Valencia Nanophotonics Technology Center

UNIVERSITAT POLITÈCNICA DE VALÈNCIA

2018 IMAGINENANO

Photonic Bandgap Biosensing Structures Biofunctionalized with Molecular Beacon Probes

Ángela Ruiz-Tórtola[*1], Francisco Prats-Quílez[1], Daniel González-Lucas[2], María-José Bañuls[2], Ángel Maquieira[2], Guy Wheeler[3], Tamas Dalmay[3], Amadeu Griol[1], Juan Hurtado[1], Helge Bohlmann[4] and Jaime García-Rupérez[1]

[1] Nanophotonics Technology Center, Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain
[2] IDM, Instituto Interuniversitario de Investigación de Reconomiento Molecular y Desarrollo Tecnológico, Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain
[3] School of biological Sciences, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, UK
[3] microTEC Gesellschaft für mikrotechnologie mbH, Duisburg, Germany

saphely

Self-amplified photonic biosensing platform for microRNA-based early diagnosis of diseases

Outline

- **Motivation**
- Sensor concept
- Oligonucleotide detection
- Influence of the MB conformational change on evanescent wave
- Conclusion

Motivation

Motivation

CONVENTIONAL METHODS

- labelling processes
- extremely laborious
- time-consuming
- expensive

Motivation

CONVENTIONAL METHODS

- labelling processes
- extremely laborious
- time-consuming
- expensive

OPTICAL BIOSENSORS

- label-free
- user friendly
- real-time analysis
- low cost

Motivation

CONVENTIONAL METHODS

- labelling processes
- extremely laborious
- time-consuming
- expensive

OPTICAL BIOSENSORS

- label-free
- user friendly
- real-time analysis
- low cost

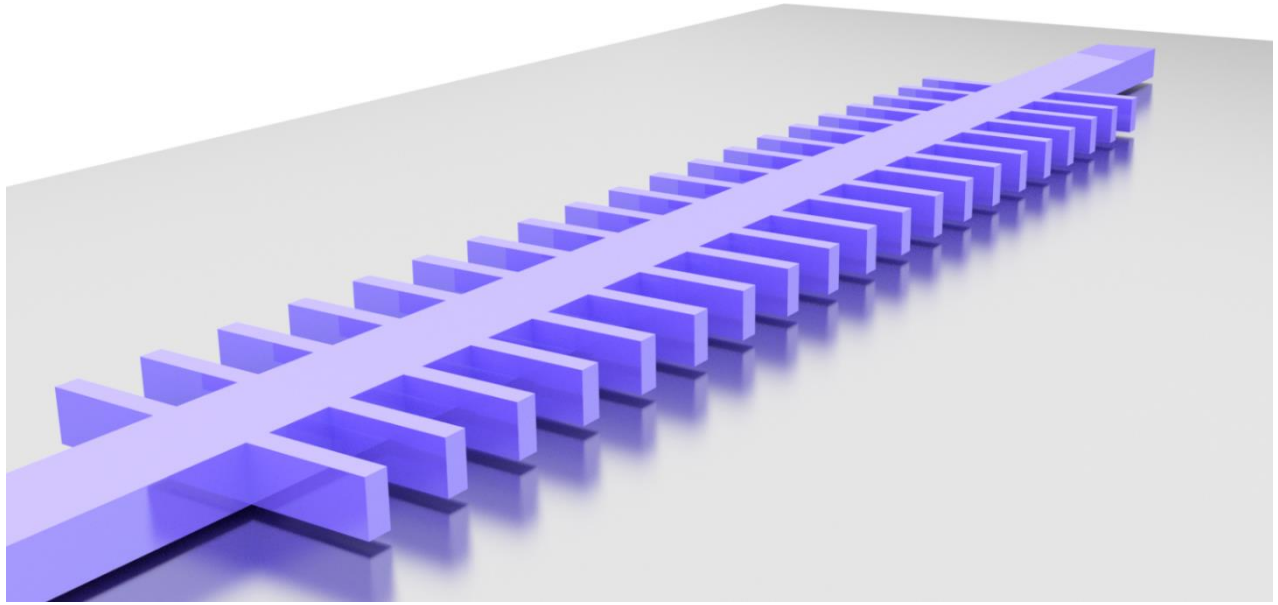
LAB-ON-A-CHIP DEVICE

Outline

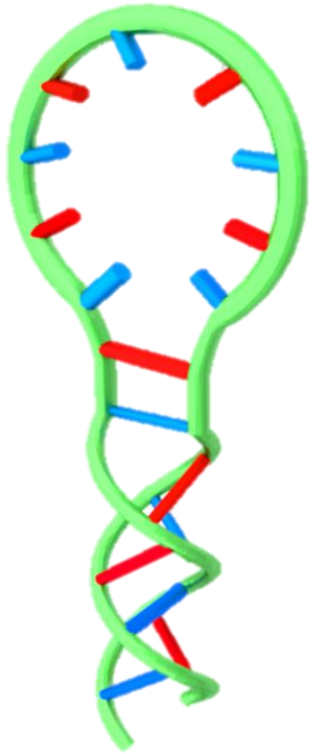
- Motivation
- **Sensor concept**
- Oligonucleotide detection
- Influence of the MB conformational change on evanescent wave
- Conclusion

Sensor concept

(i) Photonic Bandgap (PBG) sensing structure



(ii) Molecular Beacon (MB) probe



Sensor concept

(i) PBG sensing structure: working principle

PHOTONIC BANDGAP

Reflections produced at the interfaces of periodic dielectric distributions.

SLOW WAVE PHENOMENON

High interaction between the evanescent wave and the propagation medium (analytes) in periodic structures.

Sensor concept

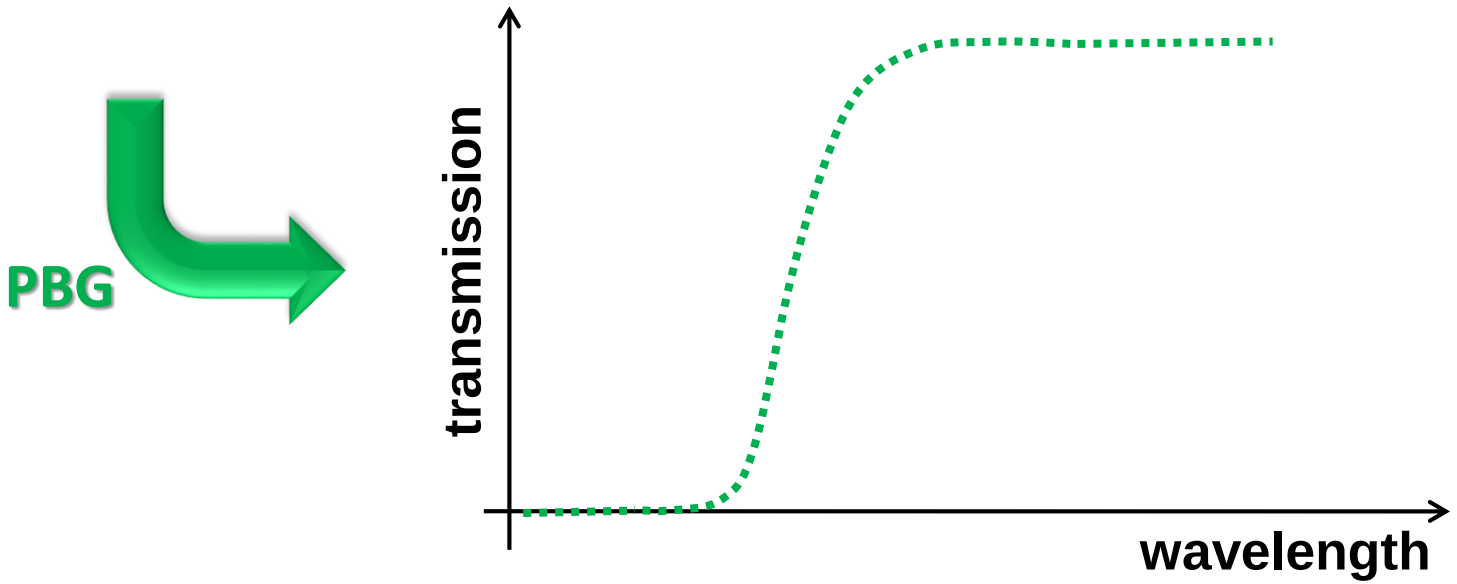
(i) PBG sensing structure: working principle

PHOTONIC BANDGAP

Reflections produced at the interfaces of periodic dielectric distributions.

SLOW WAVE PHENOMENON

High interaction between the evanescent wave and the propagation medium (analytes) in periodic structures.



Sensor concept

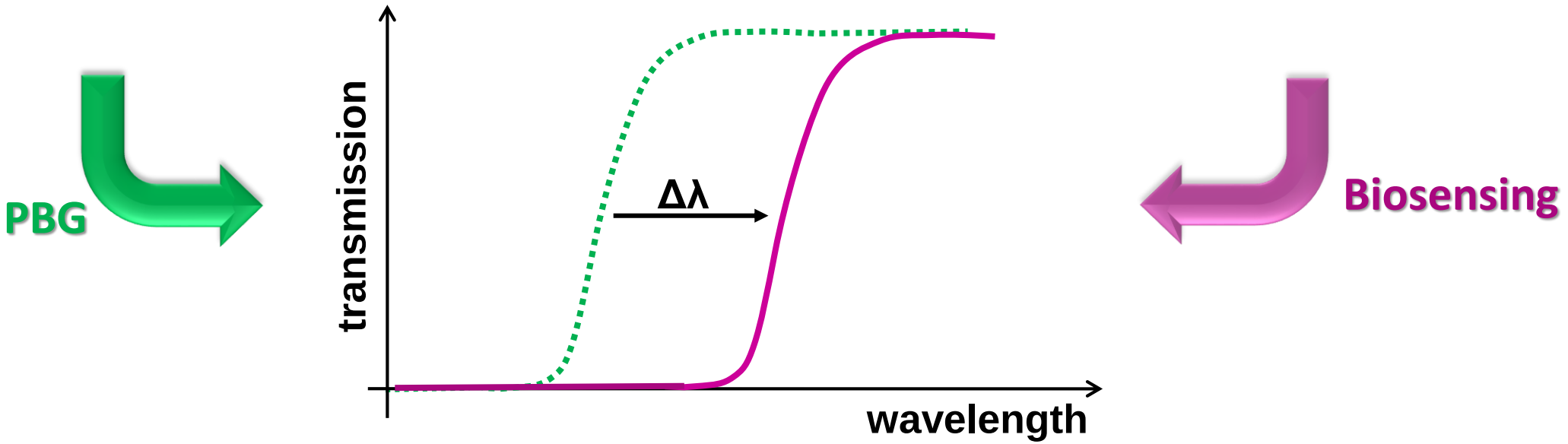
(i) PBG sensing structure: working principle

PHOTONIC BANDGAP

Reflections produced at the interfaces of periodic dielectric distributions.

