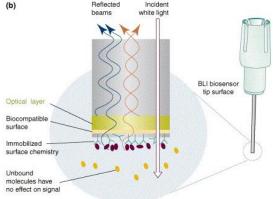
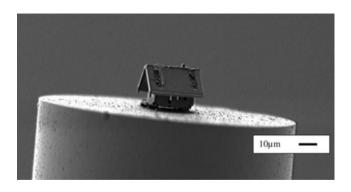
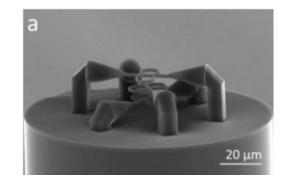




LAB ON FIBER TECHNOLOGY: TOWARDS NEW ADVANCED OPTICAL OPTRODES FOR LIFE SCIENCE APPLICATIONS







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a.cusano@unisannio.it

Optoelectronics and Photonics Group, Department of Engineering, University of Sannio, Benevento, Italy









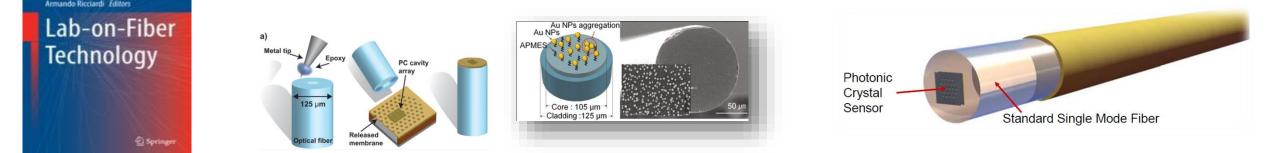
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LAB ON FIBER TECHNOLOGY:

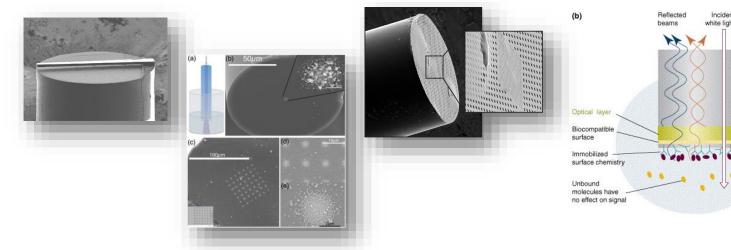


TOWARDS INTEGRATED AND MULTIFUNCTIONAL NANO-PROBES

Integration and patterning at micro and nano scale of different functional materials with desired optical, physical and chemical properties



Increased light matter interaction and creation of a technological world completely integrated within optical fibers with significant advantages in terms of functionality, performances, miniaturization, robustness, cost effectiveness and power consumption





BLI biosensor tip surface

MAIN BARRIER

Definition of a reliable *fabrication procedure able to integrate, at micro- and nano-scale,* several materials onto unconventional substrates such as the optical fibers.



THE LAB ON FIBER TECHNOLOGY



F. Chiavaioli, F. Baldini, S. Tombelli, C. Trono, A. Giannetti Biosensing with optical fiber gratings

Nanophotonics, vol. 6, no. 4, 2017

Shrinking the 'labs' onto the optical fibers



T. Guo, Á . González-Vila, M. Loyez, C. Caucheteur Plasmonic Optical Fiber-Grating Immunosensing: A Review Sensors (Basel). 2017;17(12):2732

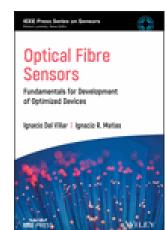
Stavros Pissadakis Lab-in-a-fiber sensors: A review Microelectronic Engineering, Vol. 217, 2019

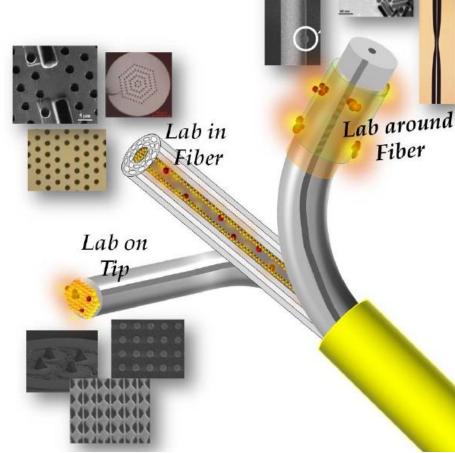
P. Vaiano, A. Cusano et al.

Lab on Fiber Technology for biological sensing applications.

Laser & Photonics Reviews, 2016, 10(6), 922-961

Editor(s): Ignacio Del Villar, Ignacio R. Matias Optical Fibre Sensors: Fundamentals for Development of Optimized Devices IEEE Press & Wiley 2020





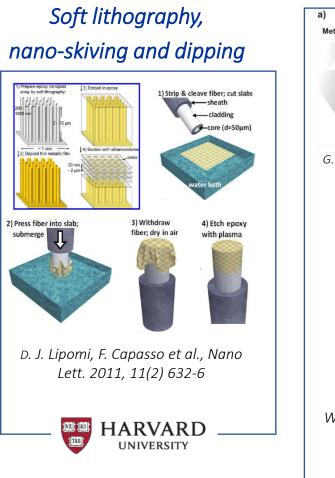


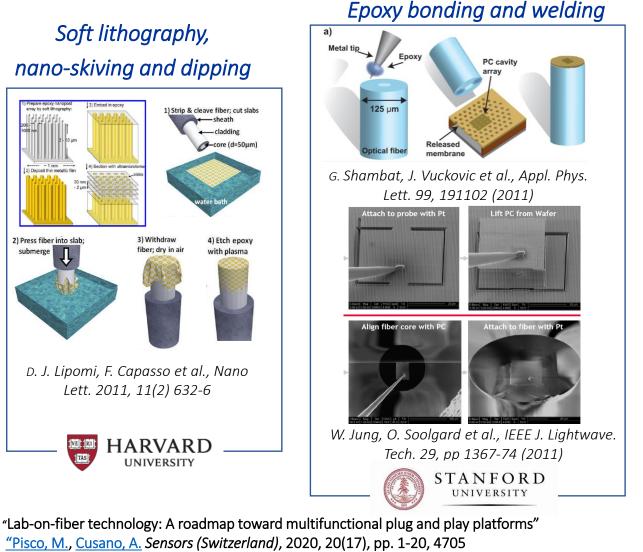
THE FABRICATION ROUTES

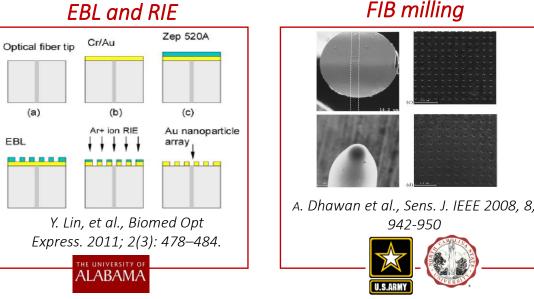


NANO-TRANSFERRING

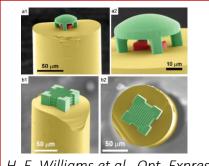
DIRECT-WRITING



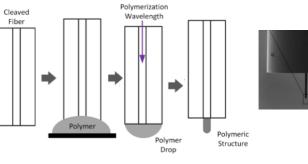




Multi-photon direct laser writing/polymerization



H. E. Williams et al., Opt. Express 19, 22910 (2011) ICF

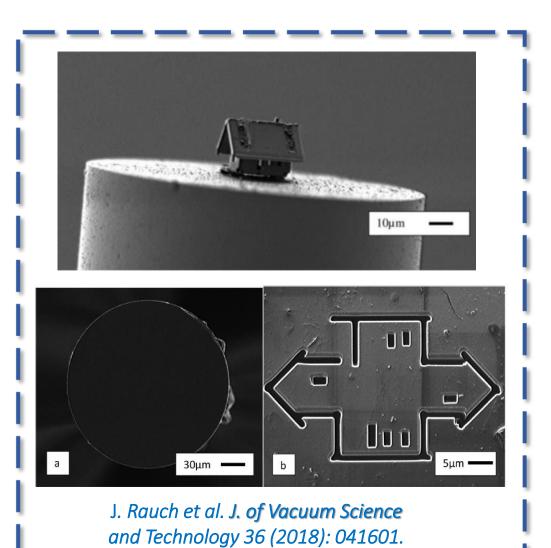


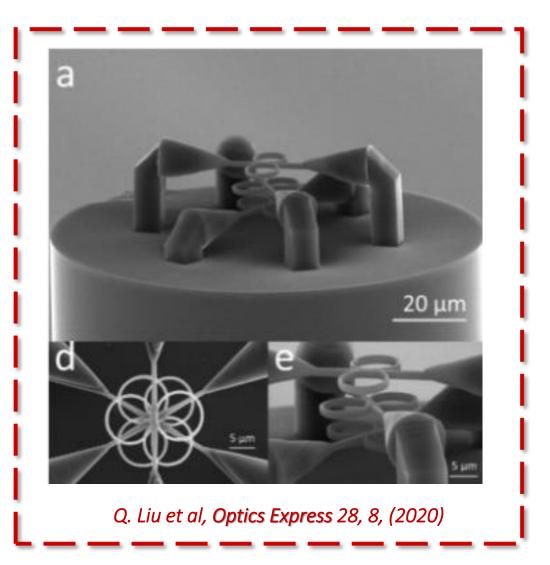
Ribeiro R. et al. Photonics 2, pp 634-645 (2015) U.PORTO_



