PASSIVATED POROUS SILICON SUPPORTED MEMBRANES TOWARD BACTERIAL DETECTION IN COMPLEX SAMPLES

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Porous Semiconductors – Science and Technology Pacific Rim Conference 2025
Adelaide (Australia) April 15-19, 2025

Louvain la Neuve, located in Belgium

Louvain la Neuve, located in Belgium

Louvain la Neuve

UCLouvain 600

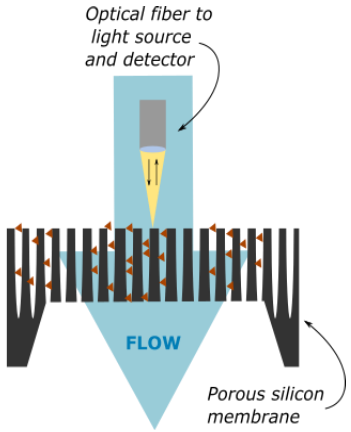
Louvain la Neuve – then (1972)

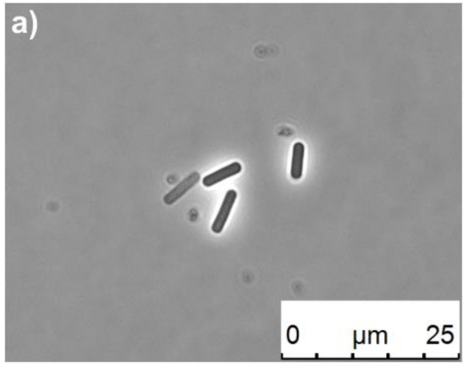
Louvain la Neuve – now

winfab
WALLONIA
INFRASTRUCTURE
NANO
FABRICATION

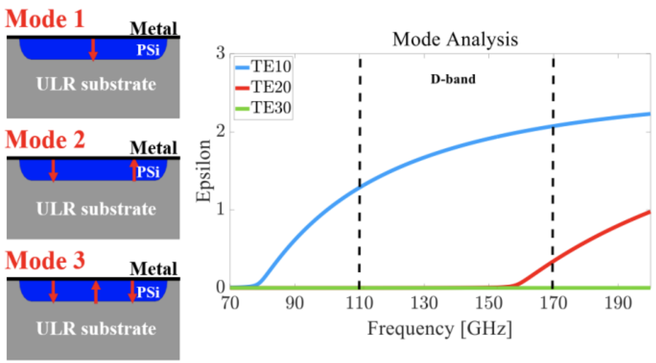
welcome
wallonia electronics
and communications
measurements

BACTERIAL DETECTION IN COMPLEX SAMPLES



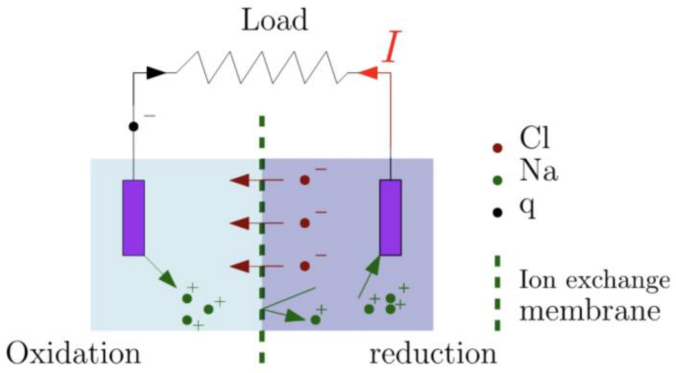


THz WAVEGUIDES



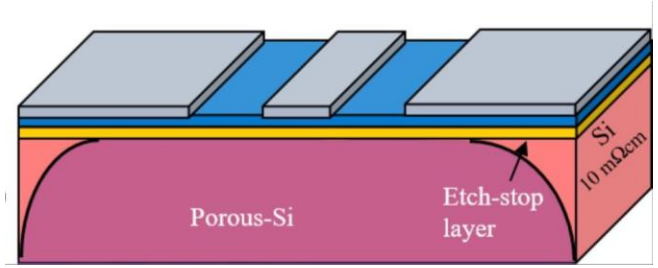
Collaboration with Prof. Dimitri Lederer's team

BLUE ENERGY & IONTRONICS

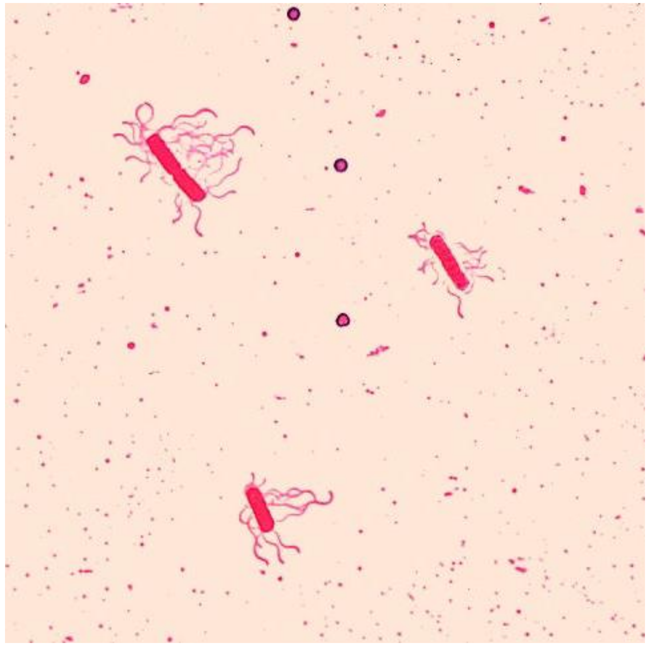


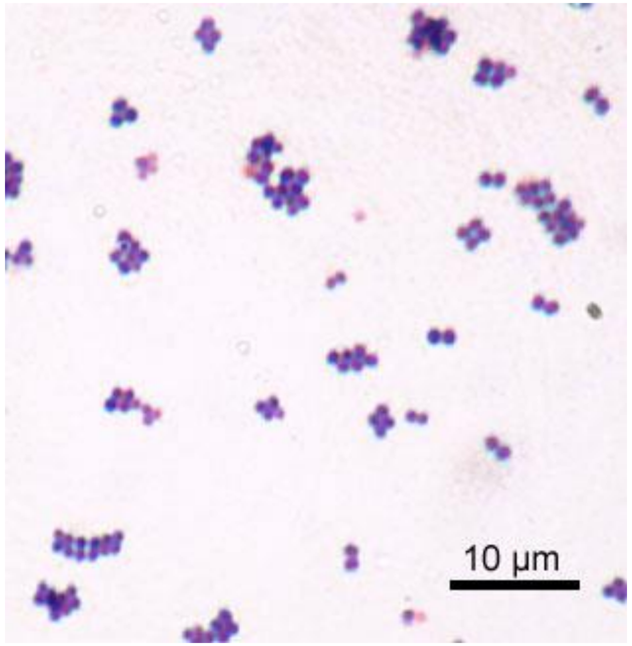
RED cell

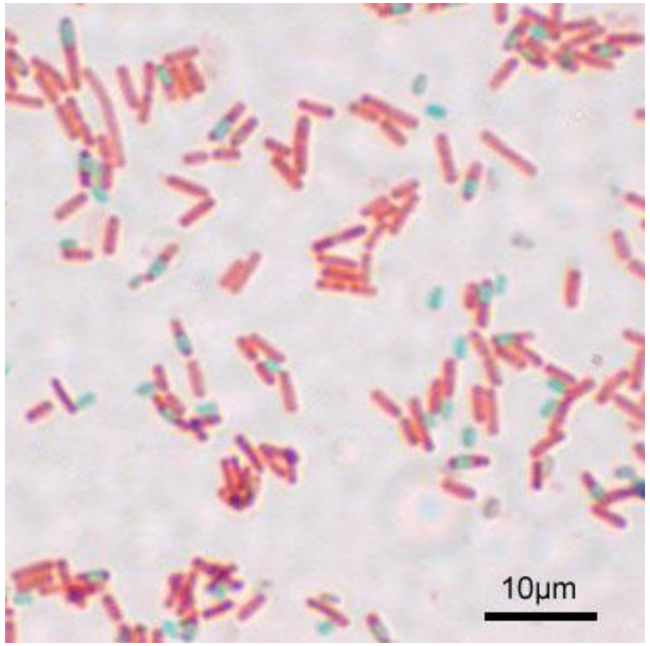
RF SUBSTRATES



Prof. Jean-Pierre Raskin's
RF SOI group







B. cereus

Gastrointestinal, respiratory tract, nosocomial, eye, CNS, urinary tract and cutaneous infections, endocarditis, osteomyelitis. The potential of this bacterium to cause life threatening infections has increased.

S. aureus (S. epidermidis)

Minor skin infections: boils, abscesses, impetigo;
More serious infections: meningitis, osteomyelitis, pneumonia, septic phlebitis, endocarditis;
MRSA, displays **antibiotic resistance**

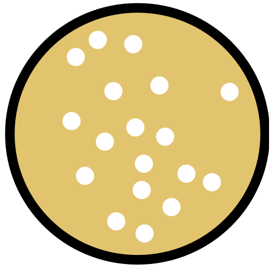
B. subtilis

« Not a frank human pathogen, but has on several occasions been isolated from human infections.
Infections attributed to *B. subtilis* include **bacteremia**, **endocarditis**, **pneumonia**, and **septicemia**. »

[https://www.epa.gov/sites/default/files/2015-09/documents/fra009.pdf]

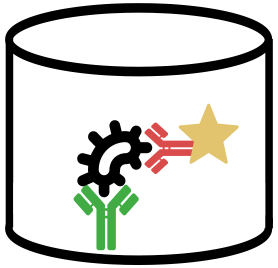
[https://www.msjonline.org/index.php/ijrms/article/view/2049]

Traditional methods for bacterial detection



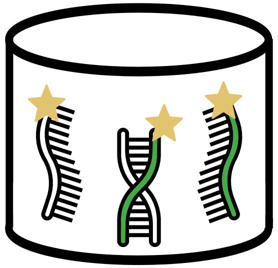
Culture

- ✓ Cost-effective
- ✓ Specific
- ✓ Sensitive (1 CFU*/mL)
- ✗ Time-consuming (>12h)
- ✗ Prone to errors



ELISA

- ✓ Fast (>2h)
- ✓ Specific
- ✓ Sensitive (1-10 CFU*/mL)
- ✗ Expensive

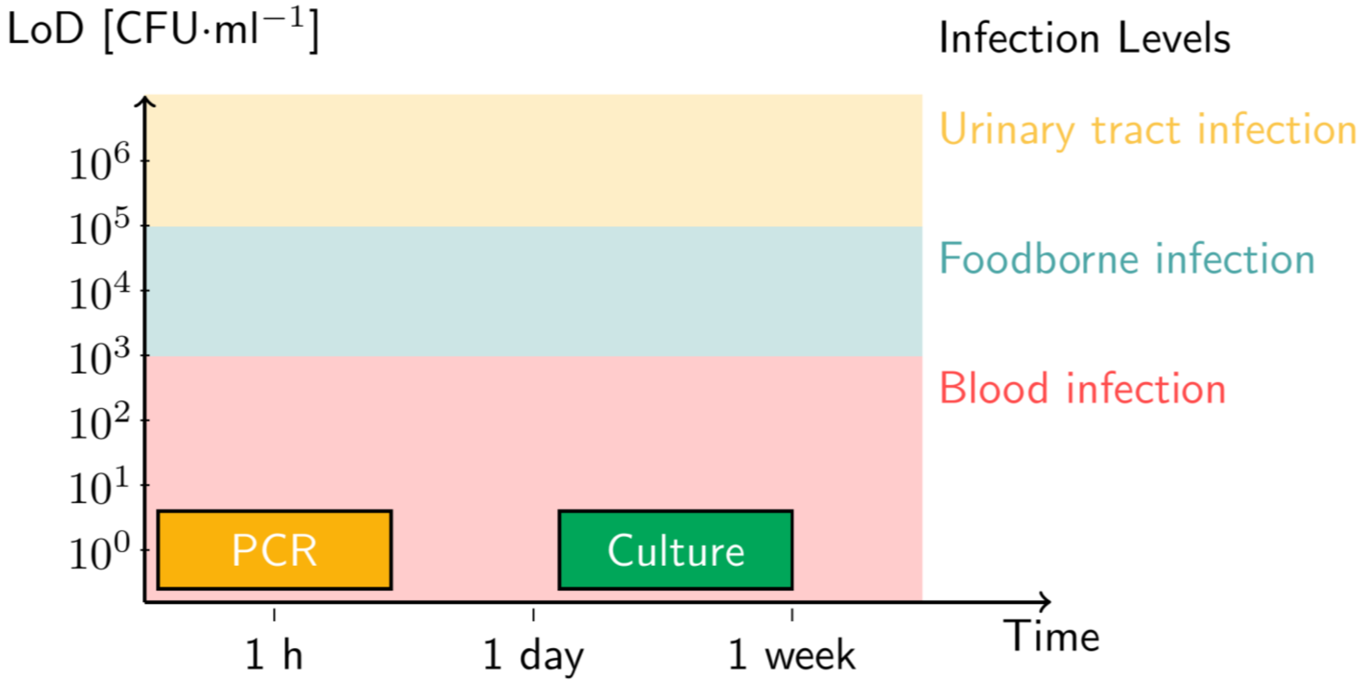


PCR

- ✓ Fast (>1h)
- ✓ Specific
- ✓ Sensitive (1 CFU*/mL)
- ✗ Expensive
- ✗ High-end instrumentation
- ✗ Prior knowledge of suspected pathogen

* CFU = Colony Forming Units

Figures of merit



Assay time
Sensitivity
Selectivity
Reliability/Robustness
Complex sample
Versatility
Cost
Portability

PSI MEMBRANES

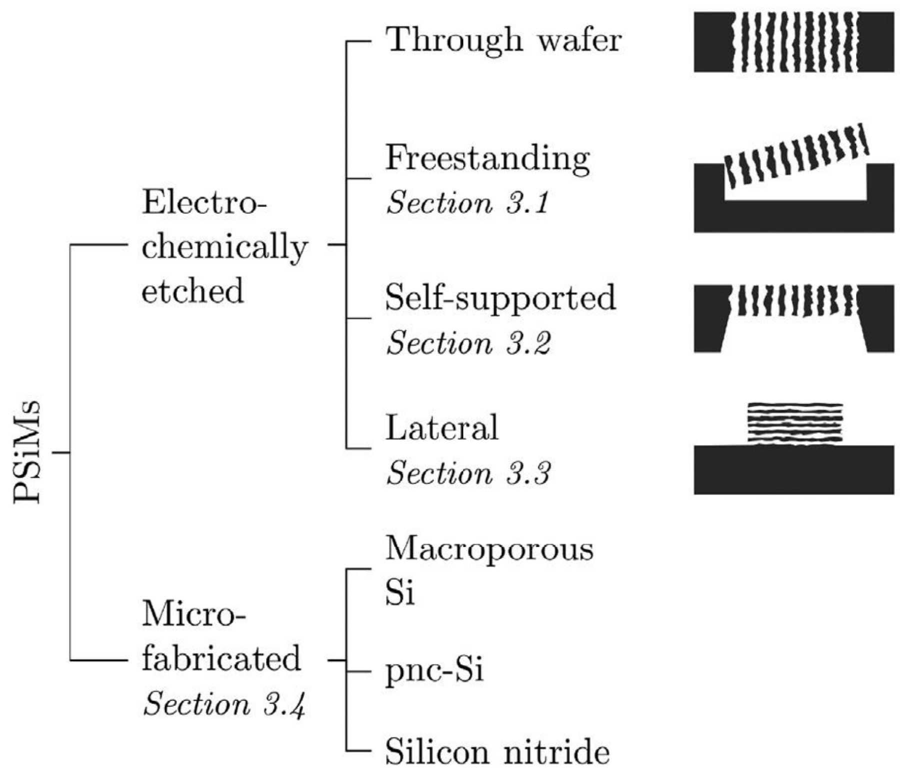
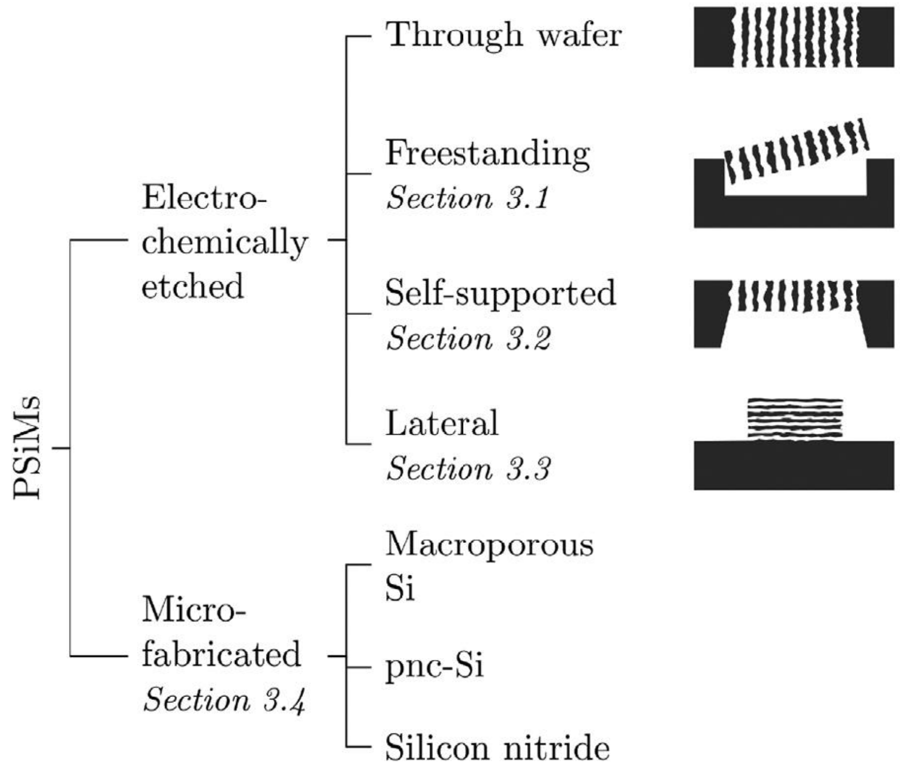


Fig. 2. Summary of porous membranes fabrication techniques.

