



4th International Conference
and Exhibition
Biosensors & Bioelectronics 2015

nanoimmunotech
global solutions in nanobiotechnology

MARIANTONIETTA PARRACINO (PhD)
Biosensing project manager

Outline

- “ NANOIMMUNOTECH
- “ Biosensors: different applications
- “ Unsolved problems of biosensors
 - “ Case study: Cancer early detection
 - “ Case study: Analytes, of interest in agro-food sector, early detection
- “ Biosensors: Why using nanomaterials?
- “ Thermal biosensor – **HEATSENS**
 - “ Oriented surface functionalization for improving the detection limit
- “ Use of HEATSENS for the detection of food pathogens/allergen and cancer marker CEA
- “ NANOIMMUNOTECH: Thermal biosensor microfluidic implementation
- “ Conclusions



NANOIMMUNOTECH

Spin-off Company from **Universidad de Vigo**



and



**Universidad
Zaragoza**



NANOIMMUNOTECH

VISION

Our main objective is to become a world leader in **Functionalization, Biosensing** and Characterization of nanometric systems.

MISION

Our commitment consists in offering products and **services**, integrally covering the **characterization, biosensors and functionalization nanoparticles** market, within the Biotechnology and Health sectors.



Biosensors: different applications

Environmental control



Security & Biodefense



Point of care screening



GLOBAL BIOSENSORS MARKET:

2013	11,39 US\$ BILLIONS
2020	22,68 US\$ BILLIONS

Industry: process control



Remote monitoring



Research laboratories

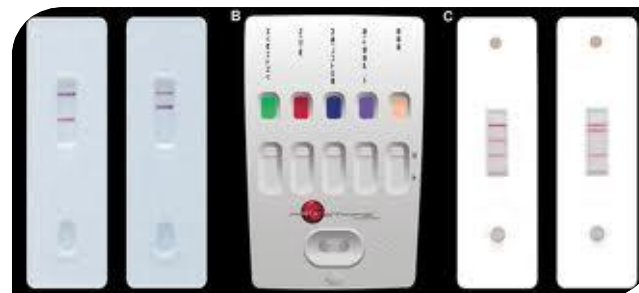


By: marketsandmarkets.com
Publishing Date: January 2015
Report Code: SE 3097



Unsolved problems of biosensors

- “ Need: lack of enough sensitivity
- “ Need: specialized users
- “ Long response times
- “ Not portable enough
- “ High Costs
- “ ...



Case study: Cancer early detection

There is a lack
of tools for
early
diagnosis

DISCOVERY OF NEW TUMOR MARKERS

Do not provide early diagnosis

Insufficient prognostic value

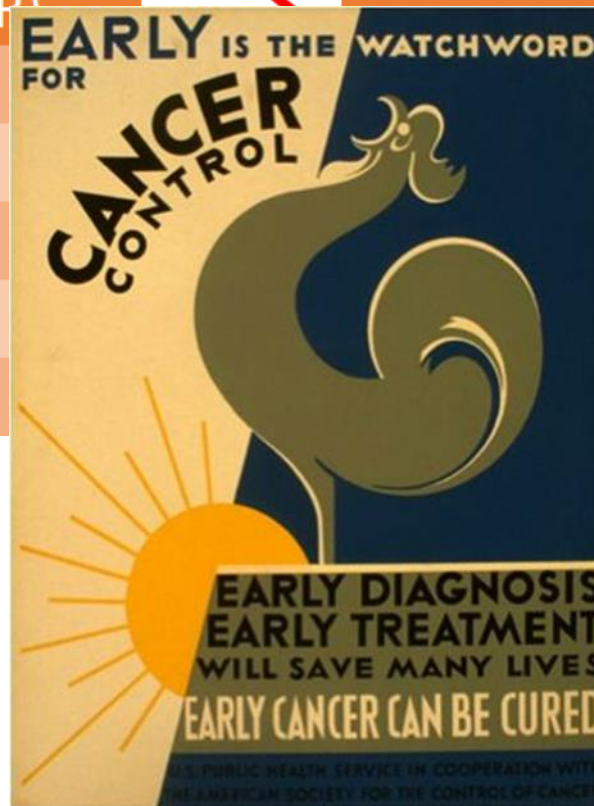
Poor recurrence predictions

Monitoring of treatment



Case study: Cancer early detection

STAGE	SURVIVAL RATE (5 YEAR)	CANCER	SURVIVAL RATE (5 YEAR)
IA	70%		15%
IB	57%		28%
IIA	45%	CTUM	64%
IIB	33%		10%
IIIA	20%		83%



Importance of early detection



Close relation with biosensor sensitivity

Case study: Cancer early detection

DISCOVERY OF NEW TUMOR MARKERS

Do not provide early diagnosis

Insufficient prognostic value

Poor recurrence predictions

Monitoring of treatment

There is a
lack of tools
for early
diagnosis

IMPROVEMENT OF DETECTION SYSTEMS

Greater sensitivity

Improving biological matrices insensitivity (*in vitro*)

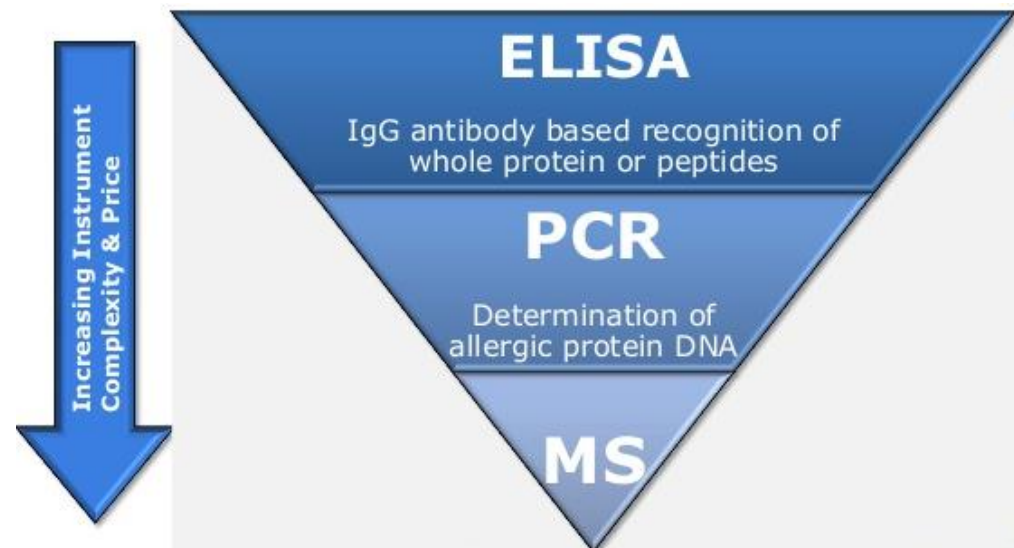
Point of care use (consulting and operating rooms...) (*in vitro*)

Specificity(*in vivo*)

Case study: Allergens detection (food industry)

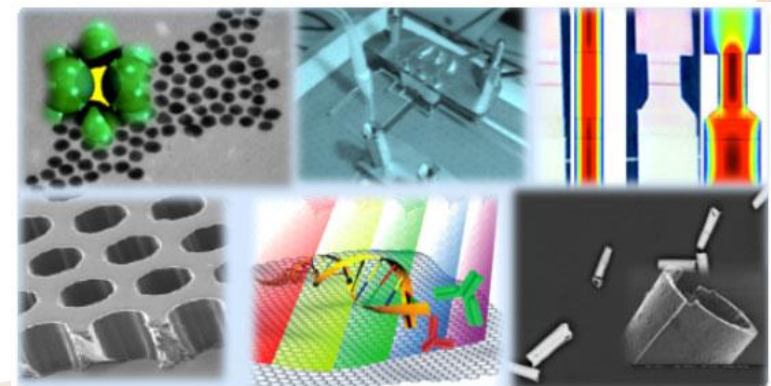
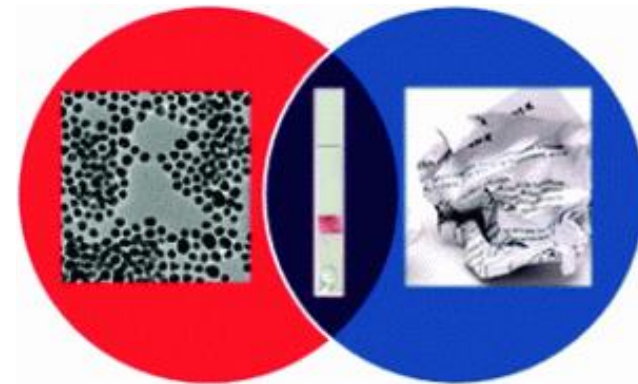
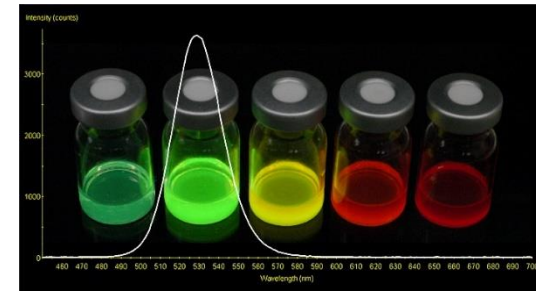


Allergen analysis: Current detection strategies



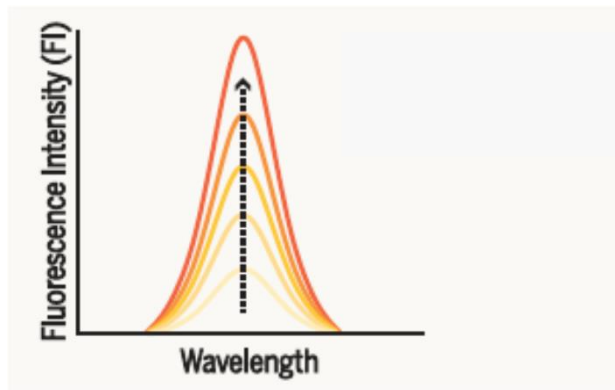
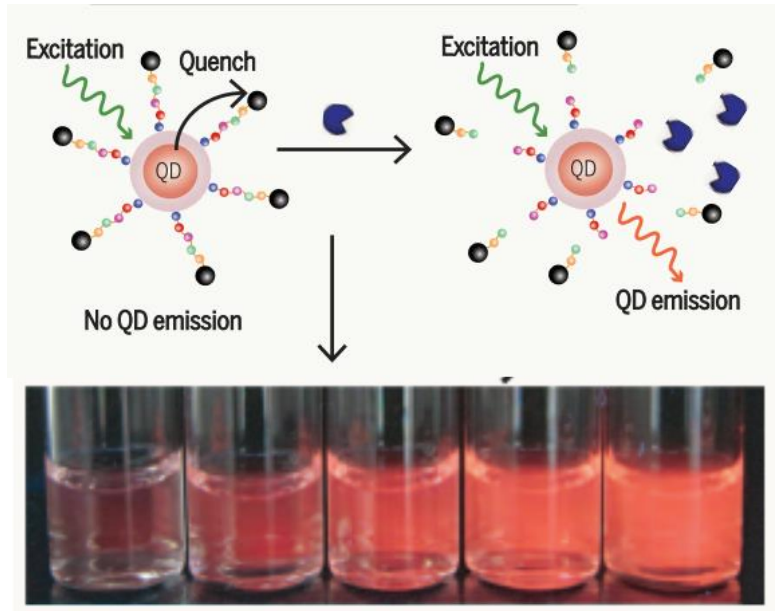
Biosensors: Why using nanomaterials?

