Method of assembly of capacitive bio-sensor for bio-molecules detection

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Overview

- Introduction
- Sensor construction
- Bio-functionalization
- Assembly process flow
- Electrical characterization
- Conclusions

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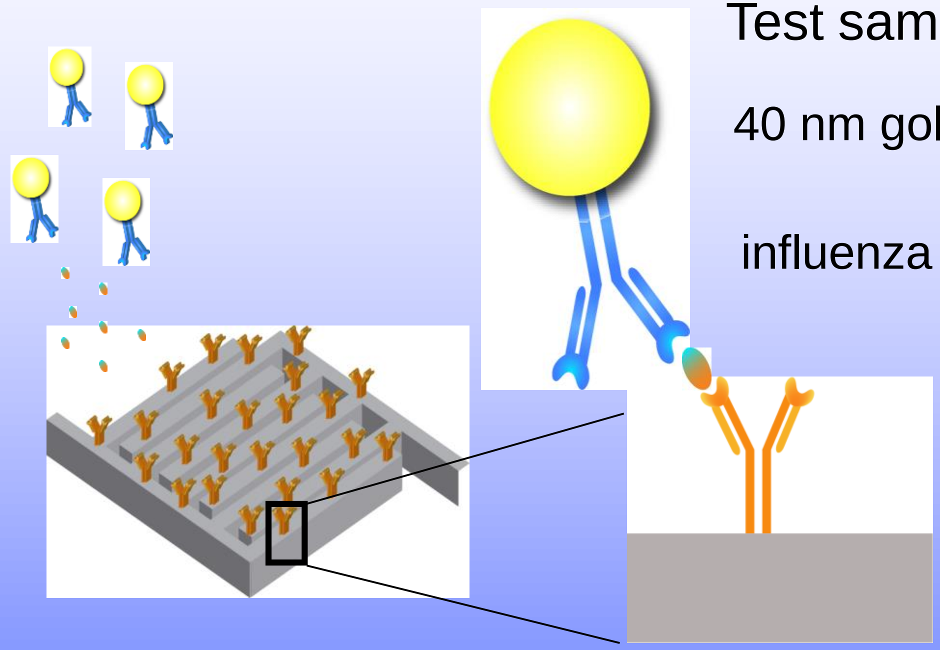
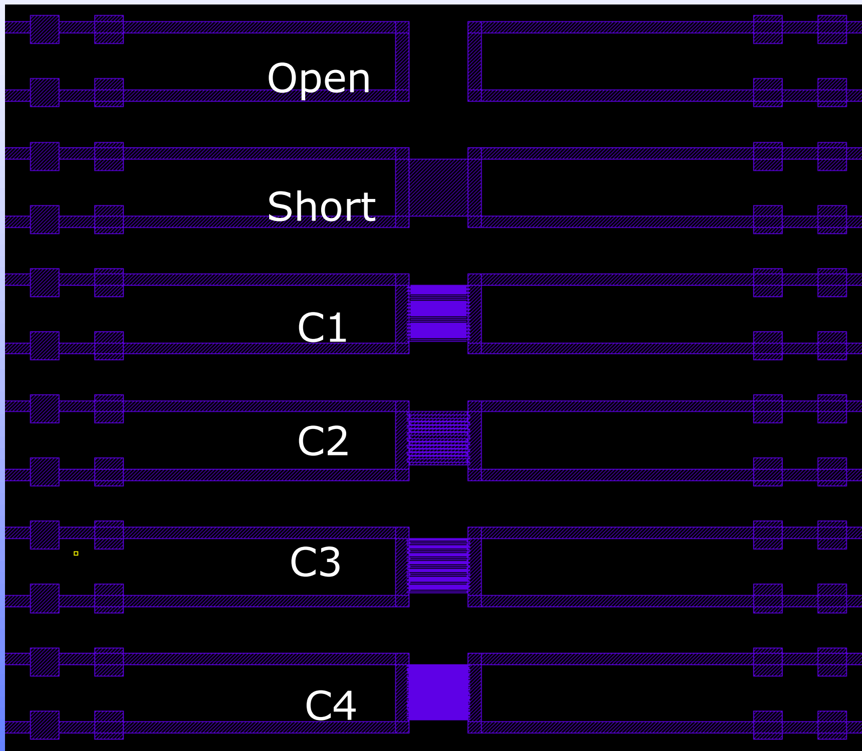
Principe of detection



The inter-digitated array microelectrodes (IDAM) is covered with a bio-functional layer (specific antibody recognizing the nucleoprotein of the Influenza A virus). The registered response is variation of the capacitance and conductivity between the IDAM. To increase the signal a 40 nm gold nano-bead are conjugated with influenza A virus.

