EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

FZU Institute of Physics of the Czech Academy of Sciences

Optical spectroscopy and biosensors for investigation of biomolecules and their interactions

Jakub Dostalek

AIT - Austrian Institute of Technology GmbH
Biosensor Technologies Unit
Konrad-Lorenz-Strasse 24 | 3430 Tulln | Austria
T +43(0) 664 2351773

FZU – Institute of Physics of the Czech Academy of Sciences,
Na Slovance 1 | Prague 182 00 | Czech Republic
T+420 776767927

jakub.dostalek@ait.ac.at | http://www.ait.ac.at | http://www.jakubdostalek.cz

Surface Plasmon Resonance Biosensors II

Content

- Sandwich assay, nanoparticle labels, enzymatic reactions coupled with SPR readout.
- Colorimetric SPR biosensors
- Multichannel SPR devices for reference compensated measurements
- Portable SPR biosensors with cell phone readout
- Miniature fiber optic sensors
- SPR imaging
- Examples of research and commercial systems. How to select an approach to solve your problem?

Amplification of Assays with SPR Readout

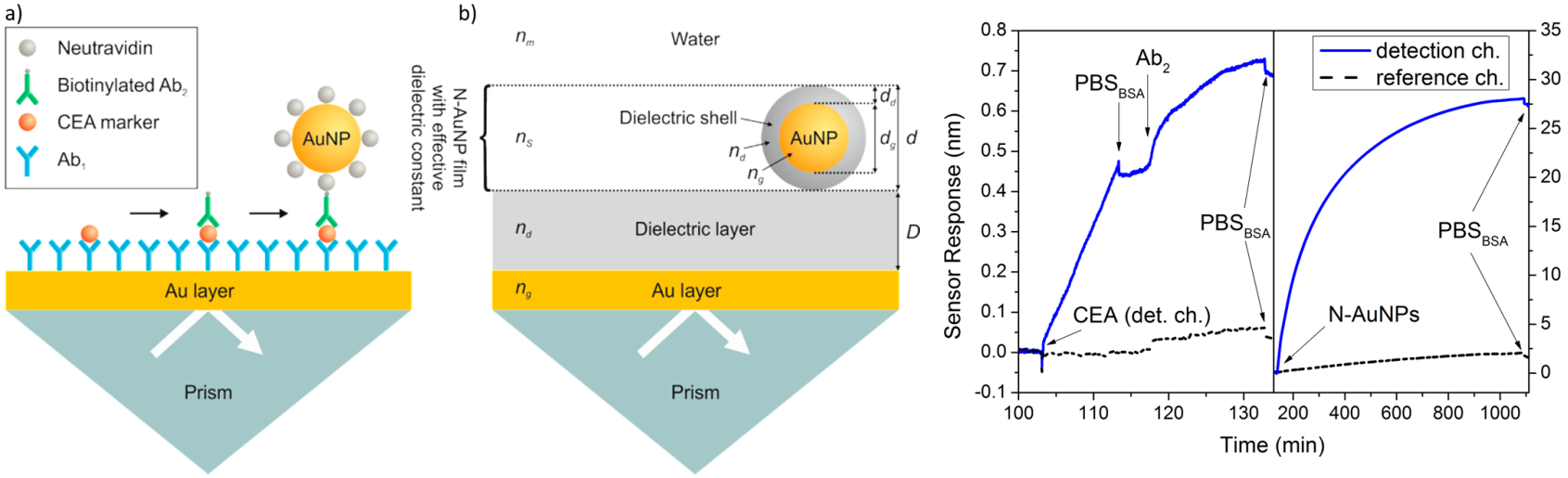
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

MINISTRY OF EDUCATION, YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Sandwich Assay Enhanced with Metallic Nanoparticles



dx.doi.org/10.1021/ac502637u

- Sandwich assay with the use of Au NP labels allows to enhance the surface mass density change associated to molecular binding event.
- Respectively, limit of detection can be enhanced. The size of metallic NP matters as smaller ones generates weaker enhancement in equilibrium, but diffuse slower.

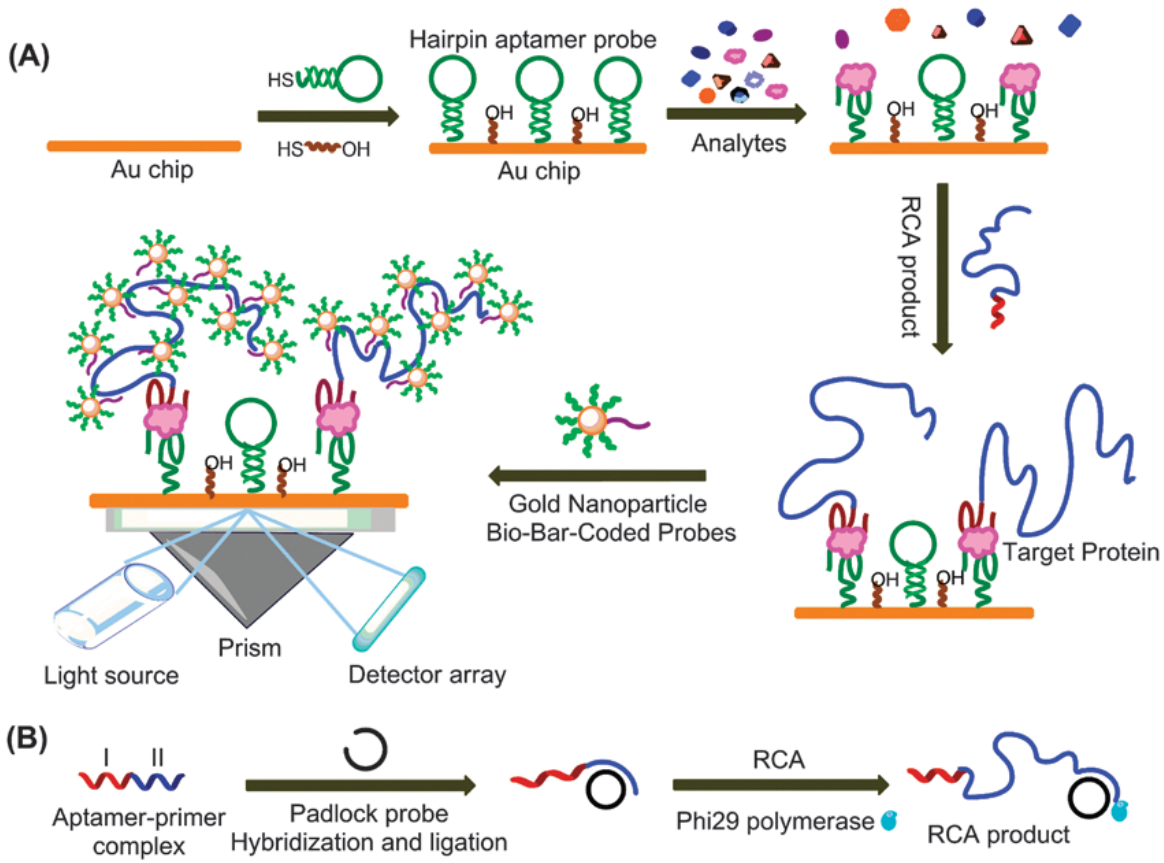
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

MINISTRY OF EDUCATION, YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

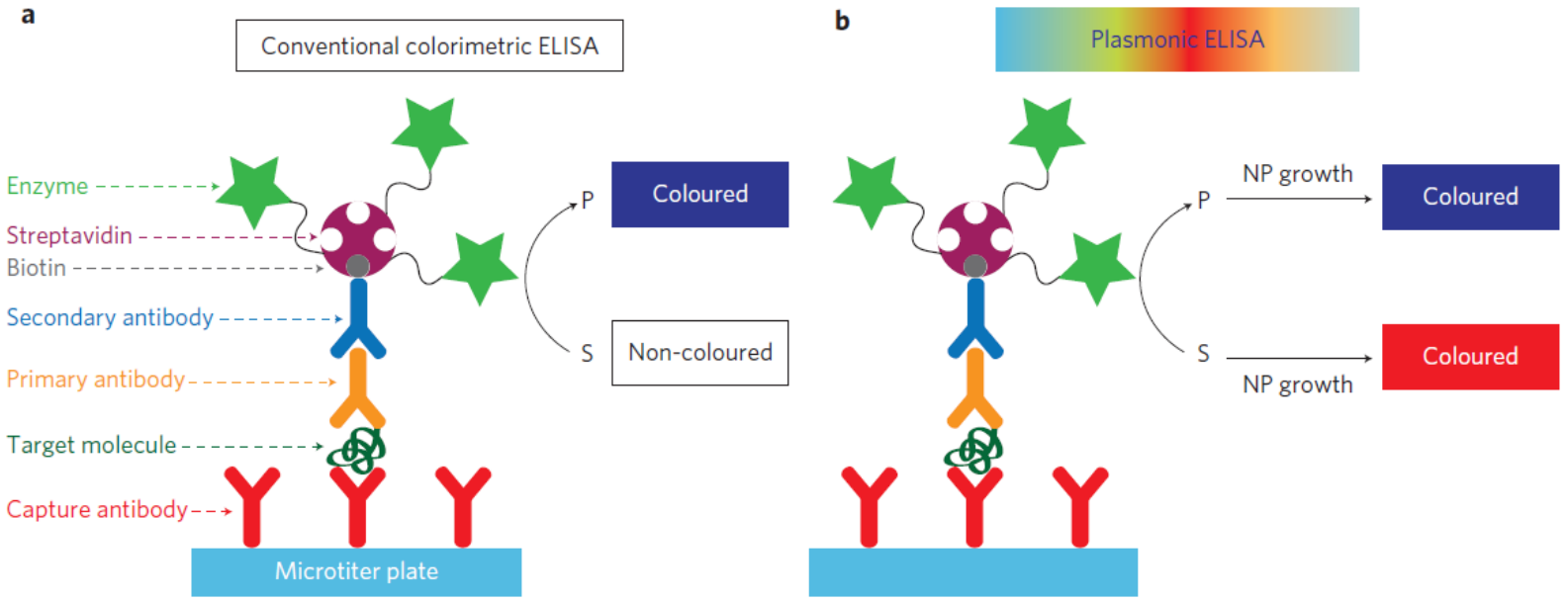
Sandwich Assay Enhanced with RCA



- Rolling circle amplification allows for generating long ssDNA strand
- Can host high number of Au NP serving as SPR sensor enhancers.

DOI: 10.1039/c3cc48223e

Sandwich Assay Enhanced with Enzymatic Synthesis of Metallic NPs



DOI: 10.1038/NNANO.2012.186

- Employing of enzymes that generates color change by synthesis of Au NPs was proposed for sensitive immunoassays readout.