- “ Sensitivity improvement
- “ New transduction technologies
- “ Better Cost-Efficiency relation
- “ Miniaturization
- “ Continuous monitoring

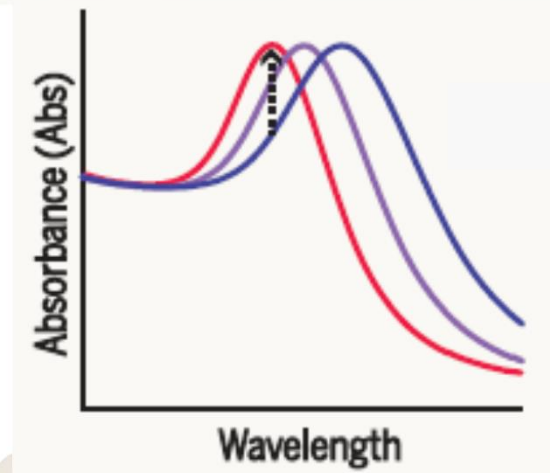
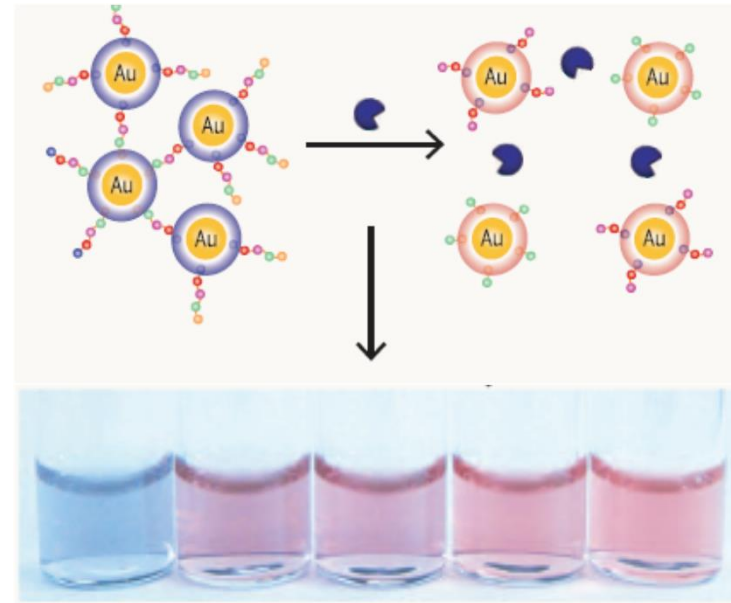


Biosensors: Why using nanomaterials in sensing?

Fluorescent Nanoparticles: QDot



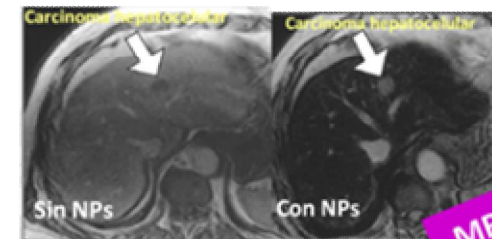
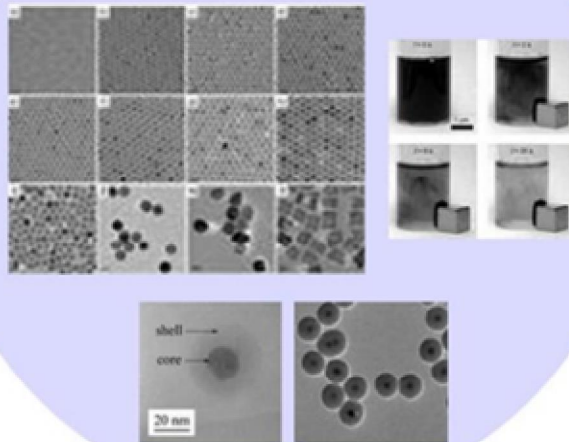
Plasmonic Nanoparticles



Biosensors: Why using nanomaterials in sensing?

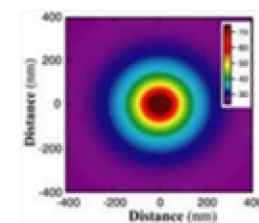
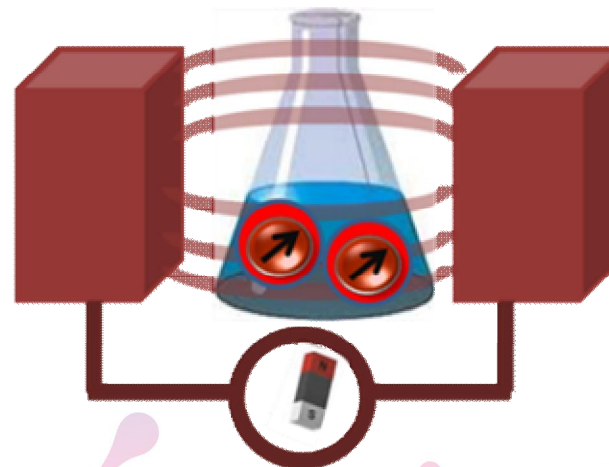
Nanodiagnosis

Magnetic NPs



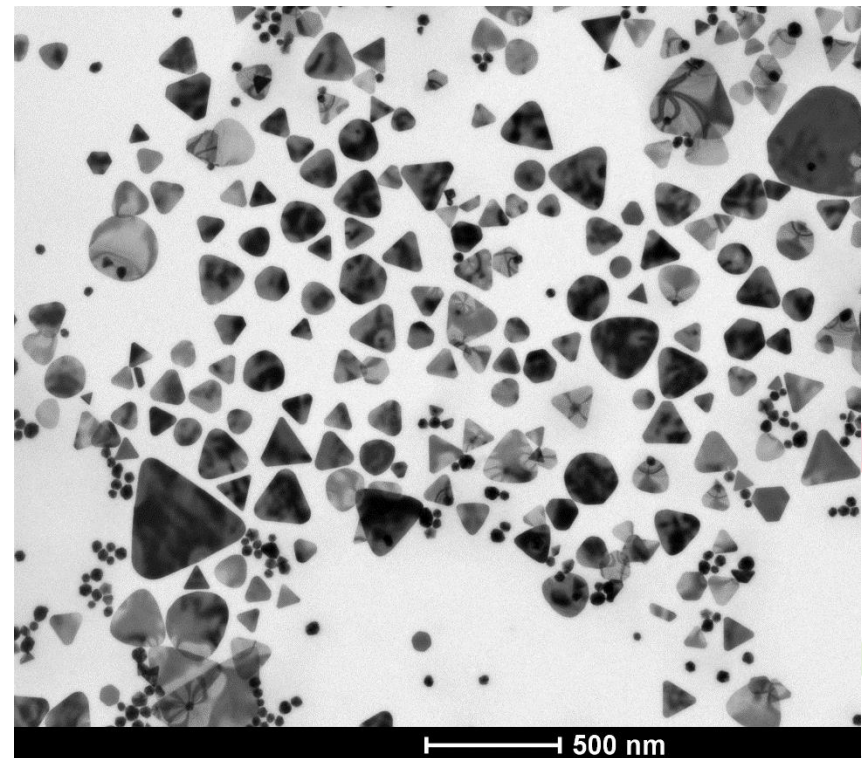
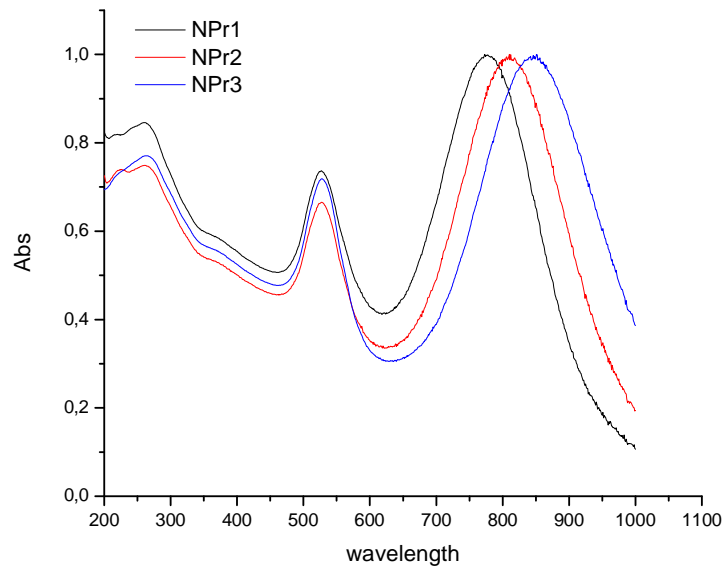
MRI

Nanotherapy



Asymmetric nanoparticles properties: AuNanoprisms

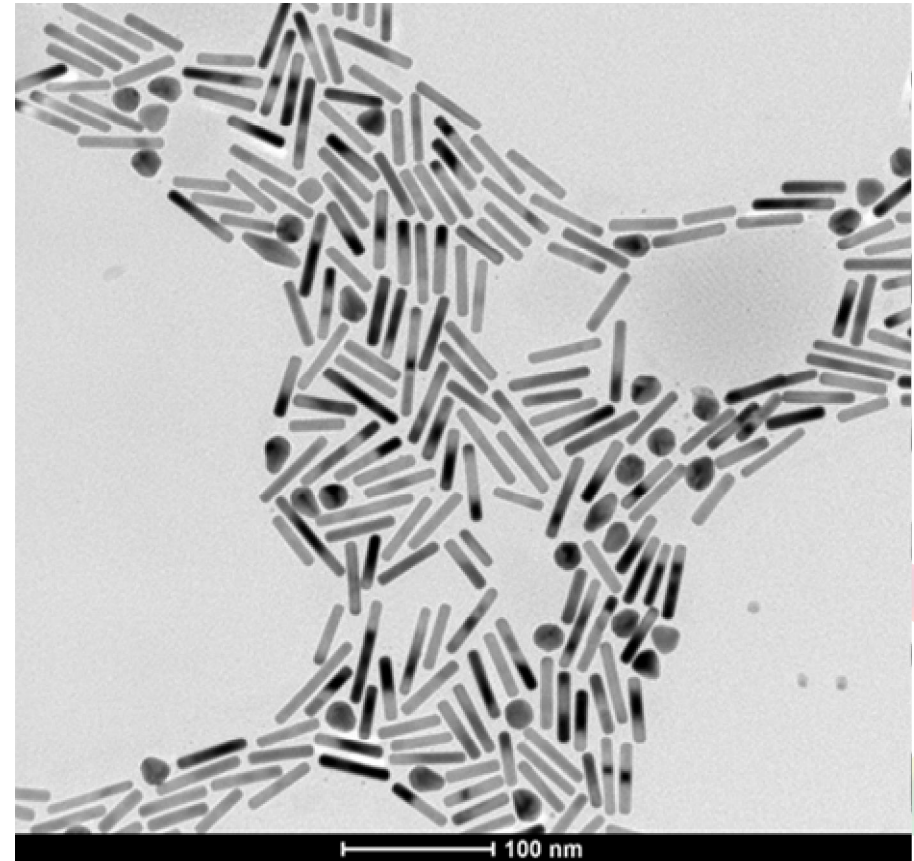
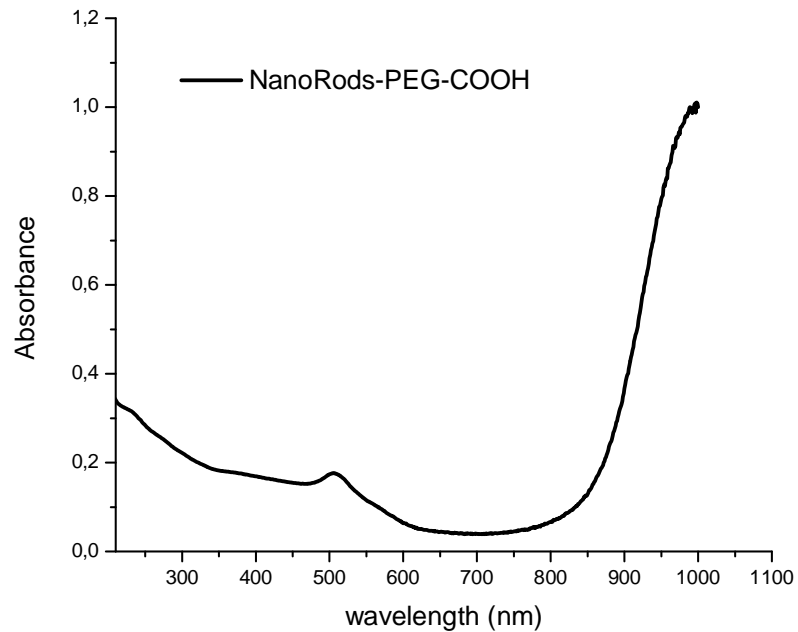
Gold Nanoprisms (NPs)



