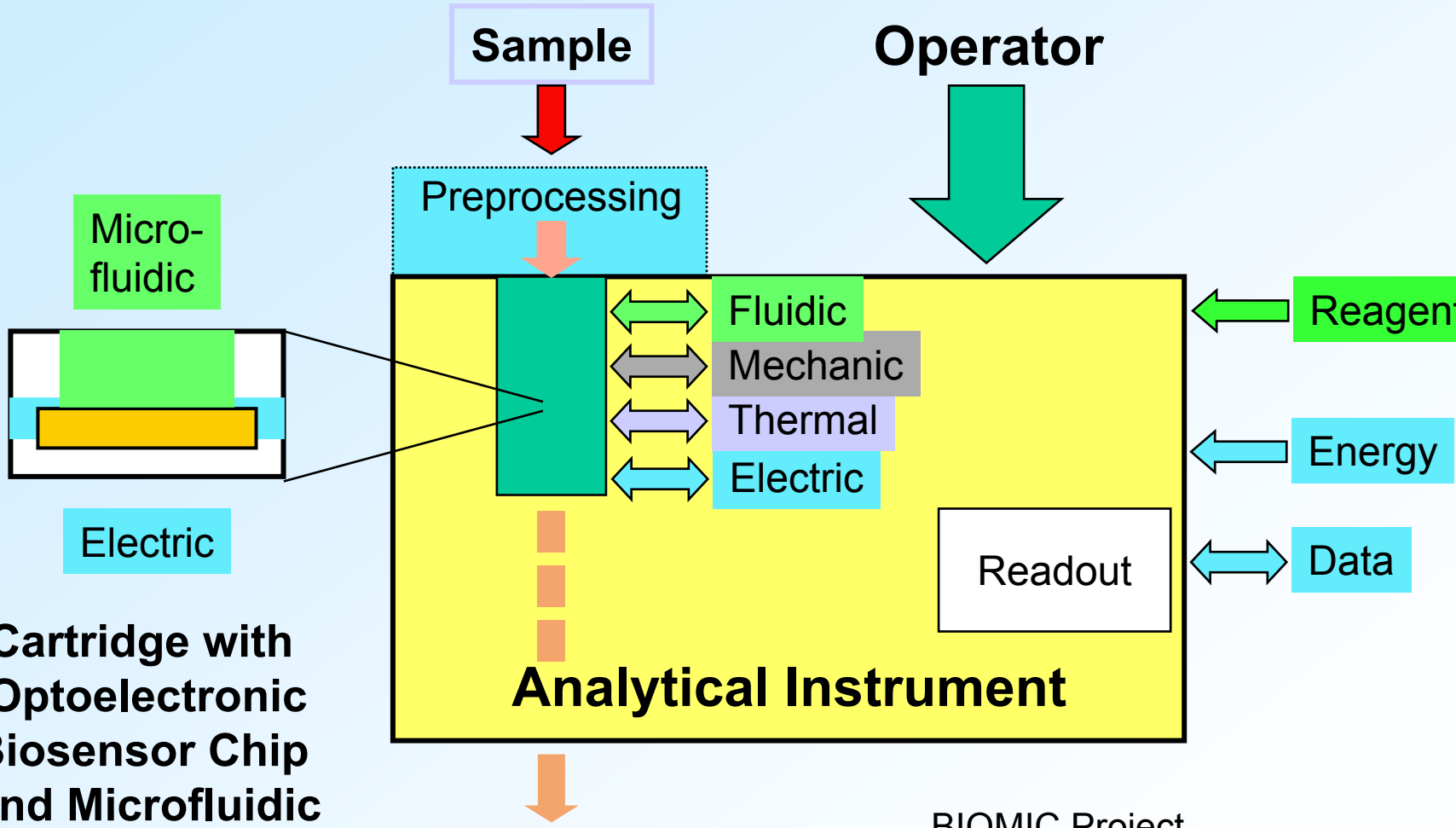
Principles of Integrated Biosensing Devices and Monolithic Optoelectronic Transducers

Lab-on-a-chip Devices

imel NCSR Demokritos

System Design Overview



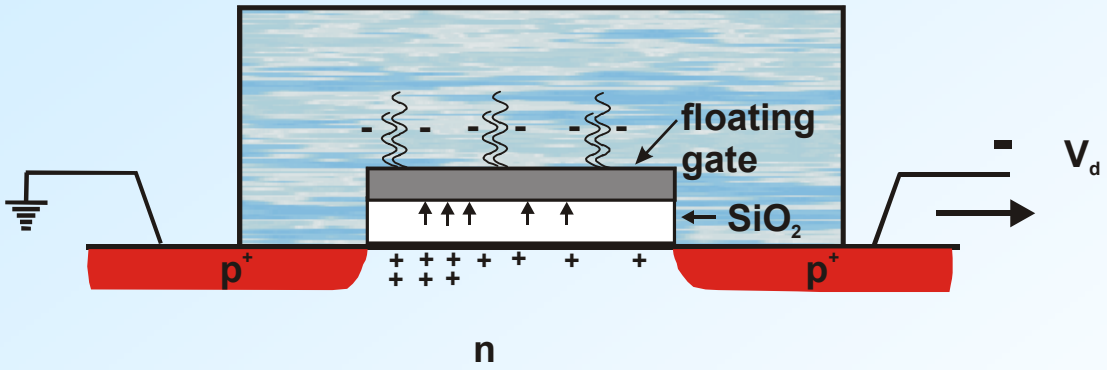
Cartridge with Optoelectronic Biosensor Chip and Microfluidic Module

BIOMIC Project

- ISFETs
- Impedance Spectroscopy Devices
- SAW Devices
- Enzymatic Detection
- SPR Resonance
- Interferometric Devices

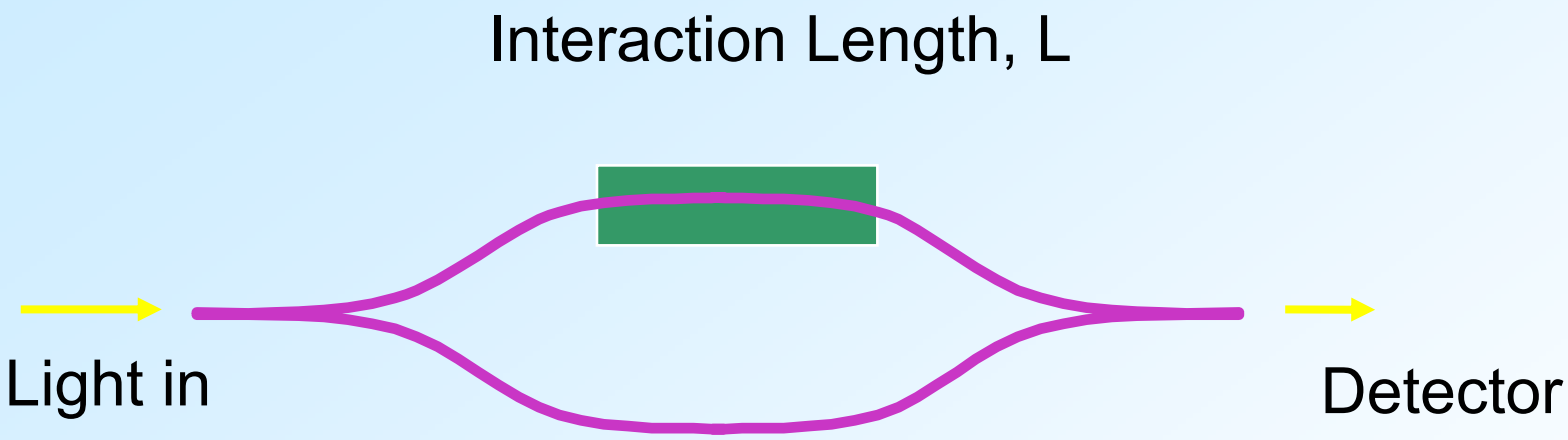
Label free detection

ISFET



$$Q_{bio} = Q_{gate} + Q_{dl}$$

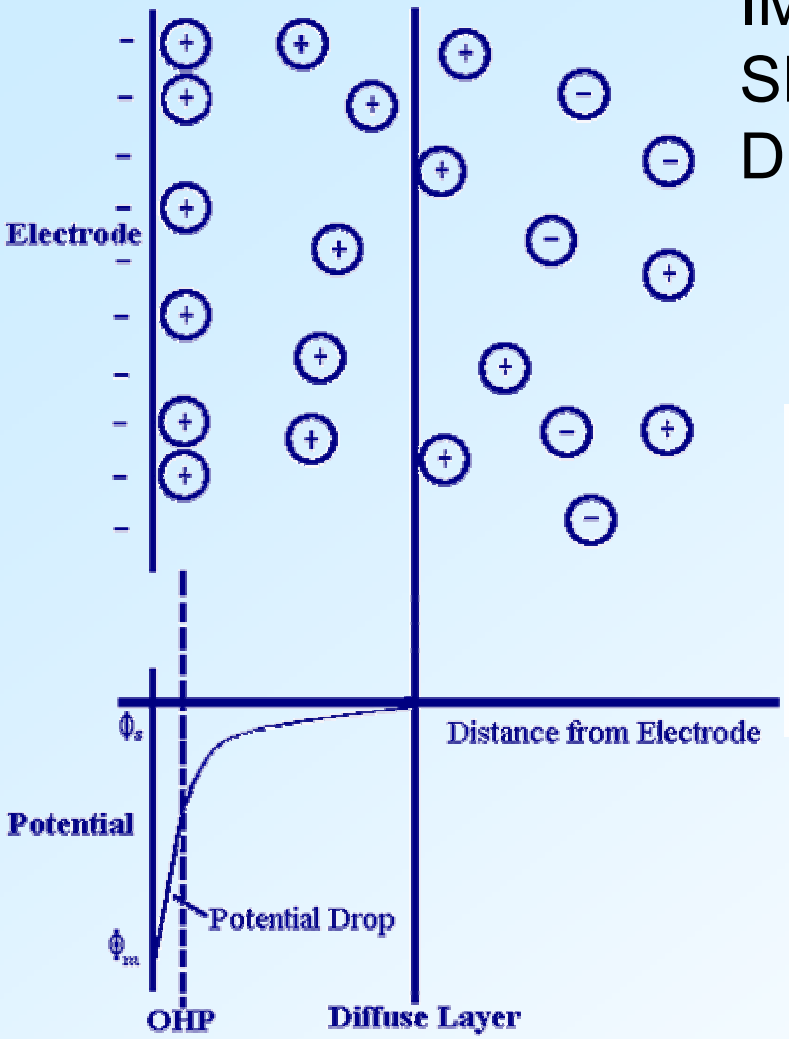
$$Q_{gate} / Q_{dl} = C_{gate} / C_{dl}$$

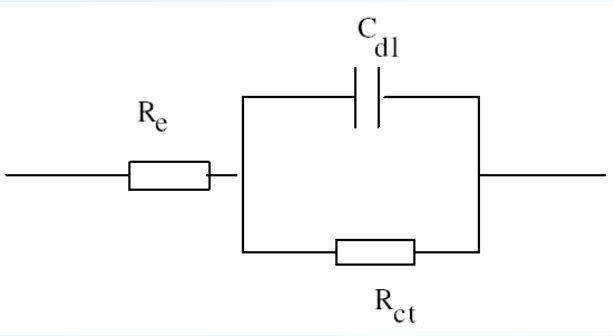


Mach-Zender Interferometer

$\Delta\varphi = 2\pi\Delta nL/\lambda$

IMPEDANCE SPECTROSCOPY DEVICES





Equivalent Circuit

Surface Acoustic Wave
Devices on piezoelectric substrates

Shear waves traveling along the
Liquid-substrate interface change their speed
And resonance if biomolecules bind on the substrate

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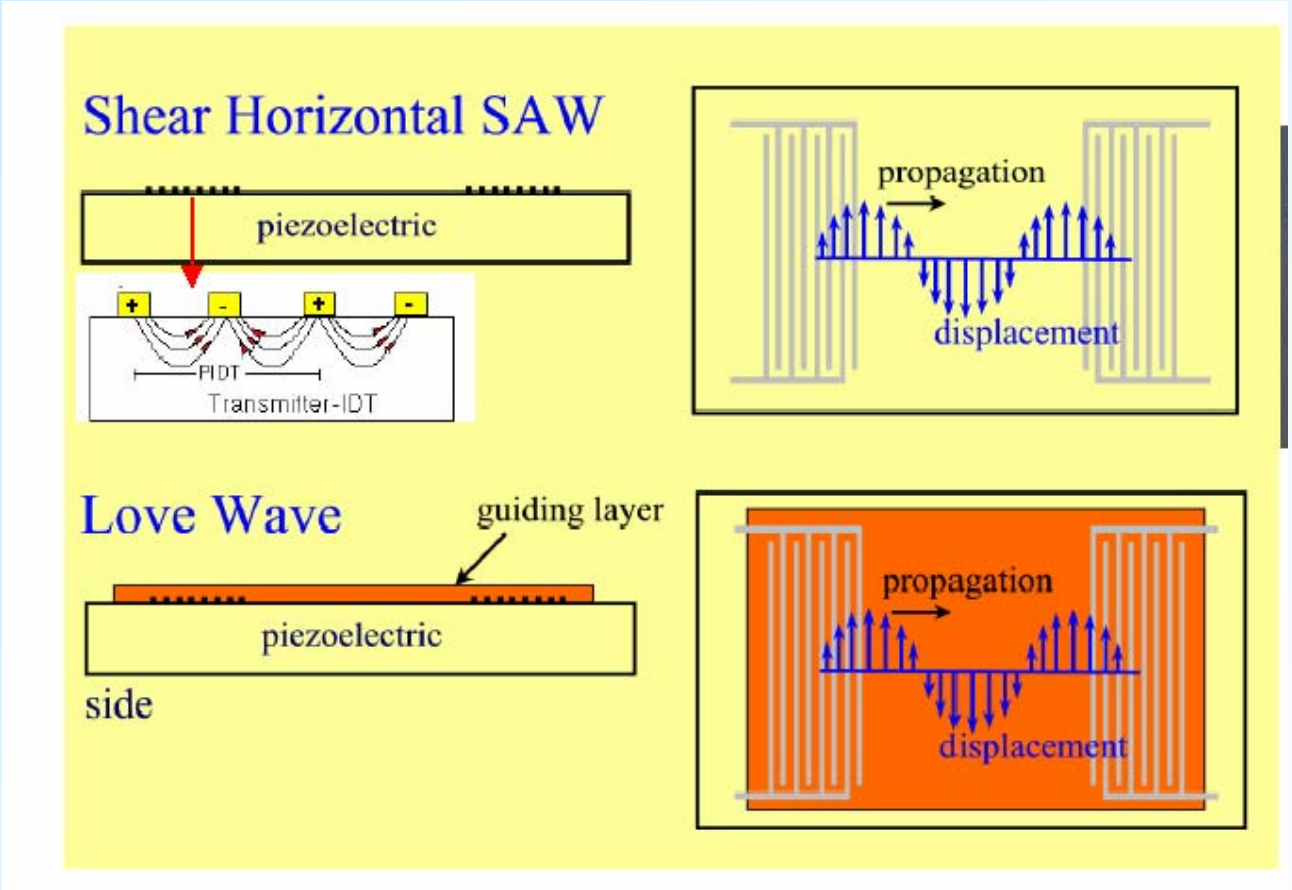


Auburn University Detection and Food Safety Center

With enzyme based electrochemical sensing, the recognition element is an enzyme that selectively catalyzes reaction of a substrate to produce an electroactive product (H_2O_2 for example)

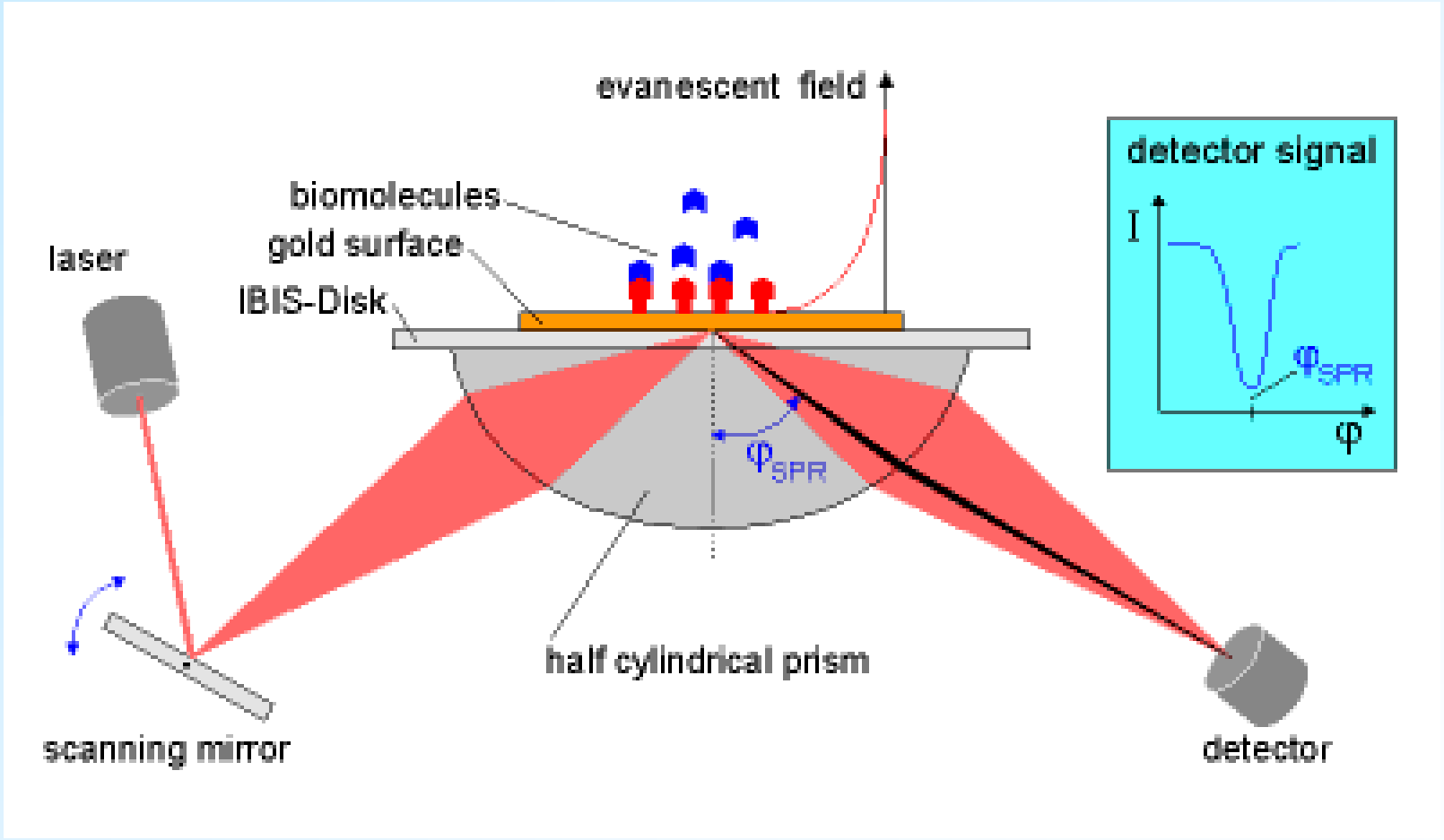
Amperometric detection measures the charge transfer in oxidation or reduction of the electroactive compound at a working electrode