TOWARDS 3D LAB ON FIBER TECHNOLOGY



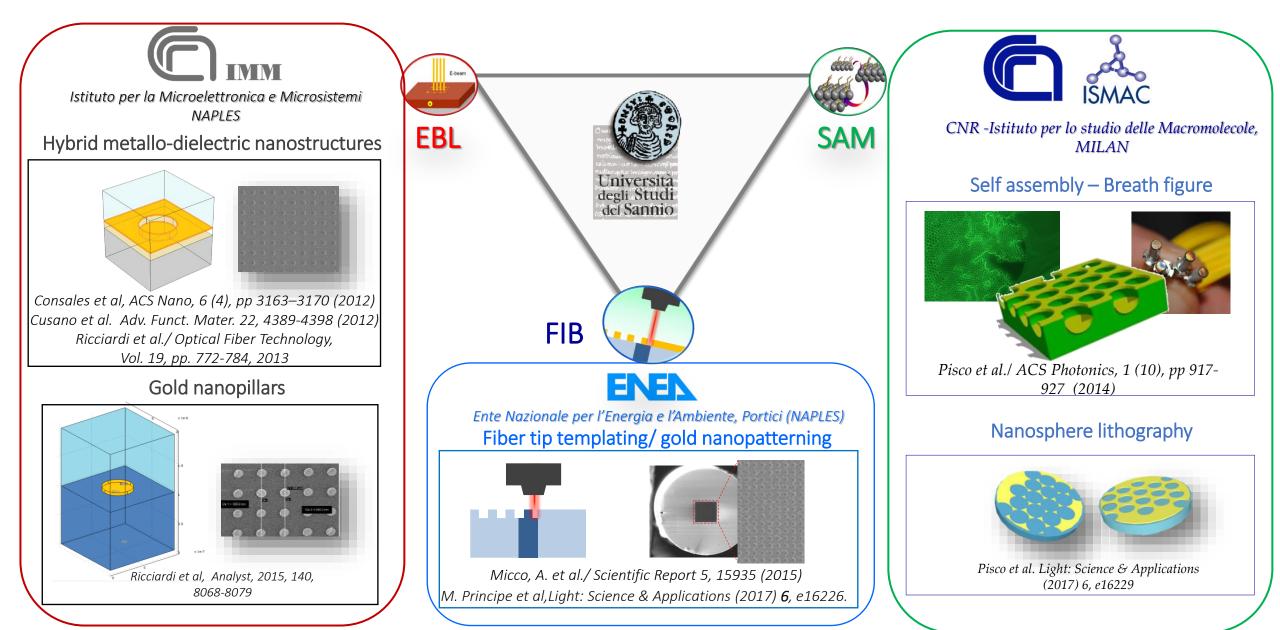






TECHNOLOGY CLUSTER

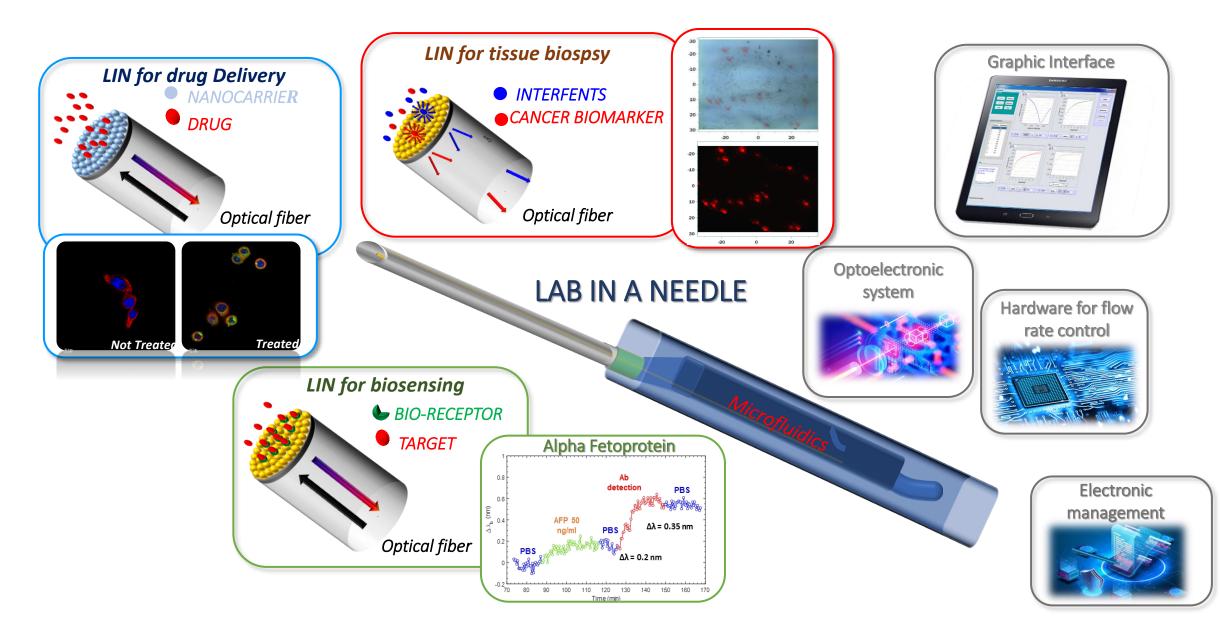






THE VISION



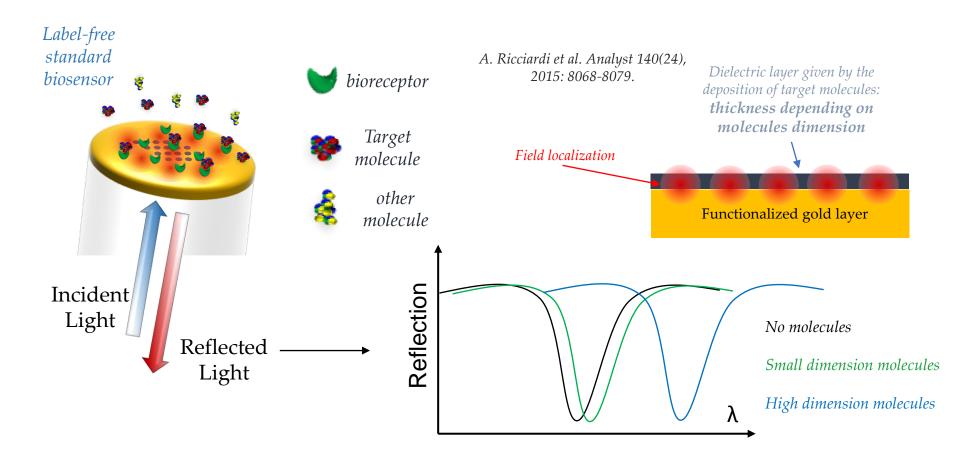






MAIN LIMITATIONS OF LAB ON TIP LABEL FREE PLATFORMS

Local refractive index changes due to the capture of the target biomarker to the bioreceptor are detected as resonant wavelength shift in the reflection spectrum.



Main limitation: the maximum wavelength shift is related to the concentration and molecule dimension.

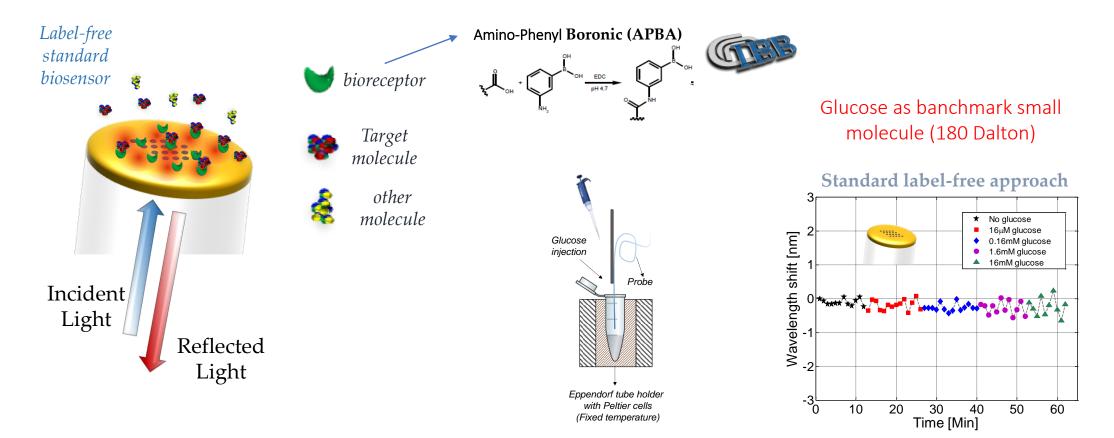




A LAB-ON-FIBER PLASMONIC DEVICE FOR BIOLOGICAL SENSING

LABEL-FREE STANDARD APPROACH

Local refractive index changes due to the capture of the target biomarker to the bioreceptor are detected as resonant wavelength shift in the reflection spectrum.



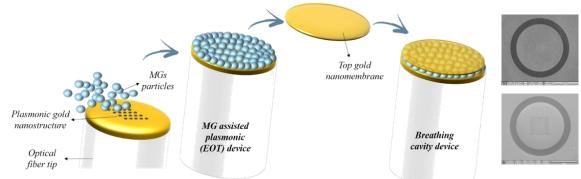
Main limitation: the maximum wavelength shift is related to the concentration and molecule dimension.



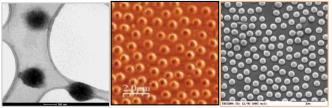


CAVITY ENHANCED LAB-ON-

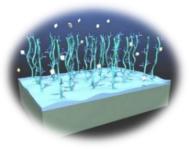
FIBER TECHNOLOGY



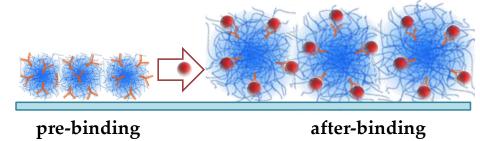
Sub-micrometer hydrogel particels i.e Crosslinked water soluble polymers (physically restricted, dimensionally stable)



MICROGELS AS AMPLIFICATION SYSTEM FOR LABEL-FREE DETECTION



Translating an interaction surface in an interaction volume



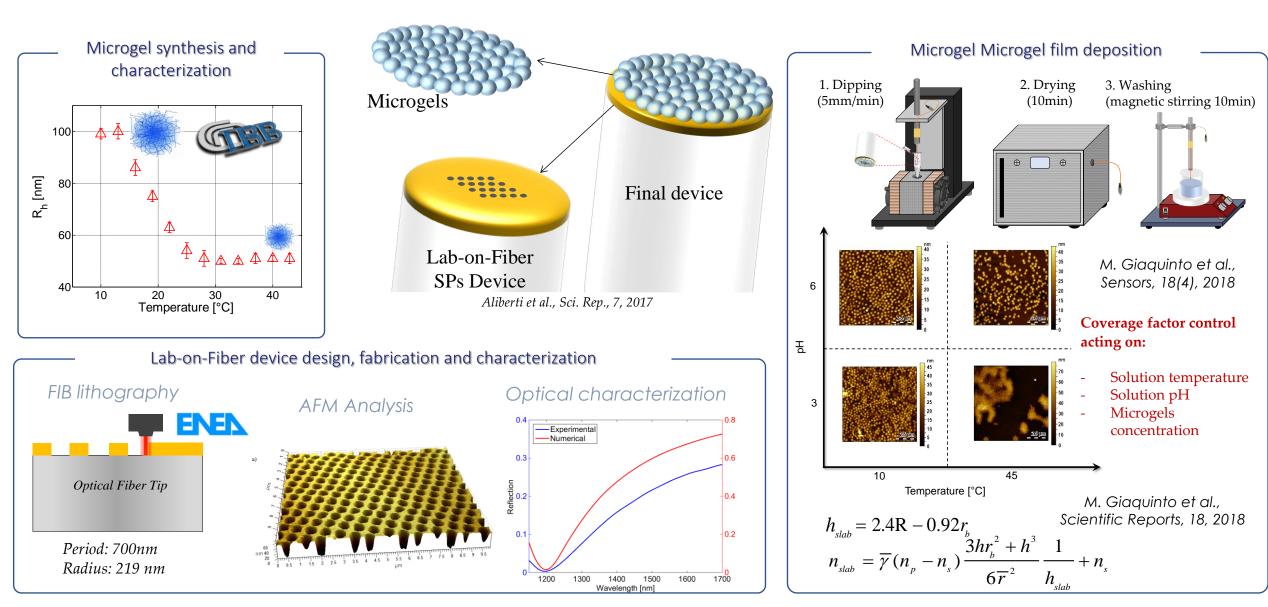
1. Amplification of the binding sites

2. Enhance the superficial changes due to binding





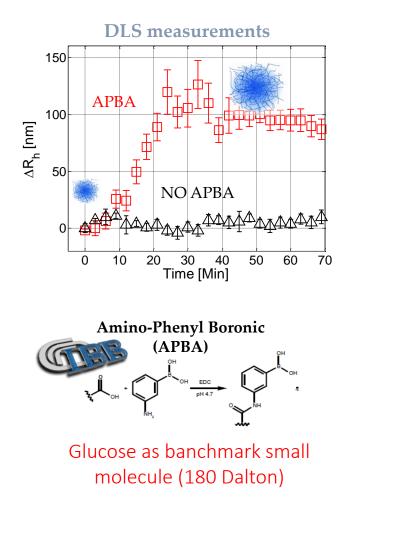
MICROGEL ASSISTED LAB-ON-FIBER OPTRODE

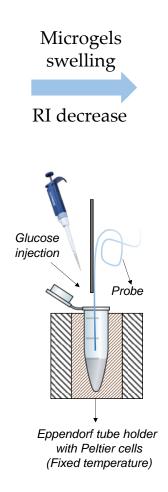




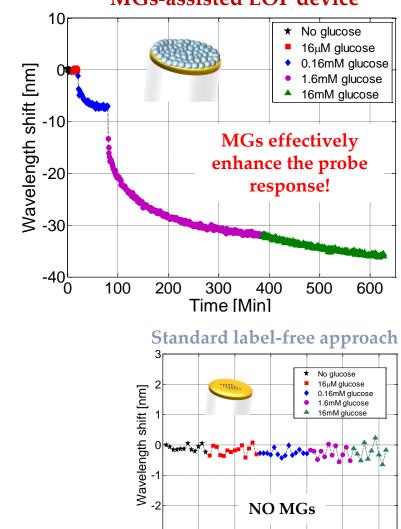


MICROGEL ASSISTED LOF OPTRODE FOR BIOSENSING





Aliberti, et al. "Microgel assisted Lab-on-Fiber biosensors", Scientific Reports, 7, 2017