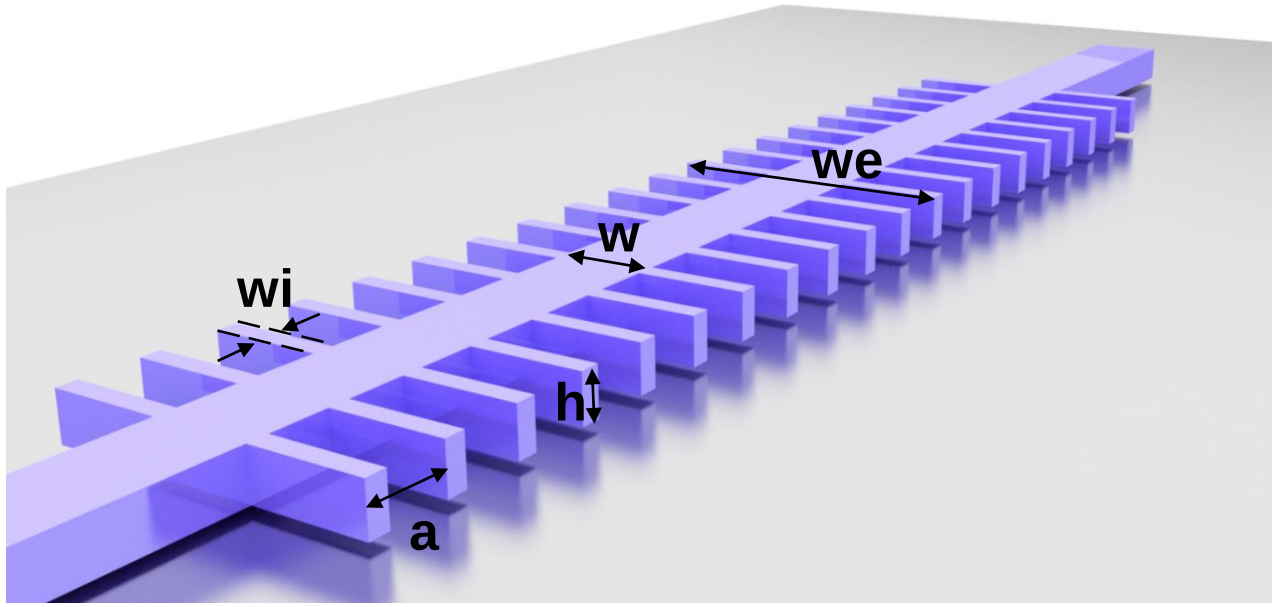
SLOW WAVE PHENOMENON

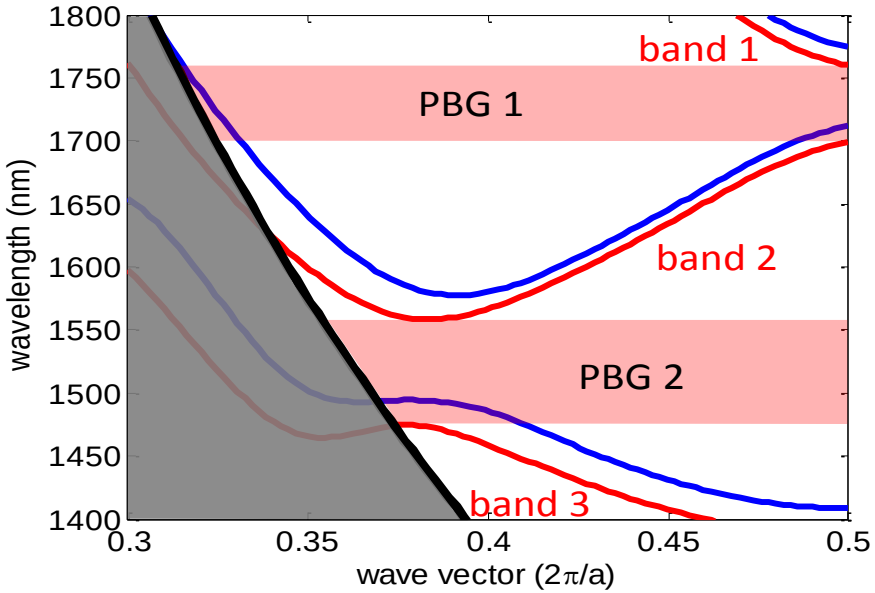
High interaction between the evanescent wave and the propagation medium (analytes) in periodic structures.

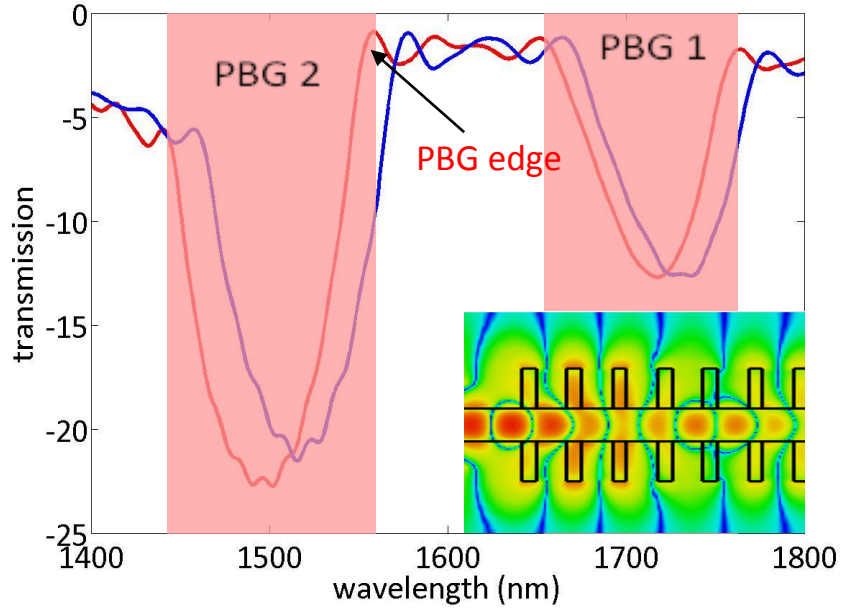


Sensor concept

(i) PBG sensing structures: design

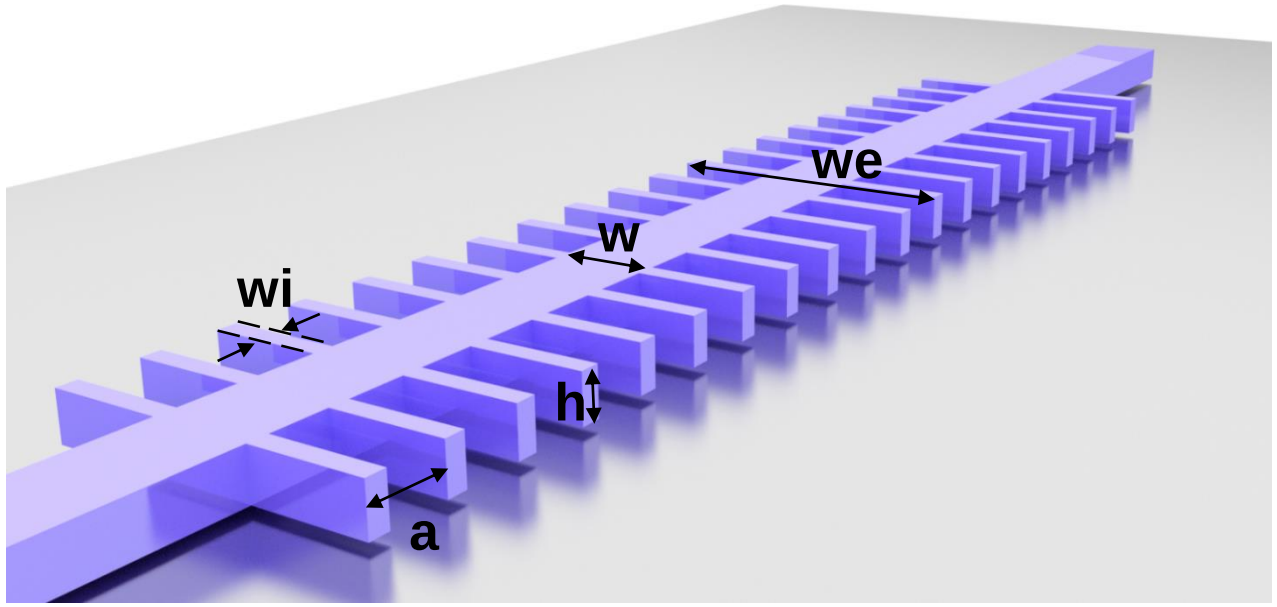


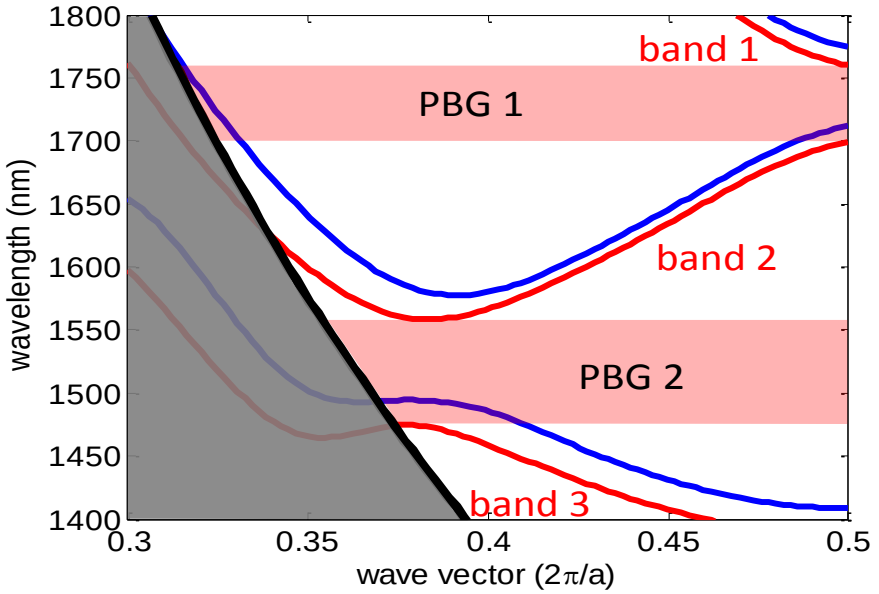


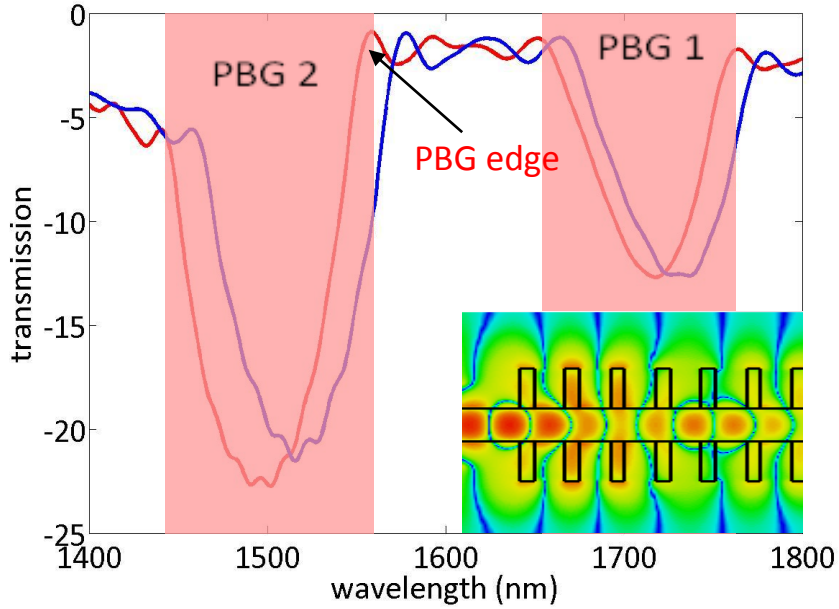


Sensor concept

(i) PBG sensing structures: design







Optimal parameters

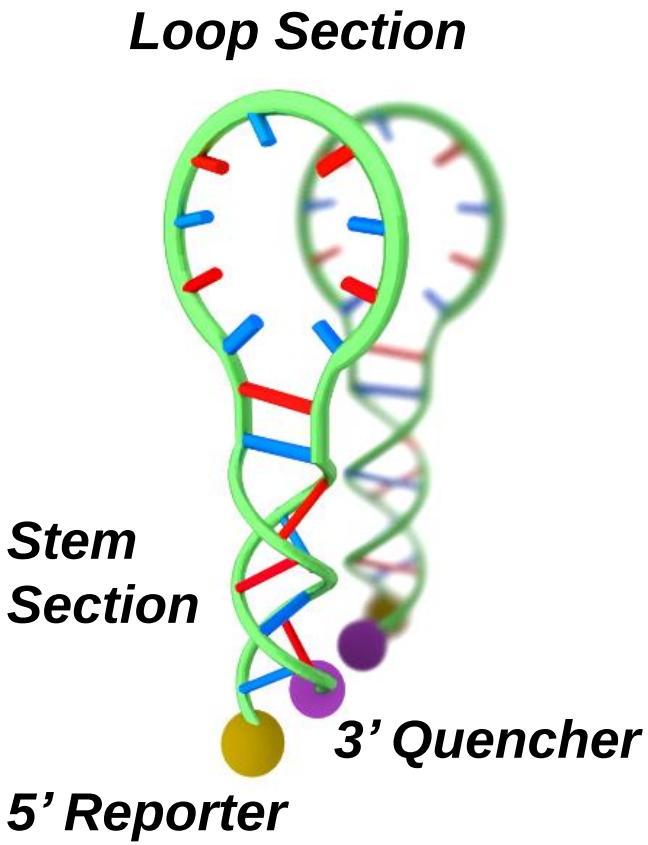
- a=380 nm
- w=460 nm
- wi=120 nm
- h=220 nm
- we=1500 nm