Pelaz B., V. Grazú Langmuir 2012

Asymmetric nanoparticles properties: AuNanoRods

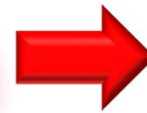
Gold NanoRods (NRs)



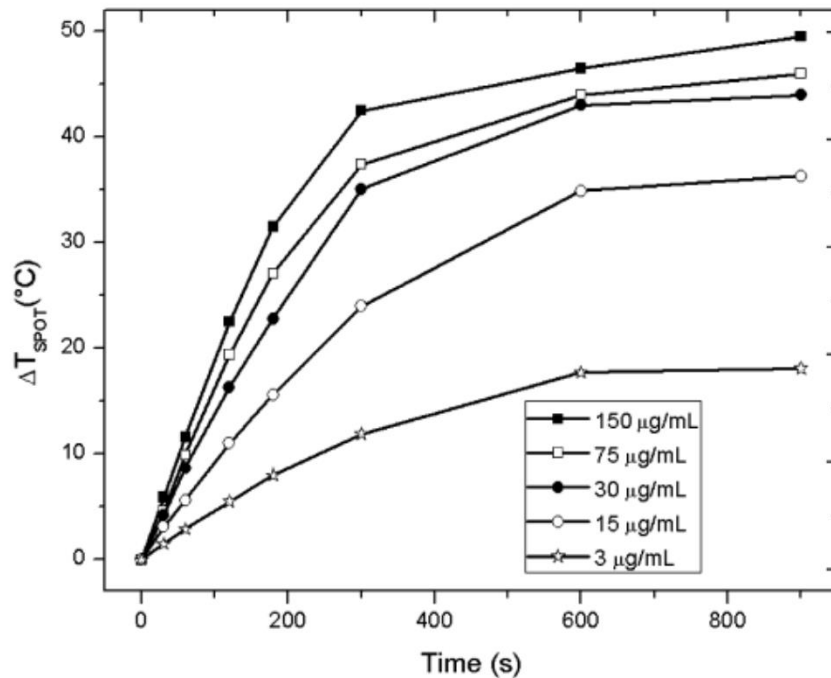
Asymmetric AuNanomaterials: thermal properties

Asymmetric nanomaterial

NIR Laser



Heat Generation
upon IR illumination



Temperature traces of
colloidal solution of
Nanoprism@PEG at
different concentrations

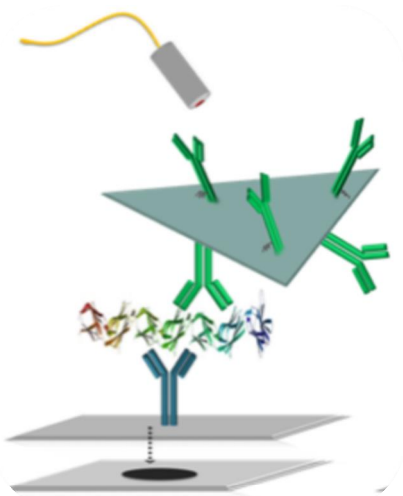
Pelaz B., V. Grazú Langmuir 2012

NANOIMMUNOTECH. Thermal biosensor development

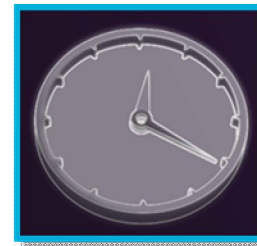


nitbiosensing
Detecting what really matters

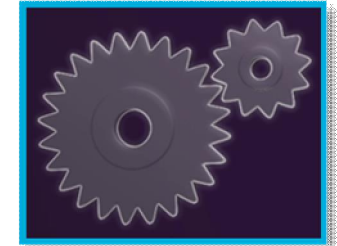
Heatsens



ULTRA-SENSITIVE



ULTRA-RAPID



ULTRA-SIMPLE

Thermal biosensor Heatsens Intellectual Property

Patent licensing
(exclusivity)

Spanish: P201231209
PCT: ES2013/070549

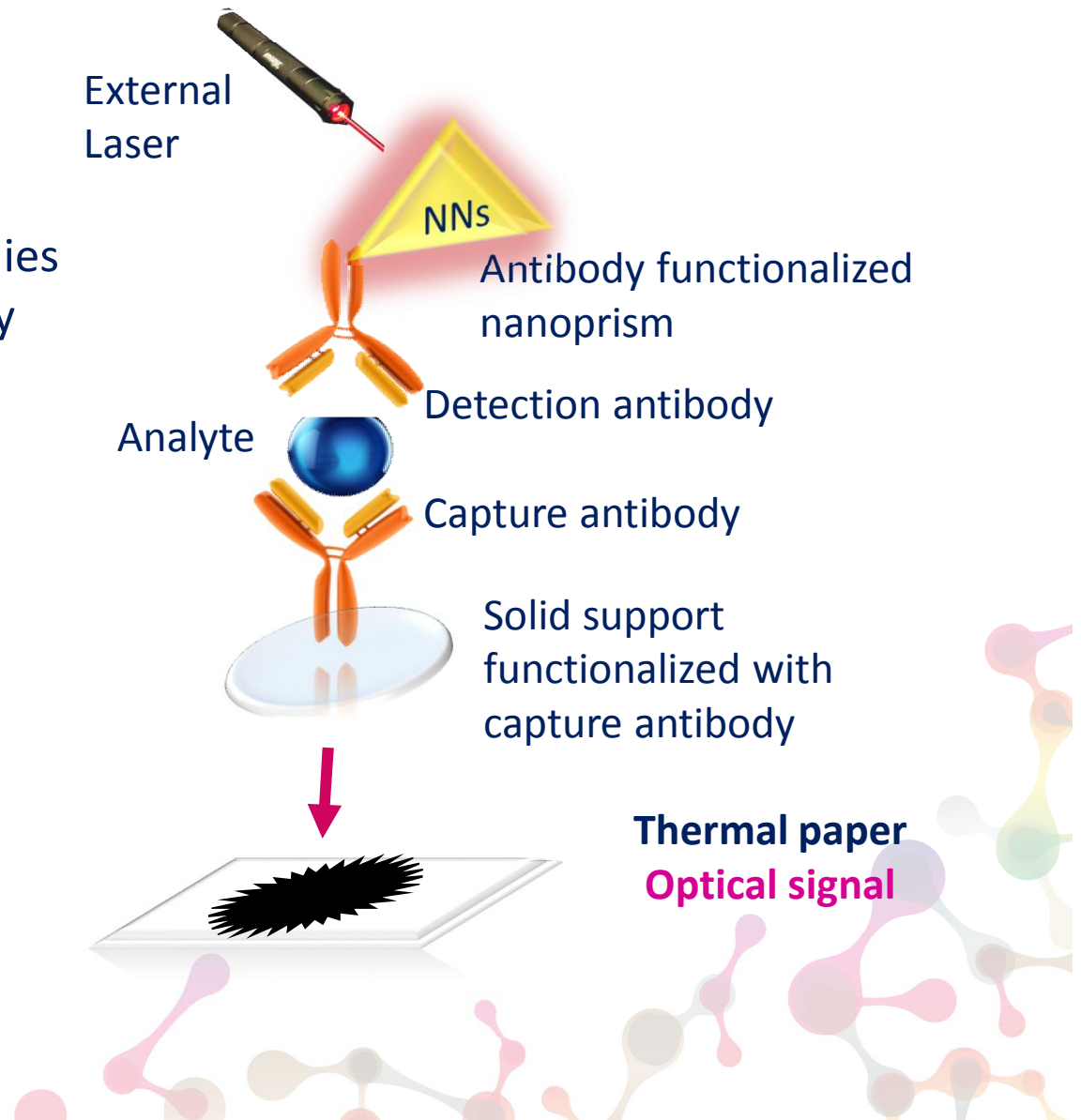
Polo et al. *Chem. Commun.* 2013, 49, 3676



Thermal biosensor Heatsens How it works?

Application example using antibodies with “Sandwich ELISA” like assay

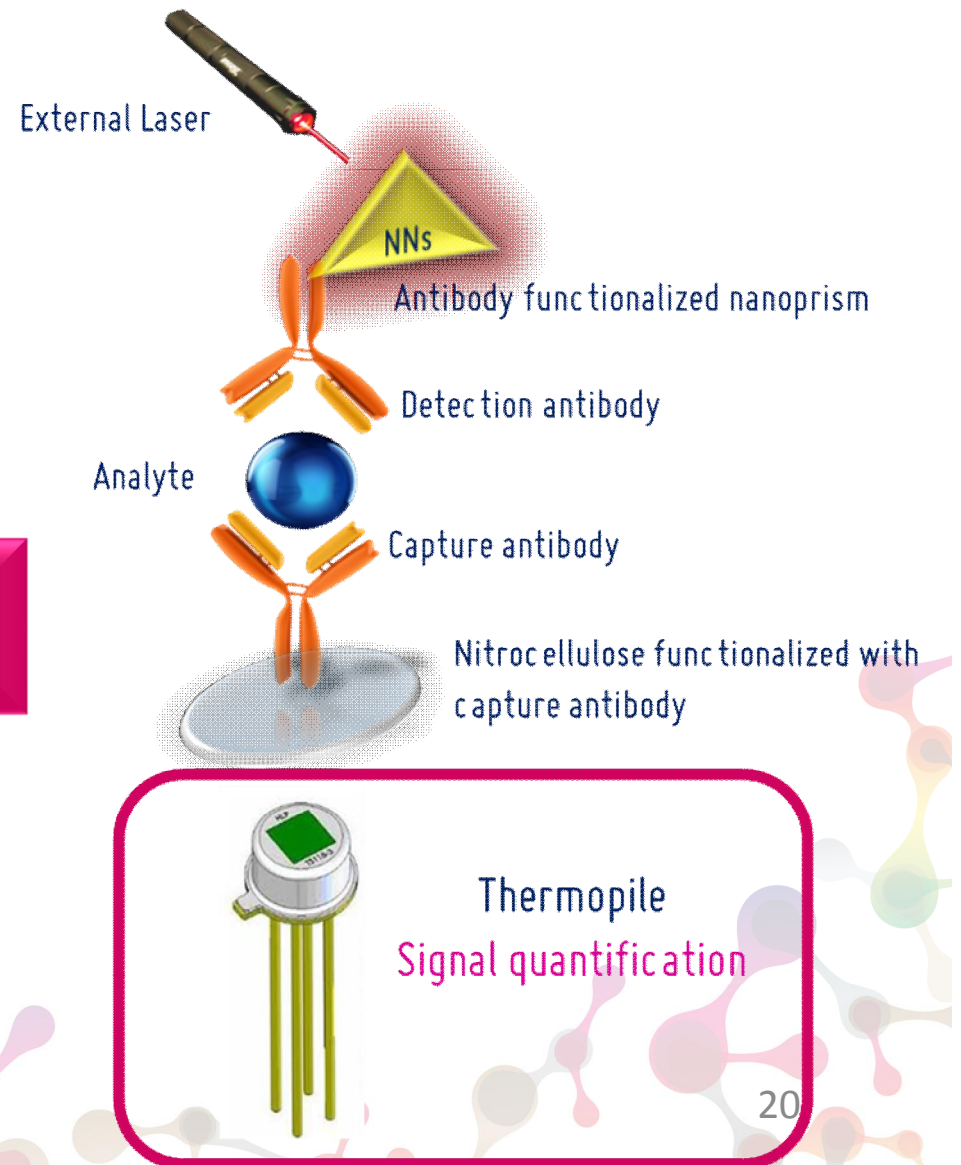
Intensity of the heat released depends on the concentration of the nanomaterial