R. Vercauteren; G. Scheen; J.-P. Raskin; L. A. Francis; Porous silicon membranes and their applications: Recent advances, *Sens. Actuator A-Phys.* ***2021***, 318, 112486, https://doi.org/10.1016/j.sna.2020.112486

Table 1
Recent advances in the applications fields of porous silicon membranes (*Note: C, F, FT, L, M, S stand for, respectively, Commercial, Freestanding, Full Thickness, Lateral, Microfabricated and Self-supported.*)

Application field	Membrane characteristics	Membrane thickness	Detailed application	Ref.
Microfluidics	M, mesoporous	15 nm	Size and charge selective filtration	[150]
	S, mesoporous	5 µm	Filtration of small biological molecules from mixtures	[81]
	L, mesoporous	10 – 20 µm	Size and charge selective filtration	[99,151,152,100,153]
	S, macroporous	215 µm	Electro-osmotic pump	[90]
Medical	F, macroporous	4.29 µm	Drug delivery patch and optical monitoring of drug release	[7]
	M, macroporous	50-60 nm	Culture of human umbilical vein vascular endothelial cells	[8]
	M, macroporous	500 nm	Reconstruction of the intestinal barrier of a trout via cell culture	[9]
	M, mesoporous	75 nm	Small-format hemodialysis with high toxin elimination capabilities	[10]
	M, macroporous	30 µm	Transmigration assay for cancer cells	[11]
	F, mesoporous	276 µm	Scaffold for the culture of oral mucosal epithelial cells	[12]
	C, macroporous	1 – 10 µm	Support for the investigation of pore-spanning lipid membranes	[154–160]
	M, mesoporous	30 nm	Cell culture of endothelial cells	[13]
	F, macroporous	12 – 15 µm	Tissue scaffold integrated with cell-laden hydrogel biomaterials	[14]
	M, macroporous	5 µm	Lung-on-chip microfluidic device	[15,161]
	M, macroporous	10 µm	Culture of intestinal epithelial cells	[16]
	S, macroporous	130 – 150 µm	Mechanical cell lysis and DNA isolation	[17,88]
	F, mesoporous	4 – 5 µm	Implantable scaffold for cell culture	[18]
Sensing	S, macroporous	~50 µm	Electrophysical NO_2-gas detector	[85]
	F, mesoporous	1.7 µm	Silver-modified sensor for SERS-based detection of miRNA	[59]
	L, mesoporous	10 µm	Interferometric transducer for solvent detection	[153]
	F, mesoporous	1.6 µm	Optical detection of ethanol vapour	[138]
	S, mesoporous	2.5 µm	Impedance spectroscopy of the formation of a lipid membrane	[94,95]
	F, mesoporous	29 µm	Electrostatic isopropanol vapour sensor	[20]
	F, mesomacroporous	5.5 µm	Optical detection of Bovine Serum Albumin	[21]
	F, mesoporous	17 – 21 µm	Optical detection of dissolved gas concentrations in liquids	[137]
	M, mesoporous	50 nm	Nanopore-based sensing of DNA translocation	[110]
	S, mesoporous	20 µm	Multi-assay solvent vapour optical detection	[162]
	F, mesoporous	870 nm	Multianalyte detection using silver-decorated sensors	[67,68]
	M, mesoporous	15 nm	Optical detection of Bovine Serum Albumin permeation	[22]
	F, mesomacroporous	4.5 µm	Electrochemical detection of MS2 bacteriophage	[71]
	F, mesomacroporous	4.5 µm	Label-free electrochemical detection of bacterial toxin	[163]
	M, mesomacroporous	50 nm	Electrochemical detection of ion-transfer across the PSiM	[113]
	C, macroporous	475 µm	3D liquid core sensor array	[164]
	S, mesoporous	340 nm	DNA translocation detection	[96,97]
	M, macroporous	50 µm	Immunoassay for specific leukocyte subsets	[103]
	S, macroporous	1 – 3 µm	Transmembranes proteins sensing	[87]
	C, mesomacroporous	10-15 nm	DNA translocation detection	[165–167]
	F, mesoporous	19.9 µm	Optical aptasensors with multiple target-binding sites	[23]
	S, mesoporous	4 – 15 µm	Optical detection of enzyme adsorption and streptadivin binding	[19,79,168]
Energy conversion	F, micro/macroporous	10 – 30 µm	Wide-gap absorber for solar cells	[66,64]
	S, mesoporous	~70 µm	Implantable glucose biofuel cell	[89]
	S, mesoporous	5 – 20 µm	Ion-exchange membrane for micro fuel cells	[27]
	S, mesoporous	50 µm	Anion exchange membrane for Glucose/O_2 micro fuel cell	[28]
	S, macroporous	125 µm	Membrane-electrode assembly for H_2/air-fed micro fuel cells	[29]
	S, macroporous	230 µm	Microfluidic electric generator	[91]
	S, mesoporous	13 µm	Monolithic Si electrode for micro fuel cells	[30,98]
	F, macroporous	50 µm	Anode for lithium-ion batteries	[63,60,65]
	F, mesoporous	200 µm	Anode for lithium-ion batteries	[31]
	M, macroporous	5 µm	Electrode grids for micro fuel cells	[32]
	S, micro/macroporous	210 µm	High-conductivity electrodes for micro fuel cells	[33]
	M, macroporous	280 µm	Ion-exchange membrane for photoelectrochemical cell	[34]
	S, macroporous	50 µm	Electrode for methanol micro fuel cell	[35]
	S, macroporous	60 µm	Cathode for self-breathing microfuel cells	[36]
	FT, meso/macroporous	500 µm	Membrane-electrode assembly for hydrogen/oxygen micro fuel cells	[57,37]
	S, mesoporous	100 µm	Proton exchange membrane for methanol micro fuel cells	[83,84]
	S, meso/macroporous	80 – 100 µm	Pervaporation membrane for methanol vapour-fed micro fuel cells	[80]
Electronics	F, mesoporous	46 µm	RF insulating and supporting substrate for microfabricated inductors	[61]
	S, mesoporous	10 µm	MEMS-based superheated loop heat pipes	[24]
	M, macroporous	600 nm	Thermal management device	[25]
	S, mesoporous	300 µm	Thermal isolation layer for high temperature micro-hotplates	[26]
	F, macroporous	2.46 µm	Flexible optoelectronics device	[72]
	F, mesoporous	1.92 µm	Modulator for photodetector	[74,75]
	FT, mesoporous	380 µm	CMOS compatible RF insulating substrate	[58]



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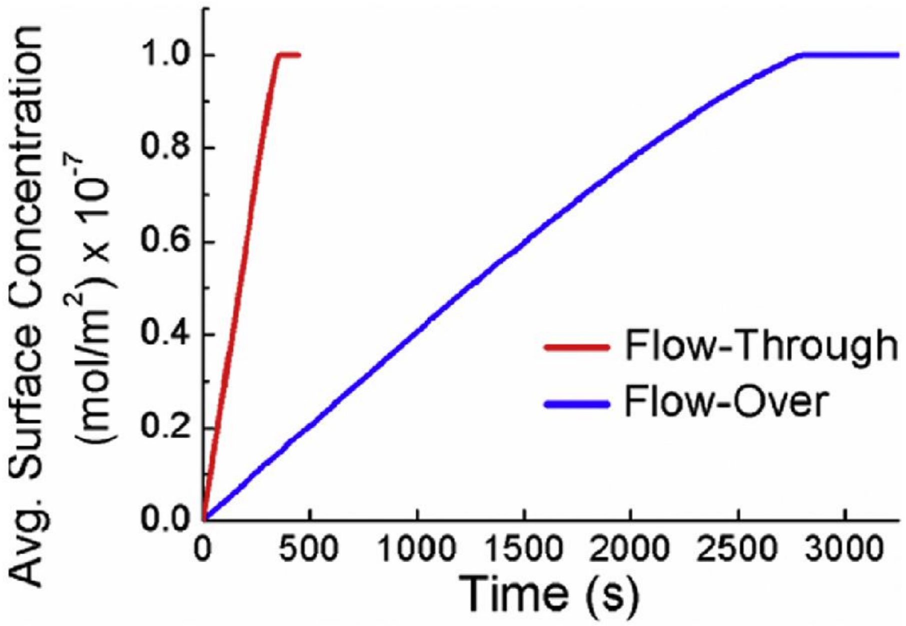
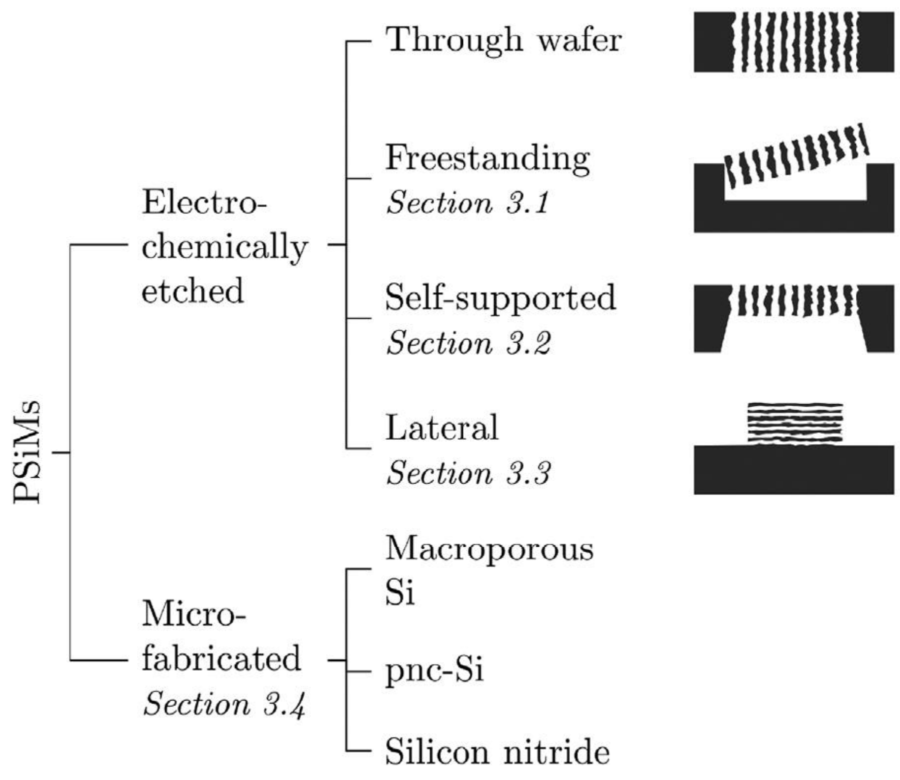


Fig. 11. Simulated average surface concentration of analyte with the same diffusivity, captured by close- and open-ended PSi sensors as a function of time; reprinted from [19], Copyright (2016), with permission from American Chemical Society.

R. Vercauteren; G. Scheen; J.-P. Raskin; L. A. Francis; Porous silicon membranes and their applications: Recent advances, *Sens. Actuator A-Phys.* ***2021,*** 318, 112486, https://doi.org/10.1016/j.sna.2020.112486



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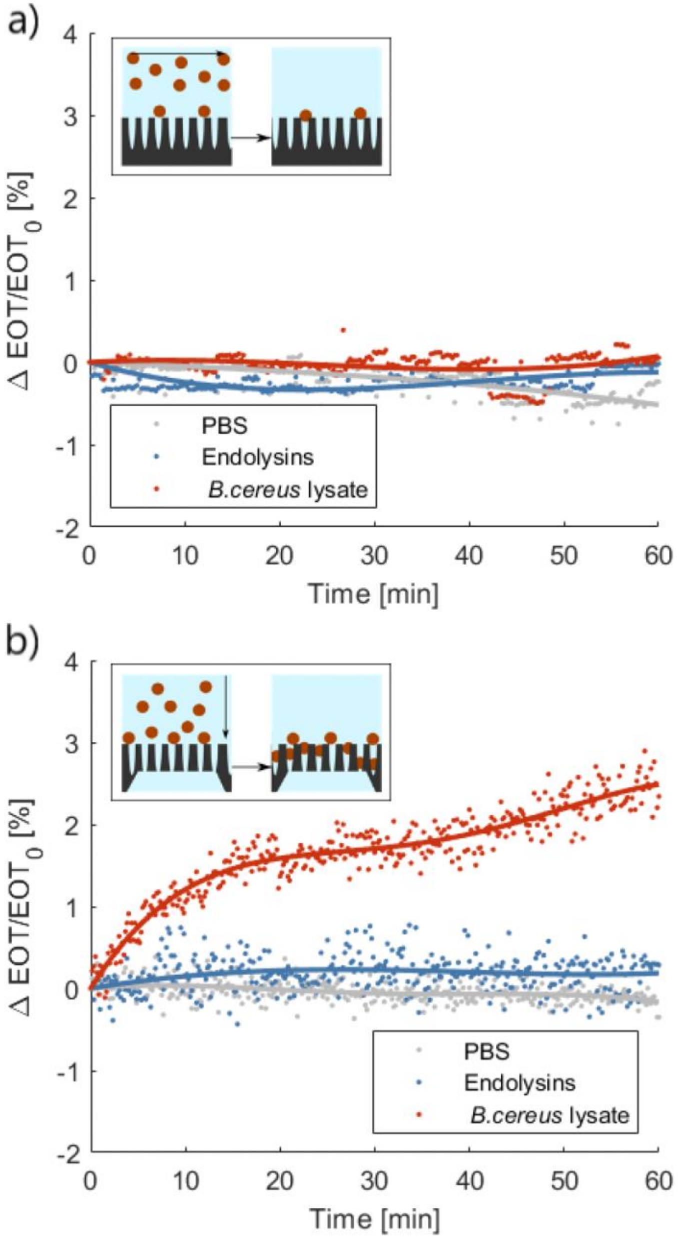

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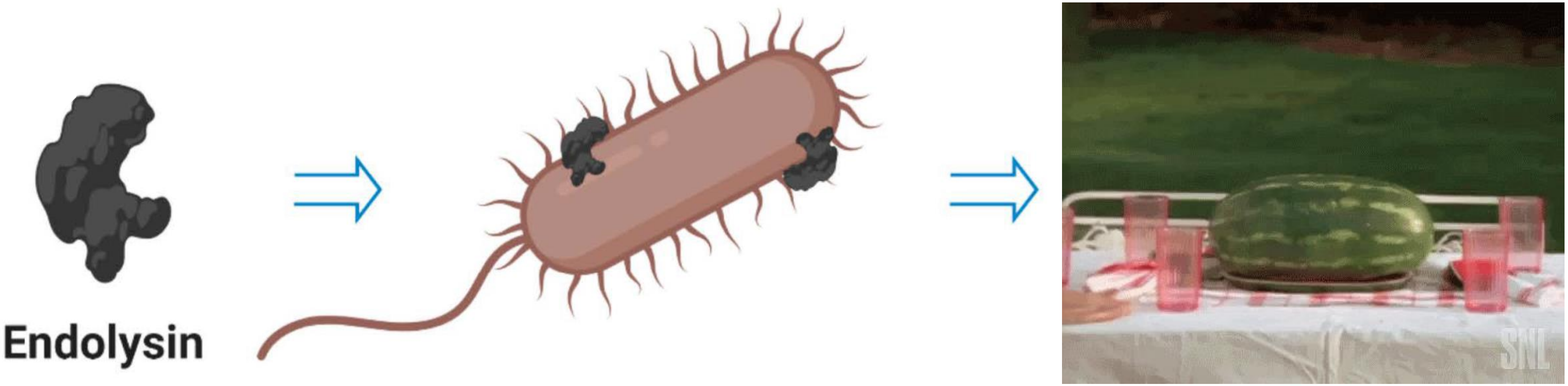
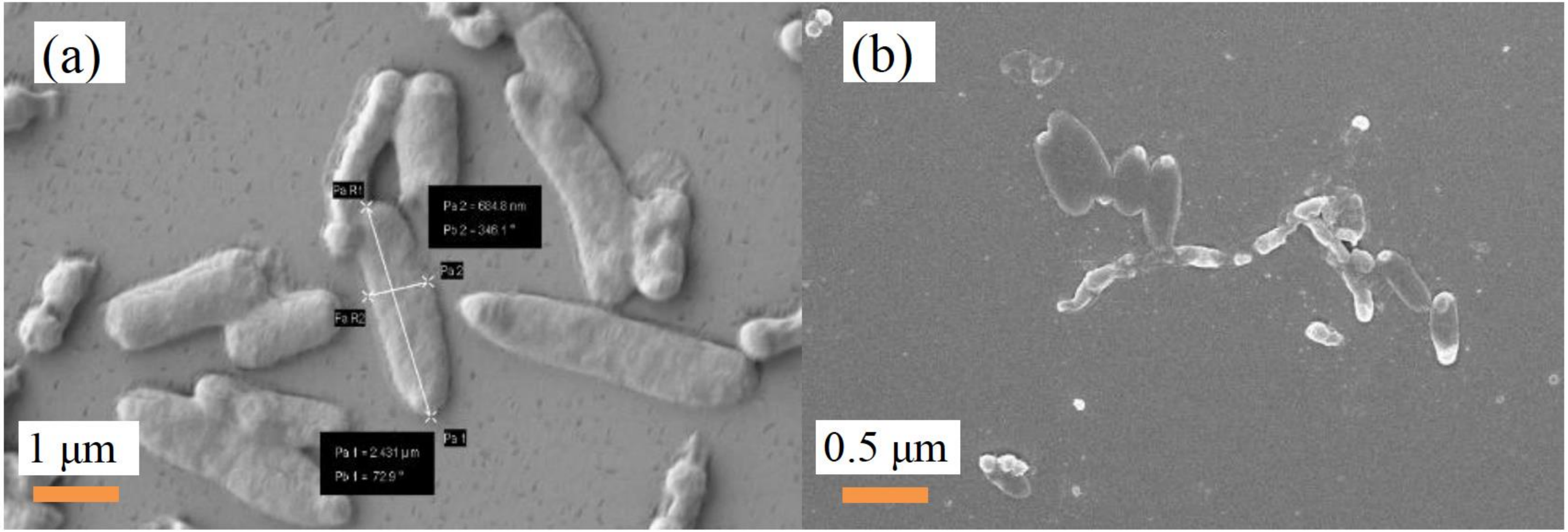


Lytic enzymes can be produced by bacteria or bacteriophage

Present "naturally"