Sensitivity 175 nm/RIU*

*Refractive Index Units

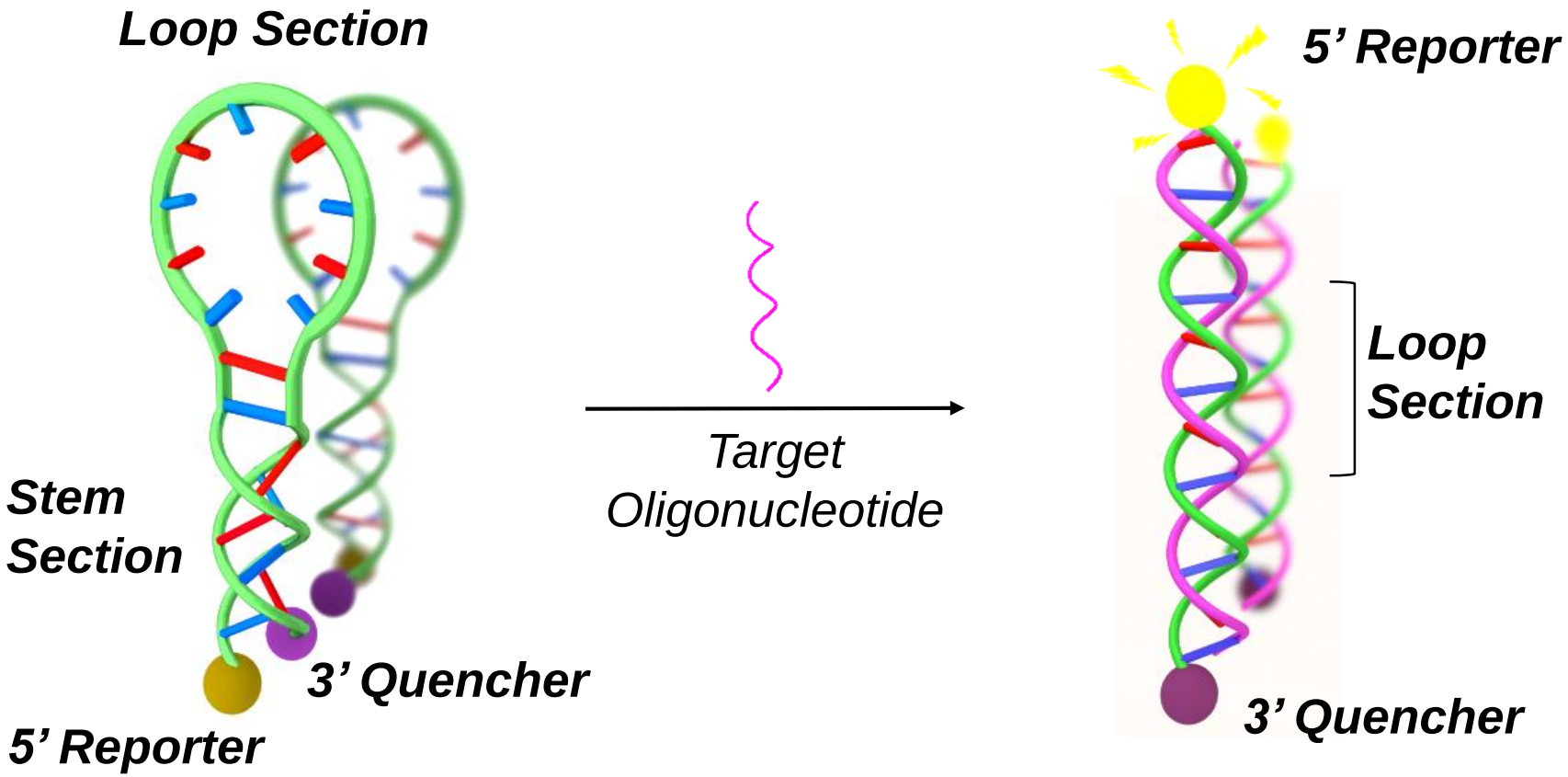
Sensor concept

(ii) MB: typical application



Sensor concept

(ii) MB: typical application

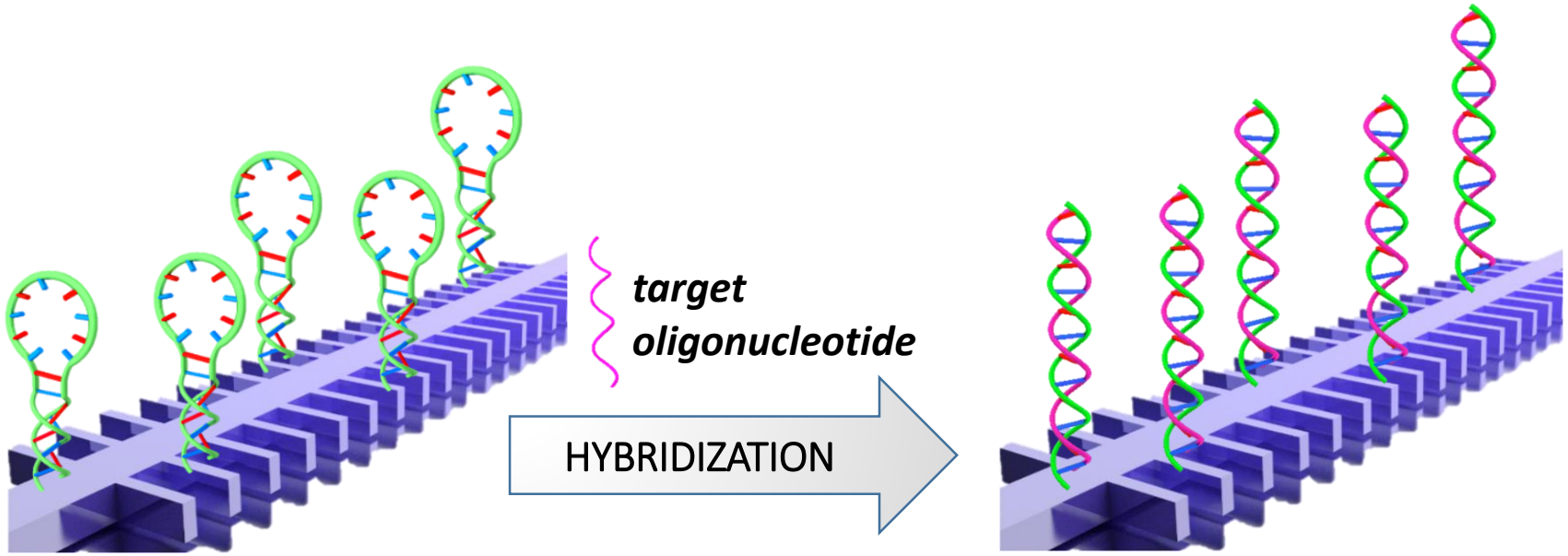


Sensor concept

(ii) MB: immobilization on PBG sensing structure surface

Thiol-ene coupling (TEC) chemistry

Immobilization density:
14 pmol/cm^2



D. González-Lucas et al., *Microchim Acta* 184, 3231-3238 (2017)

	5’	3’	Sequence (5’-3’)
Target	Cy5		AUCGACUUAAUGCUAAUCGUGAUAGGGGUGUCGAU
MB	SH		ATCGACACCCCTATCACGATTAGCATTAAGTCGAT

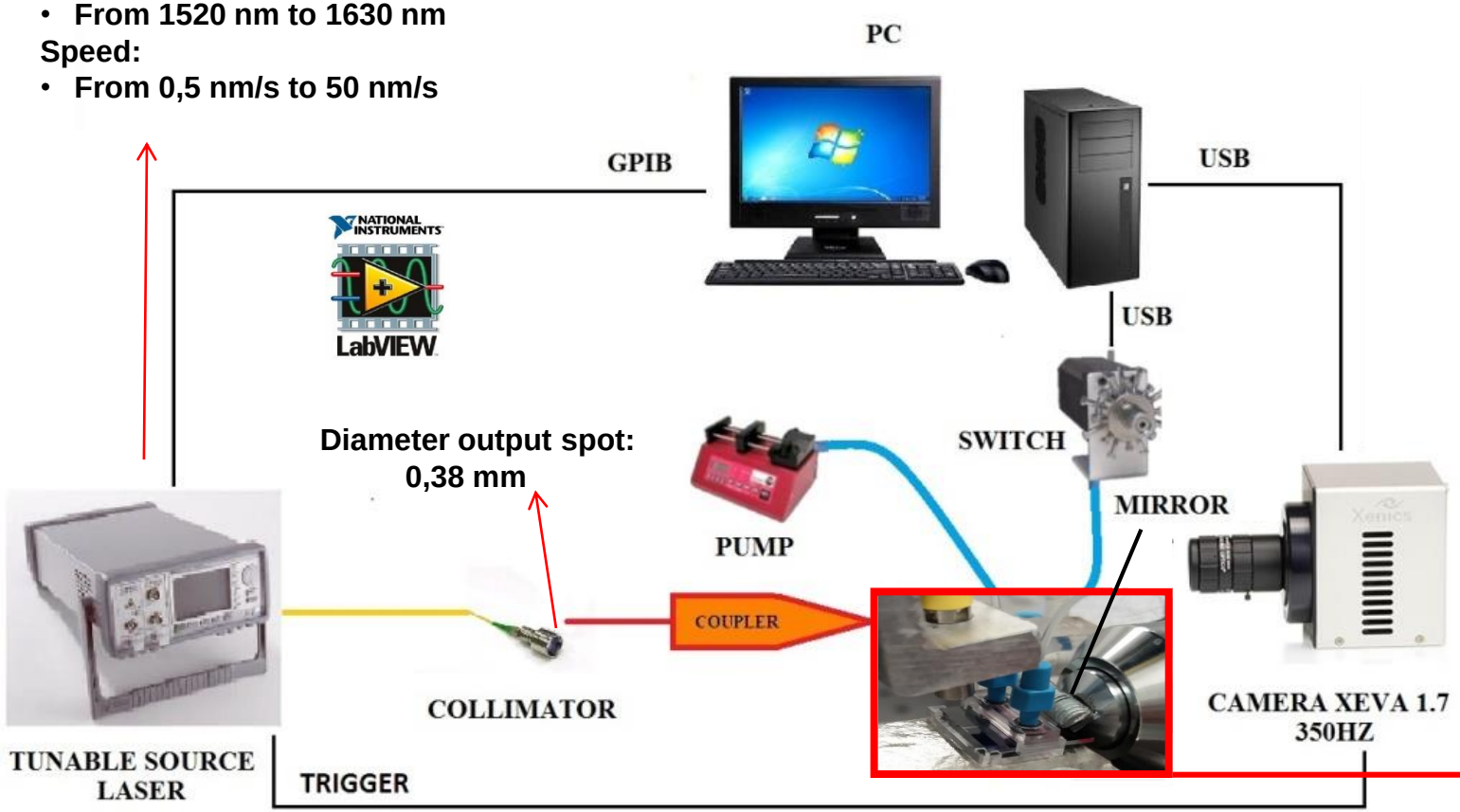
Outline

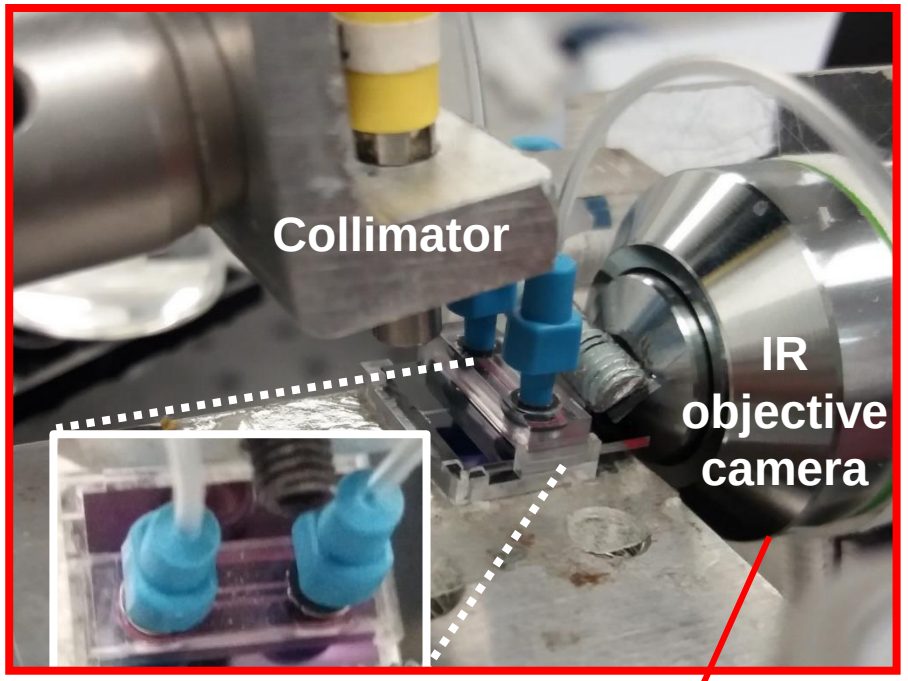
- Motivation
- Sensor concept