OPTICAL BIOSENSOR AND BIOCHIP ADVANTAGES:

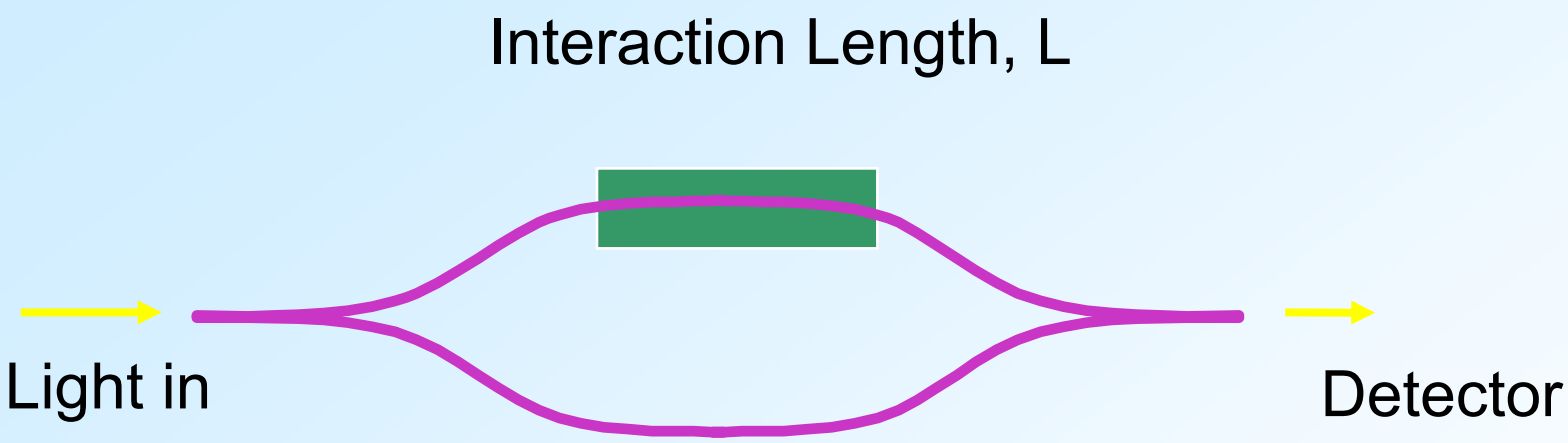
GALVANIC ISOLATION OF THE TRANSDUCER
FROM DETECTION AND EXCITATION ELECTRONICS

DIFFICULTY:

INTEGRATION OF LIGHT SOURCE



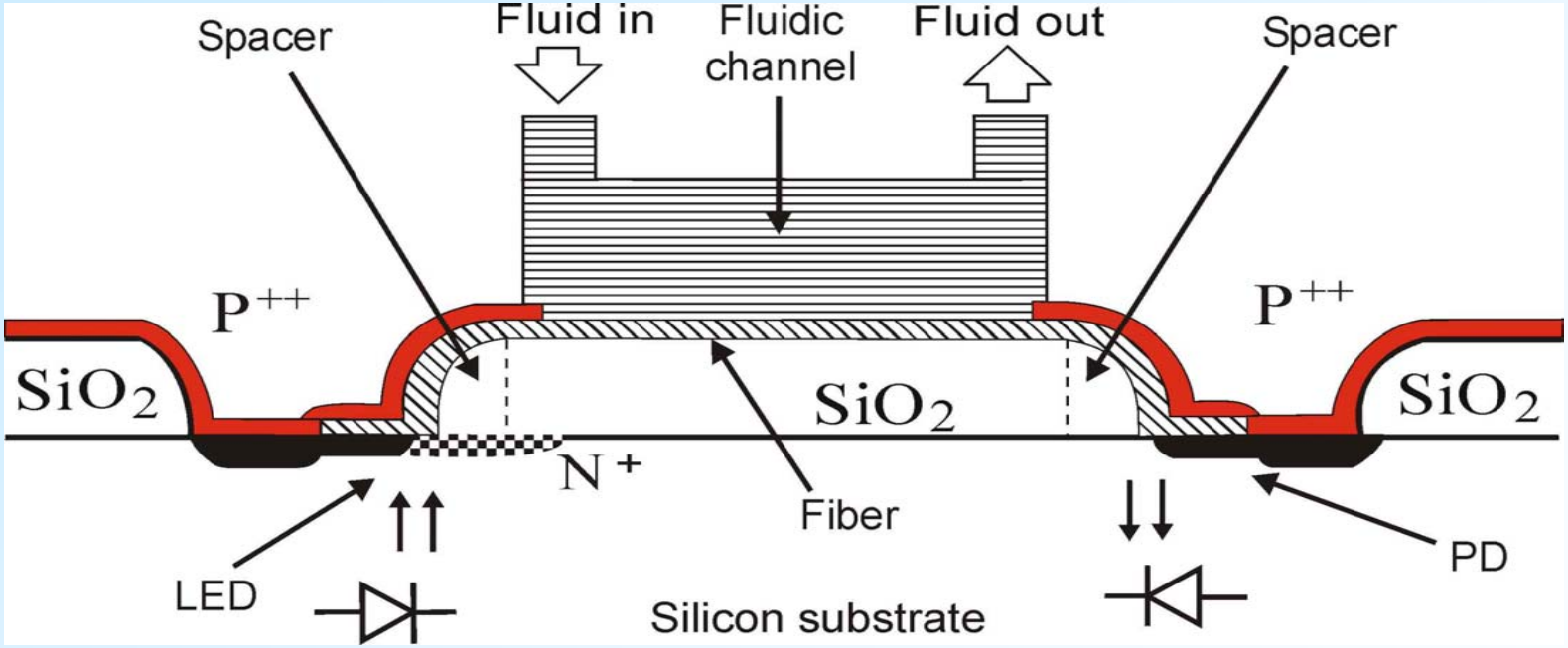
SPR PRINCIPLE
XANTEC

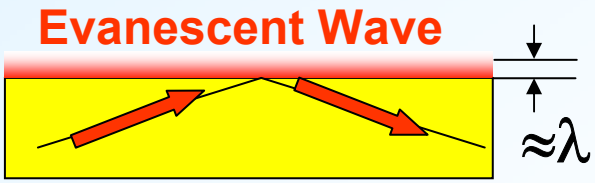


Mach-Zender Interferometer

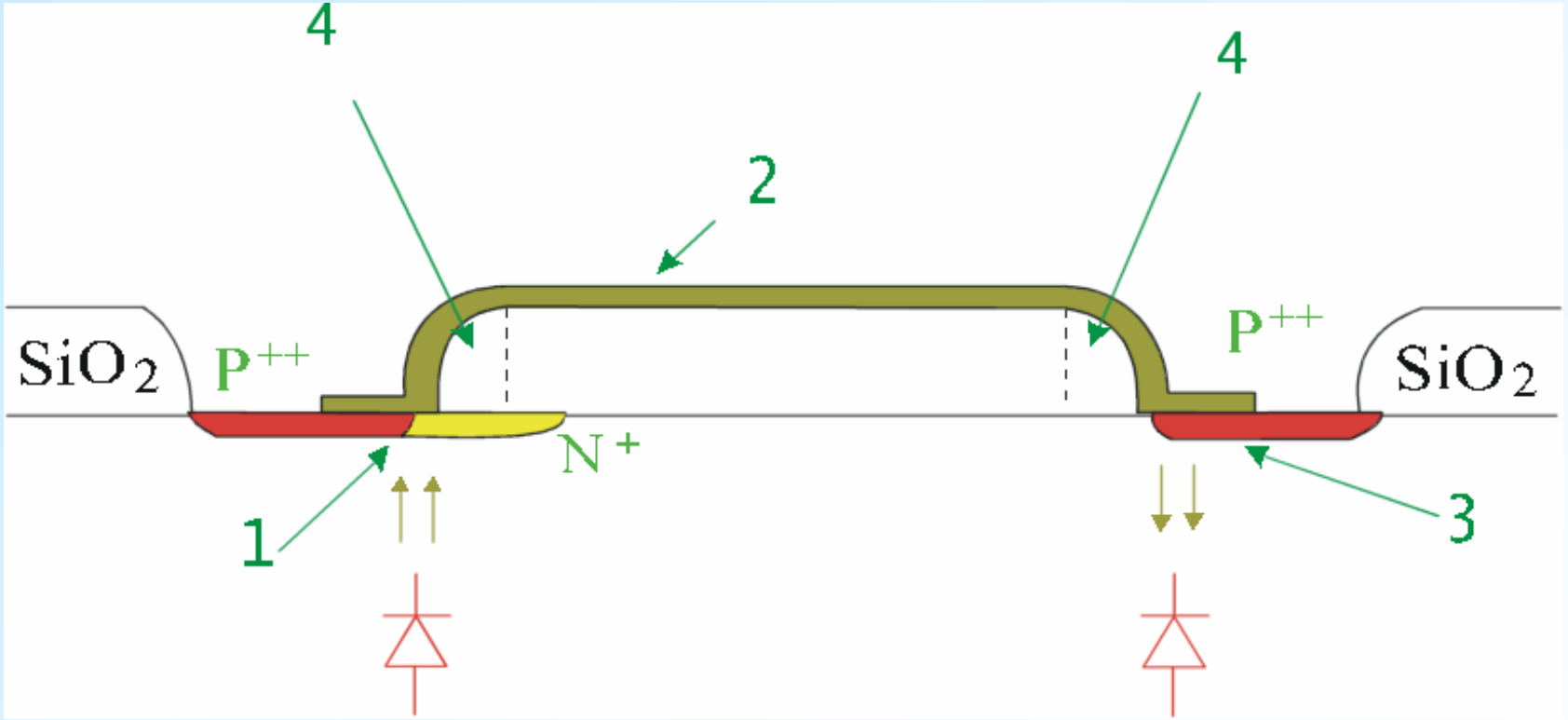
$\Delta\varphi = 2\pi\Delta nL/\lambda$

Monolithic Silicon Optoelectronic Transducers





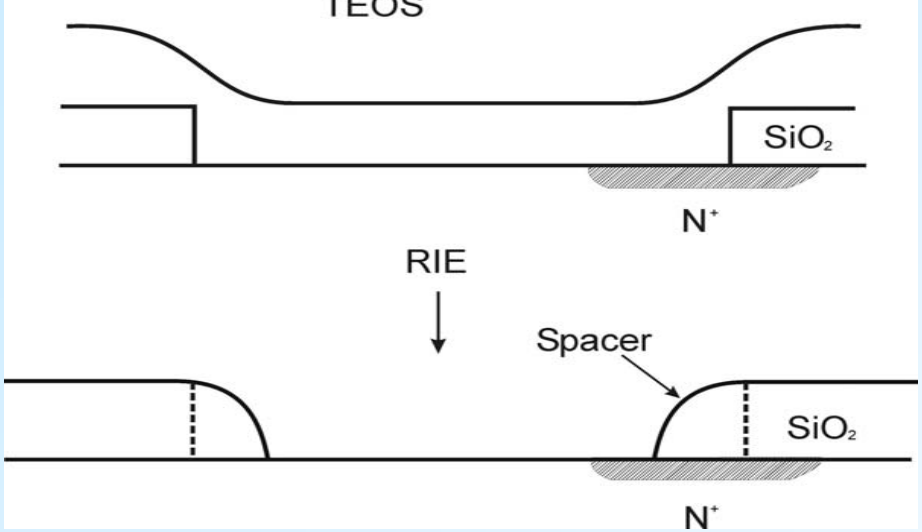
BIOMIC Project



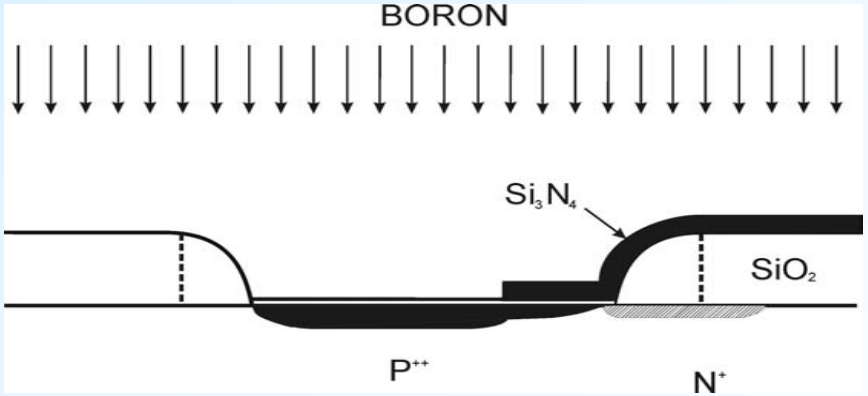
1: Avalanche diode light emitter 2: Nitride fiber