Sensor die

Sensor die layout (top view)



Sensing areas (C1…C4) configuration

Sensor	Finger width (µm)	Interspace (µm)
C1	2	4
C2	10	2
C3	5	2
C4	2	2

Si sensor die of 3.2mmx3.2mm with 4 of 200µmx200µm sensing areas (C1…C4) of different configuration IDAM (inter-digitated array microelectrodes)

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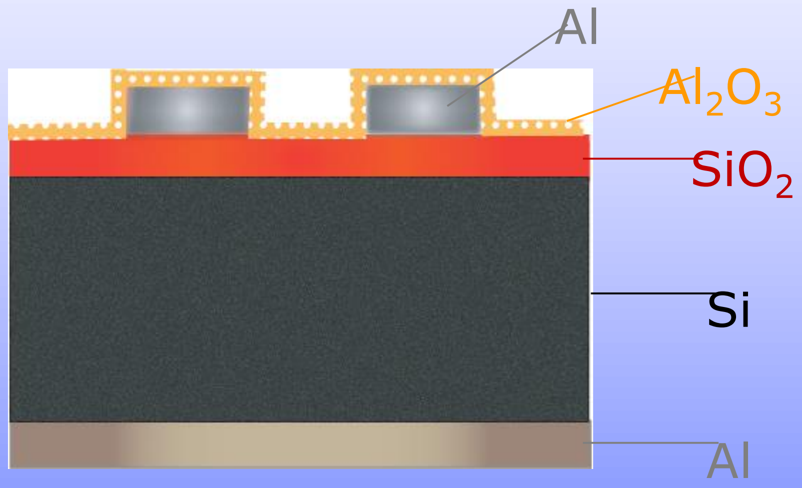
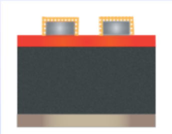
Sensor die cross sectional view



Al=800nm
SiO2=50nm
Si wafer=600µm
Al=400nm

Bio-functionalization



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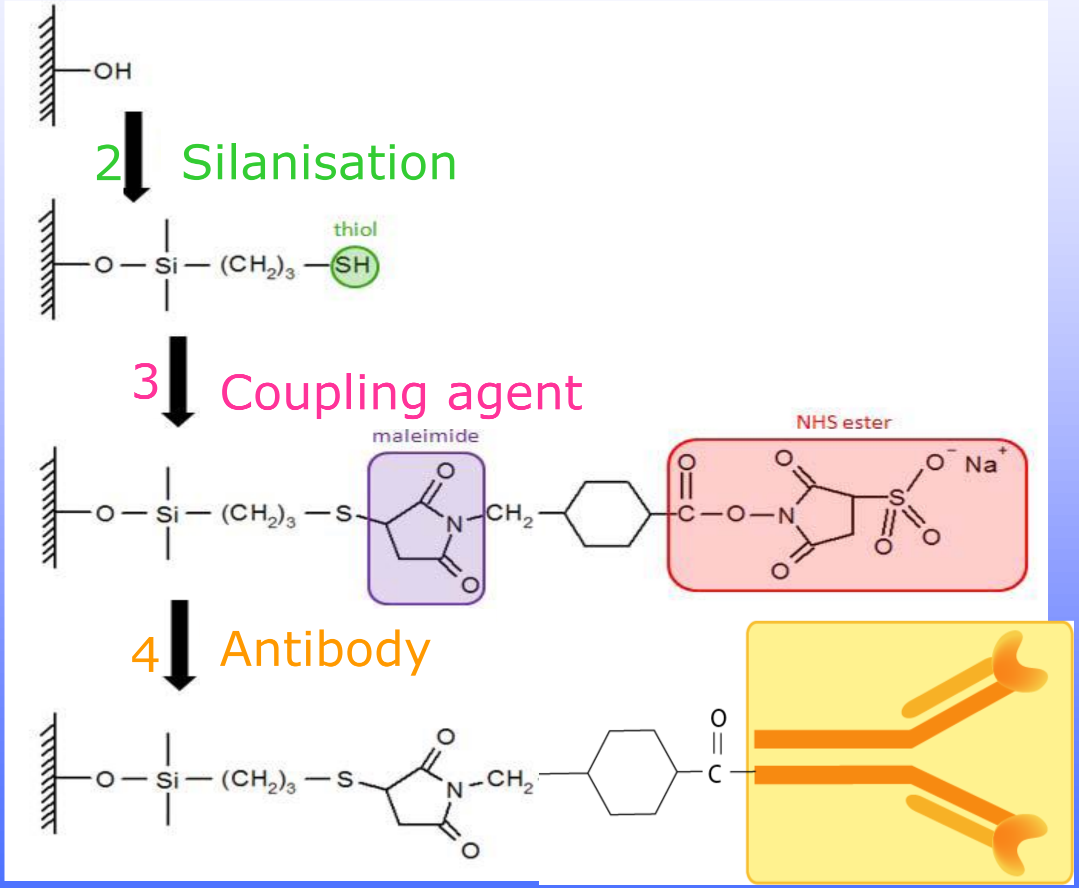
Plasma/O_2 treatment