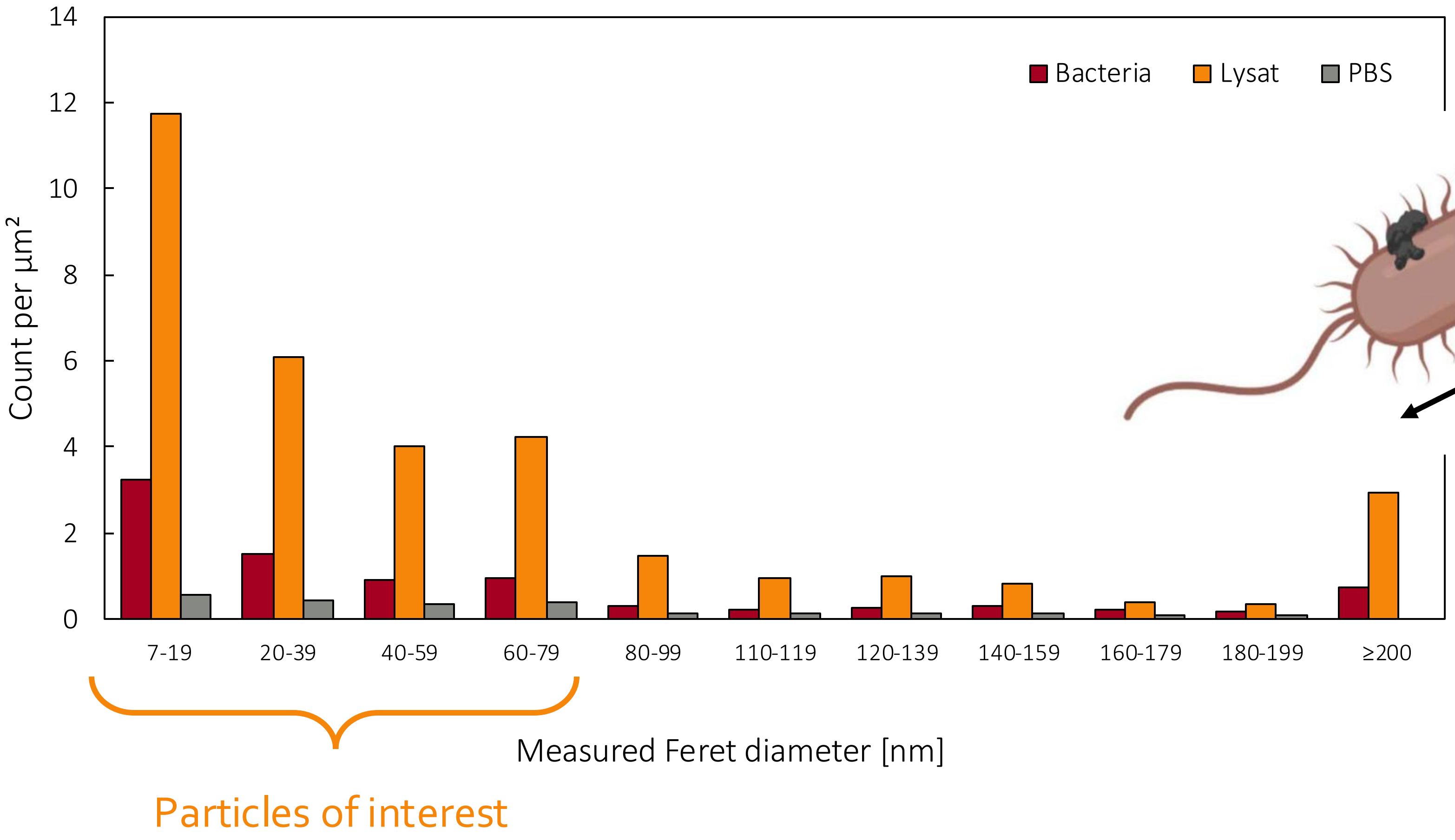
Image from Antibiotics ***2021****, 10(2), 124;* [*https://doi.org/10.3390/antibiotics10020124*](https://doi.org/10.3390/antibiotics10020124)

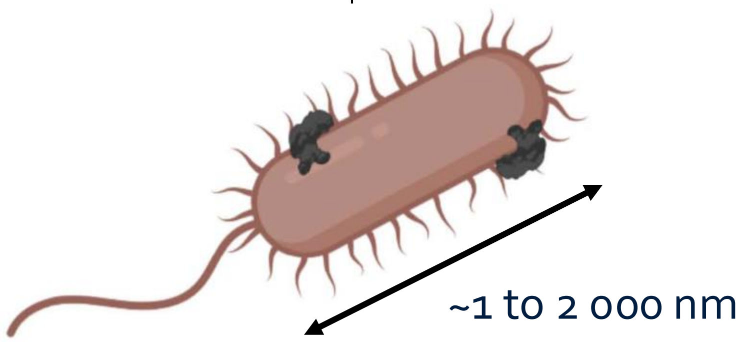


SEM observations of (a) *E. coli* bacteria and (b) *E. coli* lysate (through phage lysis).

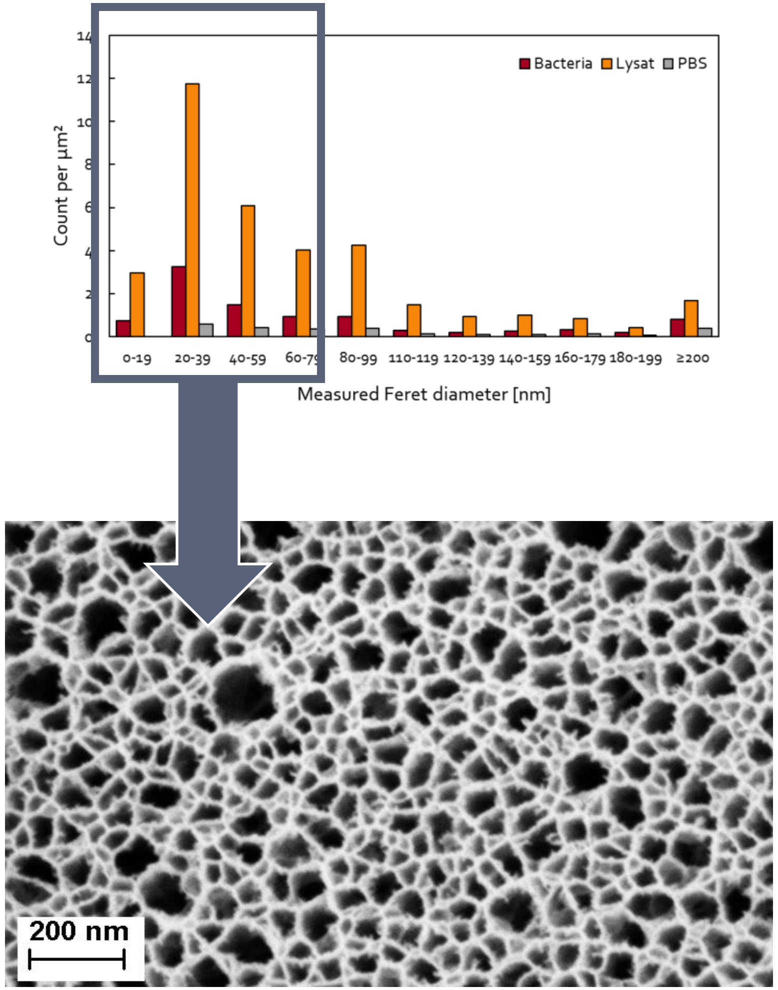
UCLouvain

Model: *Bacillus cereus* (ATCC10987)

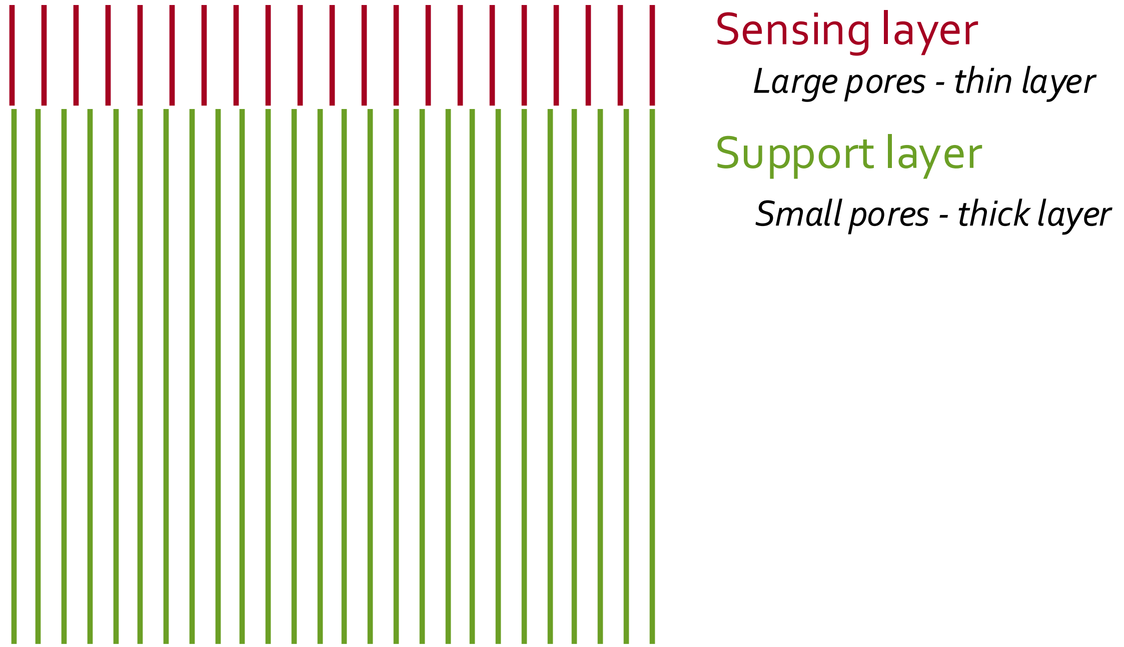


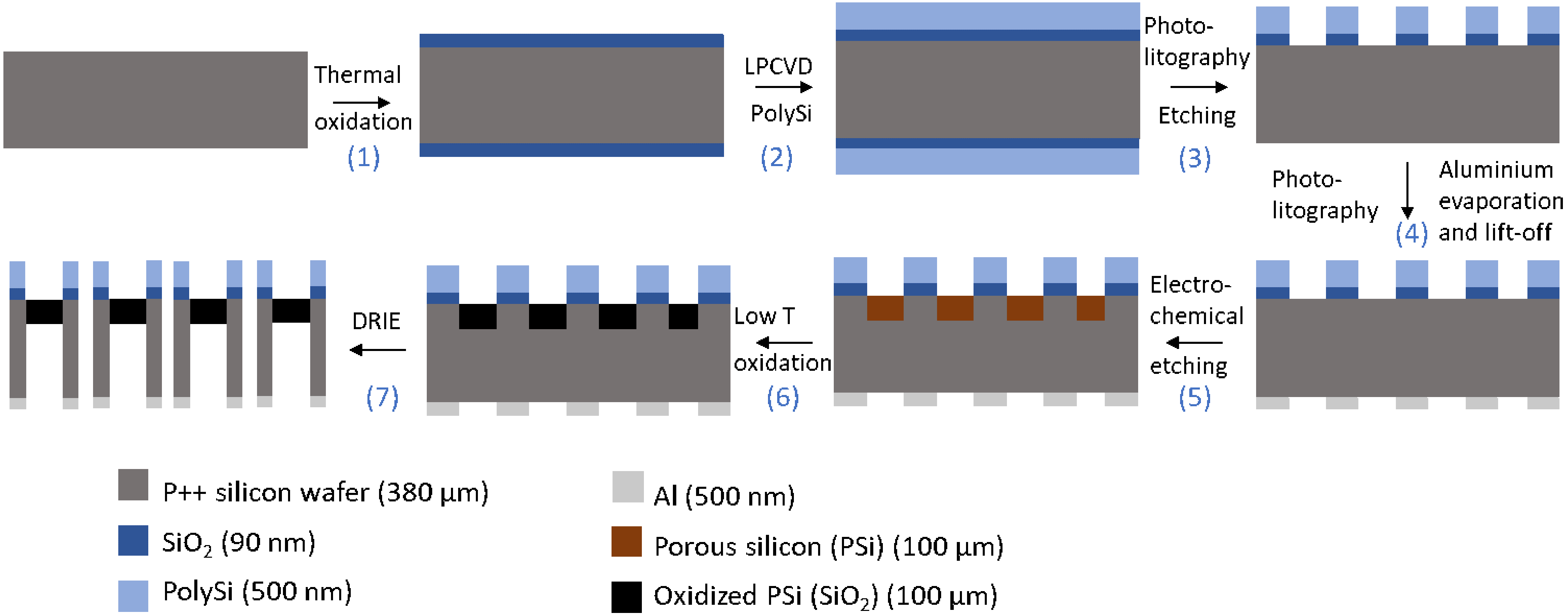


UCLouvain



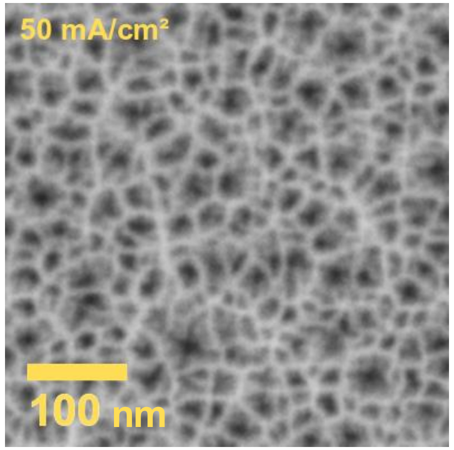
Porous silicon **interferometer**



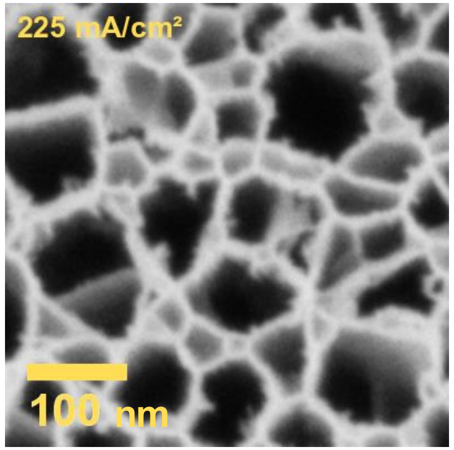

Thermal
oxidation
(1)
LPCVD
PolySi
(2)
Photo-
litography
Etching
(3)
Photo-
litography
(4)
Aluminium
evaporation
and lift-off
Electro-
chemical
etching
(5)
Low T
oxidation
(6)
DRIE
(7)
P++ silicon wafer (380 µm)
SiO2 (90 nm)
PolySi (500 nm)
Al (500 nm)
Porous silicon (PSi) (100 µm)
Oxidized PSi (SiO2) (100 µm)