-3Ľ 0

30

Time [Min]

20

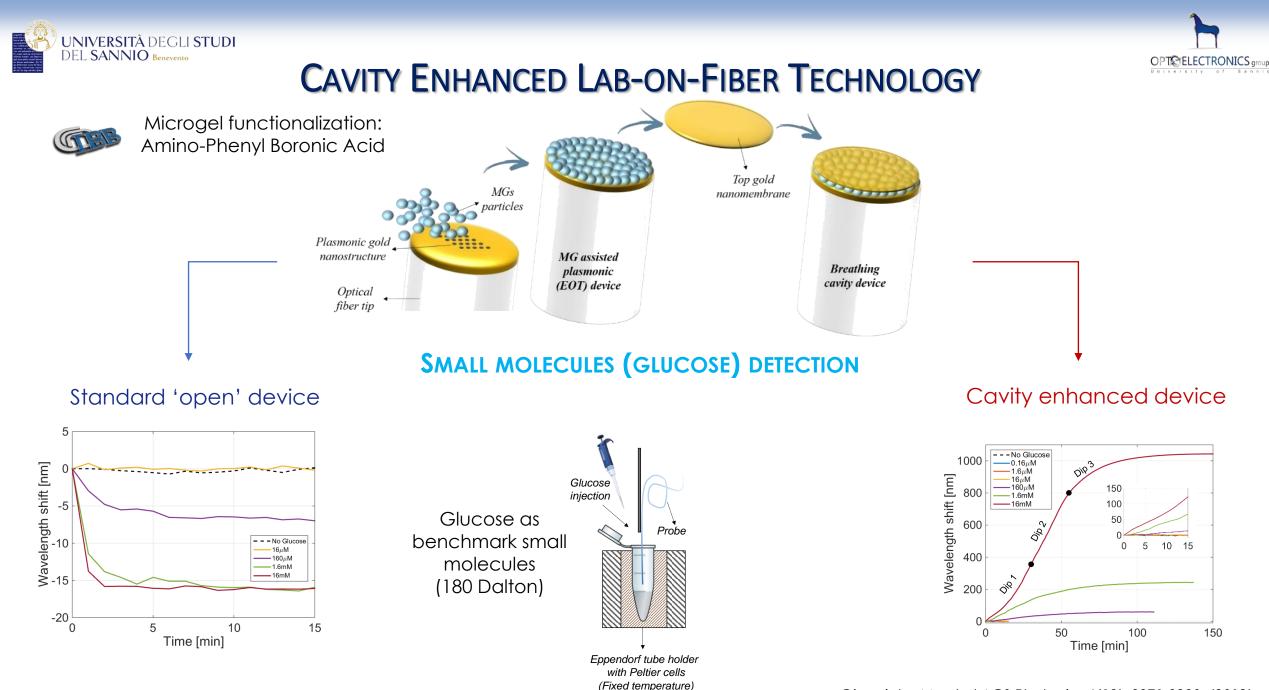
10

40

50

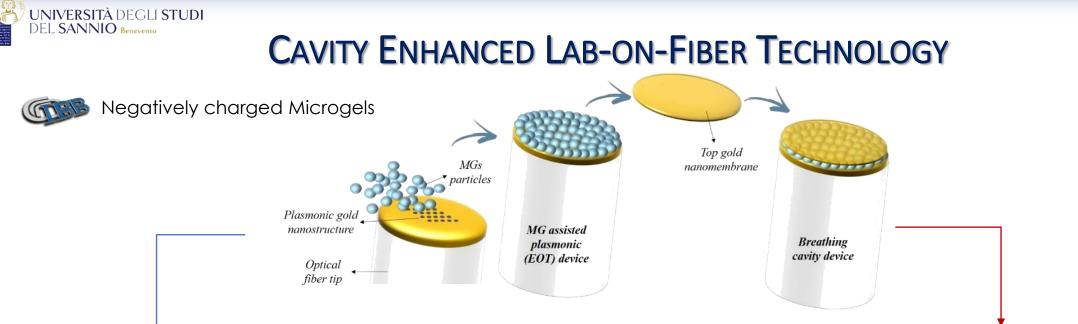
60

MGs-assisted LOF device



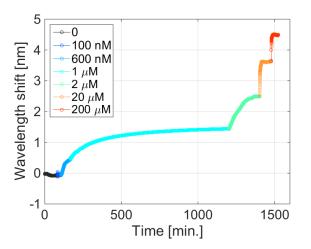
Aliberti, A. et al., Scientific reports 7(1), 14459. (2017)

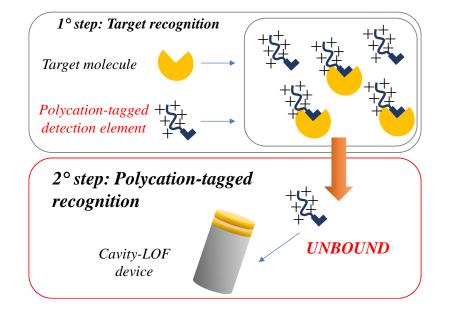
Giaquinto, M., et al ACS Photonics 6(12), 3271-3280. (2019)



POLYCATIONS DETECTION FOR INDIRECT ASSAYS

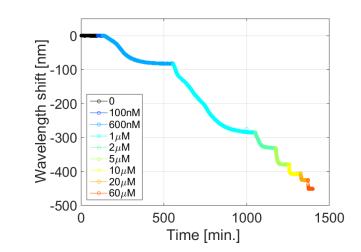
Standard 'open' device





Cavity enhanced device

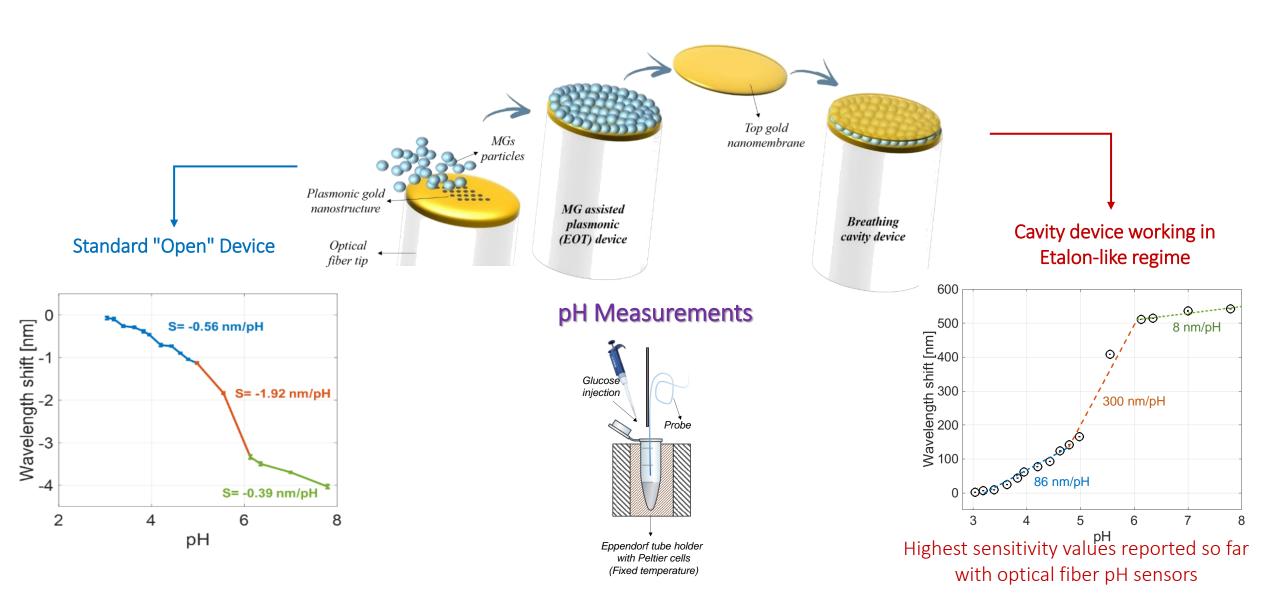
OPT ELECTRONICS group



F. Gambino, et al, Sensors and Actuators B: Chemical, 353, 2022

CAVITY ENHANCED PROBE FOR PH MONITORING

OPT ELECTRONICS group



F. Gambino, et al, Sensors & Diagnostics, 2022

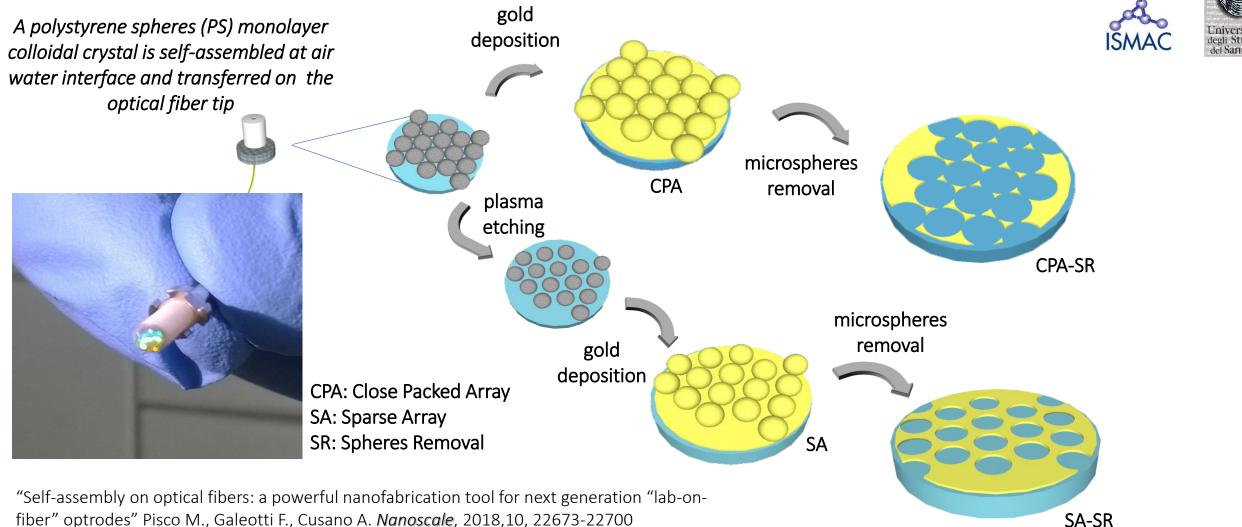
UNIVERSITÀ DEGLI STUDI

SANNIO Benevento

DFI



NANOSPHERE LITHOGRAPHY ON FIBER: TOWARDS REPEATABLE SERS SUBSTRATES



fiber" optrodes" Pisco M., Galeotti F., Cusano A. Nanoscale, 2018,10, 22673-22700

