



SAPIENZA  
UNIVERSITÀ DI ROMA

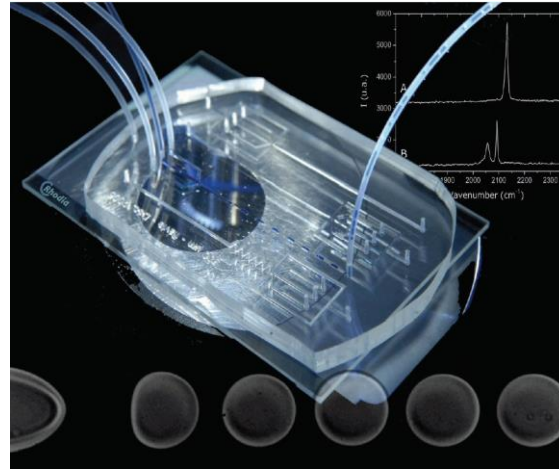
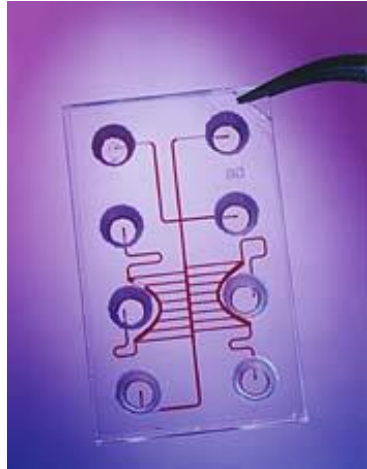
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# Lab-on-Chip systems for diverse analytical applications

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Dr. Francesca Costantini

# What is a Lab-on-Chip System?



## Microfluidic Channel

Micro/  
Nanofabrication

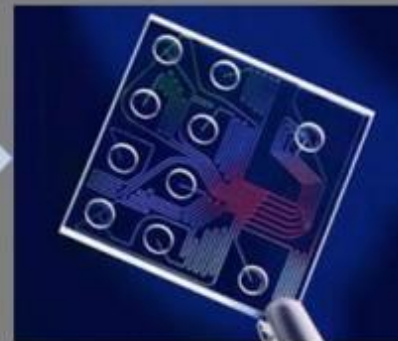
## Microfluidic Chip

Integration of heating  
and detection systems,  
Temperature control  
and samples pretreatment

## Microreactor and Lab-on-Chip Systems



Miniaturization  
Autonomy  
Integration



Agilent Tech., Inc.

# Lab-on-Chip

## Conventional approach

- High reproducibility and low limit of detection
- Number of large-scale equipment: no portability
- Requirement to make measurements in a laboratory
- Large time consuming
- High quantities of samples and reagents



## Lab-on-Chip approach

- Low fluid volume consumption (less waste, low reagents costs and less sample volume to analyze)
- Compactness of the system due to integration of much functionality ensuring analysis directly in the field (portability)
- Massive parallelization due to compactness, which allow high through-put analysis
- Novel technology not fully developed: less sensitive detection systems



# Microfluidic Applications in (bio)-Chemistry

## Microfluidic Chips for Chemistry: Microreactors

- Non-catalytic reactions
- homogenous and **heterogeneous catalytic reactions**
- photochemical reactions
- gas-phase reactions
- hazardous reactions

Lab-on-Chips for  
Industrial Chemistry

## Microfluidics for Molecular Biology: Lab-on-Chip

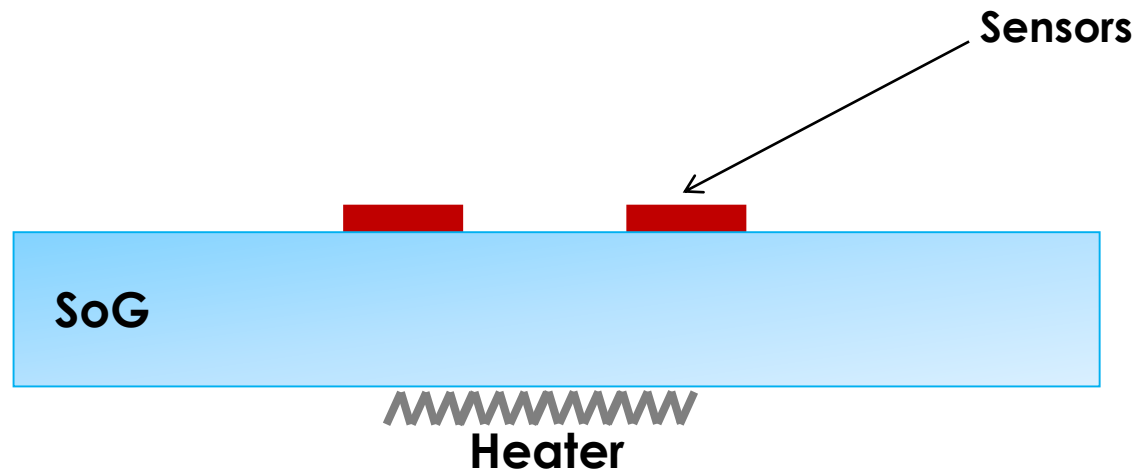
- **PCR**
- electrophoresis
- **biosensing** (immunosensors, DNA sensors)
- **sample pre-treatments**
- cell on-chip
- organ on-chip

Lab-on-Chips for  
Health-care and diagnostics

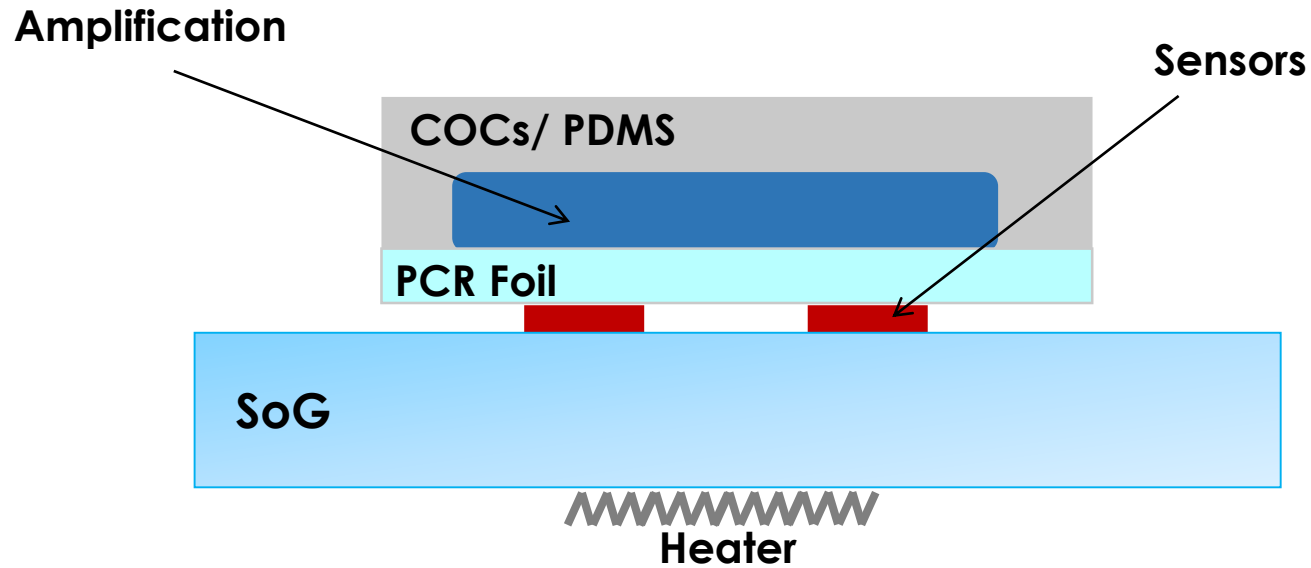
# PCR on a chip

# System-on-Glass for DNA Amplification

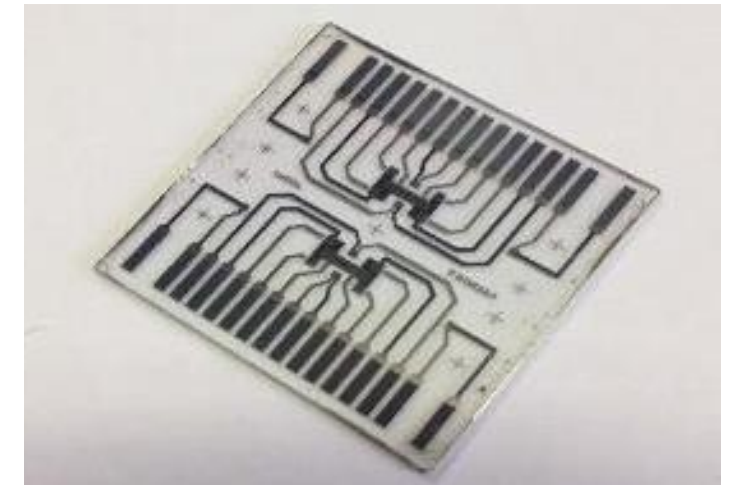
- **Multifunctional platform** integrating on a single glass substrate thin film technologies for
  - ❑ Thermal treatment (thin film heaters)
  - ❑ On-chip detection (amorphous silicon diodes)