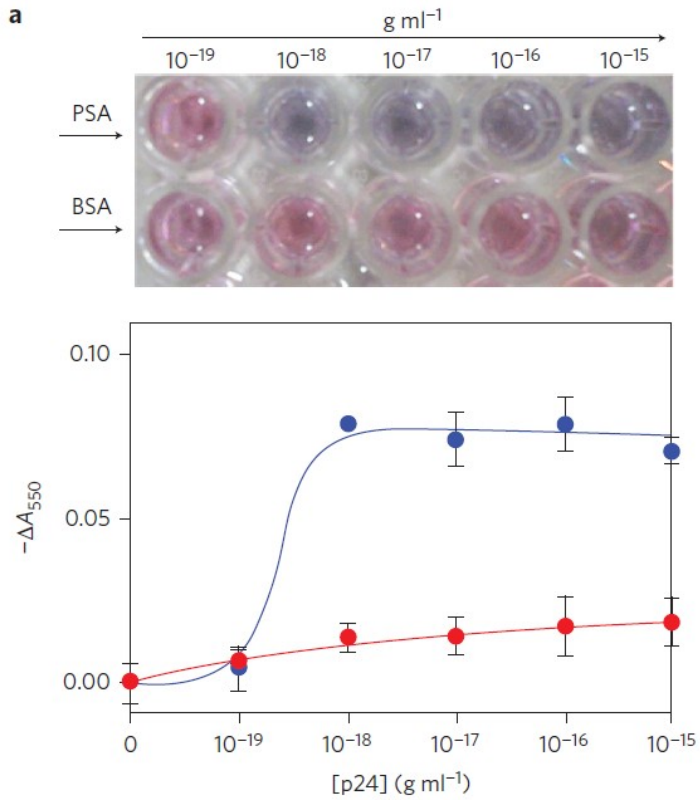
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

MINISTRY OF EDUCATION, YOUTH AND SPORTS

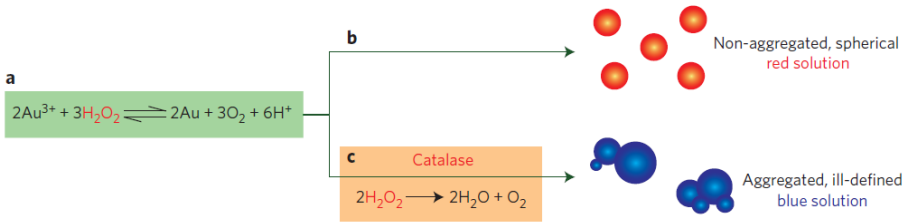
FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Sandwich Assay: Enhanced with Enzymatic Synthesis of Metallic NPs

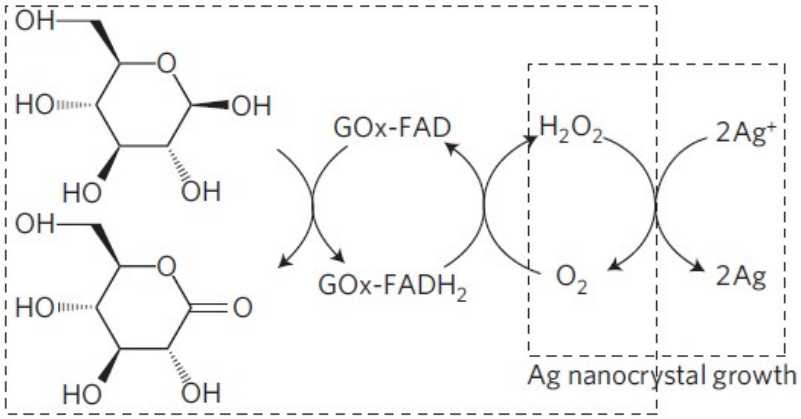


- Detection of HIV-1 capsid antigen p24 in whole serum at the ultralow concentration of 10^{-18} g/ml was reported.
- Color change due to Au NP morphology change.

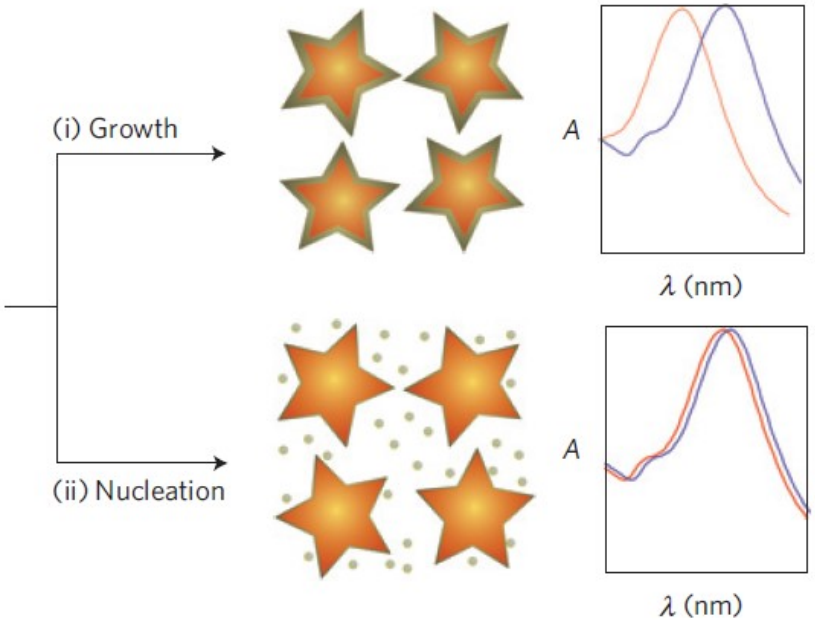


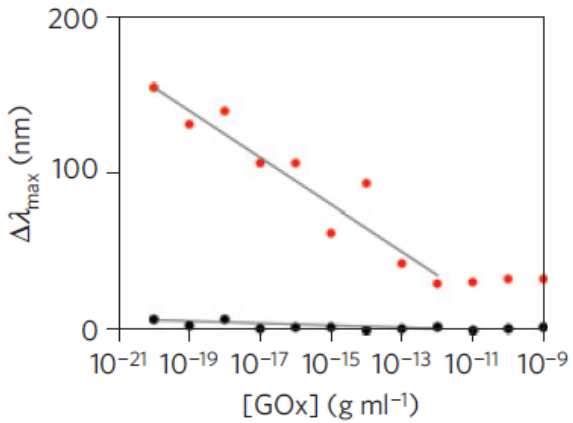
DOI: 10.1038/NNANO.2012.186

with Enzymatically Mediated-Synthesis of Metallic Nanoparticles



Biocatalytic cycle of glucose oxidase





- Detection of PSA in whole serum at the ultralow concentration of 10^{-20} M concentration was was reported based on inverse sensitivity apporach.

10.1038/NMAT3337

EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

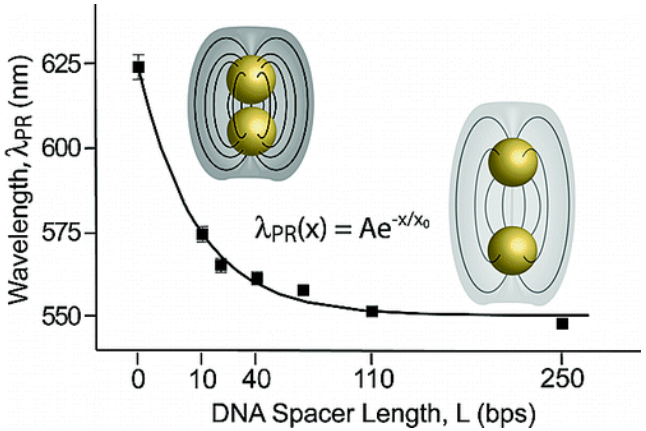
MINISTRY OF EDUCATION, YOUTH AND SPORTS

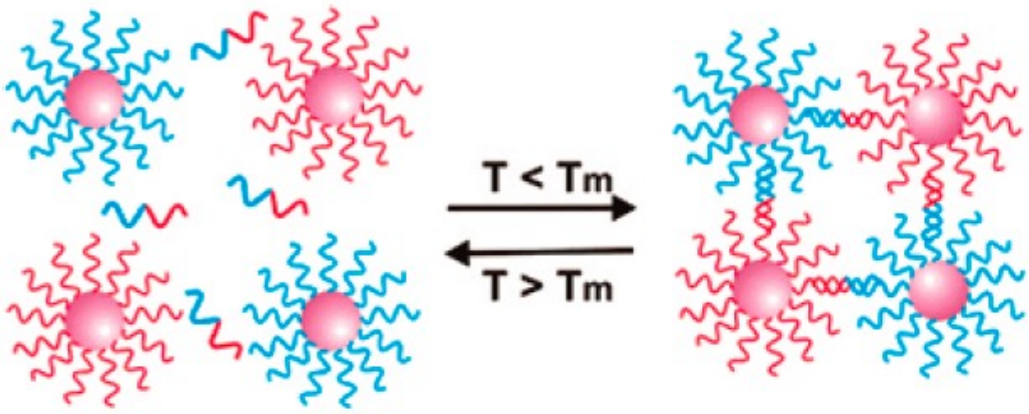
FZU Institute of Physics of the Czech Academy of Sciences

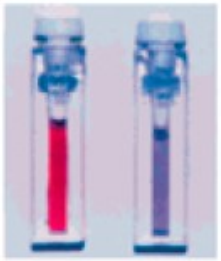
AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

LSPR Homogenous Assays

Concept of plasmonic ruler:





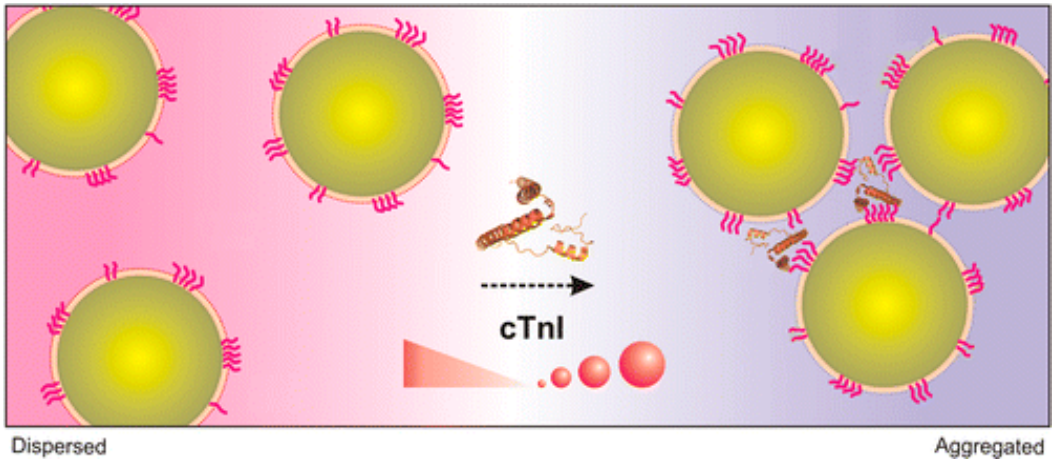


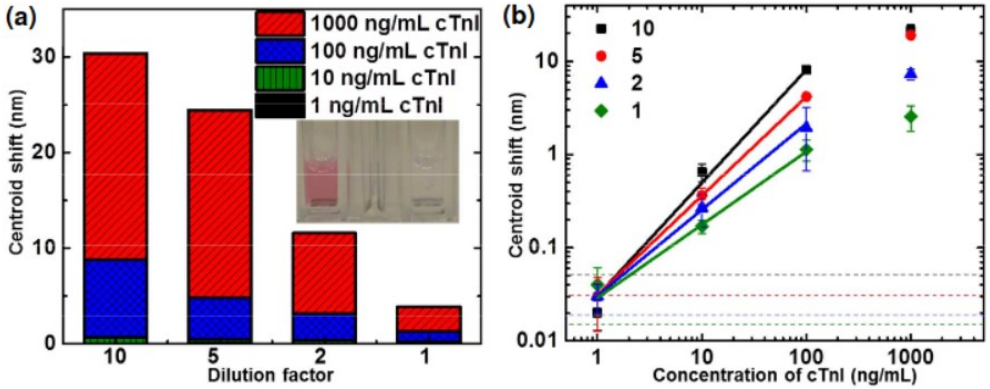
without DNA target | with DNA target

- In the presence of complementary target DNA, oligonucleotide-functionalized Au NPs will aggregate (left), resulting in a change in the color of the solution from red to blue (right).

