Optoelectronic platform based on thin film technology for biomolecular analysis

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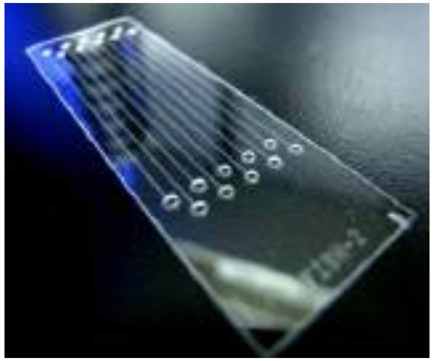
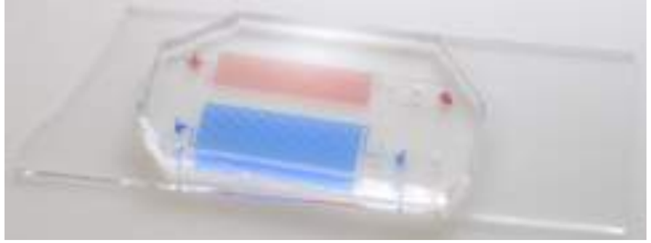
Outline

- Introduction on lab-on-chip



- Development of an optoeletronic platform for biological analysis

- Applications



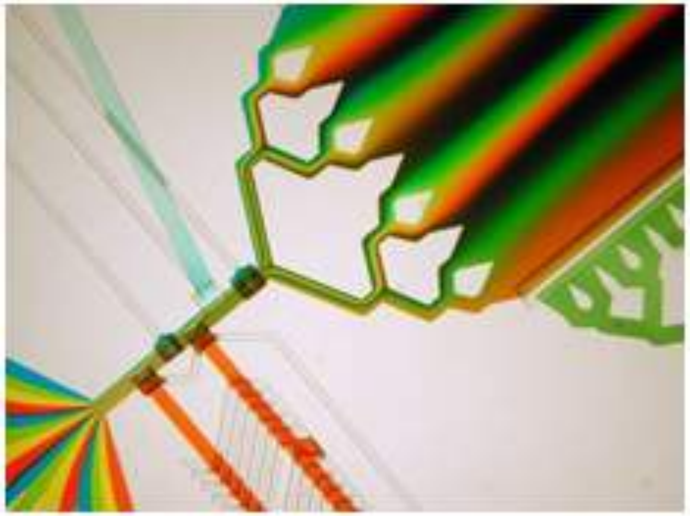
- Conclusions

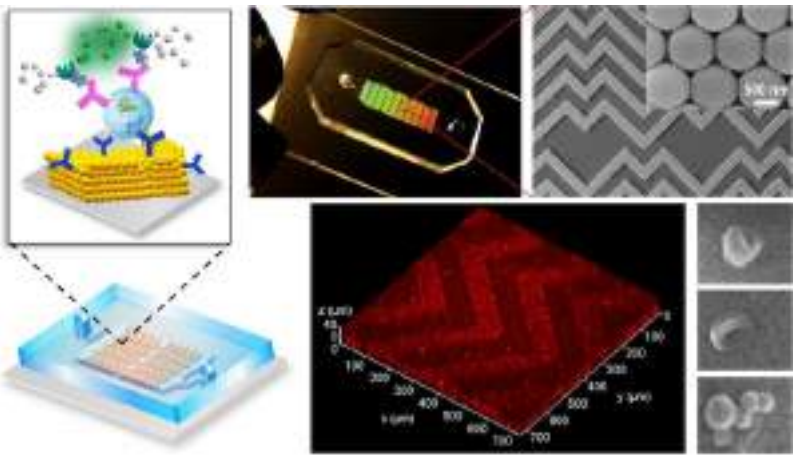
What is a lab-on-a-chip?

- A lab-on-a-chip is a **miniaturized device** that **integrates** onto a single chip one or several analyses, which are usually done in a laboratory

Function of a lab-on-a-chip

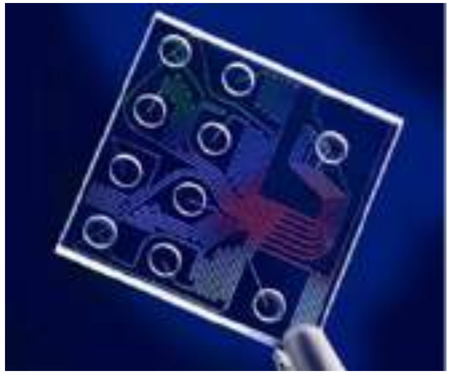
- Analysis of a sample solution for detection of a target molecule
  - sample treatment
  - handling
  - bio-chemical recognition
  - detection

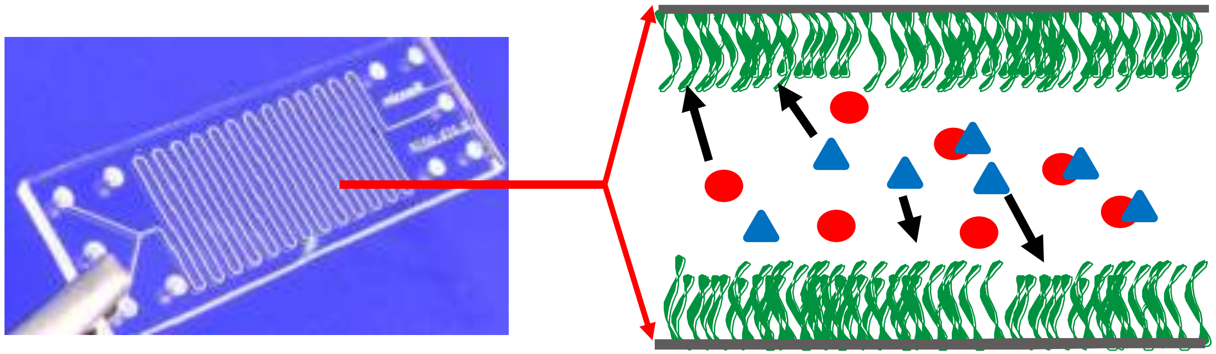




Lab-on-Chip benefits

- Main benefits come from miniaturization…
  - Small volumes (sample and reagents)
  - Faster reactions
  - Rapid thermal cycles
  - High parallelization: multiplexing





$t_d = L^2/2D$

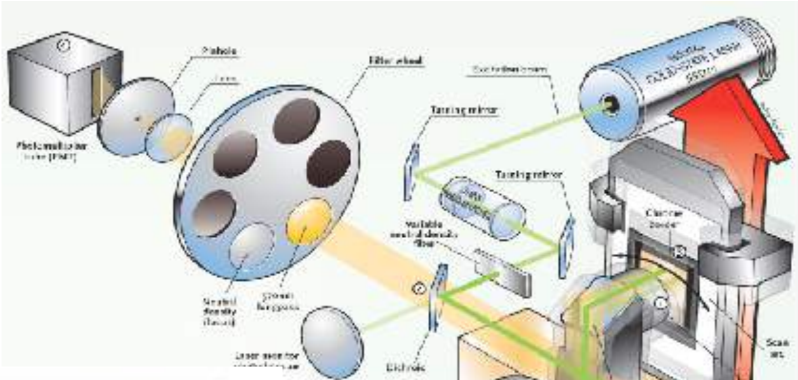
t_d= diffusion time

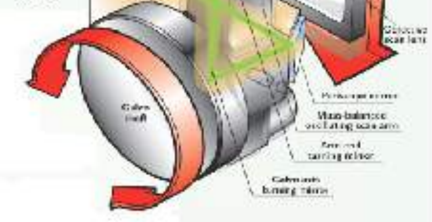
L= distance

D= diffusion coefficient

State-of-the-art: chip-in-a-lab

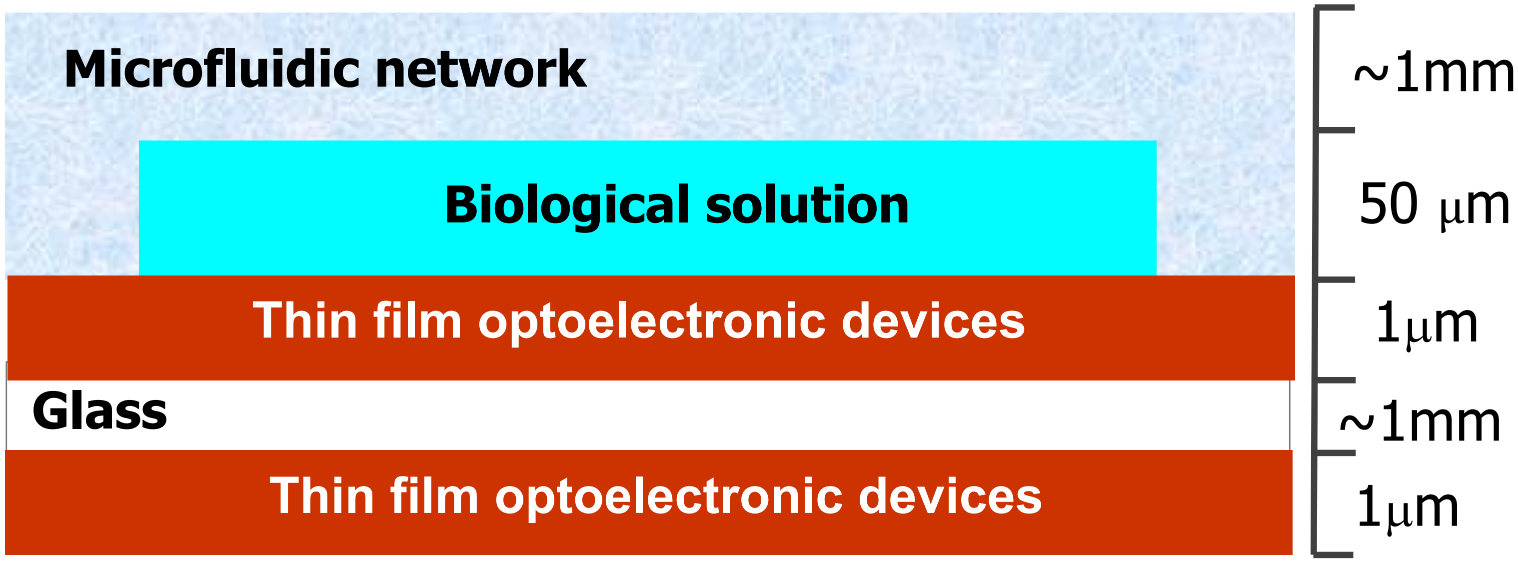
- Need of bulky instrumentation for operating microfluidic lab-on-chip:
  - fluidic actuation
    - pumps, macro-to-micro fluidic interfaces
  - excitation
    - lamps, filters, lenses
  - detection
    - microscopes, scanners, optical filters, lenses