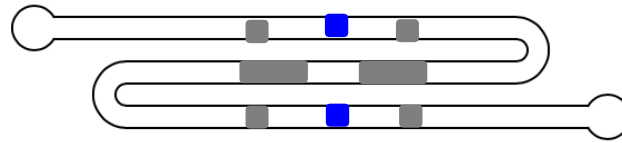
# Coupling with Microfluidics



COCs= cyclic olefin copolymers

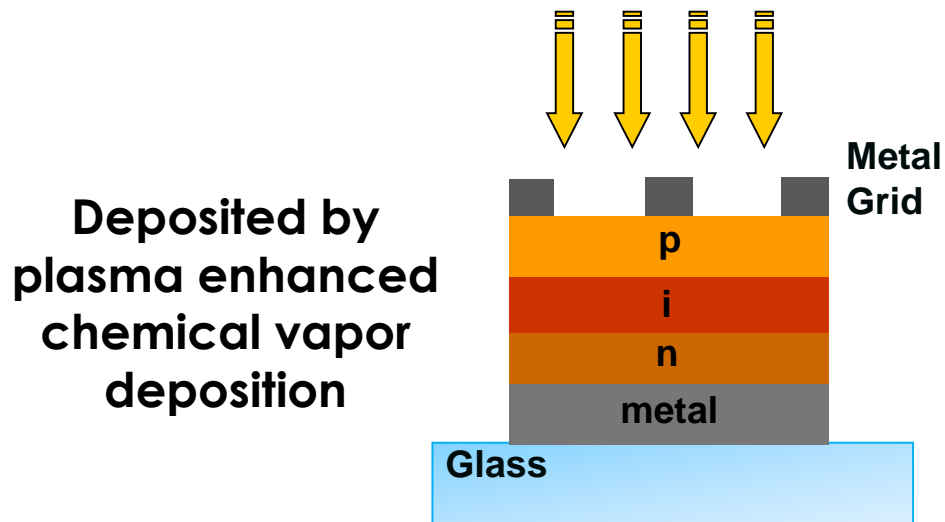


# Amorphous Silicon Diodes ( $\alpha$ -Si:H)

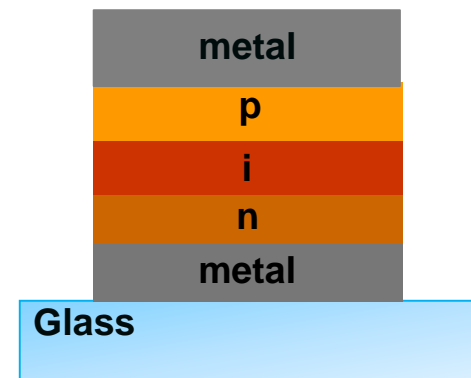


Temperature sensors: ■ (800 x 800  $\mu\text{m}^2$ )

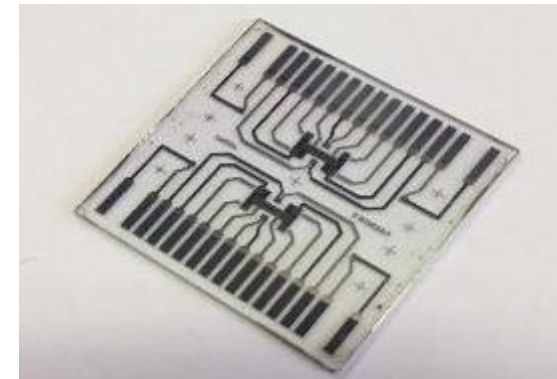
Photosensors: ■ (1100 x 1100  $\mu\text{m}^2$ ) ; ■ (3150 x 1100  $\mu\text{m}^2$ )