3: p/n Junction Detector 4: Spacers

BIOMIC Project



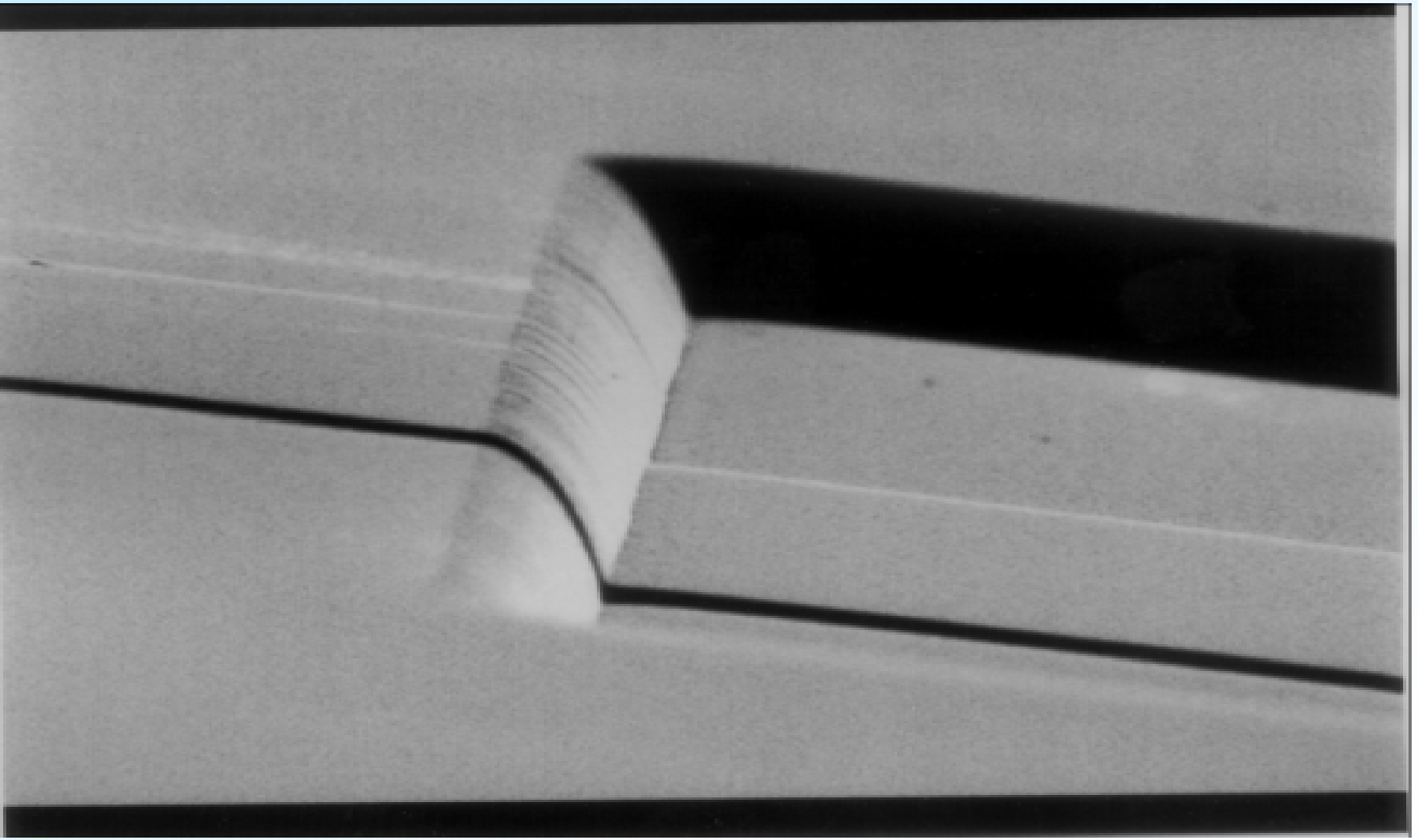
SiO_2 Spacer Formation

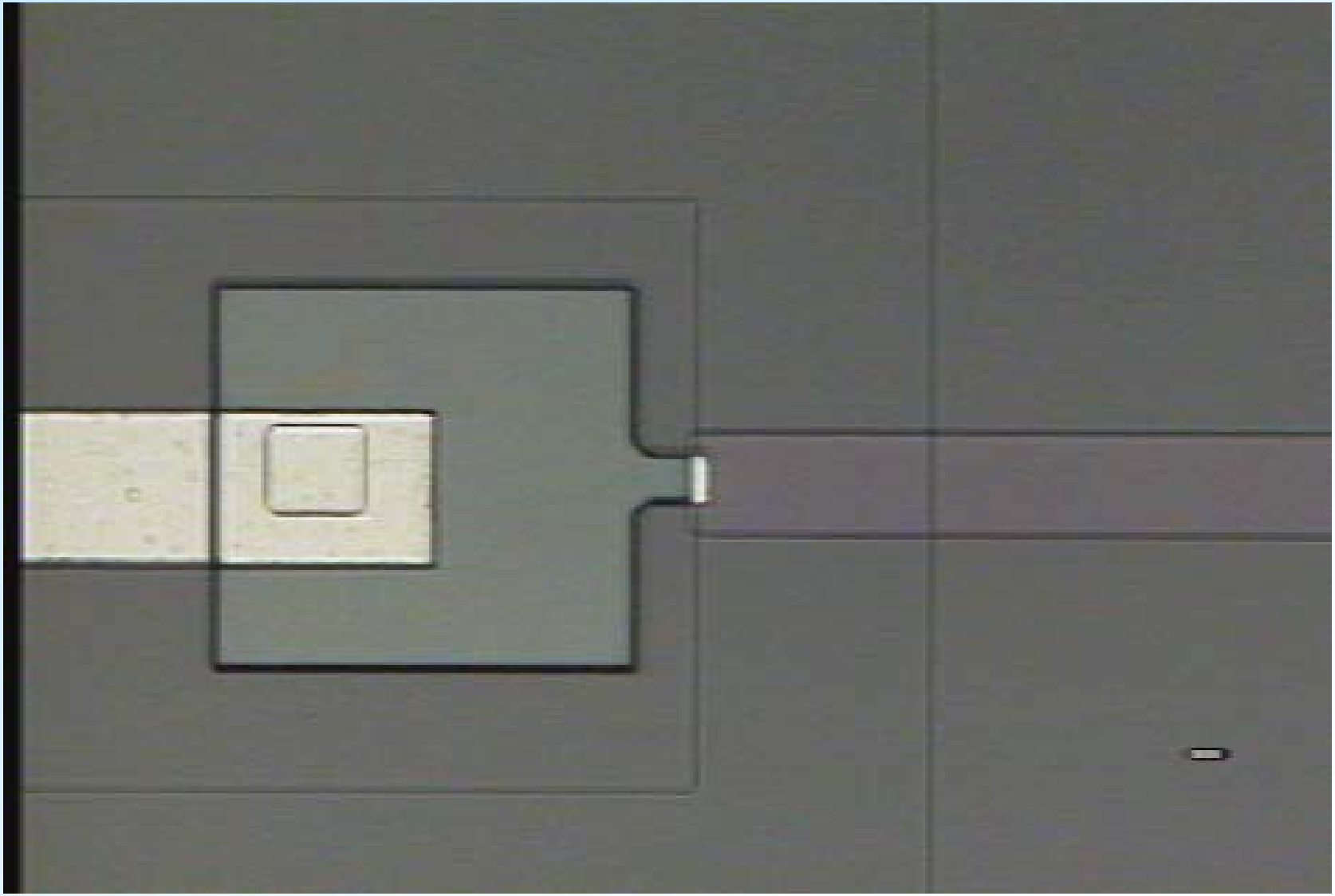


BIOMIC Project

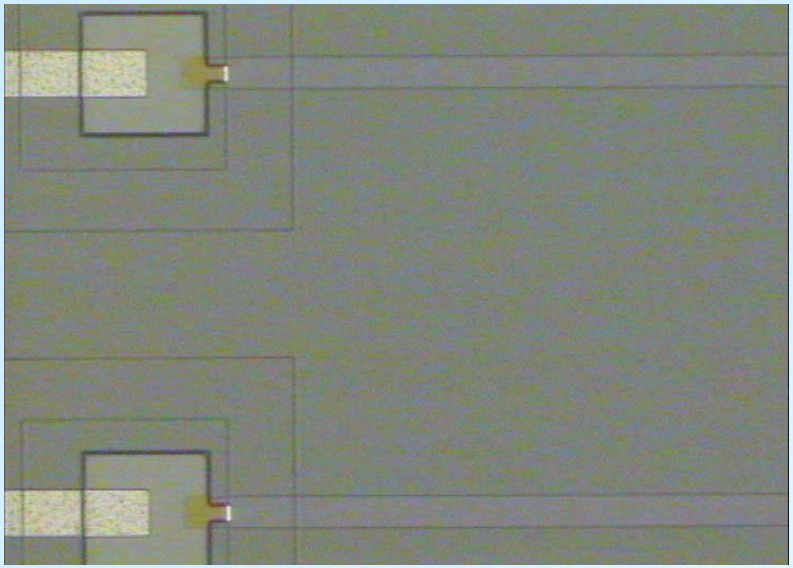
Formation of Self-aligned light emitting avalanche Diodes, silicon nitride waveguides, and detectors