- **Oligonucleotide detection**
- Influence of the MB conformational change on evanescent wave
- Conclusion

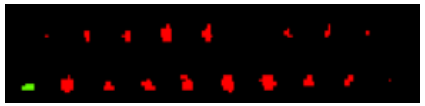
Interrogation platform

Range:
- **From 1520 nm to 1630 nm**

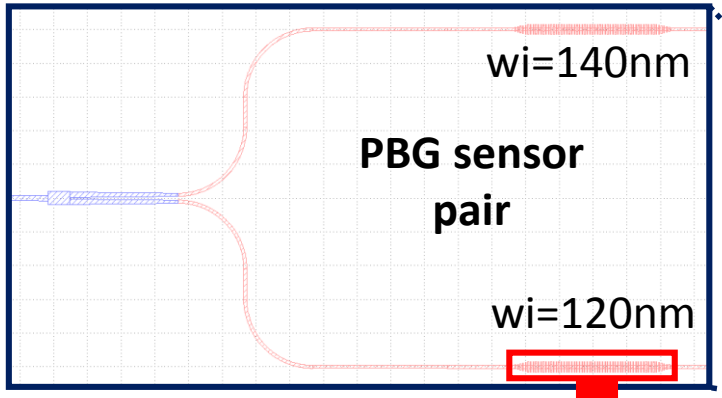
Speed:
- **From 0,5 nm/s to 50 nm/s**

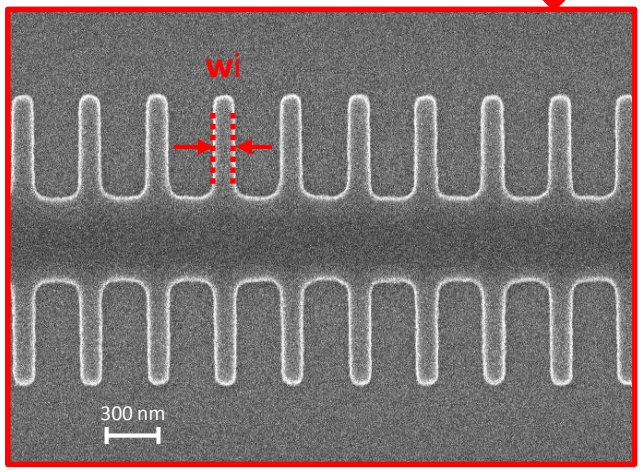






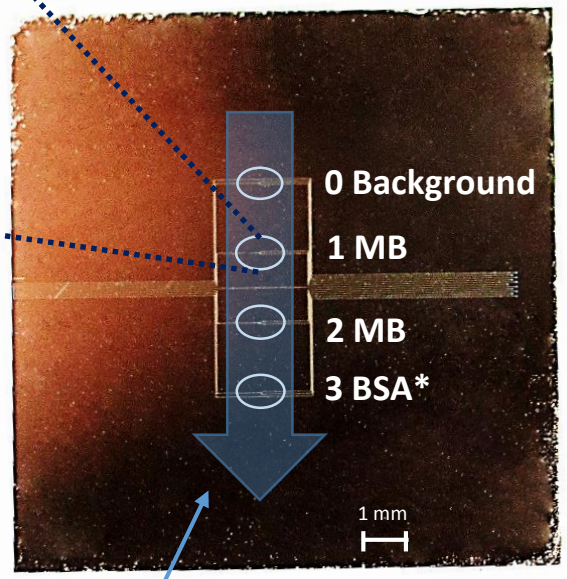
Oligonucleotide detection: **photonic chip**





SEM image of a PBG sensor

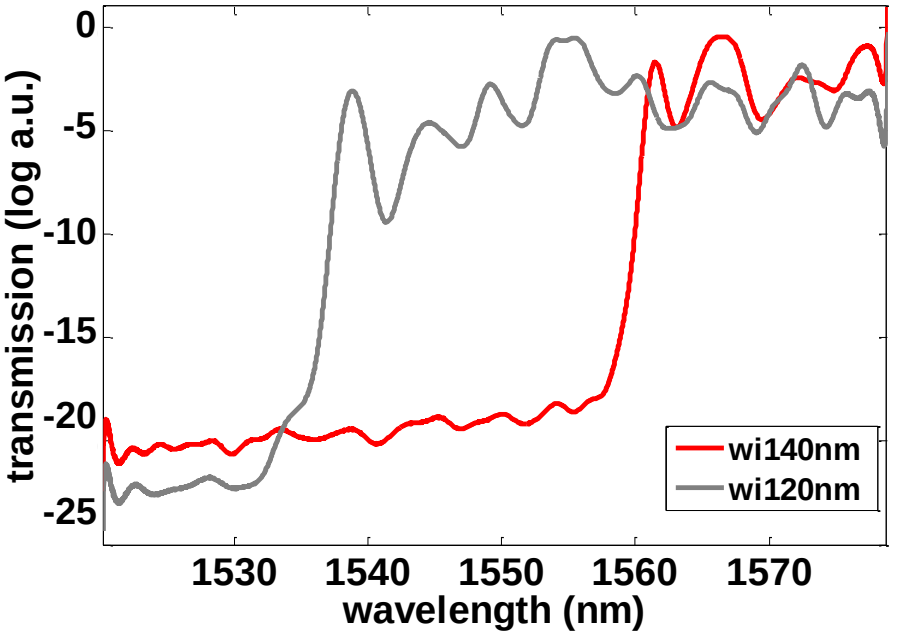
PHOTONIC SENSING CHIP



*Bovine Serum Albumin

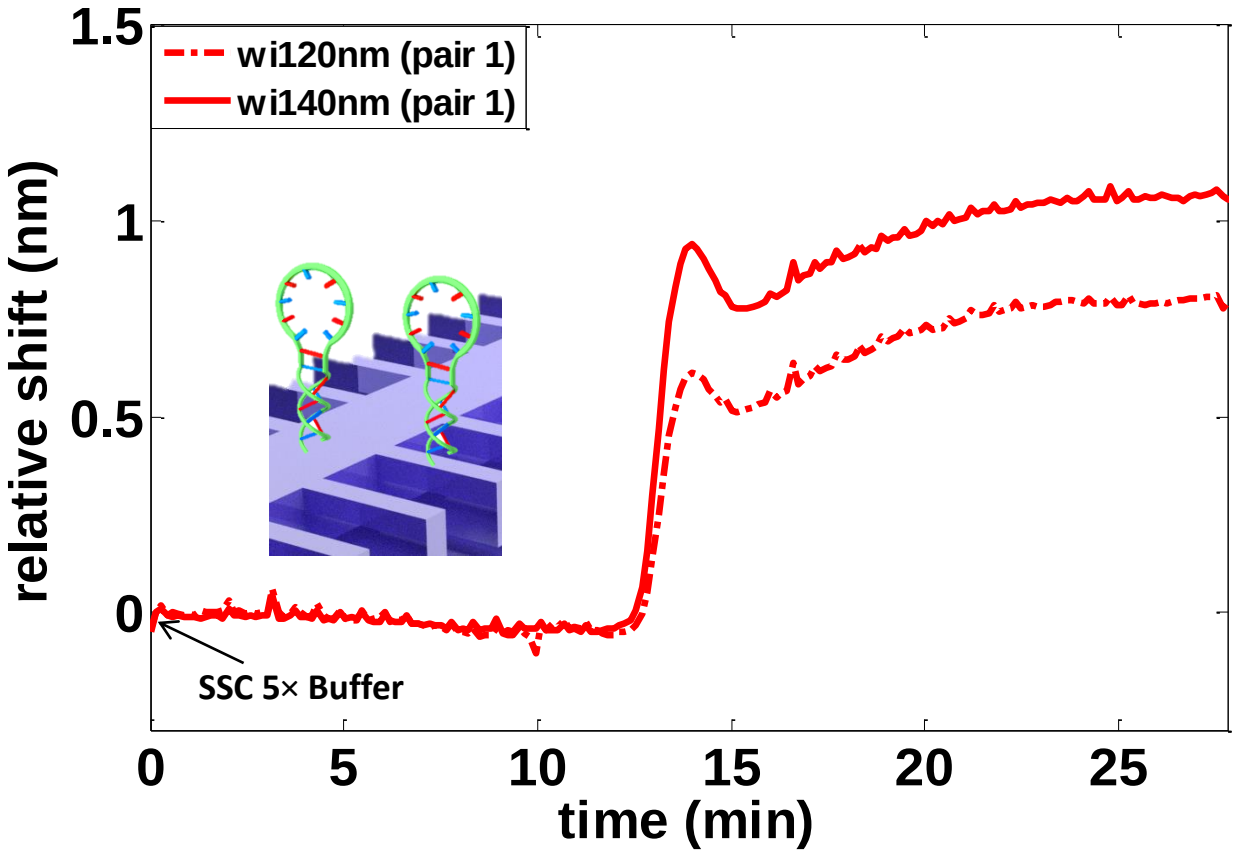
Microfluidic flow direction

Example of transmission spectrum (SSC 5× buffer*)