$\alpha$ -Si:H photosensor



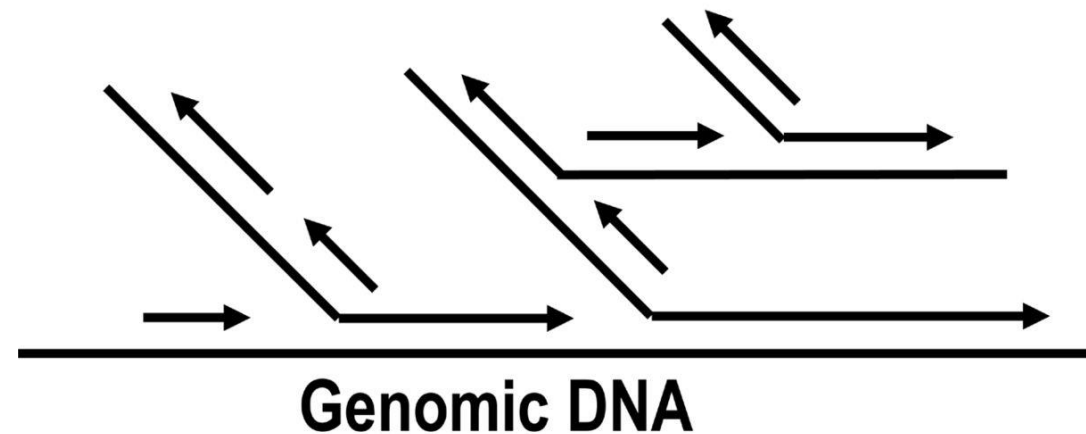
$\alpha$ -Si:H temperature sensor



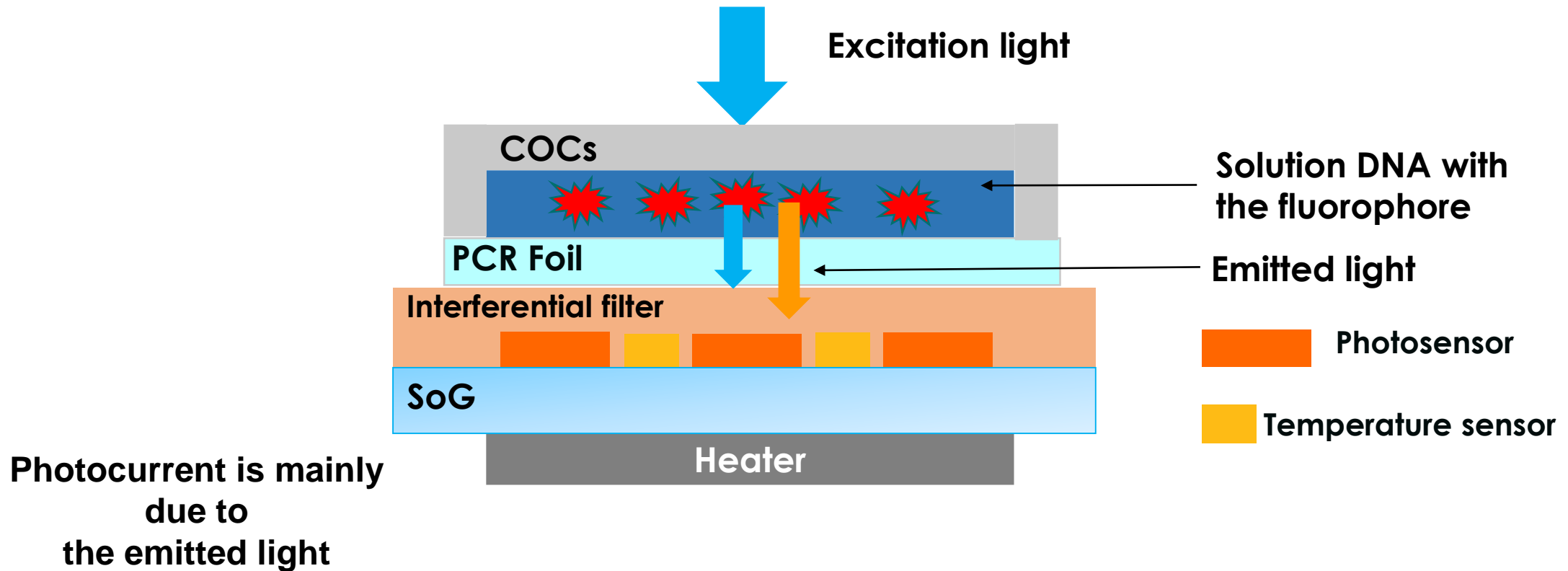


# Isothermal PCR

- 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

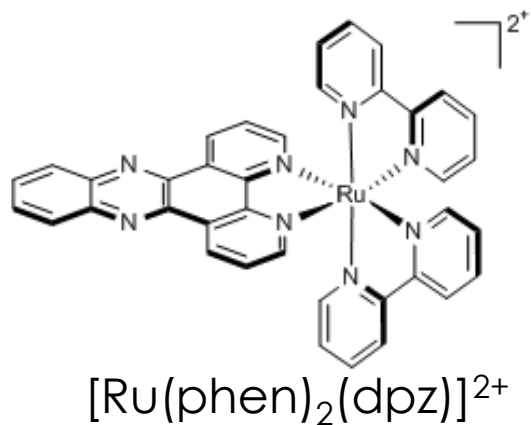


# System-on-Glass for Real-Time MDA

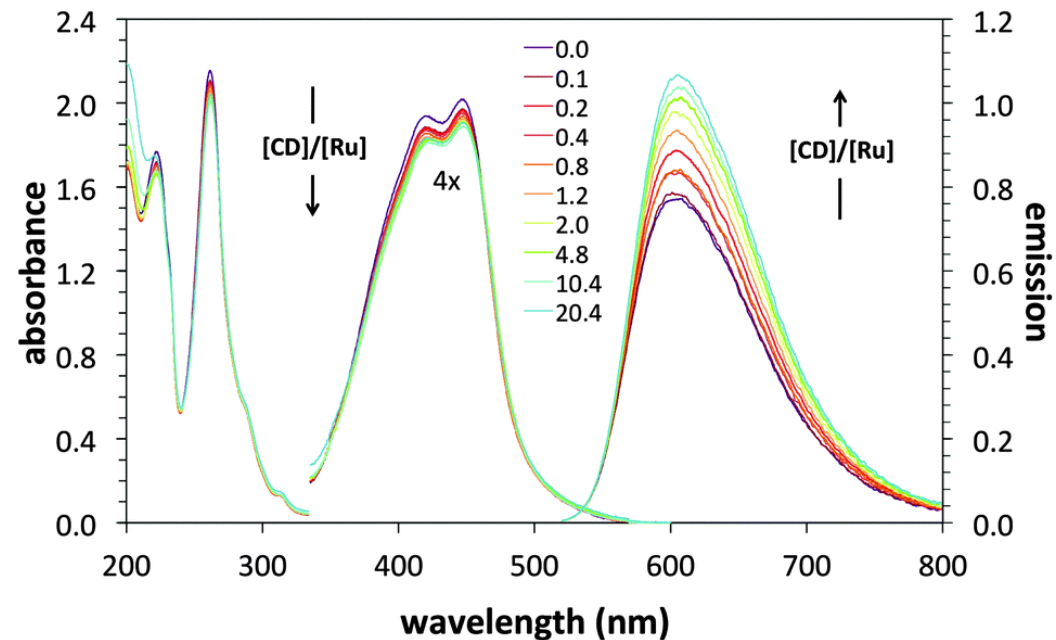


{IEEE} Trans. Biomed. Circuits Syst. **2018**, 12, 6, 1337-1344.

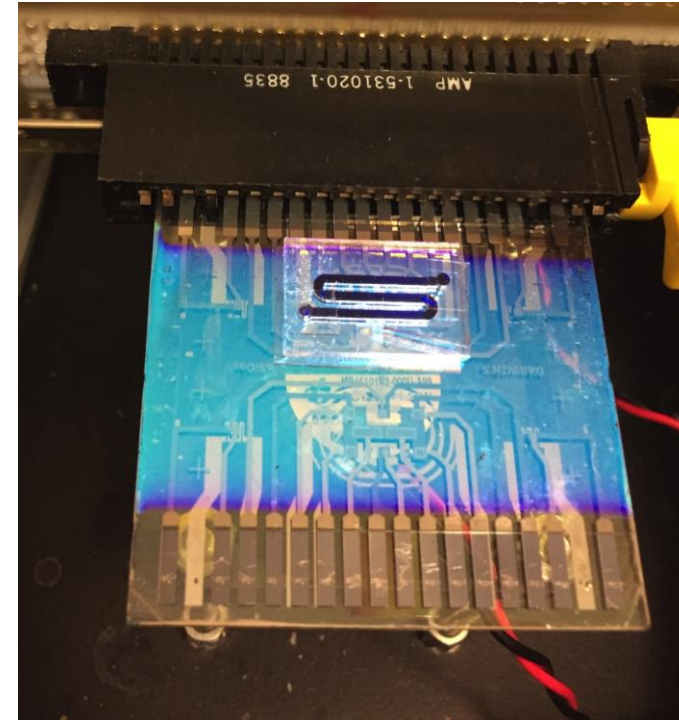
# System-on-Glass for Real-Time MDA



Ex: 450 nm, Em: 610 nm

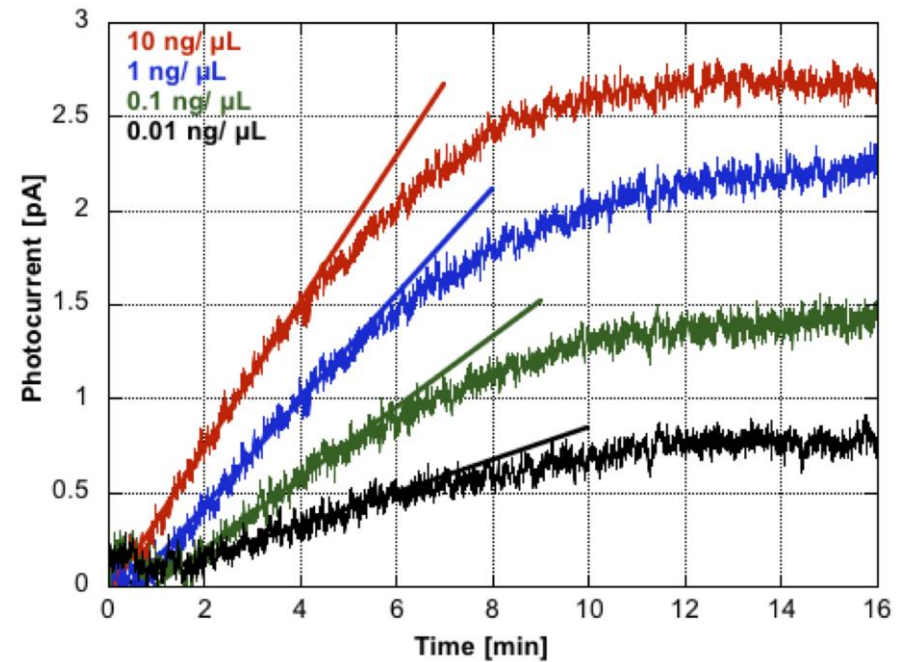
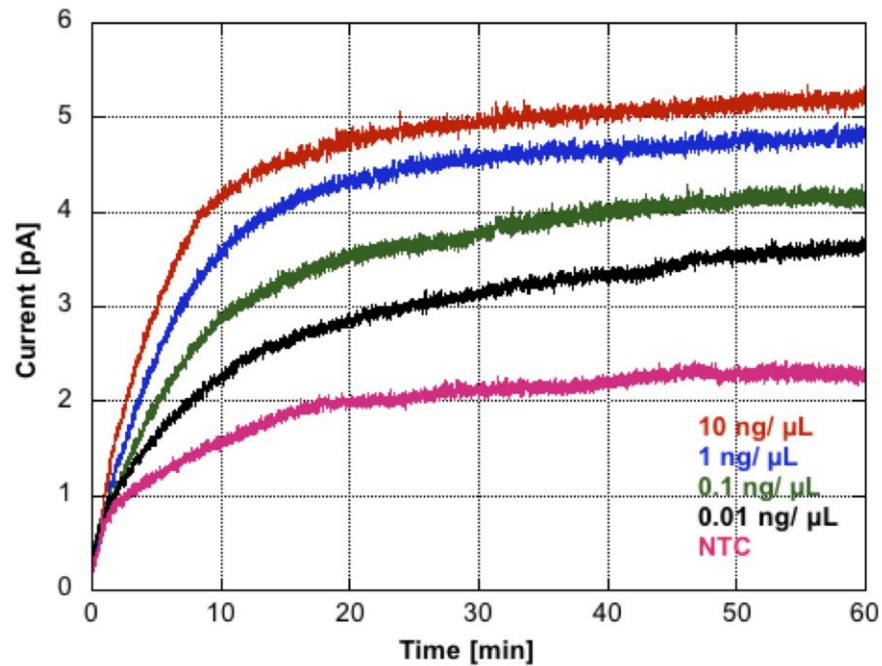