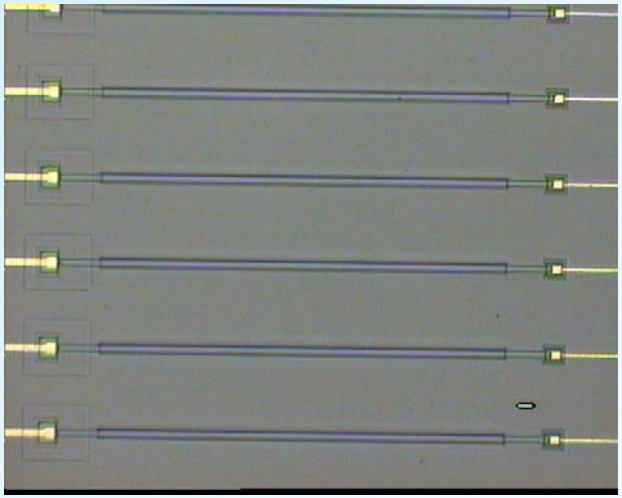
WAVEGUIDE BENDING ON THE DETECTOR SIDE





LED under excitation

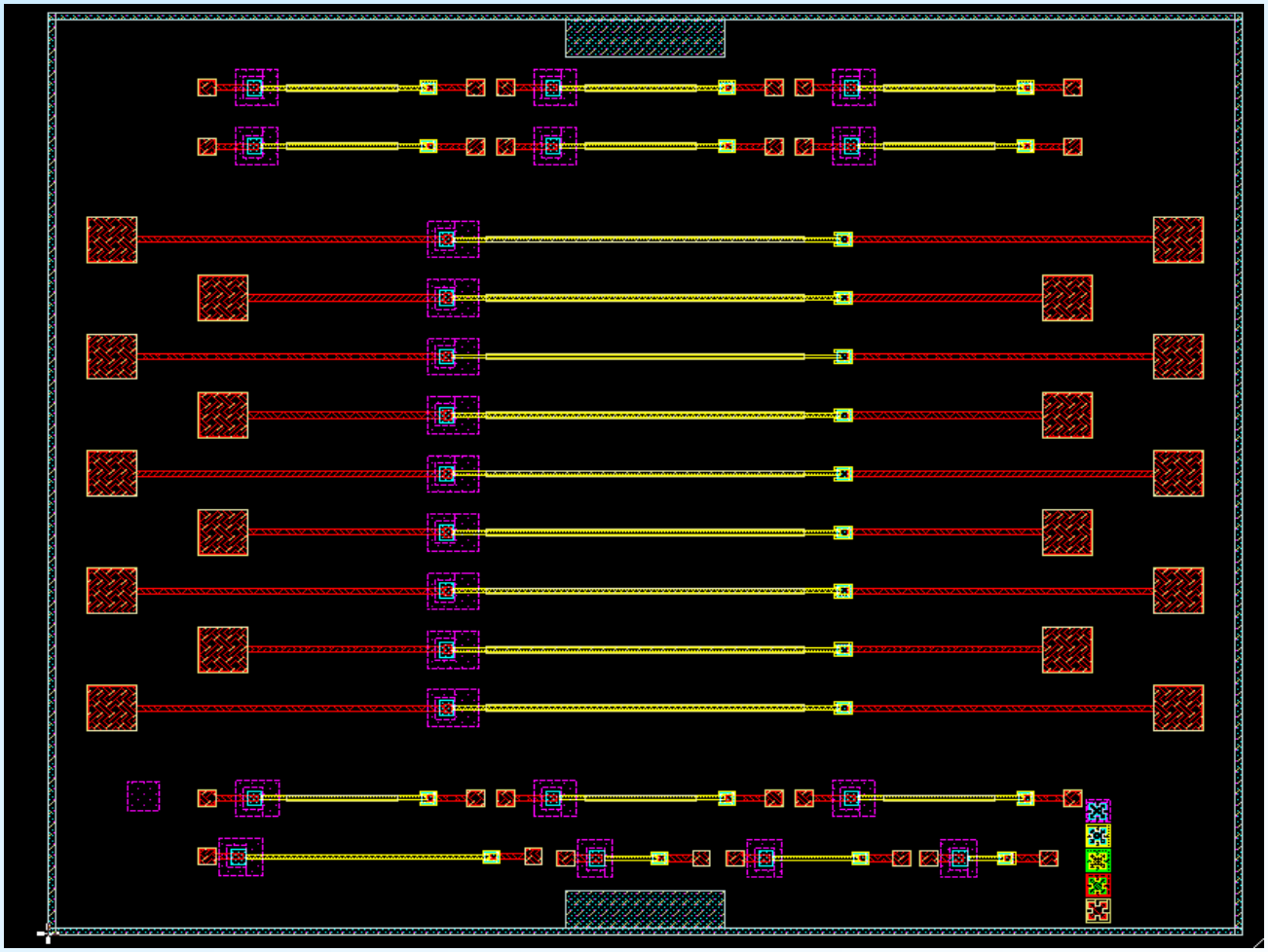




Emitters on the left,
detectors on the right

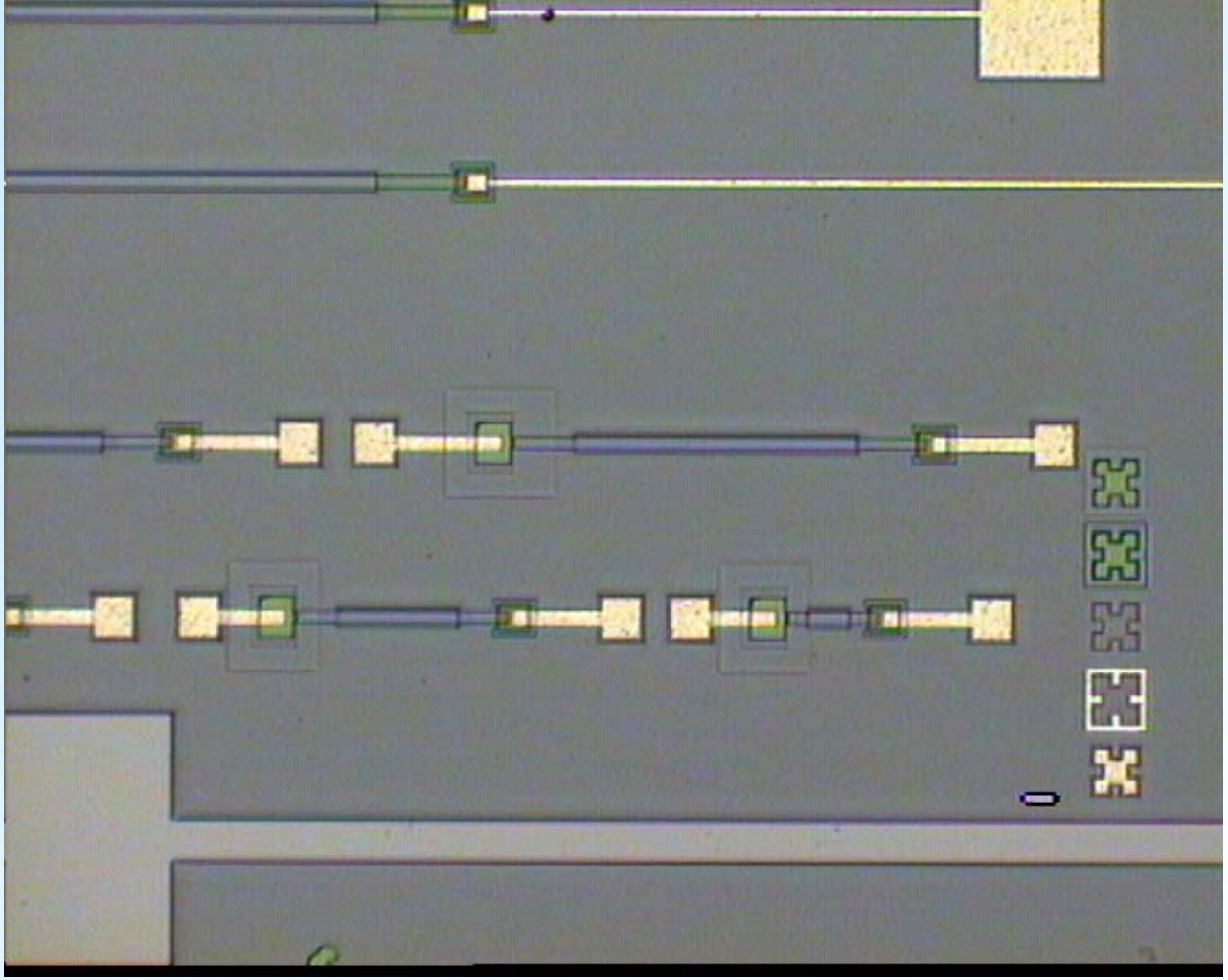
monolithic silicon optocouplers

BIOMIC Project



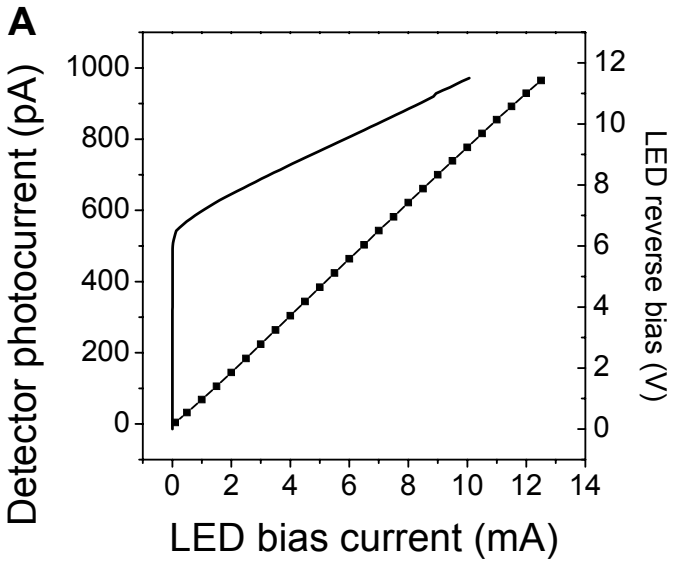
Chip Layout

BIOMIC Project

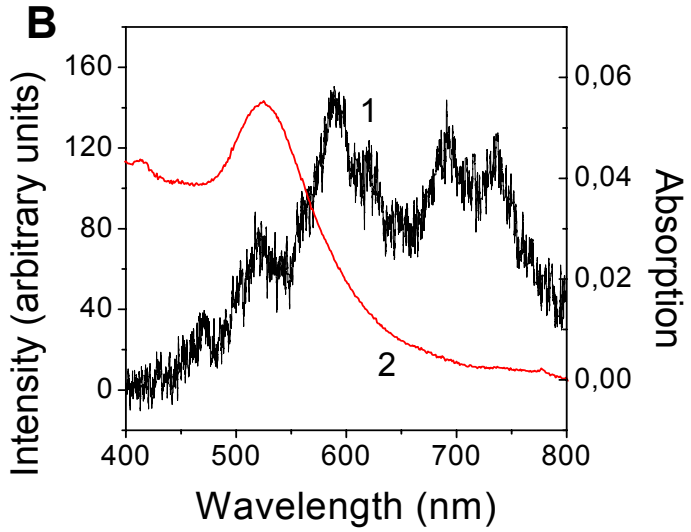


Test Devices BIOMIC Project

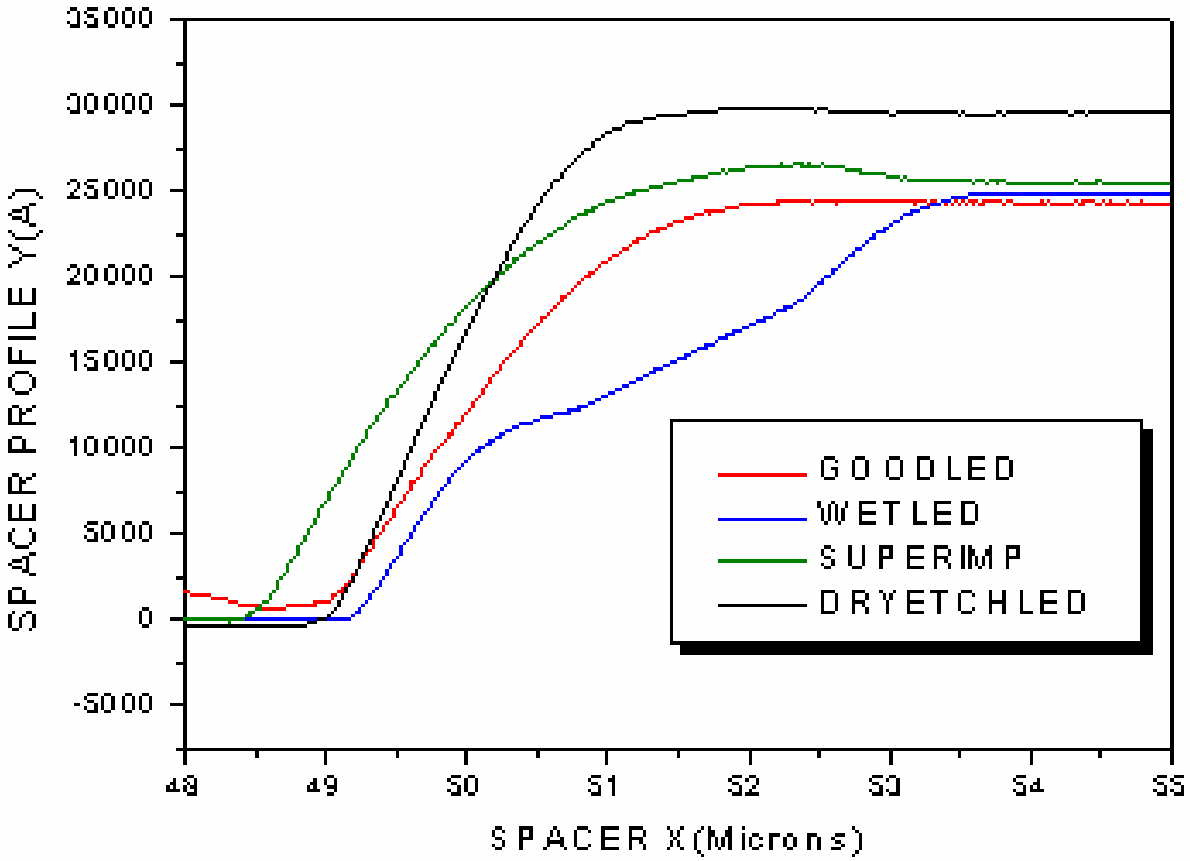
Optocoupler quantum efficiency



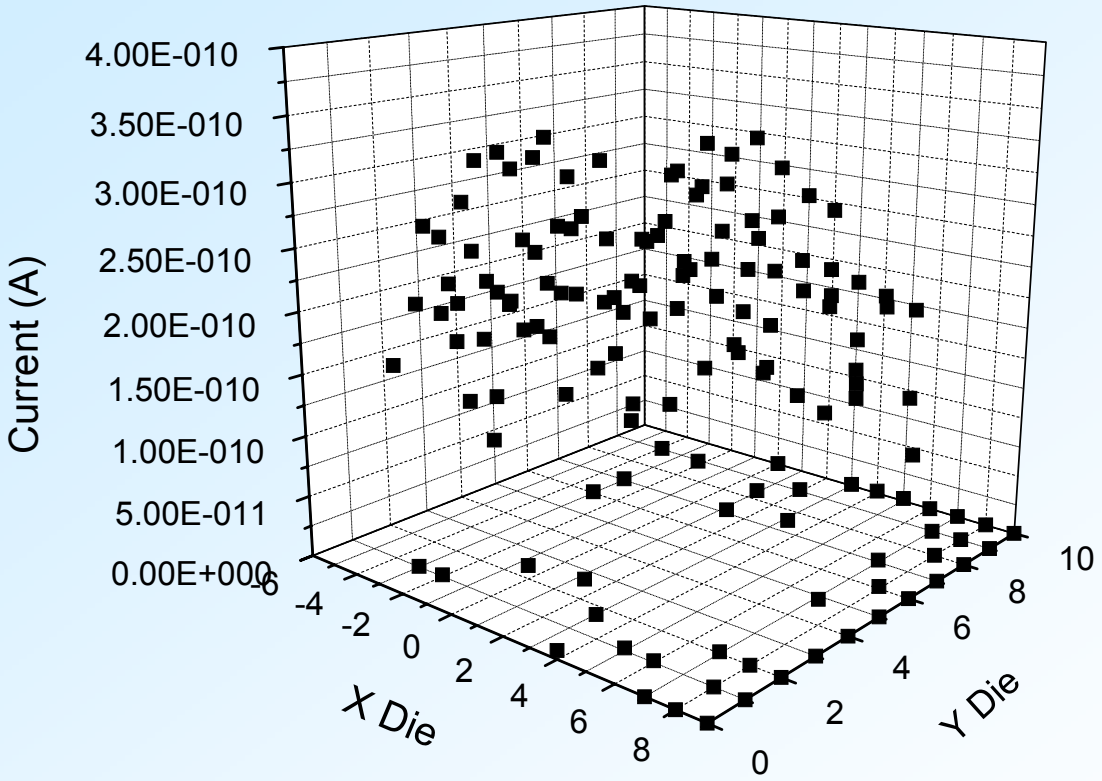
B. LED Light Spectrum
and gold nanoparticle absorption



Stylus Profilometer Spacer Profiles

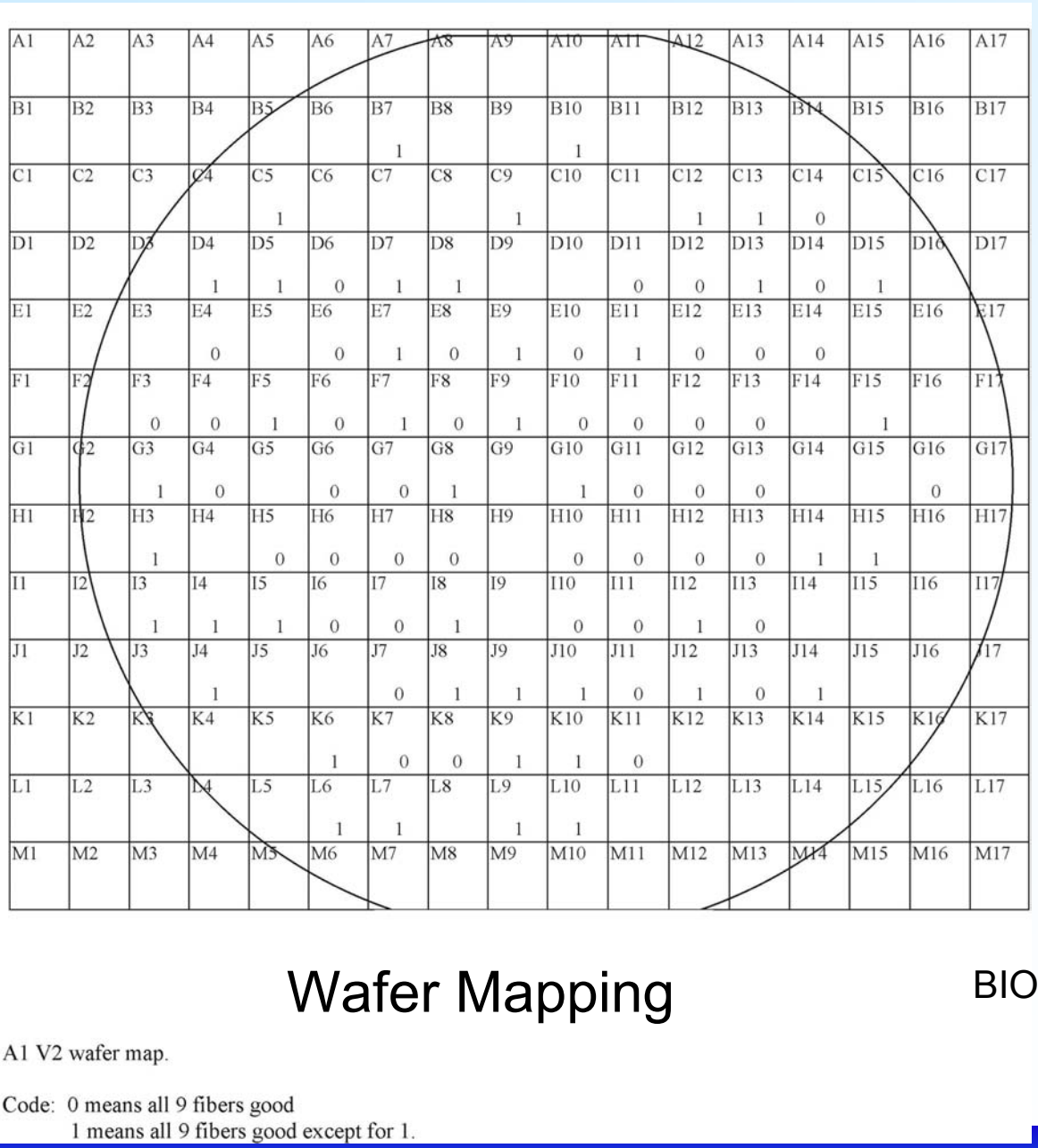


BIOMIC Project



Photocurrent variation Across the wafer

BIOMIC Project



A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12	A13	A14	A15	A16	A17
B1	B2	B3	B4	B5	B6	B7 1	B8	B9	B10 1	B11	B12	B13	B14	B15	B16	B17
C1	C2	C3	C4	C5 1	C6	C7	C8	C9 1	C10	C11	C12 1	C13 1	C14 0	C15	C16	C17
D1	D2	D3	D4 1	D5 1	D6 0	D7 1	D8 1	D9	D10	D11 0	D12 0	D13 1	D14 0	D15 1	D16	D17
E1	E2	E3	E4 0	E5	E6 0	E7 1	E8 0	E9 1	E10 0	E11 1	E12 0	E13 0	E14 0	E15	E16	E17
F1	F2	F3 0	F4 0	F5 1	F6 0	F7 1	F8 0	F9 1	F10 0	F11 0	F12 0	F13 0	F14	F15 1	F16	F17
G1	G2	G3 1	G4 0	G5	G6 0	G7 0	G8 1	G9	G10 1	G11 0	G12 0	G13 0	G14	G15	G16 0	G17
H1	H2	H3 1	H4	H5 0	H6 0	H7 0	H8 0	H9	H10 0	H11 0	H12 0	H13 0	H14 1	H15 1	H16	H17
I1	I2	I3 1	I4 1	I5 1	I6 0	I7 0	I8 1	I9	I10 0	I11 0	I12 1	I13 0	I14	I15	I16	I17
J1	J2	J3	J4 1	J5	J6	J7 0	J8 1	J9 1	J10 1	J11 0	J12 1	J13 0	J14 1	J15	J16	J17
K1	K2	K3	K4	K5	K6 1	K7 0	K8 0	K9 1	K10 1	K11 0	K12	K13	K14	K15	K16	K17
L1	L2	L3	L4	L5	L6 1	L7 1	L8	L9 1	L10 1	L11	L12	L13	L14	L15	L16	L17
M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17

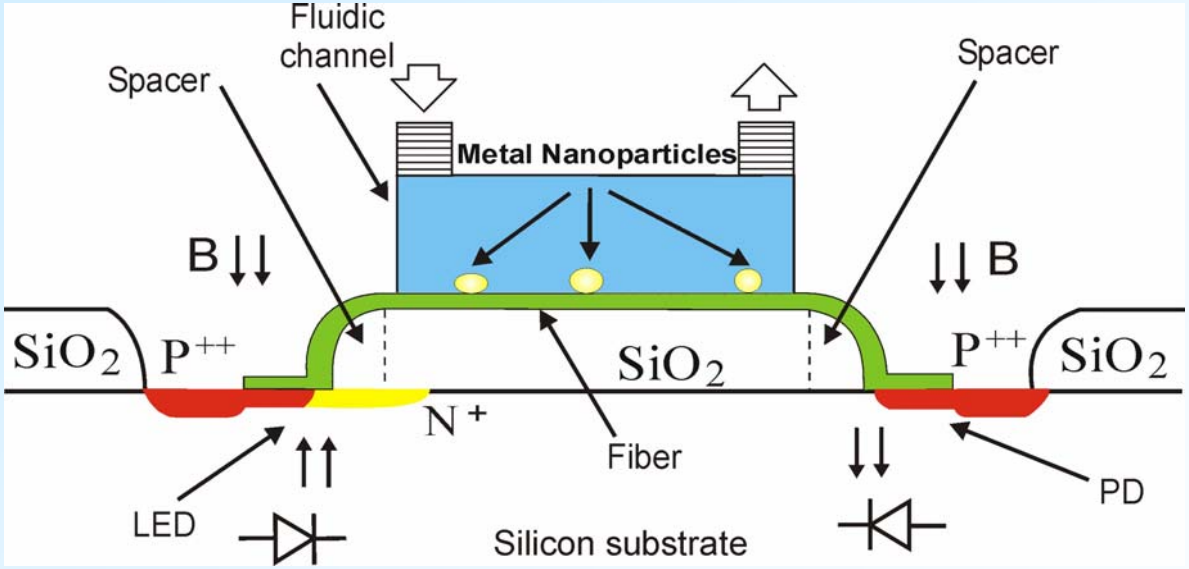
Wafer Mapping

BIOMIC Project

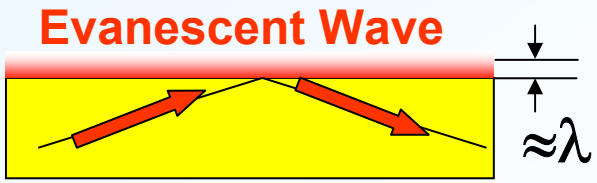
A1 V2 wafer map.

Code: 0 means all 9 fibers good
1 means all 9 fibers good except for 1.

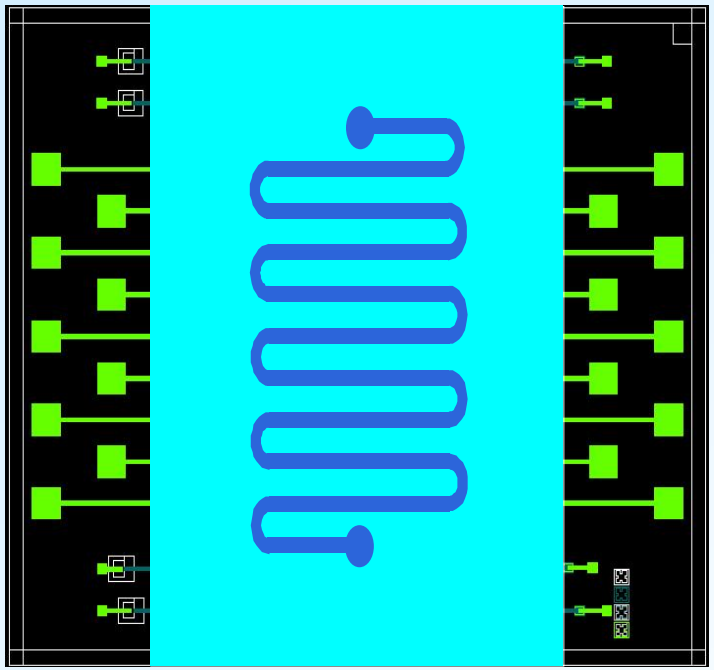
OPTOCOUPLER IS CONVERTED TO BIOSENSOR AFTER SURFACE ACTIVATIO OF THE NITRIDE FIBER BY APTES AND THEN BY THE COATING OF THE BIOMOLECULAR PROBE. GOLD NANOPARTICLE LABELS EMPLOYED

