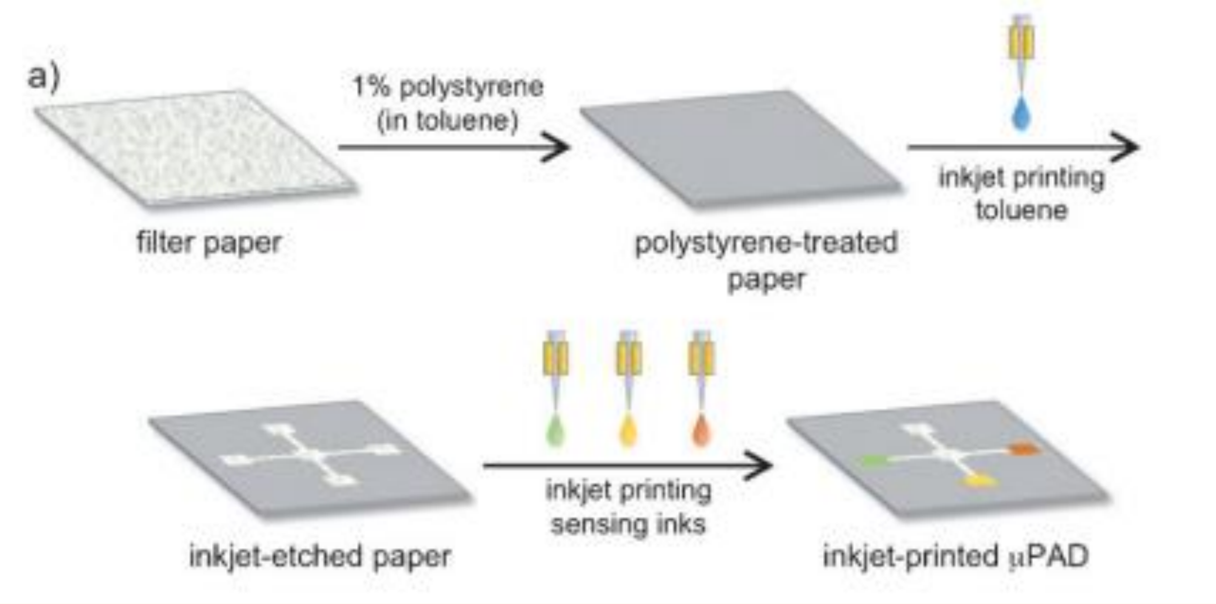
- **Advantages:** low cost, simple fabrication
- **Disadvantages:** low resolution, requires separate screens for different patterns



μPADs fabrication

Inkjet printing

- **Advantages:** high throughput, customizable ink material
- **Disadvantages:** requires modification to the printer which often reduces the lifespan of
- the equipment

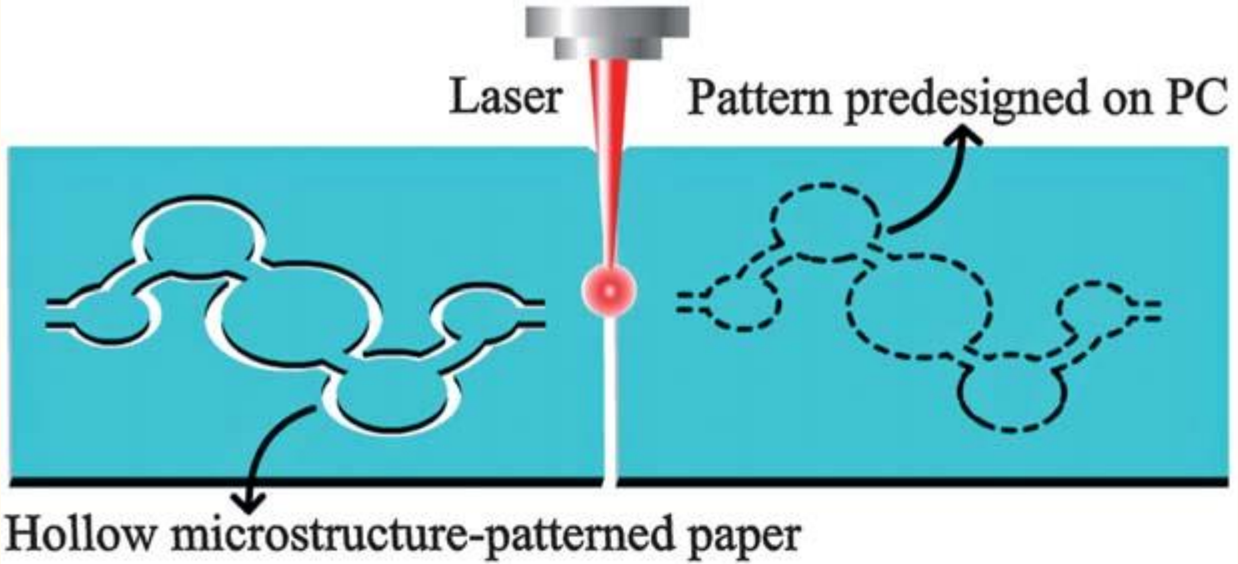


Yamada, K., Henares, T.G., Suzuki, K. and Citterio, D. (2015), Paper-Based Inkjet-Printed Microfluidic Analytical Devices. Angew. Chem. Int. Ed., 54: 5294-5310.