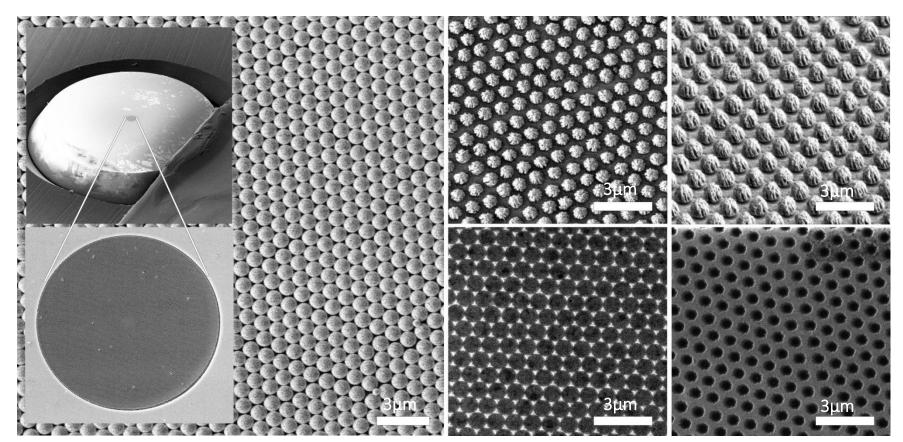






NANOSPHERE LITHOGRAPHY ON THE OPTICAL FIBER TIP

Four different kinds of structural motifs are realized directly on the optical fiber facet, each of which giving rise to a different metallo-dielectric periodic pattern



M. Pisco et al., «Nanosphere lithography for optical fiber tip nanoprobes», Light: Science & Applications (2017) 6, e16229





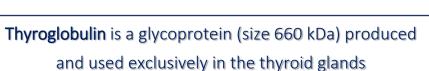


THYROID CANCER – NEON PROJECT







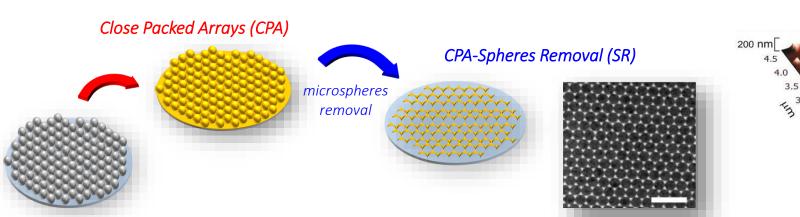


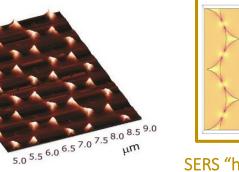


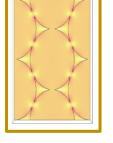
High values of Tg concentration in the lymph nodes specifically identify the presence of differentiated thyroid cancer cells



LAB ON FIBER SERS OPTRODES





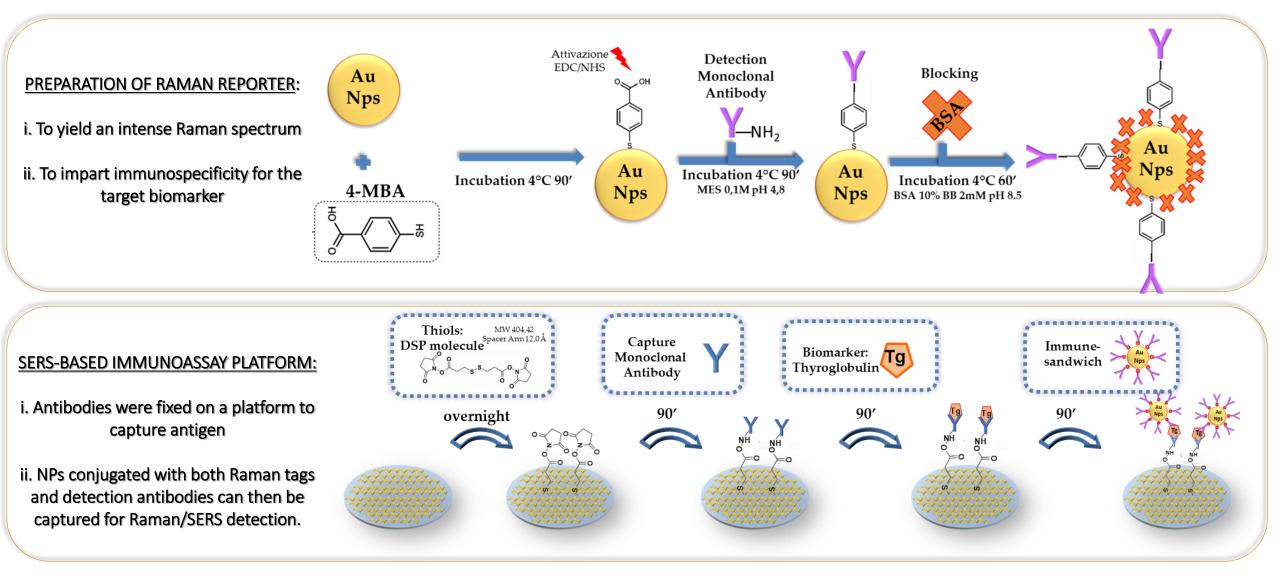


SERS "hot-spots"





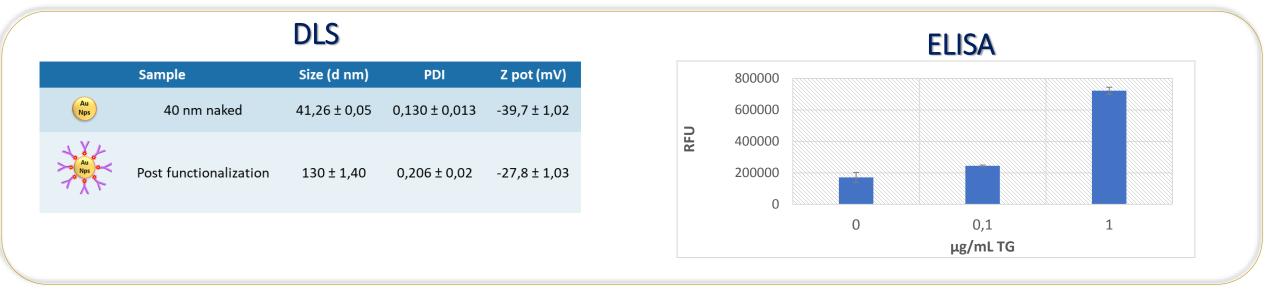
SERS PLATFORM FOR HIGH-SPECIFICITY TUMOR BIOMARKER IDENTIFICATION IN LIQUID BIOPSY





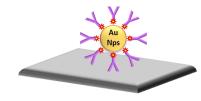
AuNps CHARACTERIZATION

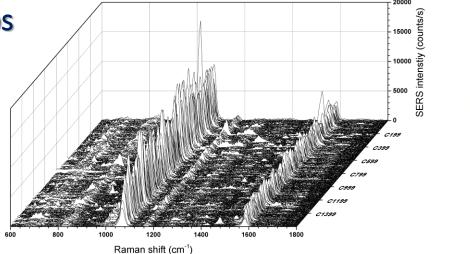




SERS signal of functionalized AuNps

The SERS spectrum of 4-MBA is dominated by the strong bands at about **1590 and 1080 cm-1** which are assigned to aromatic ring vibrations.





Red map

x (µm) The red map of 4-MBA main peak at 1080 cm⁻¹



SERS immunoassay:

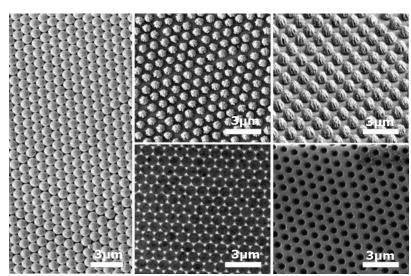


towards a Lab on Chip platform for liquid biopsy

Biosensors and Bioelectronics Volume 233, 1 August 2023, 115322

Thyroglobulin is a glycoprotein produced and used exclusively in the thyroid glands Contraction of the second seco

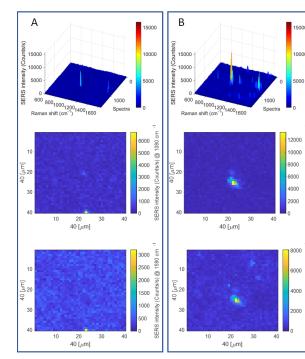
Biofunctionalized SERS substrate

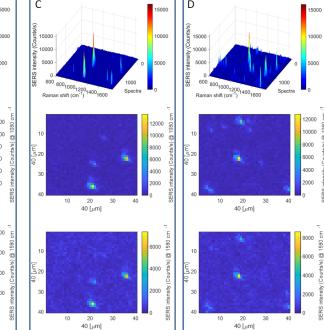


S. Managò *et al.*, Sensors and Actuators B: Chemical, 339, 2021 G. Quero, *et al.*, Sensors, Vol. 18, 3, 2018 M. Pisco *et al.*, Light: Science & Applications, 6, 2017

Azienda Ospedaliera Universitaria

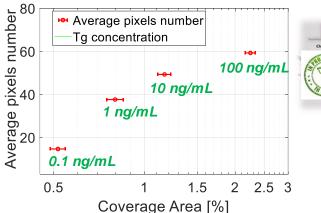


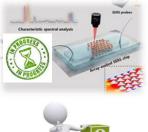






Strict correlation between average nanoparticle coverage (from AFM) and the Tg concentration (from SERS)