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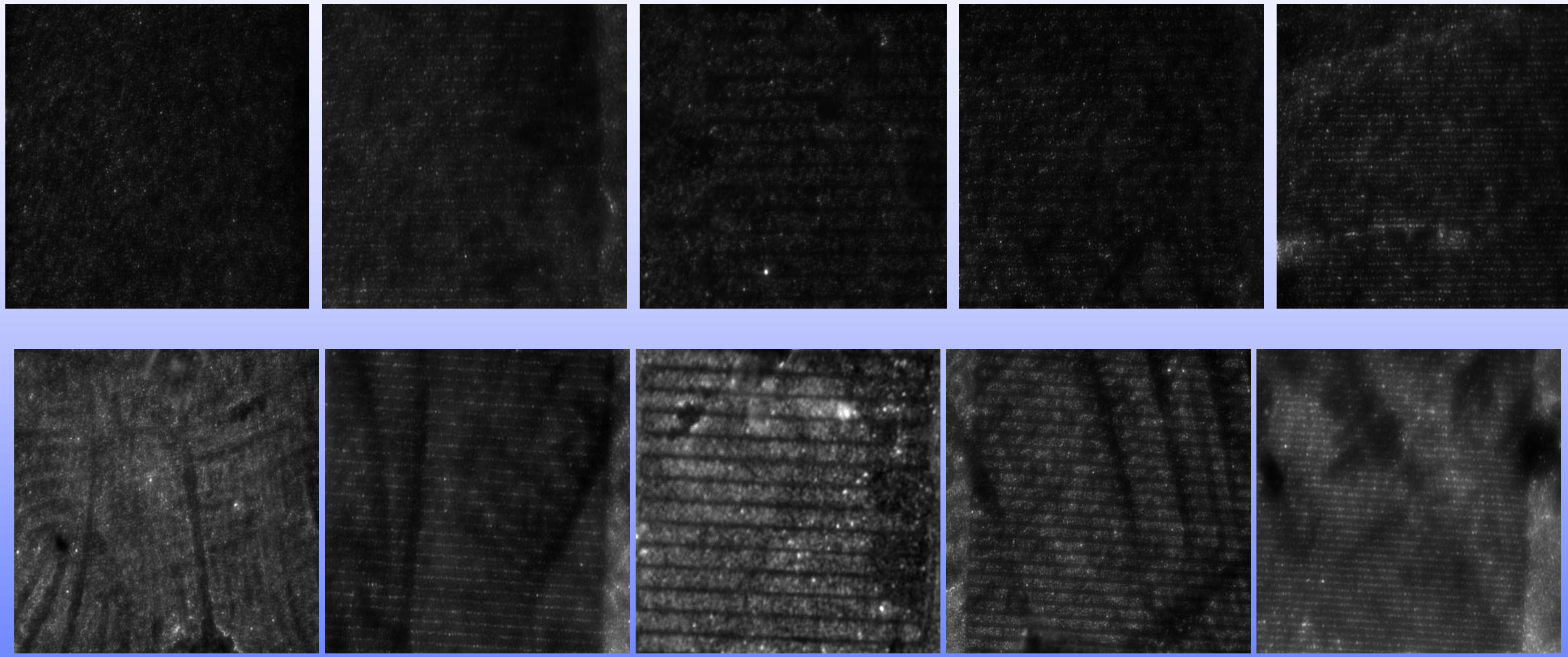
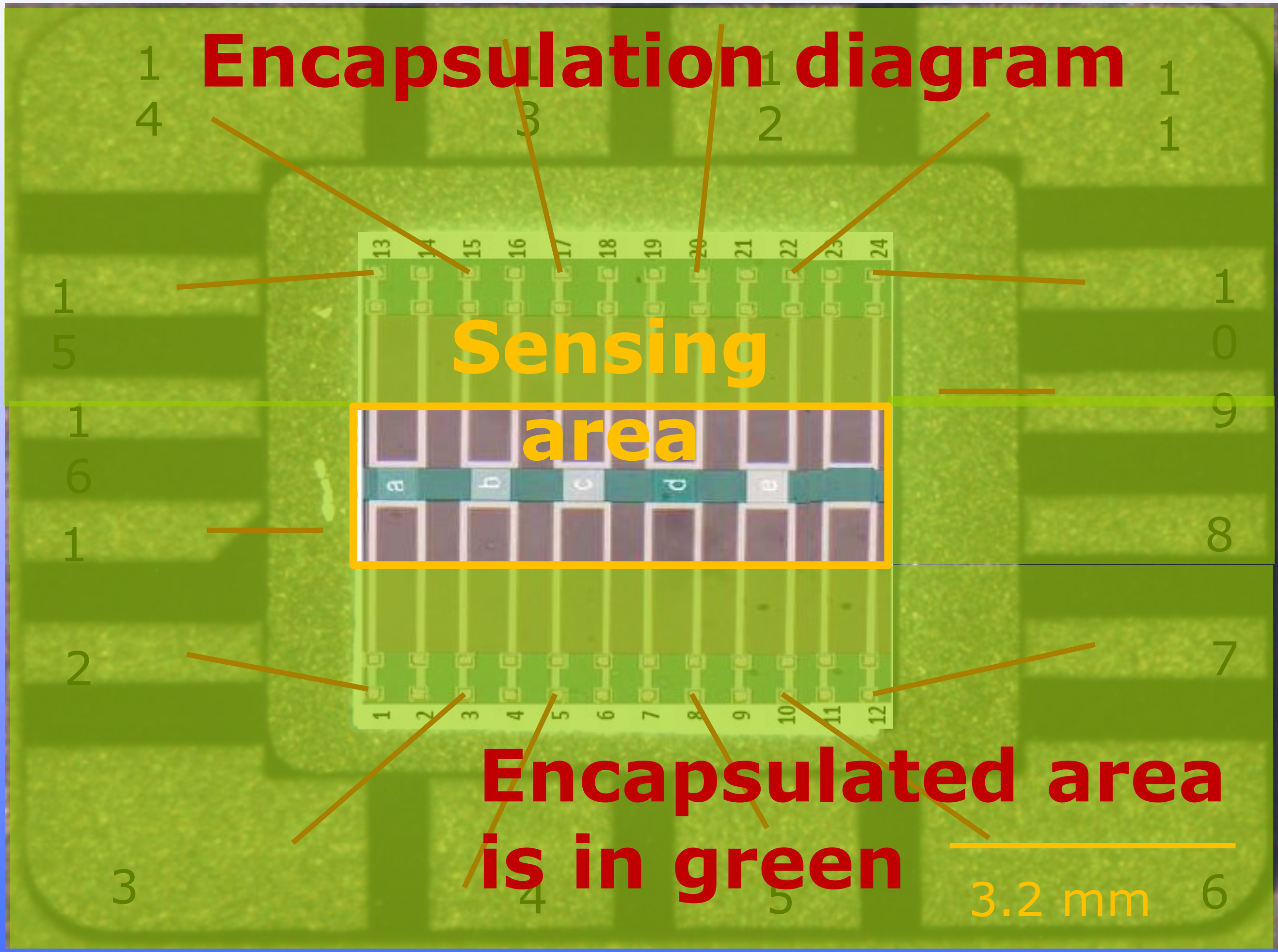
Surface analyses (confocal microscopy)