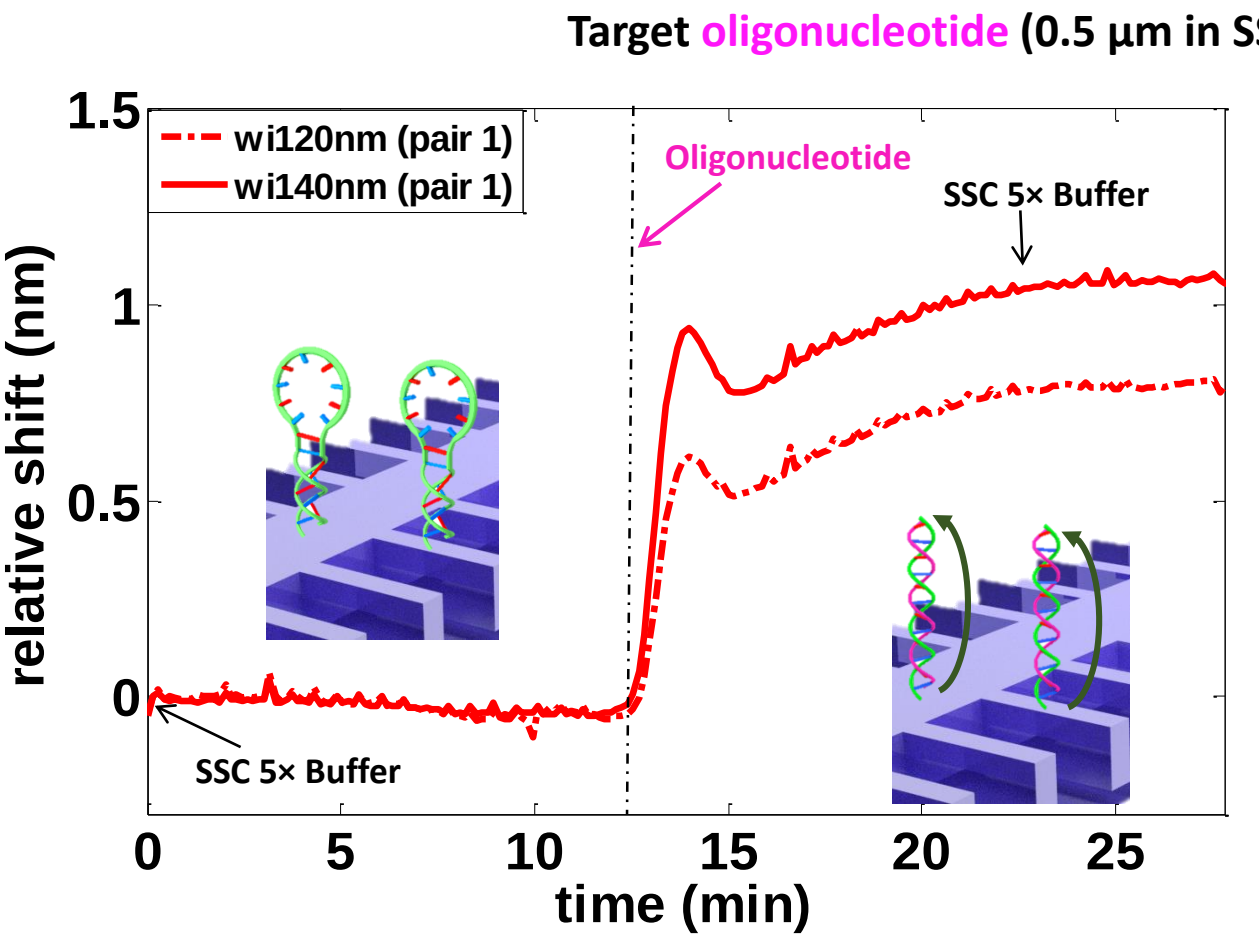


*Saline-sodium citrate

Oligonucleotide detection: **experiment**

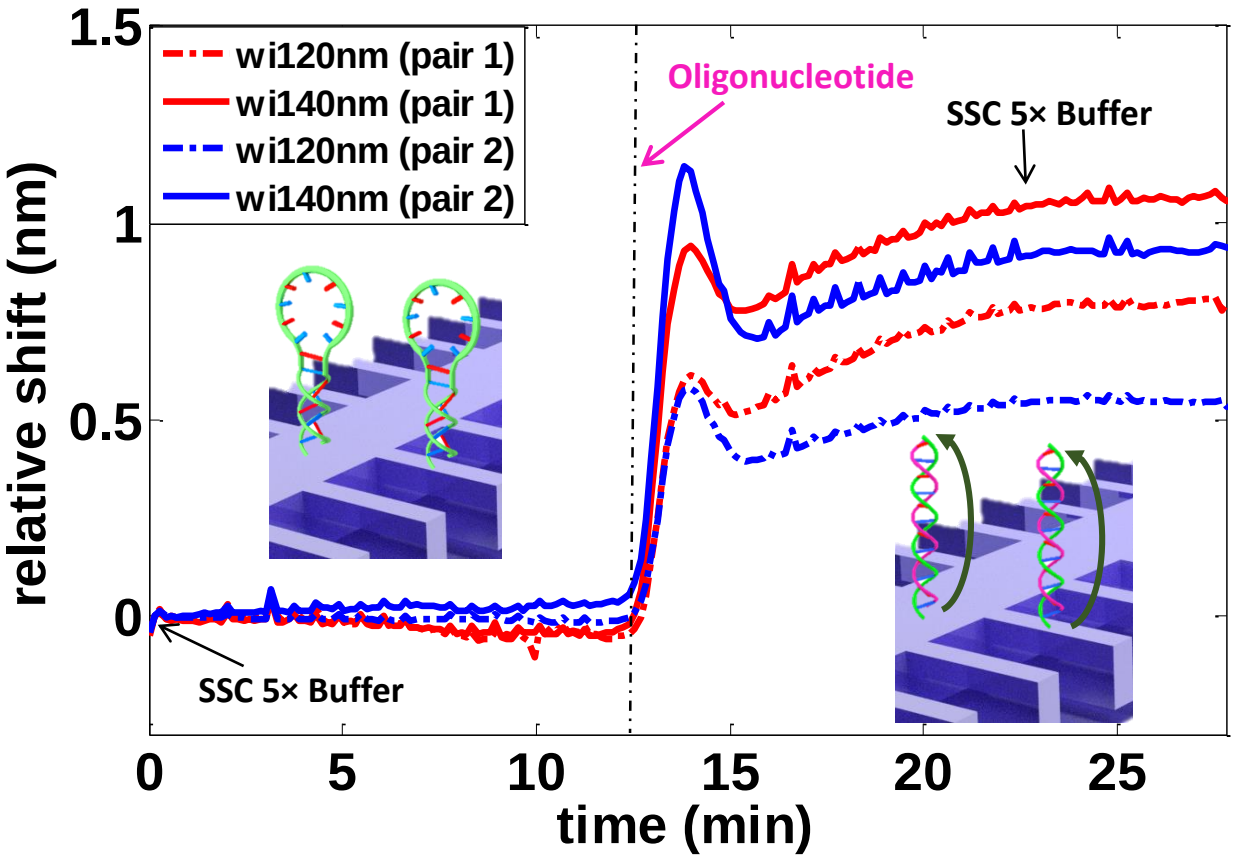


Oligonucleotide detection: **experiment**



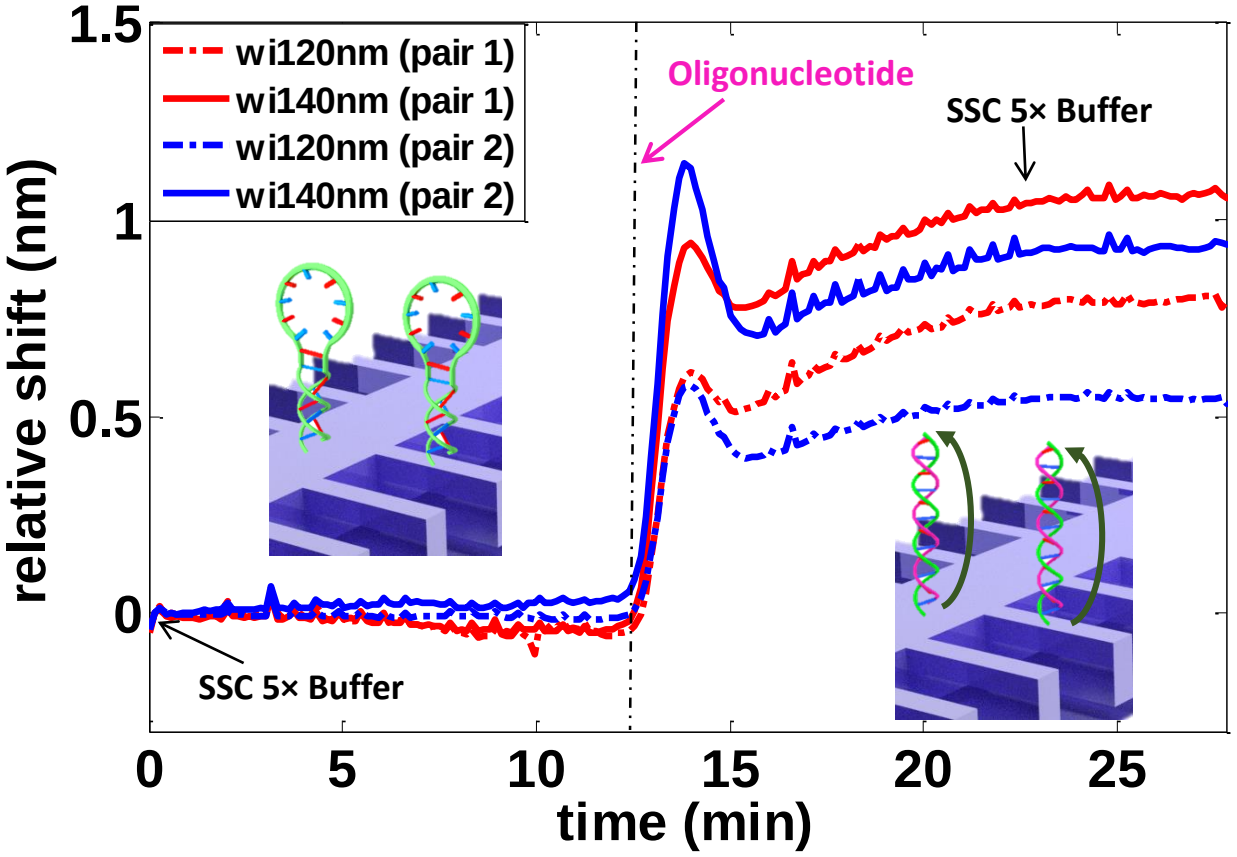
Oligonucleotide detection: **experiment**