Our goal: 'true' lab-on-chip

- **Optoelectronic platform on glass** based on thin film devices



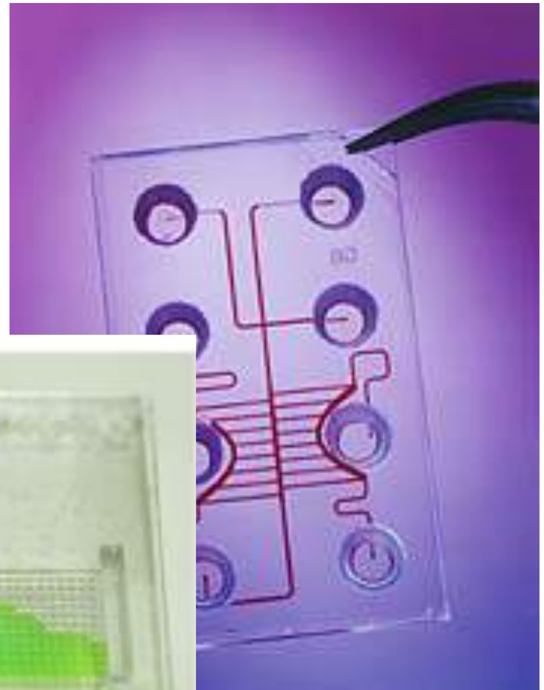
System compactness (portable system)

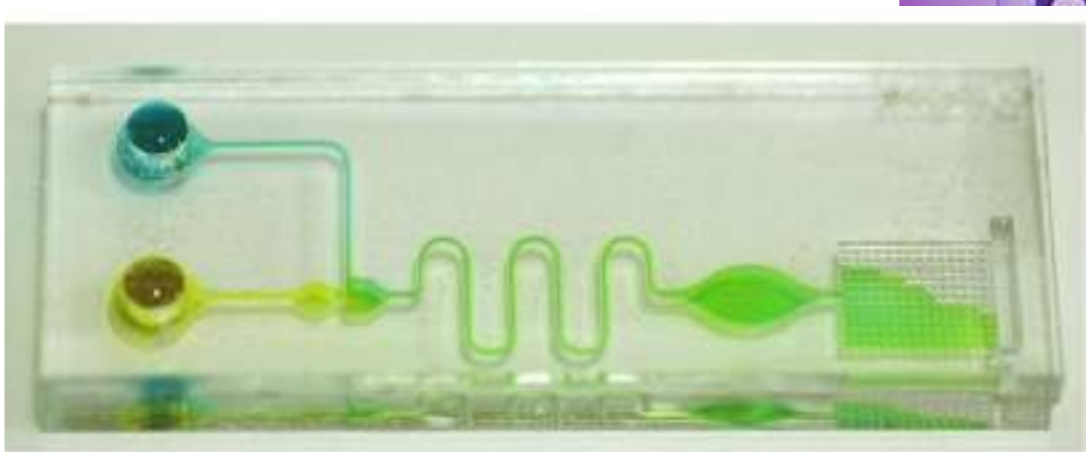
Reduced distance between bio-world and electronics

Improvement of sensitivity

Why glass?

- Material preferred by biologist and chemists:
  - transparent (optical detection)
  - biocompatible
  - easy to functionalize





Which optoelectronic devices?

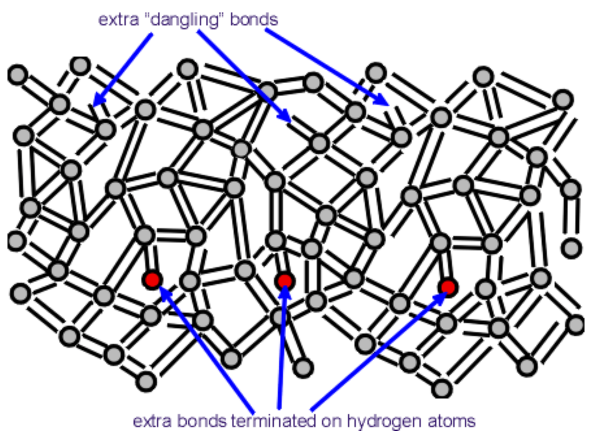
- Dependent on the implemented functions:
  - On-chip optical detection
  - On-chip thermal treatment (cell culture DNA, amplification by PCR)

- On-chip optical detection:
  - Photosensors
  - Filters

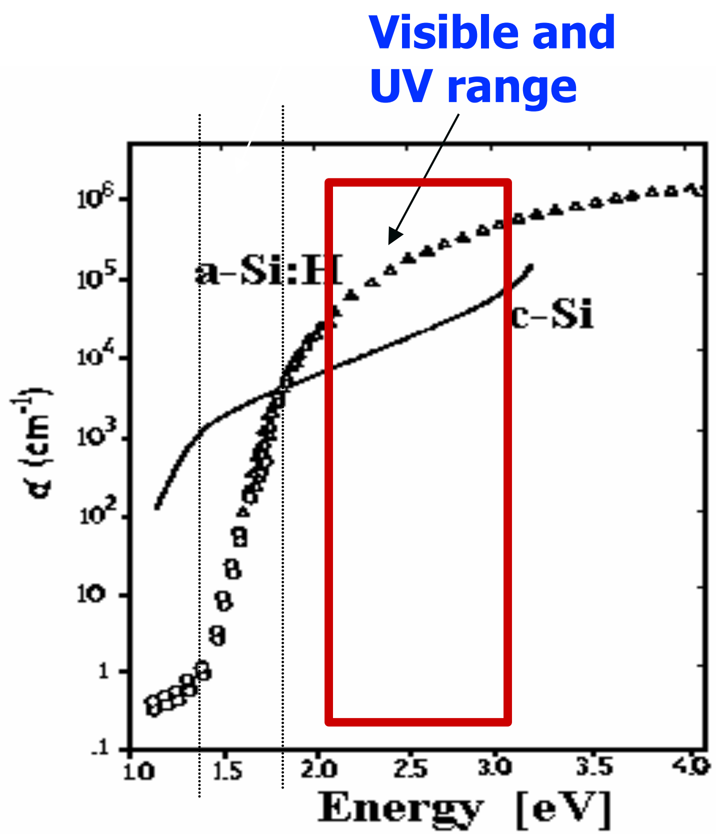
- On-chip thermal treatment:
  - Heaters
  - Temperature sensors

Material for sensors: a-Si:H

- Grown at temperature around 200 °C by PECVD from SiH_4 on:
  - glass
  - plastic
  - metals