µPADs fabrication

Laser cutting

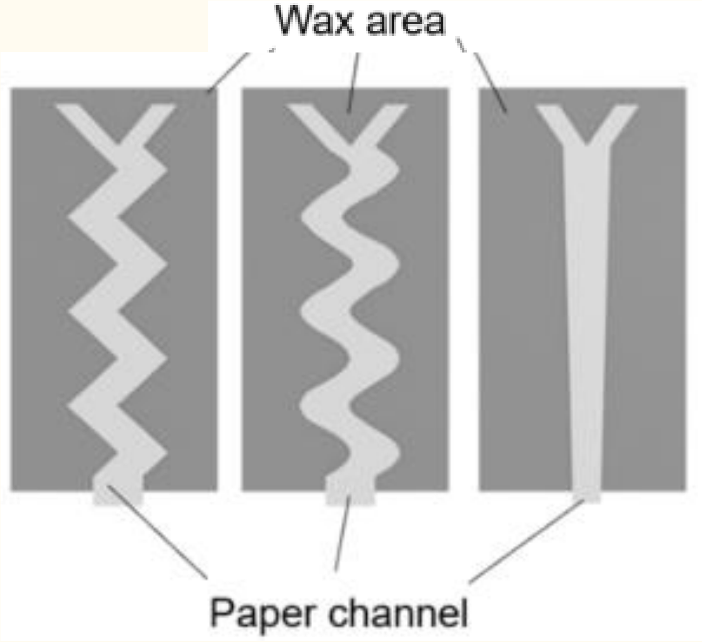
- **Advantages:** high throughput, high resolution, does not require patterning reagents
- **Disadvantages:** requires a CO2 laser cutter or craft cutter, low mechanical stability



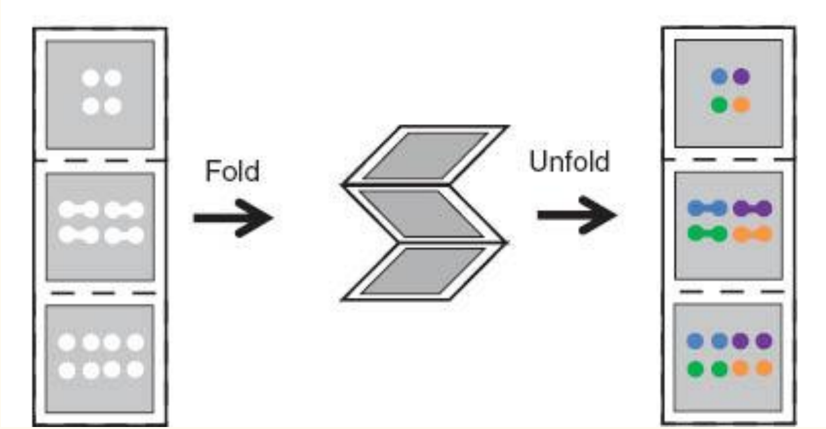
One-step patterning of hollow microstructures in paper by laser cutting to create microfluidic analytical devices. N. Jinfang, L. Yuanzhi, Zh. Yun, L. Shangwang, L. Dunnan, Zh. Songbai, Analyst, Vol. 138 (2), 2013.