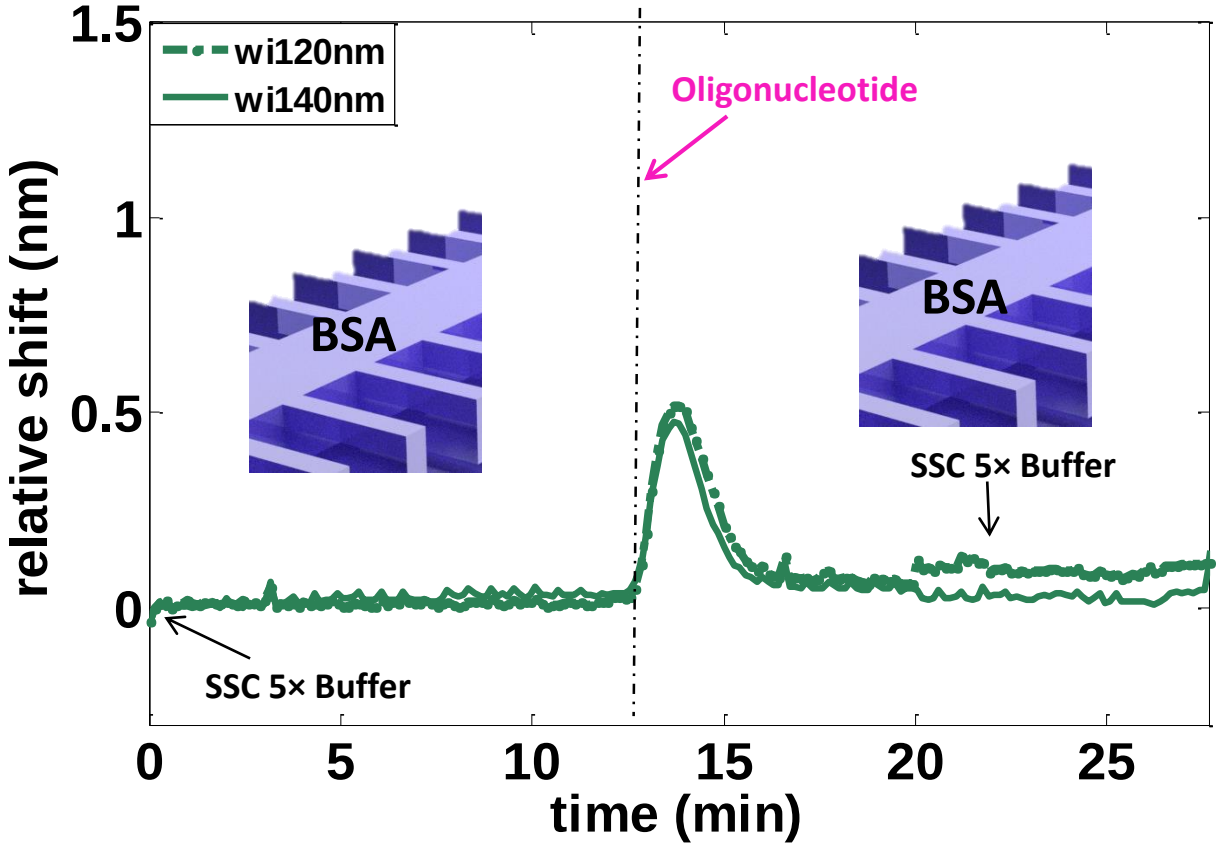
Target oligonucleotide (0.5 µm in SSC 5× buffer)



Oligonucleotide detection: **experiment**

Target oligonucleotide (0.5 µm in SSC 5× buffer)



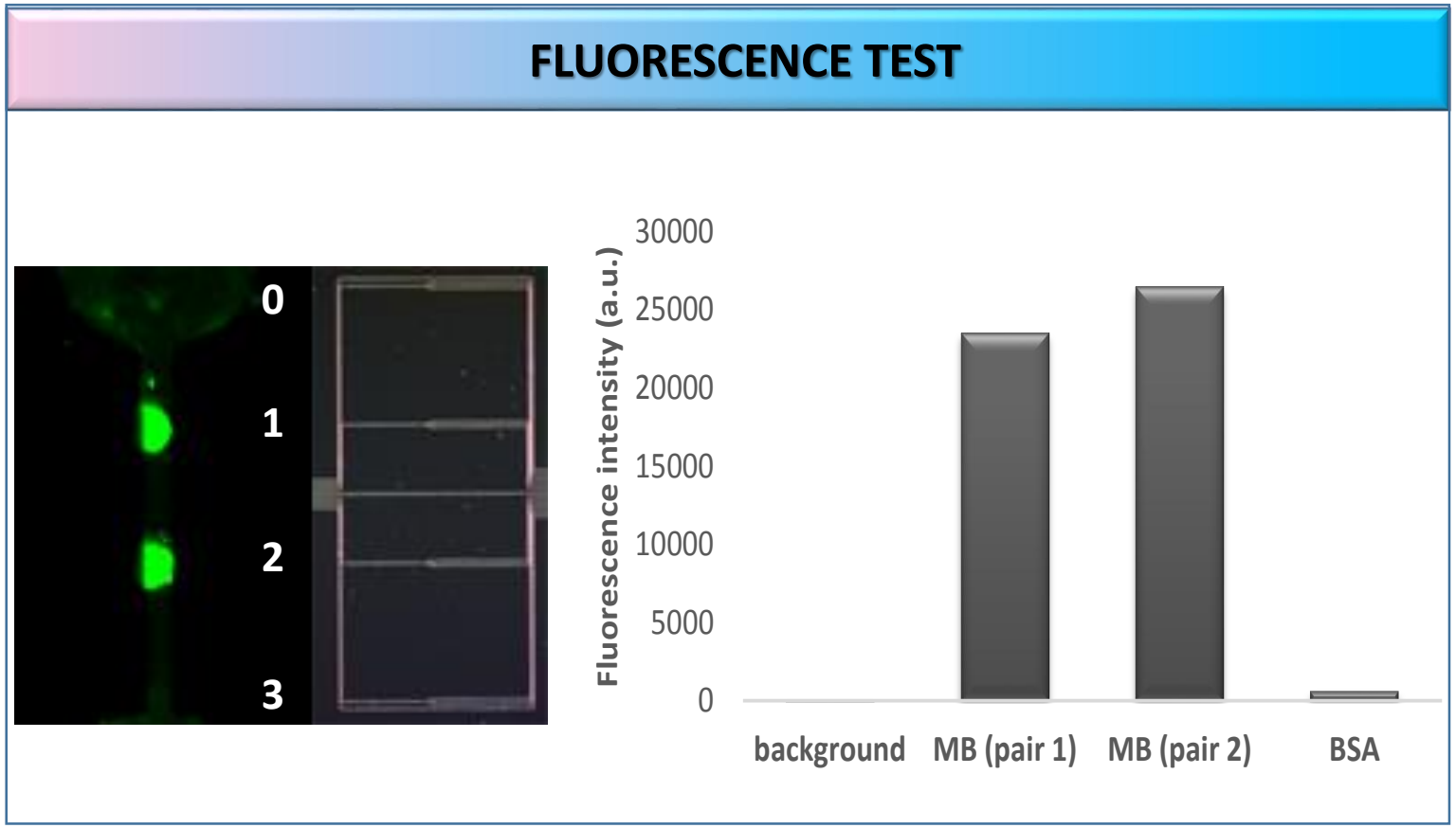


Oligonucleotide detection: **results**

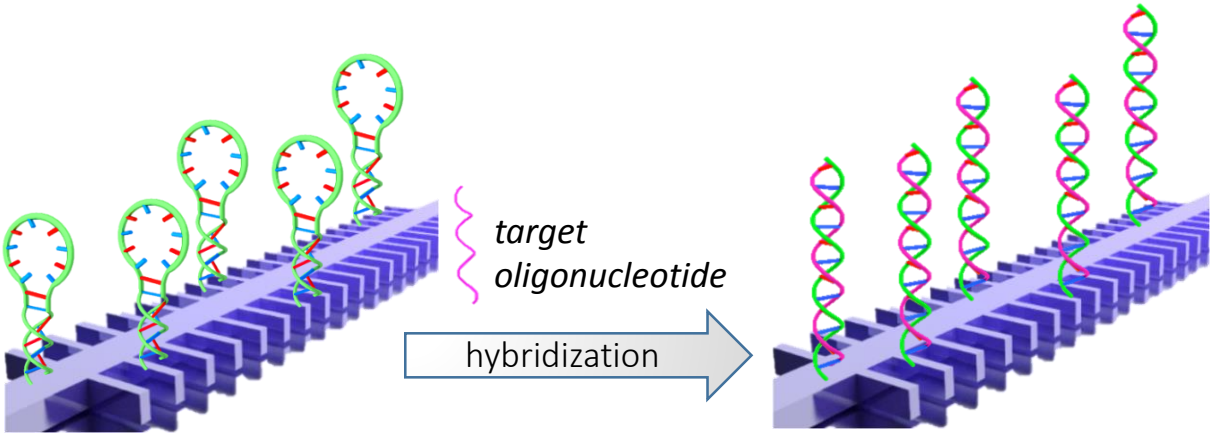
PBG Sensor pair	wi (nm)	Chemistry Biofun*	PBG edge shift (pm)
0	120	Background	NM**
	140		NM**
1	120	MB	800
	140		1100
2	120	MB	520
	140		950
3	120	BSA	-
	140		-