Rosi, N. L.; Mirkin, C. A. *Chem. ReV.* ***2005, 105, 1547***

LSPR Homogenous Assays





- Aggregation assays were developed for protein analytes such as cardiac marker troponin.
- Using of low molecular weight ligands such as peptides allows achieving stronger effect due to shorted distances between NPs.

Xiaohu Liu, Yi Wang, Peng Chen, Austin McCadden, Alagappan Palaniappan, Jinling Zhang, Bo Liedberg

10.1021/acssensors.6b00493

EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

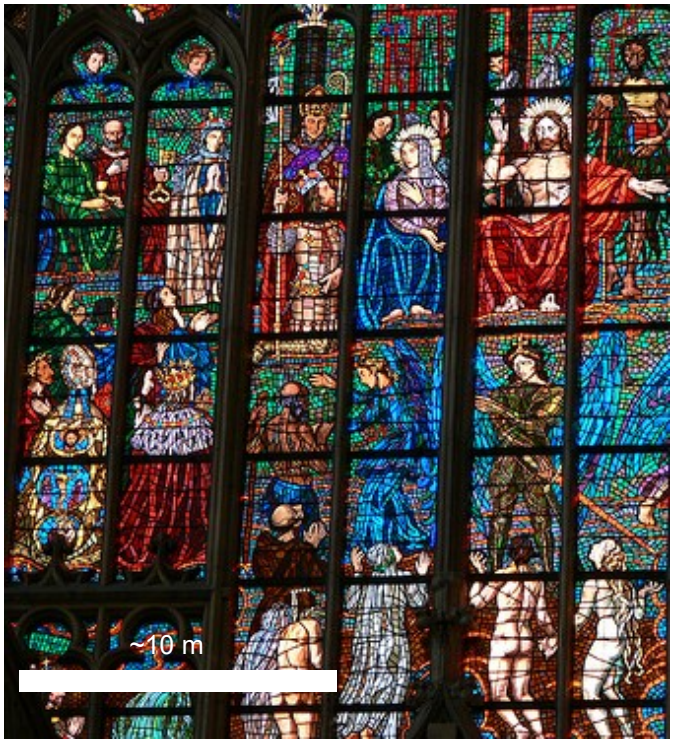
MINISTRY OF EDUCATION, YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

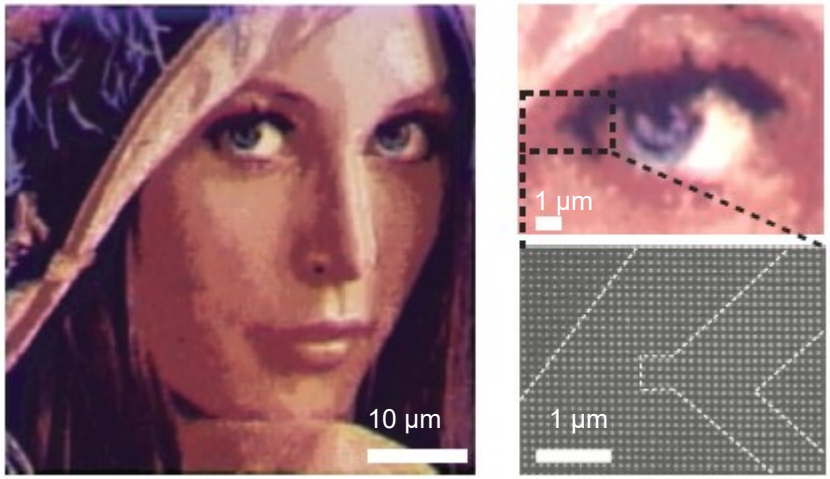
Examples of LSPs

Blend of glass with metallic nanoparticles - used for centuries in stained glass.



St. Vitus cathedral, Prague

Structures from previous slide employed for printing with diffraction limit accuracy (10^5 dpi).



Kumar et al., Nature Nanotechnology (2012) DOI: 10.1038/NNANO.2012.128

Multichannel SPR Biosensors

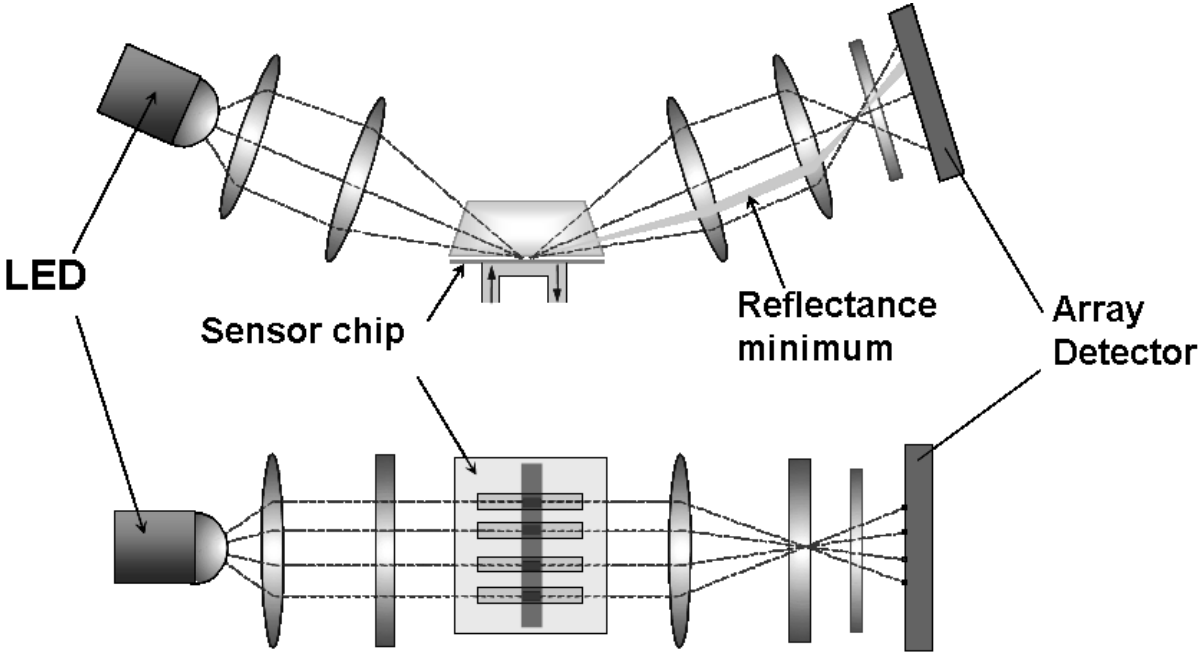
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

MINISTRY OF EDUCATION,
YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Multichannel SPR Biosensors



- Biacore design of four-channel SPR biosensor with angular interrogation (provided by S. Löfås, Biacore AB.)

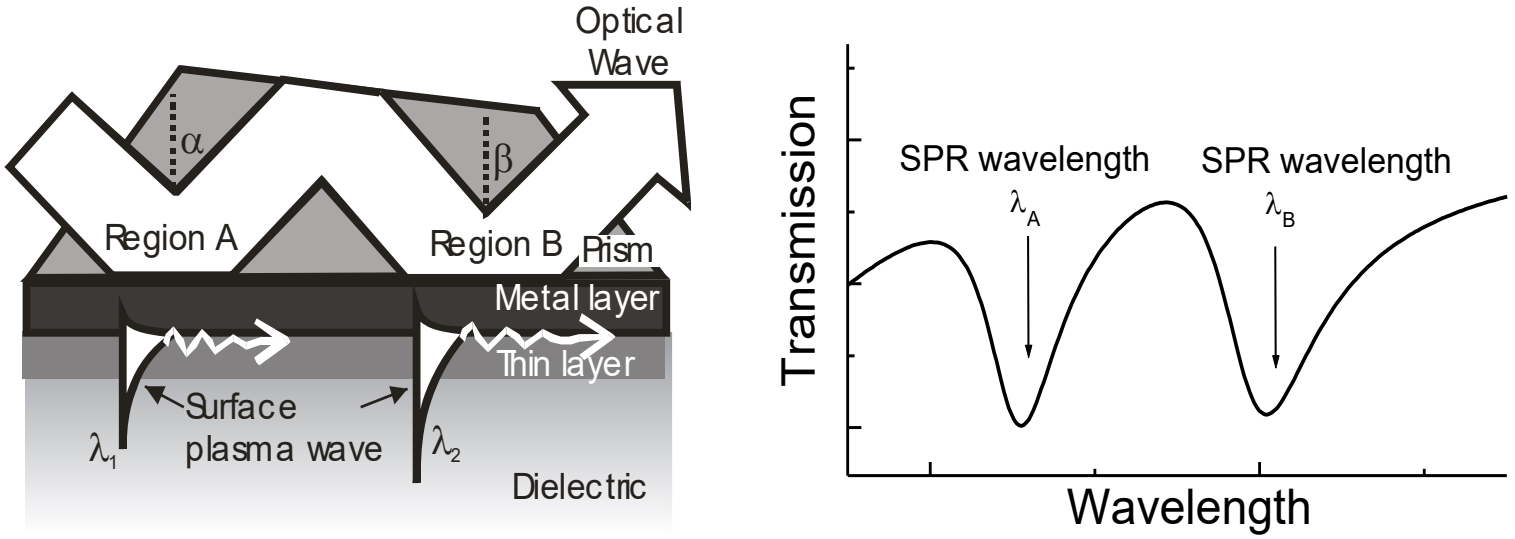
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