Confirmation by confocal microscopy of the engraftment of the capture antibody: the signal of the fluorescent marker was observed on every functionalized structure of the chip while a weak fluorescence was distinguishable on the non- functionalized chip.

Assembly schematic view



Sensing channel (configuration of 1mm width x 3 mm length and 0.5 mm high) is to doze 1-1.5 ml volume of the test sample.

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Assembly process flow

- Die attach (mounting the sensor die in the package)
- Wire bonding (electrical connection between the sensor die and the package)
- Encapsulation:
  - Protect the bond pad on the sensor die
  - Protect the wire
  - Protect the lead (bond pad) on the package
  - Define the sensing area

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Assembly process challenges

- Die attach:
  - Die pick and place normally required a direct top contact on the die
  - Permanent die fixation usually performed at elevated temperature (>40°C, typically 150°C)
- Wire bonding: standard technology requires elevated temperature (>40°C, typically 150°C)
- Encapsulation: standard technology requires elevated temperature (>40°C, typically 150°C)

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Die mounting

- Pick and place without direct contact with sensing area (no damage to the bio-functionalized layer, no damage to vulnerable IDAM)
- Permanent fixation is achieved at room temperature

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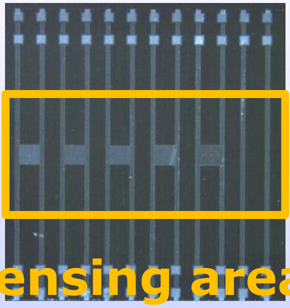
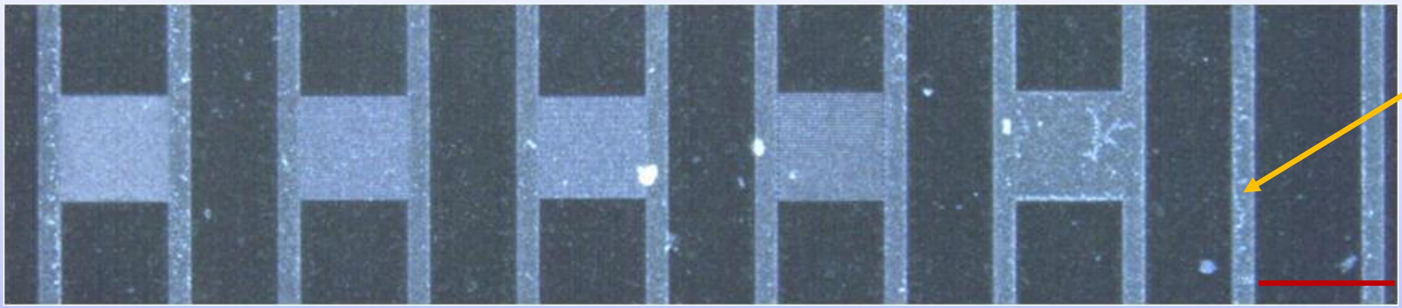
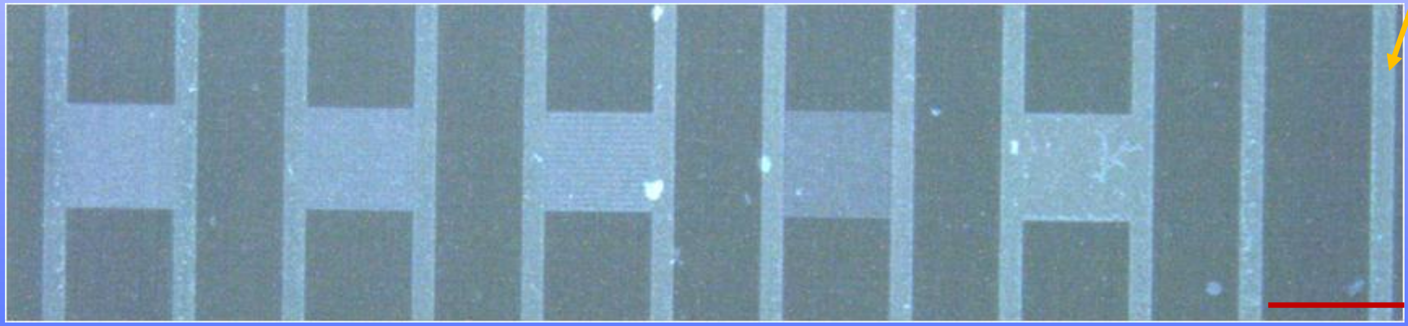
Sensing area observation