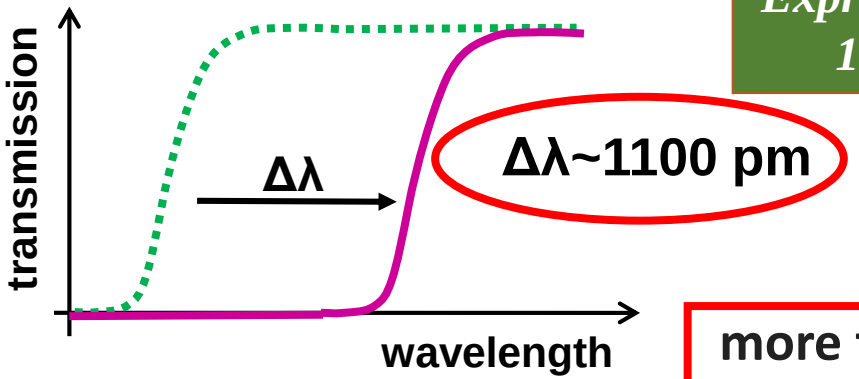
* Biofunctionalization

** Not Measured



Oligonucleotide detection: **comparison**

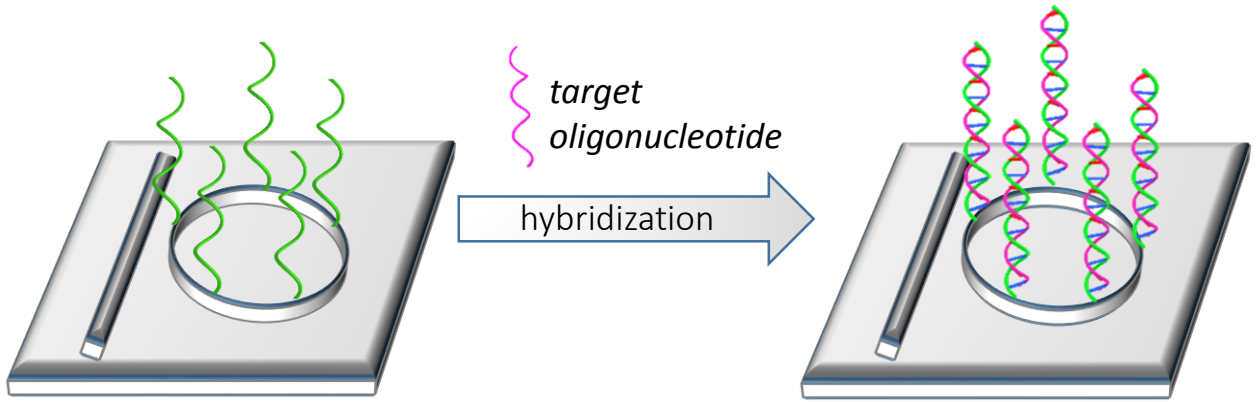


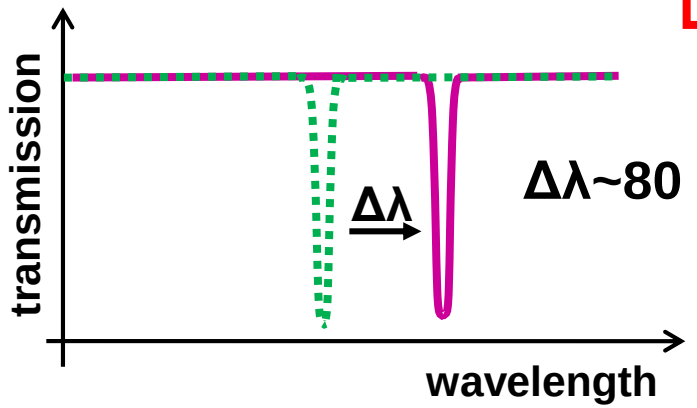


Á. Ruiz-Tórtola et al., *Biomed. Opt. Express 9(4), 1717-1727 (2018)*

Δλ~1100 pm

more than one order of magnitude





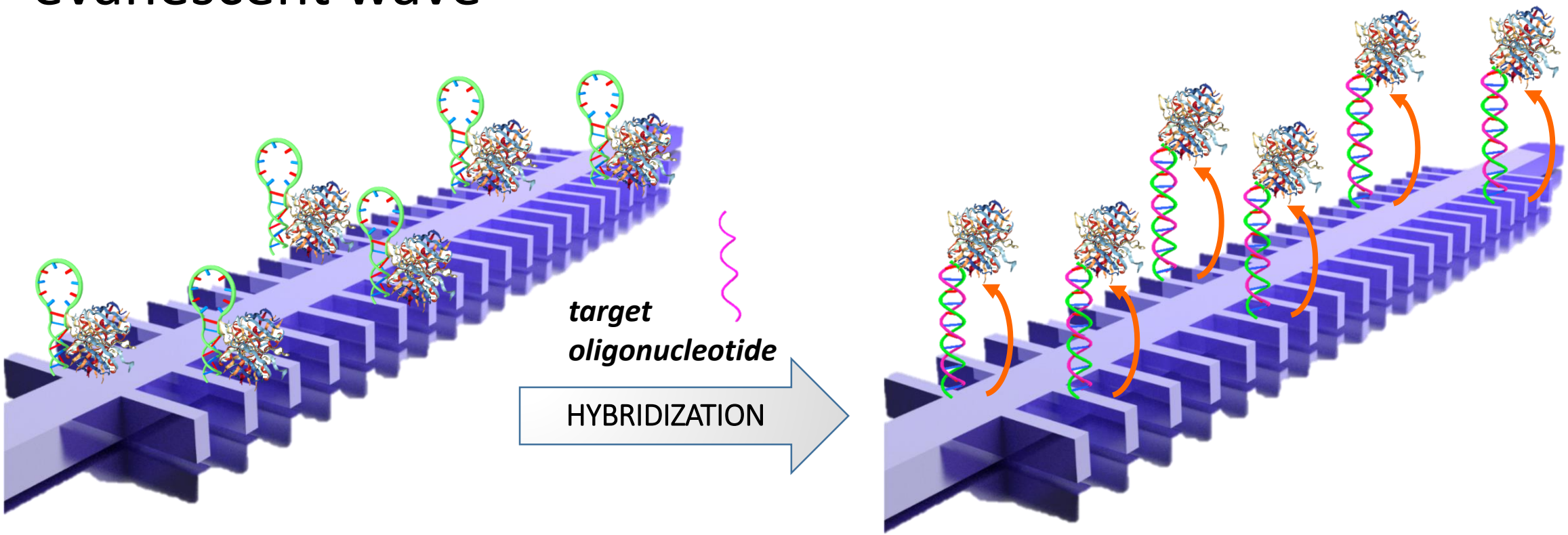
Δλ~80 pm

A. J. Qavi and R. Bailey, *Biosensors* 49, 4608-4611 (2010)

Outline

- Motivation
- Sensor concept
- Oligonucleotide detection
- **Influence of the MB conformational change on evanescent wave**
- Conclusion

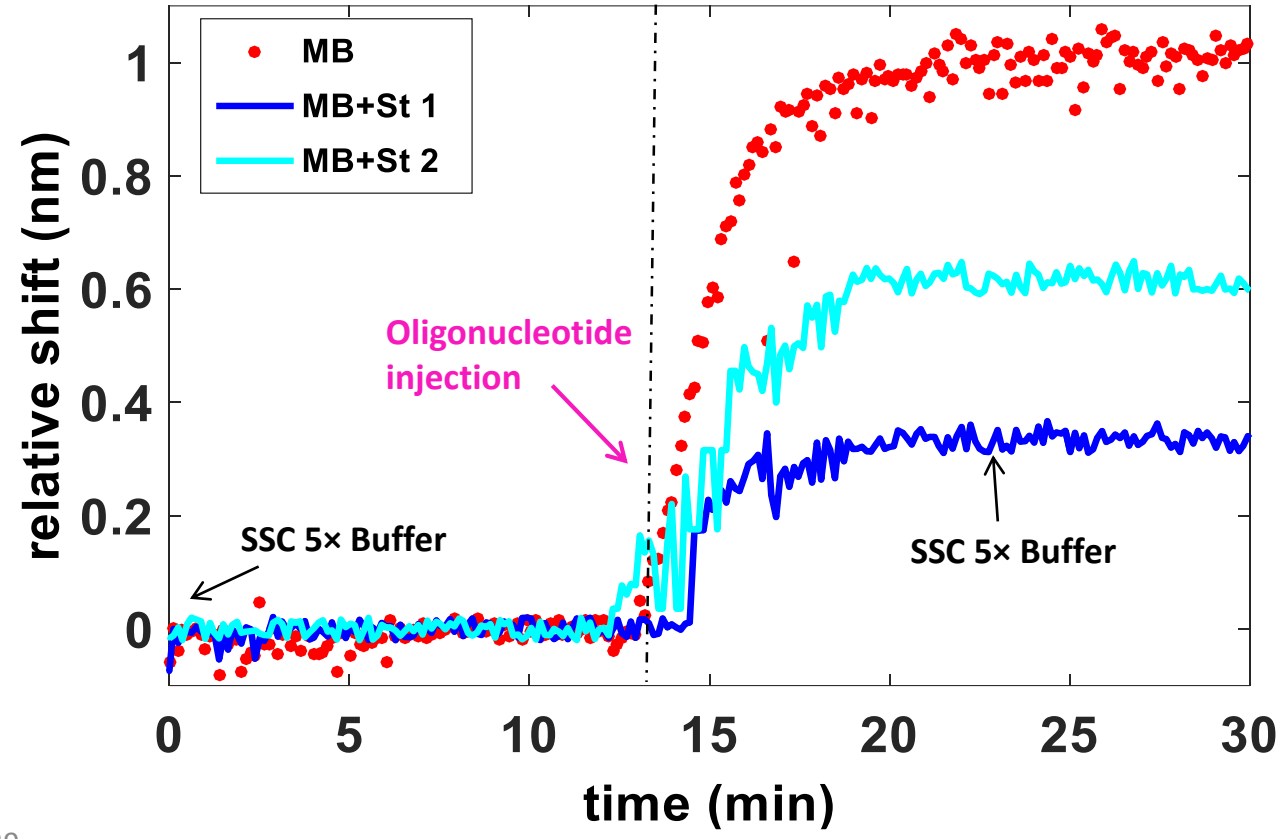
Influence of the MB conformational change on evanescent wave



Very robust biotin-streptavidin recogniticon

Bayer EA and Wilchek M, *Methods in enzymology* 184, 49-51 (1990)

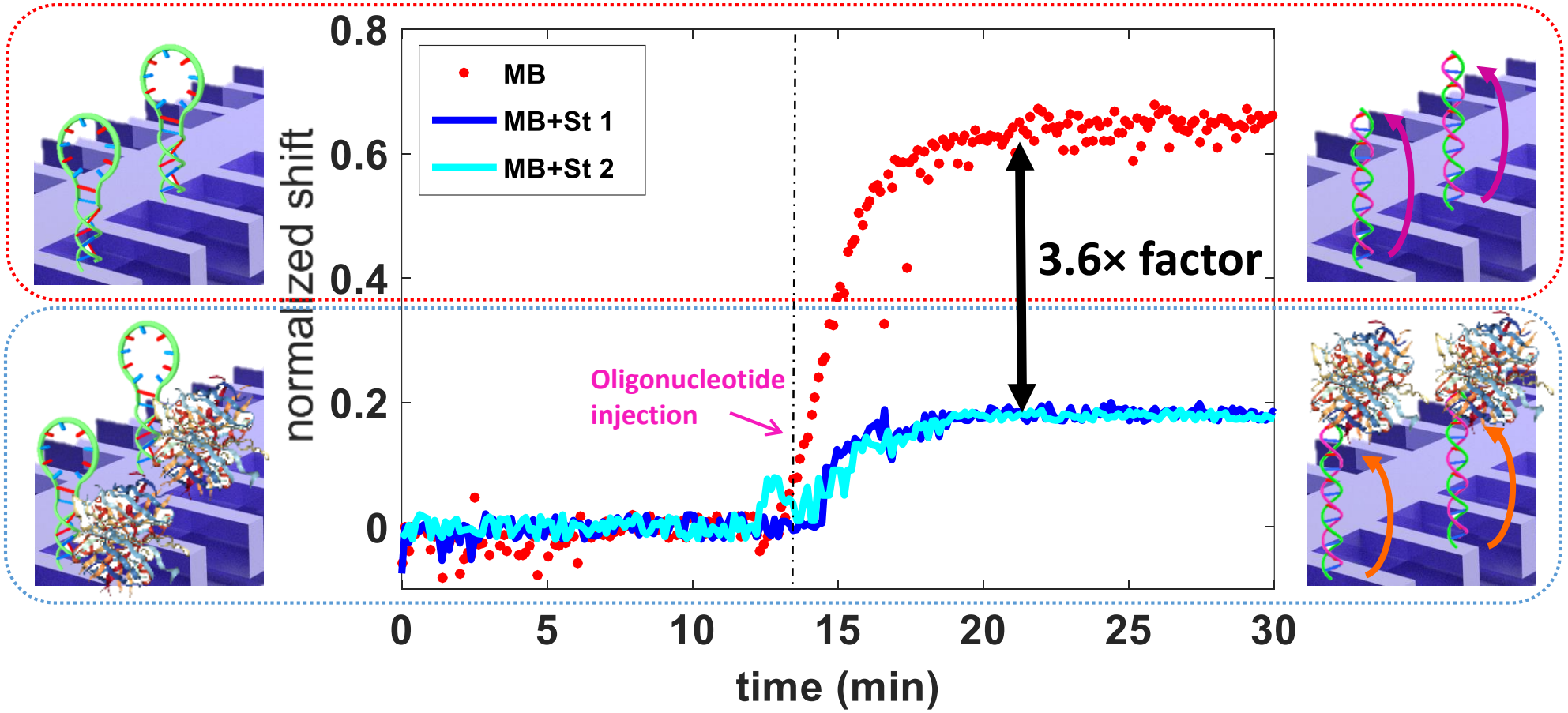
Influence of the MB conformational change on evanescent wave: **experiment**



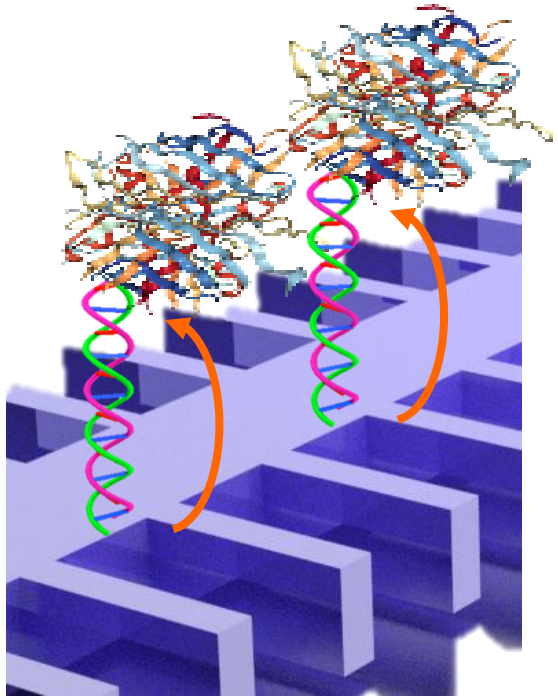
	MB	MB+St	MB+St
Oligonucleotide detection (pm)	1020	620	345
RI Calibration (pm)*	-1560	-3230	-1890
Normalized oligonucleotide detection	0,654	0,192	0,183