MINISTRY OF EDUCATION, YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

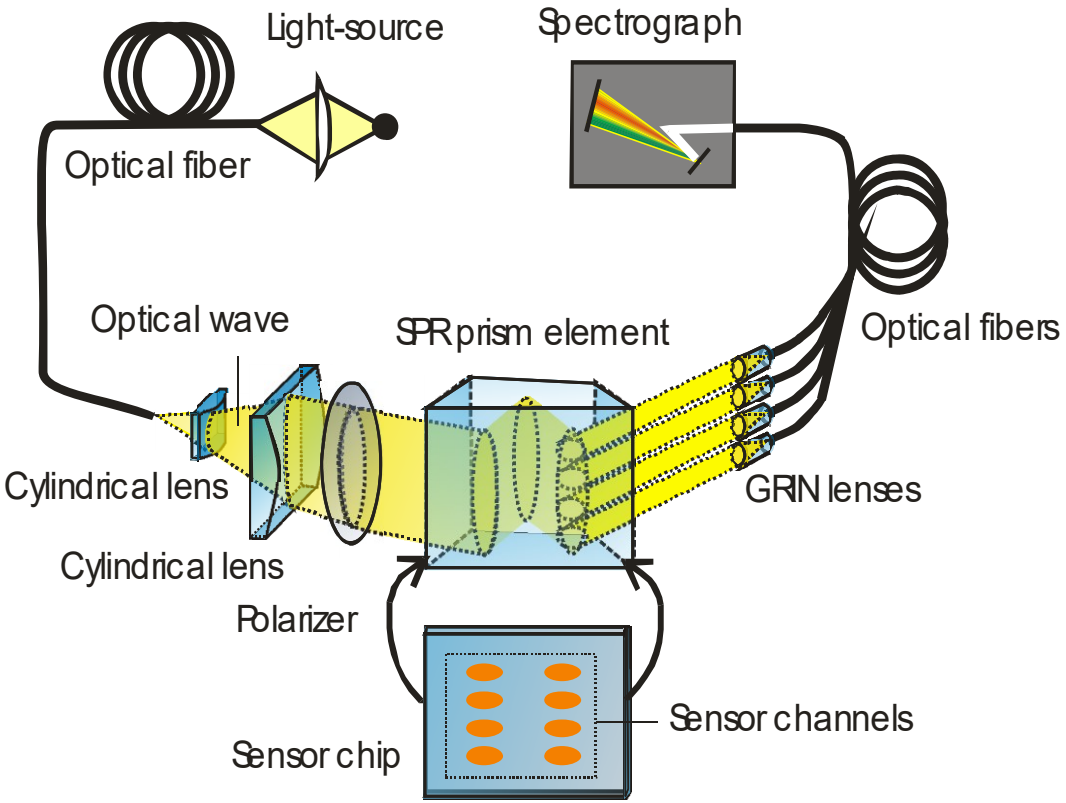
Multichannel SPR Biosensors



- Example of wavelength division multiplexing of sensing channels combined with the ATR method in Kretschmann configuration.

J. Dostalek, H. Vaisocherova, J. Homola, Multichannel Surface Plasmon Resonance Biosensor with Wavelength Division Multiplexing, Sensors and Actuators B, 108 (2005) 758-764.

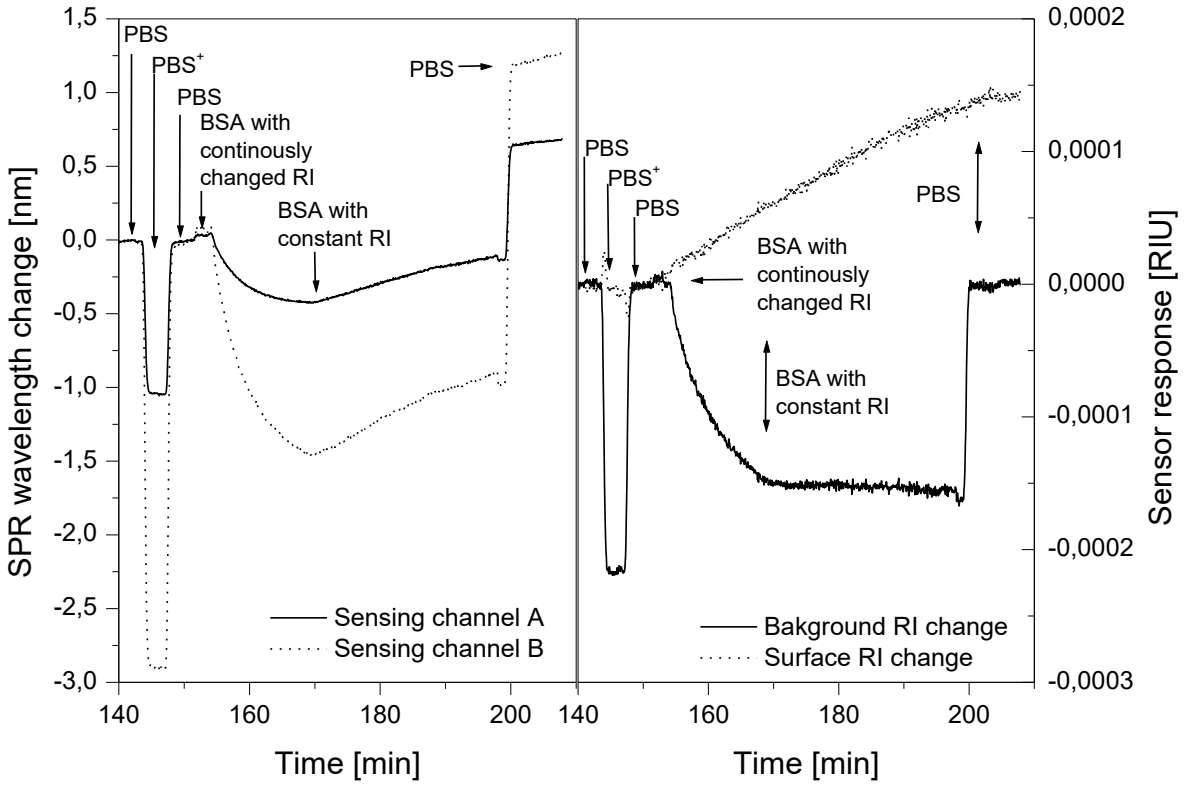
Multichannel SPR Biosensors



- Example of wavelength division multiplexing of sensing channels combined with the using of multiple optical beams.

J. Dostalek, H. Vaisocherova, J. Homola, Multichannel Surface Plasmon Resonance Biosensor with Wavelength Division Multiplexing, Sensors and Actuators B, 108 (2005) 758-764.

Referencing SPR sensor drift



- Example of reference compensated response for resolving the molecular binding at the surface from bulk refractive index changes.

J. Dostalek, H. Vaisocherova, J. Homola, Multichannel Surface Plasmon Resonance Biosensor with Wavelength Division Multiplexing, Sensors and Actuators B, 108 (2005) 758-764.

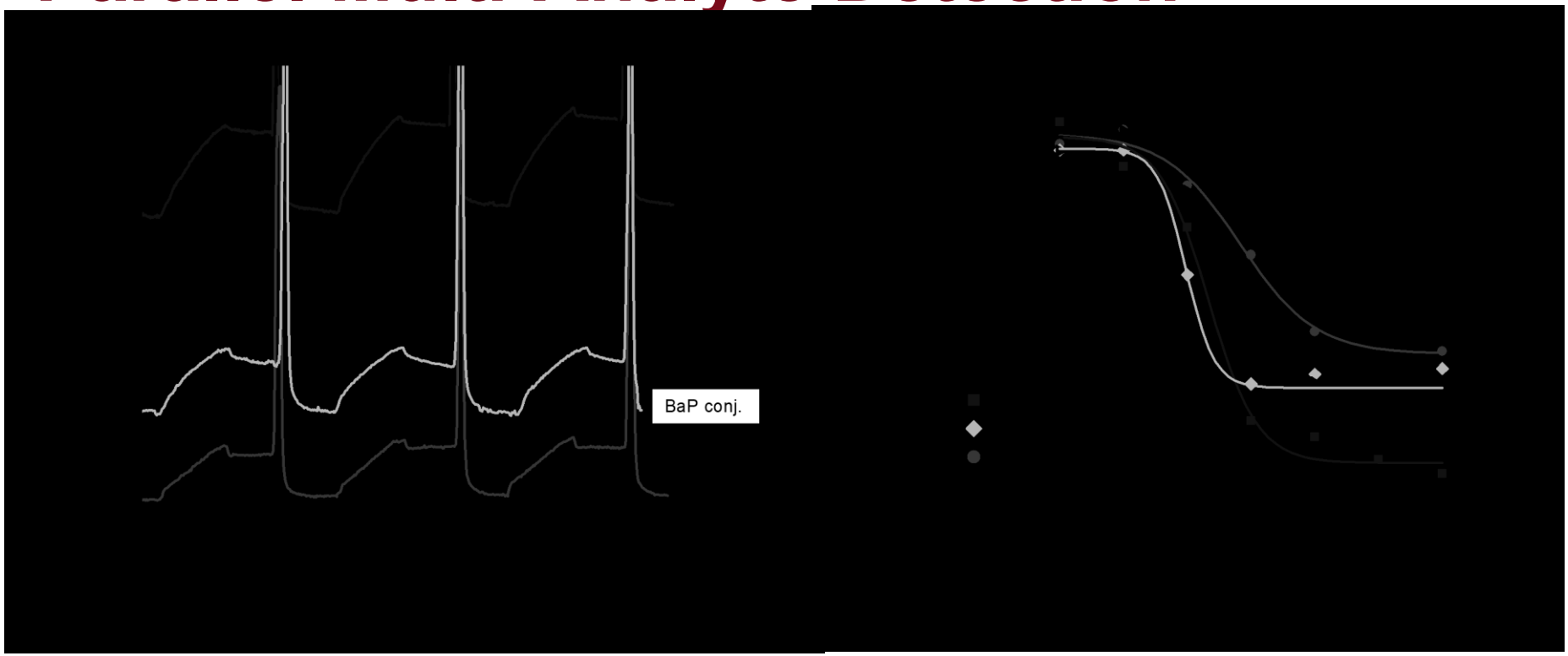
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

MINISTRY OF EDUCATION,
YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

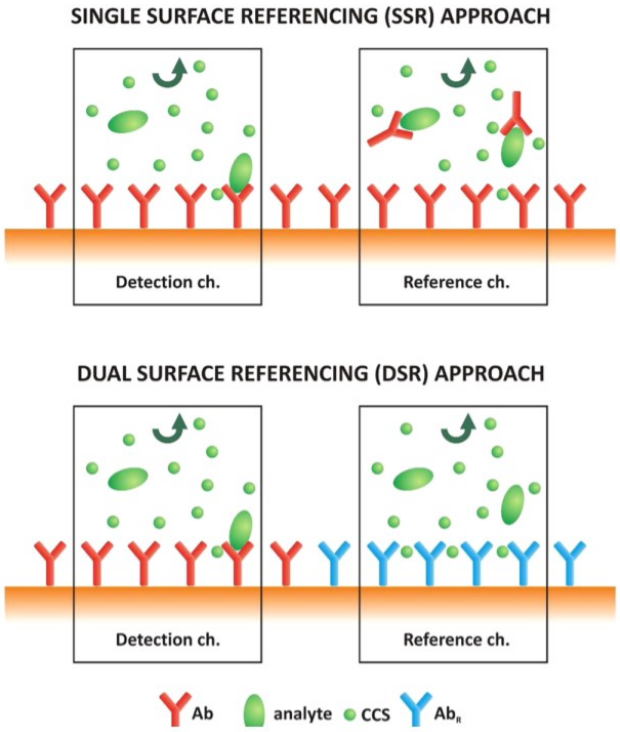
Parallel Multi-Analyte Detection



- Parallel detection of multiple analytes in the analyzed sample enabled by the multichannel SPR biosensor instrument.