# On-Chip Real-Time MDA



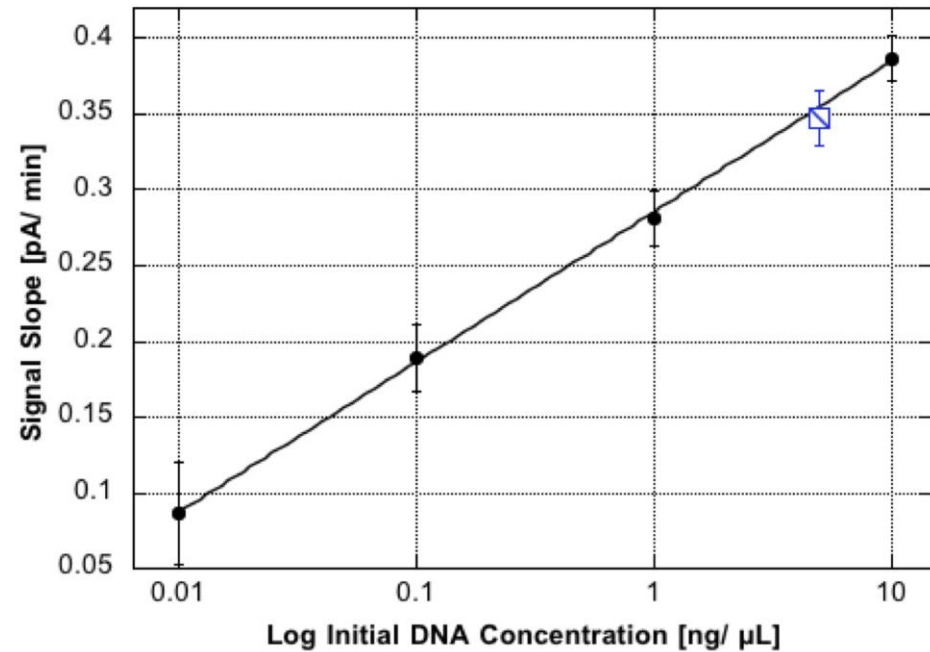
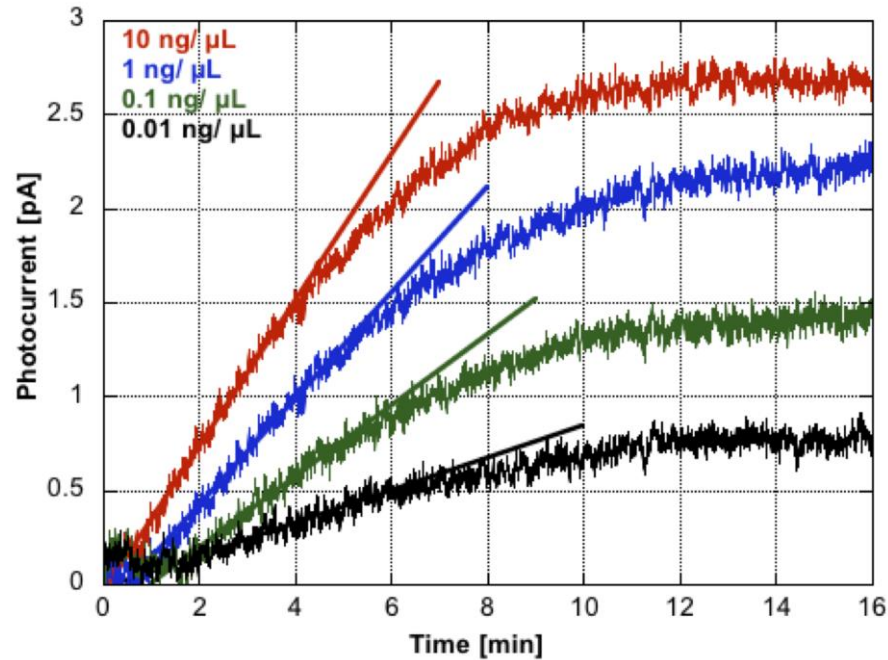
**Microfluidic Channel  
optically coupled  
with the System-on-Glass**

# Real-Time MDA



Please DO NOT take photographs.