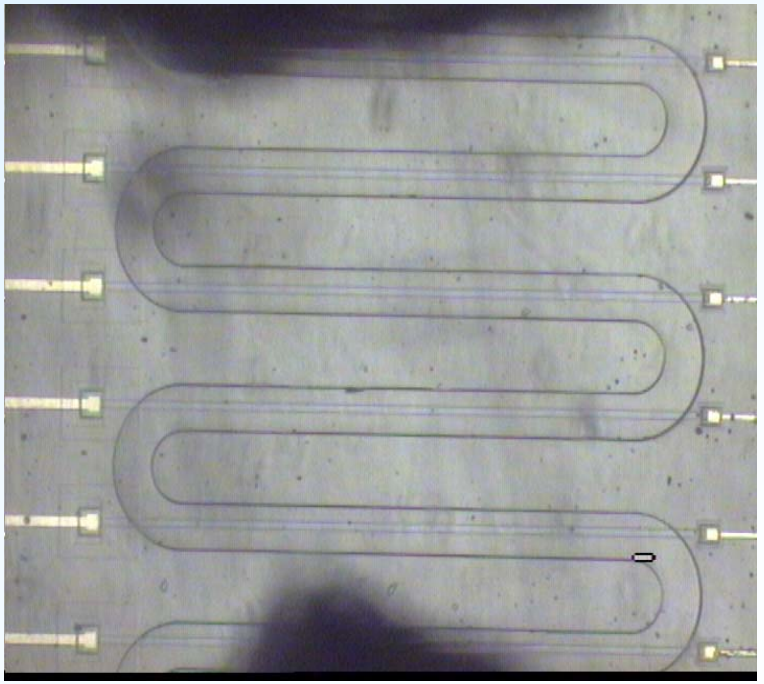


$$\Delta z = \frac{\lambda}{2\pi\sqrt{N^2 - n^2}}$$

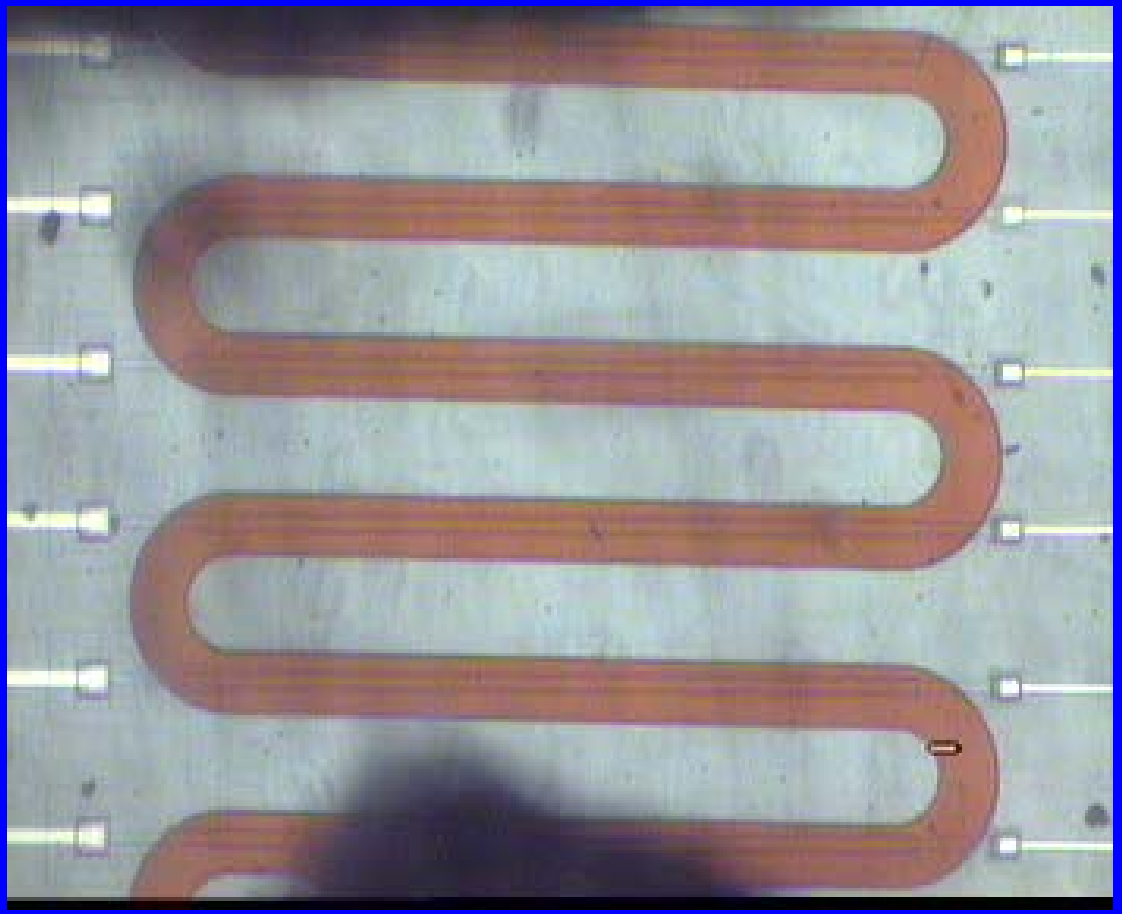


BIOSENSOR CHIP LAYOUT: NINE MONOLITHIC OPTOCOUPLERS+ SELECTIVE BIOAFFINITY LAYERS+ MICROFLUIDIC MODULE

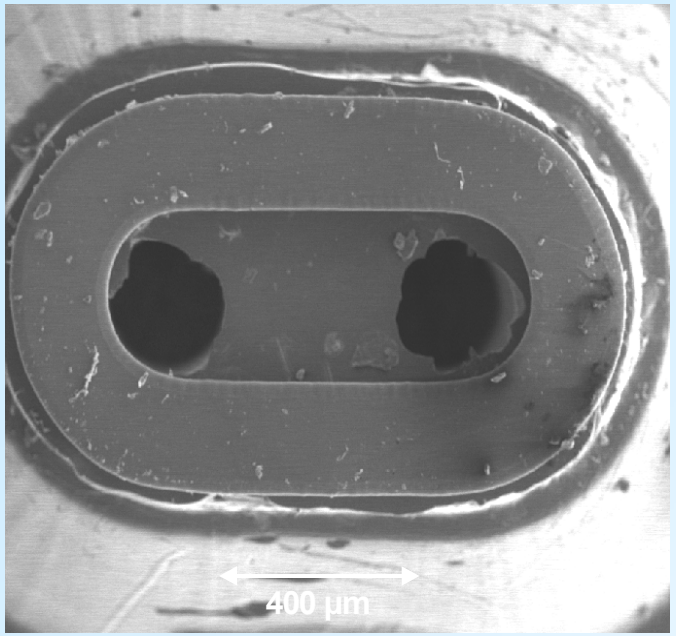


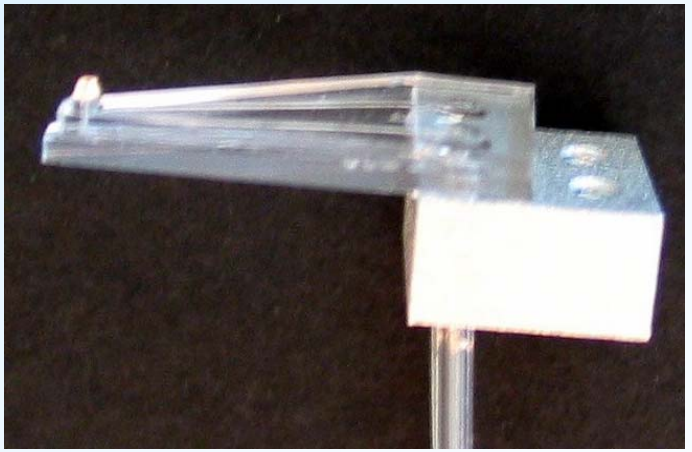


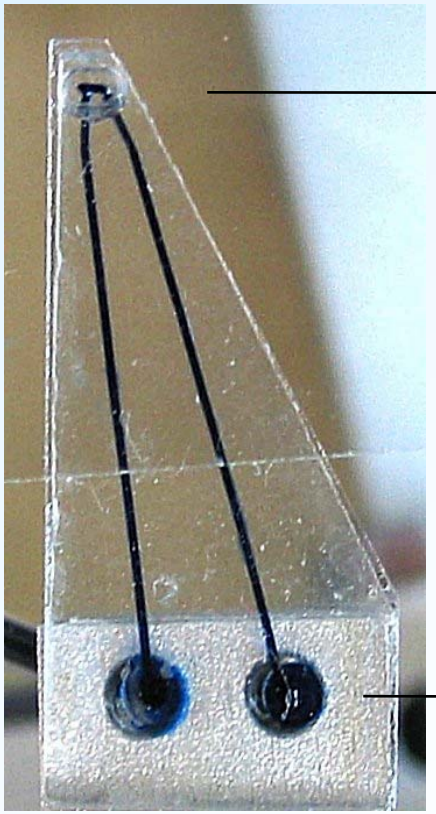
MICROFLUIDIC COUPLING



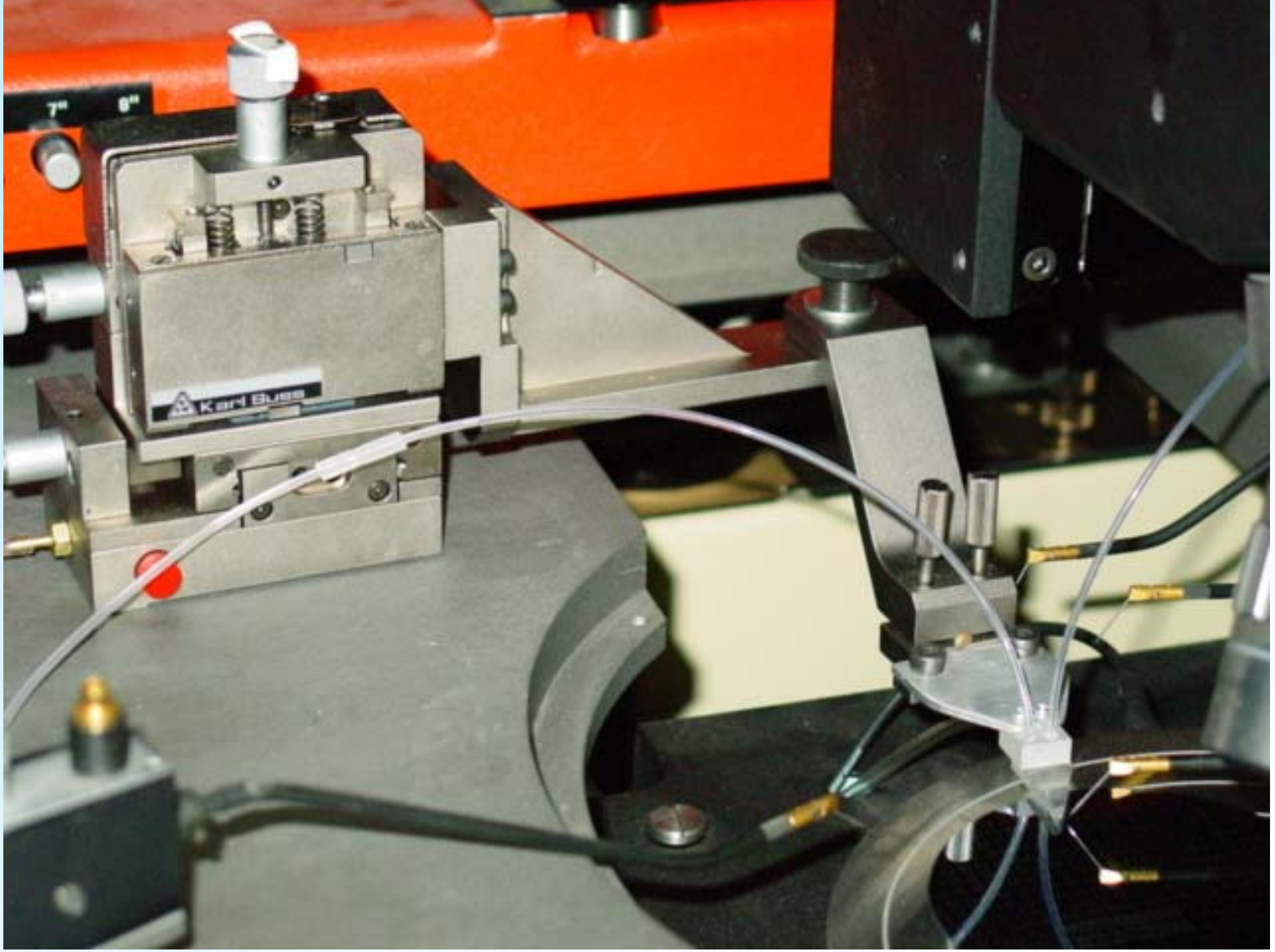
Fluidic Tip for Test Devices







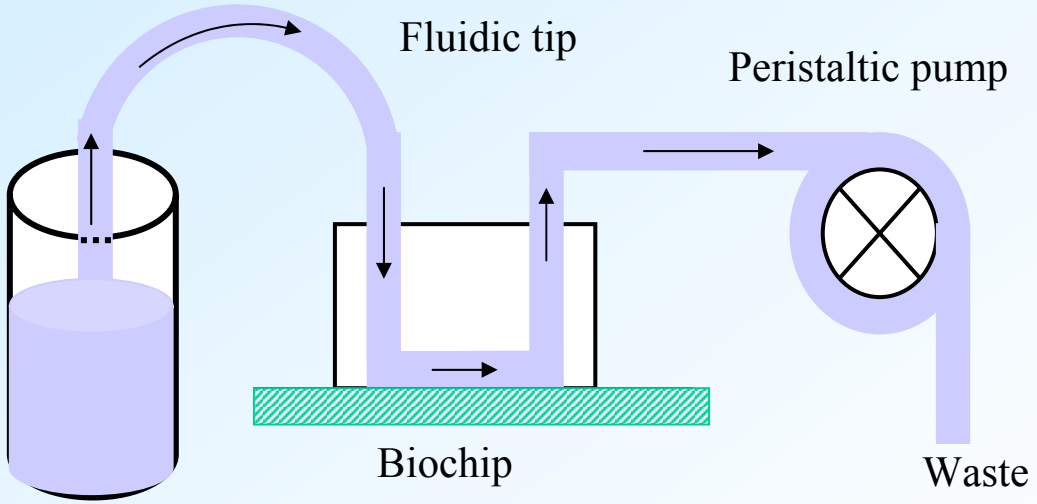
BIOMIC Project



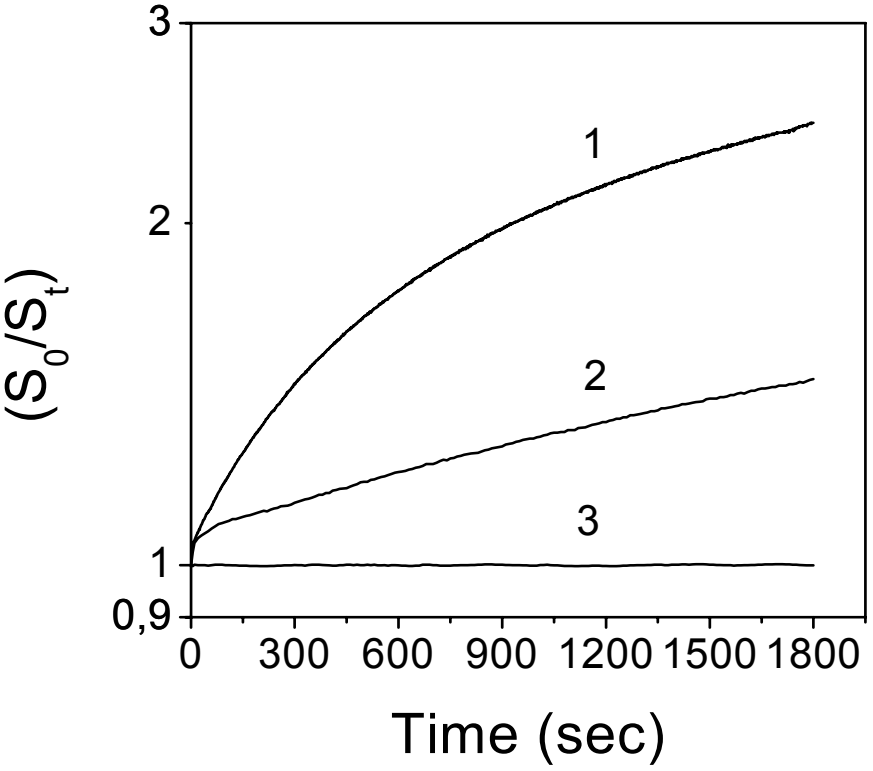
Testing in wafer prober

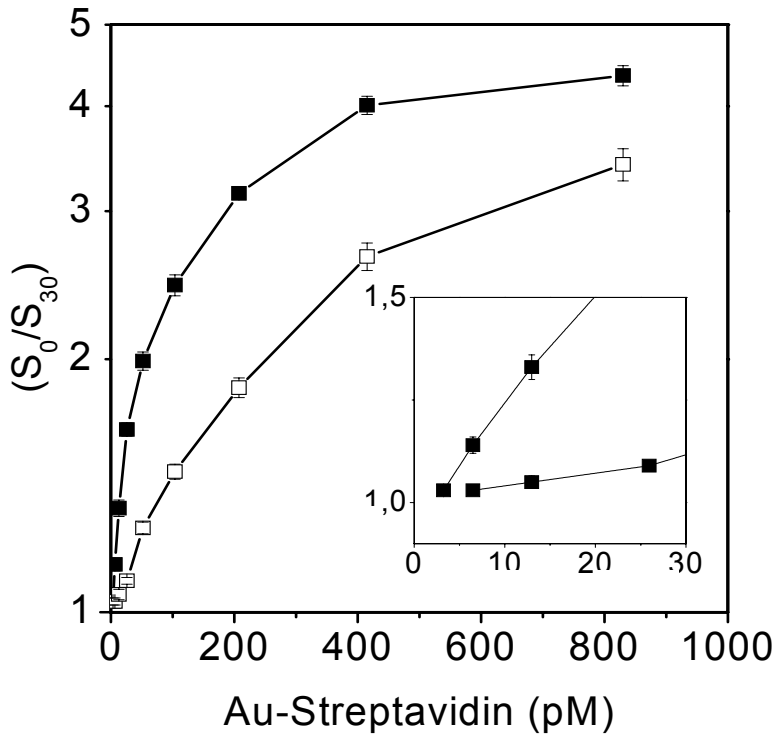
BIOMIC Project

Fluidic Diagram



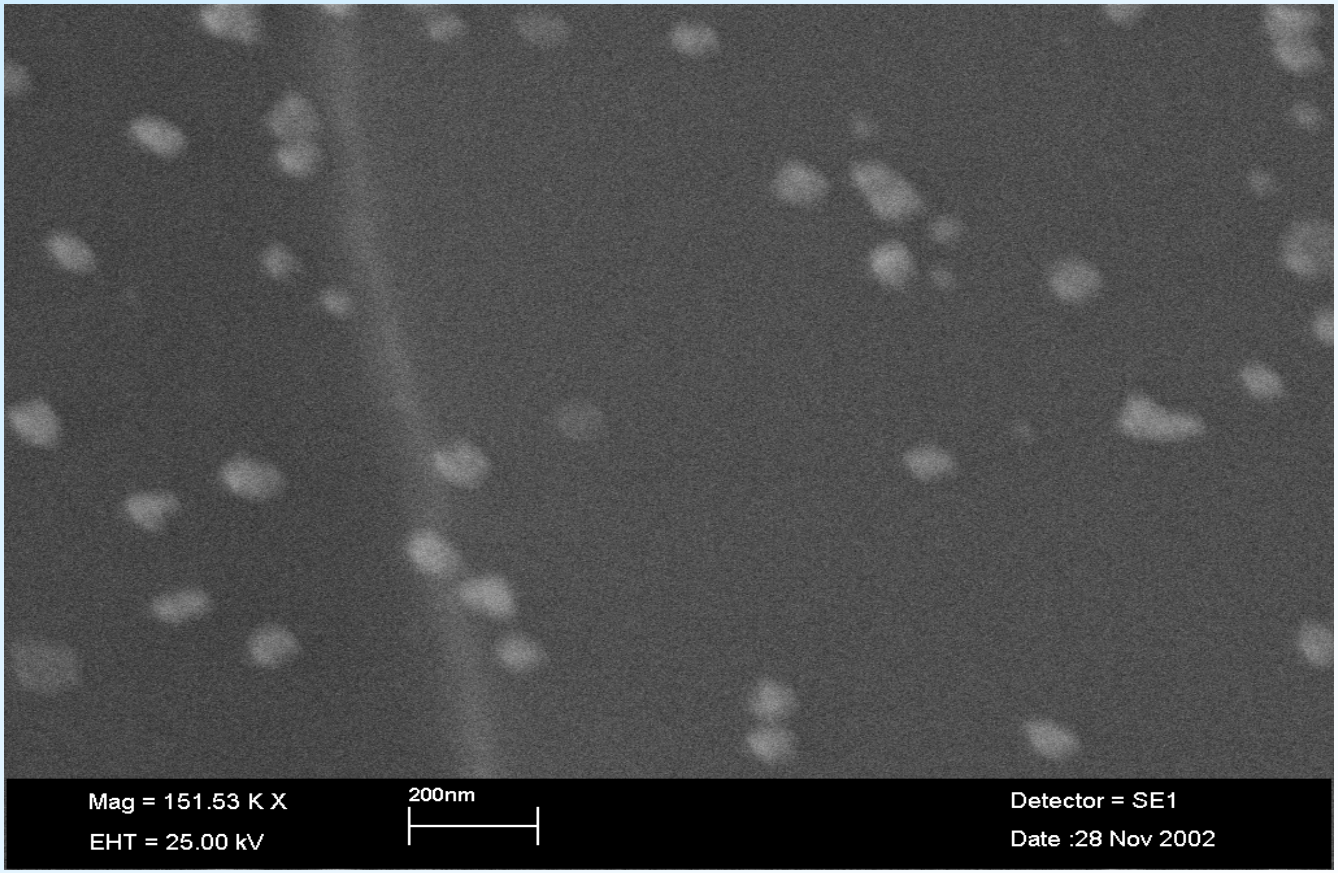
BIOMIC Project





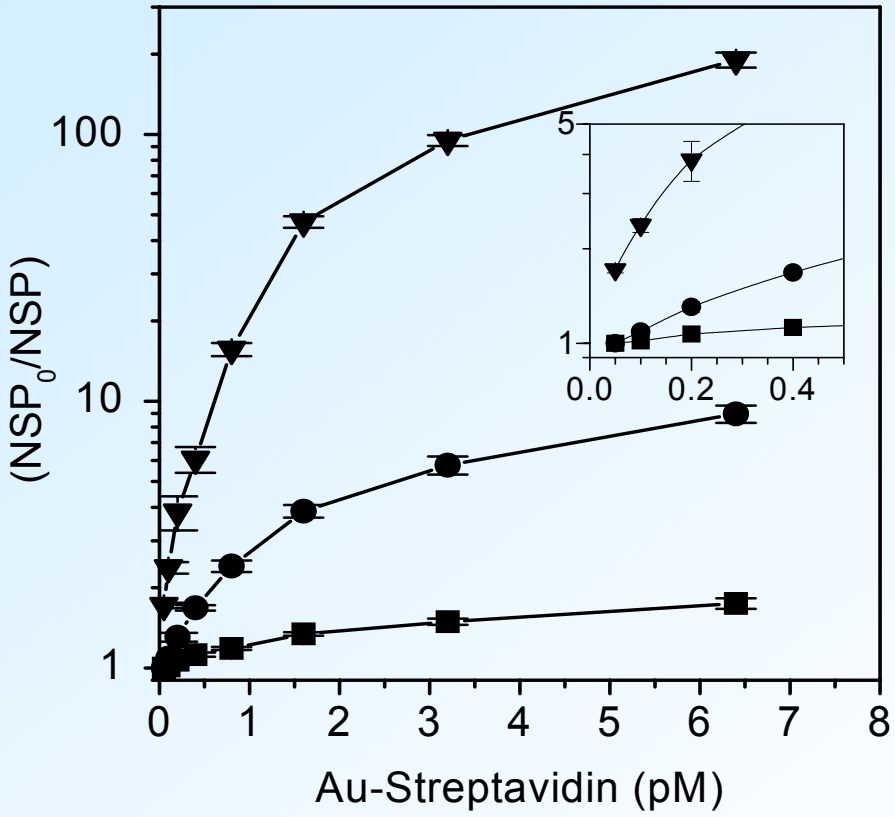
Biotin-Streptavidin model assay