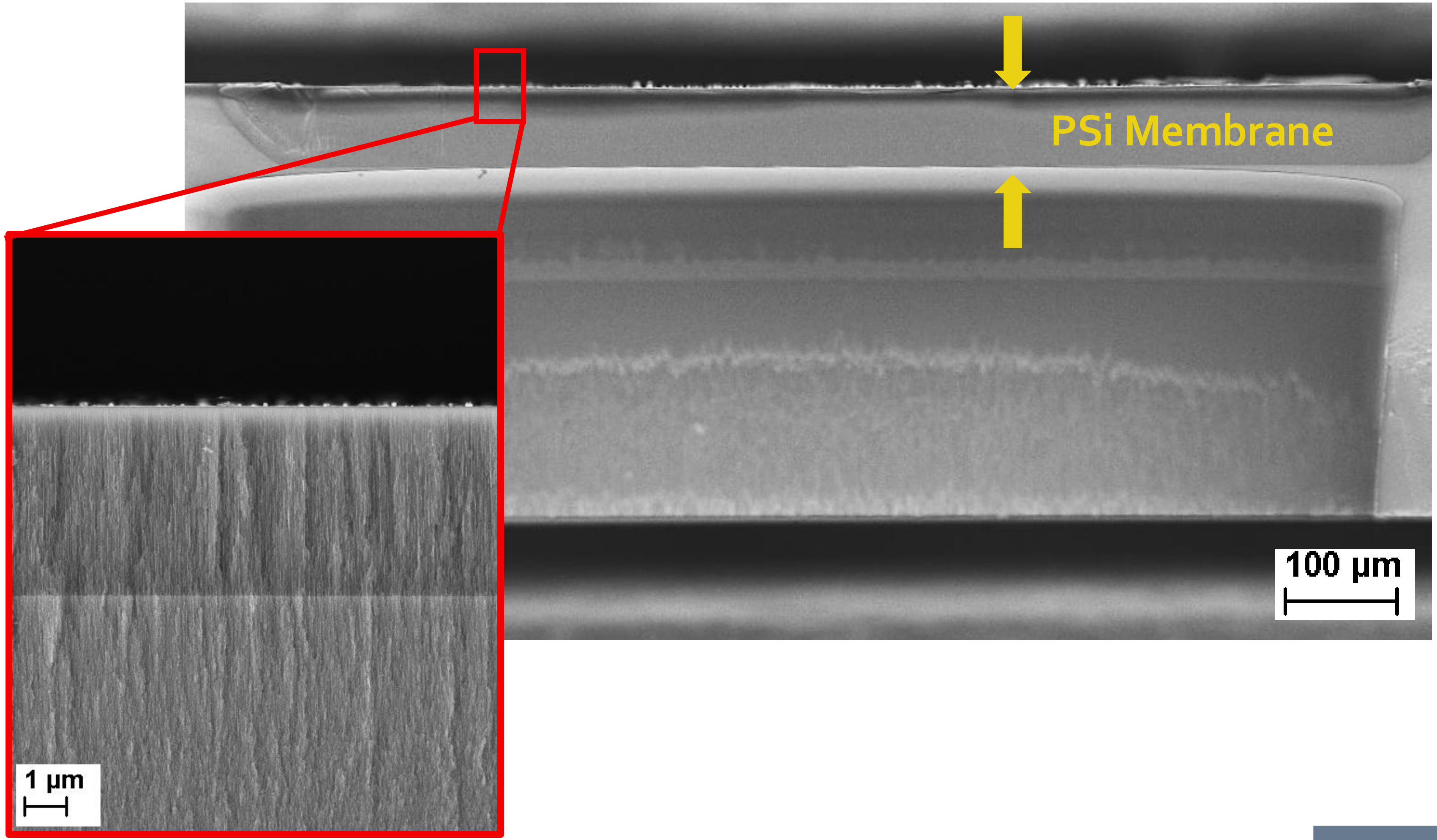
Filtration membrane

Small pores
15 nm

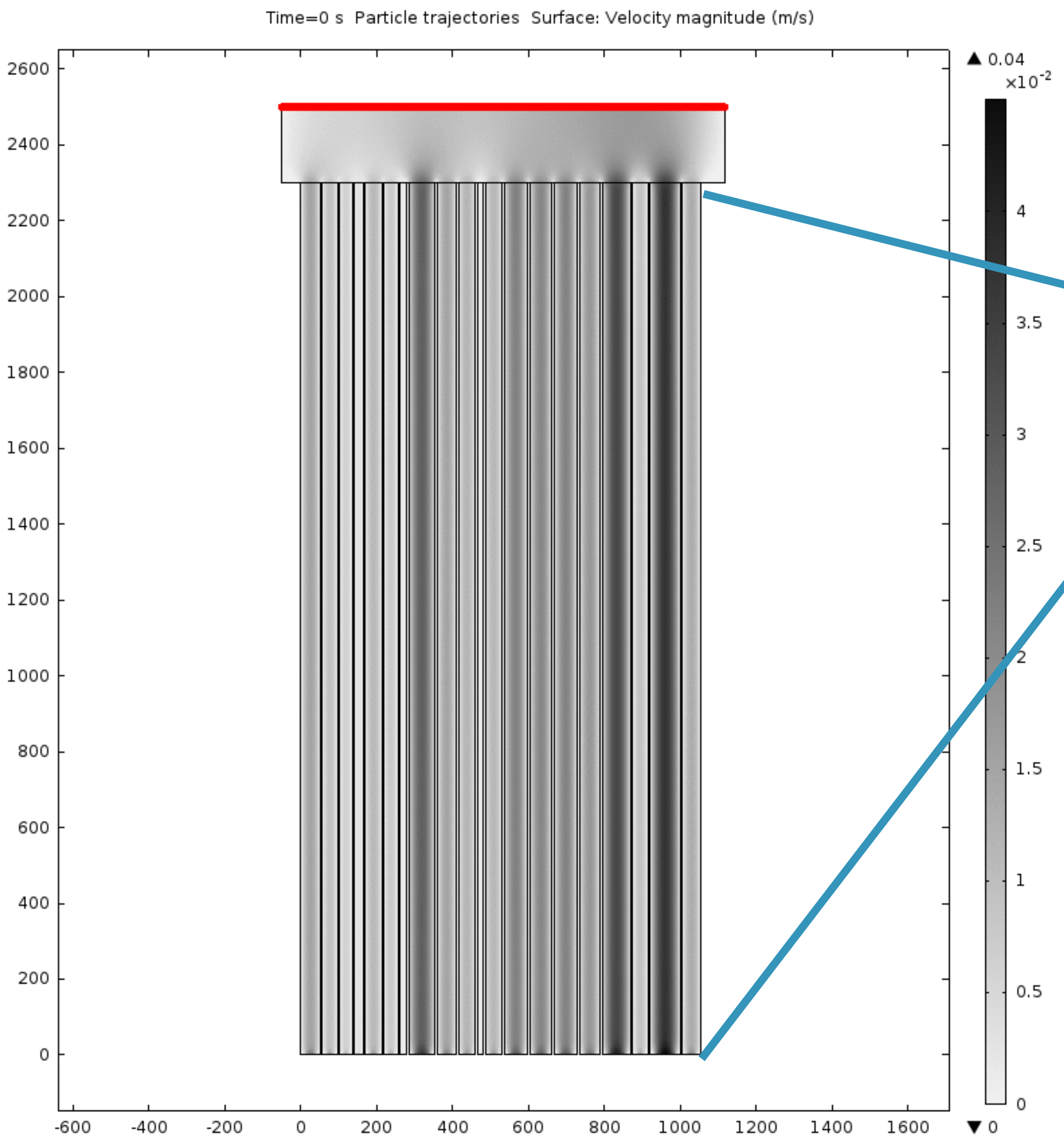


Large pores
50 nm

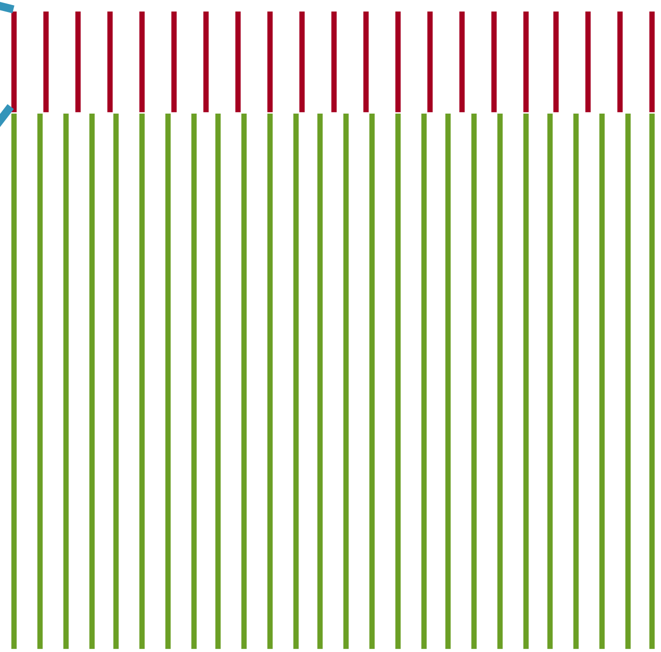




UCLouvain



F.E.M. simulation (Comsol Multiphysics)

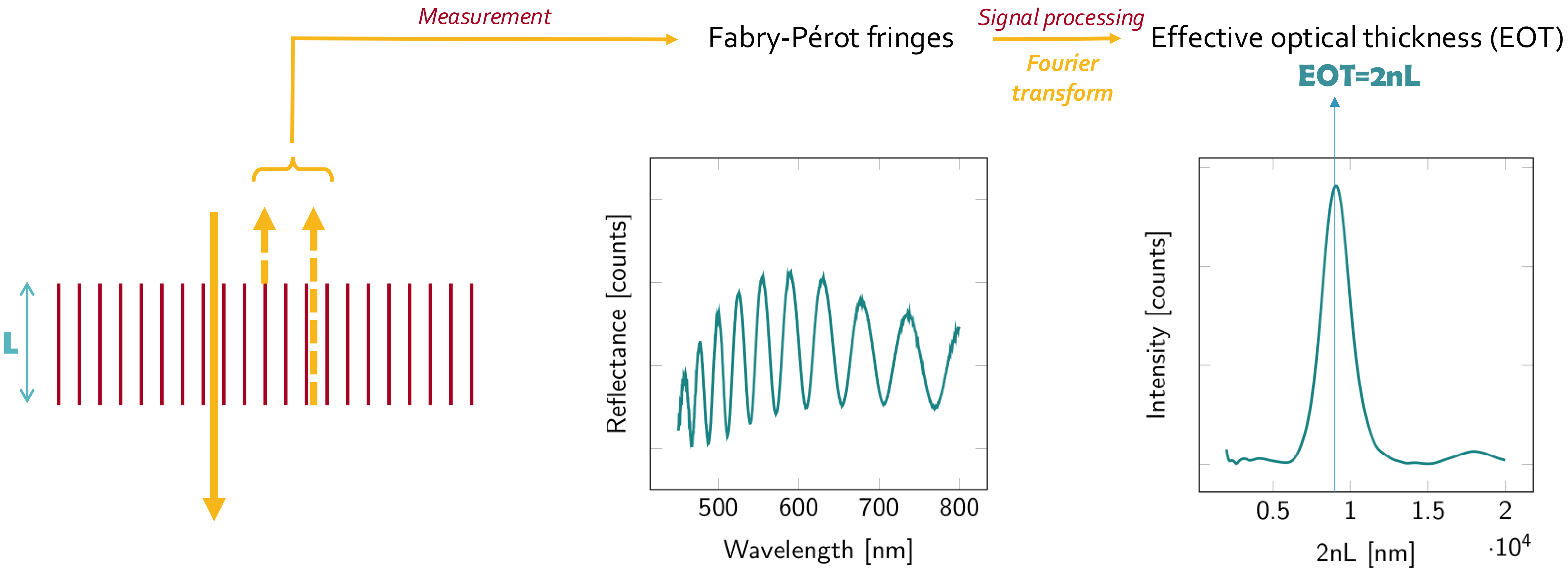


Sensing layer

Large pores - thin layer

Support layer

Small pores - thick layer


L
Measurement
Fabry-Pérot fringes
Signal processing
Fourier transform
Effective optical thickness (EOT)
EOT=2nL
Reflectance [counts]
500
600
700
800
Wavelength [nm]
Intensity [counts]
0.5
1
1.5
2
$\cdot 10^4$
2nL [nm]

UCLouvain

Measurement

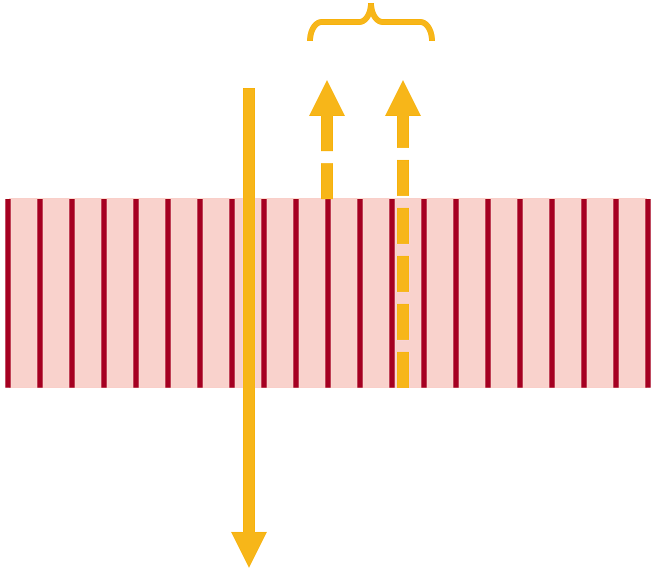
Fabry-Pérot fringes

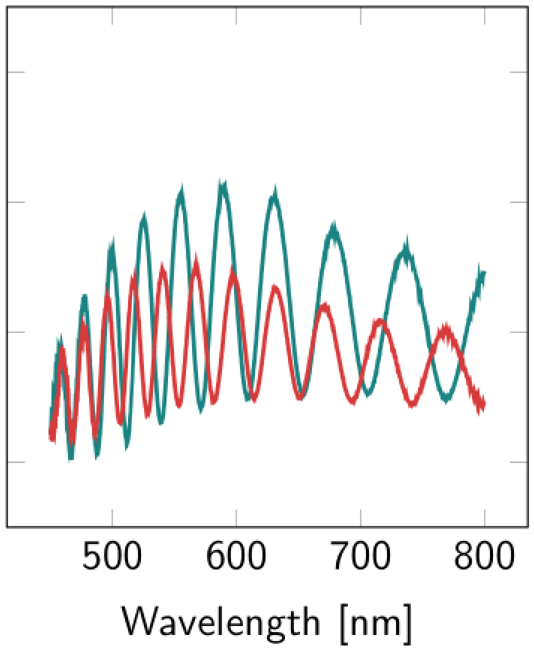
Signal processing

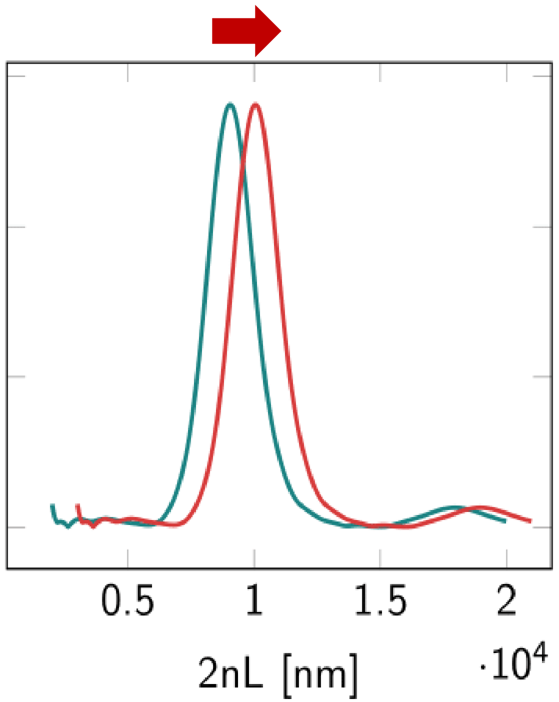
Fourier transform

Effective optical thickness (EOT)

EOT=2nL

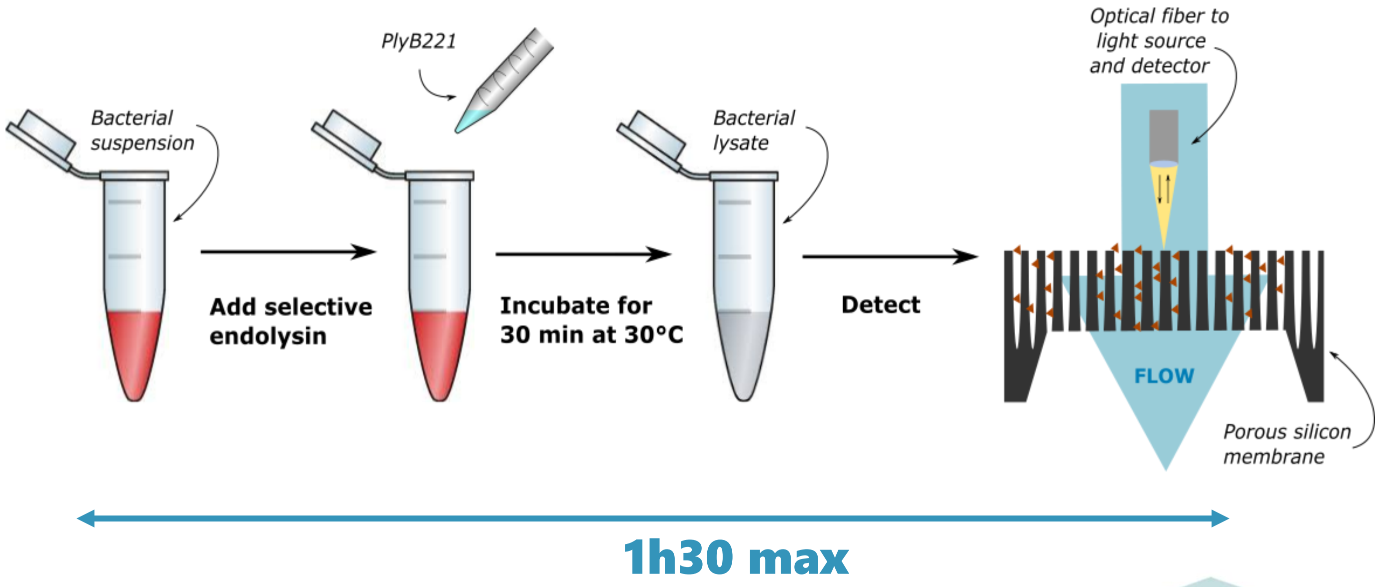


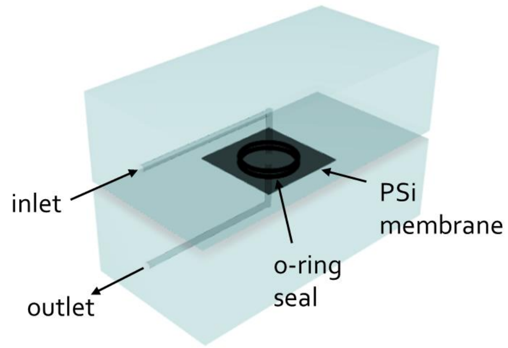


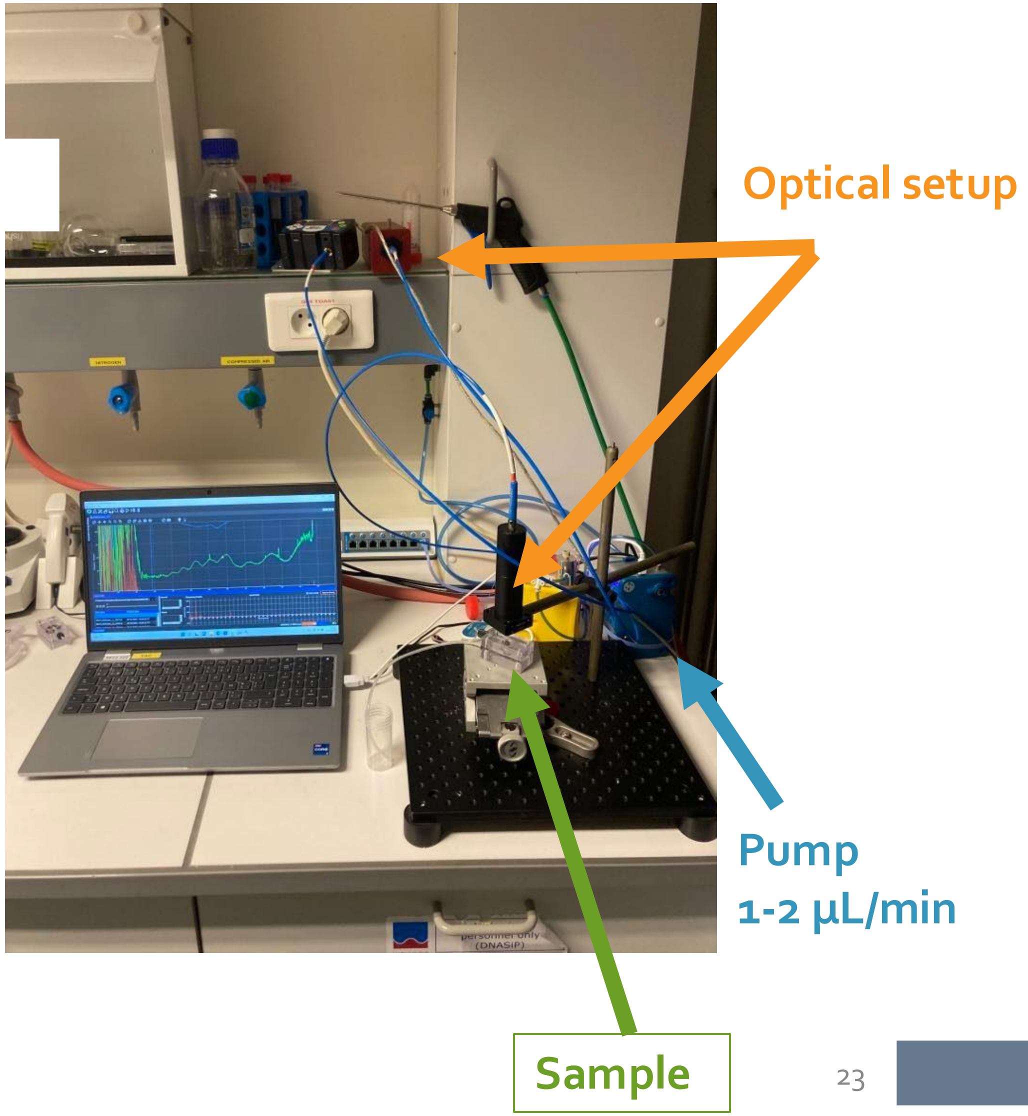


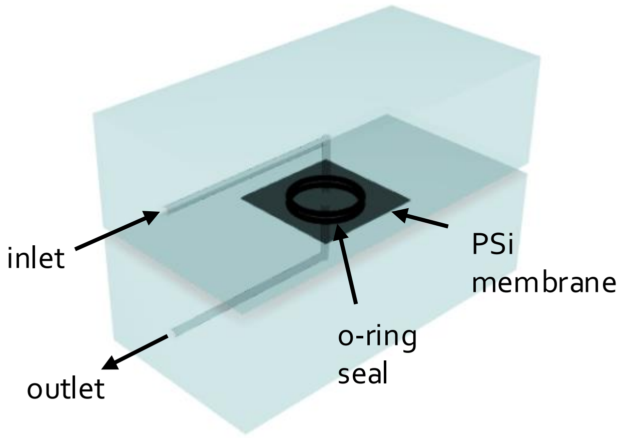
UCLouvain

The detection of *Bacillus cereus* (ATCC10987, ~10^6 CFU/mL), lysed by PlyB221 endolysins