# Real-Time MDA



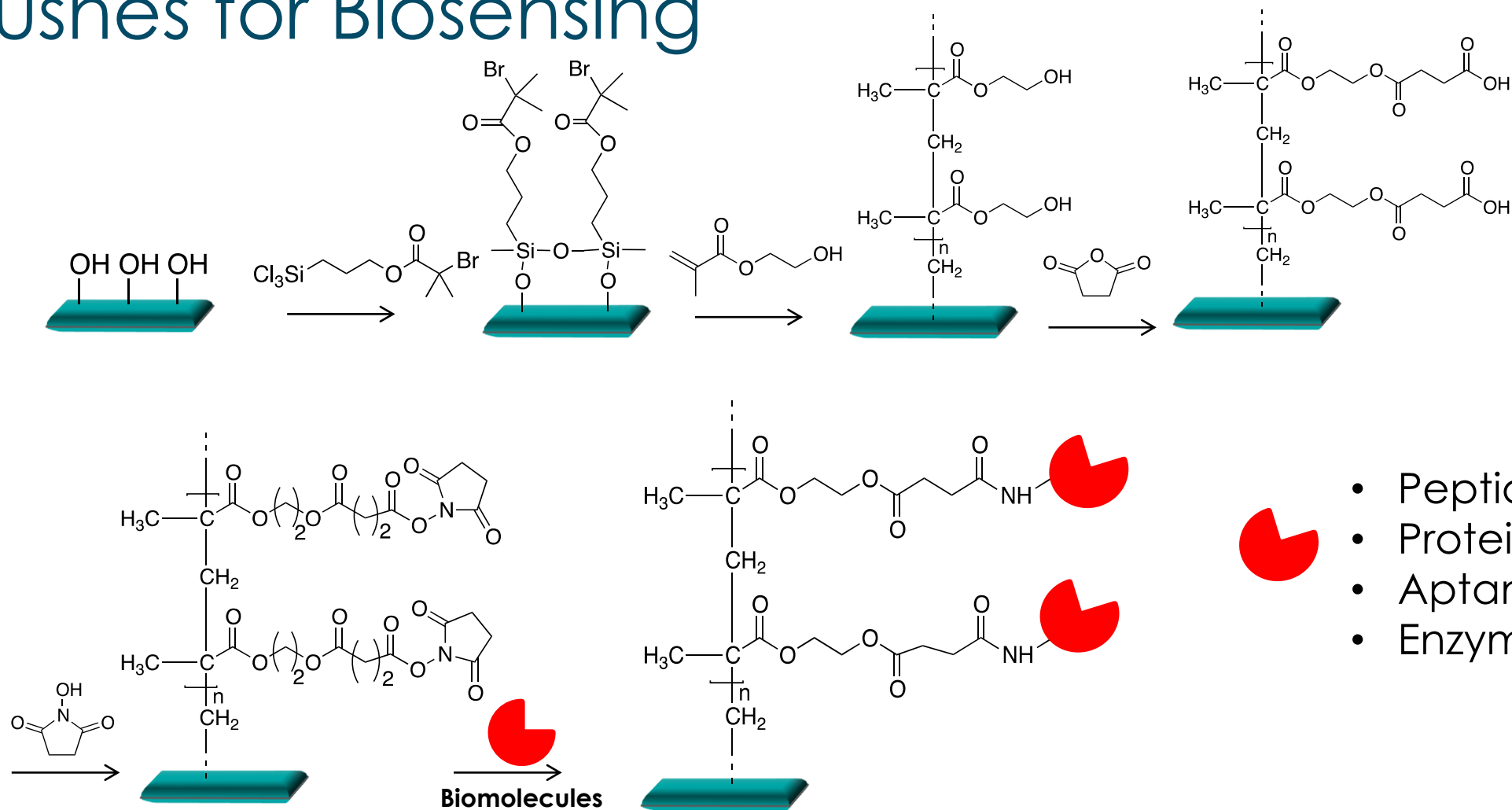
*Not published results*



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# Mycotoxin biosensing

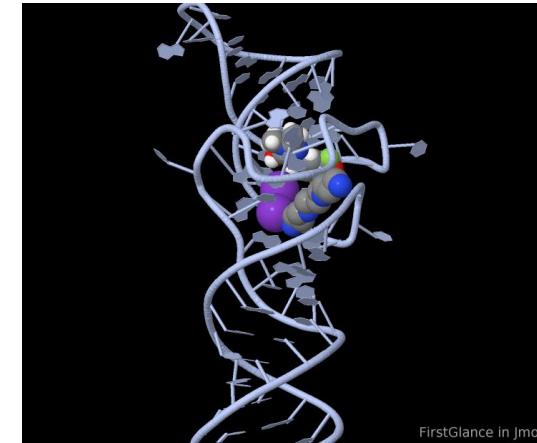
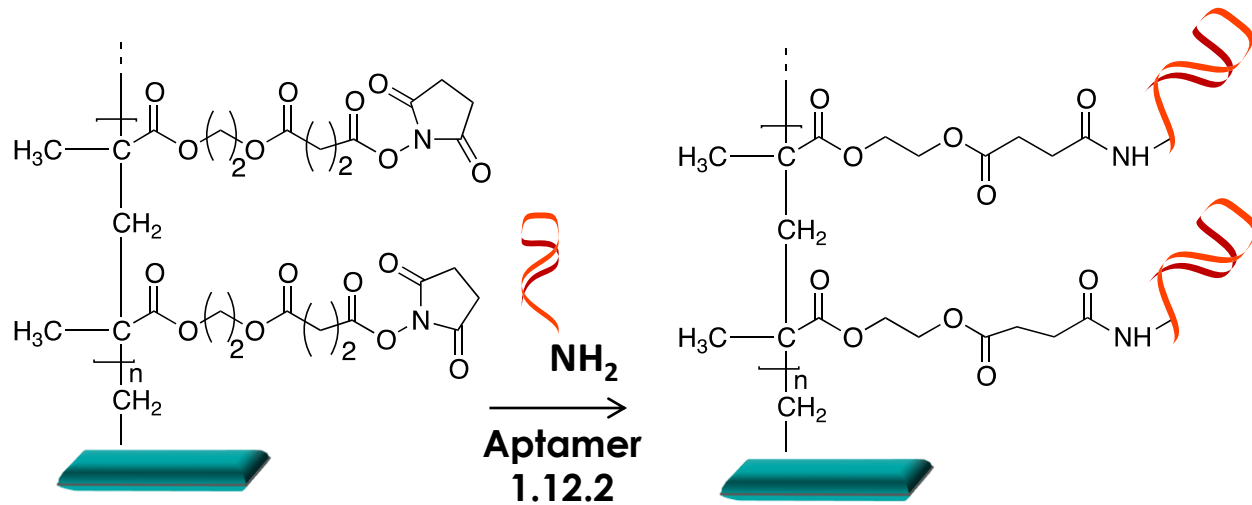
# PHEMA (polidrossietilmetacrilato) Polymer Brushes for Biosensing



- Peptides
- Proteins
- Aptamers
- Enzymes



# PHEMA Brushes for Aptamer Assays

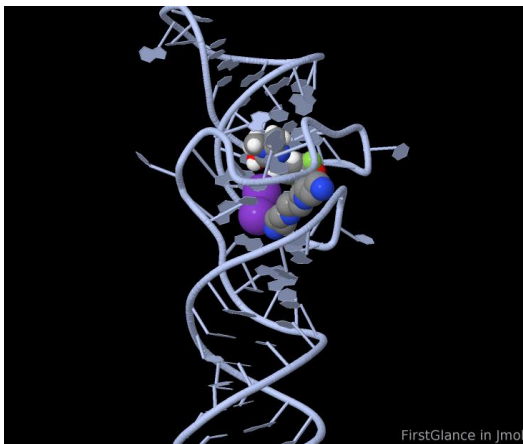
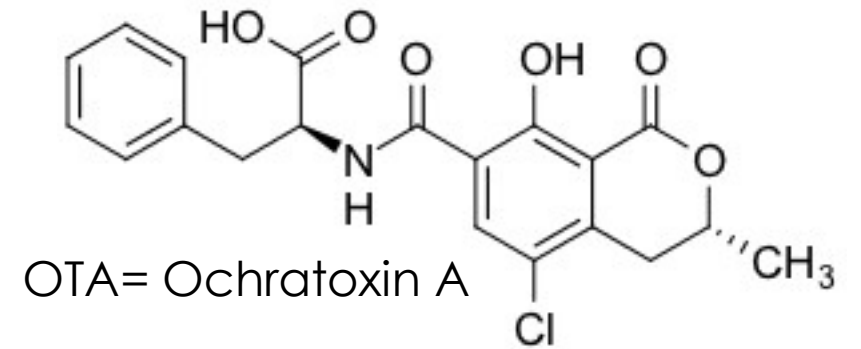
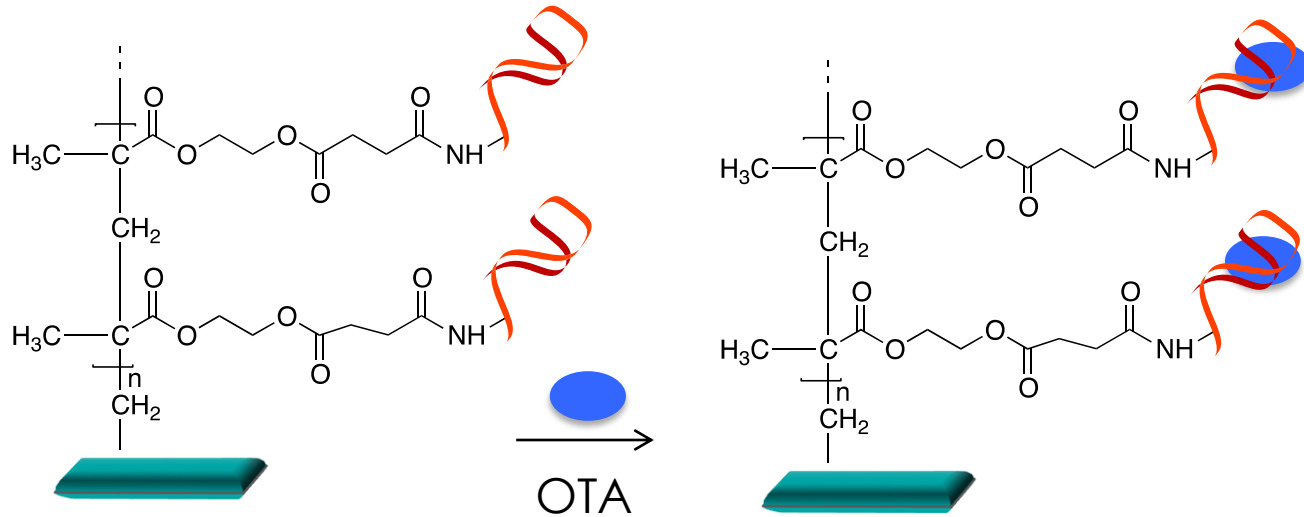