Silver Plating to Increase Sensitivity

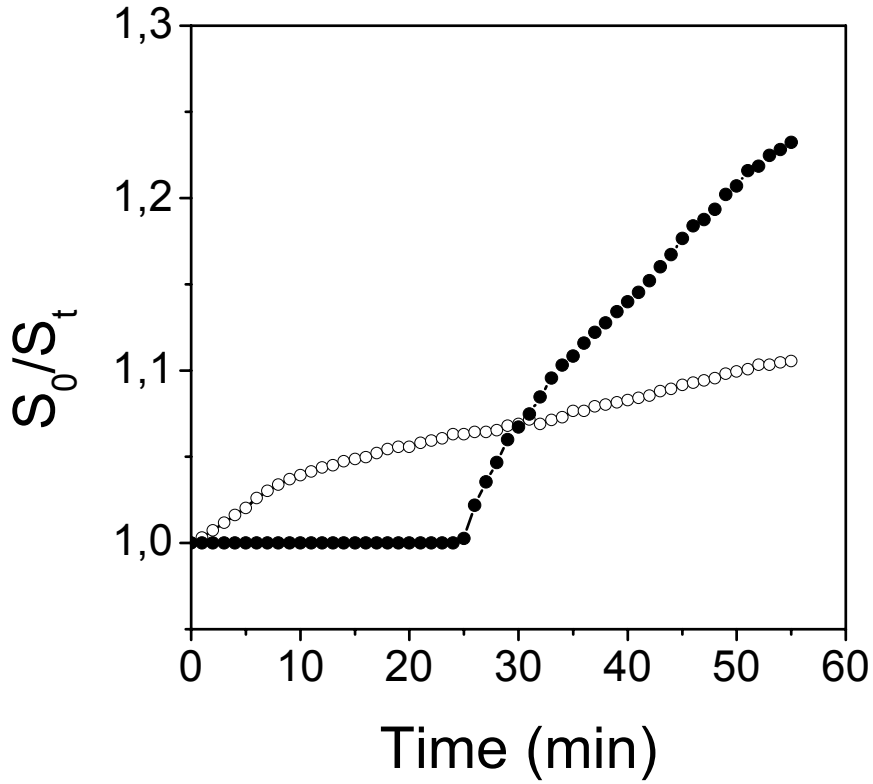


SEM: Silver Plating, Gold, 1/10.000

sensitivity enhancement

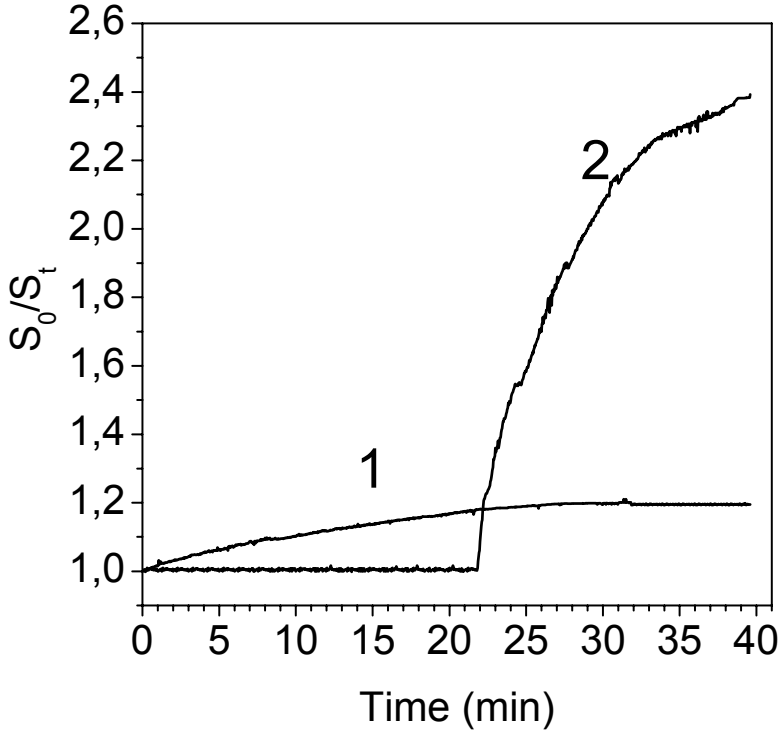


silver plating: 5, 10, 20 min



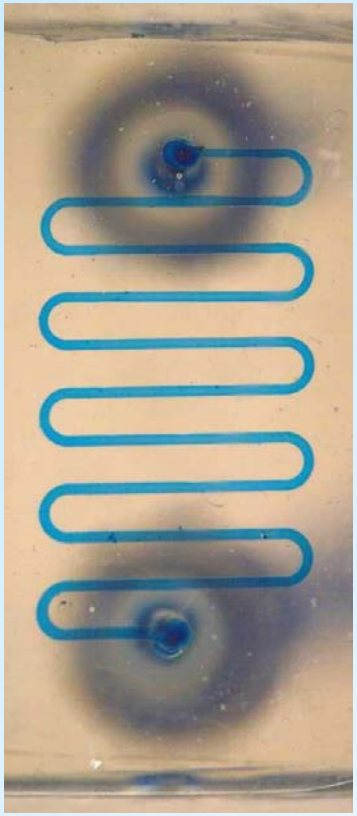
Real time dual analyte assay.

nM Au-anti-mIgG solution for 25 min, 52 pM Au-streptavidin (●

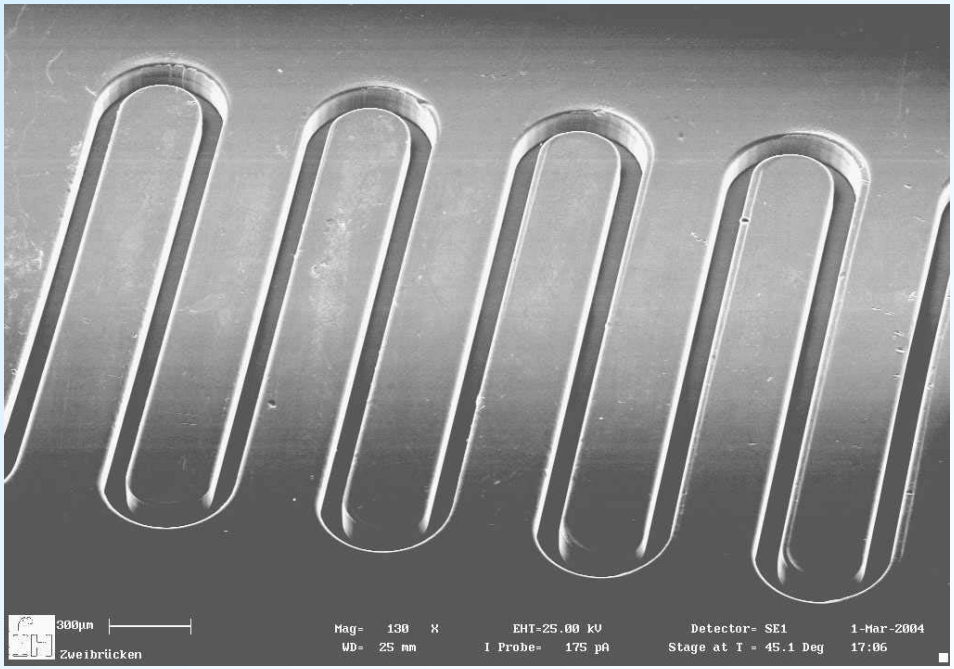


Real time dual analyte assay:

1 nM Au-anti-I Rabbit IgG solution for 25 min, 104 pM Au-streptavidin

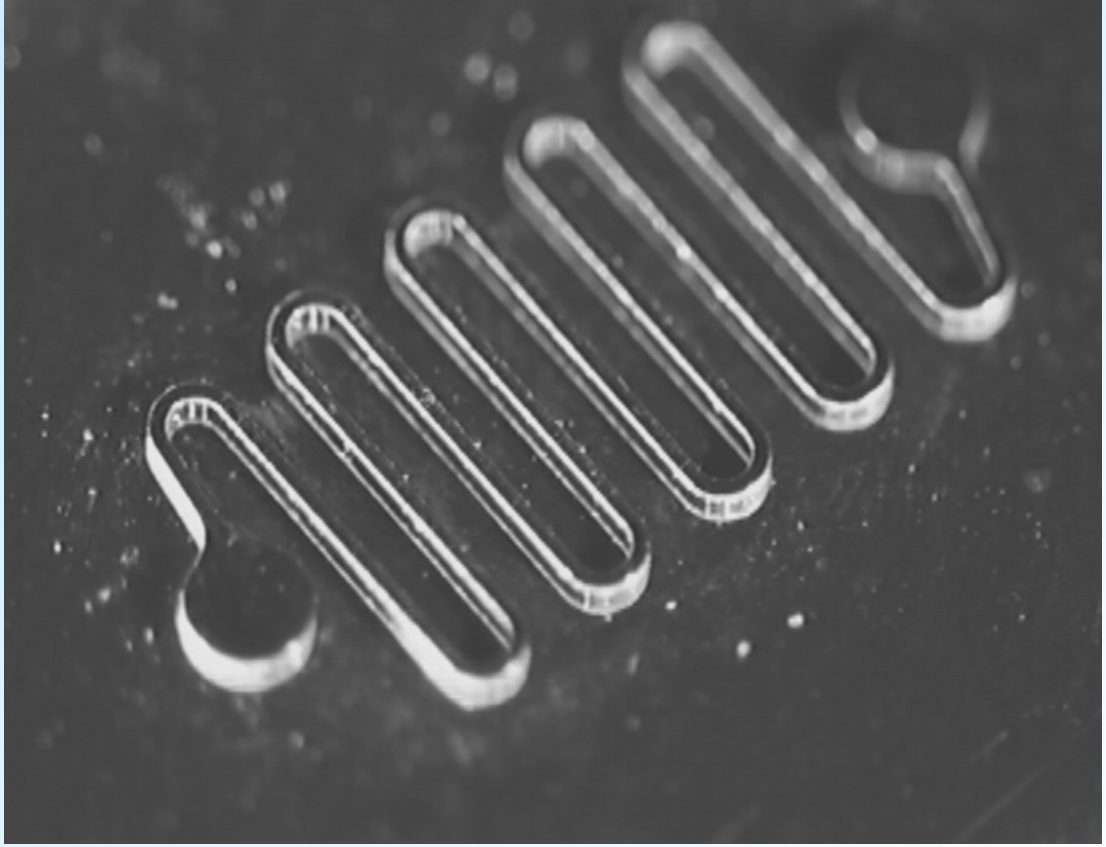


PDMS Fluidics



SEM of injection molded fluidic module

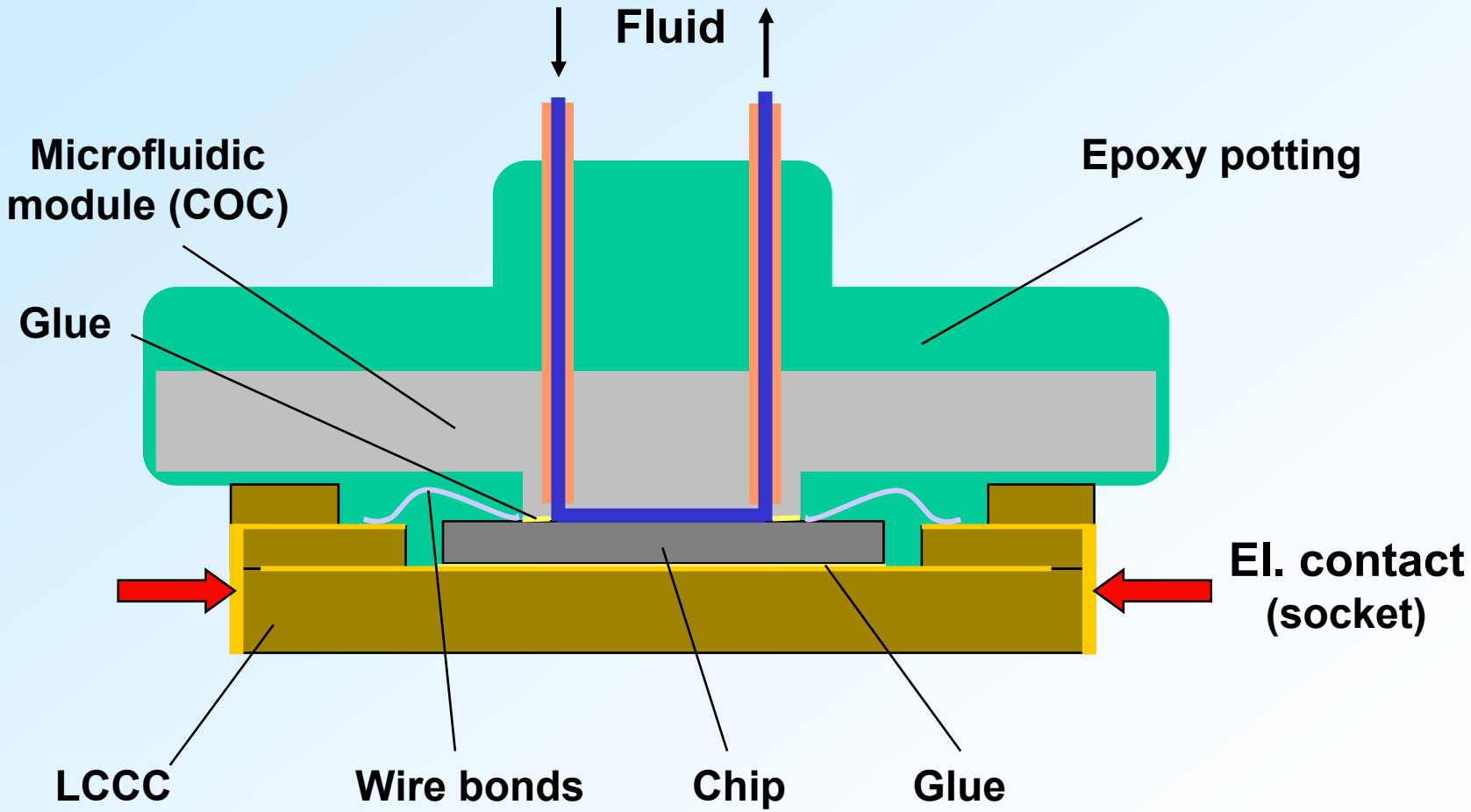
BIOMIC Project



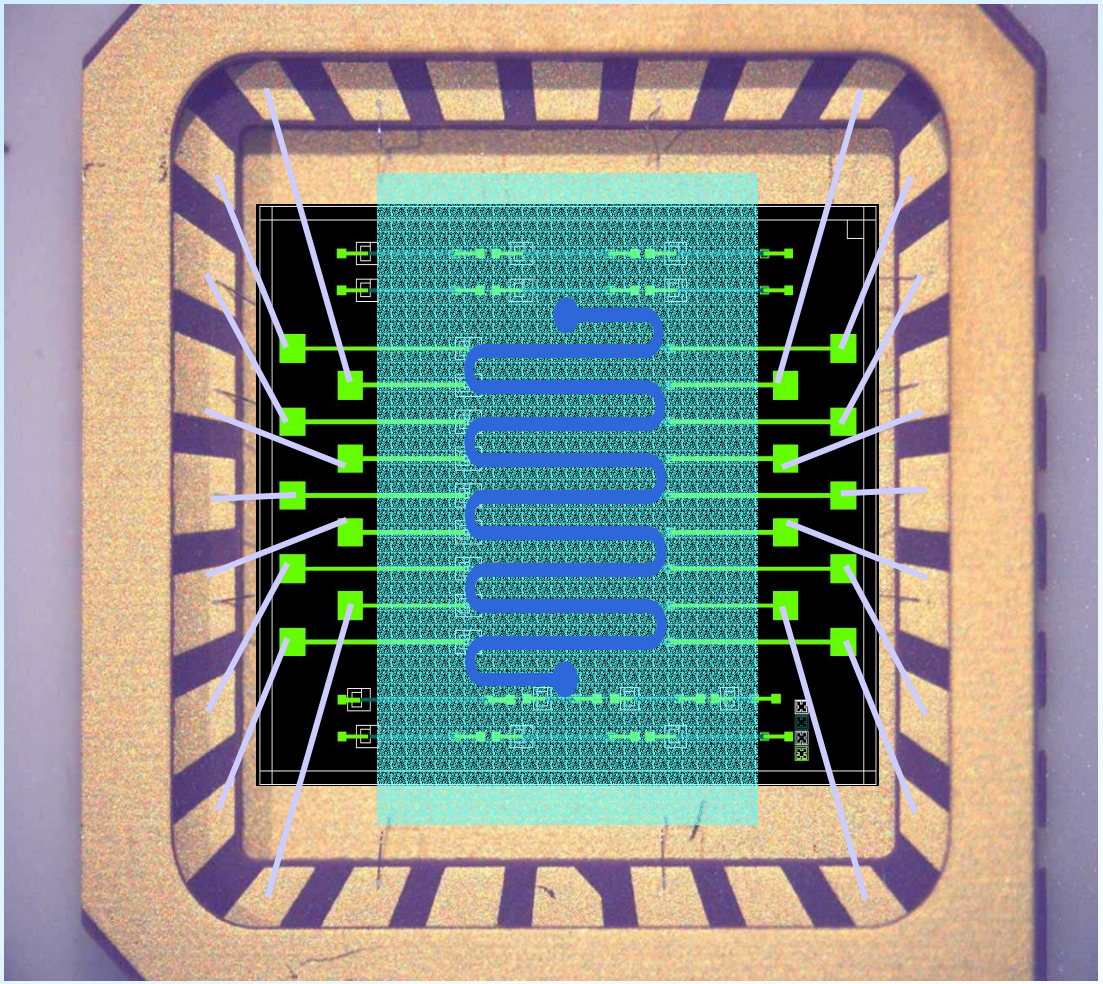
Micro-machined Nickel Mould insert for injection moulding of the fluidic structure