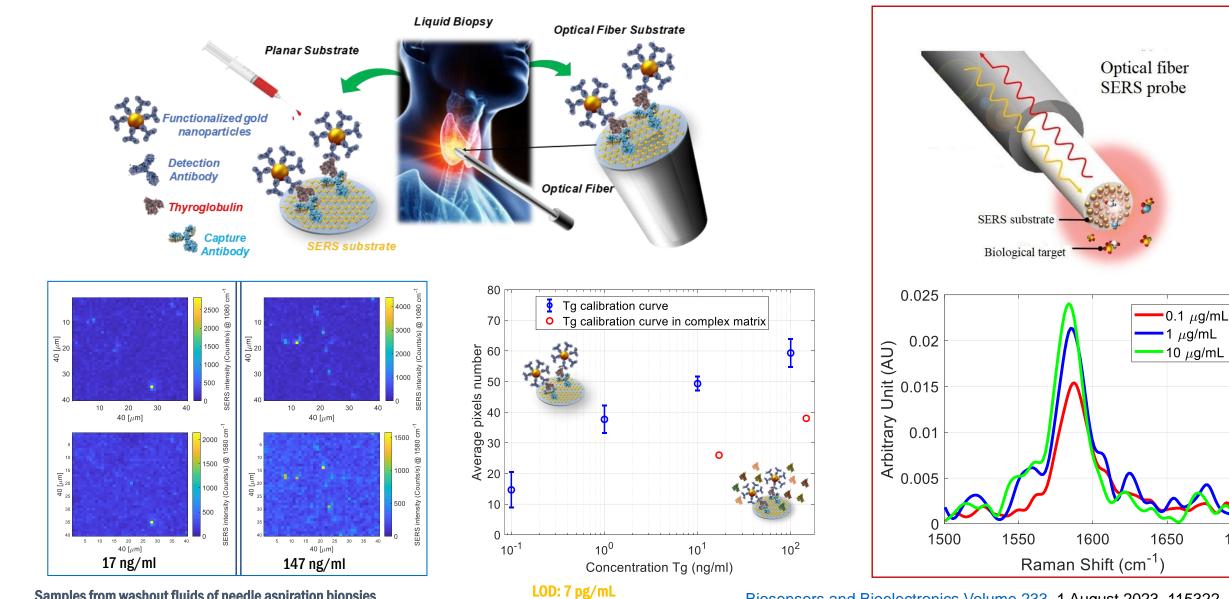


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1700

Human Tg detection and SERS optrodes



Samples from washout fluids of needle aspiration biopsies

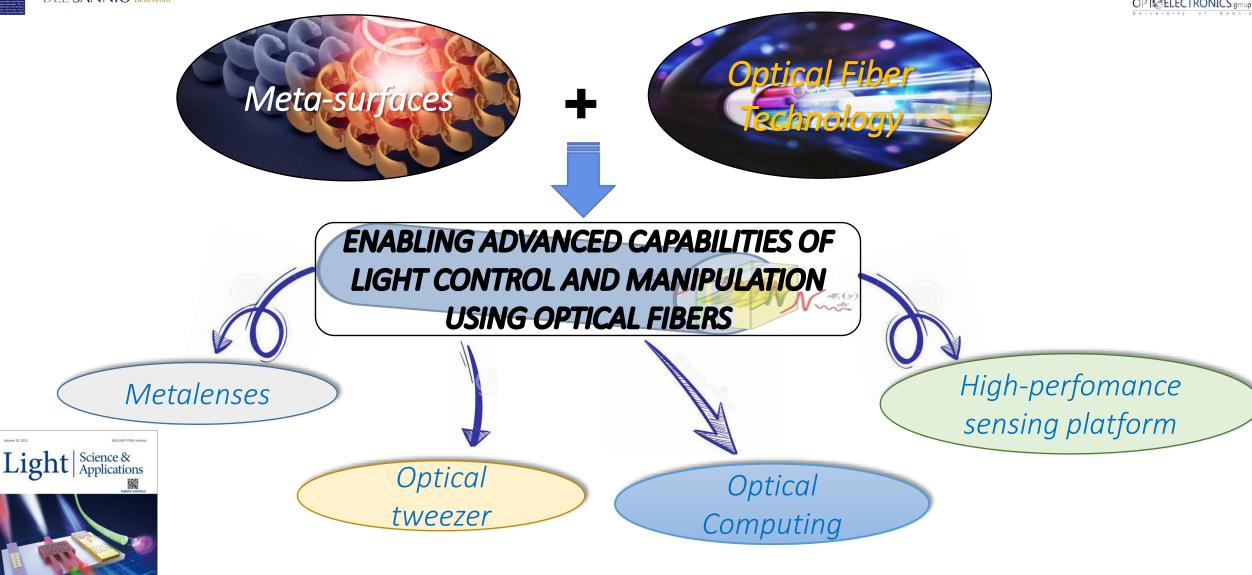
Biosensors and Bioelectronics Volume 233, 1 August 2023, 115322



meta-waveguides for integrated photonics

(



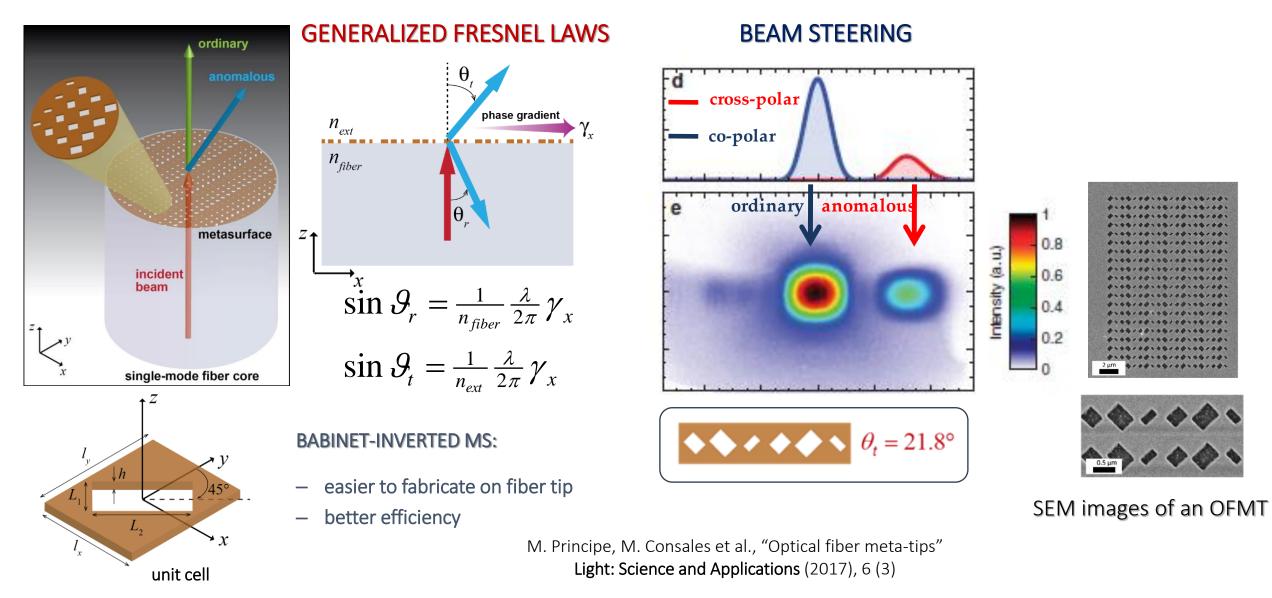


[Meng Y.,Cusano A. et al. "Optical meta-waveguides for integrated photonics and beyond" Light Science & Applications (in press December 2021)





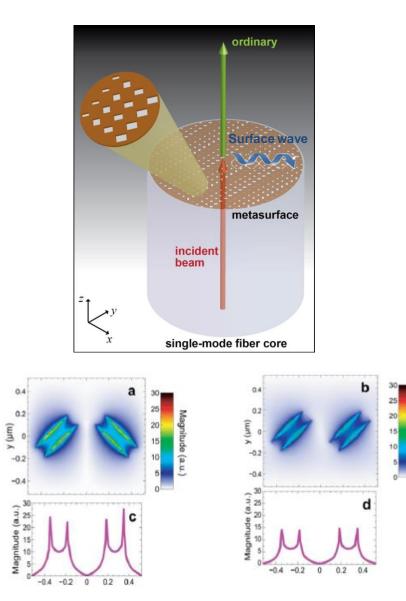
OPTICAL FIBER META TIPS (OFMTs) FOR BEAM STEERING APPLICATIONS

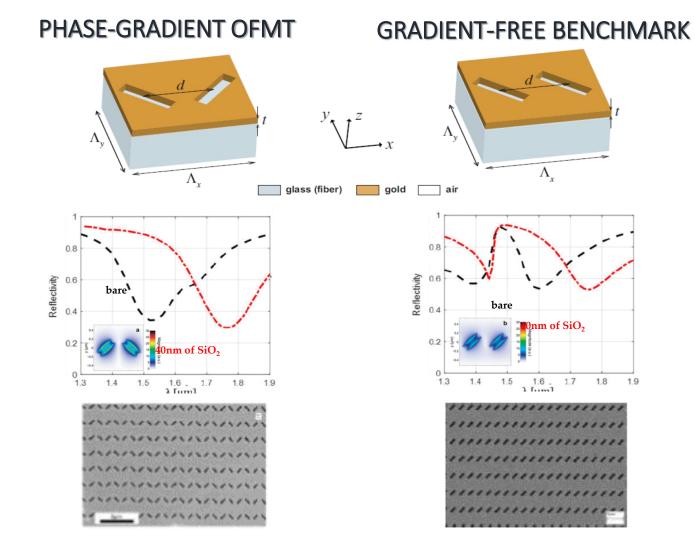




OFMTs AS ADVANCED PLATFORMS FOR SENSING







A. Cusano et al., "Optical fiber meta-tips" Light: Science and Applications (2017)

A. Cusano et al. "Evaluation of Fiber-Optic Phase-gradient Meta-tips for Sensing Applications", Nanomat. and Nanotech. (2019)

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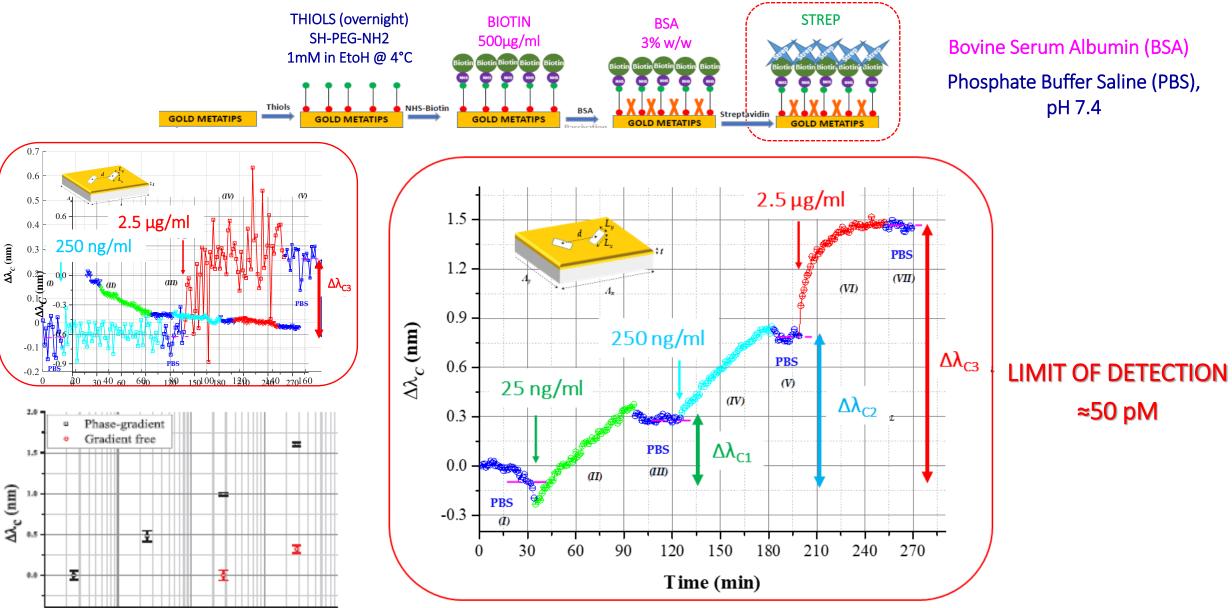
 10°

10

Streptavidin Concentration (µg/ml)

10





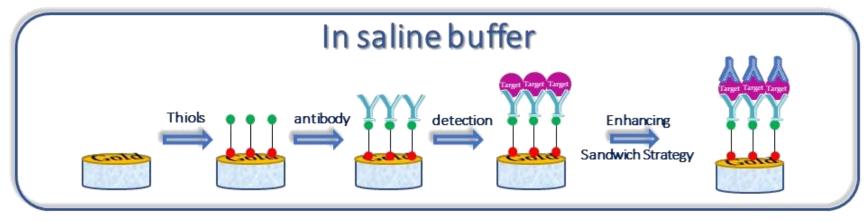
M. Consales, M. Principe et al, "Metasurface-Enhanced Lab-on-Fiber Biosensors", Laser Photonics Rev. 2020, 2000180.