# Aptameri

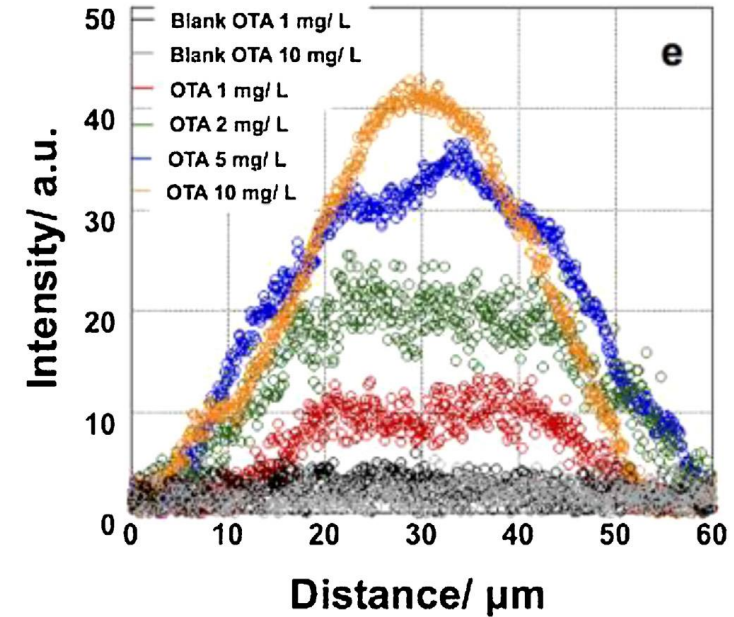
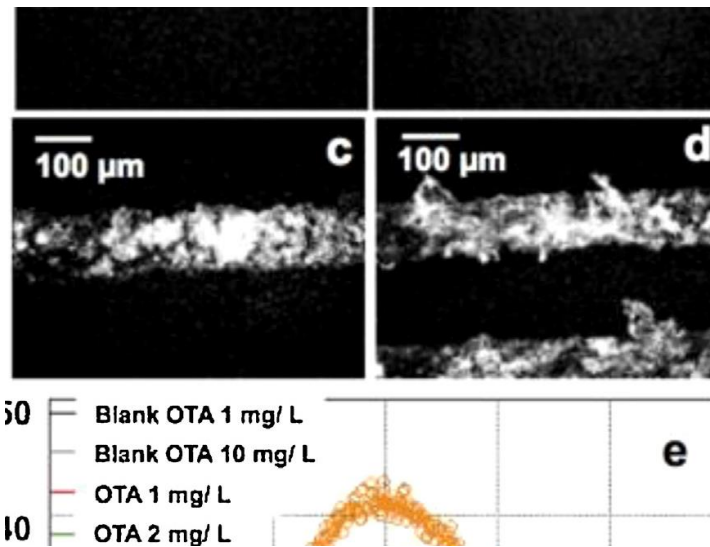
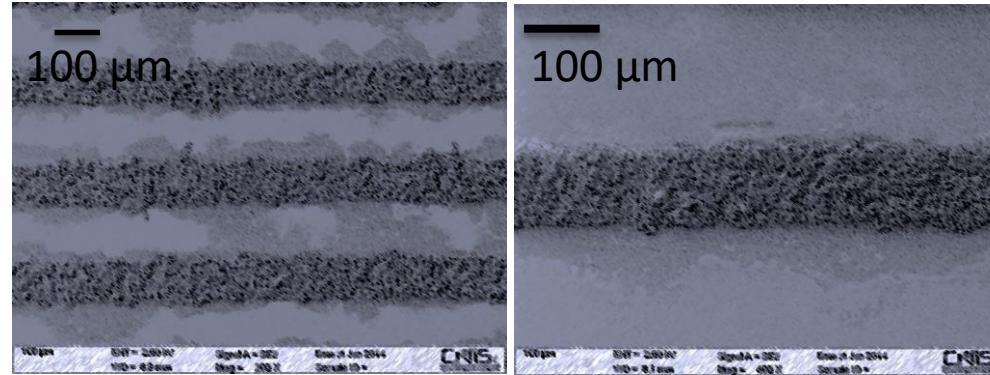
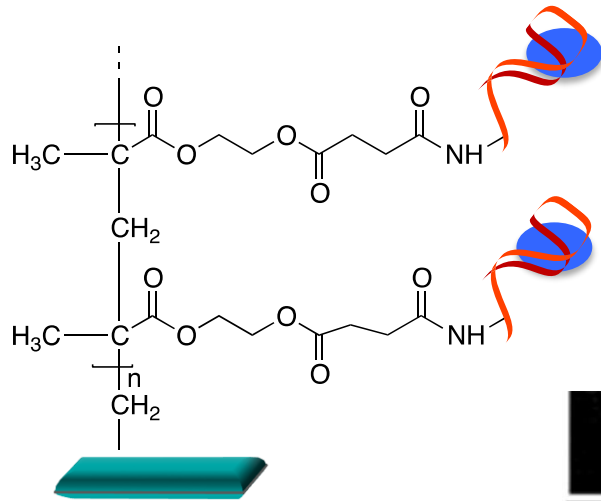
Corte sequenze oligonucleotidiche di DNA o RNA a singolo filamento in grado di legarsi con elevata selettività a diversi target che possono essere macromolecole di origine organica, inorganica o biologica ( $K_d$  simili a quelle degli **ANTICORPI**)



# PHEMA Brushes for Aptamer Assays



# PHEMA Brushes for Aptamer Assays



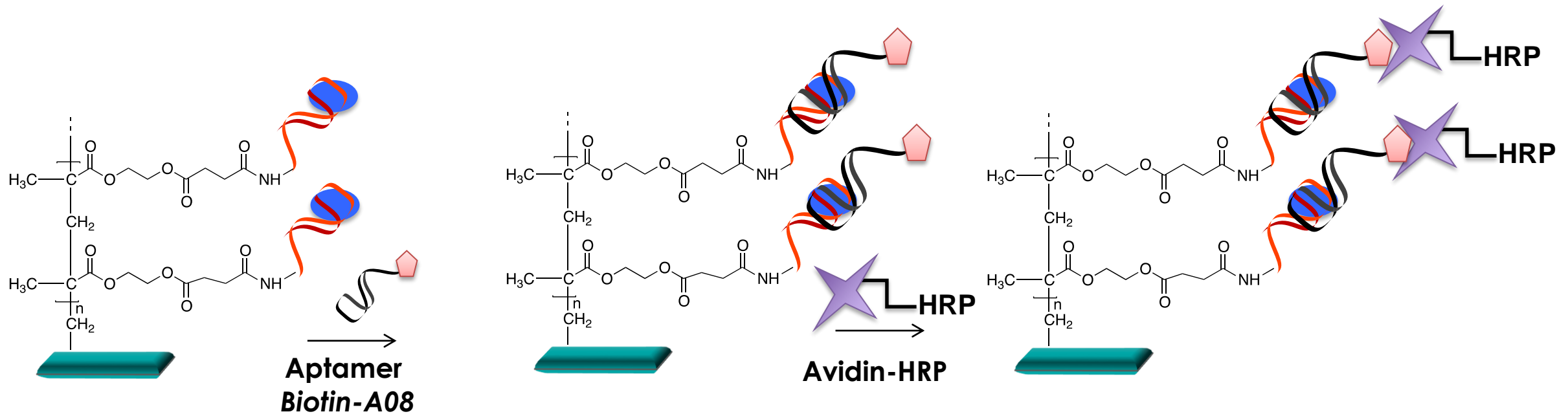
F. Costantini et al., *Sensors and Actuators B*, 230 31–39, 2016

Congresso Micotossine, Roma 10 Giugno 2019

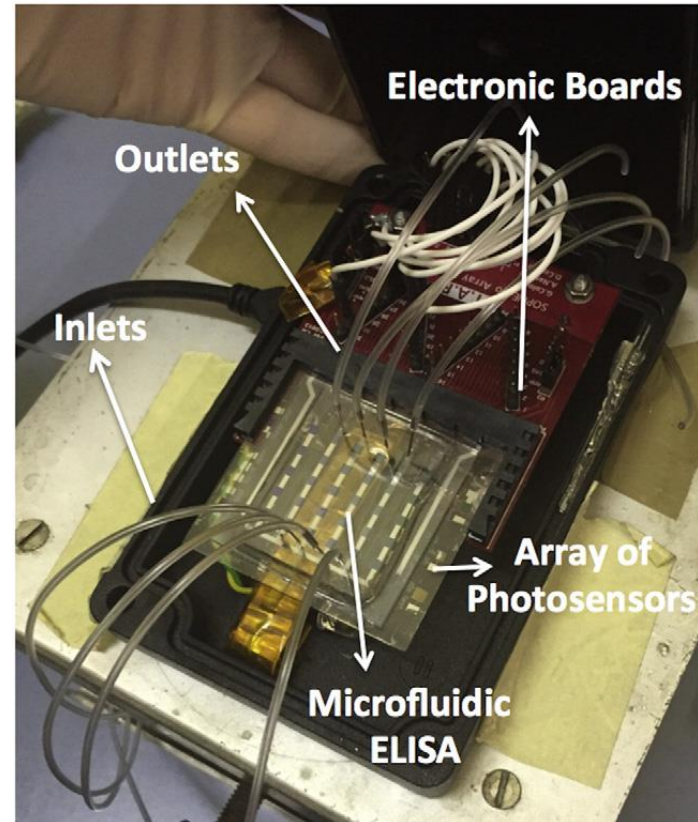
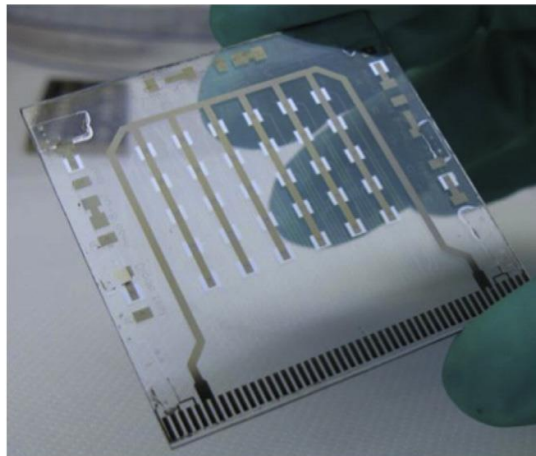
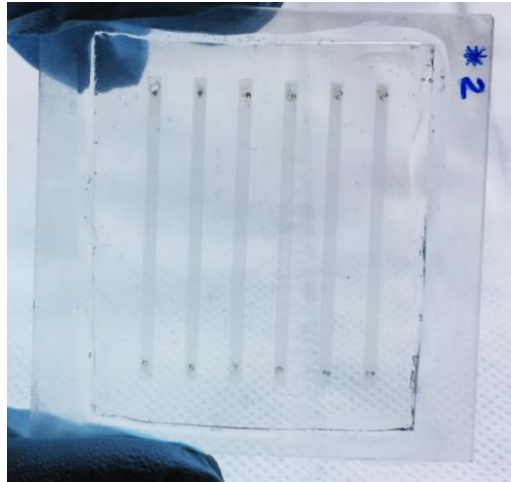