BIOMIC Project

Packaging with LCCC



BIOMIC Project



Fluid Footprint and Wire-Bonding Scheme

BIOMIC Project

Packaging of Optoelectronic Biochip

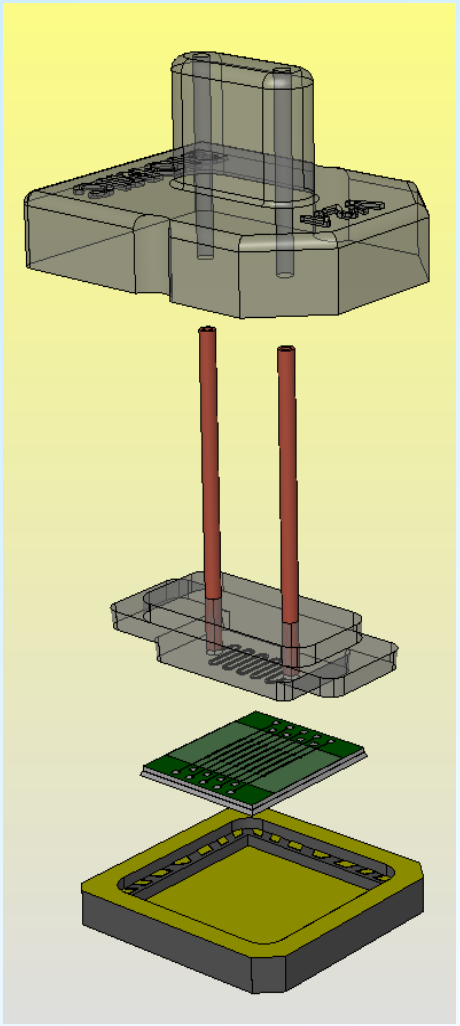
Components

Case

Injection molded microfluidic module

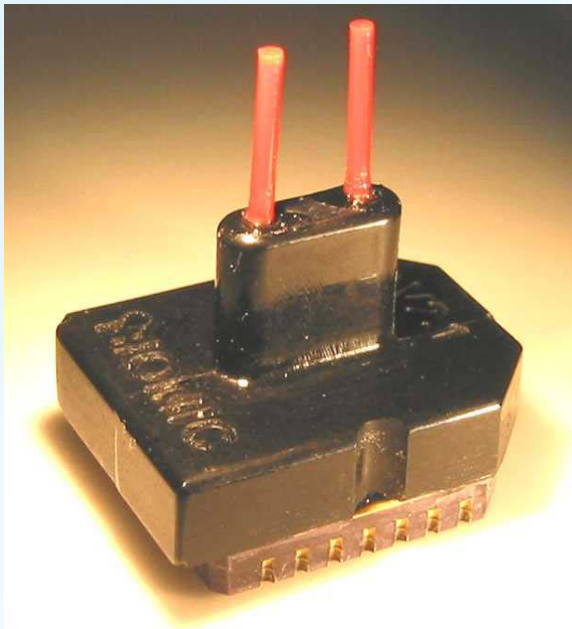
Biochip

Chip carrier LCCC



Processes

Potting with black epoxy



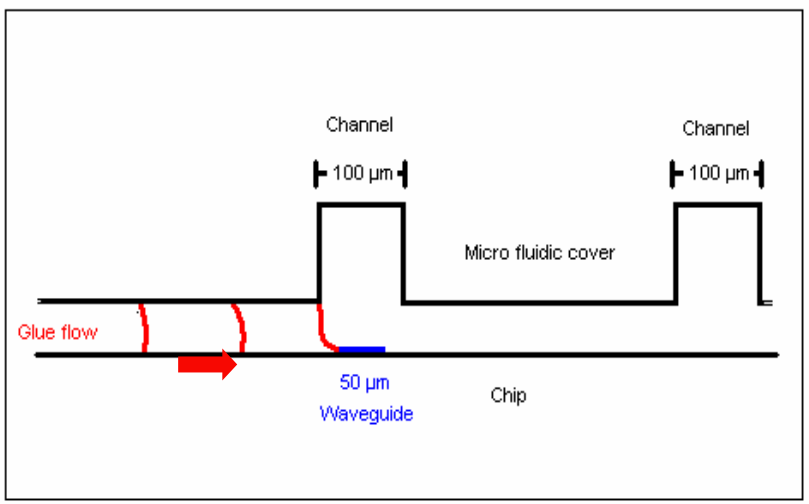
Underfill gluing

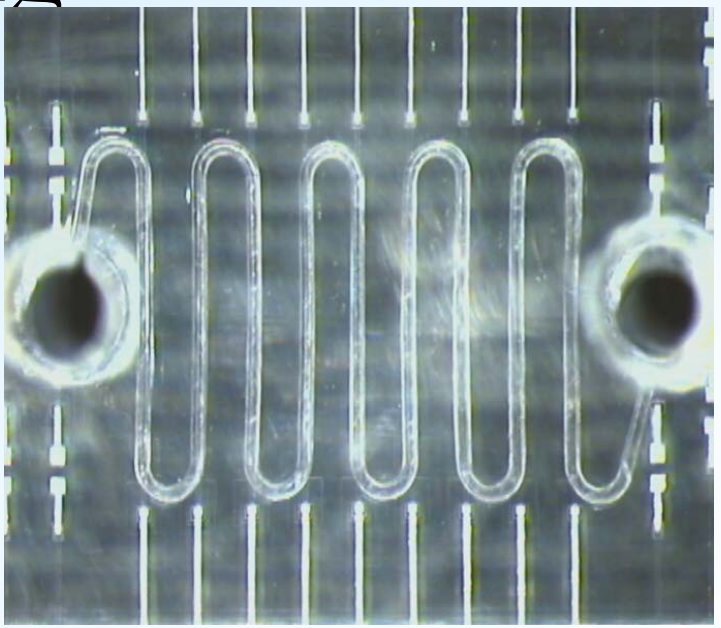
Wire bonding (wedge-wedge)

Conductive gluing of chip into carrier

BIOMIC Projec

Microfluidic Module Gluing





Underfill or capillary gluing

Glued onto chip

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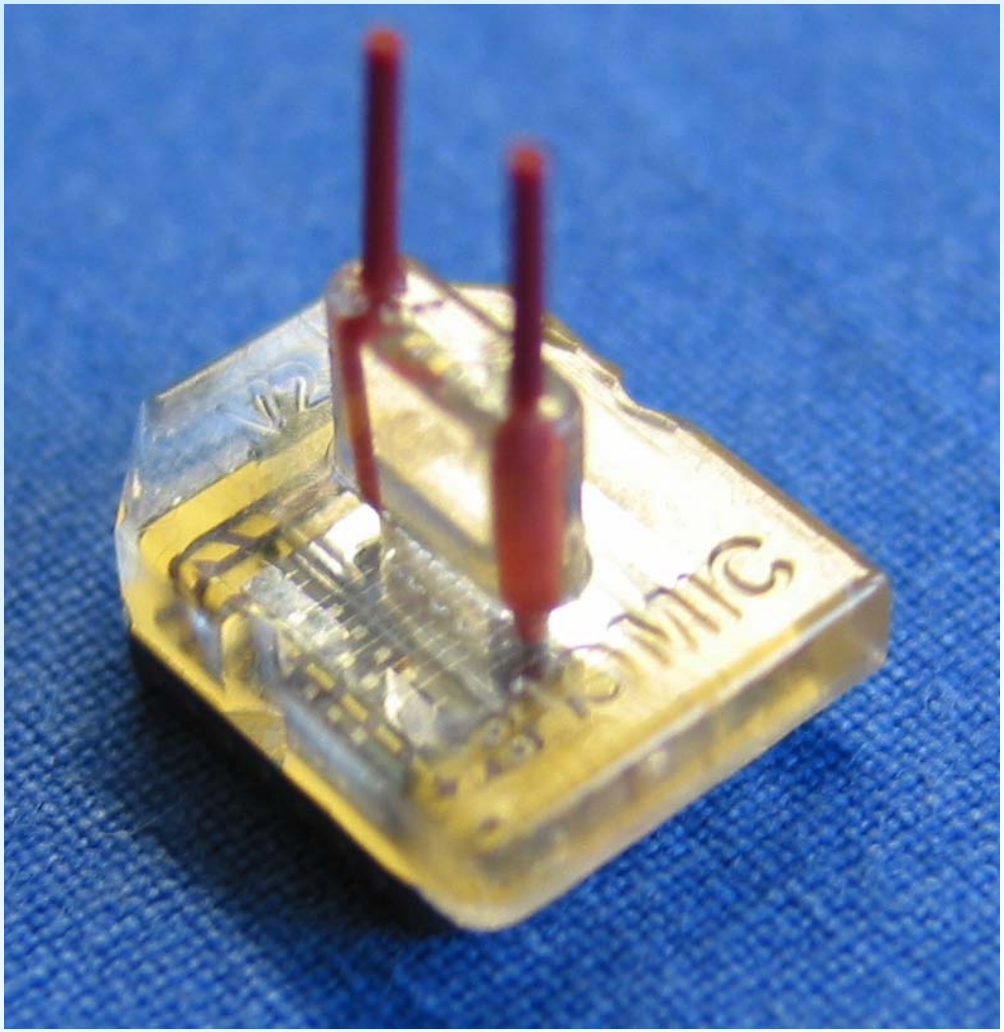
Packaged Chips



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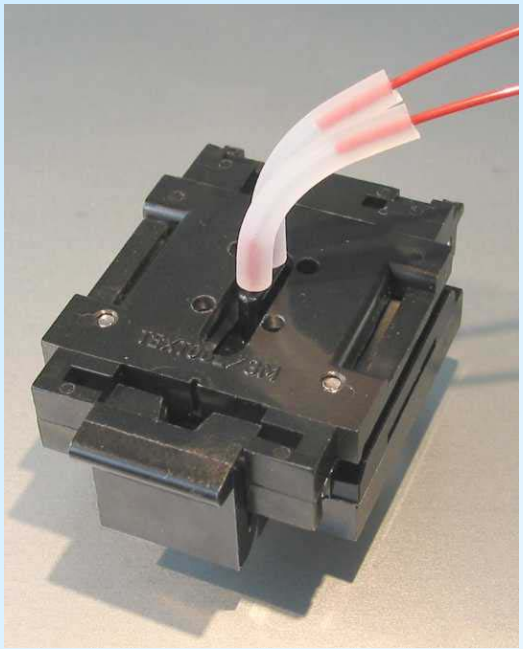
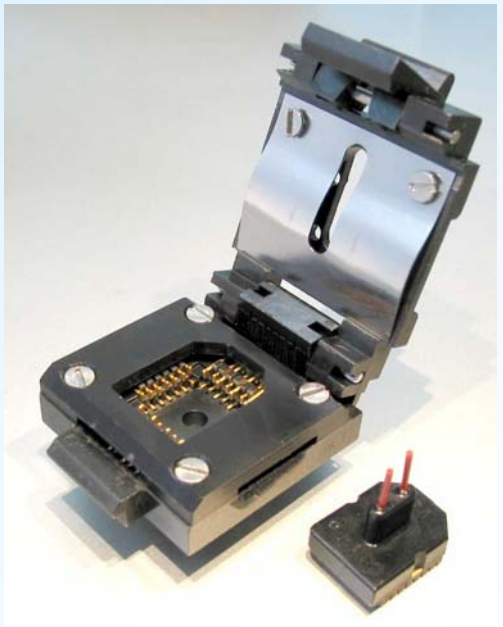
ADAPTATION OF TEST SOCKET





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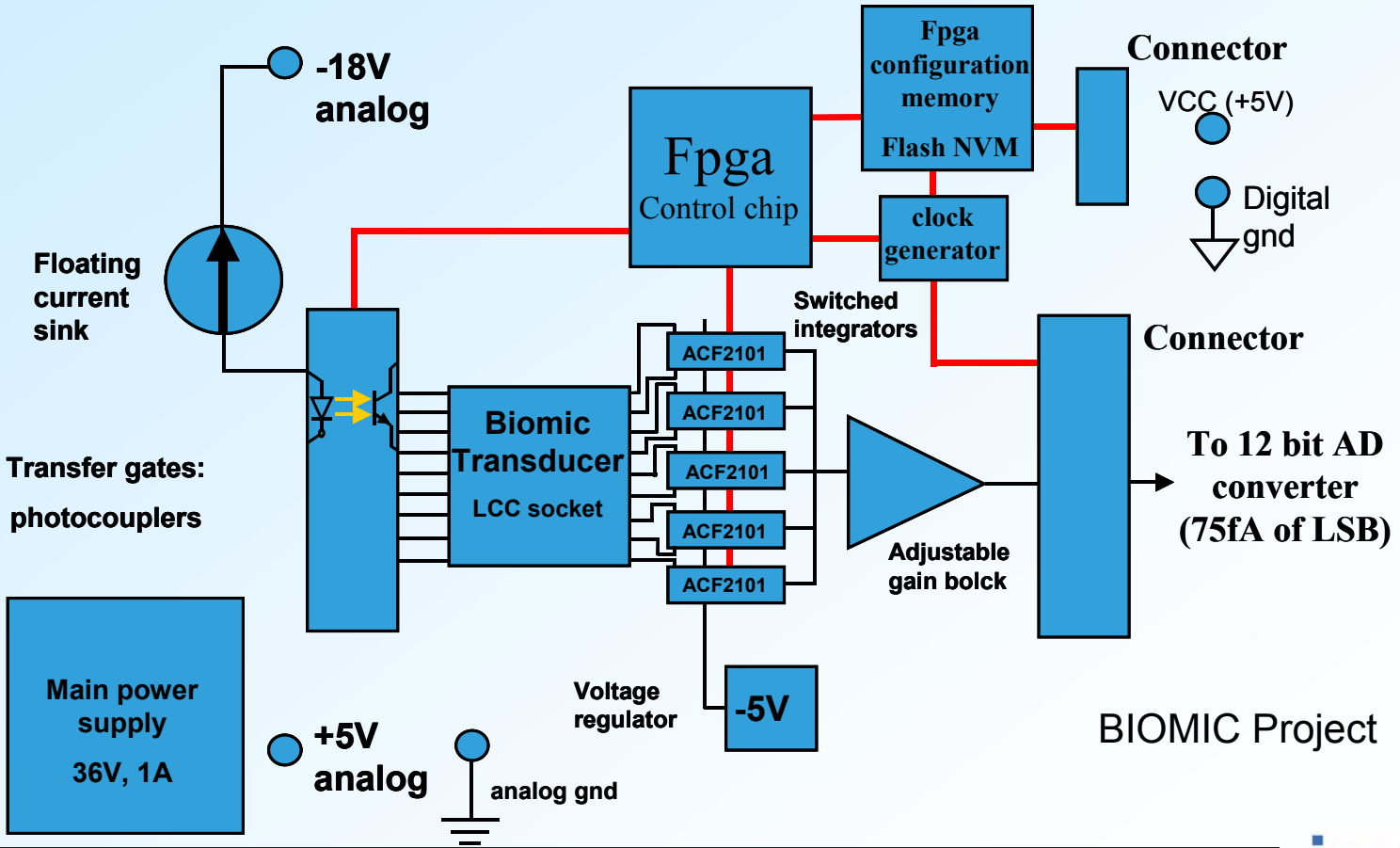
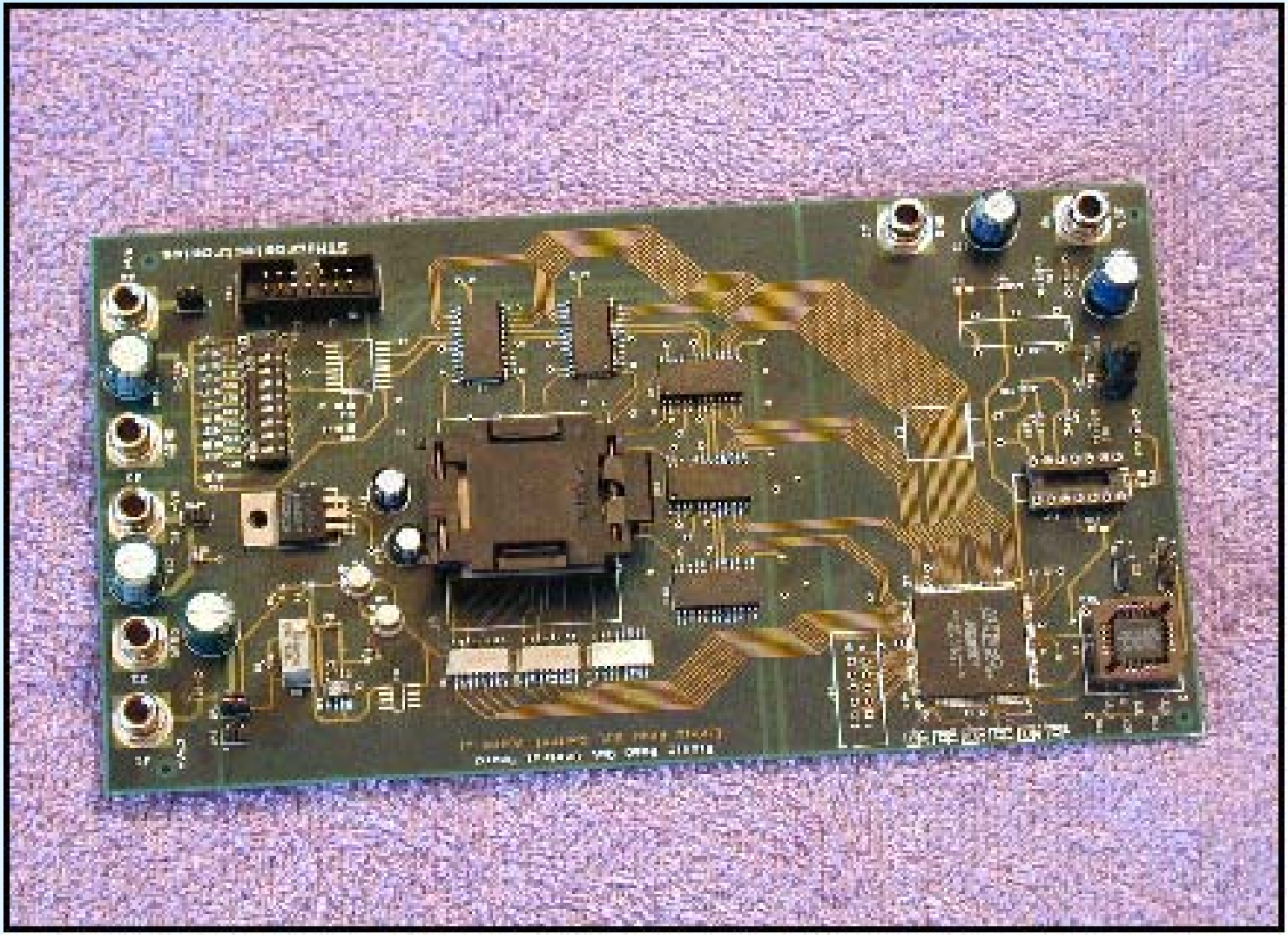
SCHEMATIC OF READOUT ELECTRONICS