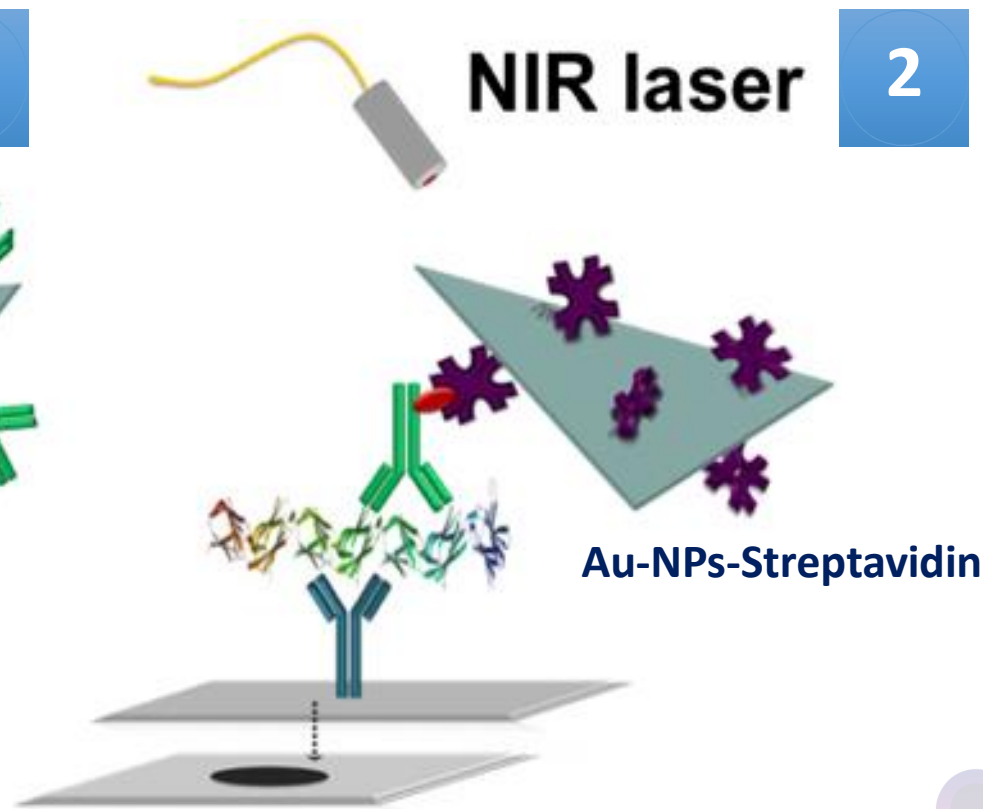
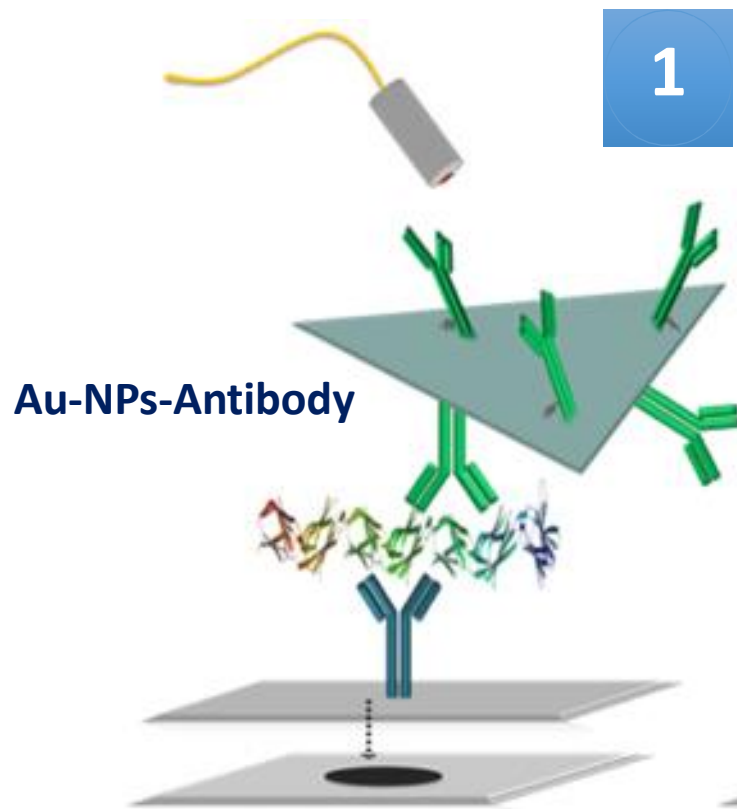
Thermal biosensor – Heatsens – How it works?

Application example using antibodies
with “Sandwich ELISA” like assay

Quantitative Measurement
of the heat released

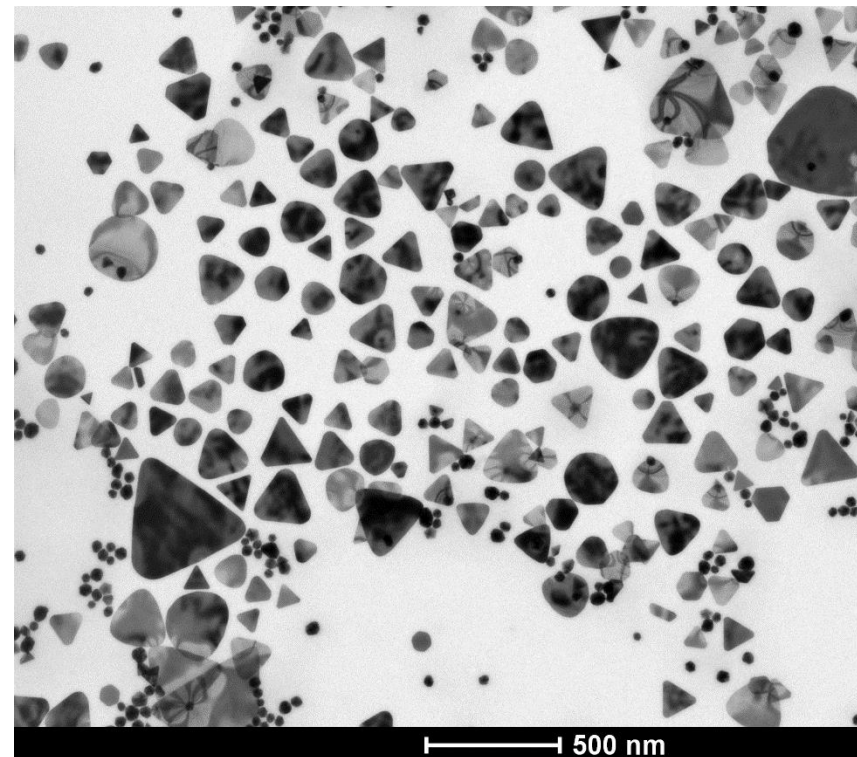
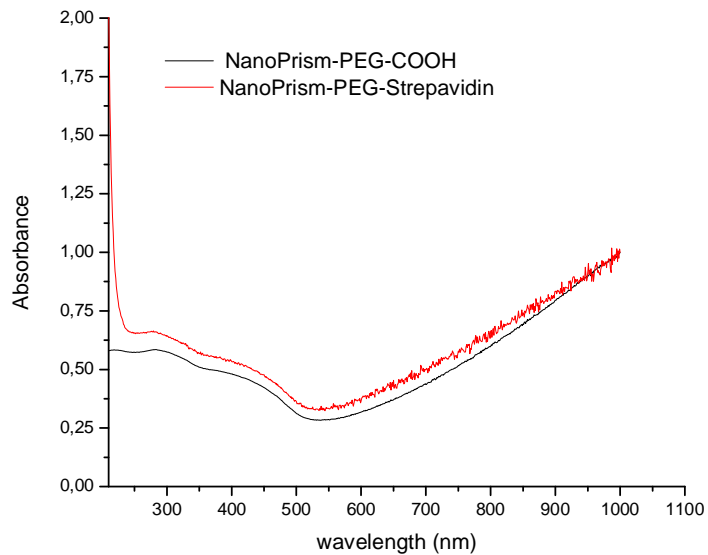


Thermal biosensor – Heatsens – Different possibilities



Au NanoPrism@streptavidin functionalization

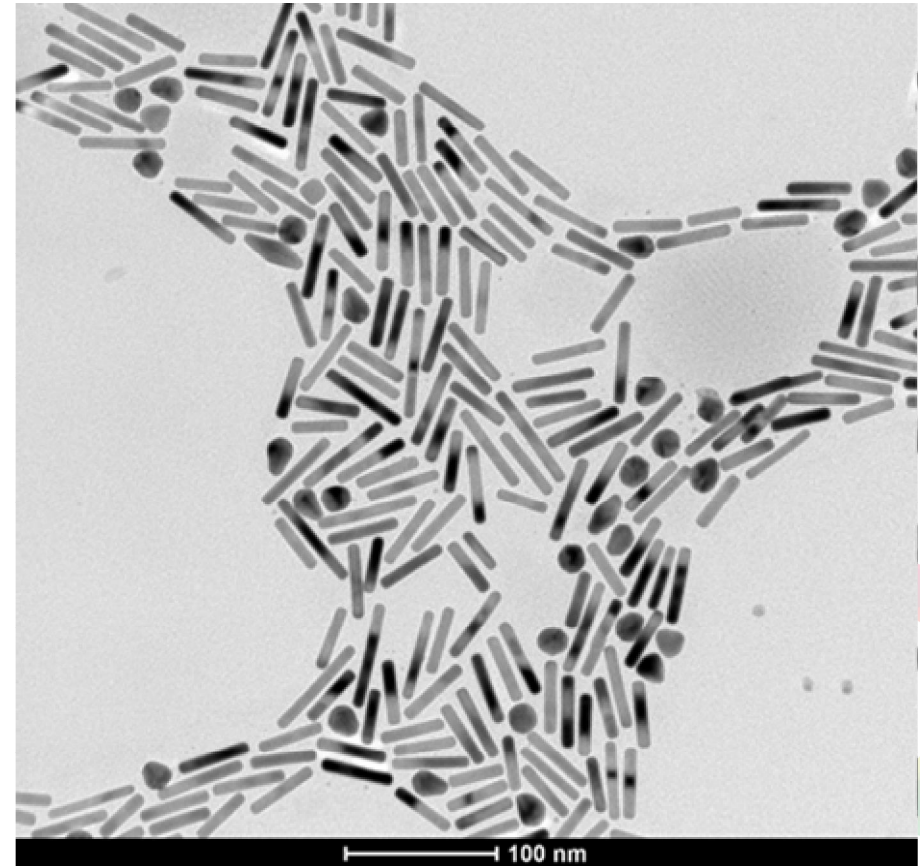
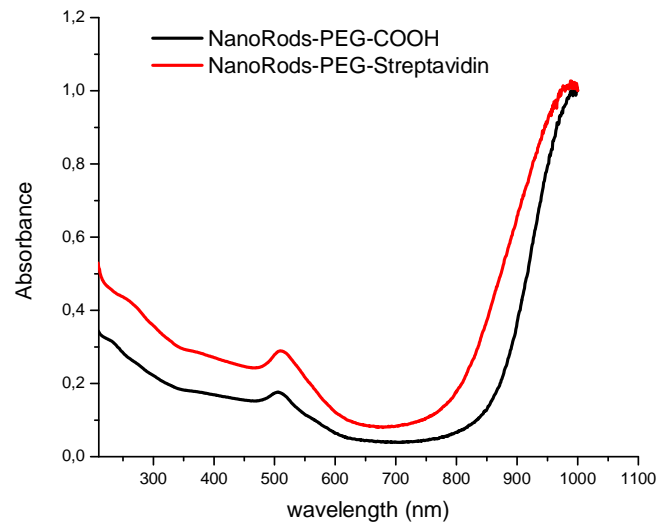
Gold Nanoprisms (NPs)