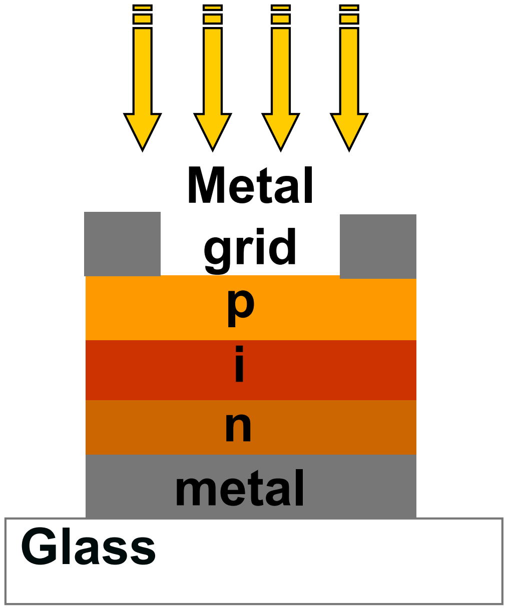
- Eg ≈ 1.7eV

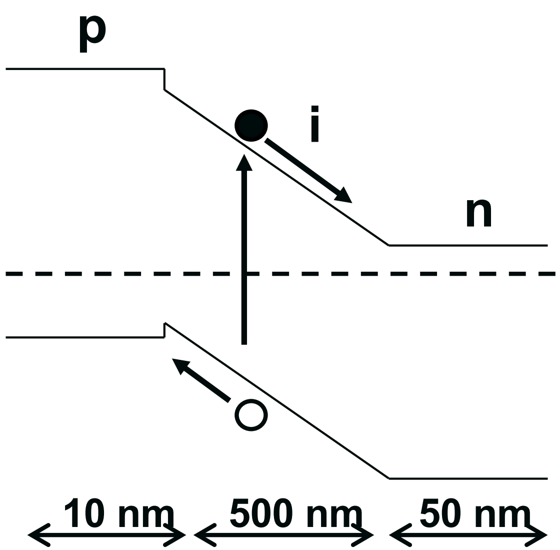


Ideal for on-chip optical detection

a-Si:H photosensors

- Stacked structures





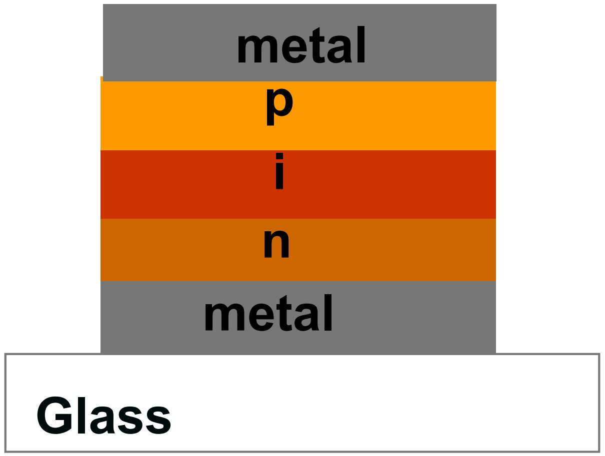
$I_{ph} = \sigma P$

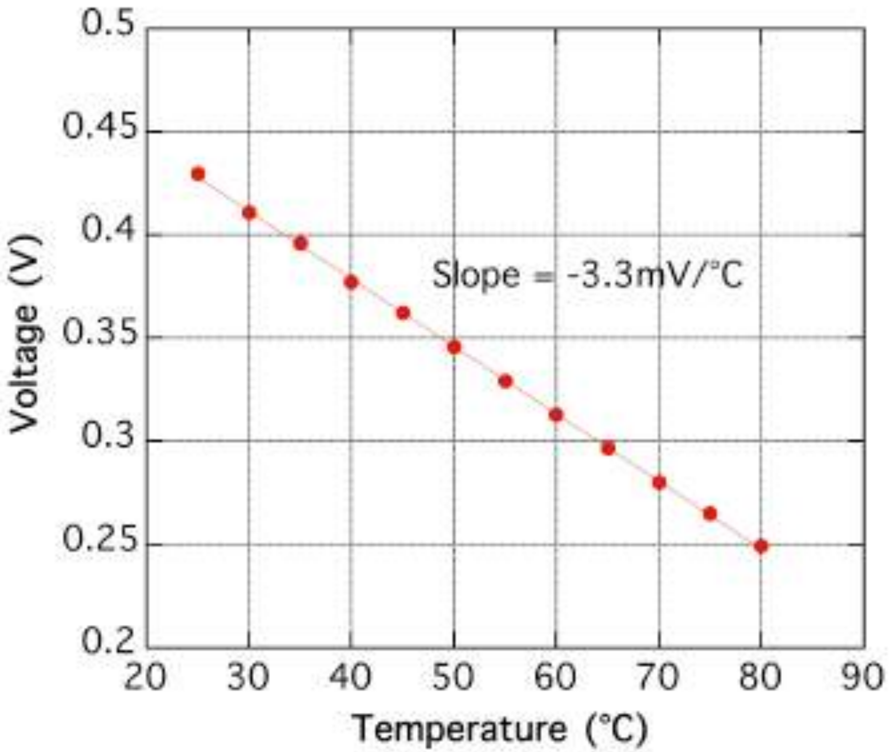
Intrinsic region: active region (collection by drift)

Doped layers: only for the built-in voltage

a-Si:H temperature sensors

- Stacked structures



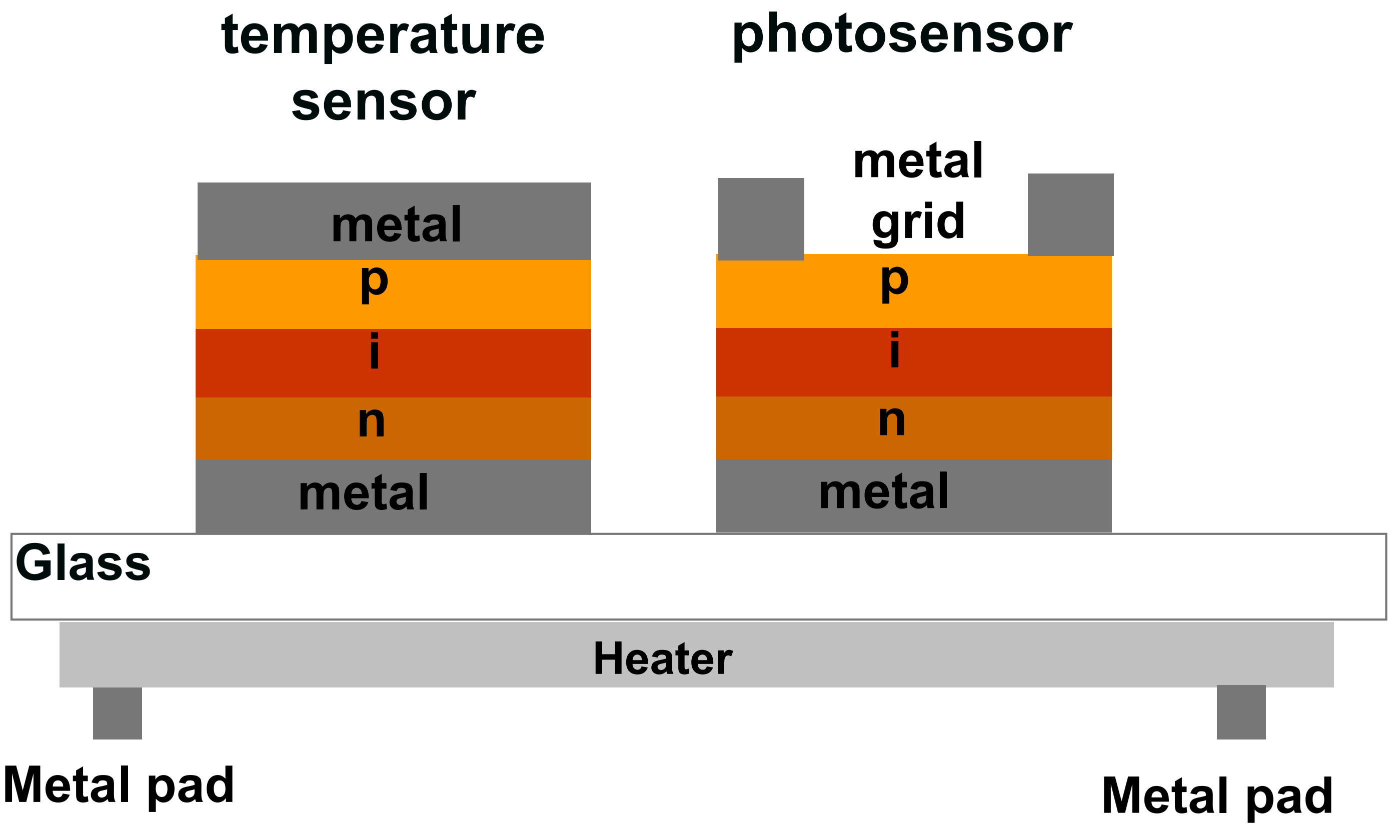


Forward constant current I=10nA

Linear behavior

Challange

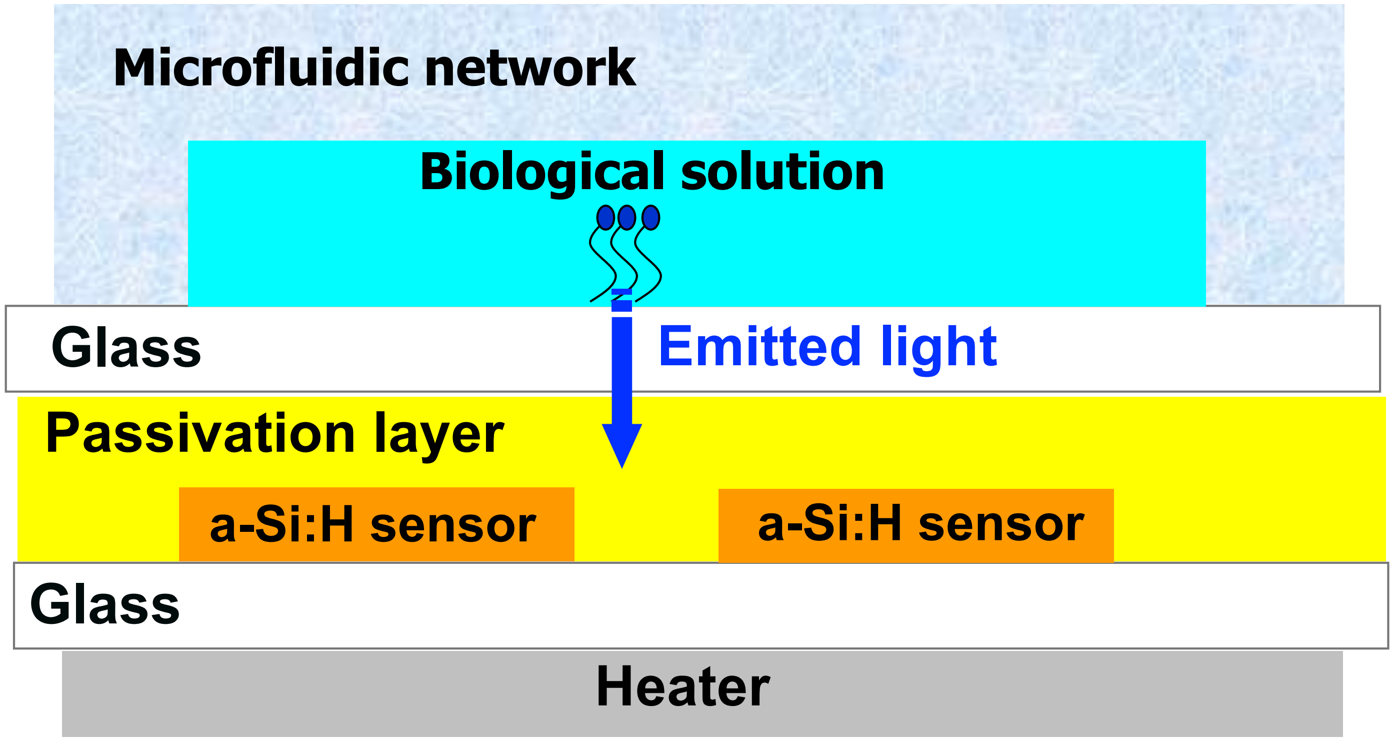
- Integration of heaters and a-Si:H sensors



Another challange….