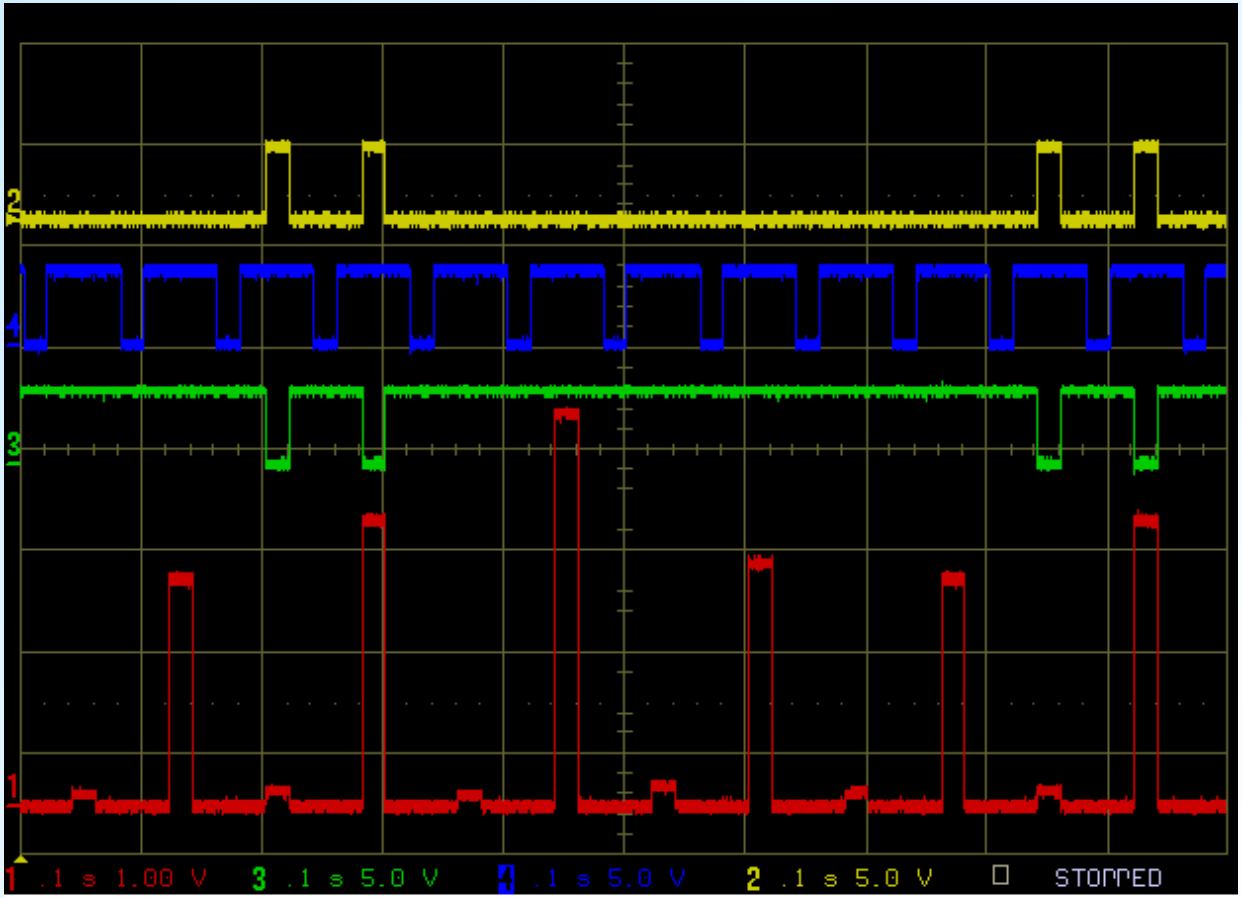


READ-OUT ELECTRONICS FOR PORTABLE BIOANALYTICAL MICROSYSTEM



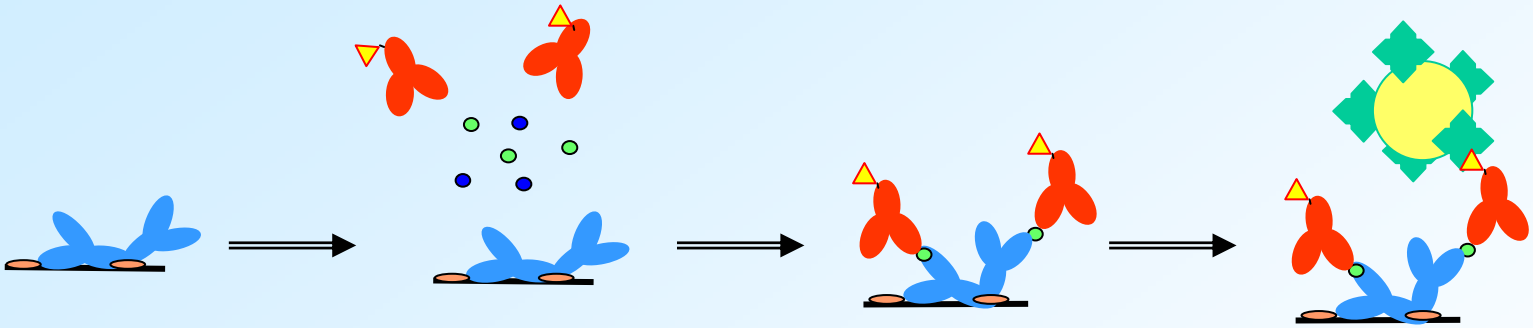
BIOMIC Proje

MULTIPLEXED SIGNAL SEQUENCE OF THE NINE OPTOCOUPLERS



BIOMIC Proje

Non-competitive assay configuration



Coating antibody

biotinylated antibody

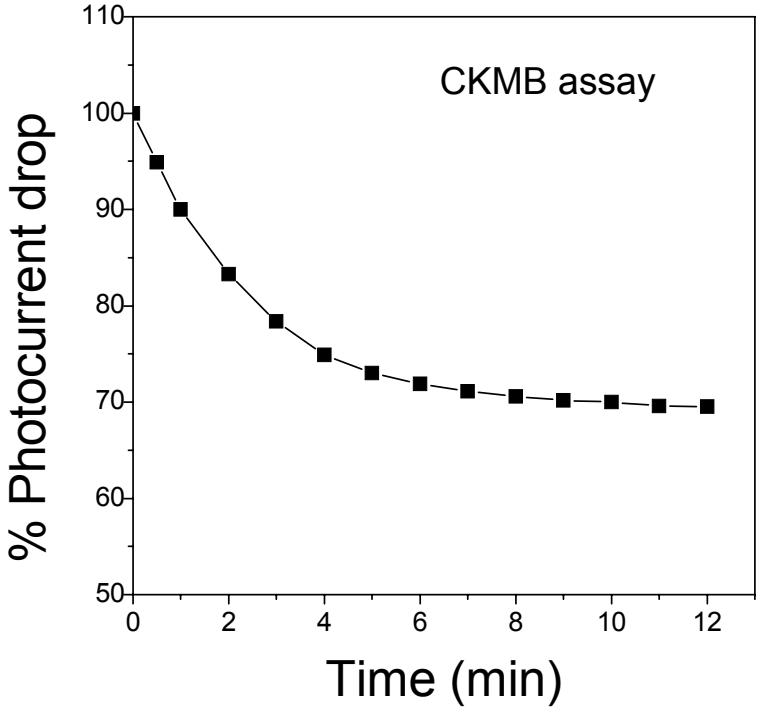
Gold labelled strepavidin

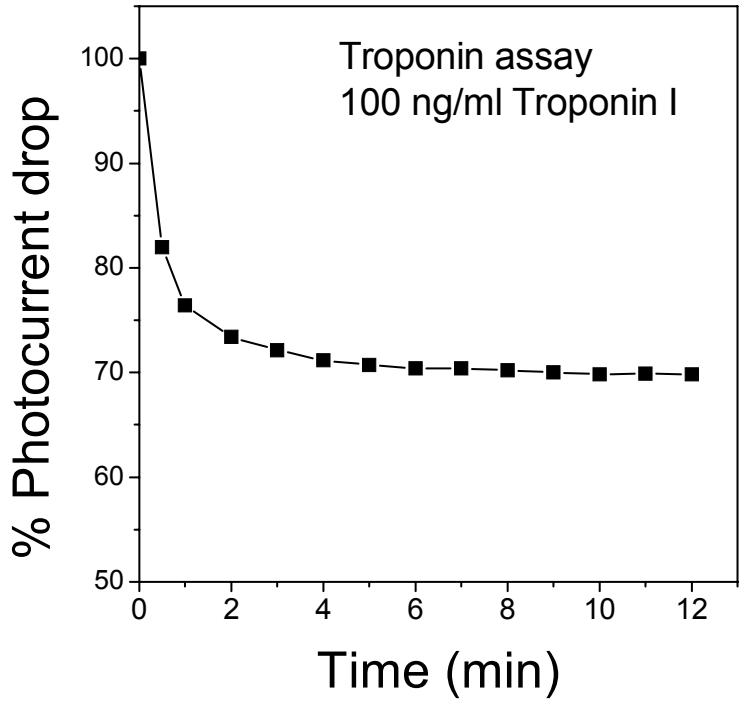
Blocking agent

Other analyte

Determined analyte

Detection of Cardiac Markers





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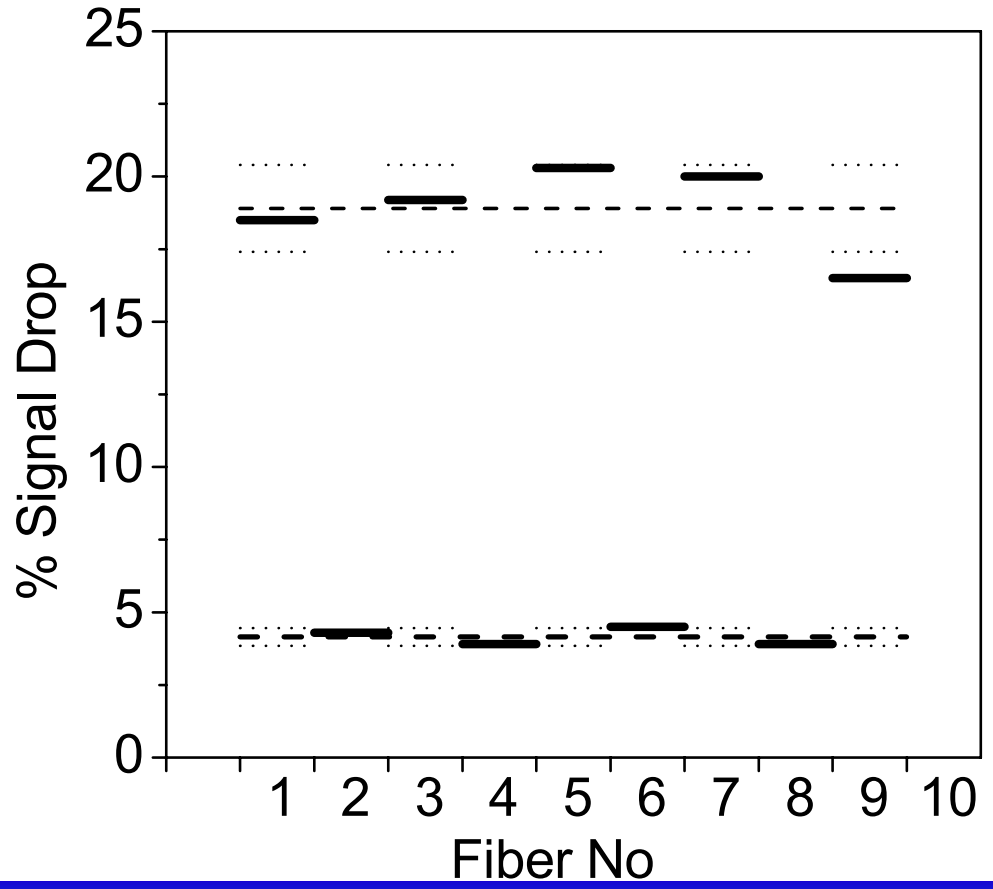
Coating: 5 mg/L Mab anti-CKMB, 1 h, RT

Assay: 1:1 standard solution 300ng/mL, CKMB:biotinylated Mab anti-CKMB 2.5 mg/L, RT Detection: Streptavidin Gold labeled (8.4 nm) (no silver plating)

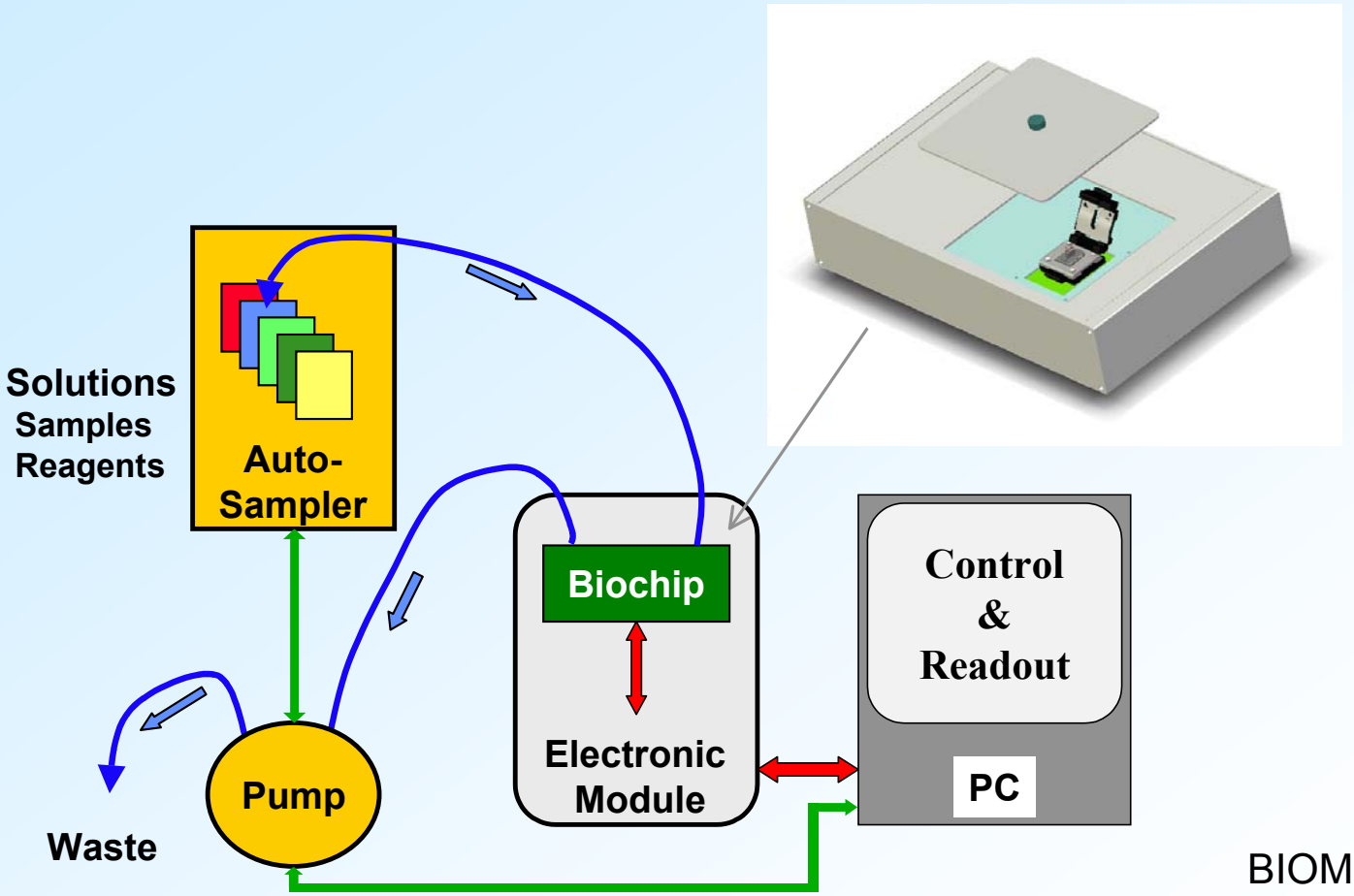
SNP DETECTION IN DNA

Odd fibers: wild-type, 5′-Biotin-GCGGGAG**C**GCCCCAC AAACTCCAGGATCTTTTGA-3

Even fibers: mutant, 5′- Biotin-GCGGGAG**T**GCCCCACAAACTC CAGGATCTTTTGA-3′



BIOMIC Project



BIOMIC Project

CONCLUSIONS:

MINIATURIZED MONOLITHIC SILICON OPTOCOUPLERS FOR PORTABLE MULTIANALYTE BIOSENSING