Design and modofication

- **2D lateral flow**

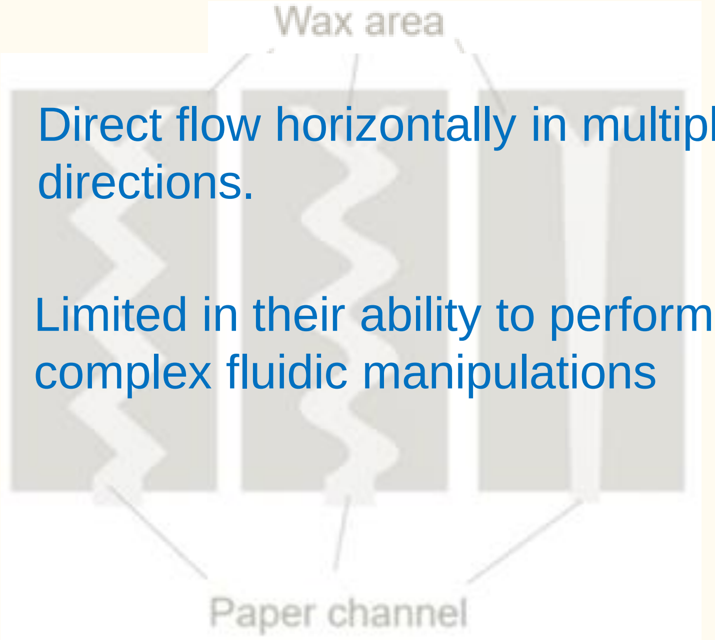


- **3D flow through**



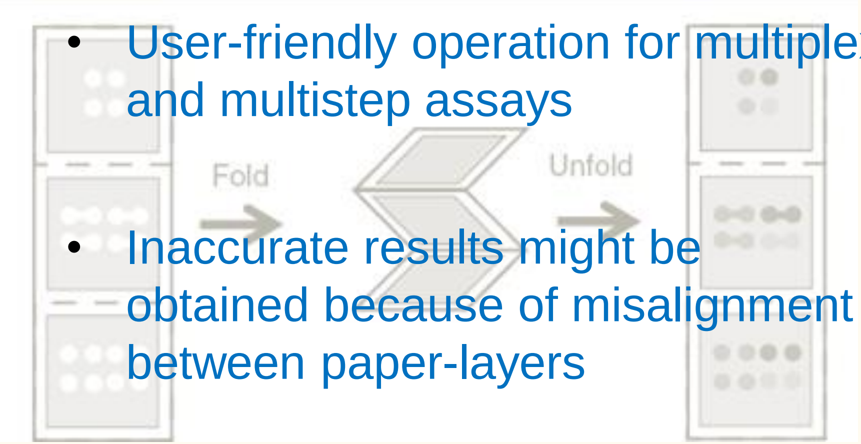
Design and modofication

- **2D lateral flow**



- Direct flow horizontally in multiple directions.
- Limited in their ability to perform complex fluidic manipulations

- **3D flow through**

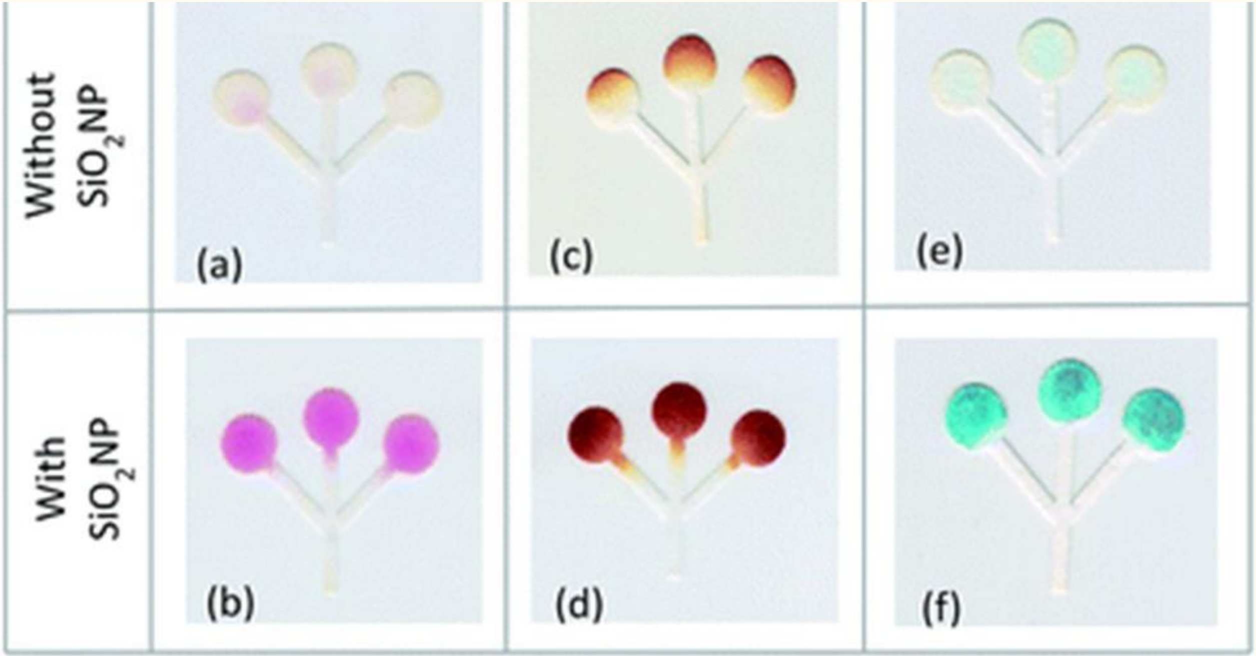


- User-friendly operation for multiplex and multistep assays
- Inaccurate results might be obtained because of misalignment between paper-layers

Design and modofication

- In paper-based devices, the solution wicks through the device in part due to the hydrophilic nature of the fibers.
- Interaction analyte - fiber nonspecific adsorption of the analyte (polar or charged)
- pH change effect – concentrate or release molecules (Changing protonation of amine groups)
- Example: Celulose-Chitosan-Glutaldehide-Protein
- Chemical modification – oxidation of cellulose with sodium periodate
- Remain stationary molecules in specific zones

Design and modofication



Evans, E.; Moreira Gabriel, E. F.; Benavidez, T. E.; Tomazelli Coltro, W. K.; Garcia, C. D. Modification of microfluidic paper-based devices with silica nanoparticles. Analyst 2014, 139, 5560−5567.

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Design and modofication

- Controlling the flow rate in paper
  - Multistep assays,
  - Adjusting residence time over a detection zone,
  - Increasing electrochemical signal,
  - Decreasing assay time

- Lucas Washborn eq.