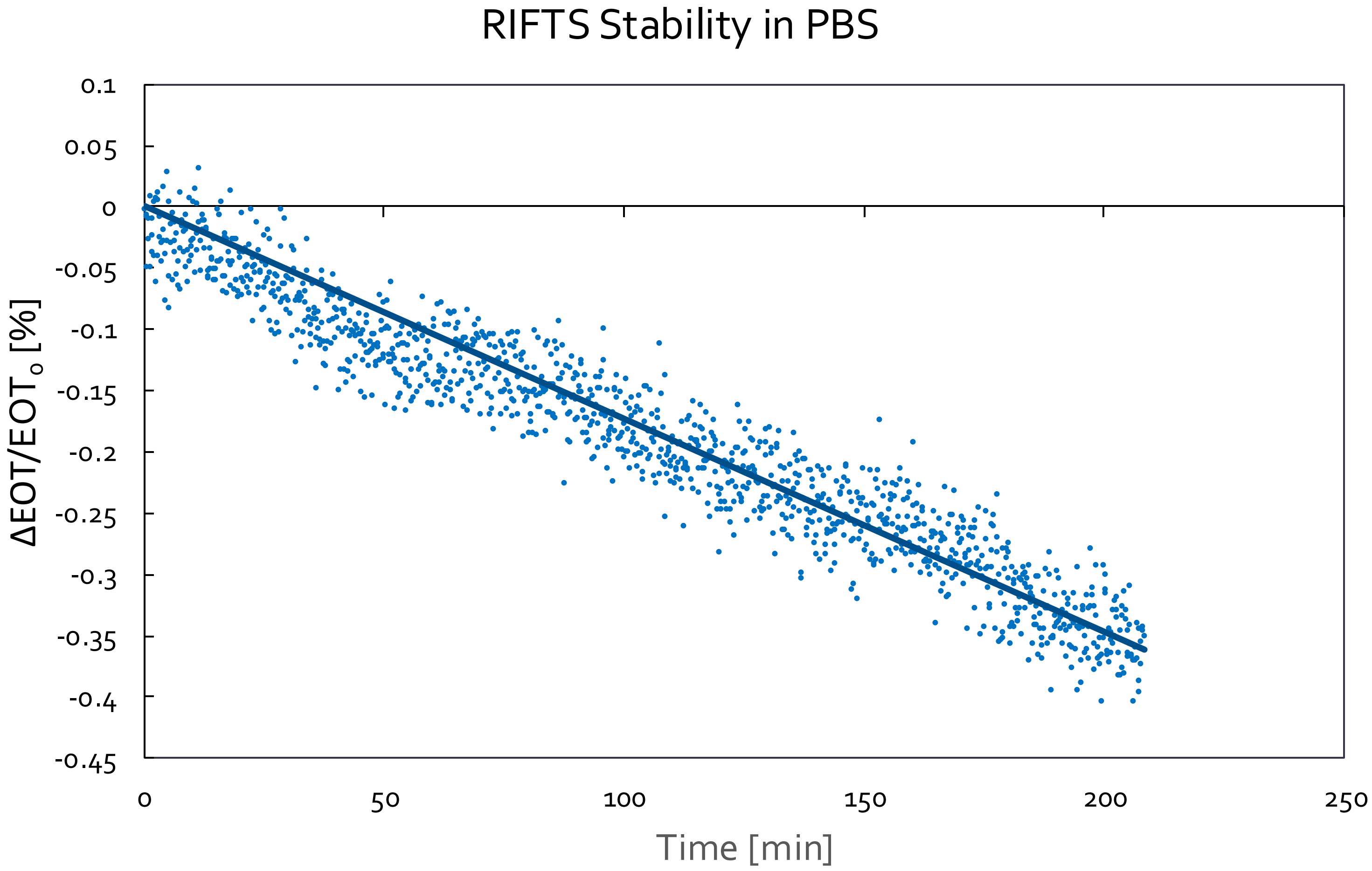


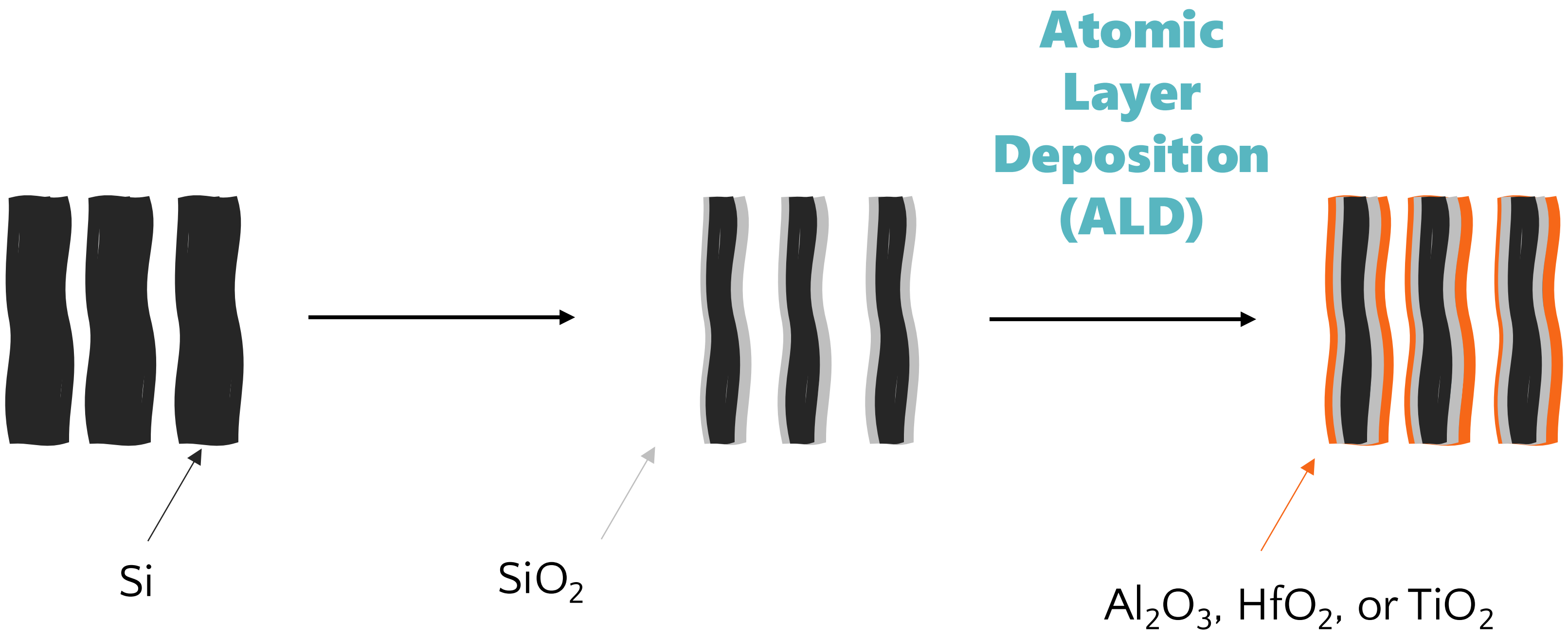






C. Whyte Ferreira, UCLouvain, 2021



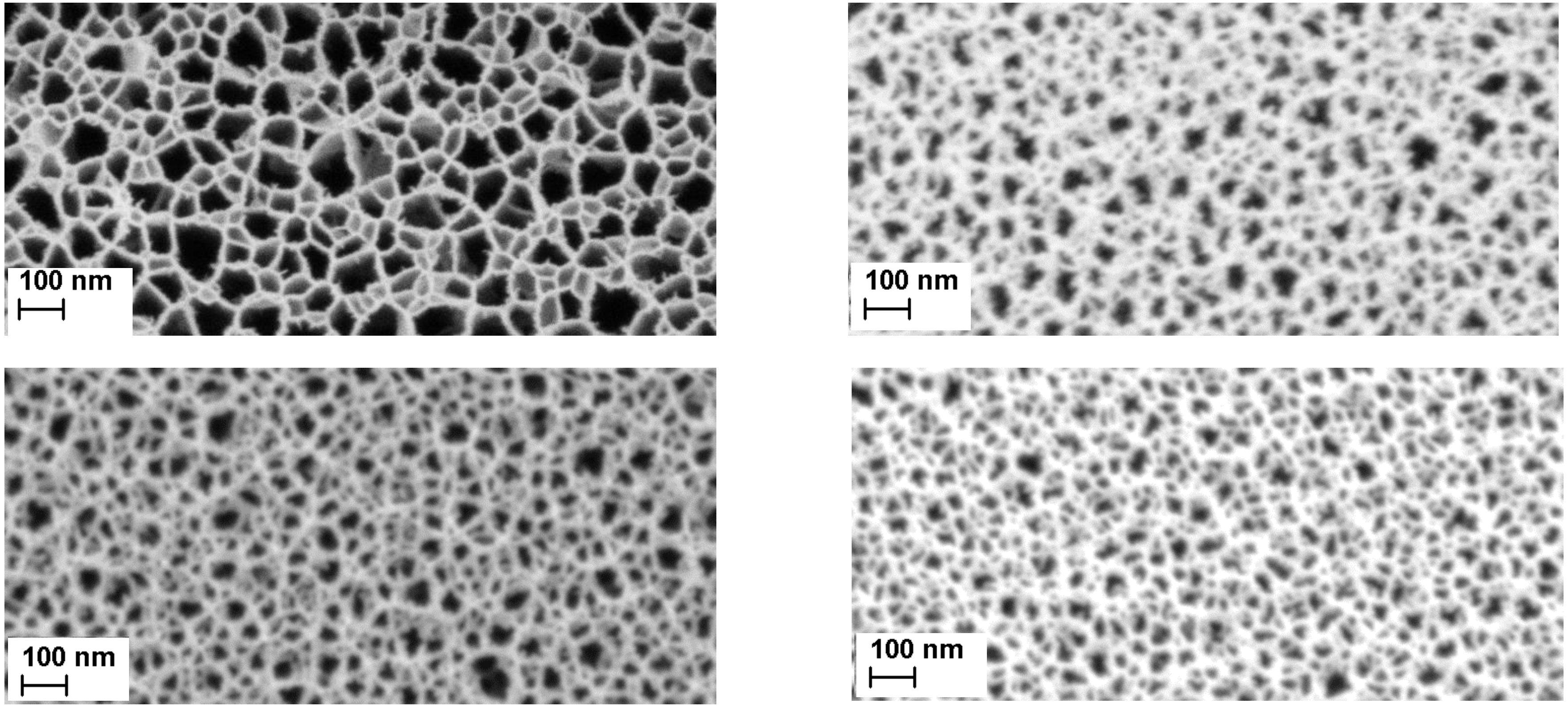

Atomic
Layer
Deposition
(ALD)
Si
SiO_2
Al_2O_3, HfO_2, or TiO_2

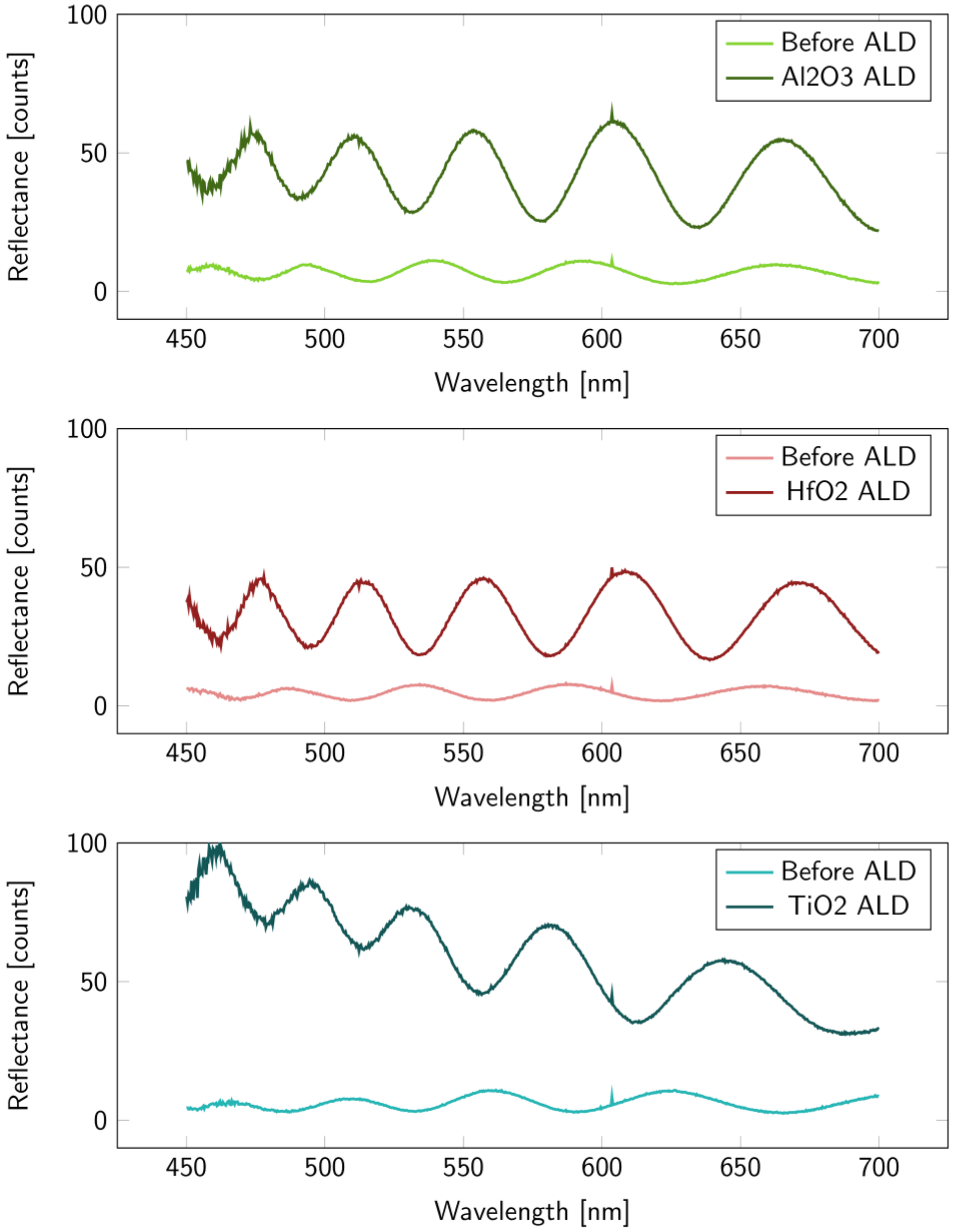
ALD PASSIVATION

UCLouvain

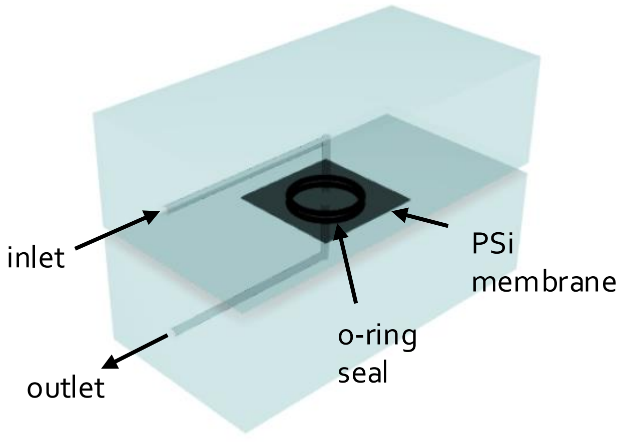
SiO_2 HfO_2

Al_2O_3 TiO_2





Reflectance is improved



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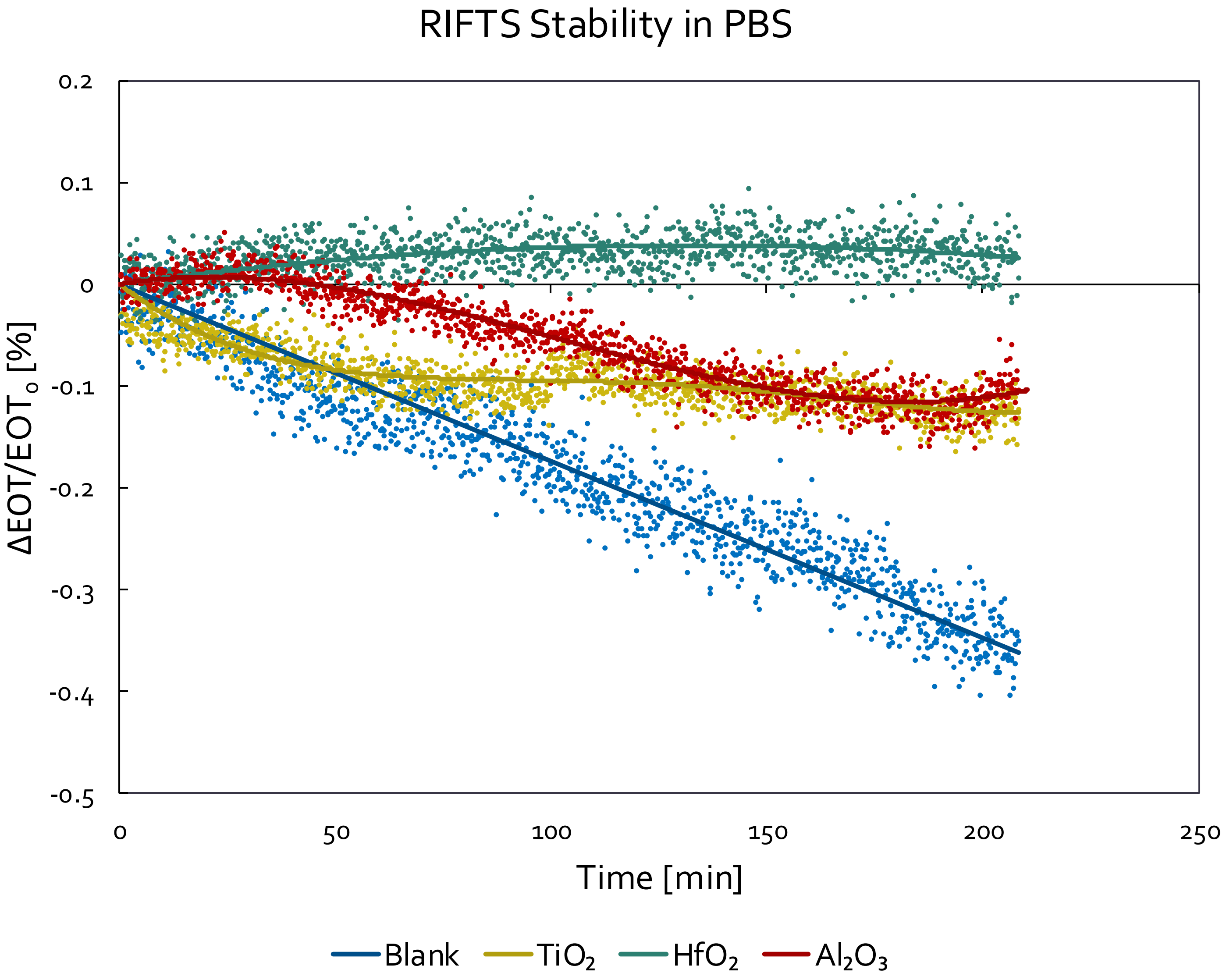
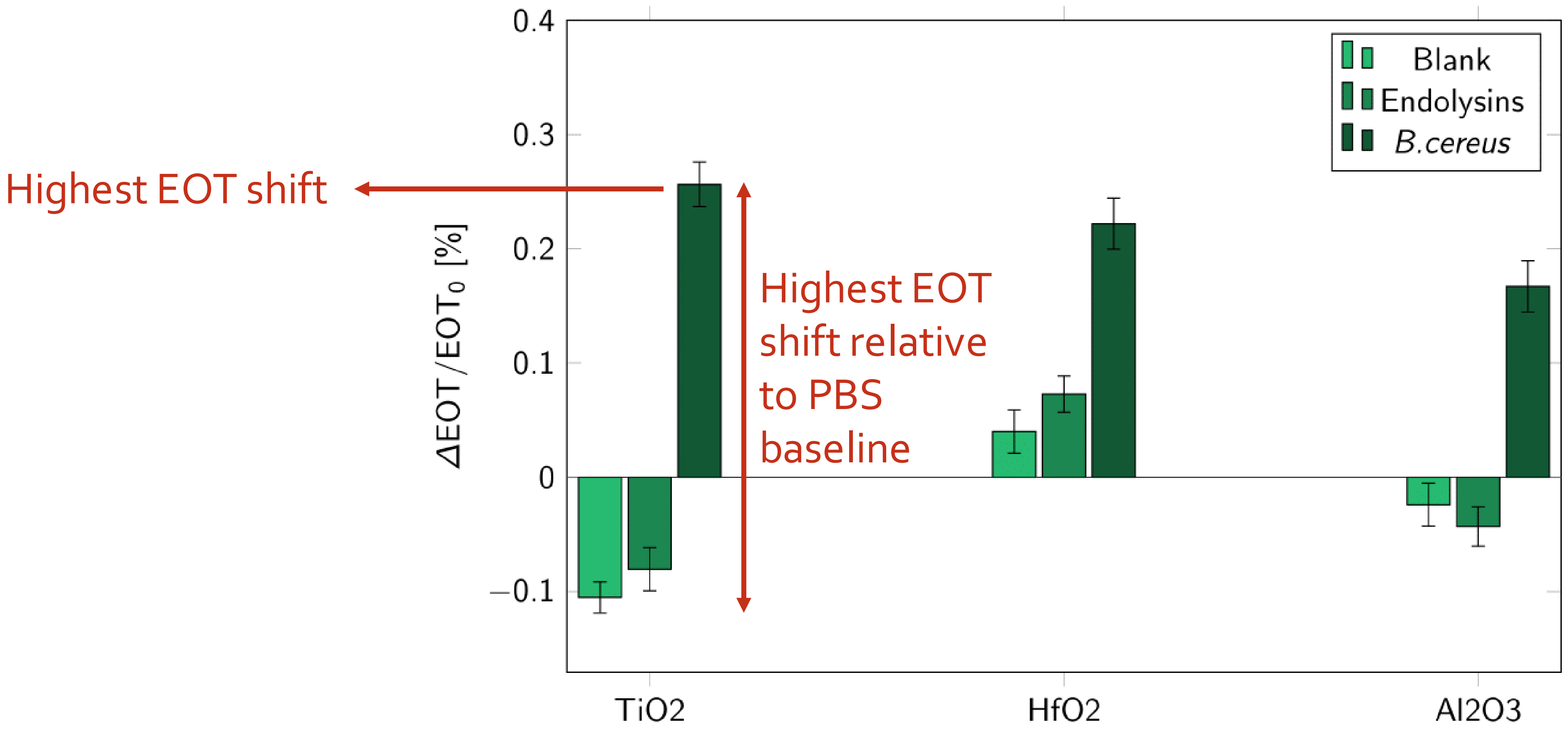