J. Dostalek, J. Pribyl, P. Skladal, J. Homola, Multichannel SPR biosensor for detection of endocrine disrupting compounds, Analytical and Bioanalytical Chemistry, (2007) 389:1841-1847

Design of Reference Channel



- Compensating for unspecific sorption and bulk refractive index change

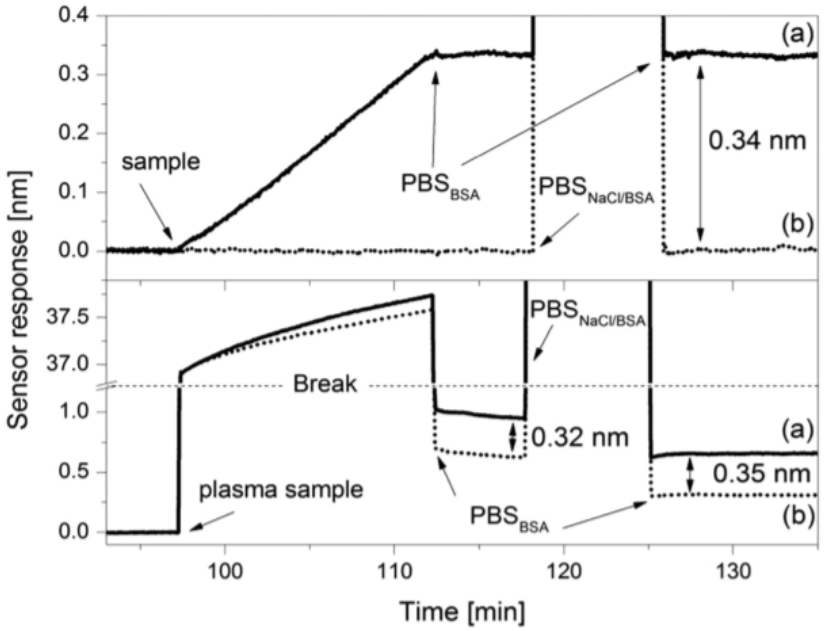
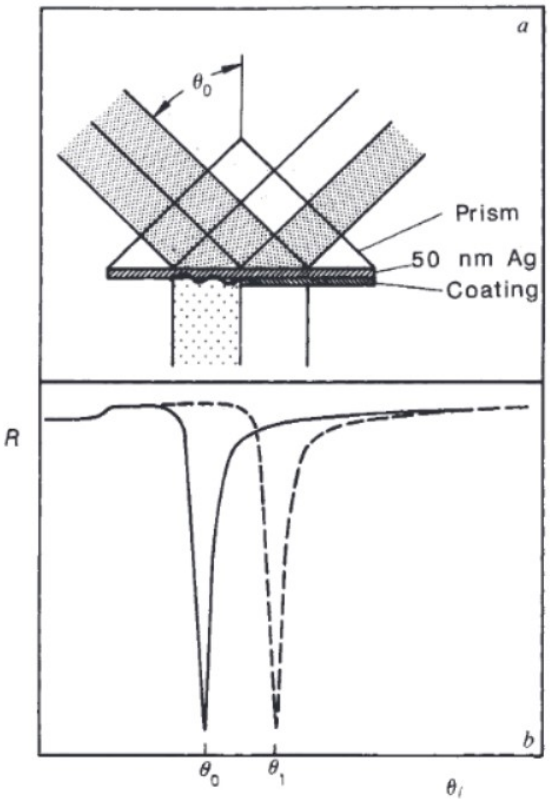


Figure 2. Reference-compensated detection of CEA in PBS$_{BSA}$ (upper graph) and 50% human blood plasma P$_1$ (lower graph) for the SSR approach. Curve (a) denotes the response to the concentration of CEA of 500 ng/mL (detection channel). Curve (b) presents the sensor response to the mixture of 500 ng/mL CEA with an addition of 5000 ng/mL Ab$_{CEA}$ (reference channel).

dx.doi.org/10.1021/ac401062m | Anal. Chem. 2013, 85, 5637−5640

SPR Imaging / Microscopy

Invention in 1988



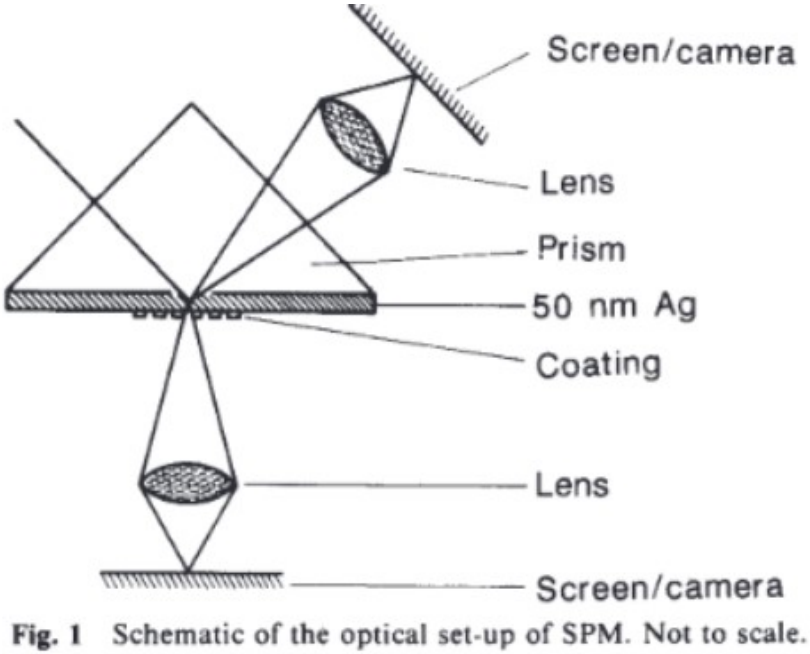
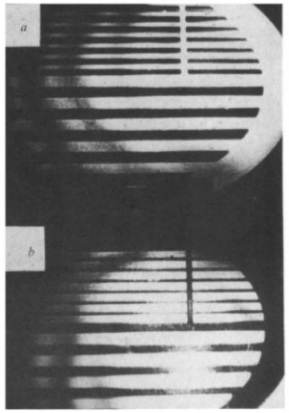


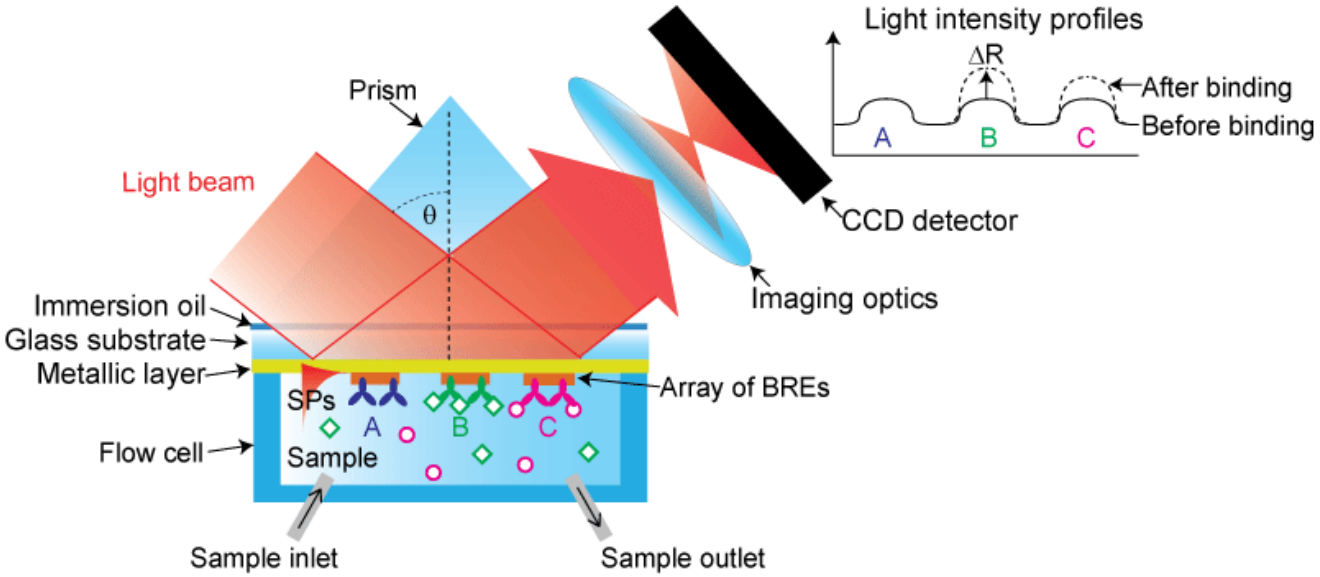
Fig. 1 Schematic of the optical set-up of SPM. Not to scale.



- Rothenhaesler and Knoll invented the method coined the term Surface Plasmon Microscopy – SPM.

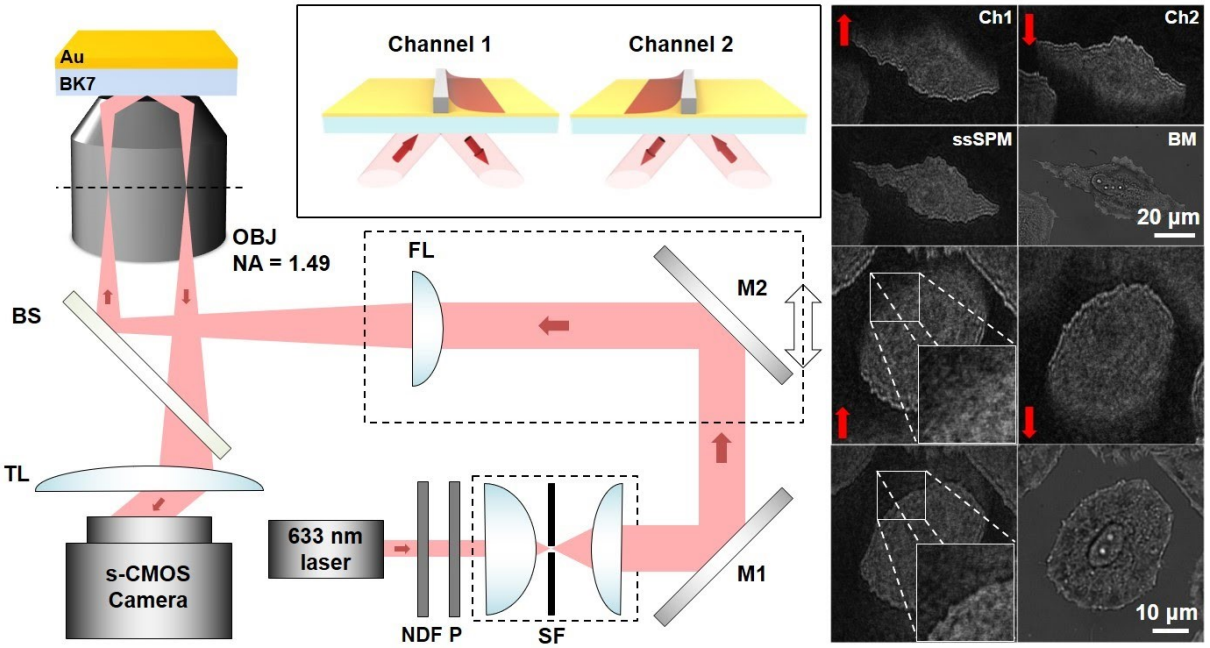
https://www.nature.com/articles/332615a0

Surface Plasmon Imaging - SPRI



- Surface plasmon imaging (SPRI) is technique used for probing of arrays of spots, imaging of cells….
- Spatial resolution typically of several μm, utilizing intensity modulation of SPR with refractive index resolution of typically 10^{-5}.