As received



After encapsulation



No visual damage induced during the assembly flow

Wire bonding

- Industrial standard is Au wire bonding. Cu wire bonding emerges. It total they counts for 90%. They requires elevated temperature (typically 150-220°C)
- We interconnect the sensor die using Al wire bonding (room temperature process)
- Al wire bonding is currently used for special application (military, space etc)

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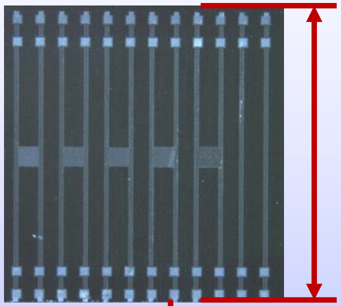
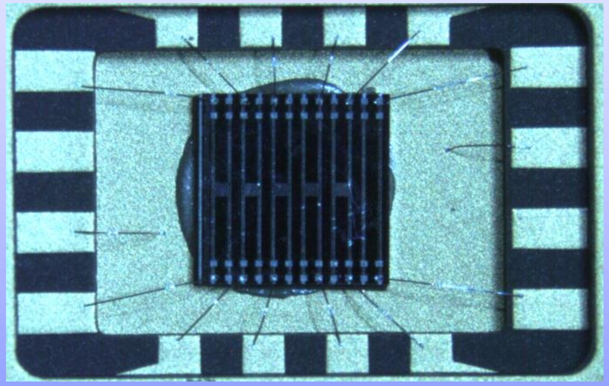
Process flow

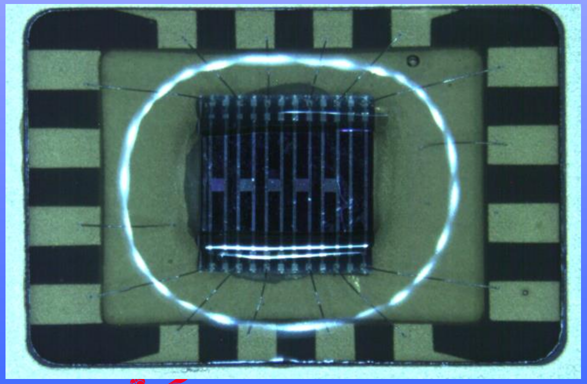


“As received sensor die (after bio-functionalization)



Sensor die mounted into package and wire bonded

Encapsulated sensor die (transparent encapsulant)



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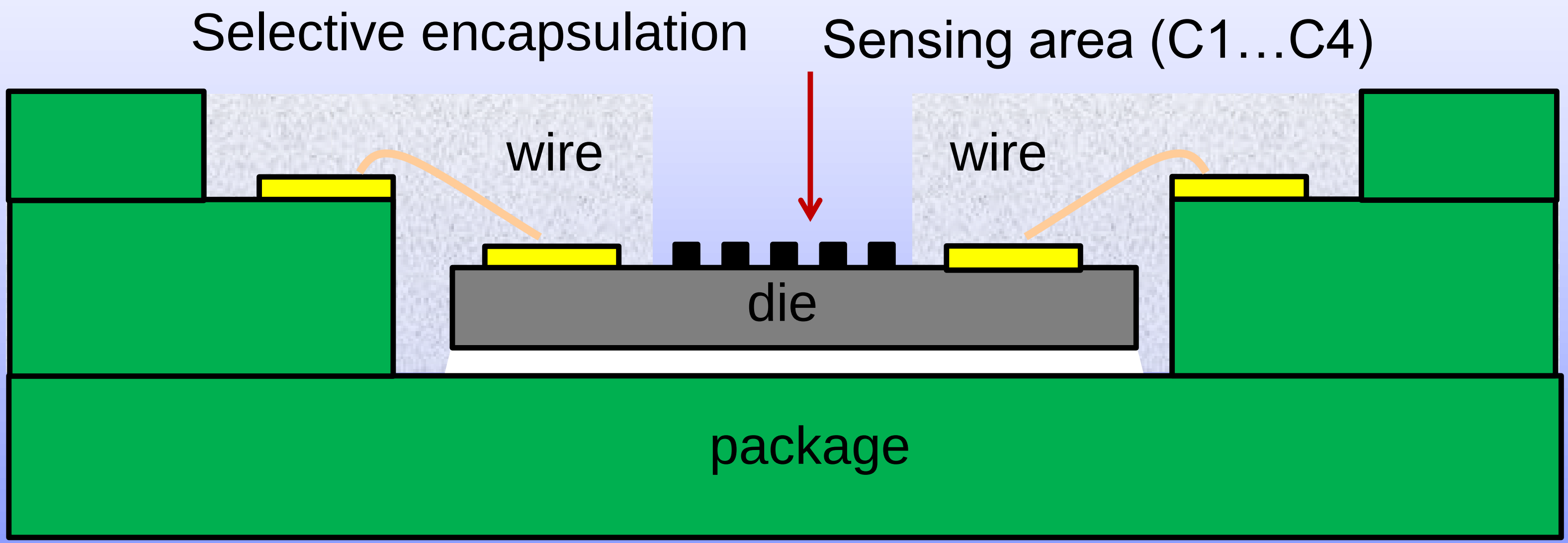
Assembled sensor: cross sectional view