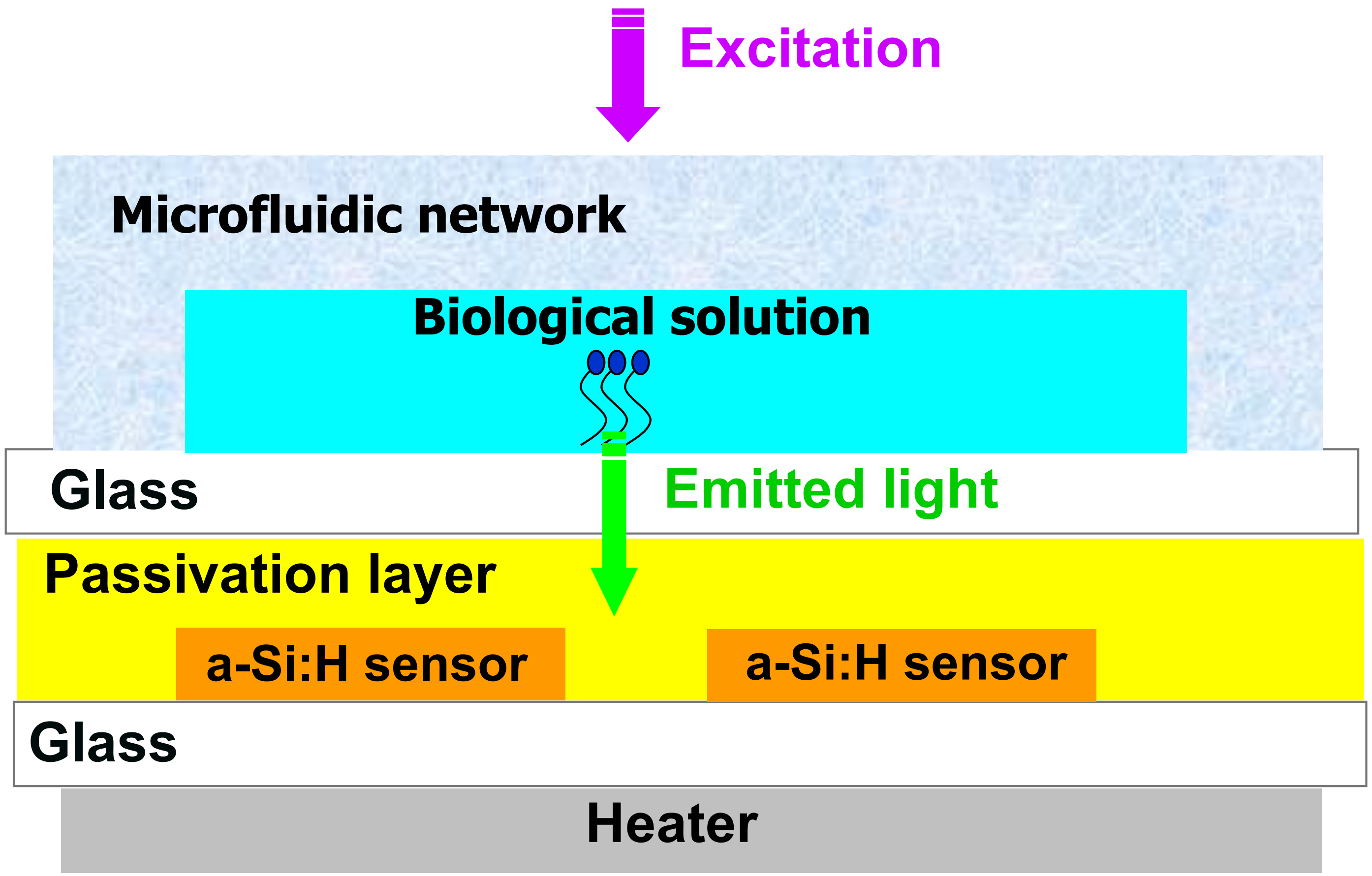
On-Chip
Optical detection

Chemi/bio-luminescence



No optics needed for focusing the emitted light

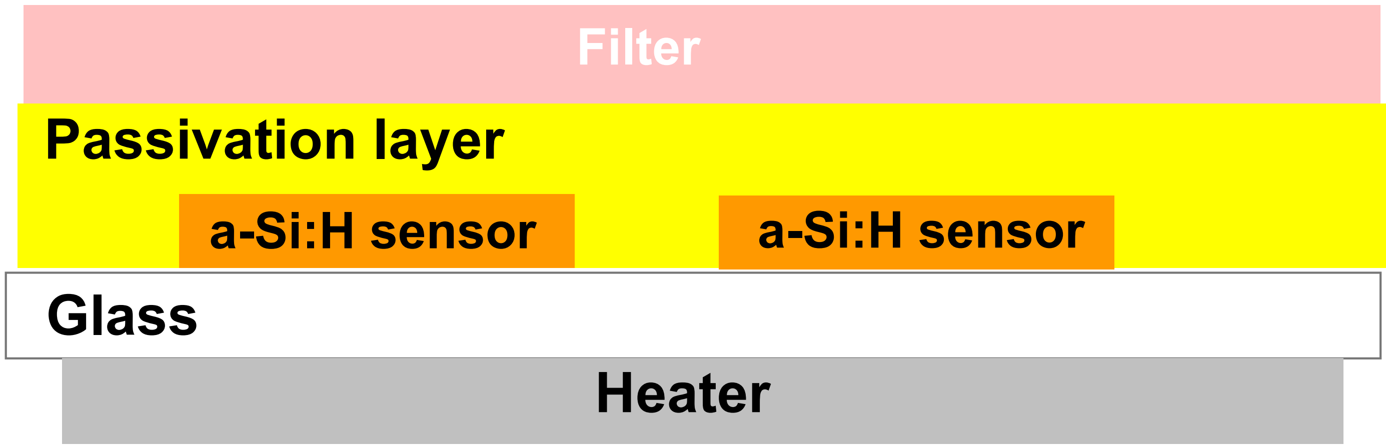
Fluorescence



Need to reject the excitation light

Integration with a filter

- Rejection of the excitation light



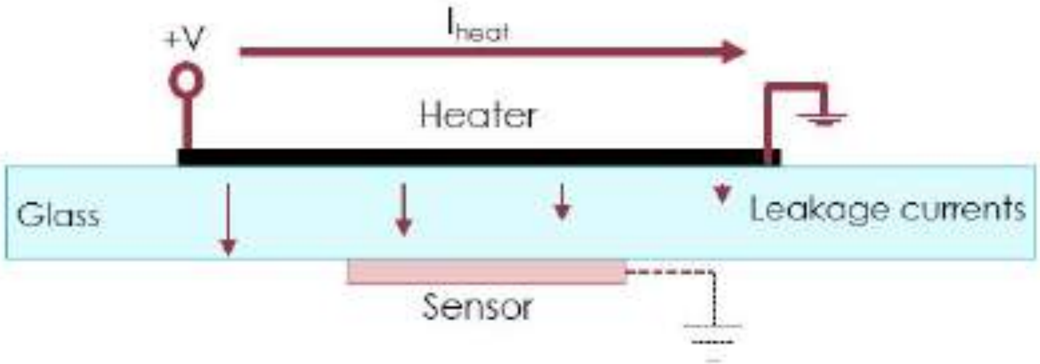
Integration issue

- Compatibility of different technological steps
  - Temperature deposition
  - Choice of materials for selective etching
  - Sequences of technological steps

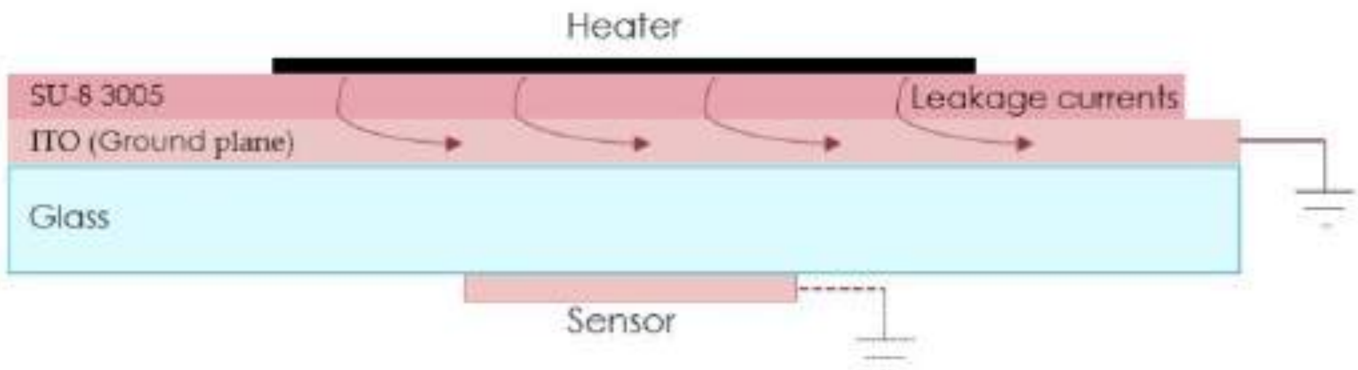
- Cross-talk between different devices
  - Leakage currents
  - Maximum power