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# ALISA (aptamer-linked immobilized sorbent assay) in the Aptamer Functionalized Chip

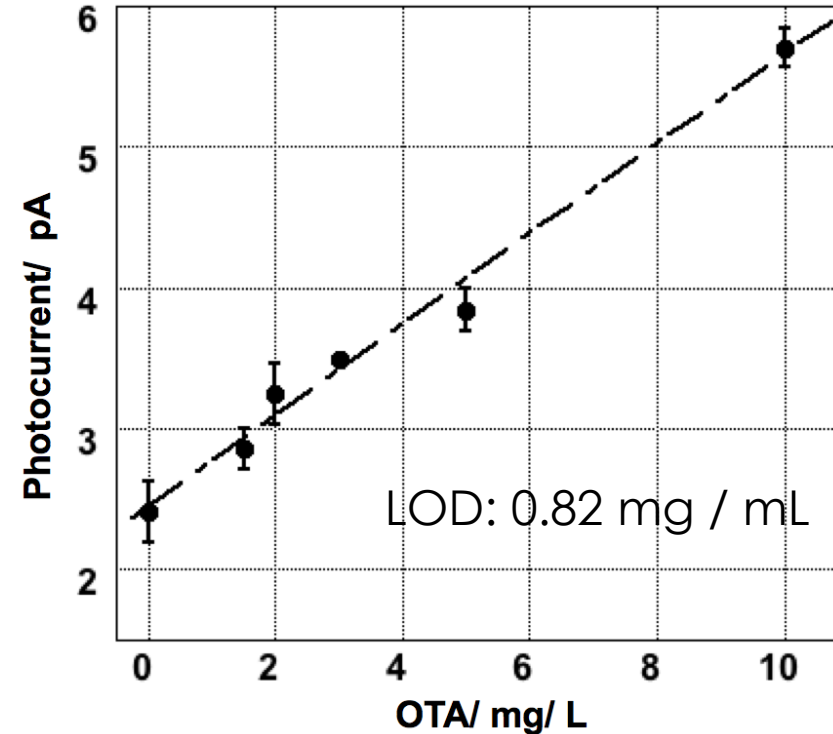
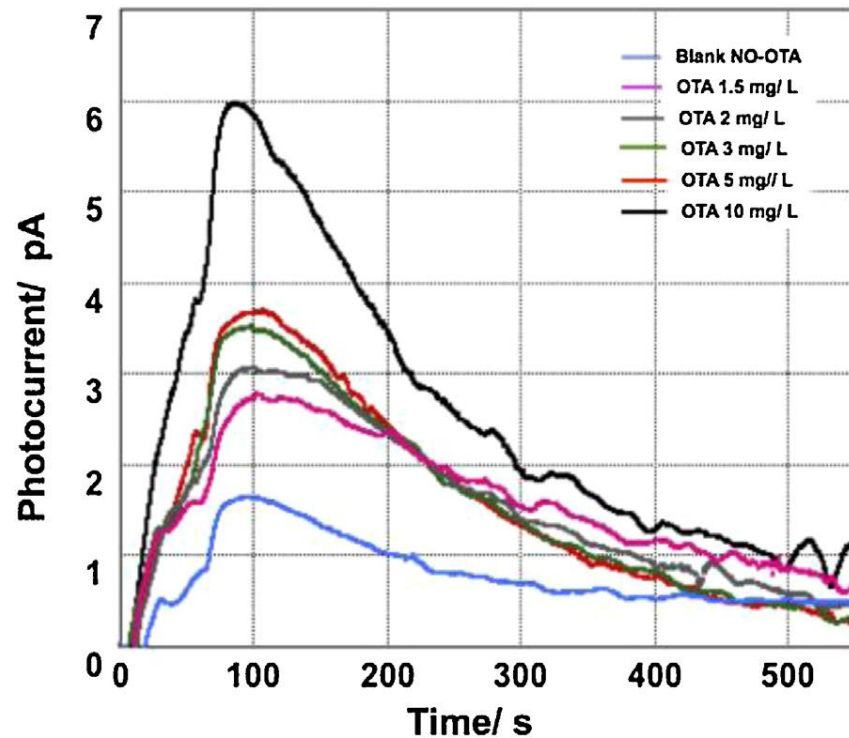


# $\alpha$ -Si:H sensors coupled with the microfluidics



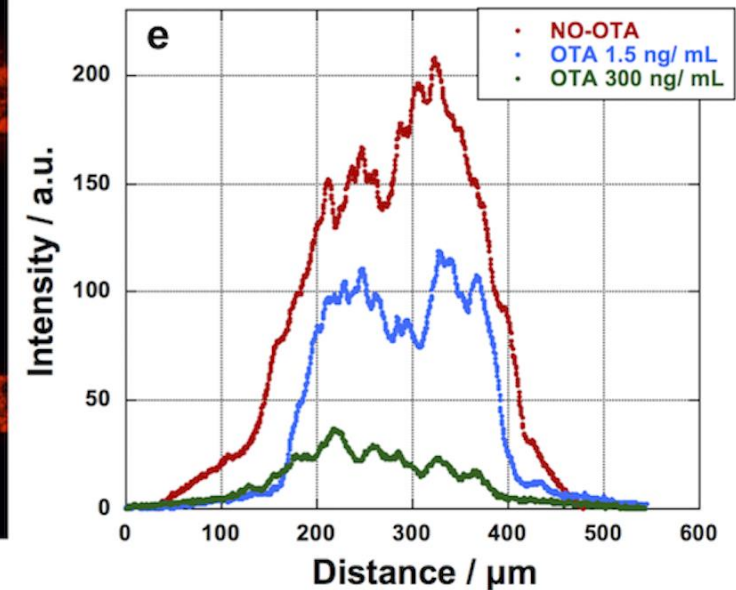
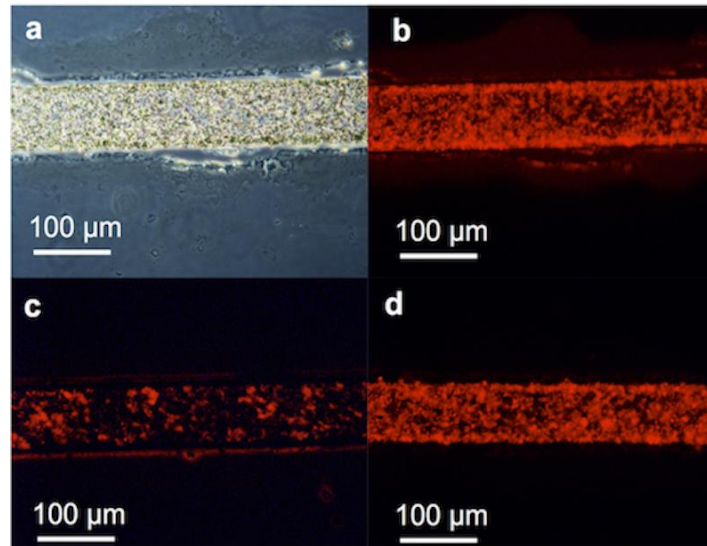
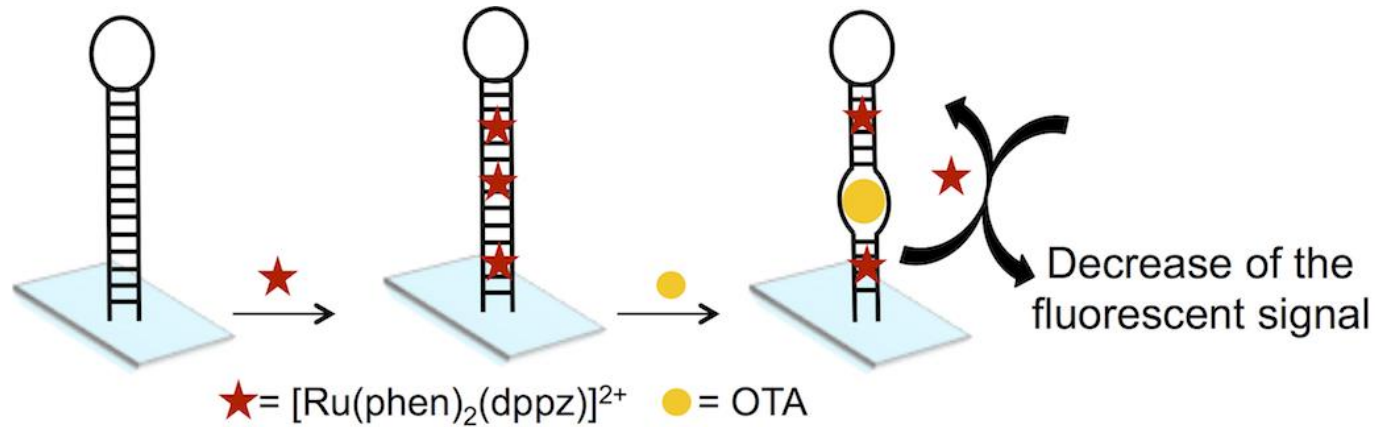
F. Costantini et al., *Sensors and Actuators B*, 230 31–39, **2016**