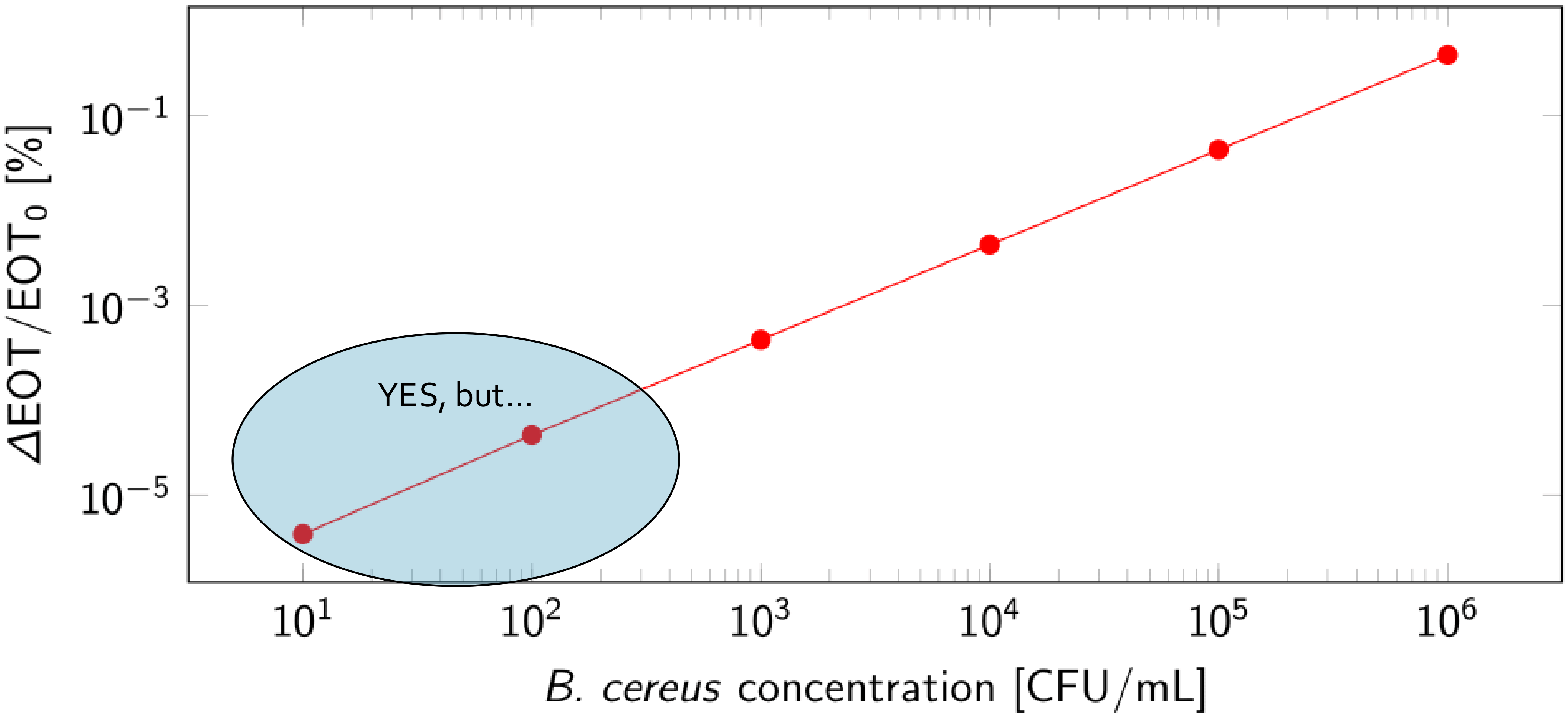


UCLouvain



The detection of *Bacillus cereus* (ATCC10987, ~10^6 CFU/mL), lysed by PlyB221 endolysins, shift after 1h

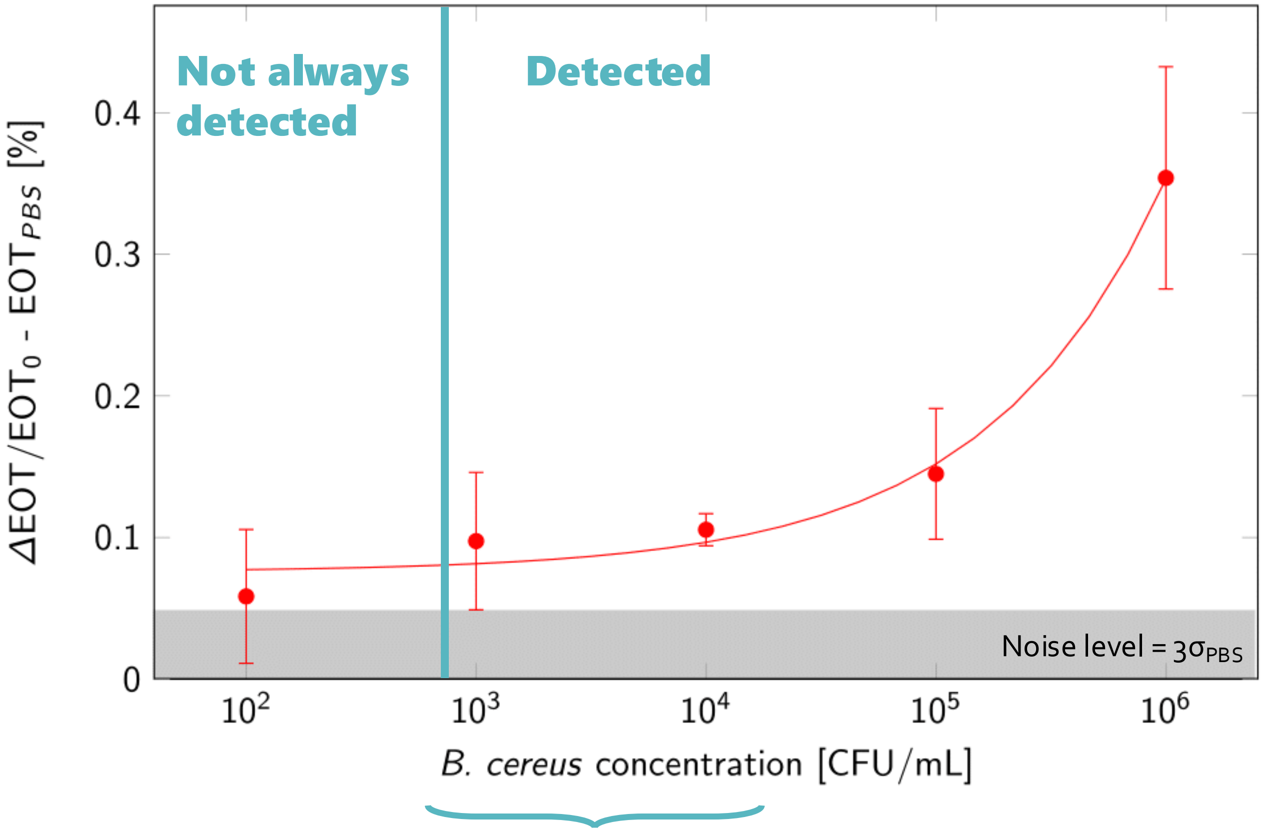
UCLouvain



YES, but...
10^{-1}
10^{-3}
10^{-5}
ΔEOT/EOT0 [%]
10^1
10^2
10^3
10^4
10^5
10^6
B. cereus concentration [CFU/mL]

UCLouvain

Sensitivity ✓



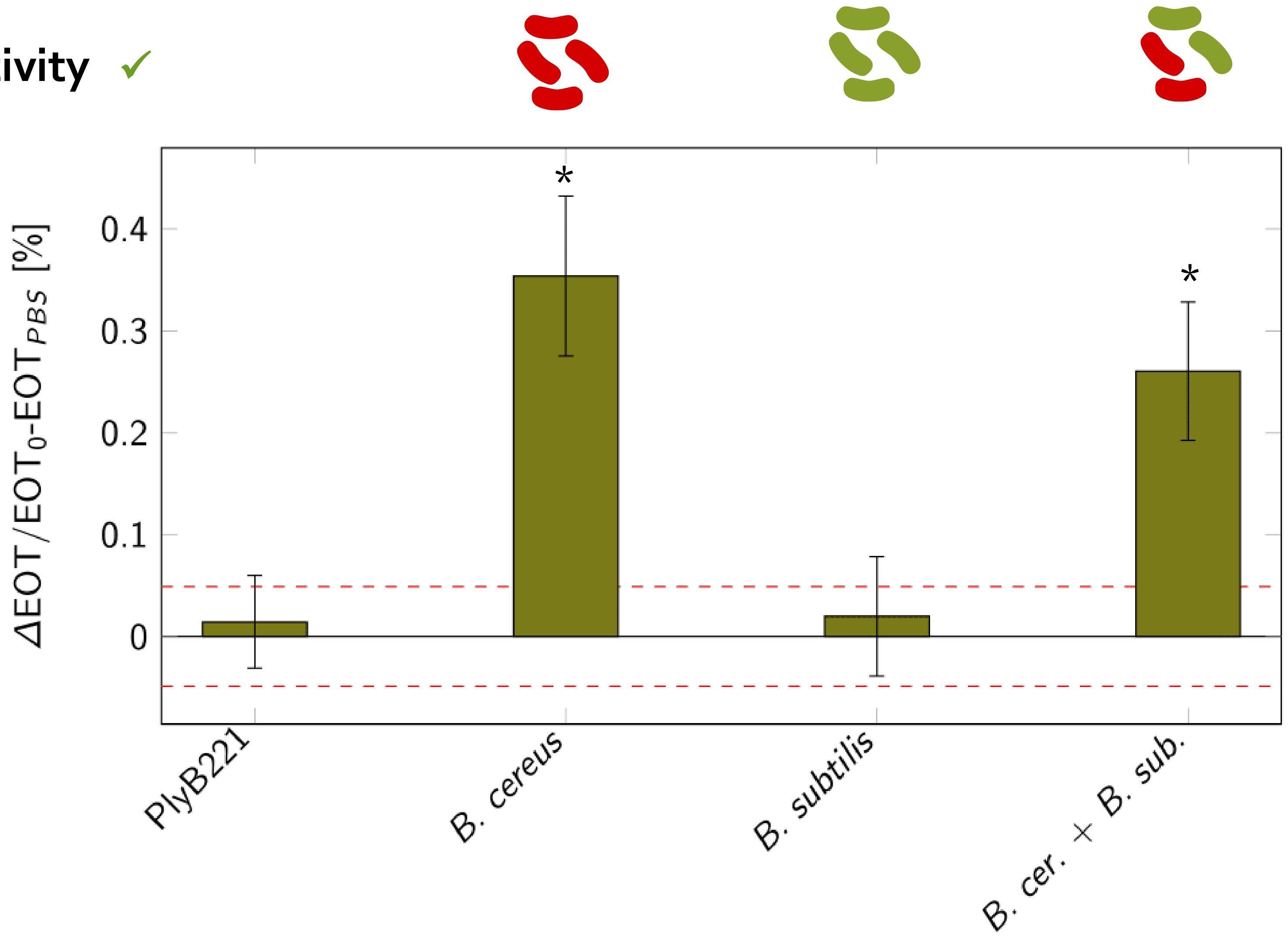
Infection levels for foodborne infection

10^2 CFU/mL ⇨ Detected but not *reliably* *(p-value>0.05)*

10^3 CFU/mL ⇨ **Limit of Detection (LoD)** *(p-value<0.05)* !