Integration issue

Leakage currents through the glass



Solution: ground plane to collect leakage currents



Integration issue

- Filter temperature deposition lower than 200°C
  - Deposition techniques

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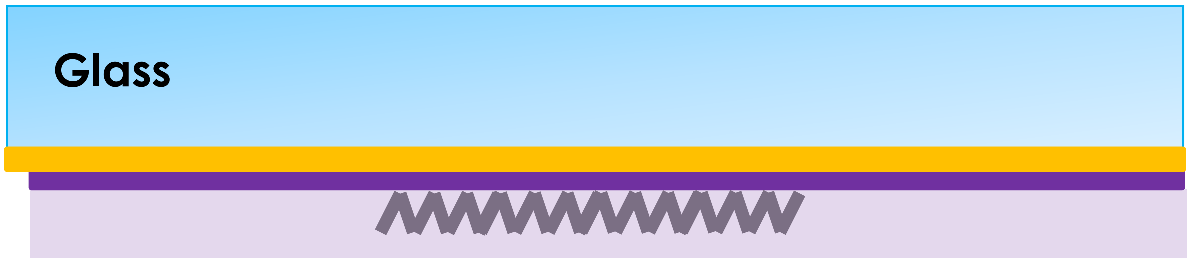
- Electron Beam Physiscal Vapor Deposition at room temperature

Fabrication steps

1) Ground plane (ITO) and passivation (SU-8)

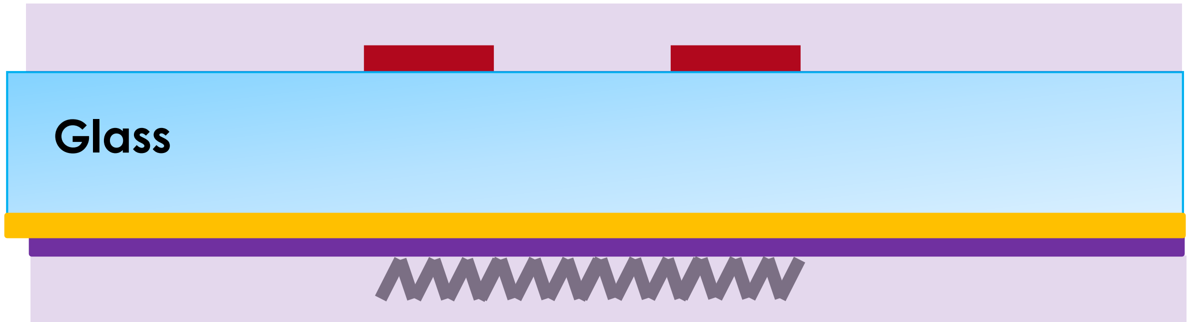
Fabrication steps



1) Ground plane (ITO) and passivation (SU-8)

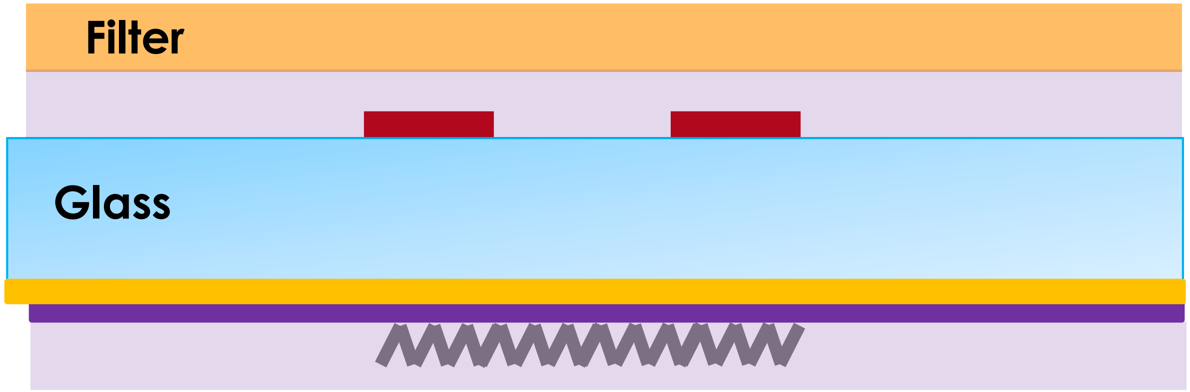
2) Heaters and passivation (SU-8)

Fabrication steps



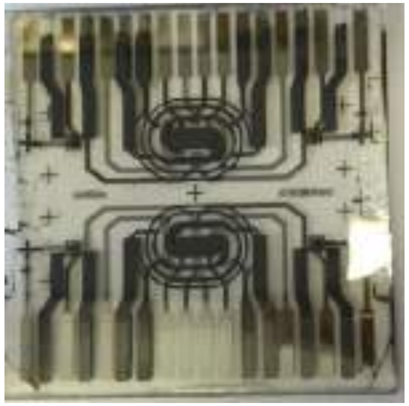
1) Ground plane (ITO) and passivation (SU-8)
2) Heaters and passivation (SU-8)
3) a-Si:H sensors and passivation (SU-8)

Fabrication steps

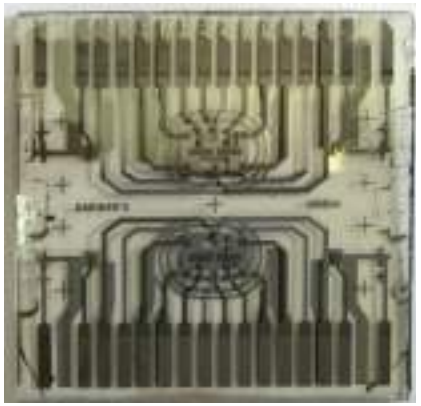


1) Ground plane (ITO) and passivation (SU-8)
2) Heaters and passivation (SU-8)
3) a-Si:H sensors and passivation (SU-8)
4) Filter

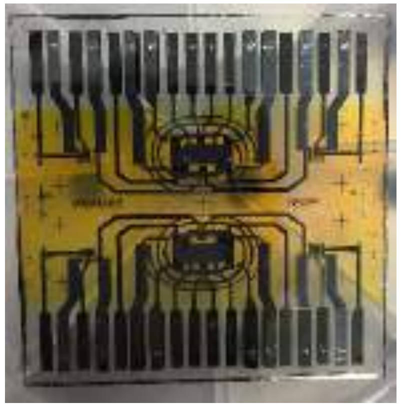
Fabricated optoelectronic platform



Integrated device (heater side)