# ALISA in the Aptamer Functionalized Chip



	Analysis type	HPLC (mg/L)	ALISA (mg/L)
OTA extracted from bier	OTA extract 1	2.42 ± 0.54	2.7 ± 0.43
	OTA extract 2	3.26 ± 0.28	2.9 ± 0.70

# Label-free Fluorescent Aptasensor Assay

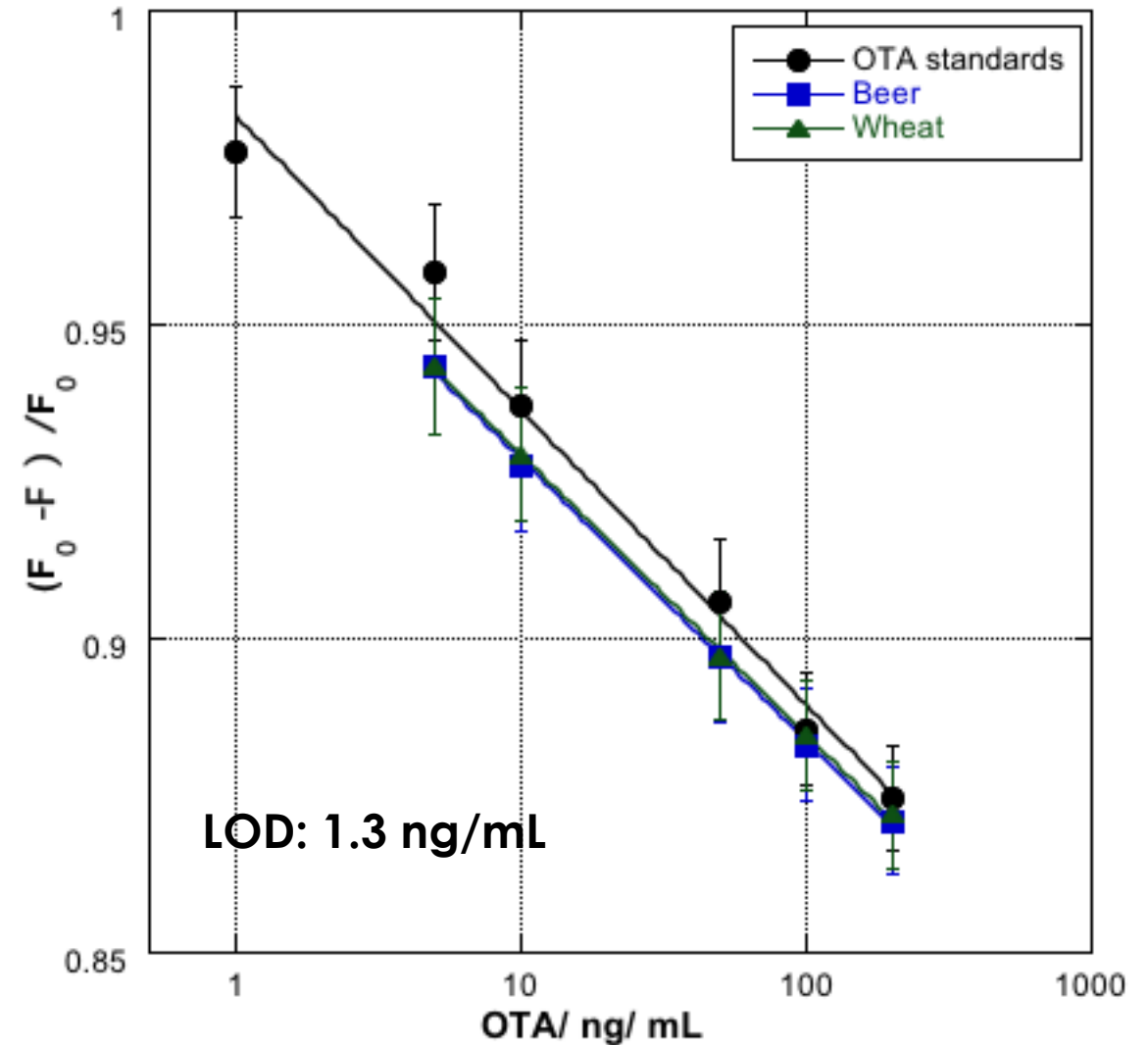
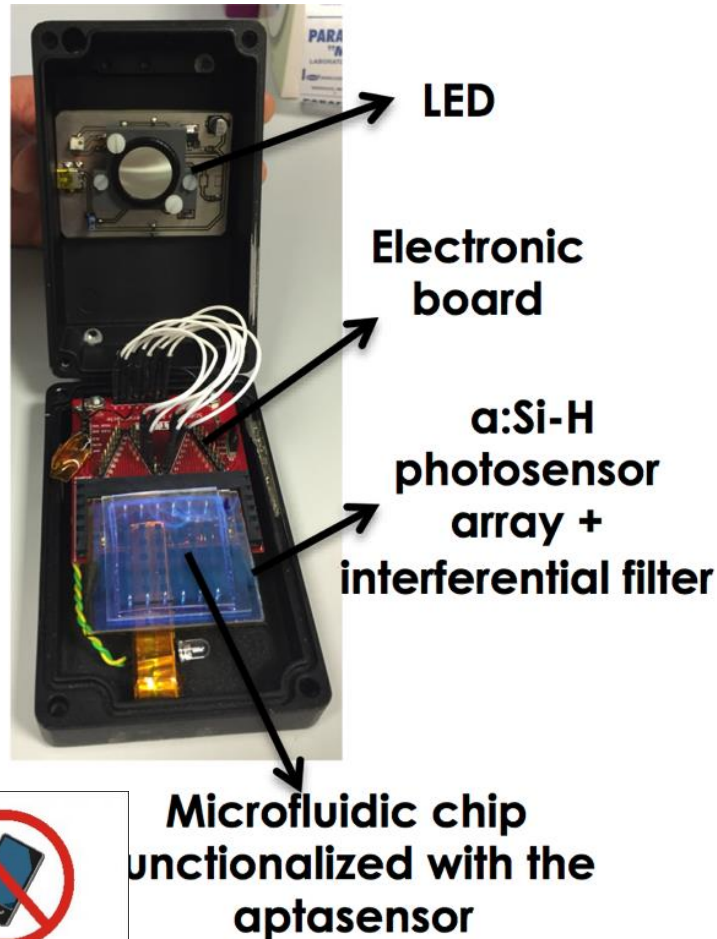


Please DO NOT take photographs.

*Not published results*



# Label-free Fluorescent Aptasensor Assay



Not published results



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Aptameri	Anticorpi
Corte sequenze oligonucleotidiche a DNA o RNA (15 ed 80 nucleotidi)	Costituiti da catene polipeptidiche
Generati da un processo di selezione <i>in vitro</i> (SELEX) con elevato grado di purezza ed elevata riproducibilità (circa 8 settimane)	Selezionati <i>in vivo</i> attraverso meccanismi multipli di risposte immunitarie indotte nei sistemi biologici (circa 6 mesi)
Possono essere ottimizzati nella regione d'interesse con opportune modifiche e possono essere variati i parametri cinetici	difficoltà di modifiche strutturali
Possono rigenerati dopo una denaturazione (variazioni di temperatura, pH)	Stabili e attivi solo in condizioni analoghe all'ambiente cellulare, la denaturazione è irreversibile

# Summary

- Different types of DNA amplifications have been conducted and showed good potential of applicability as portable system to be used directly in-the-field;
- The PHEMA brushes developed for the biosensing system showed low non-specific absorption and they are responsive when wetted with buffer, allowing the interaction of the target with the selected receptor (i.e. aptamer etc...).
- The functionalized devices showed good applicability for OTA detection when coupled with the array of amorphous silicon photosensors;

# Acknowledgements

UNIVERSITY OF TWENTE. **MESA+**  
INSTITUTE FOR NANOTECHNOLOGY



Prof. D. Caputo and G. de Cesare,  
Dr. N. Lovecchio DIET



Dr. R.M Tiggelaar, Prof. Han Gardeniers and Dr. B. Bruijne  
MCS



Prof. A. Nascetti  
SIA



Prof. C. Manetti  
DIBA



Prof. M: Reverberi  
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Prof. M. DeRosa  
Chemistry Department



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