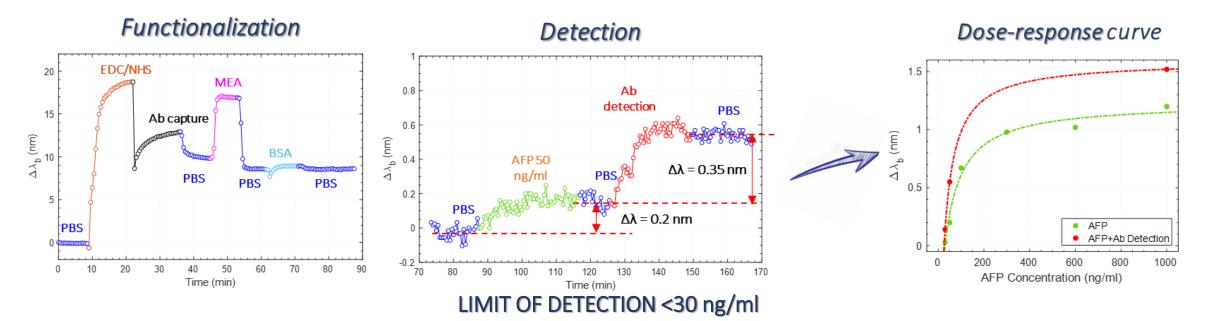


HEPATOCELLULAR CARCINOMA



OPTICAL FIBER METATIPS: AFP DETECTION



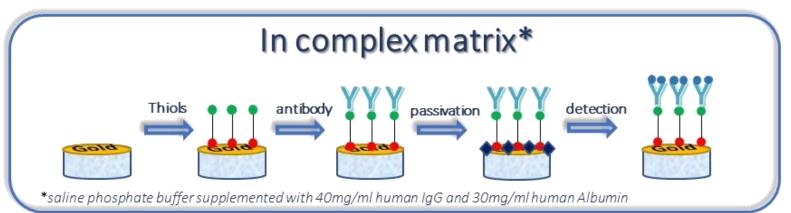


THE SANDWICH STRATEGY ALLOWS TO REDUCE THE LOD OF A FACTOR OF ABOUT 3

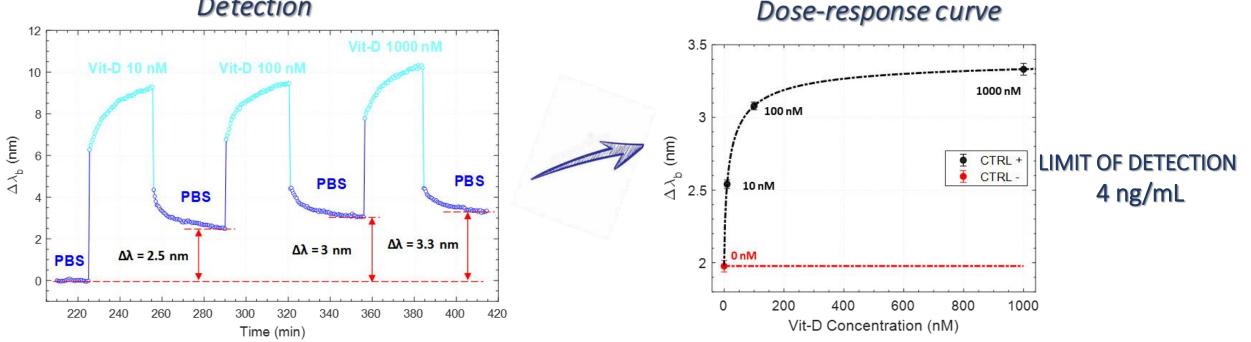


OPTICAL FIBER METATIPS: VITAMIN D DETECTION

OPT@ELECTRONICS group

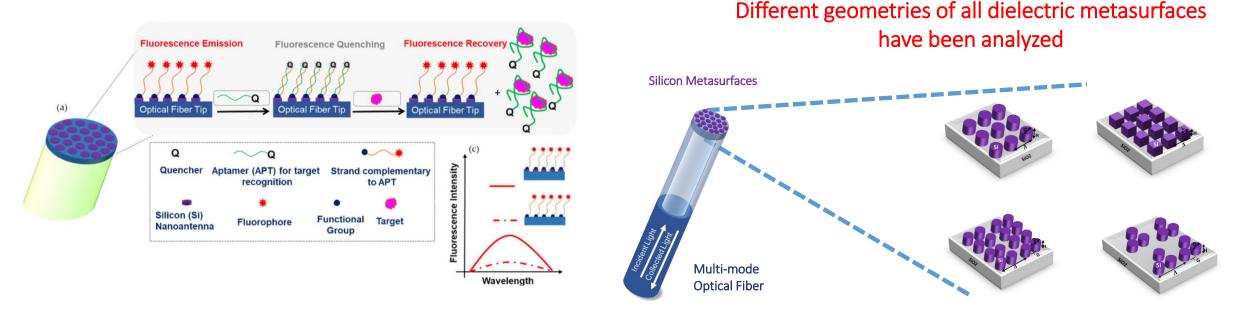


Detection





All-Dielectric Fluorescence Enhancing Metasurfaces: Towards Advanced MS-Assisted Optrodes



A FEM-based numerical environment has been developed in order to optimize the dielectric MS to maximize the fluorescence enhancement factor:

Fluorescence enhancement of Dipole at a distance 7 nm from the Structure				
	Cylindrical (D=160,H=120)	Square (L=150,H=90)	20 nm Gap Dimer (D=120,H=85)	Trimer (D=100,H=105)
Average Fluorescence Enhancement	163	147	1020	880

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SANNIO Benevento

Fluorescence Enhancement Factors of two/three orders of magnitudes can be obtained.

Alhalaby, H. et al., "Enhanced Photoluminescence with Dielectric Nanostructures: A Review". Results in optics 2021, 3, 100073.

Alhalaby, H. et al., "Design and Optimization of All-Dielectric Fluorescence Enhancing Metasurfaces: Towards Advanced Metasurface-Assisted Optrodes". Biosensors 2022, 12, 264.



RISK FACTORS

GENDER

2.2

FAMILY HISTORY OF BREAST

CANCER

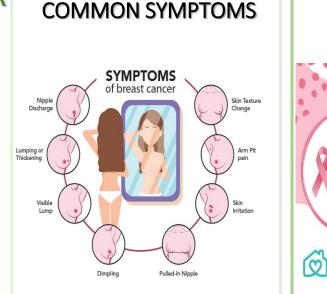
BREAST

DENSITY

AGE



THERAPY



TRASTUZUMAB (140KD)

PERSONAL

CANCER

HISTORY OF BREAST

Trastuzumab is a mAb that binds the domain IV of HER-2. It is used to treat breast cancer patients (~=30%) in which HER-2 is overexpressed and spontaneously homodimerizes or forms heterodimers with other HER

Doxorubicin (MW 543 Da)

Doxorubicin is used widely for managing intermediate-tohigh-risk breast cancer patients and is mainstays of treatment for triple-negative breast cancer.

CARRIERS FOR BREAST CANCER

OPT ELECTRONICS group

THERMORESPONSIVE MICROGELS FOR <u>DOXORUBICIN</u> RELEASE

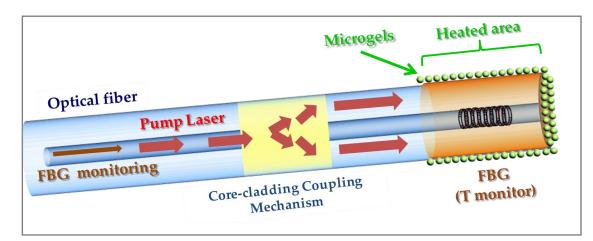
PLGA NANOPARTICLES FOR
<u>TRASTUZUMAB</u> DELIVERY



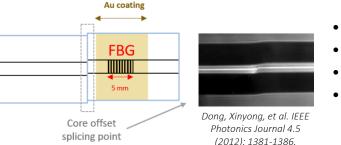




A LAB-ON-FIBER PLATFORM FOR LIGHT-TRIGGERED DRUG DELIVERY



CORE-CLADDING LIGHT COUPLING MECHANISMS

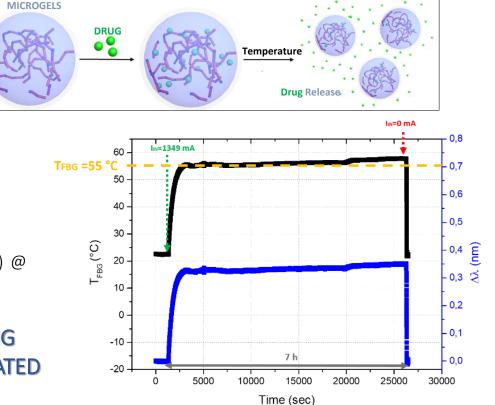


- SMF-28e optical fiber
- Core offset of ~ 6 μ m
- 150 nm Au layer
- 6340 ComboSource from Arroyo Instrument) @ 1485 nm with an output power of 500 mW

LIGHT TRAVELLING IN THE FIBER CORE IS TRANSFERRED TO THE CLADDING REGION AND HEATS THE METALLIC COATING WHERE THE MGS ARE INTEGRATED

Berruti et al. Journal of Lightwave Technology, 2021.

- MGs integration along the lateral surface of a thermal heating device, based on a gold-coated optical fiber
 - Light-triggered drug release by inducing surface heating



Optical actuation

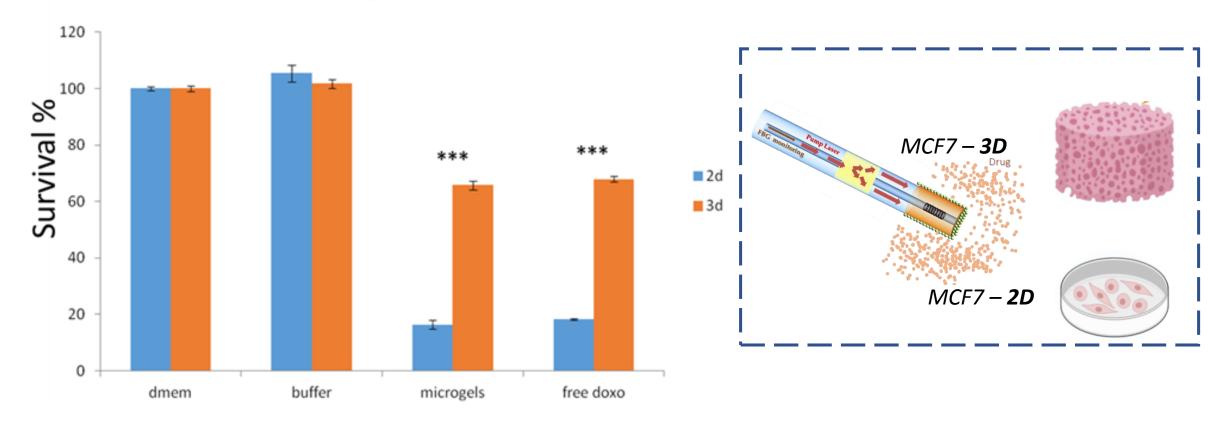


MCF7

Cytotoxicity assays on MCF7 2D and 3D cell culture





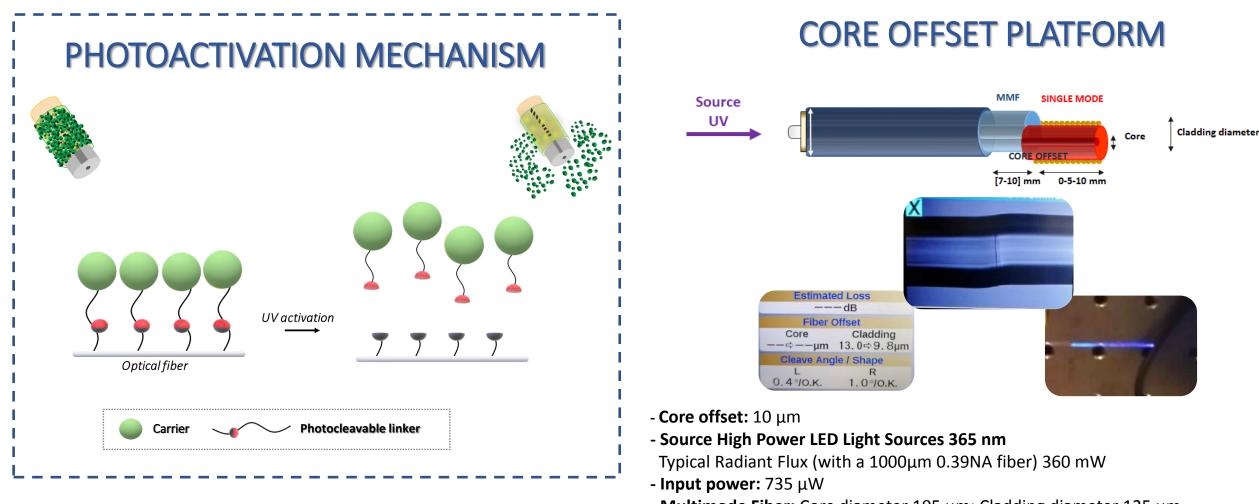


Doxorubicin released from optical fiber show cytotoxicity comparable to free doxorubicin in 2D and 3D tests