Encapsulation challenges

- Partial encapsulation to define accurately the sensing area (1mm x 3 mm and 0.5 mm high):
  - dam (high viscosity) and encapsulant (lower viscosity)
  - Industrial process: partial molding
- UV curable encapsulant (UV spot intensity: 18.5W/cm2 irradiance maximum output, wave length of 320-500nm), maximum 20 sec
- Such UV exposure causing no direct damage to bio-functionalized layer of the sensor (tested experimentally)

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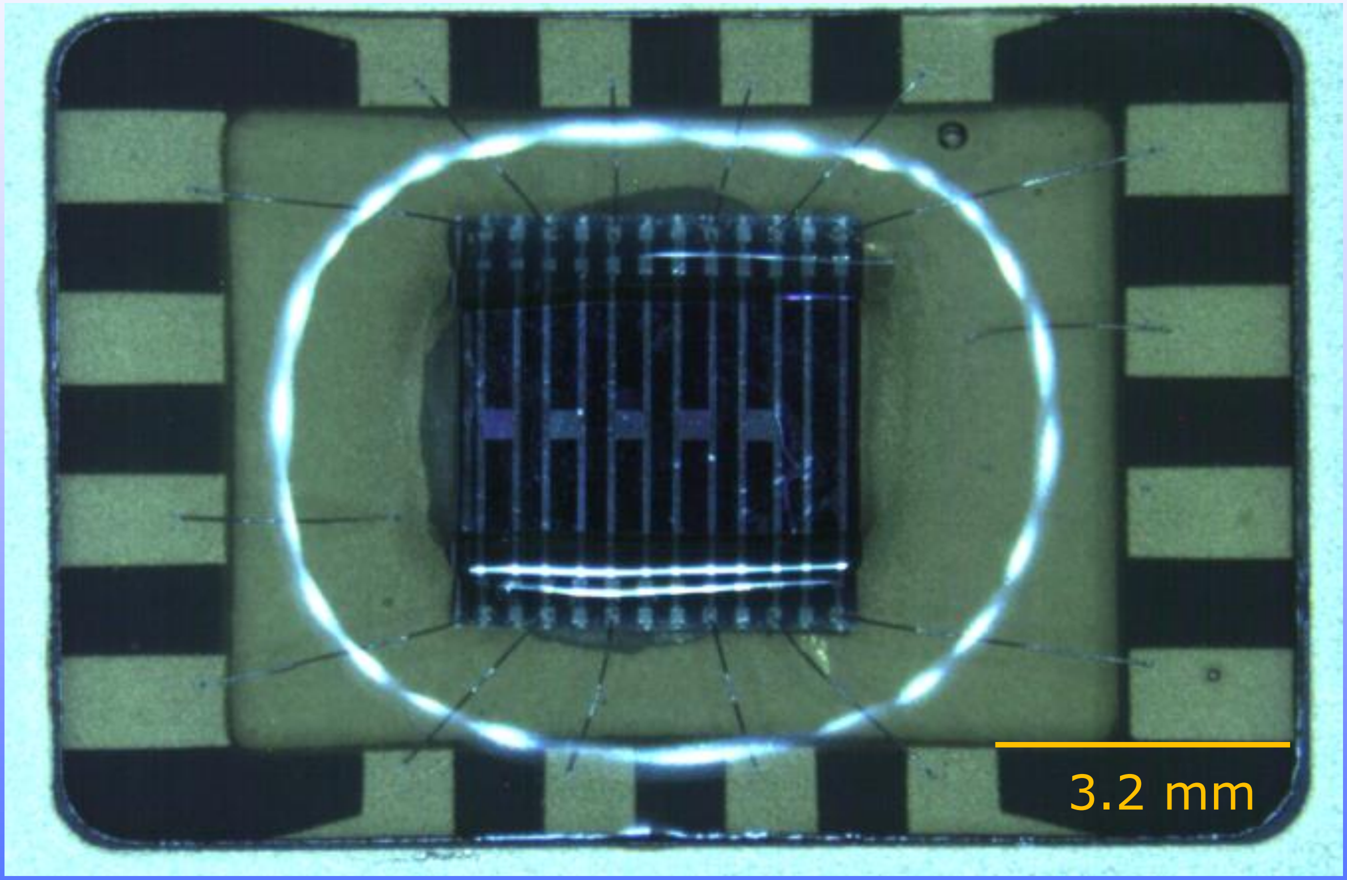
Assembled sensor (top view)