Pelaz B., V. Grazú Langmuir 2012

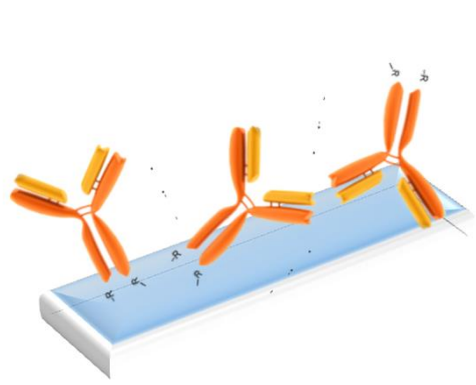
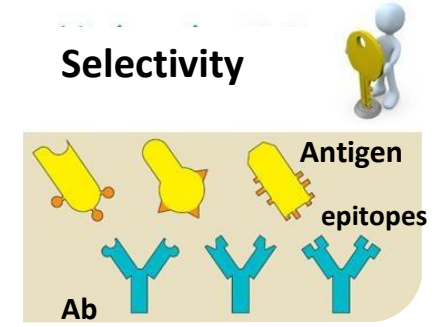
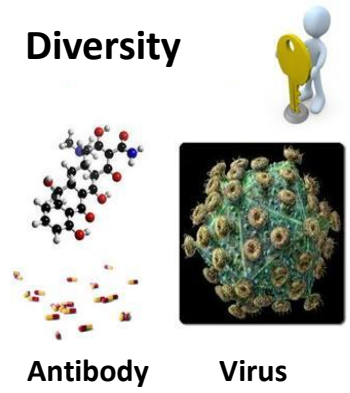
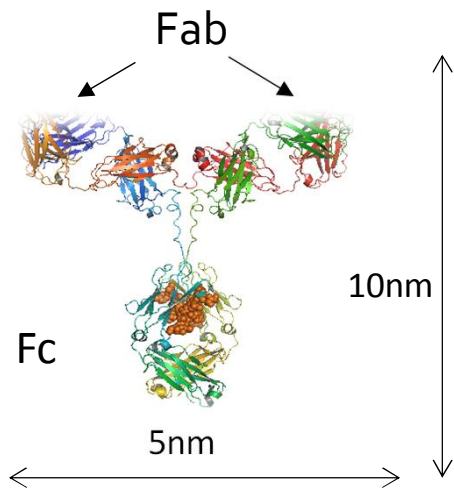
Au NanoRods@streptavidin functionalization

Gold NanoRods (NRs)

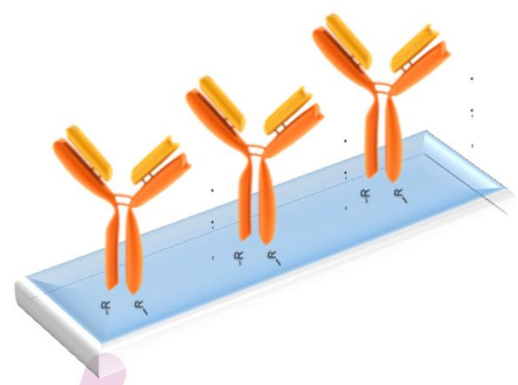


Thermal biosensor – Heatsens – Oriented support surface immobilization

Antibody (Ab)



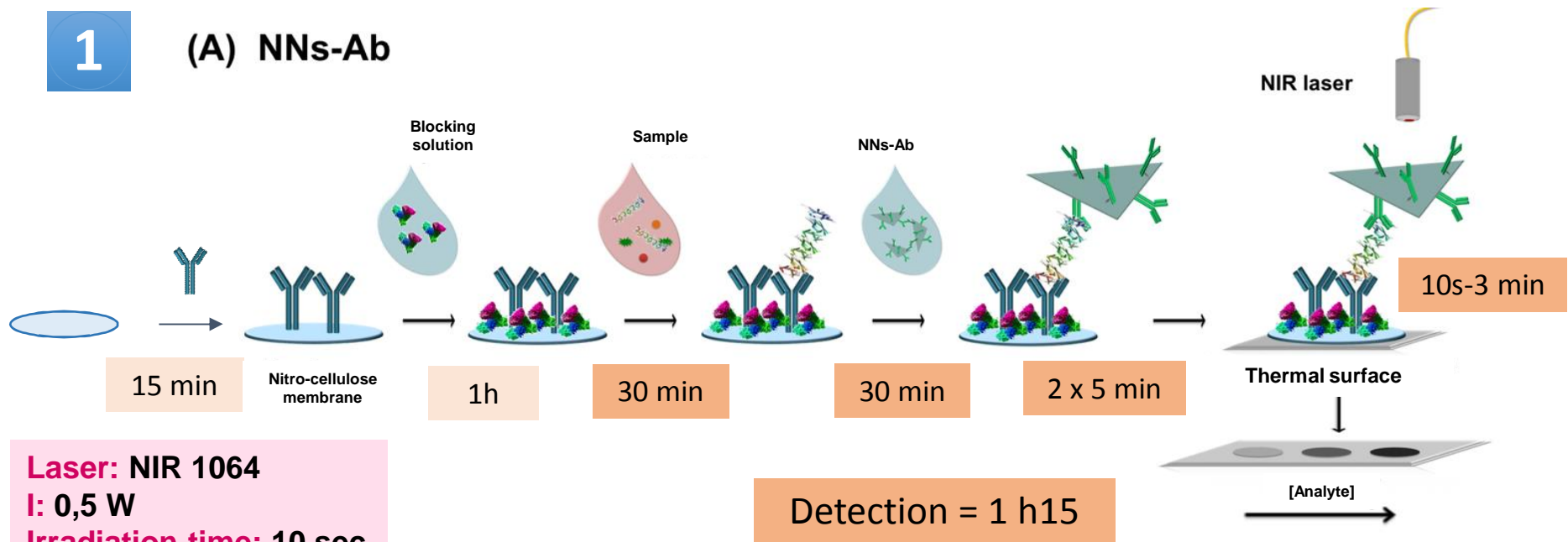
Oriented surface functionalization



Improving of sensitivity of biosensor platform








Thermal biosensor – Heatsens – Deatection of the CEA

1 (A) NNs-Ab



Laser: NIR 1064
I: 0,5 W
Irradiation time: 10 sec

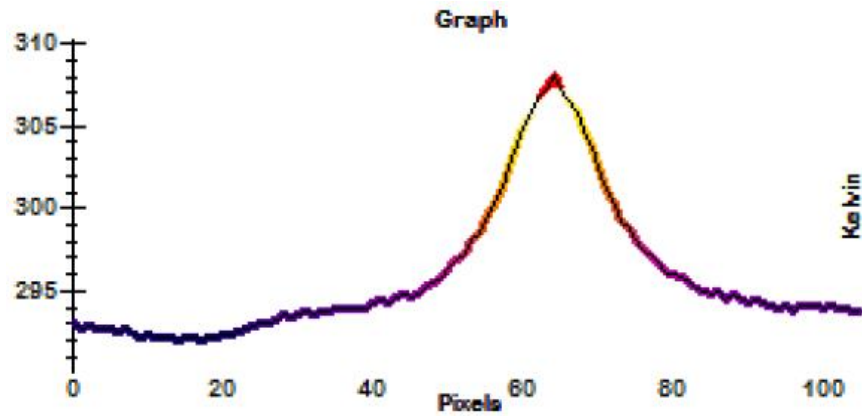
Note: Detection time for a final comercial device will depend on the EBR, assay format, pre-treatment of the materials delivered to the customer,... hopefully it will be lower that the one shown

CONTROL	SAMPLE 0 ng/mL	SAMPLE 1 ng/mL	SAMPLE 5 ng/mL	SAMPLE 10 ng/mL	SAMPLE 25 ng/mL	SAMPLE 50 ng/mL
						

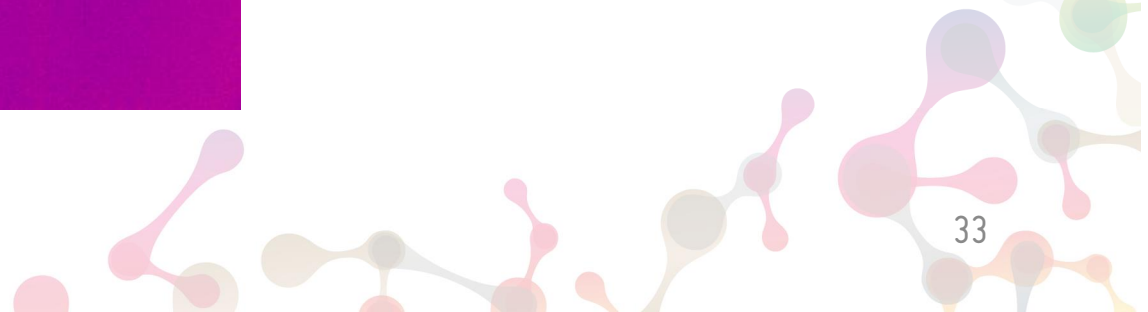
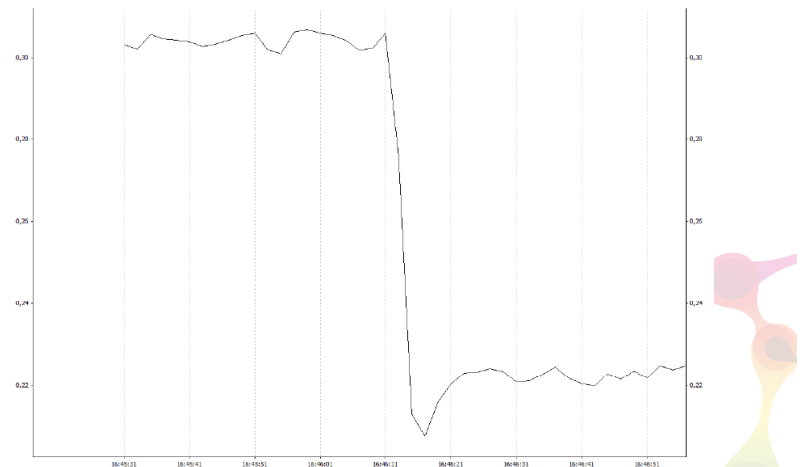
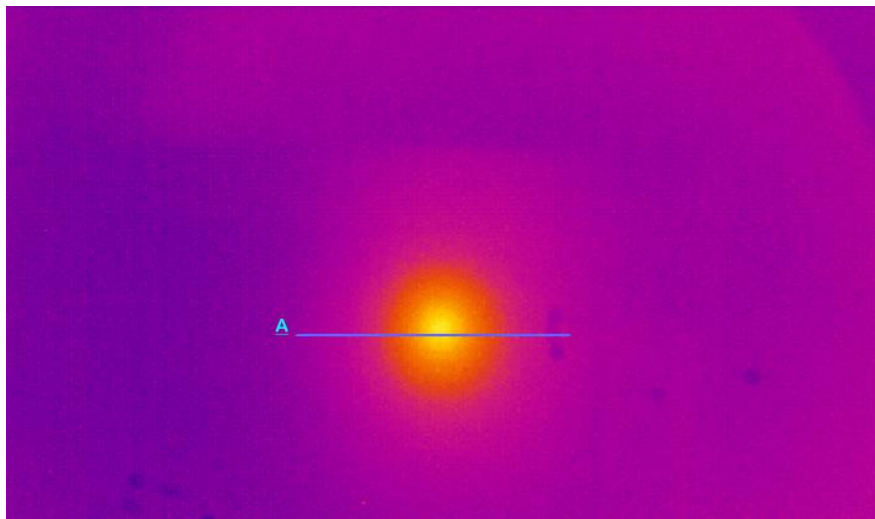
[CEA] ↑