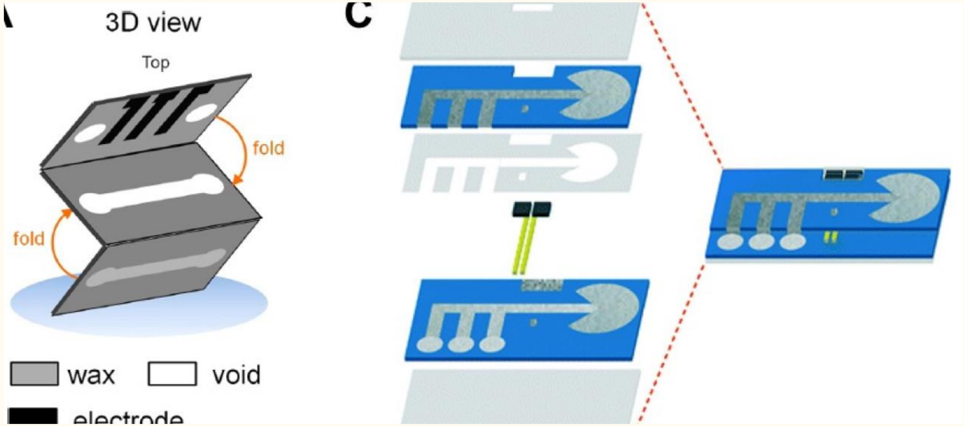
$$L = \sqrt{\frac{\gamma r t \cos \varnothing}{2\eta}}$$

L -distance the fluid travels,
γ-surface tension,
r -radius of the capillary,
t -time,
ø is the contact angle,
η - liquid viscosity

Design and modofication

- Increasing the flow rate in paper

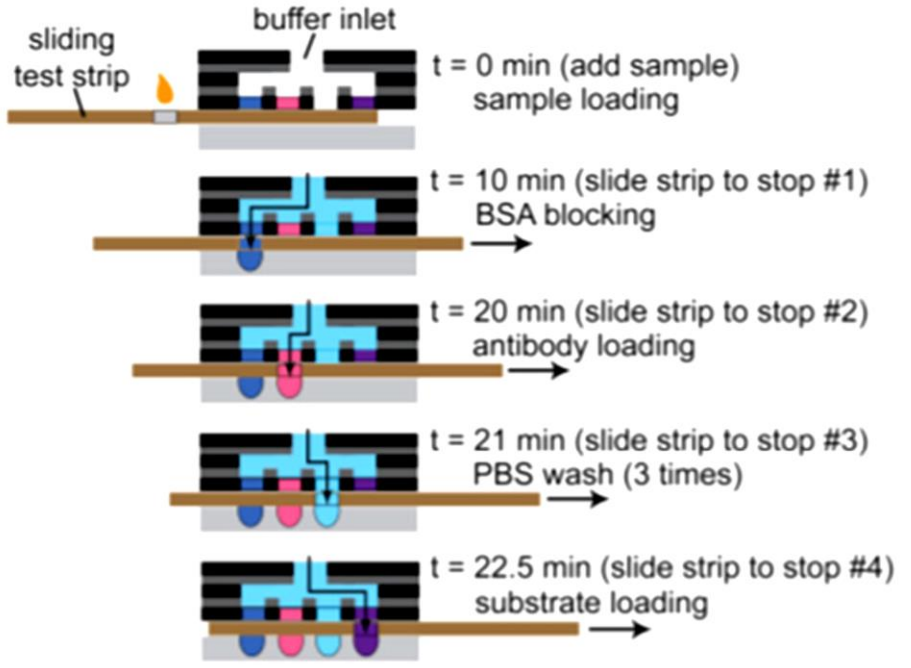
- Increasing pore radius (sandwiched paper between two polyester films)