OPTICAL-FIBER PLATFORM FOR UV-TRIGGERED TRASTUZUMAB-BASED CARRIER DELIVERY



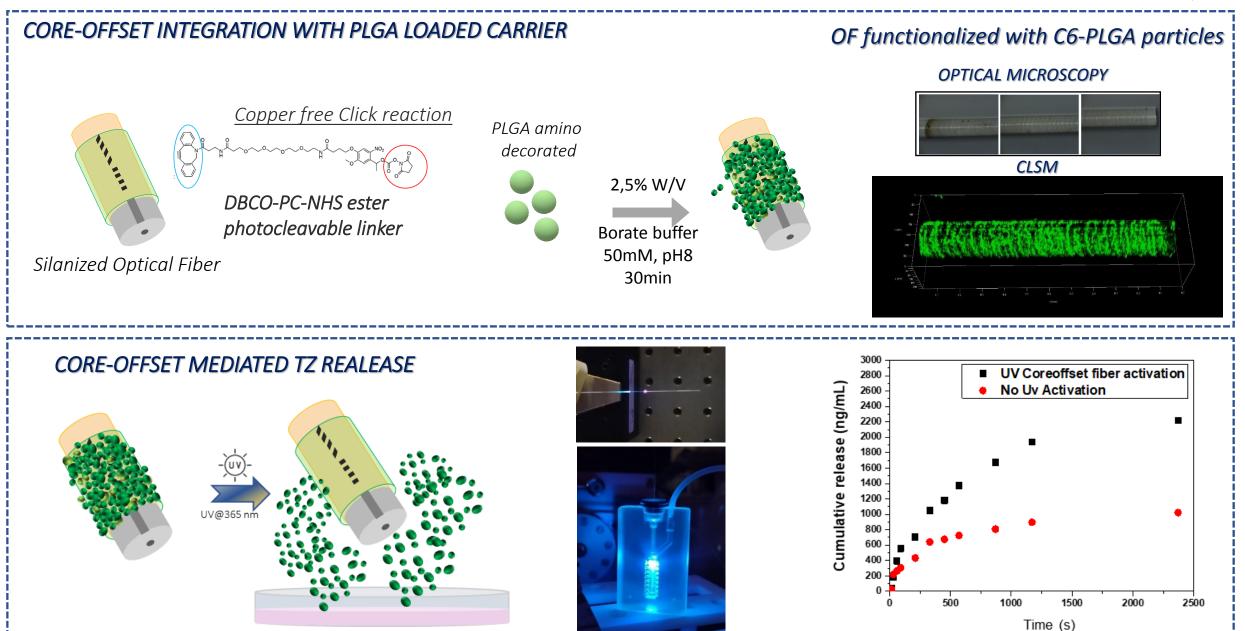


- Multimode Fiber: Core diameter 105 μ m; Cladding diameter 125 μ m
- Single mode fiber SMF-28: Core diameter 8.2 μ m; Cladding diameter 125 μ m



CORE-OFFSET MEDIATED DRUG DELIVERY



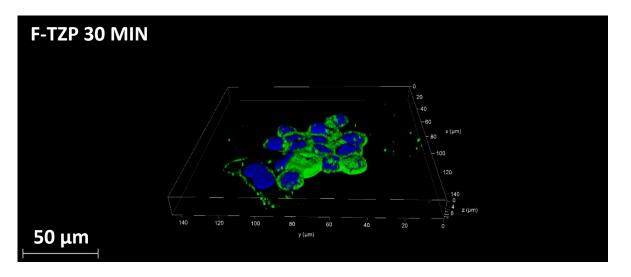


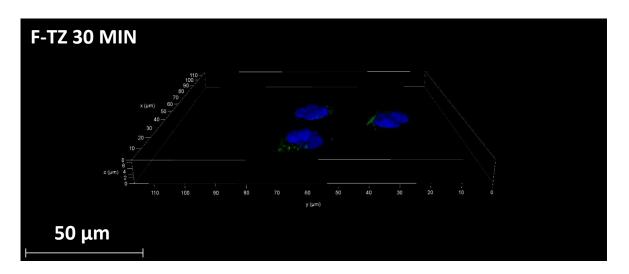


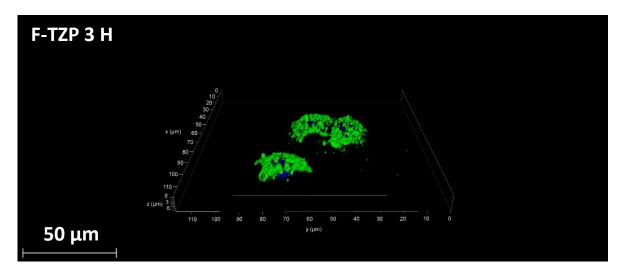
POLYMERIC PARTICLES FOR TRASTUZUMAB RELEASE

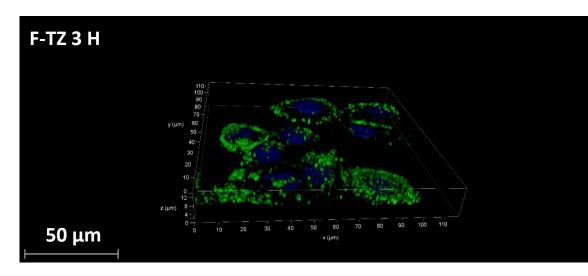


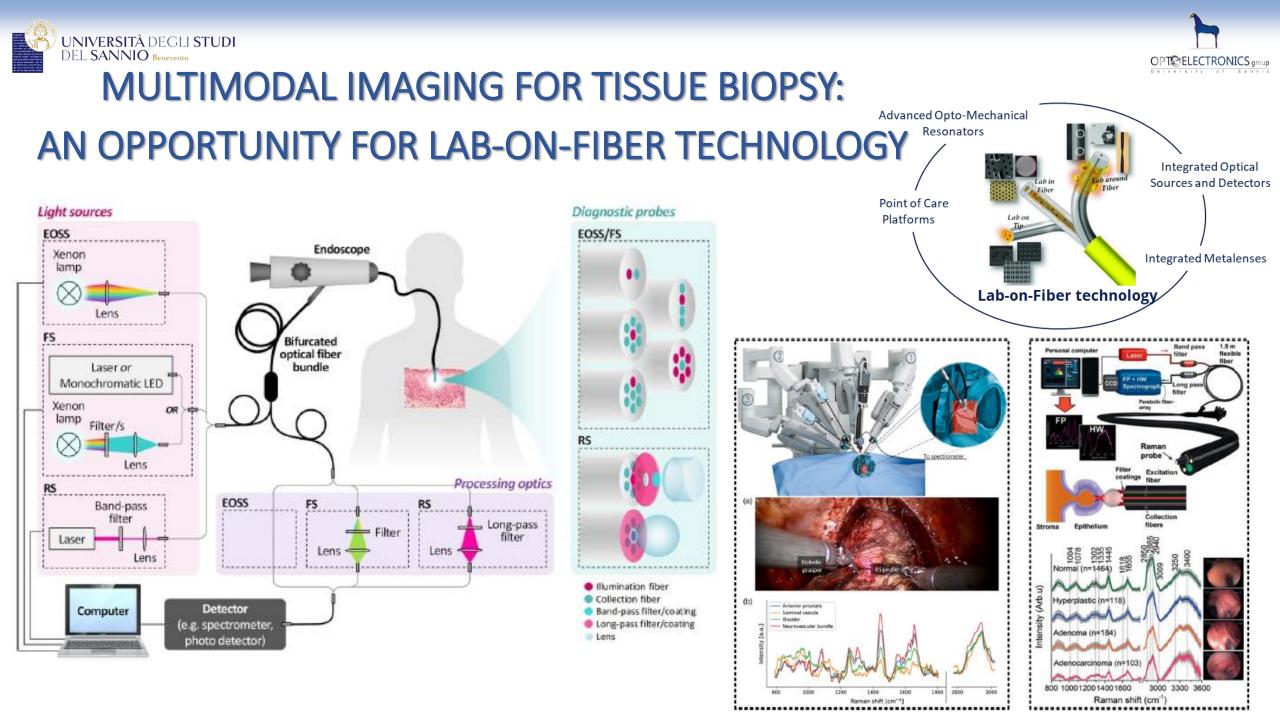
TZ-FITC PLGA particles internalization by CLSM in SKBR3 cell line: z-stack













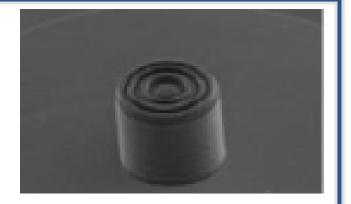
LAB-ON-FIBER: A STEP-AHEAD INTEGRATED FLAT OPTICS



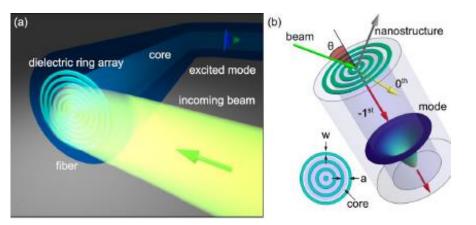
Single-mode liber Functionalized fiber Trapped object Light in-coupling

M. Plidschun Light Science & Applications 2021

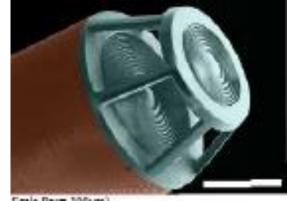
METALENSES ON OPTICAL FIBER



W. Hadibrata et al. Nano Letters 2021



O. Yermakov ACS Photonics 2020



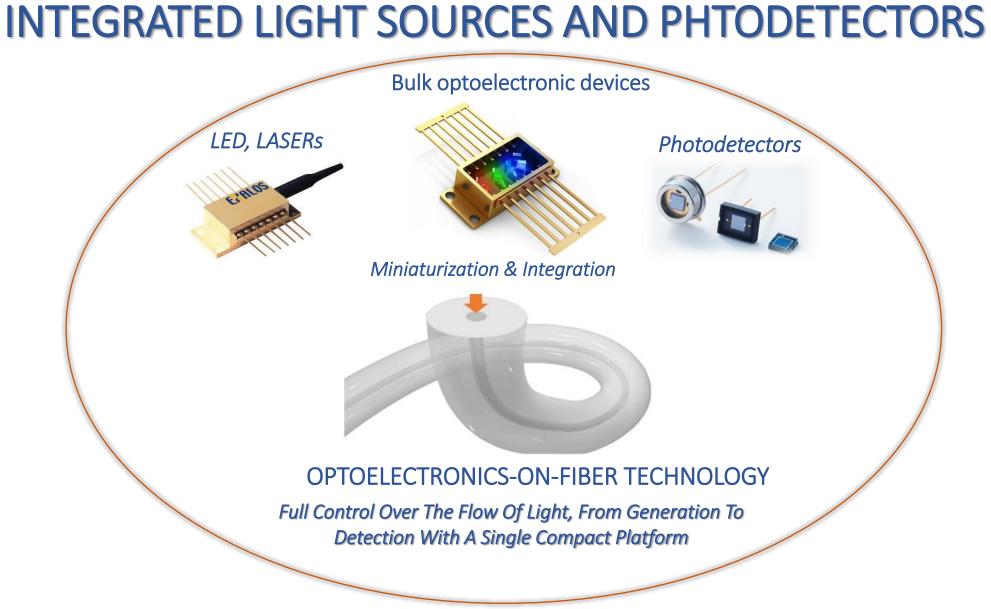
Scale Bar# 100um)