Analyte: Colon adenocarcinoma
✓ CEA antigen

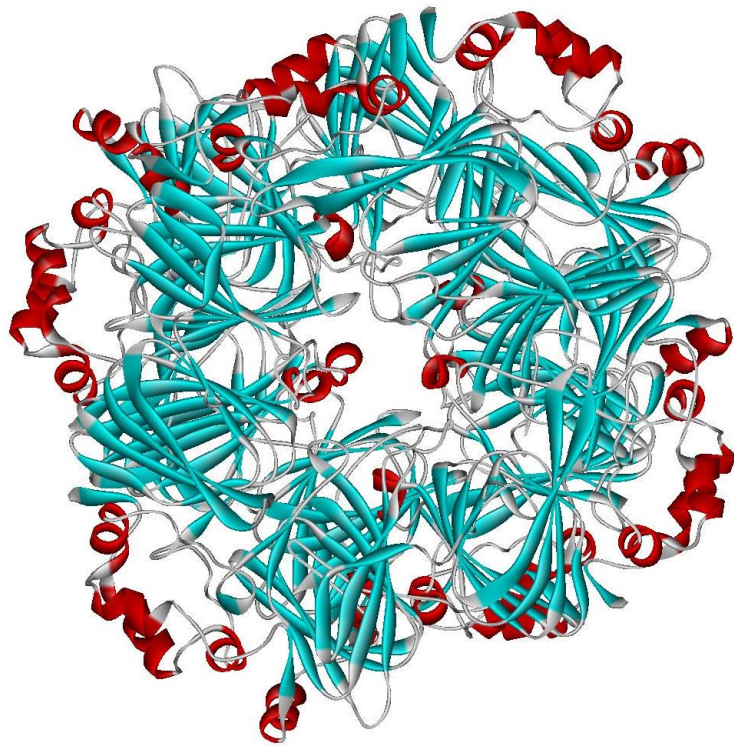
Thermal biosensor – Heatsens



QUANTITATIVE DETECTION
0,1ng/ml CEA



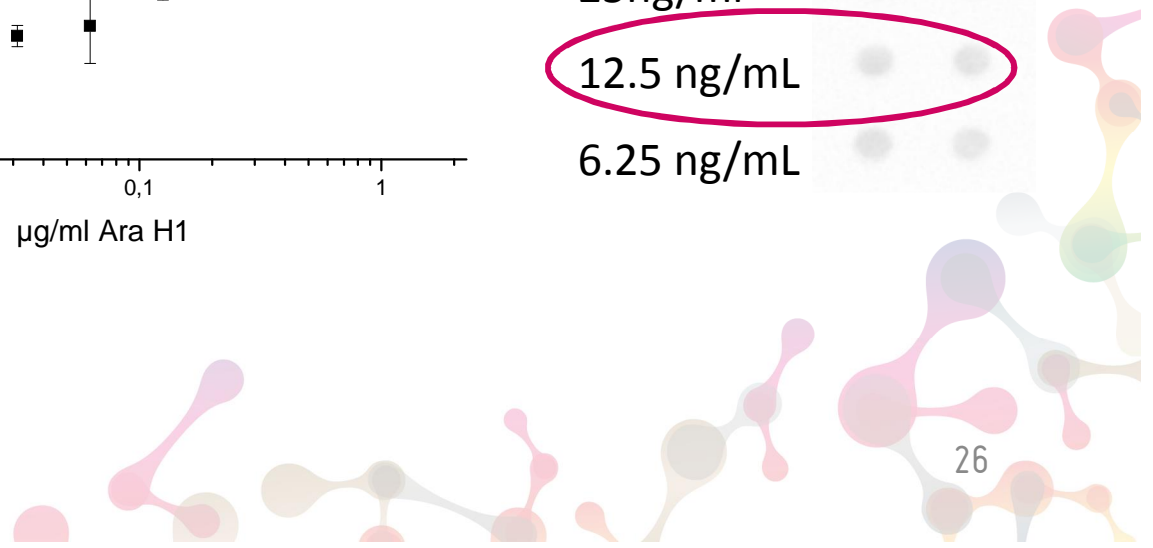
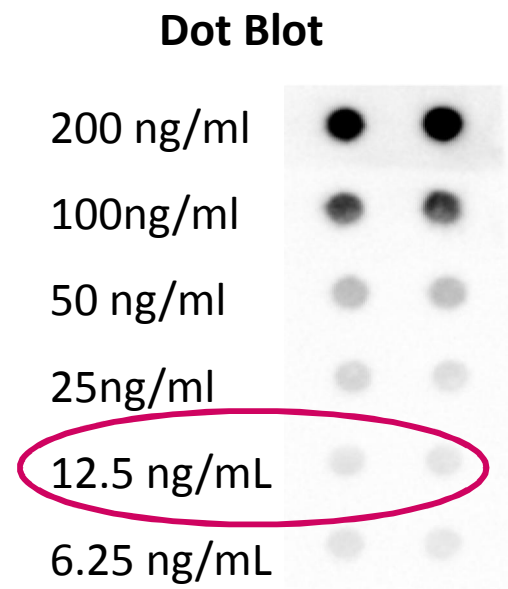
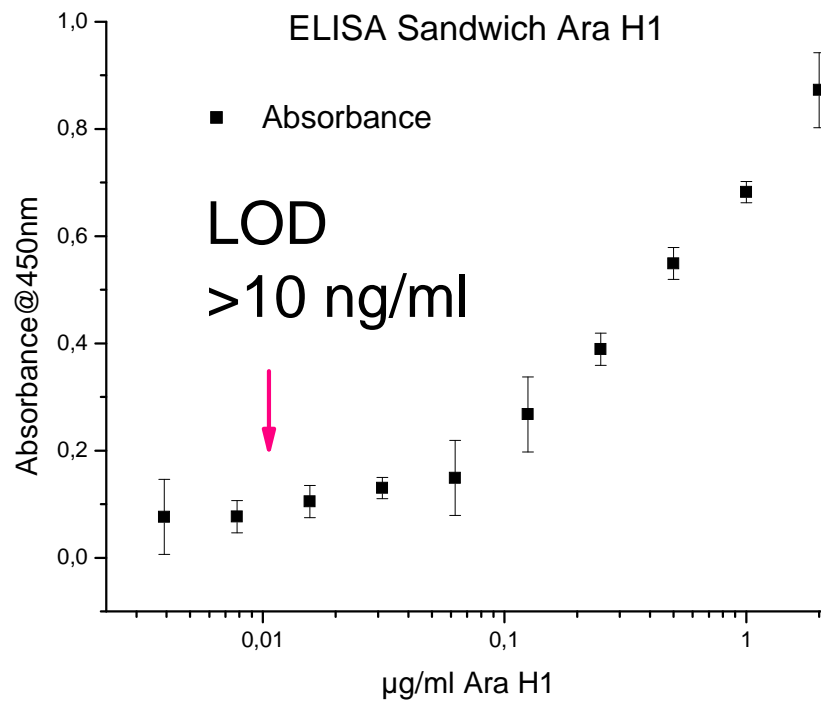
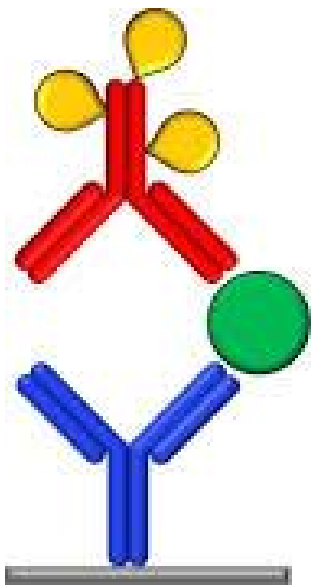
AraH1: a major peanut allergen



Ara h 1 plays an important role in peanut allergic reactions

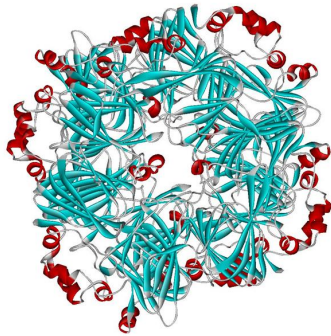
Ara h 1 makes up 12% to 16% of the total protein in peanut extracts and is classified as a major peanut allergen because it provokes sensitization in 35% to 95% of patients with this allergy

Detection of the AraH1

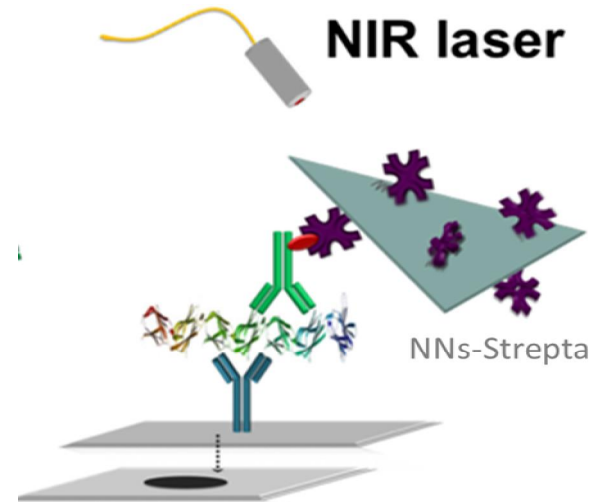








Thermal biosensor – Heatsens – Detection of the AraH1

[Ara H1]