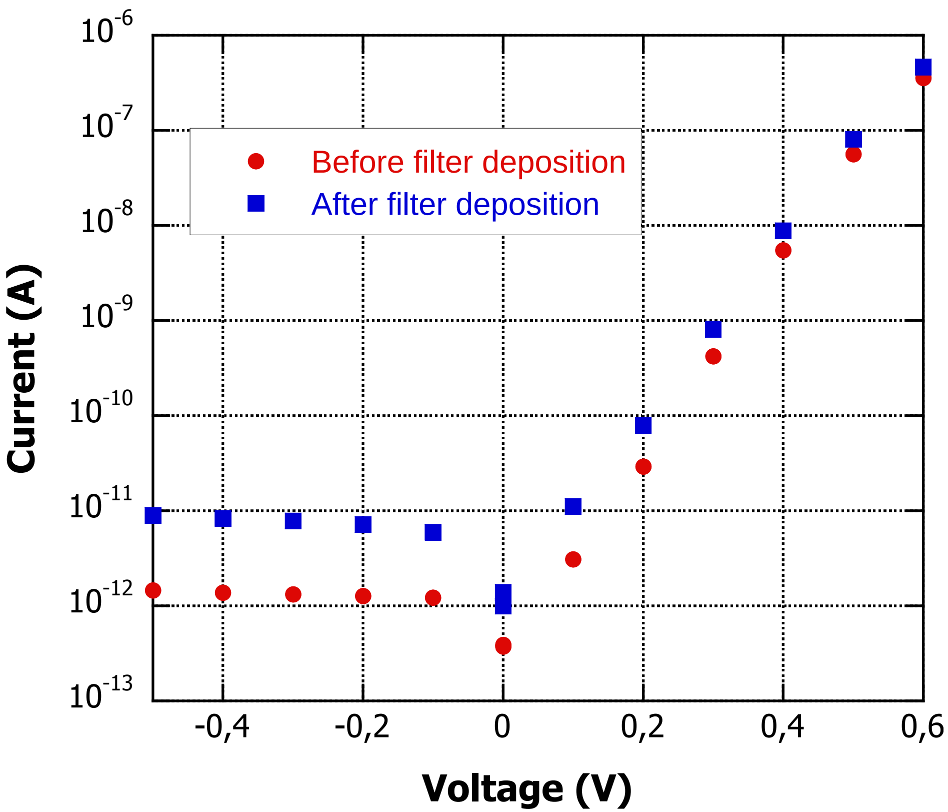


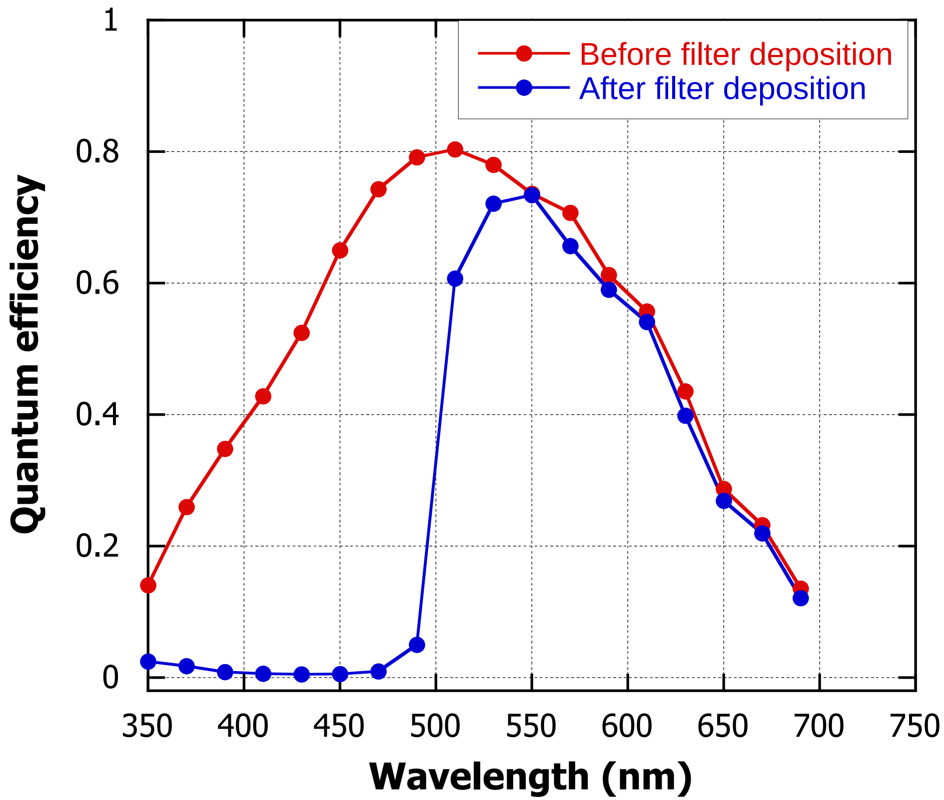
Integrated device (sensor side)



Integrated device+ Filter (sensor side)

Sensor characterization

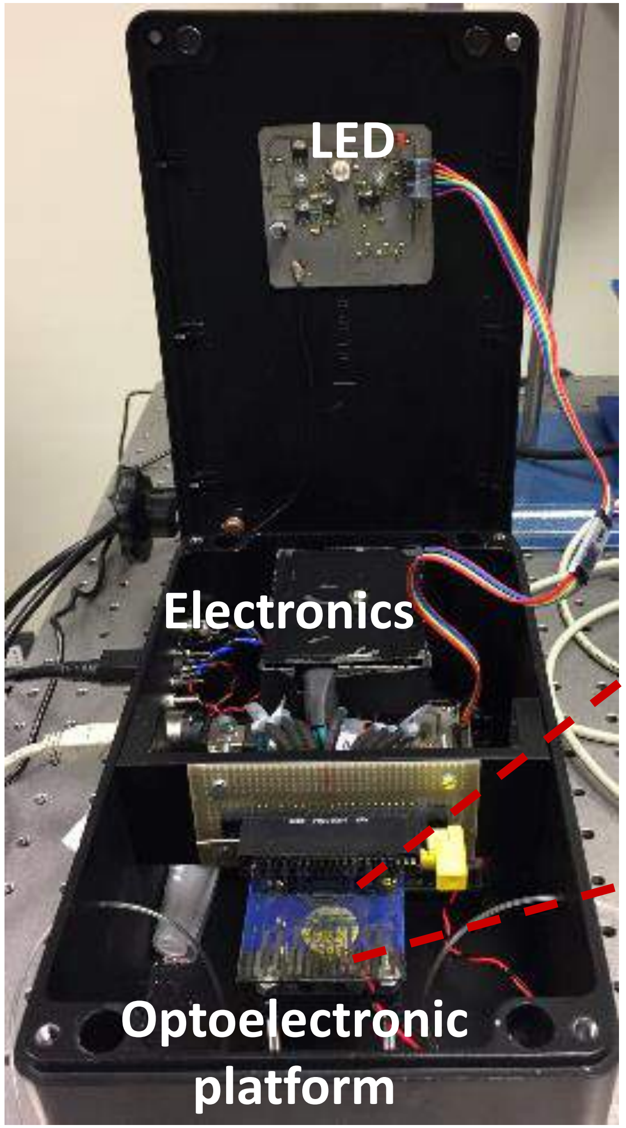


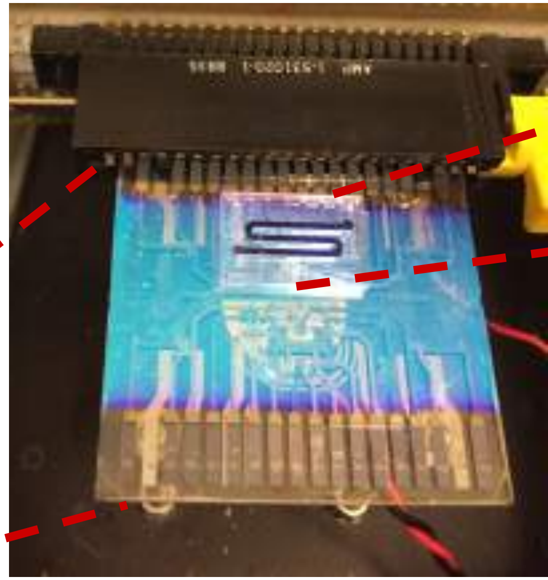


Dark current noise around 10^{-15} A

Rejection of the excitation source

Whole system





Microfluidic network
optically coupled
with the optoelectronic platform

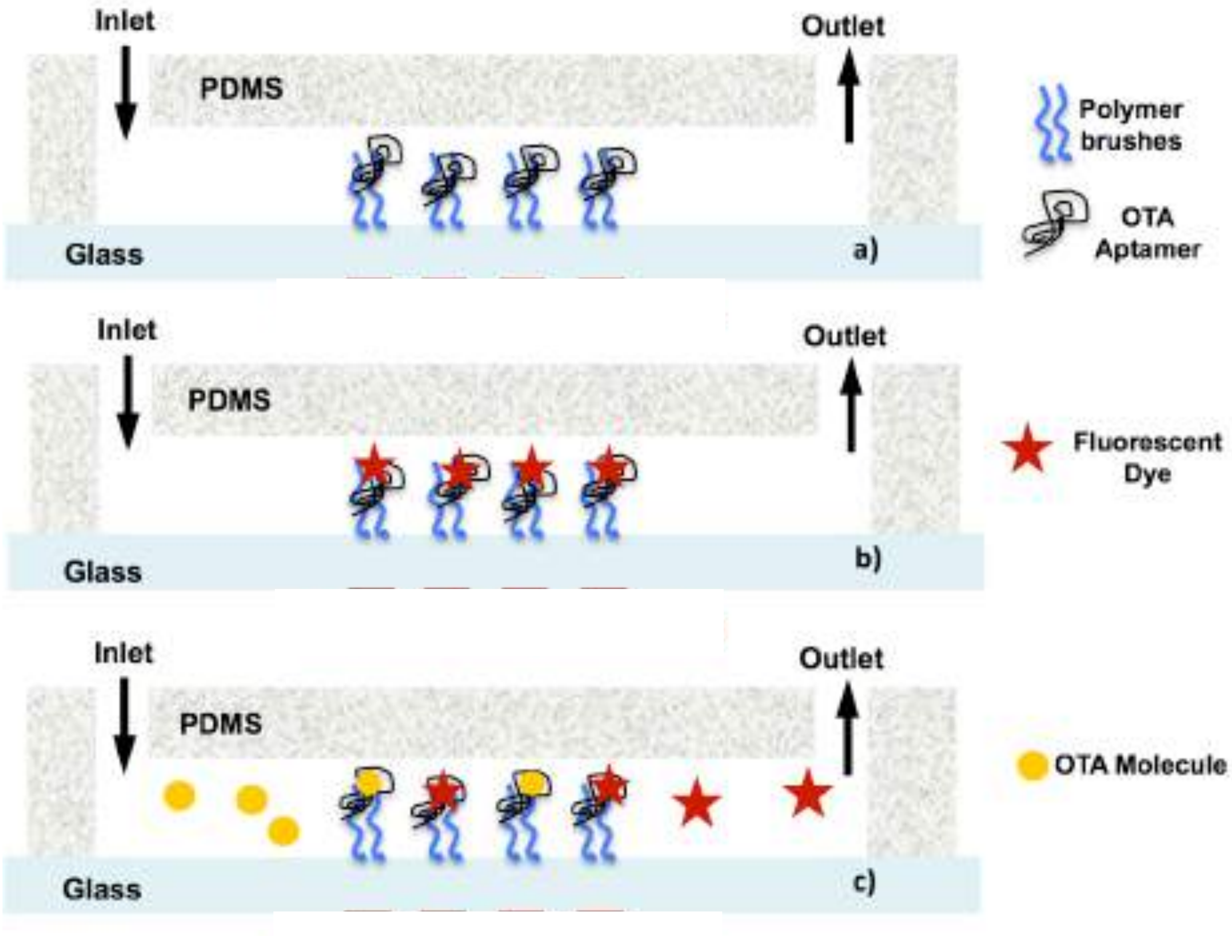
Applications

- Biosensing
  - Mycotoxin

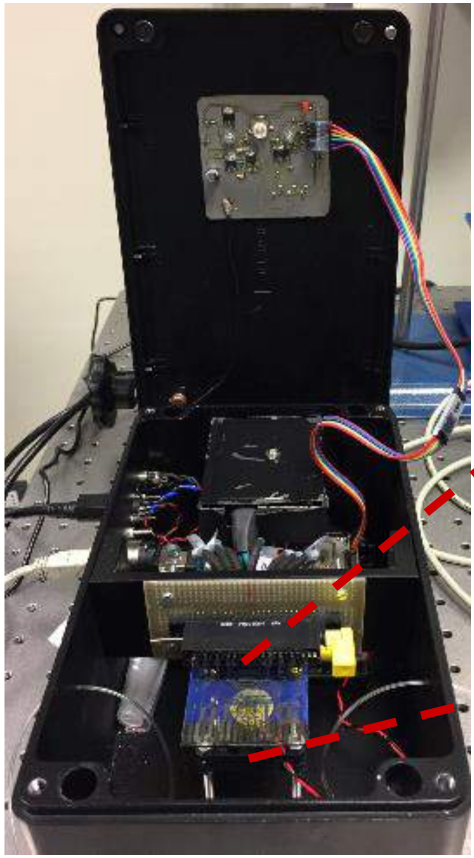
- DNA amplification
  - qPCR
  - Isothermal