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Electrical characterization

- Capacitance and conductivity measurements (PO_4 buffer; 20 mM, pH 8)(freq=100 kHz): the measurements were performed with a LCR meter with different bias voltages. Different dilutions of (left) antibody conjugated with gold bead, in contact with antibodies (initial concentration= 10^{13} beads/mL) or (right) different dilutions of the Influenza A virus were tested.
- For the measurements of the Influenza A virus, the signal was enhanced with an anti-Influenza antibody conjugated with a gold nano-bead. The same trend was observed for both targets.

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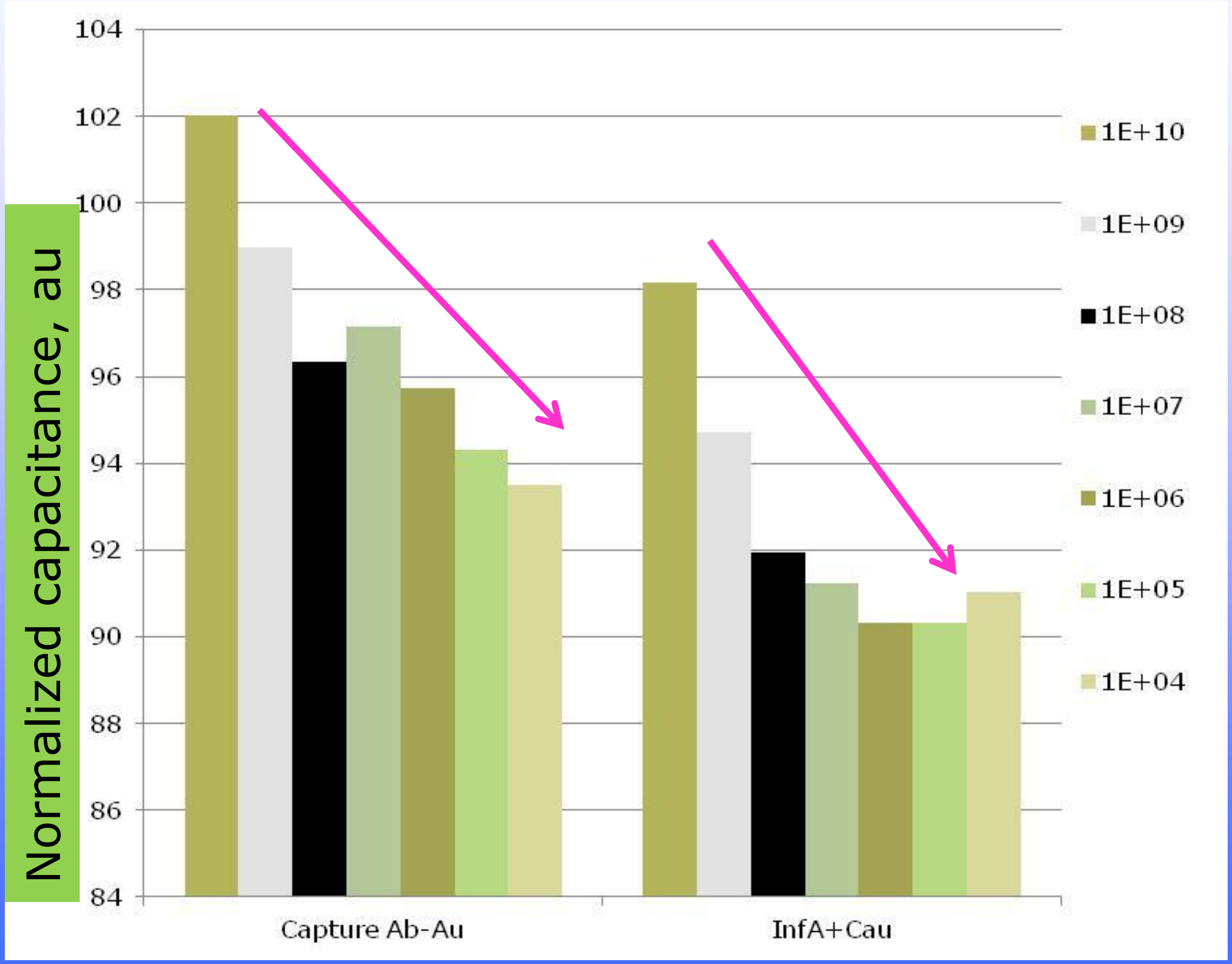
Capacitance



Ab-Au: antibody conjugated with gold nano-bead
InfA+Cau: Influenza A virus enhanced with an anti-Influenza antibody conjugated with a gold nano-bead