Laser: NIR 1064
I: 250mW/mm²
Irradiation time: 1 sec



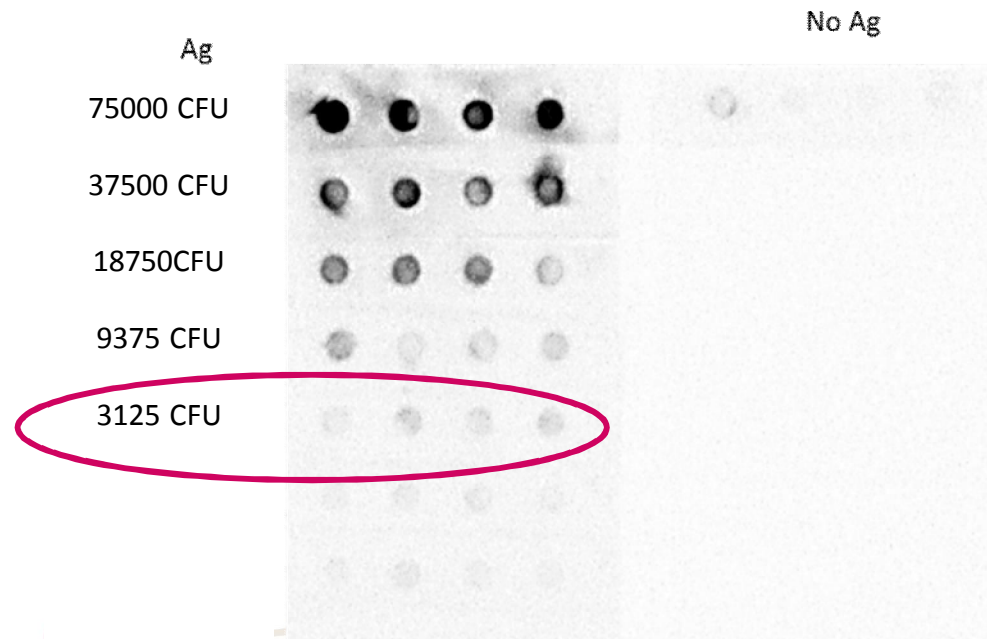
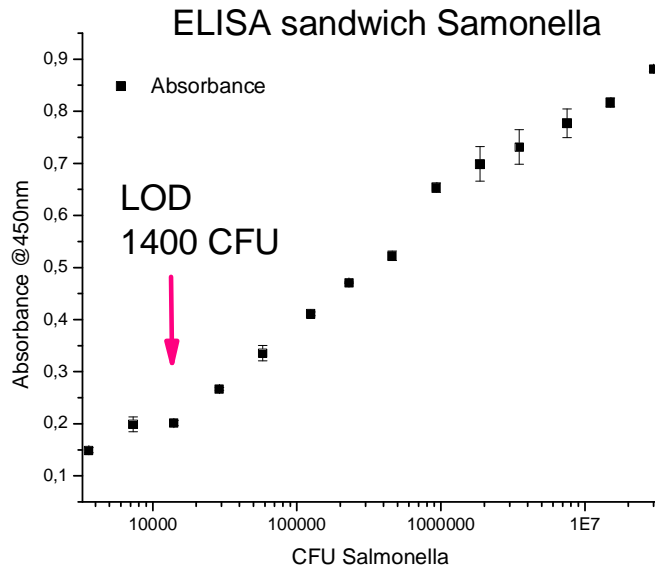
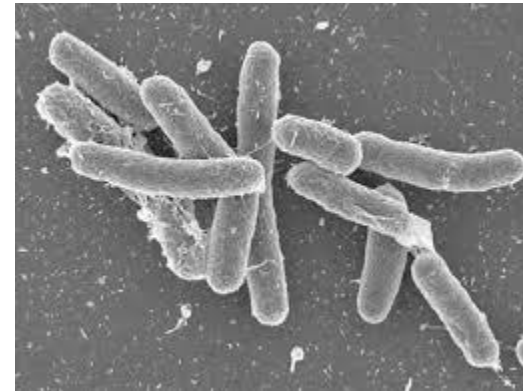
Ara H 1 200 ng/ml	Ara H 1 100ng/ml	Ara H 1 50 ng/ml	Ara H 1 25ng/ml	Ara H 1 12.5 ng/mL	Ara H 1 6.25 ng/mL
					

↓ [Ara H1]

Thermal biosensor – Heatsens – Detection of the Salmon

Salmonella Typhimorium

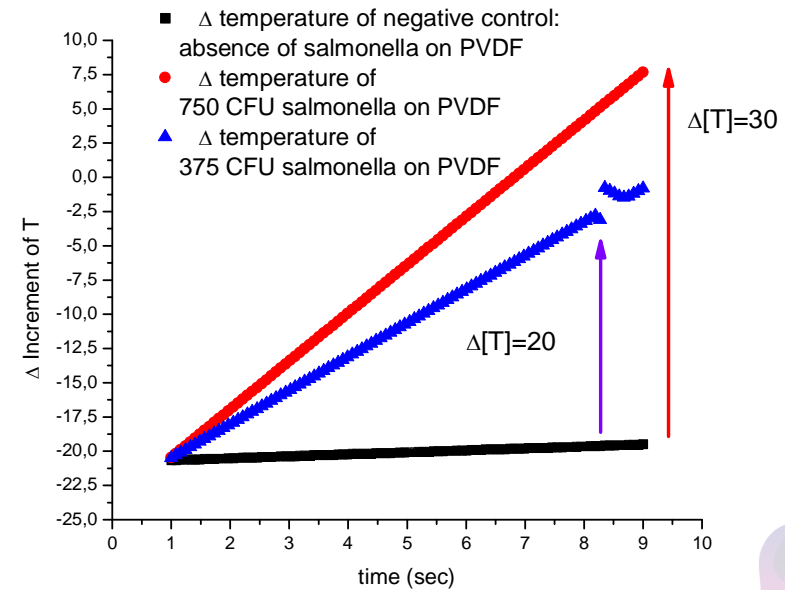
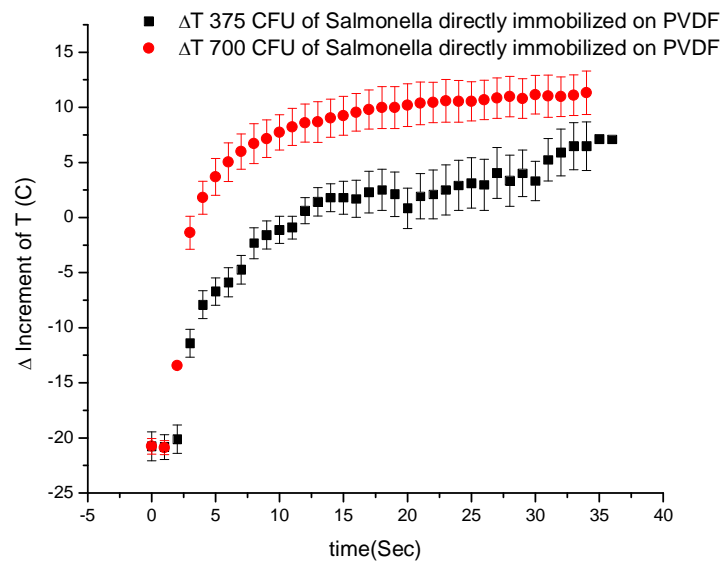
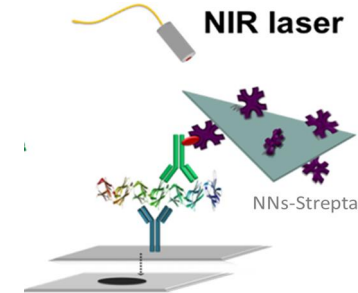
the most common cause of food poisoning



Thermal biosensor – Heatsens – Detection of the AraH1

[Salmonella T.]

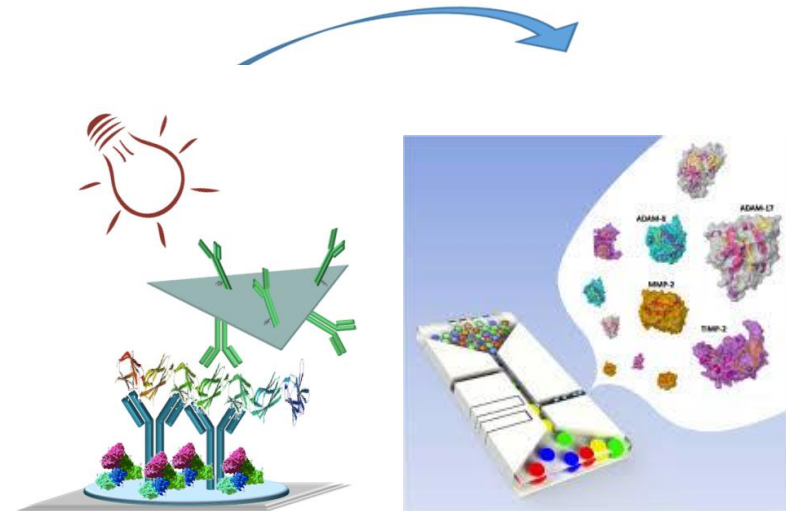
Laser: NIR 1064
I: 250mW/mm²
Irradiation time: 1 sec



[Salmonella T.]

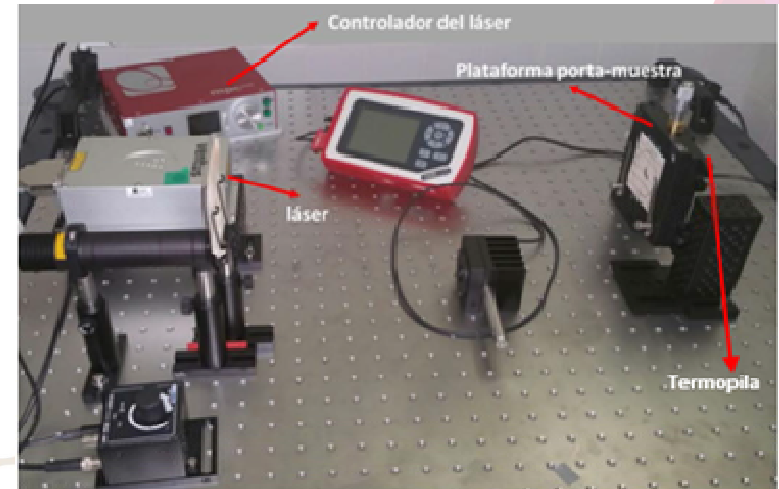
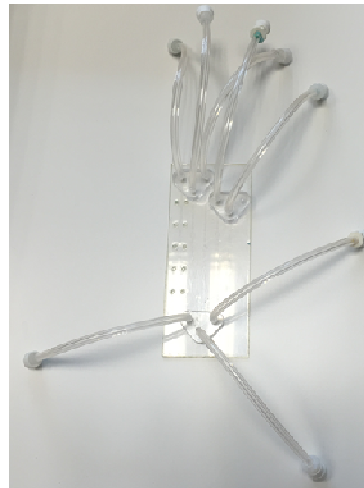
Thermal immunosensor microfluidic implementation

Nanomaterial → signal transduction
from optical
to thermal signal allowing:
Microfluidic-based platform with
integrated thermal detection for point-
of-care testing within the medical and
agro-food sector.