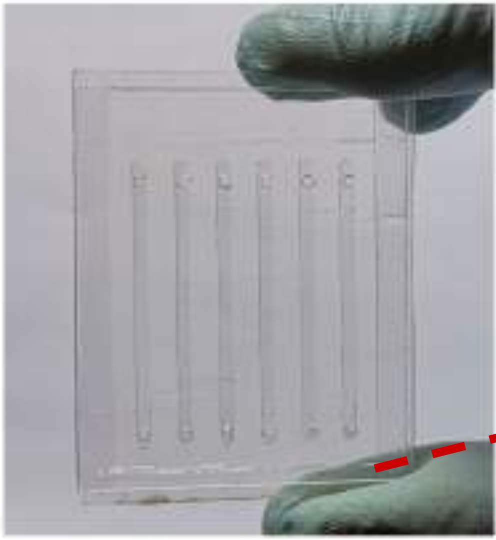
Mycotoxin detection

- Detection of Ochratoxin A (OTA) through aptamer

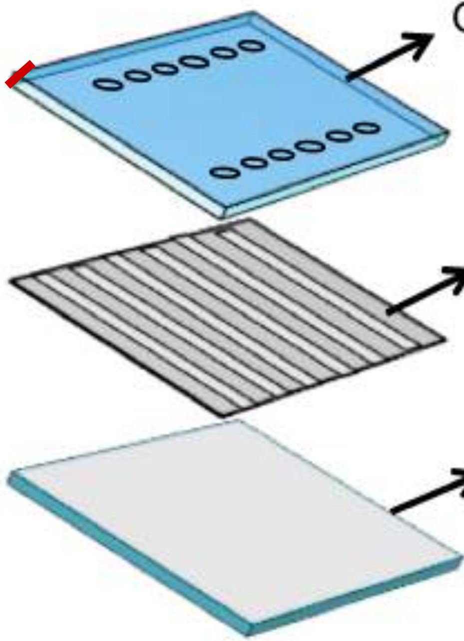


Experimental set-up



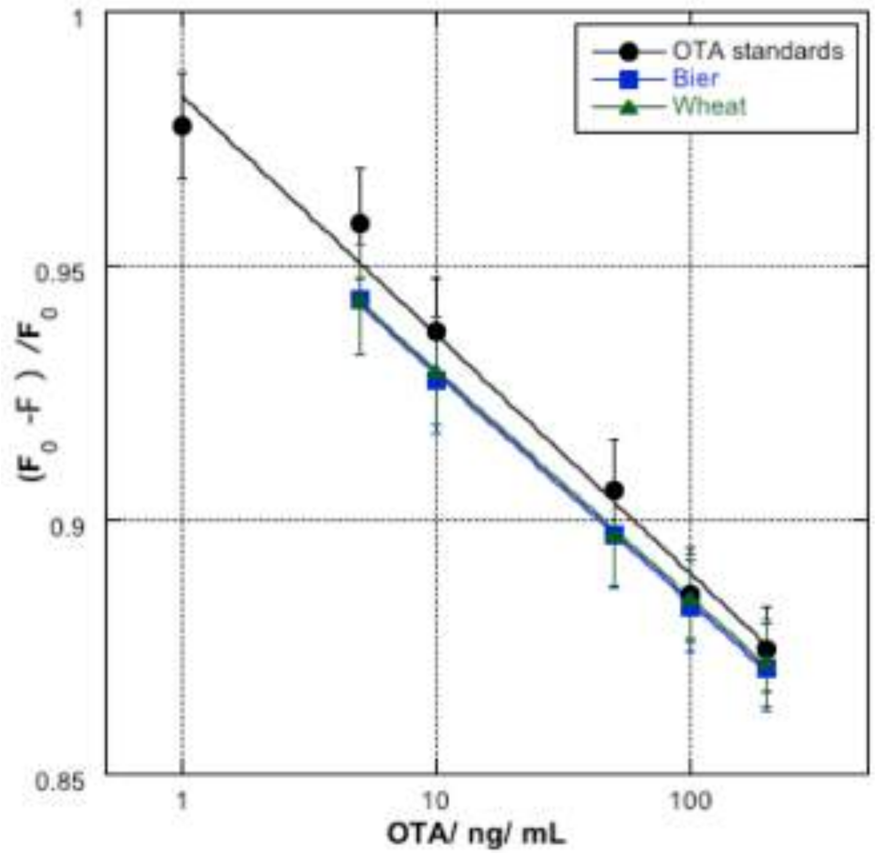


Microfluidic Channels



Results

- Experiments performed on OTA standards and extracts of beer and wine



Limit of detection (LOD)= 1.56ppb

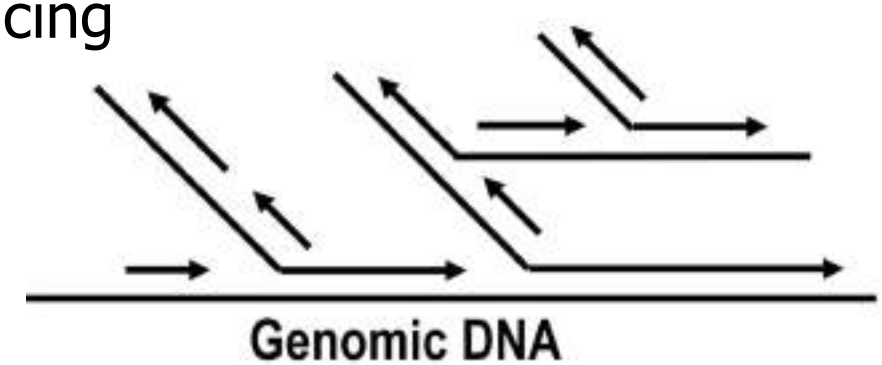
Applications

- Biosensing
  - Mycotoxin

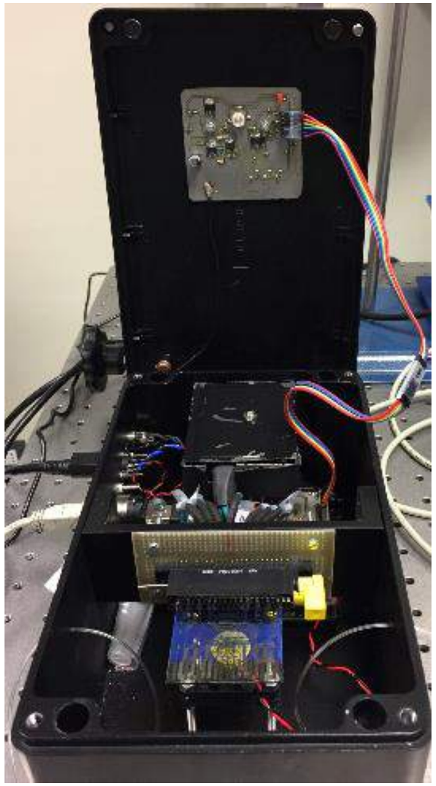
- DNA amplification
  - qPCR
  - Isothermal

Isothermal PCR

- MDA = Multiple Displacement Amplification
  - Isothermal amplification technique (30-35 ° C)
  - From 1-10 DNA copies 20-30 µg DNA can be obtained
  - Application are:
    1. single cell genome sequencing
    2. genetic study
    3. Forensic