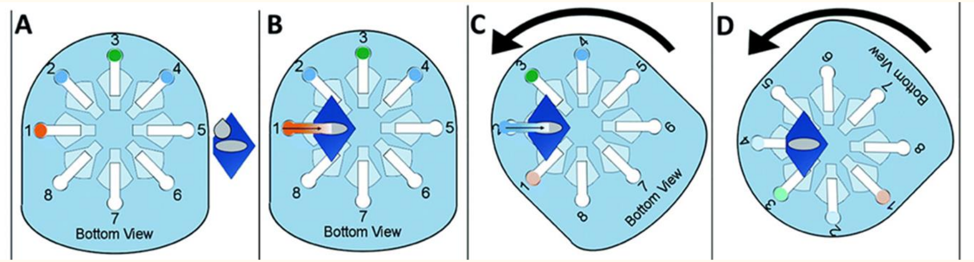


- Limitation for fast-flow devices-require a larger volume of fluid

Design and modofication

- Valving





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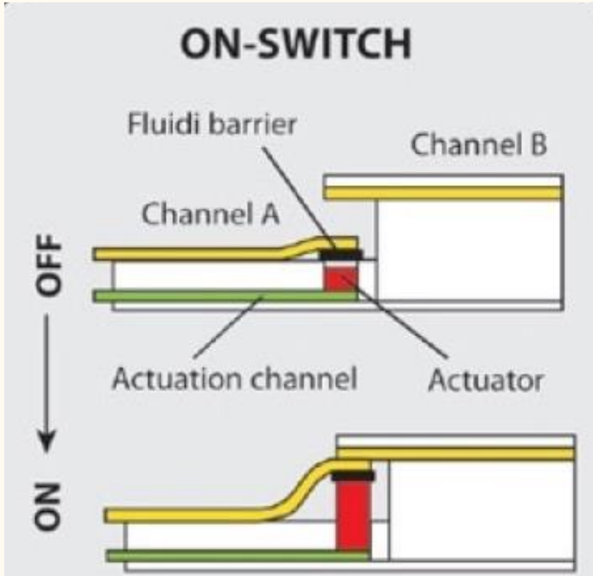
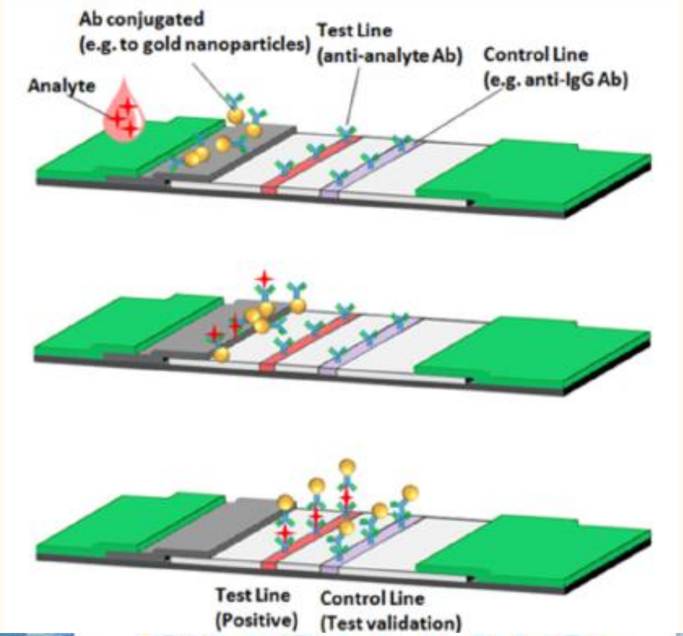
Design and modofication

- Valving
  - Passive valves – dissolvable barriers (sugars, polymers etc.)
  - on/off paper switches
    (swelling after absorbing fluid)
  - Electromagnet to control a paper switch
    modified with magnetic PDMS
    (controlled with Arduino)



Design and modofication

- μPADs are designed to decrease the cost and complexity
  (ideal workflow involves one-step sample addition and simple readout)



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Design and modofication

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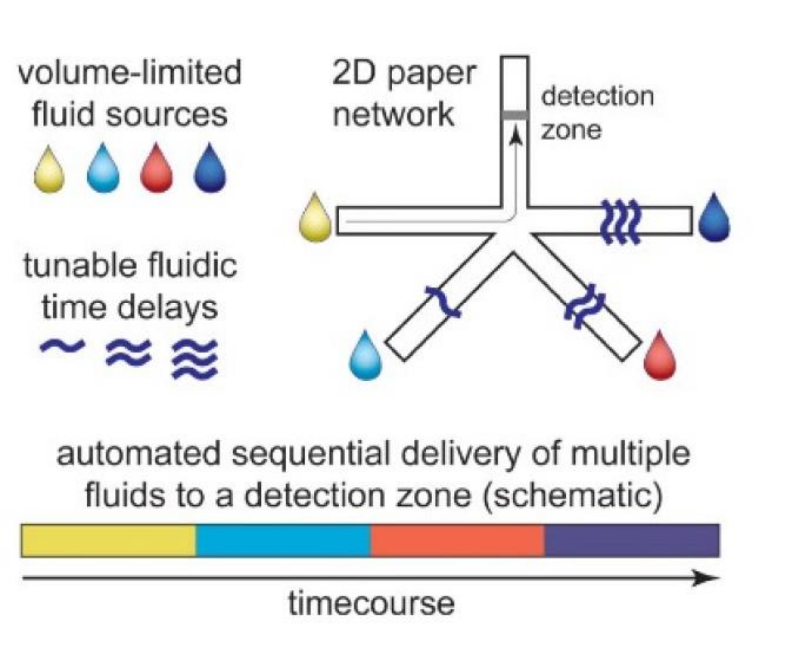

Lutz, B.; Liang, T.; Fu, E.; Ramachandran, S.; Kauffman, P.; Yager, P. Dissolvable fluidic time delays for programming multi-step assays in instrument-free paper diagnostics. Lab Chip 2013, 13, 2840−2847.

Detection methods

- Colorimetric detection
  - pH-induced color change
  - Metal–ligand complexation reactions
  - Enzymatic conversion of chromogenic substrates

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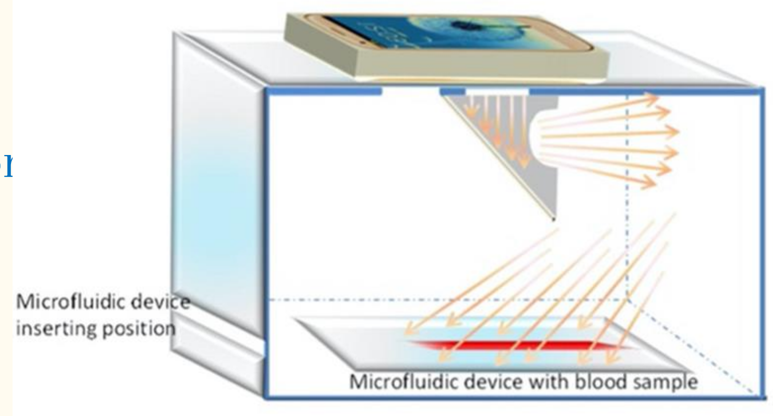
Detection methods

- Colorimetric detection
- Qualitative (yes/no result to confirm analyte presence),
- Semiquantitative (an estimate of analyte concentration),
- Quantitative (a more accurate analyte concentration).