Surface Plasmon Microscopy - SPM



https://sites.google.com/site/taehwangson89/

- Implemented with using a microscope with scanned objective lens to form the image.
- Spatial resolution typically of better then SPRI.

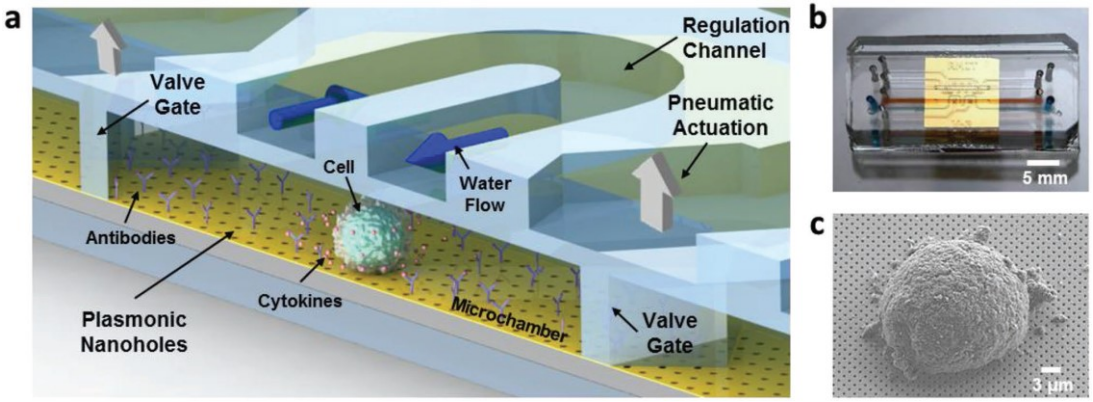
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

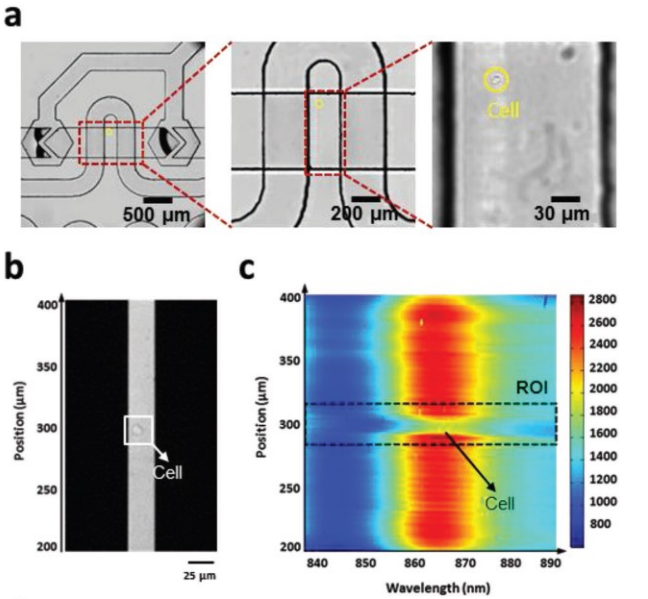
MINISTRY OF EDUCATION, YOUTH AND SPORTS

FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Surface Plasmon Microscopy – Other Implementations



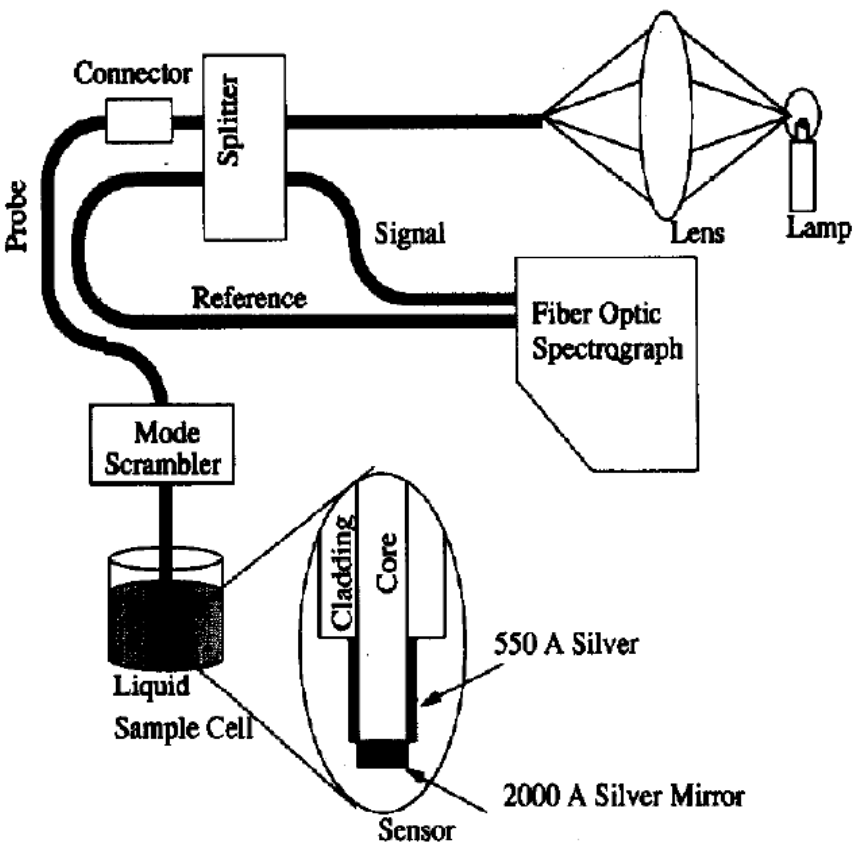


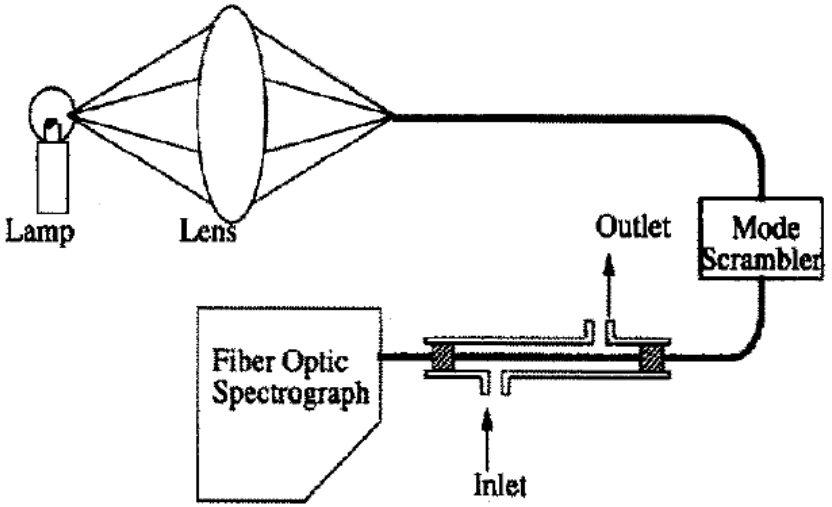
- Arrays of nanoholes that perforate thin metal films can be used for spectral imaging of diffraction-coupled SPR resonance.
- Employed in multiplexing of sensing channels (Oh group) and cellular assays (Altug group).

DOI: 10.1002/smll.201800698

Fiber Optic Probe SPR Biosensors

Multimode – SPR Fiber Optic Probe

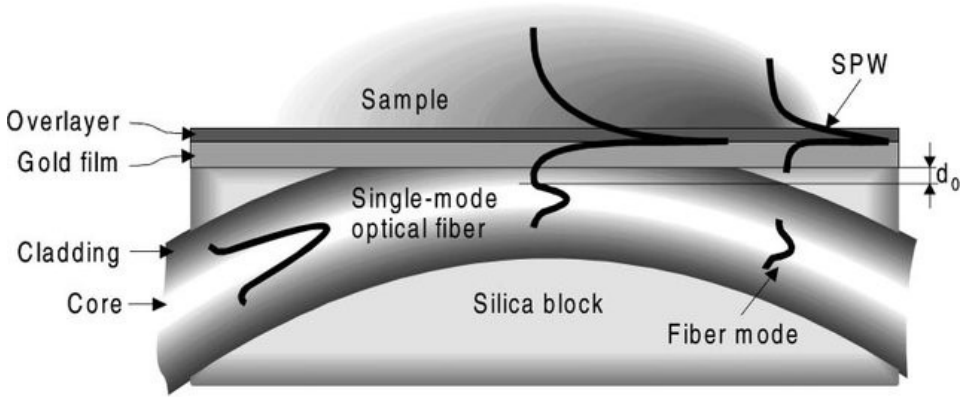


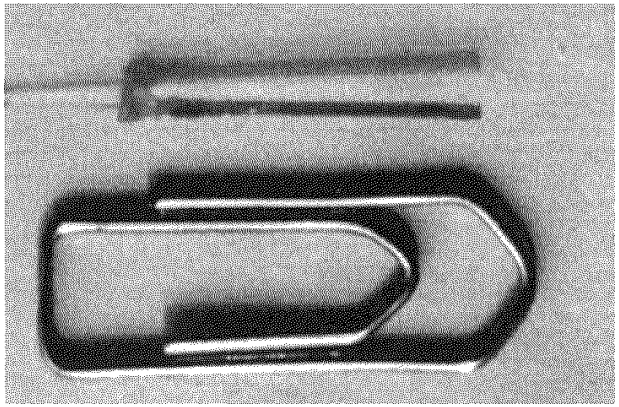


- Miniature optical probe for SPR measurement at the tip / surface of multimode optical fiber.