Multianalytes detection

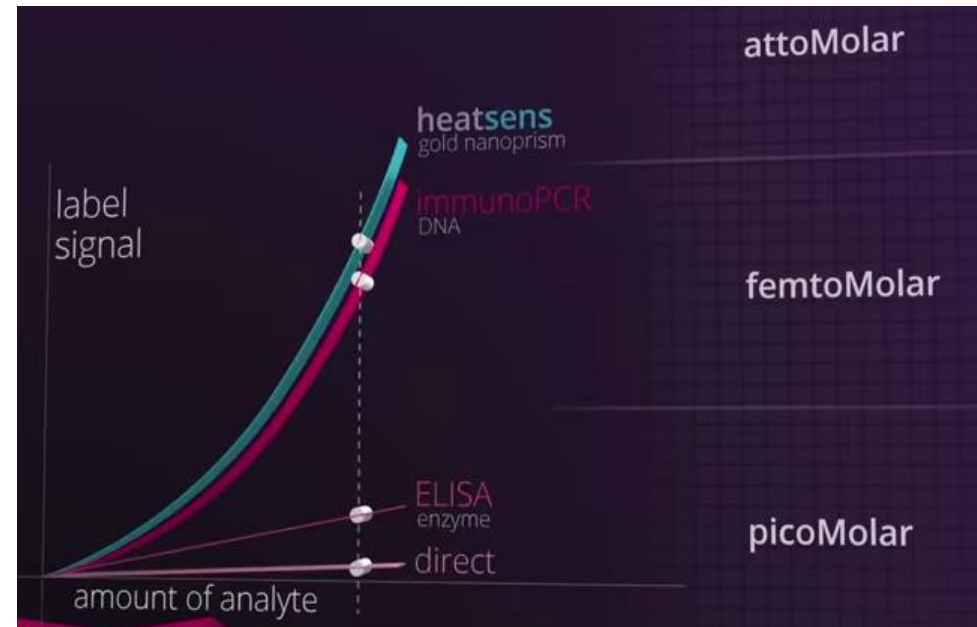
- ✓ Detection in complex matrix
- ✓ subFemtomolar detection
- ✓ Easy to handle



Thermal biosensor – Heatsens – Resume

Gold nanoparticles → Recognition transduction

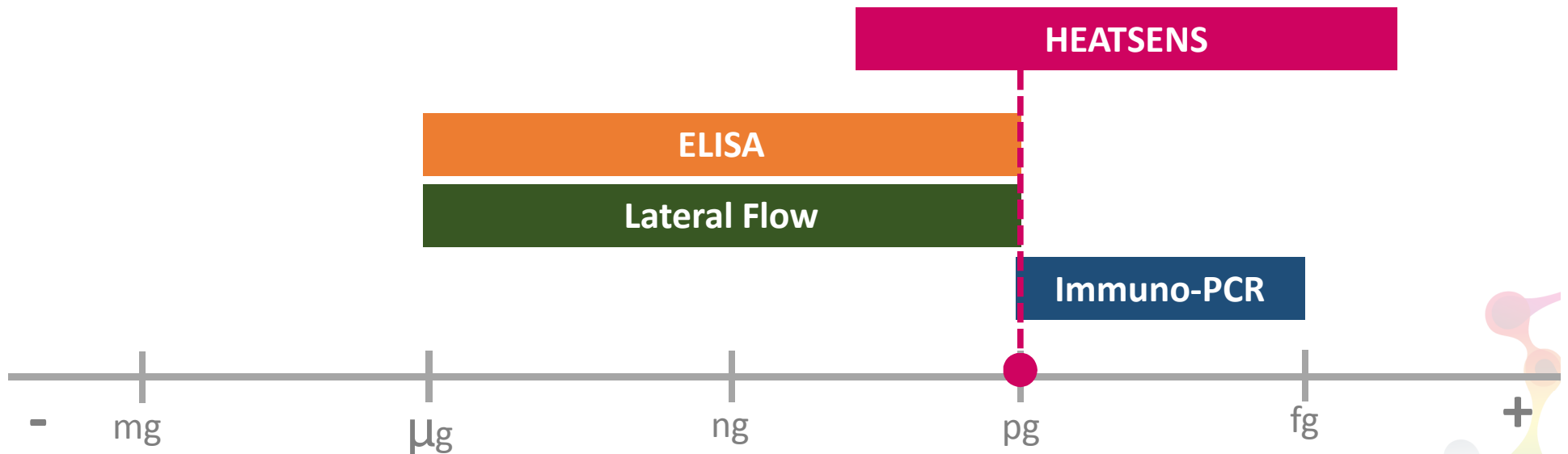
- “ Analyte detection
- “ Thermal transduction of the signal
- “ Detection
 - “ LOD CEA antigen **0,01ng/ml**
(LOD ELISA 28.7ng/ml)
 - “ LOD Ara H1 <<< **4ng/ml** LOD of ELISA
 - “ LOD Salmonella <<<**300 CFU**



Thermal biosensor – Heatsens – Positioning

Positioning related with:

Sensitivity - LOD



* Comparative study considered for most molecules

Sensitivity achieved for the PoC with CEA and no optimization implemented

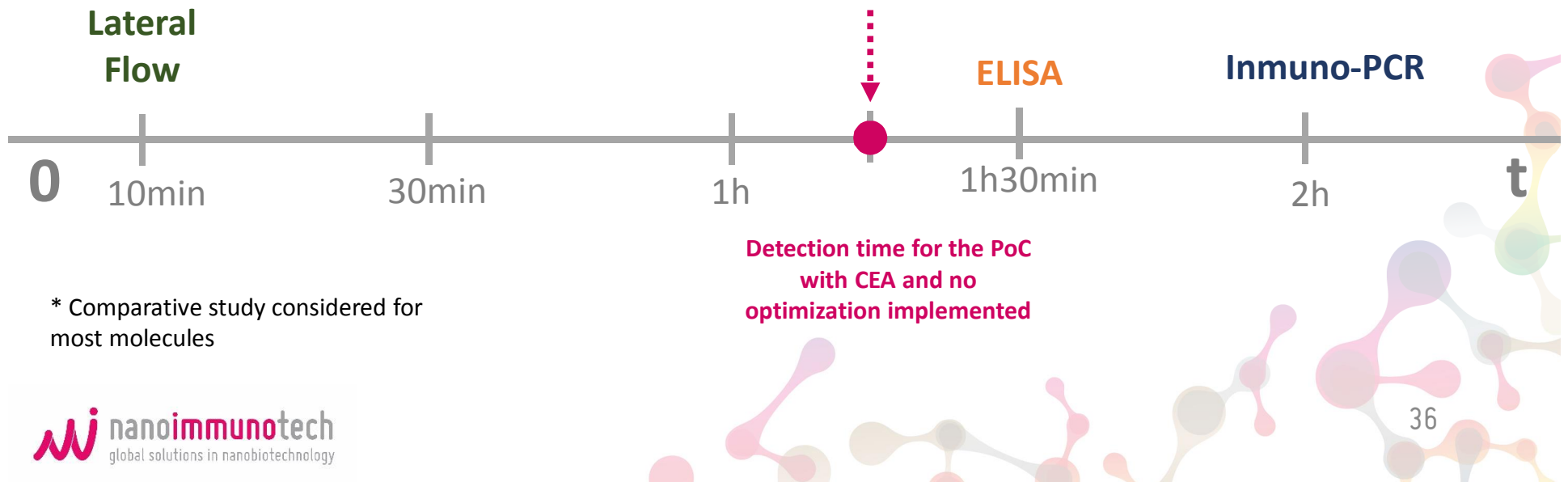
Thermal biosensor Heatsens Positioning

Positioning related with:

Detection time

HEATSENS detection time will depend on different factors, among others: analyte that must be detected, quality and volumen of the analyte, assay format and number of optimization assay stages.

HEATSENS



* Comparative study considered for most molecules

Thermal biosensor – Heatsens – Positioning

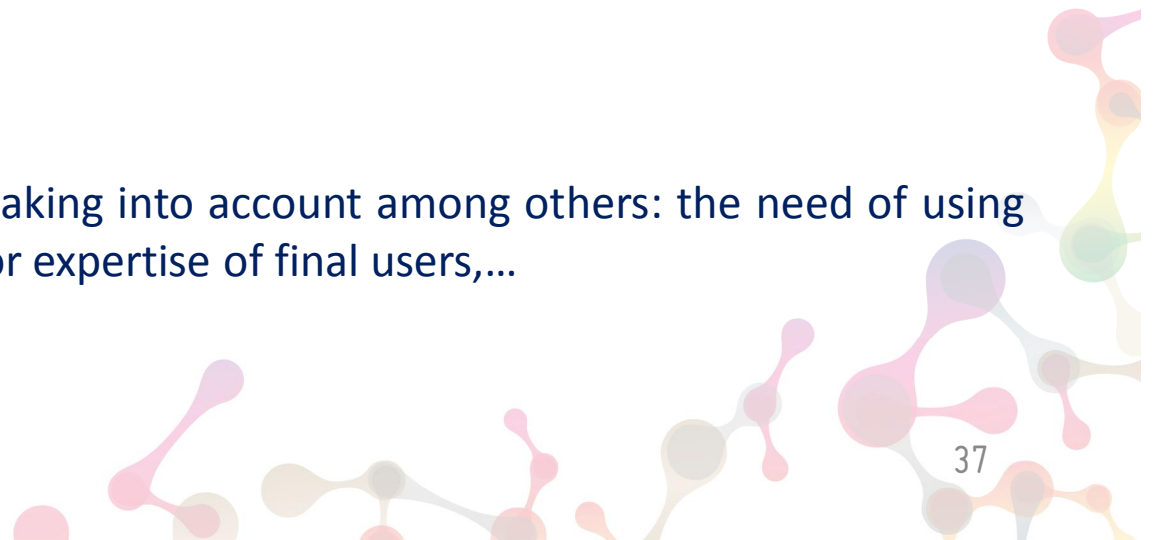
Positioning related with:

HEATSENS consists in a easy methods of trasduction



* Comparative study considered for most molecules

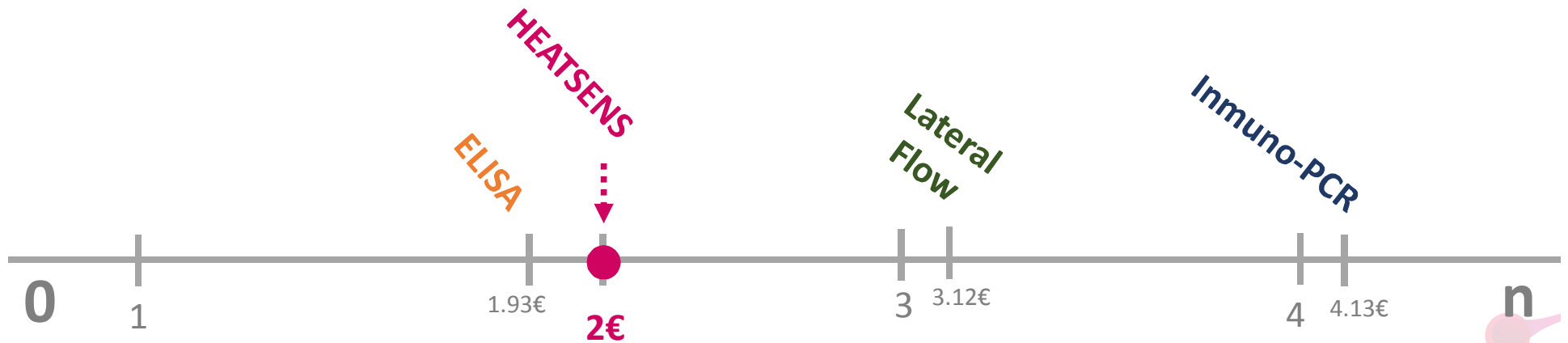
Complexity has been measured taking into account among others: the need of using additional devices, qualification or expertise of final users,...



Thermal biosensor Heatsens Positioning

Positioning related with:

Low Cost



* It has been considered laboratory assay costs for biomarker detection





Thanks for the attention



nitbiosensing

Detecting what really matters

maparracino@nanoimmunotech.es

www.nanoimmunotech.es