Labopuce implantable sous cutanée: un mini-laboratoire sous la peau

Lab-on-a-Chip implants: a mini-lab under the skin

Giovanni De Micheli
Outline

- Motivation, objectives and overview
- The *nanobiosensor* technology
- Control and readout circuit for multi-target biosensing
- Microelectronic circuits for data acquisition and energy harvesting
- System biocompatibility
- Conclusions and outlook
Objectives

- Continuous real-time monitoring of chronic patients
- Current devices are external and limited to a single measurement
- Tracking multiple metabolites
- Wireless, batteryless implant
- Driver technology for a wide set of applications
Prototype: implant

20 x 4.2 x 3 mm

Diagram showing components:
- Silicon chip for sensor read-out and control
- Wire bonding
- Substrate with antenna for remote powering and data transmission
- Sensor platform component
- Bio-sensors
- Porous biocompatible membrane
- Bio-compatible bi-directional diffusion barrier
- Potted material for wire bonding protection
- IC CMOS for RF and detection
- Temperature Sensor
- pH Sensor
- Molecular Sensors
- Inductive coil
- WE geometries
- Electrode 500 µm array
- Electrode 10 µm array
- Temperature sensor
- pH sensor
- Pads for IC integration
Prototype: external patch

**FEATURES**
- Remote powering through inductive link
- Short-range bidirectional communication
- Long-range comm. with remote devices

**ADVANTAGES**
- Improved wearability
- Direct placement over implant area
- Stand alone
- Battery-powered
Android User Interface
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The *nanobiosensor* concept

**CARBON NANOTUBES**

**CNTs + PROBE ENZYMES**

3.6 nm

4.9 nm

5.2 nm
Carbon nanotube benefits

Sensor sensitivity is enhanced by CNT nanostructuration

C. Boero, S. Carrara et al., IEEE PRIME, 2009

~ 7.5 times more

C. Boero, S. Carrara et al. / IEEE CME 2010
### Nanobiosensors sensitivity and range

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Sensitivity (µA/mM cm²)</th>
<th>Range (mM)</th>
<th>Detection limit (S/N = 3σ) (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>27.7</td>
<td>0.5 – 4</td>
<td>73</td>
</tr>
<tr>
<td>Lactate</td>
<td>40.1</td>
<td>0.5 – 2.5</td>
<td>28</td>
</tr>
<tr>
<td>Glutamate</td>
<td>25.5</td>
<td>0.5 – 2</td>
<td>195</td>
</tr>
<tr>
<td>ATP</td>
<td>3.42</td>
<td>0.5 – 1.4</td>
<td>208</td>
</tr>
</tbody>
</table>
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Control and Readout IC

- A biosensing **platform**
- Low power
- Remotely powered
- Flexible and programmable
- High accuracy

Layout of the fabricated IC (0.18um technology)
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Inductive Link

- Wireless power transfer through inductive link
- Bidirectional data communication
IronIC Patch

Power Transmission
- Up to 15 mW transmitted within 6 mm in air
- Up to 1.2 mW transmitted within 17 mm tissue

Data Transmission
- Downlink communication up to 100 kbps
- Uplink communication up to 66.6 kbps
- Bluetooth communication (Class-2)

Battery Life
- Stand-by mode: 10 hours
- Power mode: 1.5 hours
Multi-layer Receiving Inductors

- Higher link efficiency (up to 35% higher)
- Higher voltage gain (up to one order of magnitude higher)
Power & Data Transmission

Downlink Bitstream – 100 kbps
Uplink Bitstream – 66.6 kbps
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Biocompatibility

Challenges
Prevent Cu leaking (coil)
Prevent CNT diffusion (sensors)
Prevent circuit corrosion
Prevent sensors biofouling

Solutions:
Parylene C inner coating
USP class 6 Silicone external coating
CNT entrapement in chitosan + outer membrane

Investigations:
Cytotoxicity tests
In-vivo tests
In vivo inflammation

- Subcutaneous implant in mice
- No significant inflammation after **30 days**
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Conclusions

- Continuous care of chronic patients is possible through specialized bio-electronics
- Significant improvement over the state of the art:
  - FDA-approved wearable glucose monitoring systems
- Electronic implants represent a near-future technology and can be more patient-friendly
- Challenges include the plurality of technologies as well as the interaction with the human body
Thank you

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