https://doi.org/10.1016/0925-4005(93)80021-3

Singlemode – SPR Fiber Optic Probe





- Better accuracy in discriminating of SPR changes is possible with single mode fibers (in principle birefringent fiber allows for suppress the sensitivity to movement / bending of the fiber

https://www.sciencedirect.com/science/article/pii/S0925400598002056#FIG4

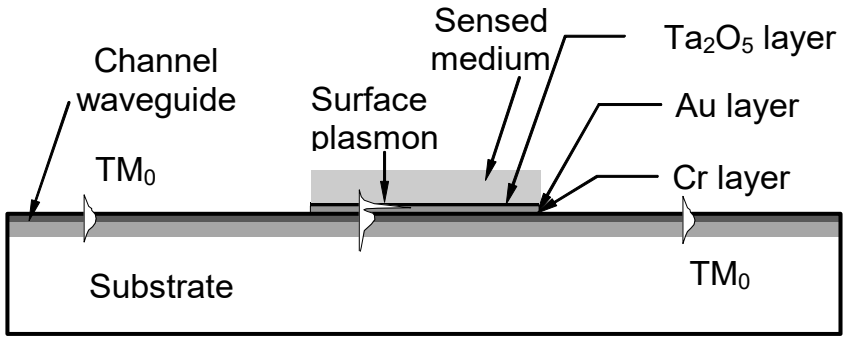
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research, Development and Education

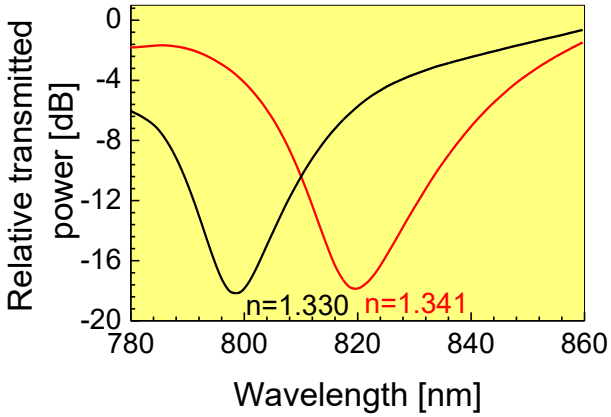
MINISTRY OF EDUCATION, YOUTH AND SPORTS

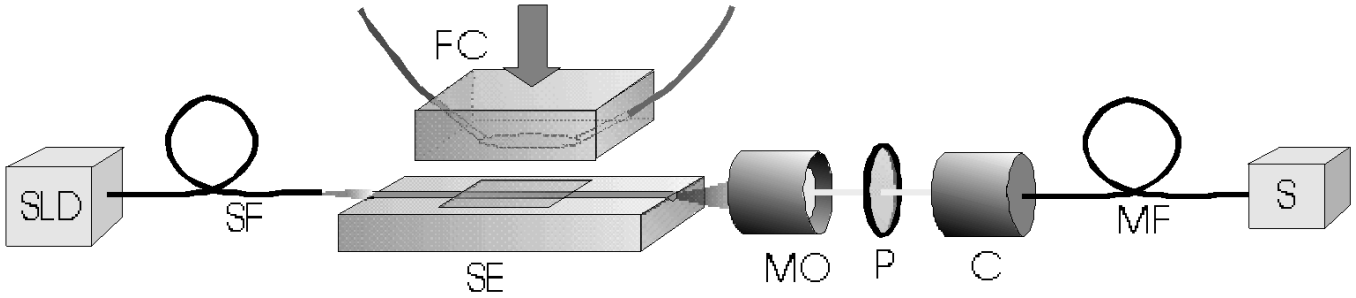
FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Optical Waveguide-Coupled SPR







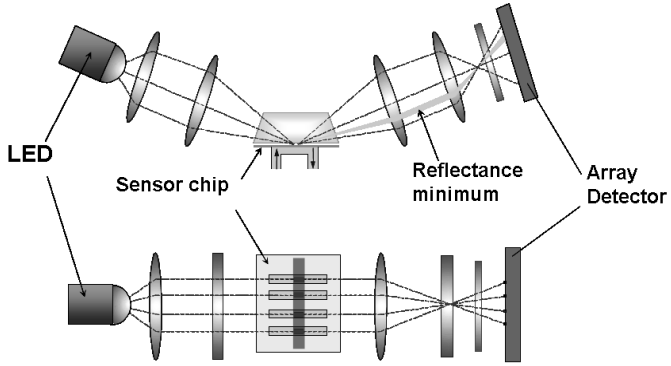
- Using integrated optical waveguides allows for similar level of miniaturization with potential for multiplexing.

J. Dostalek, J. Ctyroky, J. Homola, E. Brynda, M. Skalsky, P. Nekvindova, J. Spirkova, J. Skvor, J. Schröfel: Surface plasmon resonance biosensors based on integrated optical waveguides, Sensors and Actuators B, 76 (2001), 8-12.

Commercial SPR Biosensors

BIACORE

Parameter	Biacore T200
Affinity range	fM to mM
Analysis temperature	4°C to 45°C (maximum 20°C below ambient temperature)
Analysis time per cycle	Typically 2 to 15 min
Application[1]	Kinetics/affinity characterization, kinetics/affinity screening, single-cycle kinetic analysis, fragment screening, epitope mapping[1], immunogenicity, concentration free concentration analysis, thermodynamics, comparability, sample recovery MS
Association rate constant (k_a)	Proteins 10^3 to 3×10^9 $M^{-1}s^{-1}$ LMW molecules 10^3 to 5×10^7 $M^{-1}s^{-1}$
Automation	48 h unattended operation
Baseline drift	< 0.3 RU/min
Baseline noise	< 0.03 RU (RMS)



- Originally Pharmacia, GE Healthcare, now Cytiva. Covering the interaction analysis market, drug development.

https://www.cytivalifesciences.com/en/us/solutions/protein-research/products-and-technologies/spr-systems

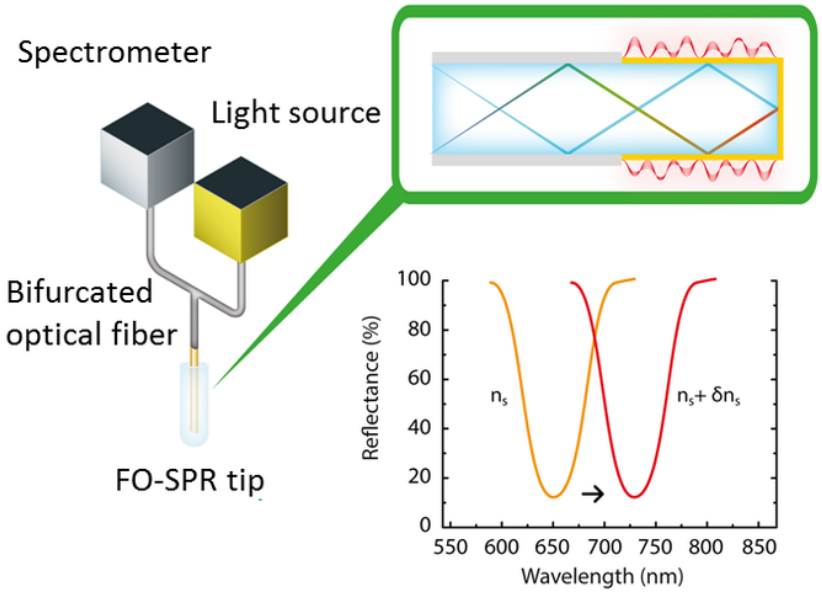
EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

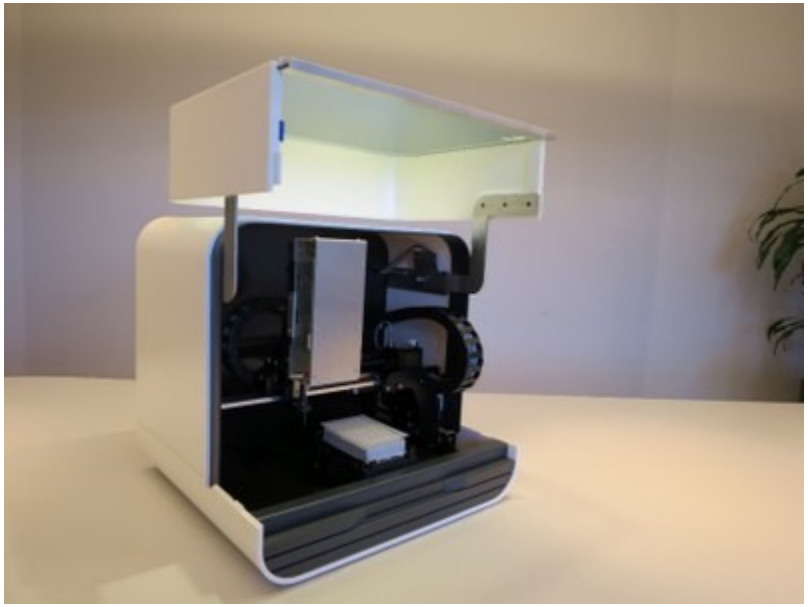
MINISTRY OF EDUCATION, YOUTH AND SPORTS

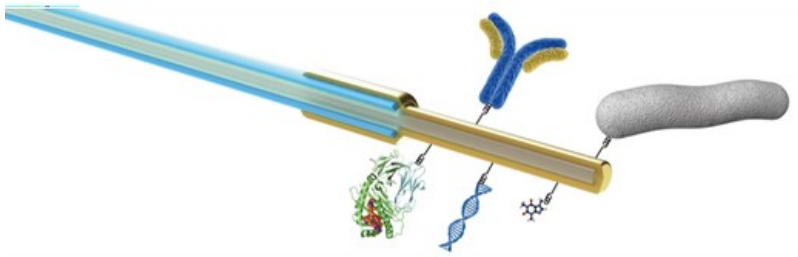
FZU Institute of Physics of the Czech Academy of Sciences

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

FOX DIAGNOSTICS



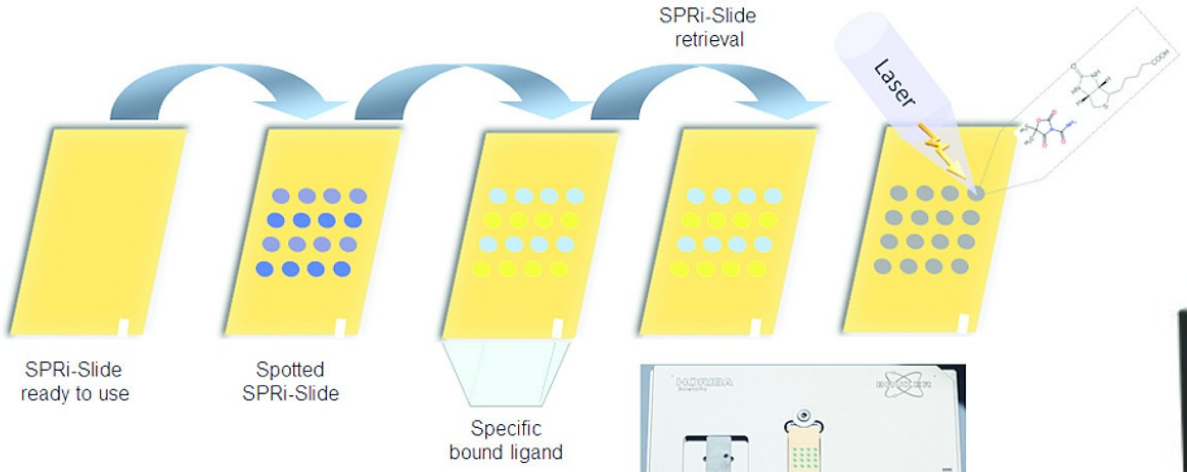


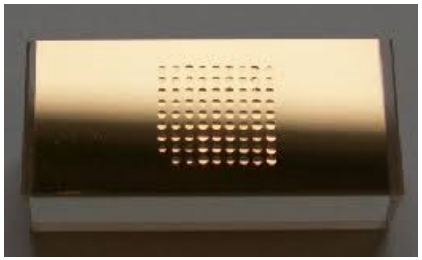


- Coupled with microtiter plates for sample delivery replacing the fluidic system (similar to Octet technology)