A. Asadollahbaik et al. ACS Photonics 2020

JNIVERSITÀ DEGLI STUDI LAB-ON-FIBER: A STEP-AHEAD

OPT ELECTRONICS group

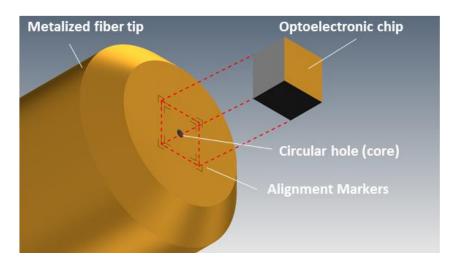
SANNIO Benevento





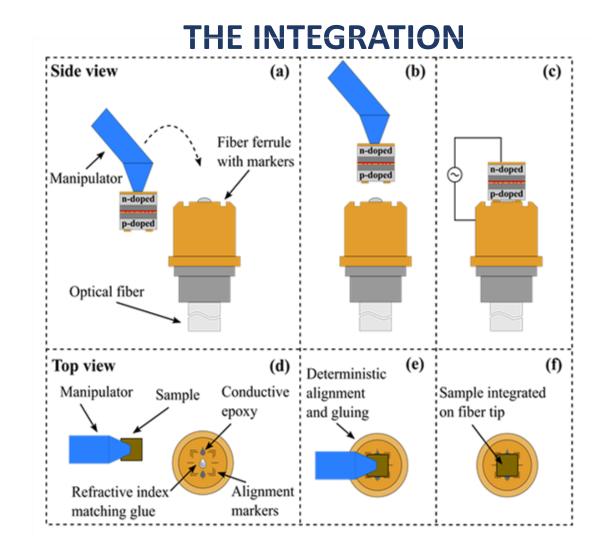
THE DEVELOPED PROCESS





- 1) Optoelectronic Chip is fabricated on a planar substrate and cleaved
- 2) Fiber is metalized and circular holes and alignment markers are written
- 3) The chip is transferred and bonded onto the fiber tip (after depositing conductive and refractive index matching glues)

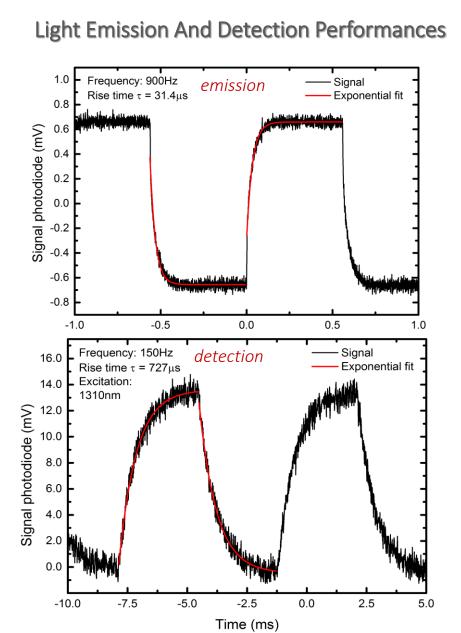
Procedure for the manufacturing of a monholitic connection between alight source and an optical fiber.102020000010336 (2020)equally shared by University of Sannio and Stuggart UniversityRicclP<0</td>C

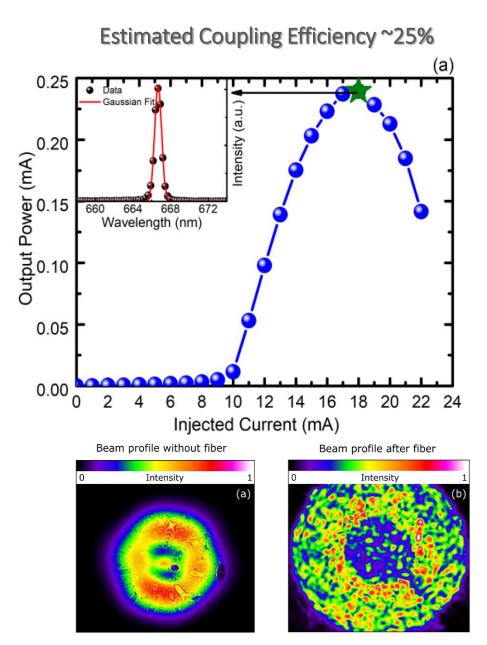


Ricciardi, A., Zimmer, M., Witz, N., Micco, A., Piccirillo, F., Giaquinto, M., Kaschel, M., Burghartz, J., Jetter, M., Michler, P., Cusano, A., Portalupi, S. L., Integrated Optoelectronic Devices Using Lab-On-Fiber Technology. Adv. Mater. Technol. 2022, 2101681.



VCSEL



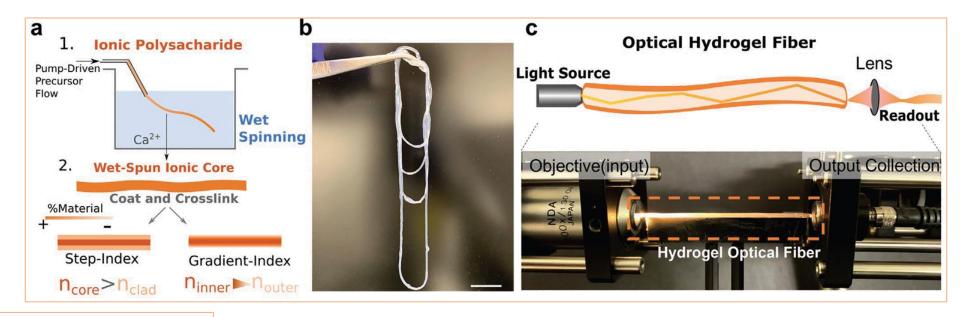


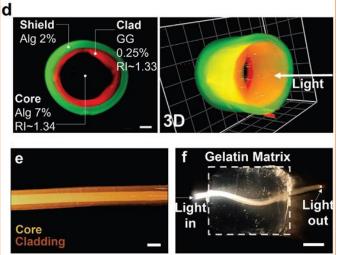


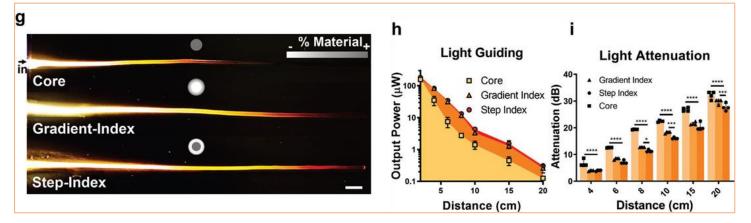




TOWARDS MULTILAYERED LIVING OPTICAL FIBERS





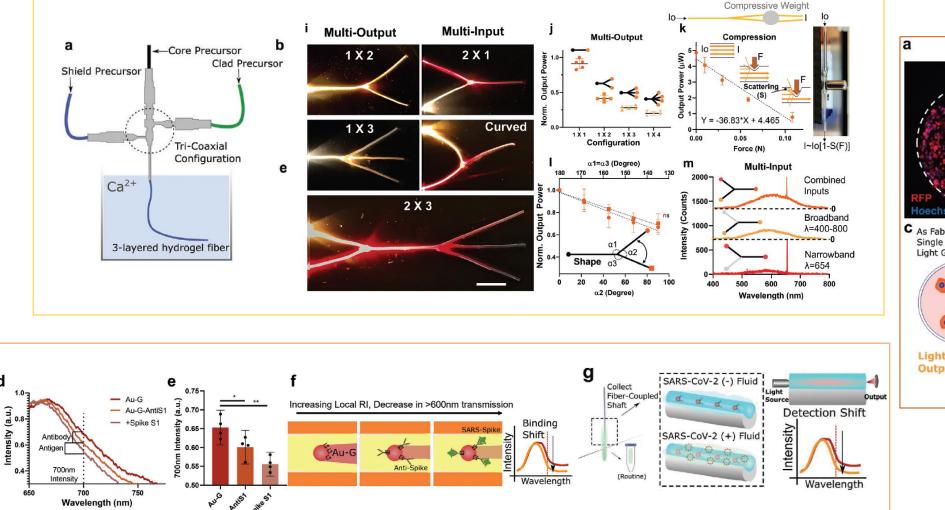


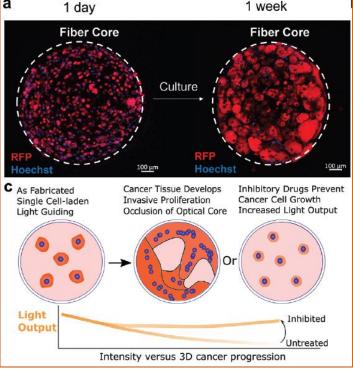
Adv. Mater. 2021, 2105361

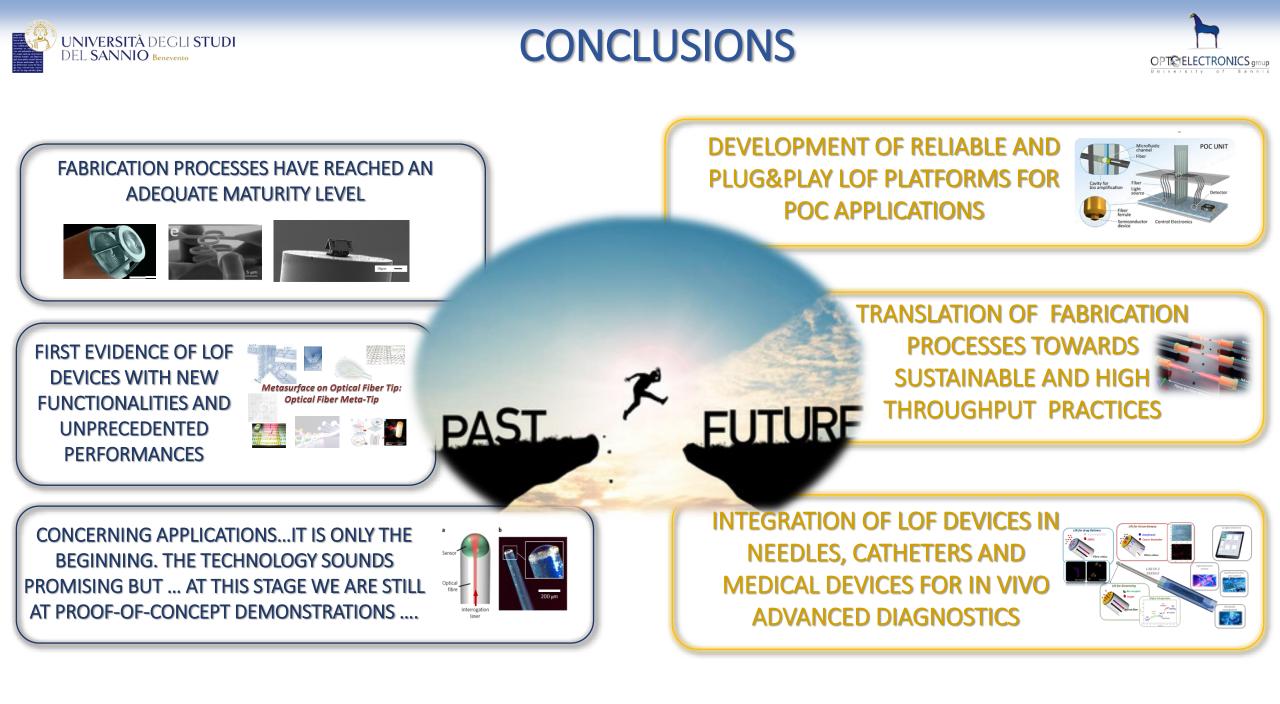


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DEL SANNIO Benevento ADVANCES IN BIOMATERIAL-BASED PHOTONICS OF ELECTRONICS GOUP AND BIOSENSING PLATFORMS











THANK YOU FOR YOUR KIND ATTENTION!