Detection methods

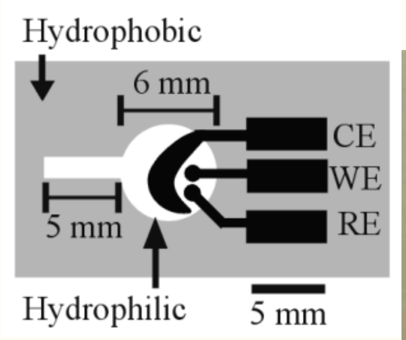
Colorimetric detection

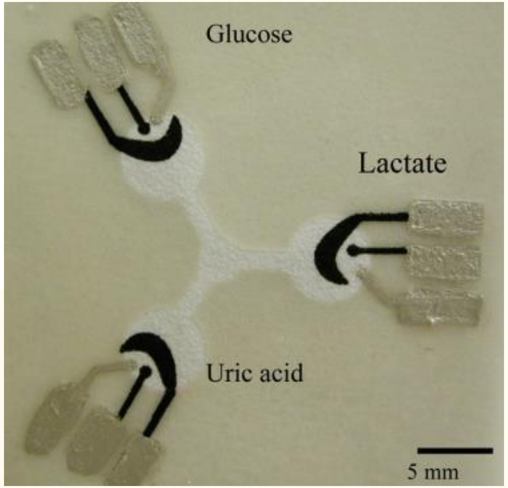
- CCD charge-coupled devices
- CMOS complementary metal-oxide senso



Detection methods

- Electrochemical detection ***e*PADs**
  - 3 electrode
  - Electrode materials
  - Modification WE





Wijitar Dungchai, Orawon Chailapakul,Charles S. Henry. Electrochemical Detection for Paper-Based Microfluidics. Anal. Chem. 2009, 81, 5821–5826

Detection methods

- Incorporating electrodes in PADs
  - Screen printing
  - Stencil printing
  - Inkjet printing
  - Pencil/pen drawing
  - Microwire placement
  - Laser scribing
  - Sputtering

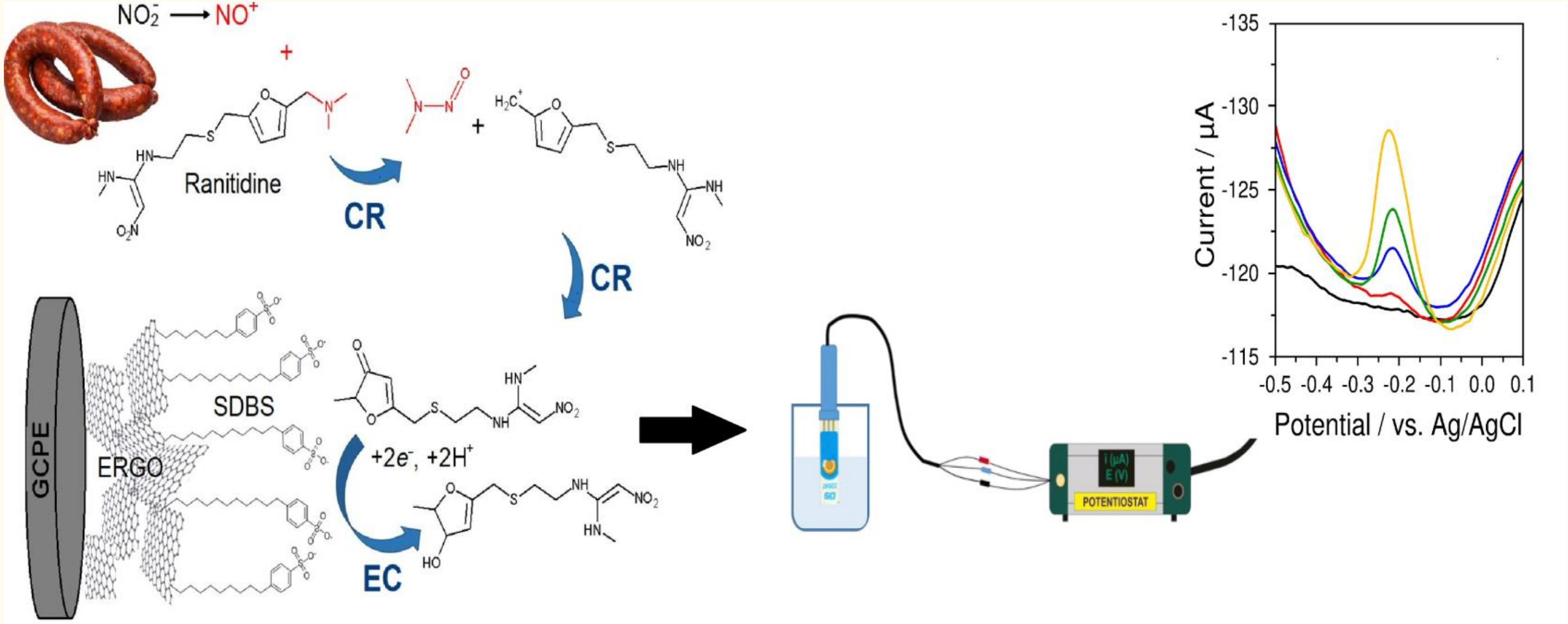
Detection methods

- Detection techniques for ePADs
  - Stripping voltammetry
  - Differential pulse voltammetry (DPV)
  - Square wave voltammetry (SWV)
  - Chronoamperometry
  - Coulometry