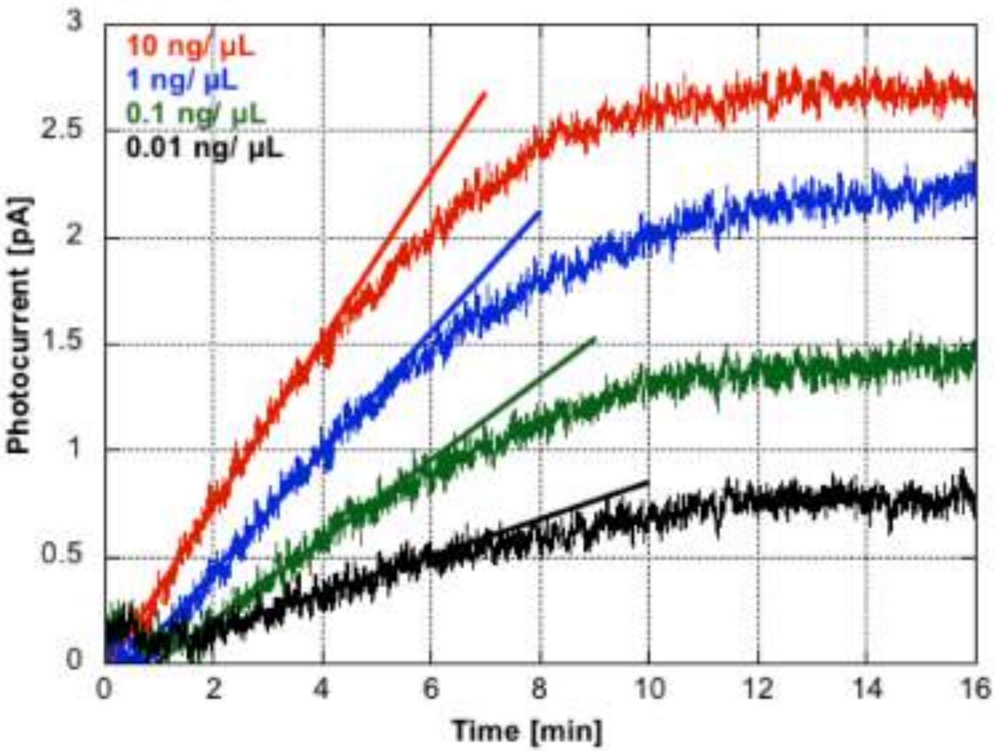
On-Chip Real-Time MDA

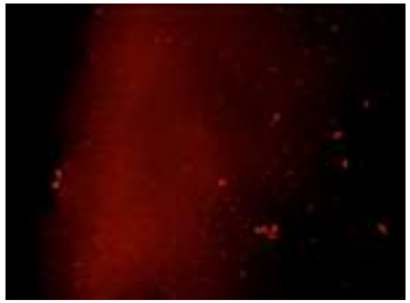


**Microfluidic Channel
optically coupled
with the optoelectronic platform**

Real-Time MDA

- On-chip real-time DNA amplification





DNA 0.5 ng/µL

DNA 0.05 ng/µL

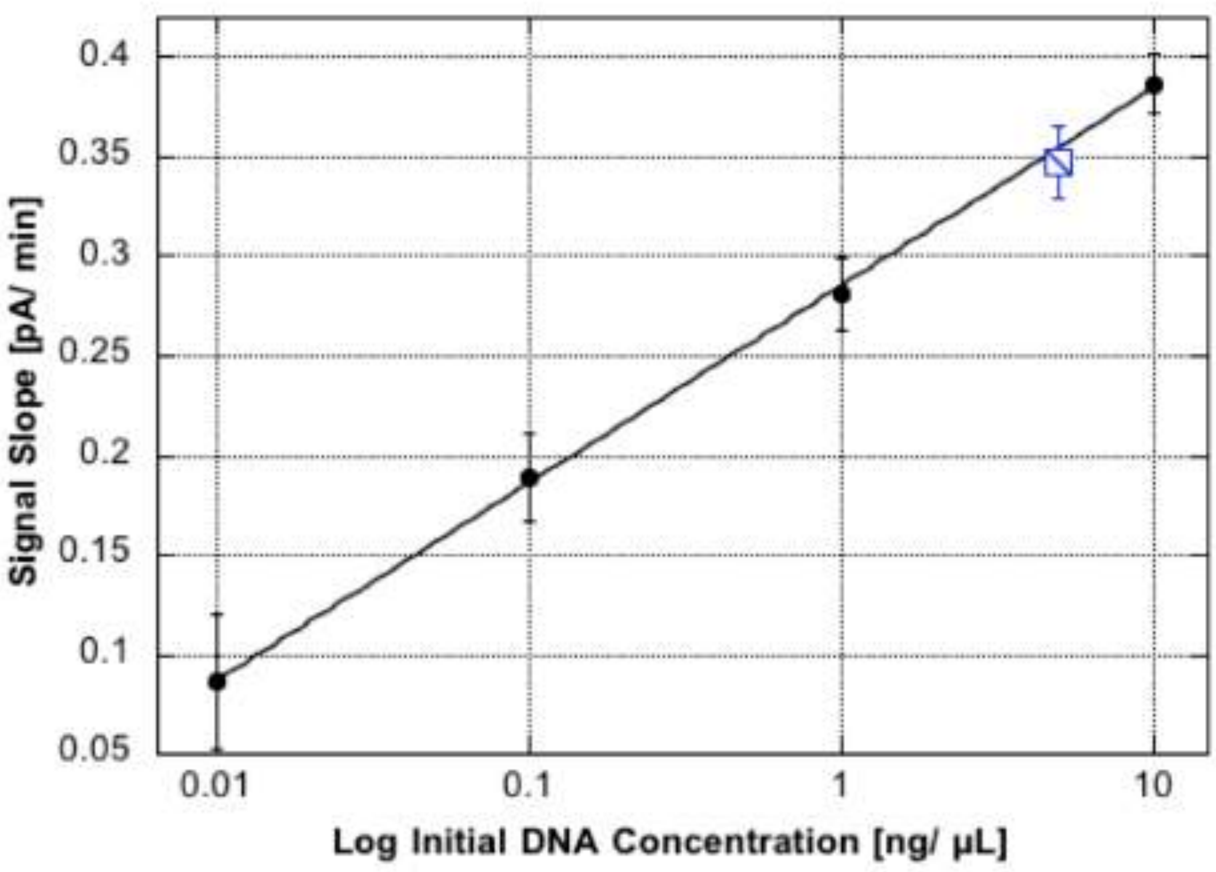
Blank

Water

Sensors and Actuator B: Chemical 293 (2019) 16-22

Real-Time MDA

- On-chip real-time DNA amplification



Sensors and Actuator B: Chemical 293 (2019) 16-22

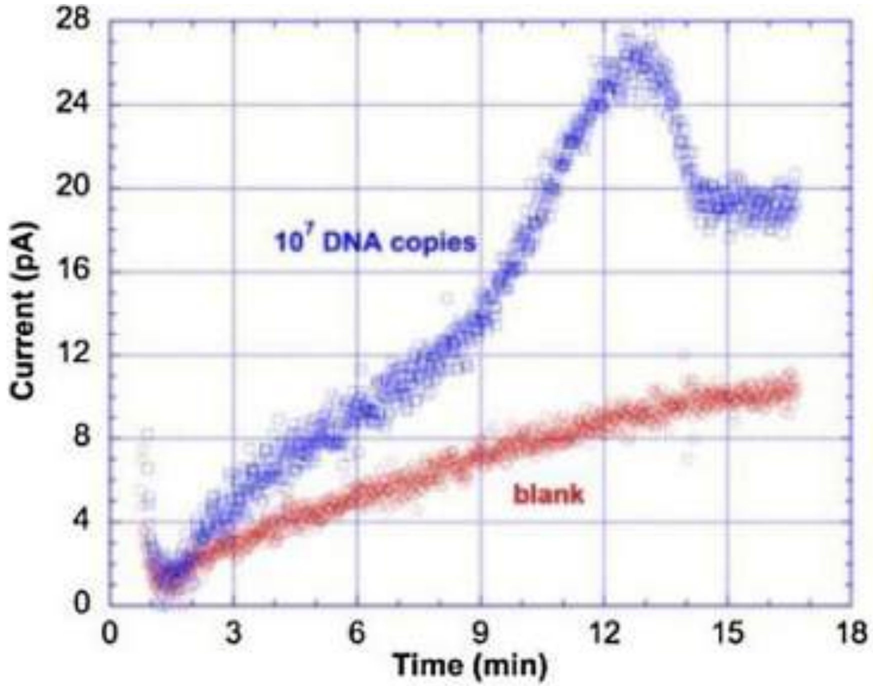
LAMP-BART DNA amplification

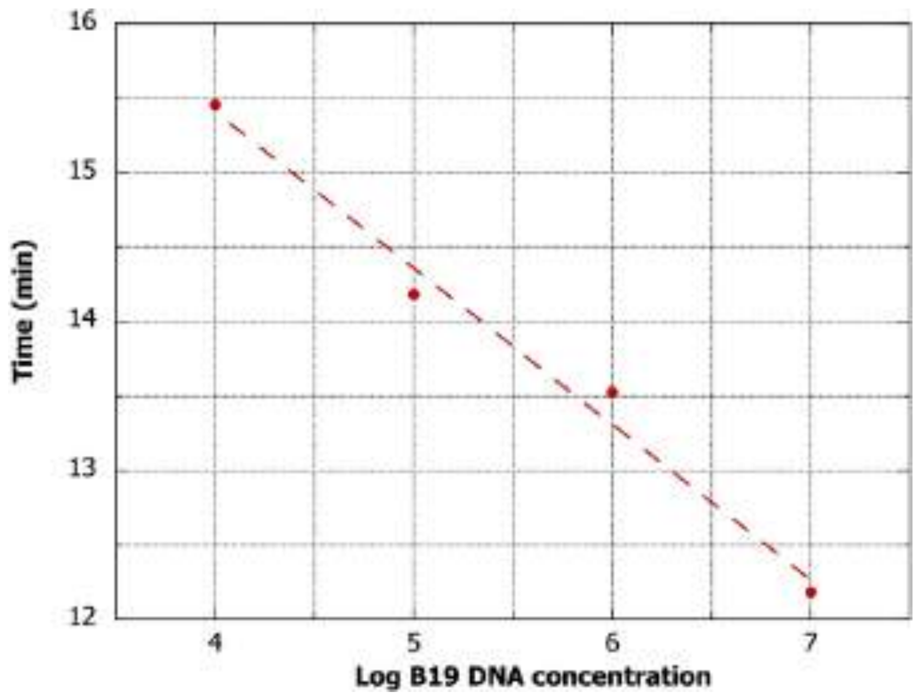
- Loop-mediated isothermal amplification (LAMP) technique was optimized to specifically amplify parvovirus B19 DNA and coupled with Bioluminescent Assay in Real Time (BART) technology to provide real-time detection of target DNA with real time monitoring of T and light

- Optimum T ≈ 65 °C

LAMP-BART DNA amplification

- Peak dependent on the initial amount of DNA





Conclusions

- Design and fabrication of lab-on-chip based on thin film optoelectronic devices
- Integration with microfluidic networks, whose internal walls have been chemically functionalized
- Application in diagnostics, clinical and agrofood fields
- Collaboration with chemists, biologists and physicians: **interdisciplinarity**