https://www.foxbiosystems.com/

HORIBA

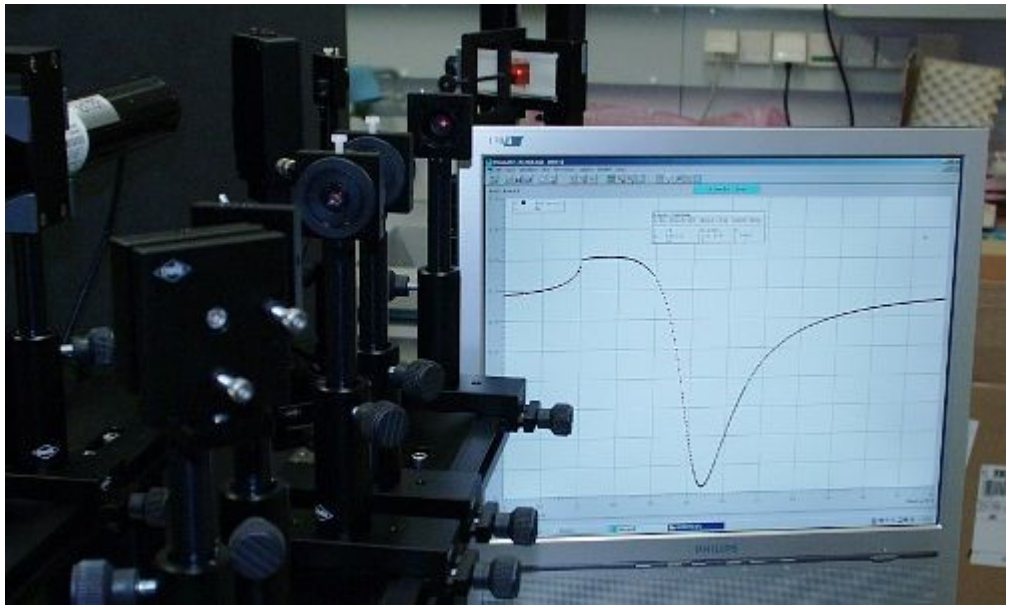


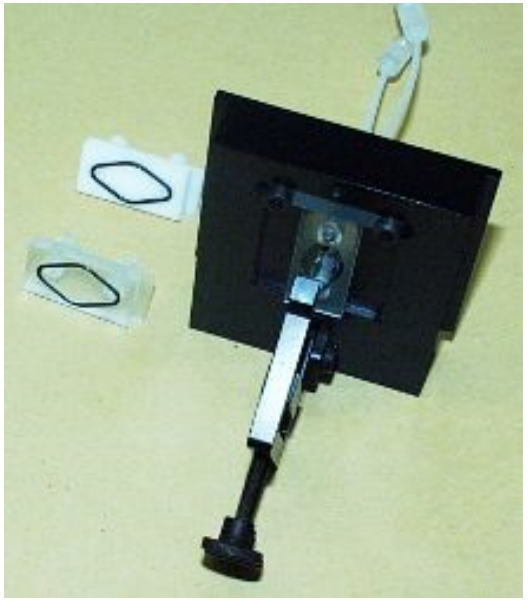


- Implemented SPR imaging (SPRI) for array detection format. Prims coupler-based with recyclable prims-shape chips.

https://www.horiba.com/uk/scientific/products/surface-plasmon-resonance-imaging-spri/spri-platform/spr-imaging-systems/

RESTEC

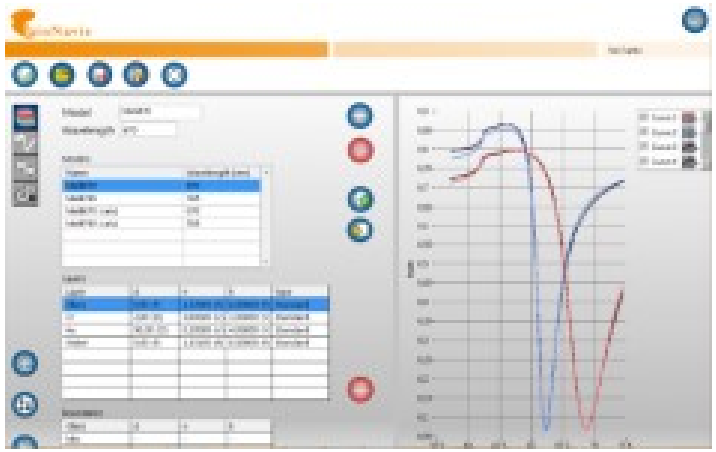




- Continuation of Mainz SPR biosensors, supporting combination with fluorescence detection.

http://www.res-tec.de/

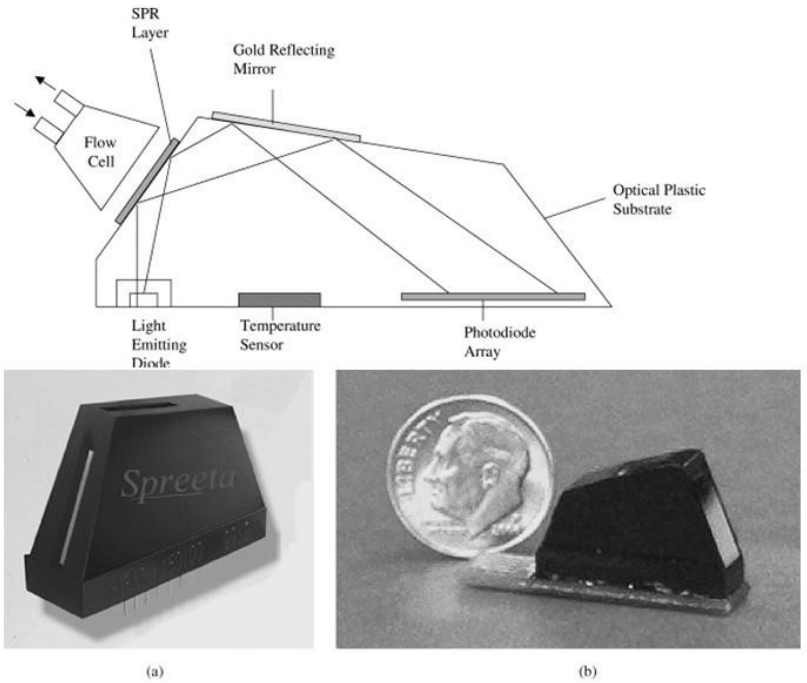
BIONAVIS

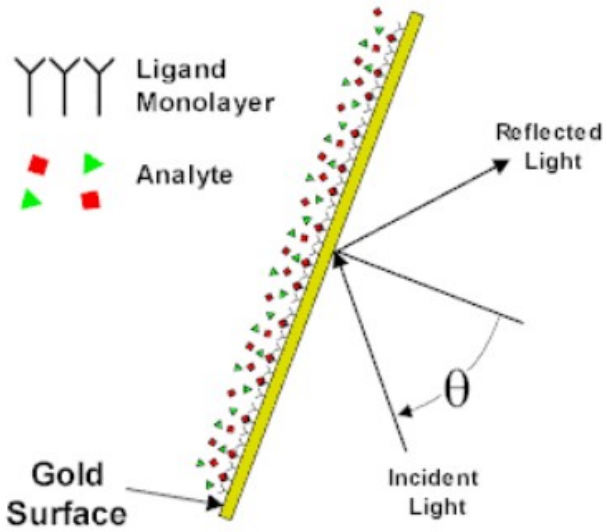


- Conceptually similar to ‘Mainz’ design of SPR with versatile applications in life sciences and materials research.
- Up to four flow chambers, angular interrogation of SPR at multiple wavelength for air and aqueous samples.

https://www.bionavis.com/

TEXAS INSTRUMENTS

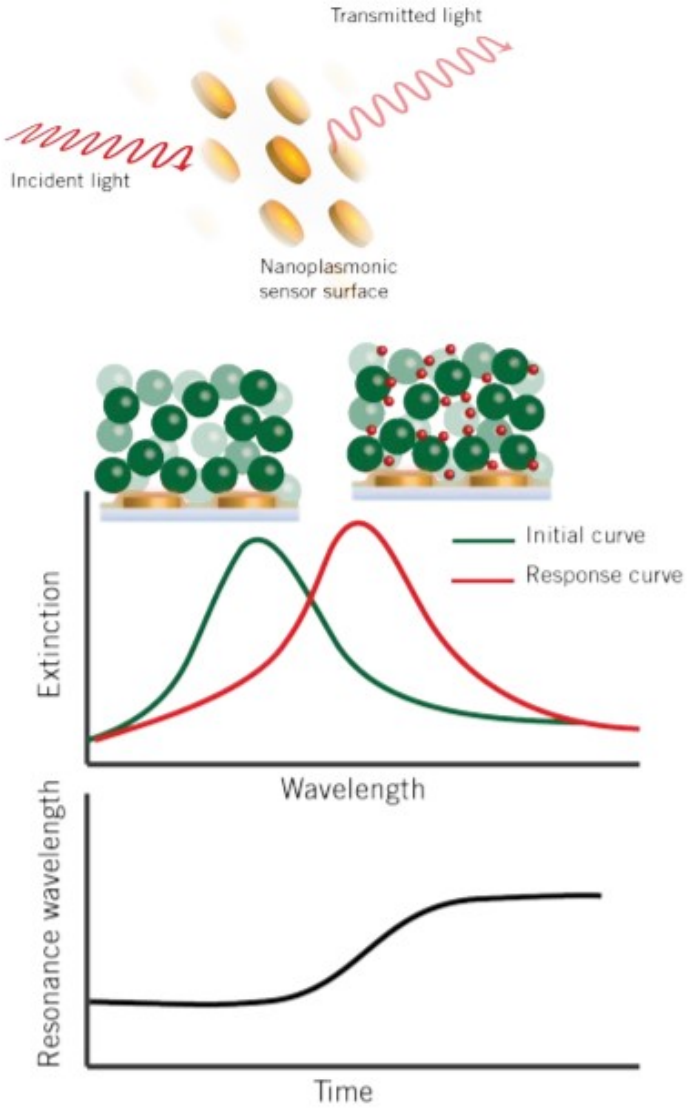




- Developed for low cost miniaturized sensing where the chip was fabricated as disposable with polymer prism. Angular spectroscopy of SPR.

http://www.aigproducts.com/surface_plasmon_resonance/spr_considering.htm

INSPLORION



- LSPR-based sensor on quasiperiodic arrays of gold nanoparticles and transmission-based tracking of resonant wavelength.

https://www.insplorion.com/