Detection methods

- Detection strategies ePADs
  - Enzyme
  - Antibodies
  - Aptamers
  - Molecularly Imprinted Polymers (MIP)

***e*PADs** for the determination of nitrate and nitrite in human saliva



L. Berisha, G. Jashari, V. Veseli, E. Shabani, F. Lushaj, F. Maxharraj, and A. Maloku. Flow injection analysis of ranitidine based on derivatization reaction producing 2-Methylfuran cation as a sensitive and selective amperometric detector. Electroanalysis 2022. DOI:10.1002/elan.202200318

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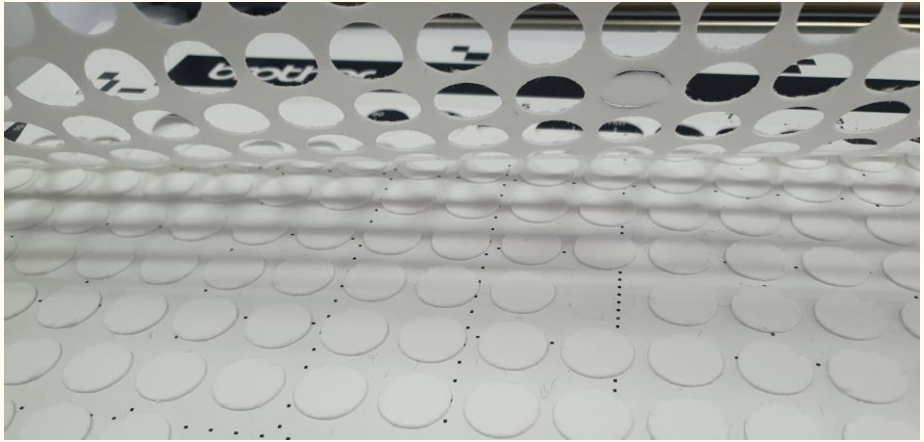
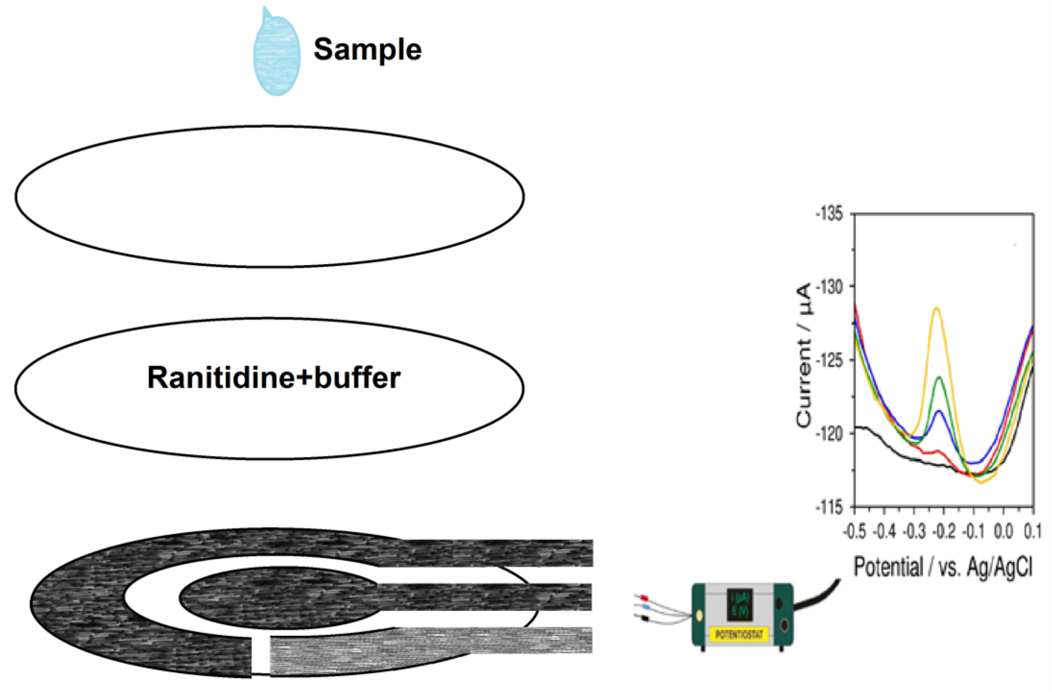


ePADs for the determination of nitrate and nitrite in human saliva

- NO_2^-

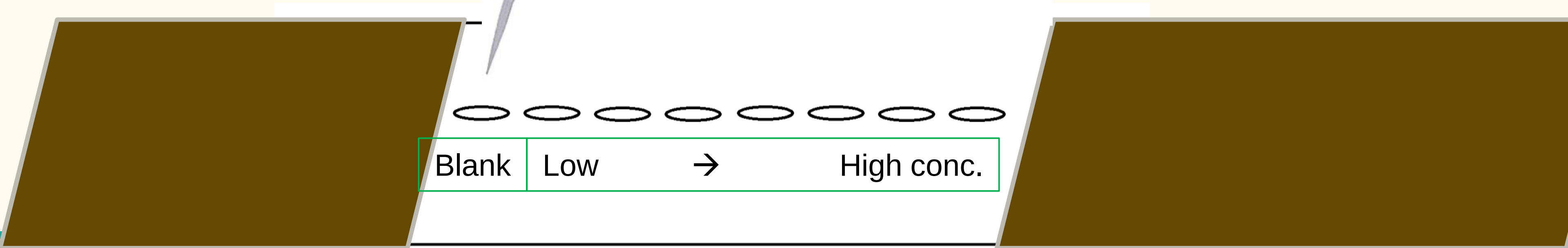


Class activity
"Integration of digital imaging technology and Microfluidic paper based analytical device for Iron determination"