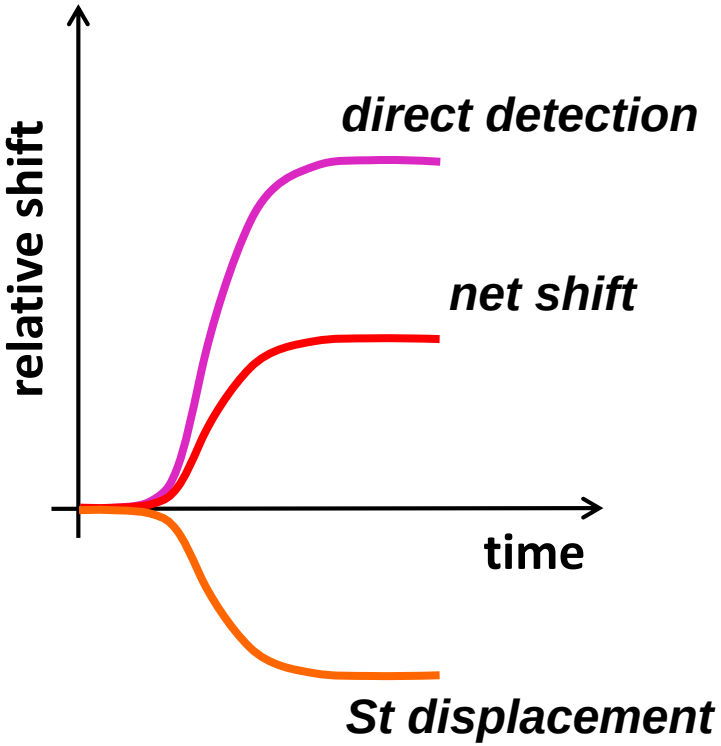
*SS5× buffer to DIW (Deionized water)

Influence of the MB conformational change on evanescent wave: **experiment**



Influence of the MB conformational change on evanescent wave: **discussion**





So significantly large positive shift measured for the direct oligonucleotide detection

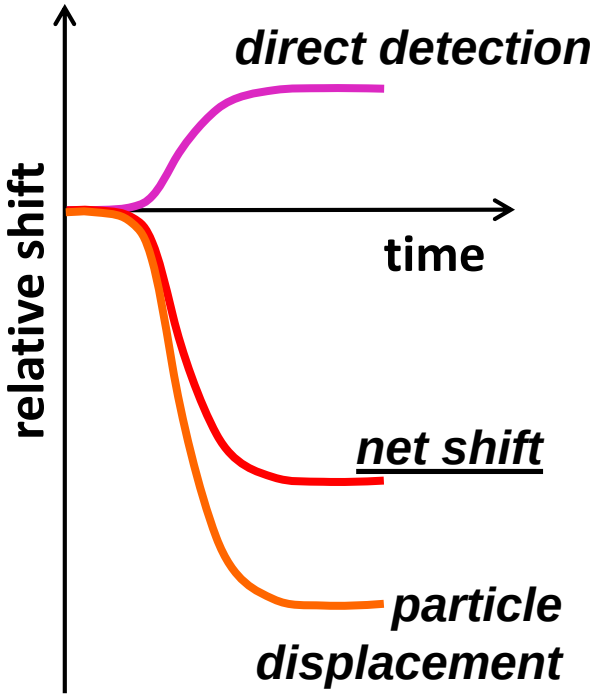
SMALLER POSITIVE NET SHIFT

The MB conformational change removes the streptavidin from the surface providing a PBG edge backshift (decrease in the index refractive)

Influence of the MB conformational change on evanescent wave: **discussion**

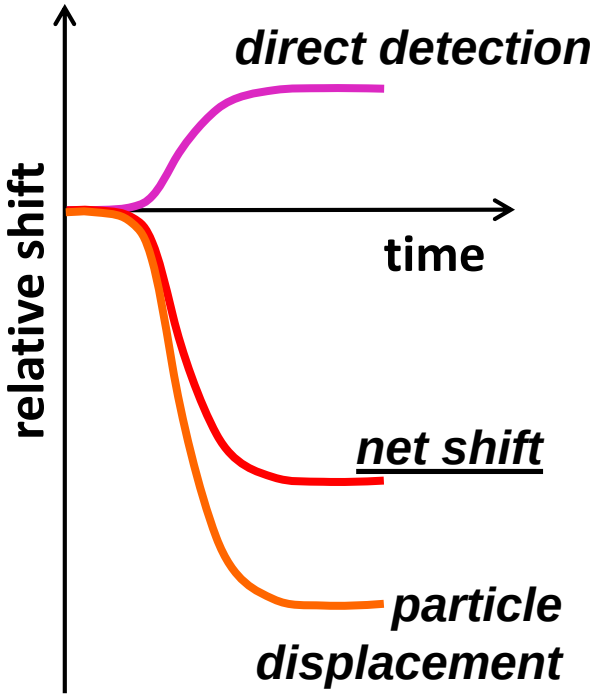
Influence of the MB conformational change on evanescent wave: **discussion**

LABELLING THE MB WITH HIGH REFRACTIVE INDEX PARTICLE

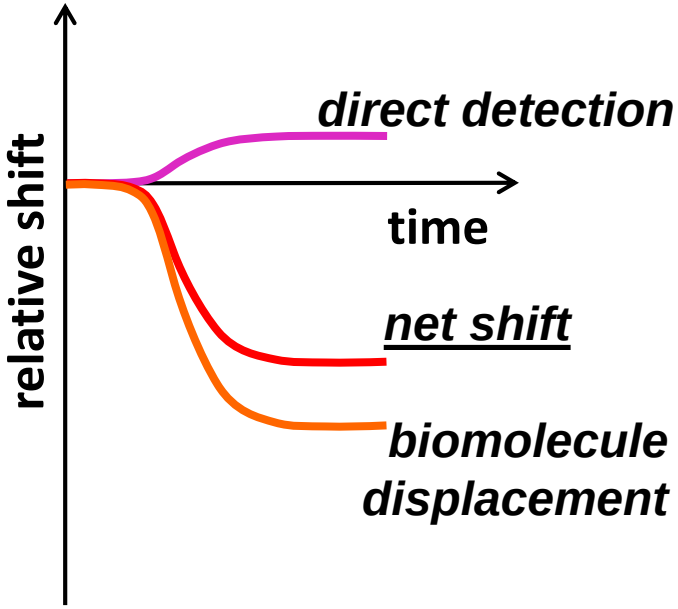


Influence of the MB conformational change on evanescent wave: **discussion**

LABELLING THE MB WITH HIGH REFRACTIVE INDEX PARTICLE

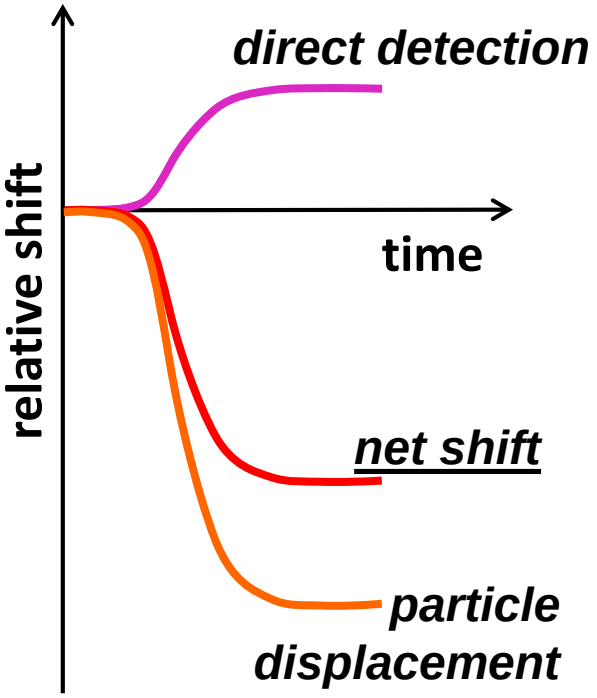


DETECTION OF LOW MOLECULAR WEIGHT TARGETS

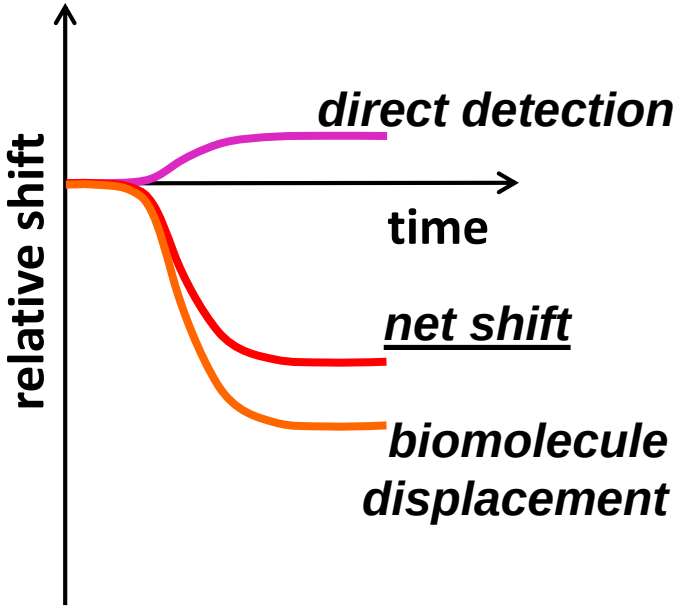


Influence of the MB conformational change on evanescent wave: **discussion**

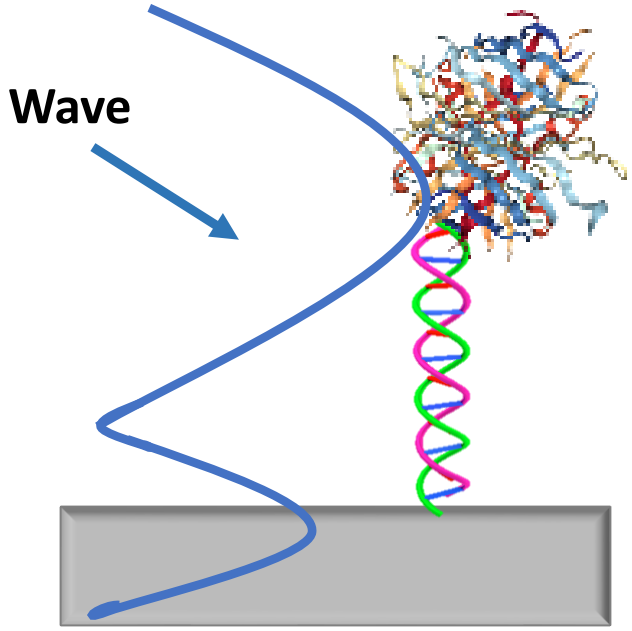
LABELLING THE MB WITH HIGH REFRACTIVE INDEX PARTICLE



DETECTION OF LOW MOLECULAR WEIGHT TARGETS



EXCITATION OF SEVERAL OPTICAL MODES



Outline

- Motivation
- Sensor concept
- Oligonucleotide detection
- Influence of the MB conformational change on evanescent wave
- **Conclusion**

Conclusion

- **OLIGONUCLEOTIDE DETECTION**
  - Efficient recognition → **Label-free detection**
  - Remarkable PBG edge shifts (~1100 pm) → **Extremely high sensitivities**
  - Higher sensitivities by properly selecting the dimensions → **Sensor footprint below 100 µm²**
  - Sensor configuration → **Promising candidate for multiplexed photonic sensing chips.**

- **INFLUENCE OF THE MB CONFORMATIONAL CHANGE ON THE EVANESCENT WAVE**
  - Different interaction for streptavidin-labelled and non-labelled MBs with the evanescent wave
  - Exploitations:
    - Replace streptavidin with a higher refractive index particle
    - Direct detection of low molecular weight targets
    - Design of the photonic sensing structure exciting several optical modes


saphely.eu
Thank you for your attention
saphely
Self-amplified photonic biosensing platform for microRNA-based early diagnosis of diseases
This project is funded by the Horizon 2020
Framework Programme of the European Union