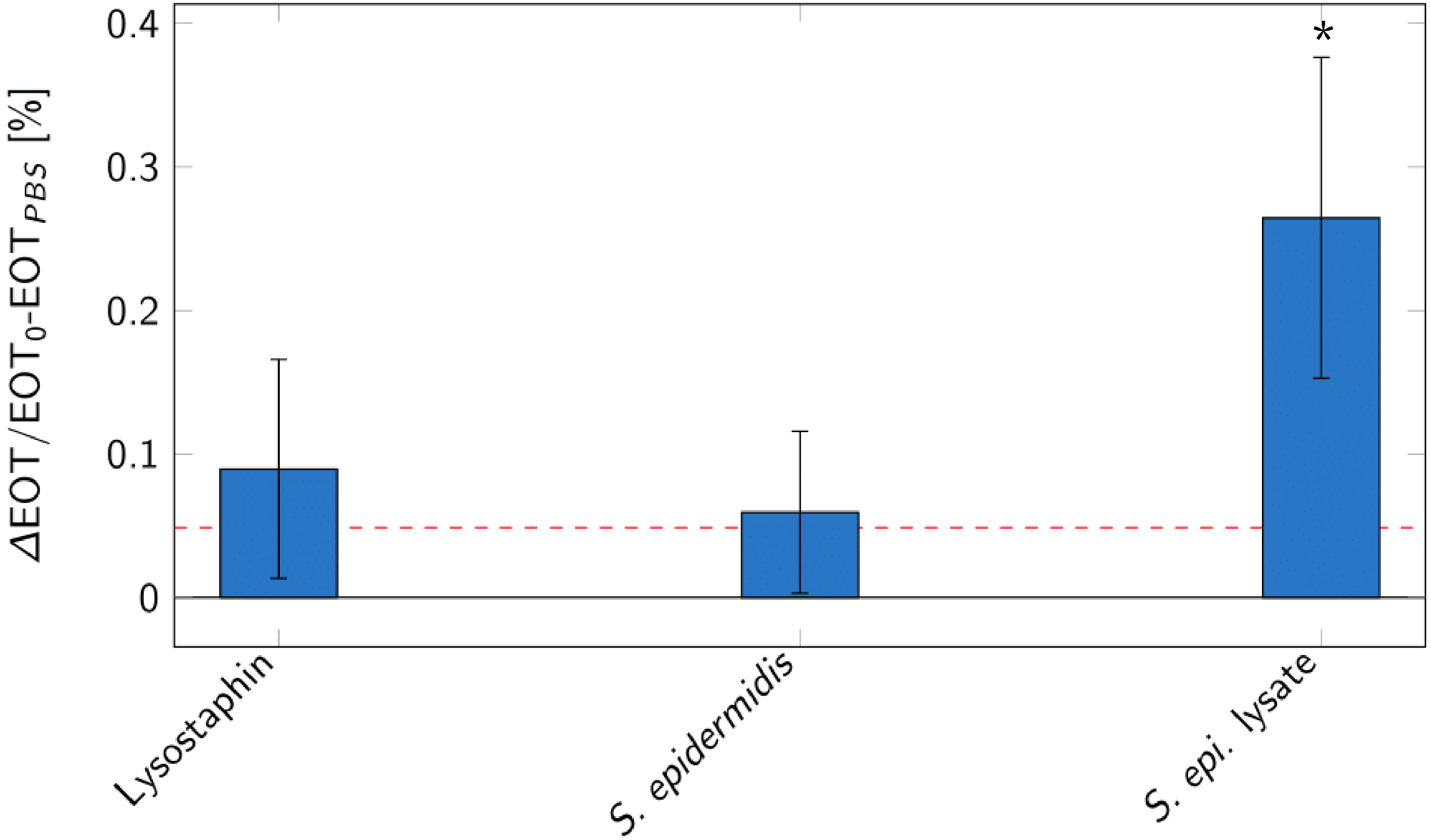
UCLouvain

Selectivity ✓



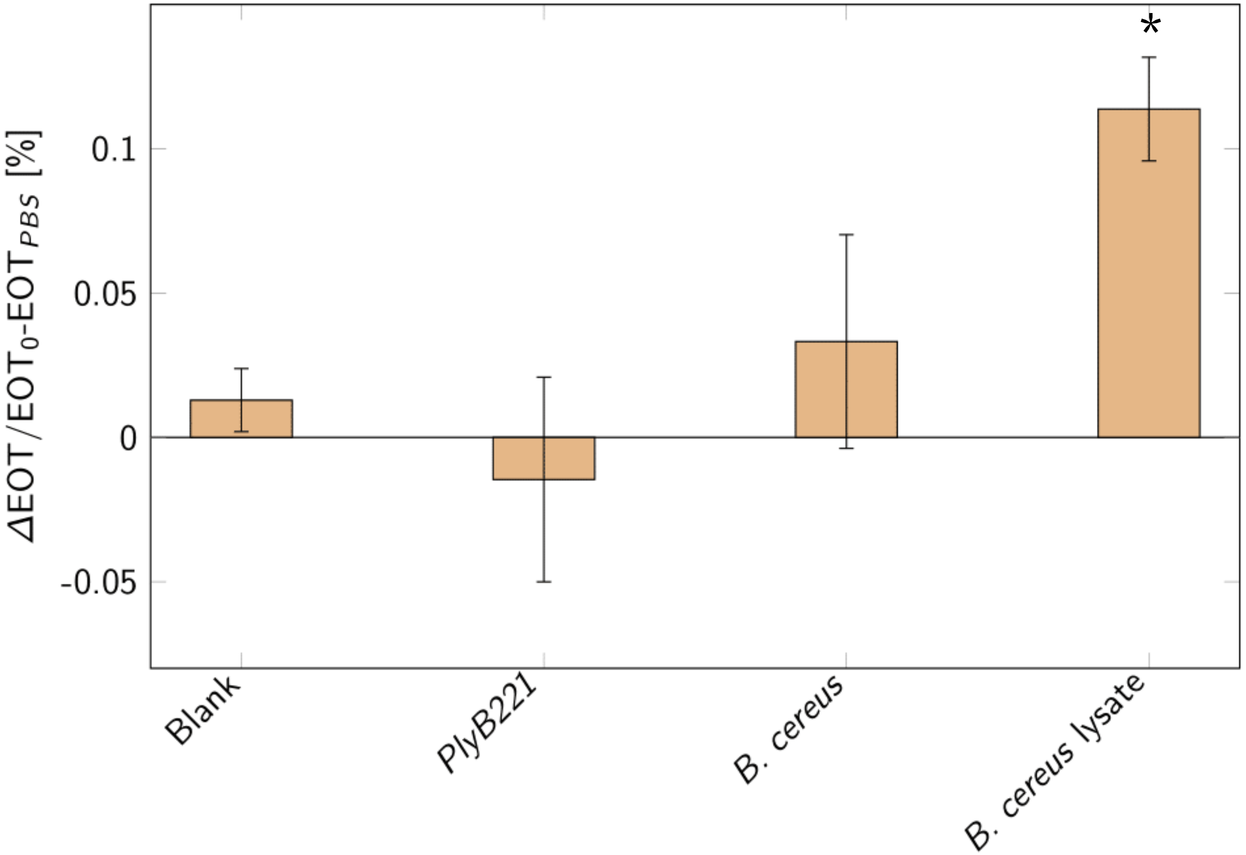
Versatility ✓

The detection of Staphylococcus epidermidis (ATCC35984, ~10⁶ CFU/mL), lysed by lysostaphin

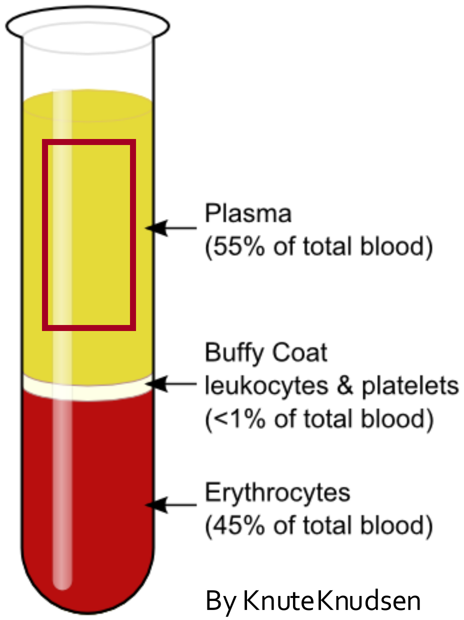


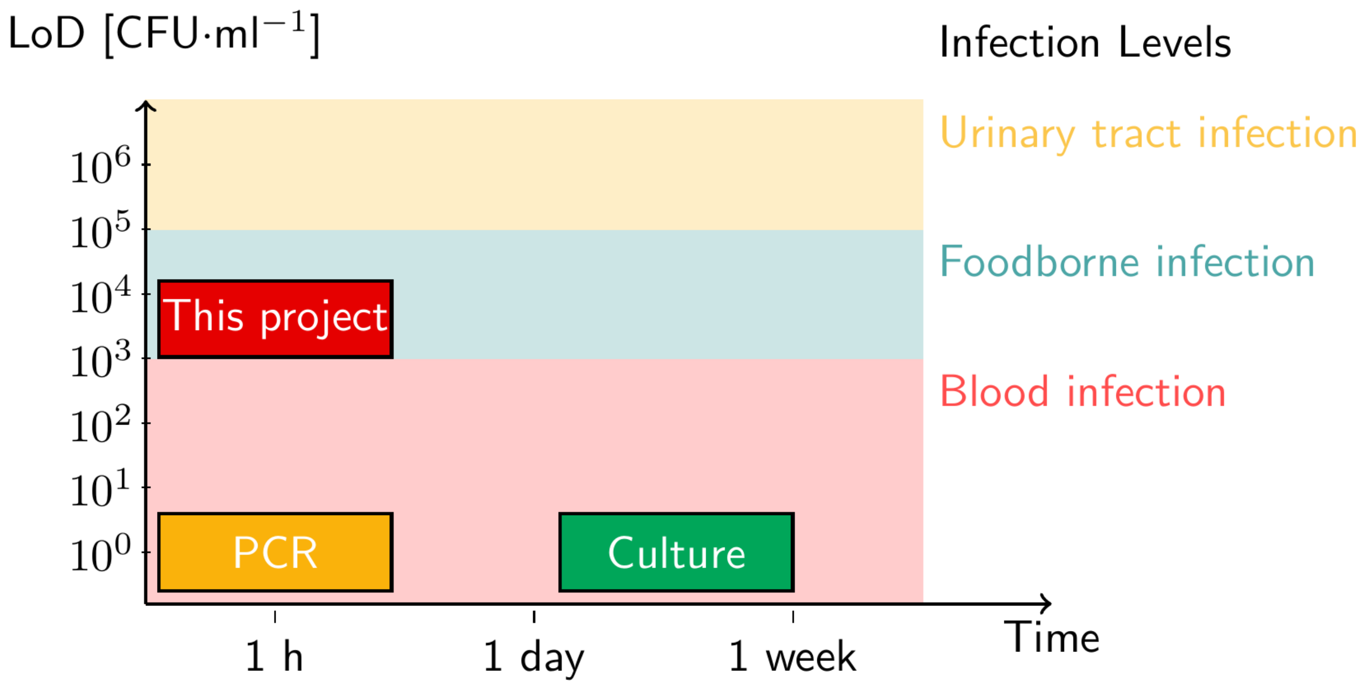
UCLouvain

Complex sample: human plasma ✓ → Blood without white blood cells, red blood cells and platelets



The detection of *Bacillus cereus* (ATCC10987, ~10^6 CFU/mL), lysed by PlyB221 endolysins, shift after 1h



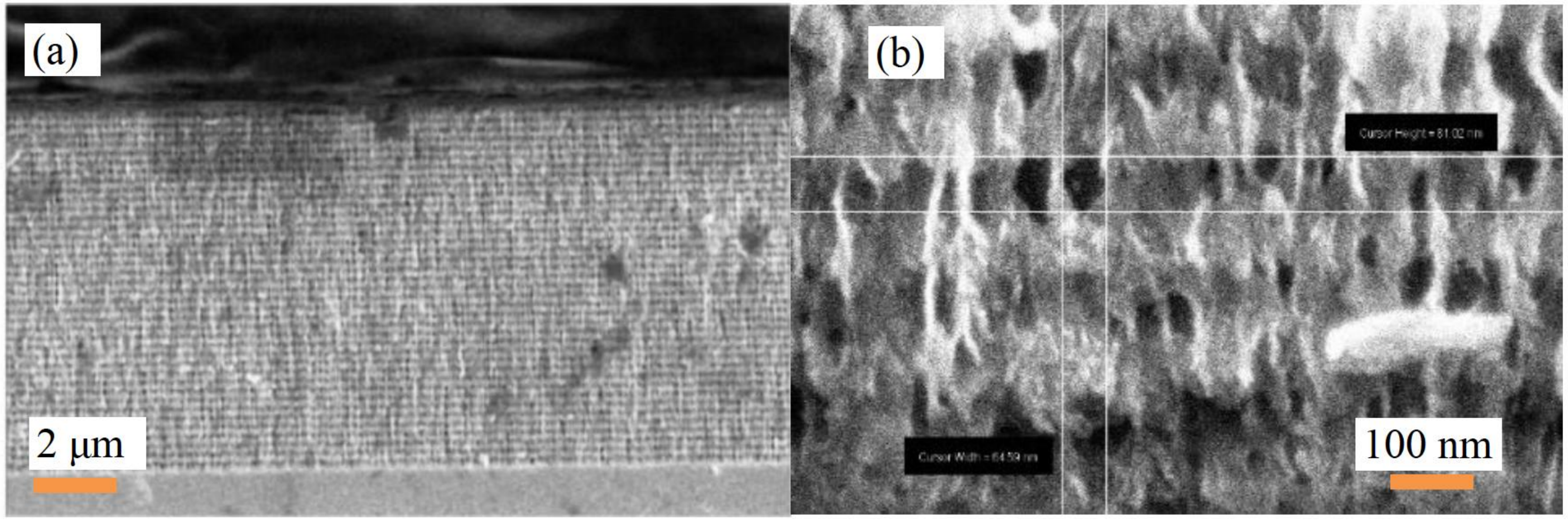


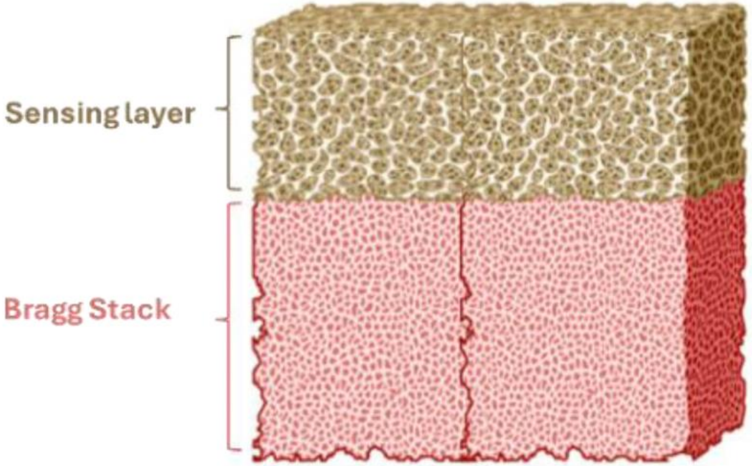
Assay time ✓
Sensitivity ✓
Selectivity ✓
Complex sample ✓
Versatility ✓

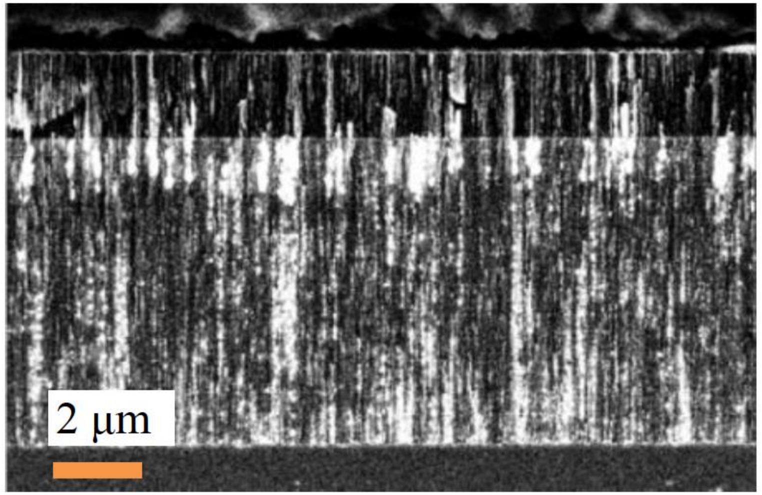
Cost ±
Reliability/Robustness ±

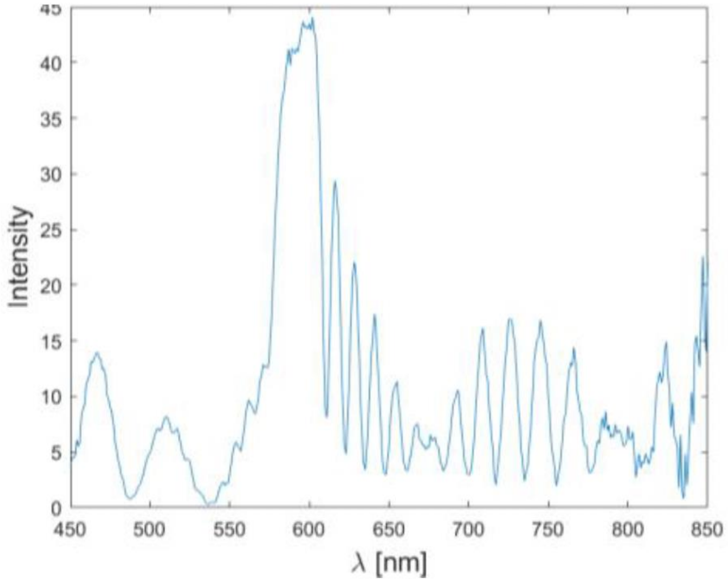
Portability ✘ ⇨ bench-top device for now

⇨ Promising results, but improvements are (always) possible!