- *1st install mobile app* **RGB Color Detector**

Calibration solutions

- Place 7 chips containing o-phenantroline
- After 10 min.



Calibration solutions

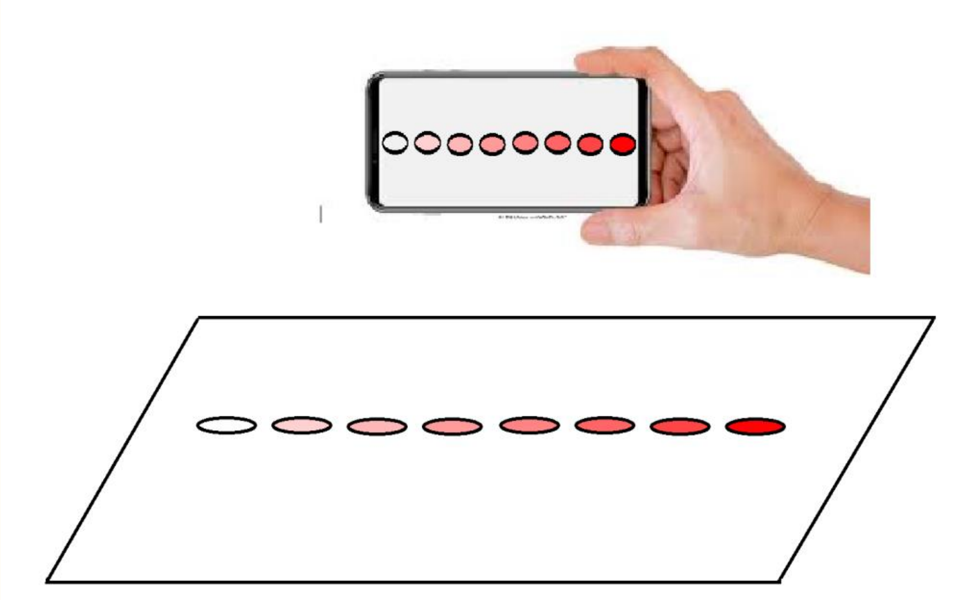


Image analysis

- ImageJ (open source)
- RGB Color Detector

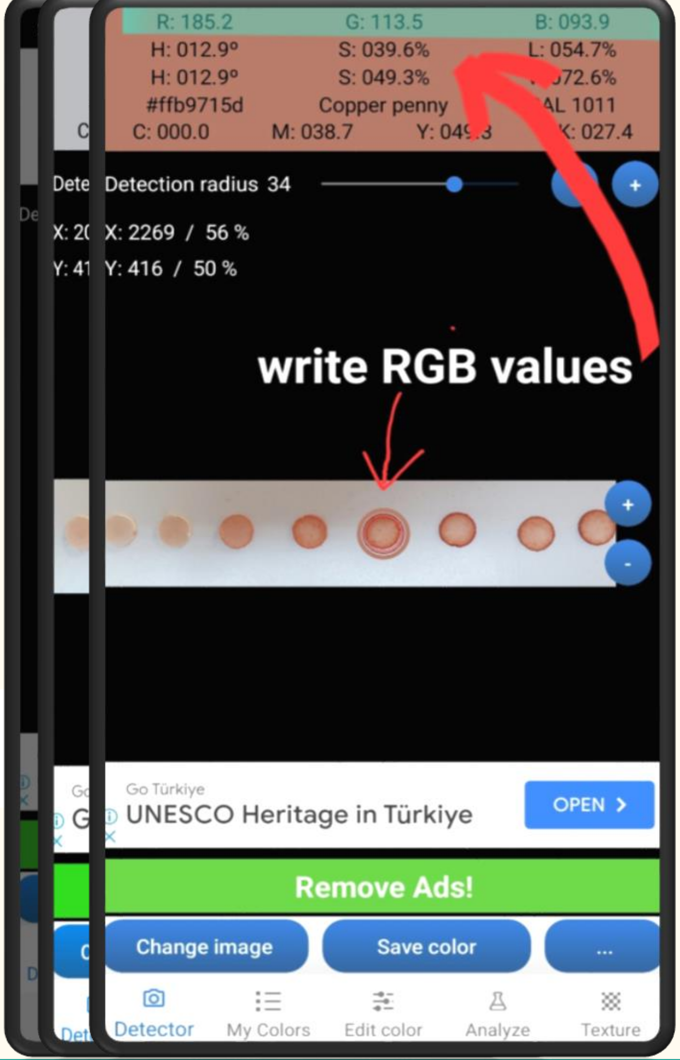


Image analysis

How to convert R G B channels value to absorbance?

Channel sensitivity?