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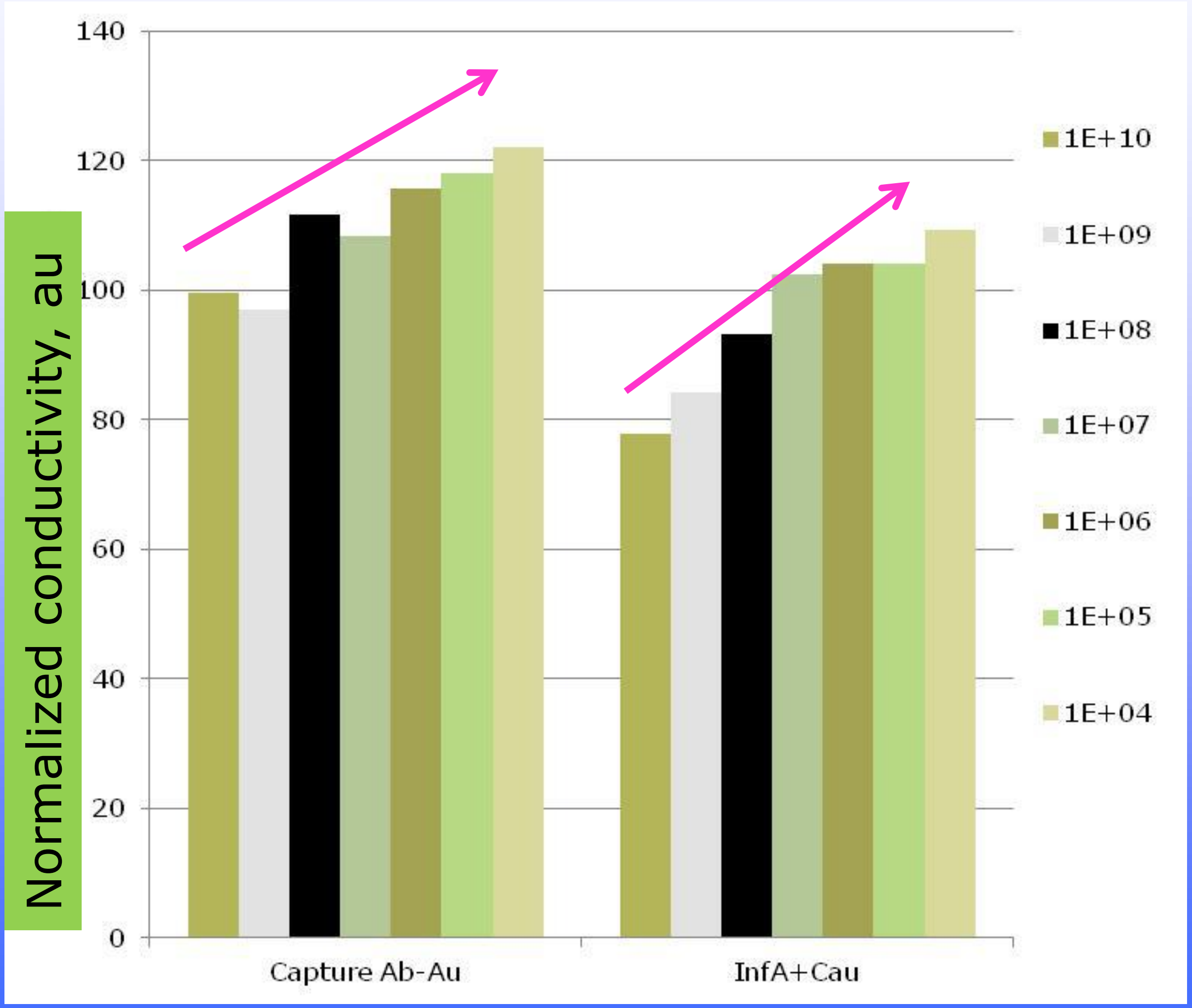
Conductivity



<u>Ab-Au:</u>
antibody conjugated with gold nano-bead
<u>InfA+Cau:</u>
Influenza A virus enhanced with an anti-Influenza antibody conjugated with a gold nano-bead

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Sensor performance summary

- We demonstrated inter-digitated capacitive biosensor can be used for the quantification of the Influenza A virus
- The demonstrated sensor can detect to 10^{10} times dilution of the Influenza A virus while a commercial immuno-chromatographic test could only detect a 10^{4} times dilution
- We successfully developed a process for applying bio-functional layer on IDAM. The layer is suitable for conjugating specific antibody and Influenza A virus
- The capacitance and conductance measurements are coherent with the test sample concentration
- Among all tested sensors (C1…C4), the C4 (2 µm/2 µm = line/space) is the most sensitive one.

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Conclusion

- We developed a convenient method for the assembly of the bio-functionalized sensor
- The process temperature is below 37°C; there is no direct contact between the die handling tool and the bio-functionalized area of the bio-sensor
- Additionally, the UV exposure, specifically intensity and time are limited to a sustainable level for inducing no damage to the bio-sensor
- The realized sensor performs detection and semi-quantification of influenza A viruses.

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Questions

Thanks for your attention:

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