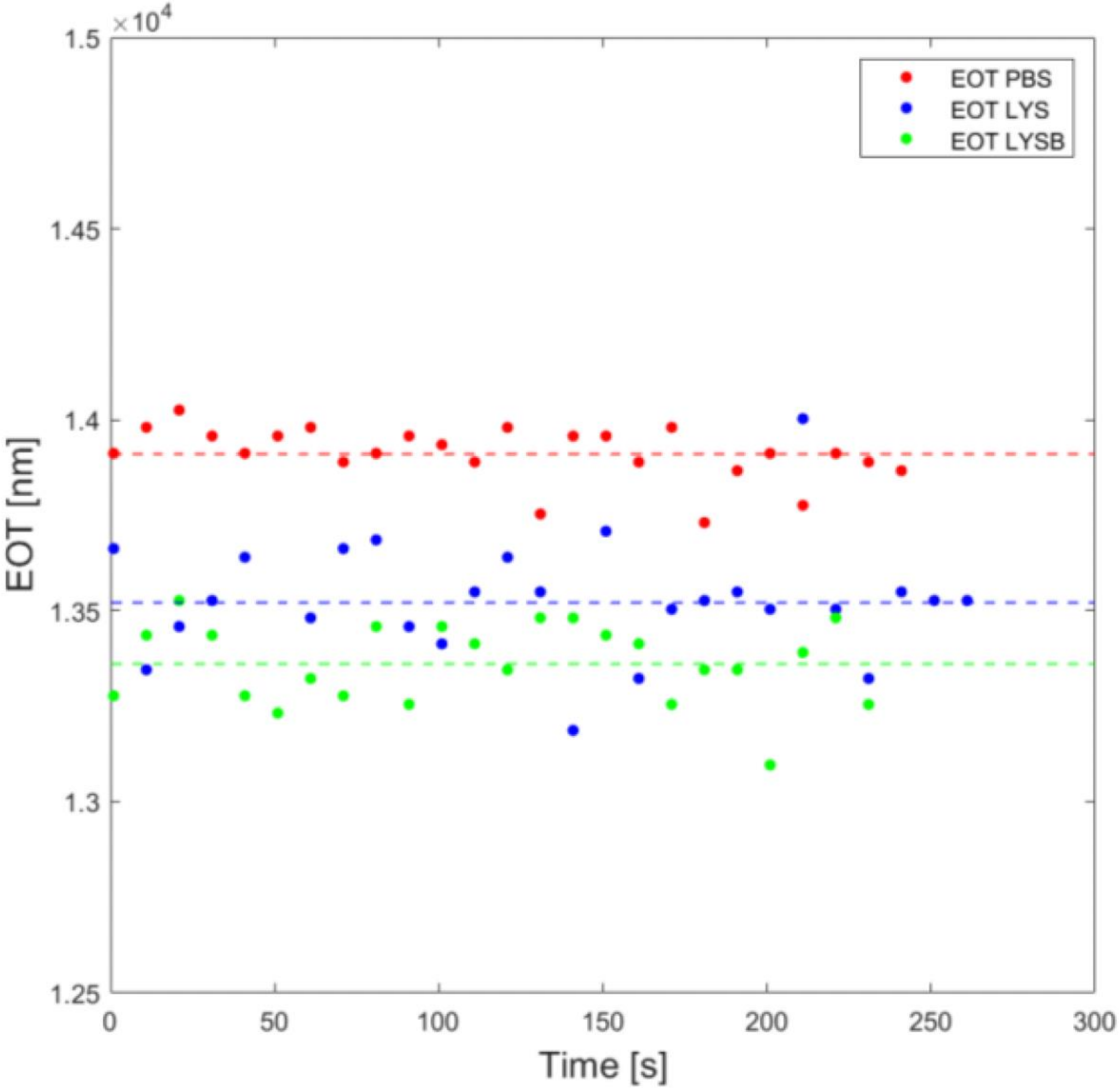






Work of E. Colomer Clavel and C. Gevers

UCLouvain



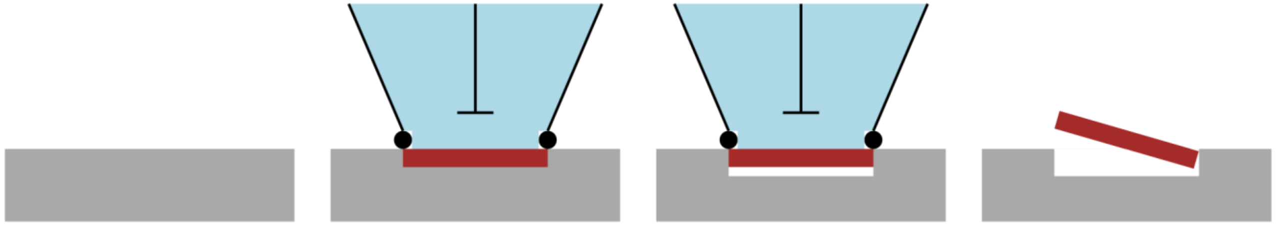
4% EOT shift

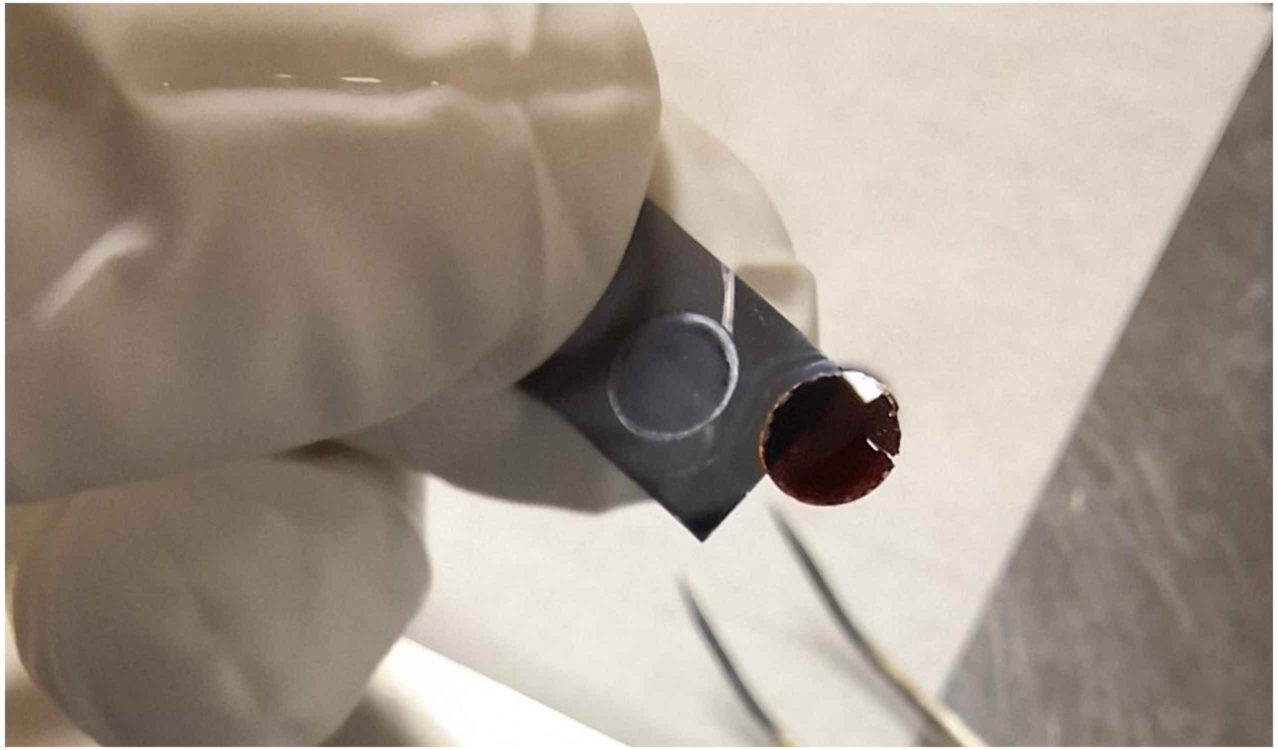
Theoretical LoD

PSi	$2.15 \cdot 10^{-1}$ RIU
PSi+Bragg mirror	$1.35 \cdot 10^{-3}$ RIU

Work of E. Colomer Clavel and C. Gevers

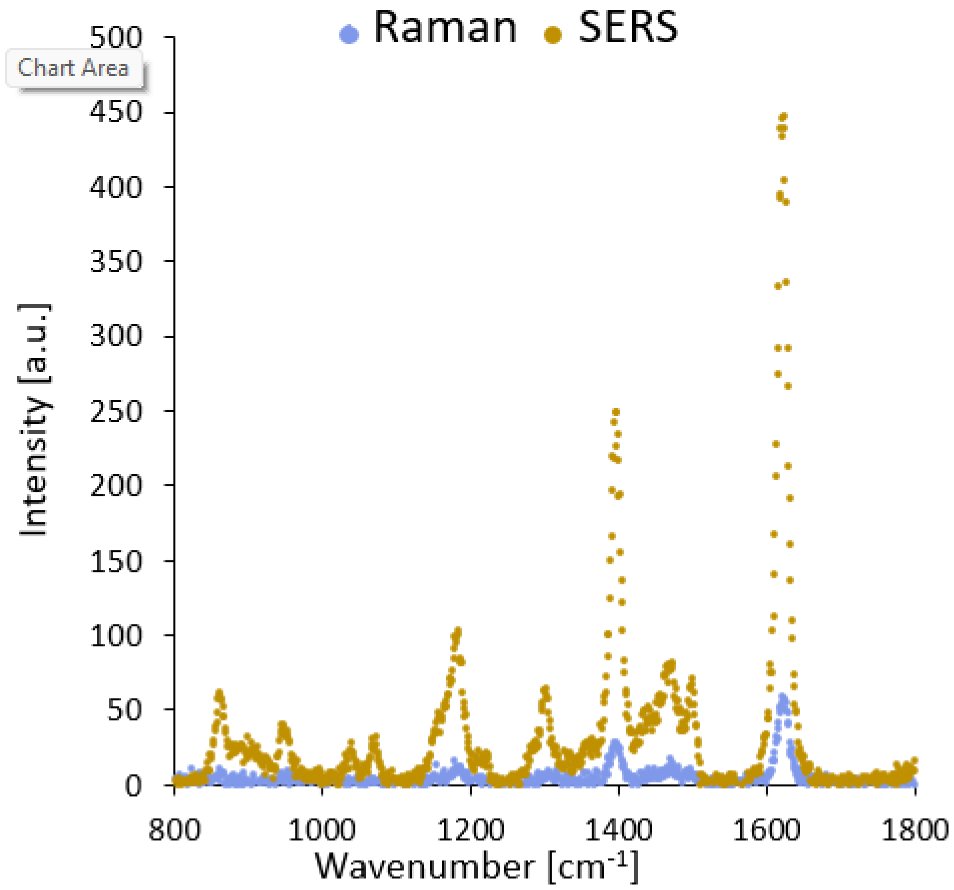
Much simpler method to achieve the fabrication of membranes, if we cope with the mechanical fragility …



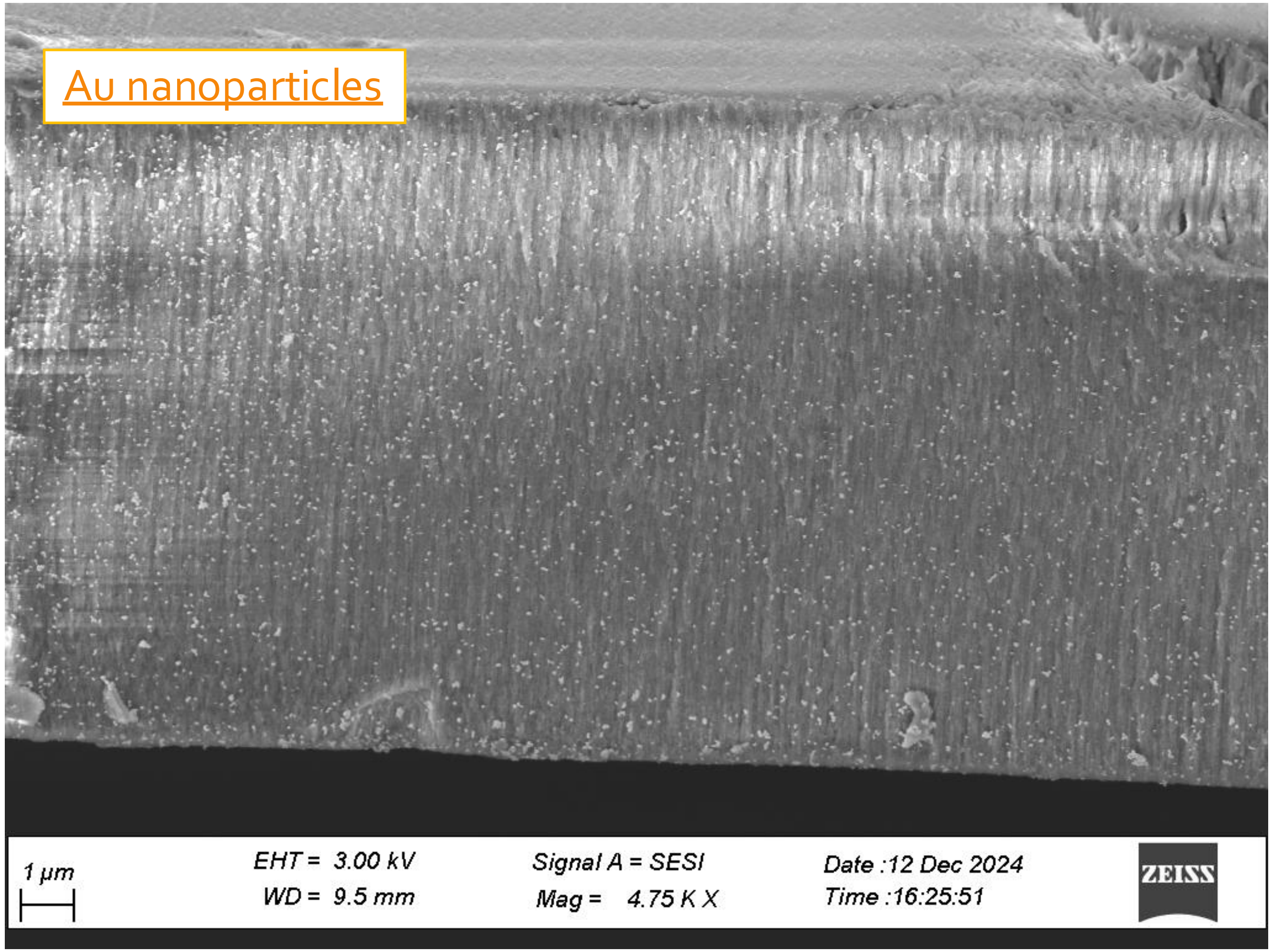


Work of R. Hanus
& C. Gevers

Star-shaped Au NPs

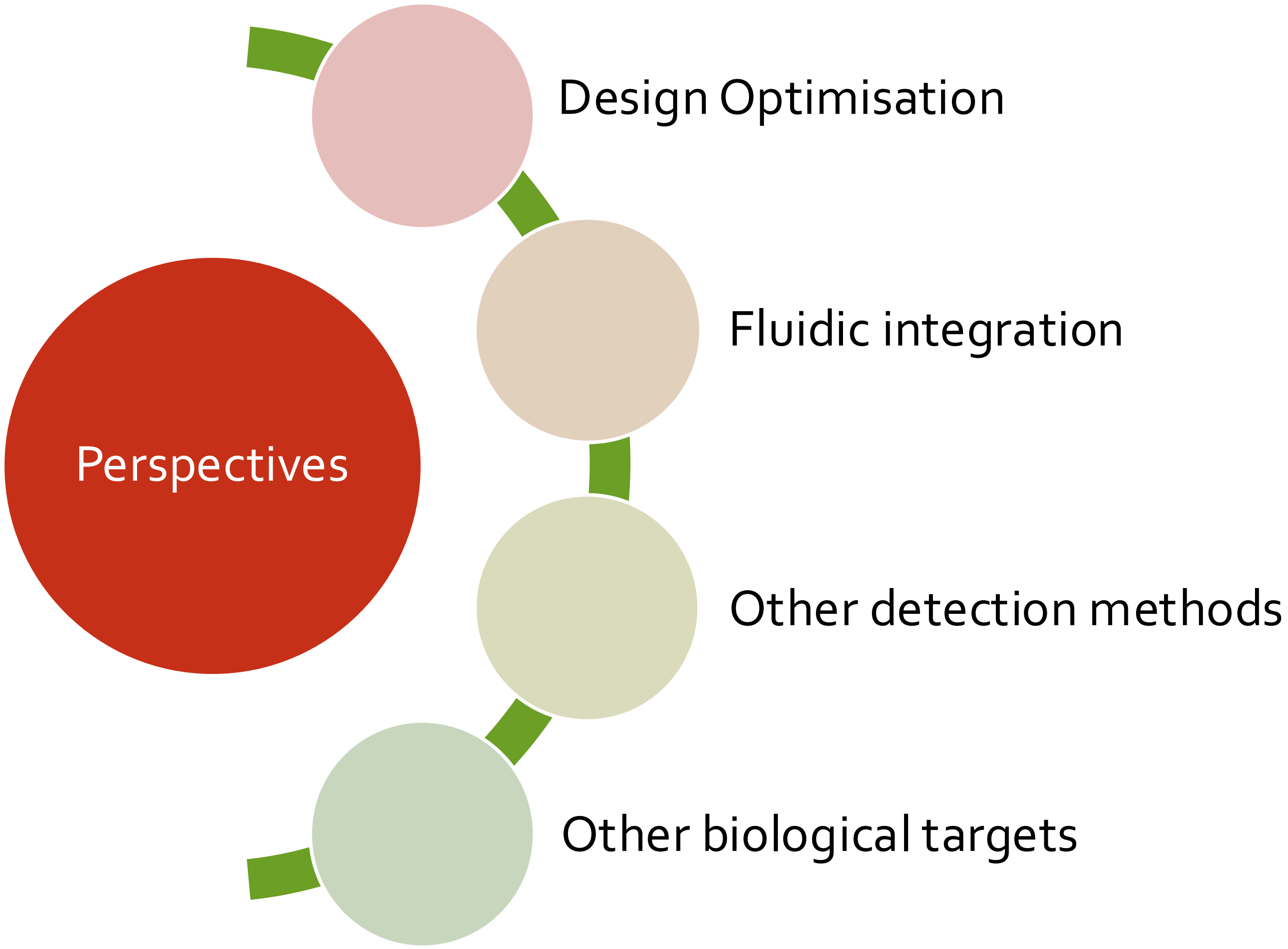


Methylen blue mediation $5{\cdot}10^{-7}$ M



Work of C. Gevers & L. Lejeune

Under submission


Perspectives
Design Optimisation
Fluidic integration
Other detection methods
Other biological targets

- Dr. ir. Roselien Vercauteren for the bulk of the work (and the wonderful slides!)
- Ir. Clara White Ferreira for the ALD investigation and helping with the membrane fabrication
- Elia Colomer Clavel for a fantastic investigation on the Bragg mirrors
- Pr. em. Jacques Mahillon and his team, in particular to Audrey Leprince and Manon Nuytten for endolysin synthesis
- Pr. Sophie Hermans and Louise Lejeune for Au NPs
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- UCLouvain's cleanroom WINFAB technical team for assistance

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  - UCLouvain

Thank you for your attention!

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