



**EDMI** Microsystems and Microelectronics

**MICRO-614:** Electrochemical Nano-Bio-Sensing  
and Bio/CMOS interfaces

# **Lecture #1 - Introduction**

## **Human Metabolism Monitoring by Electrochemical Sensing: Present & Future!**

# The Time' forecast on Human++

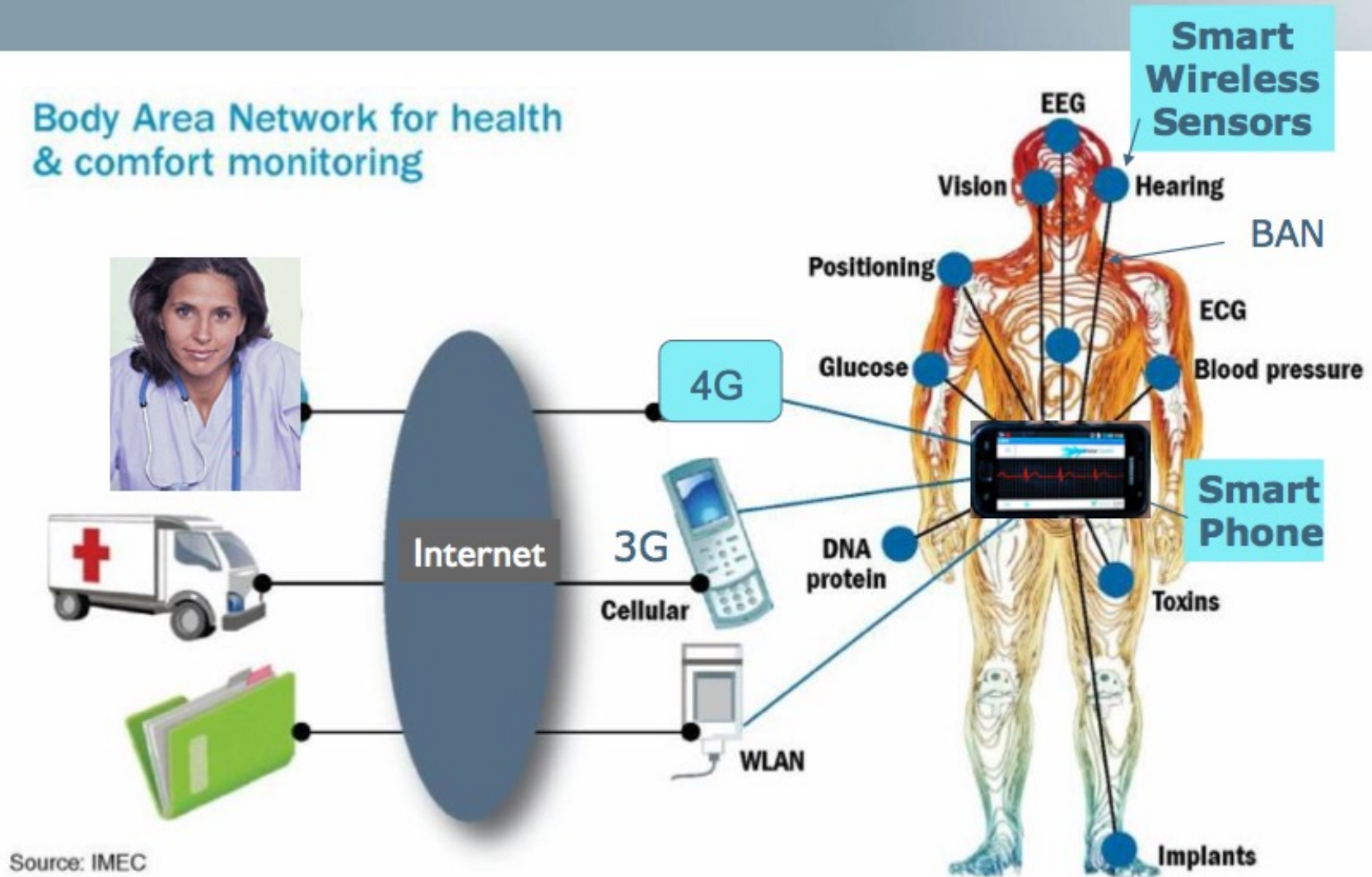


[TIME, February 2011]

(c) S.Carrara

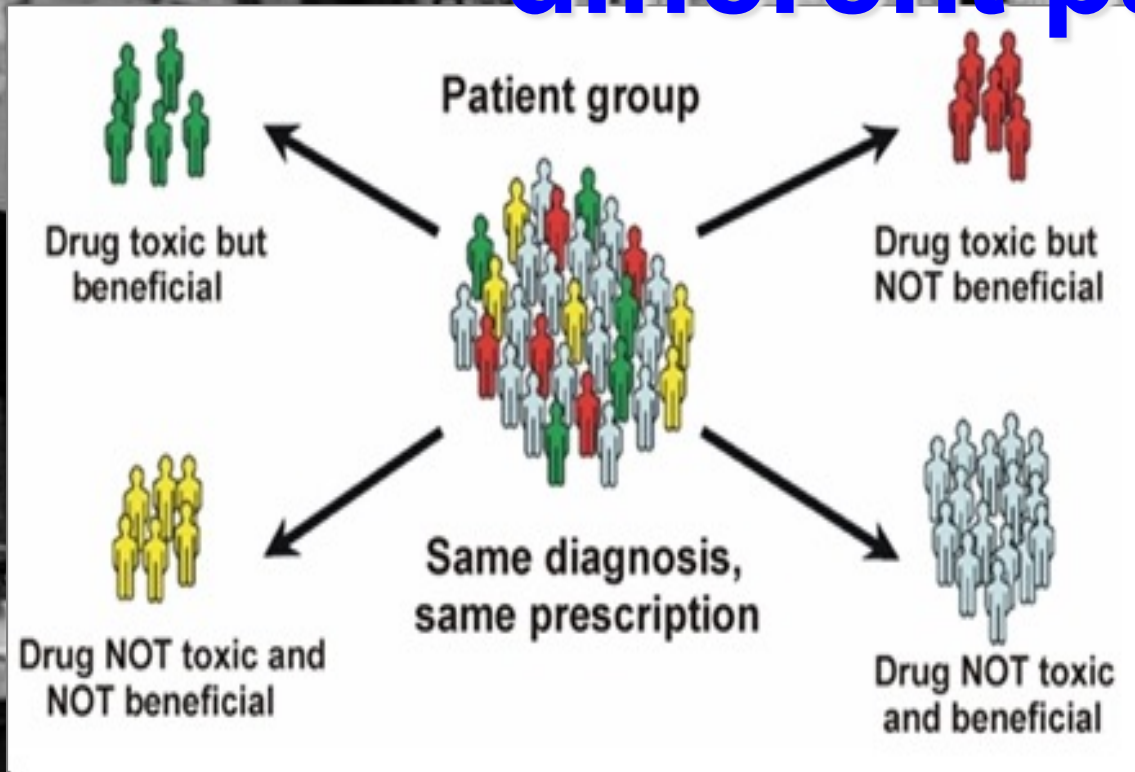
# Fully-Connected Human++

Body Area Network for health  
& comfort monitoring



Courtesy, Hugo De Man (IMEC)

# Different outcomes for different patients



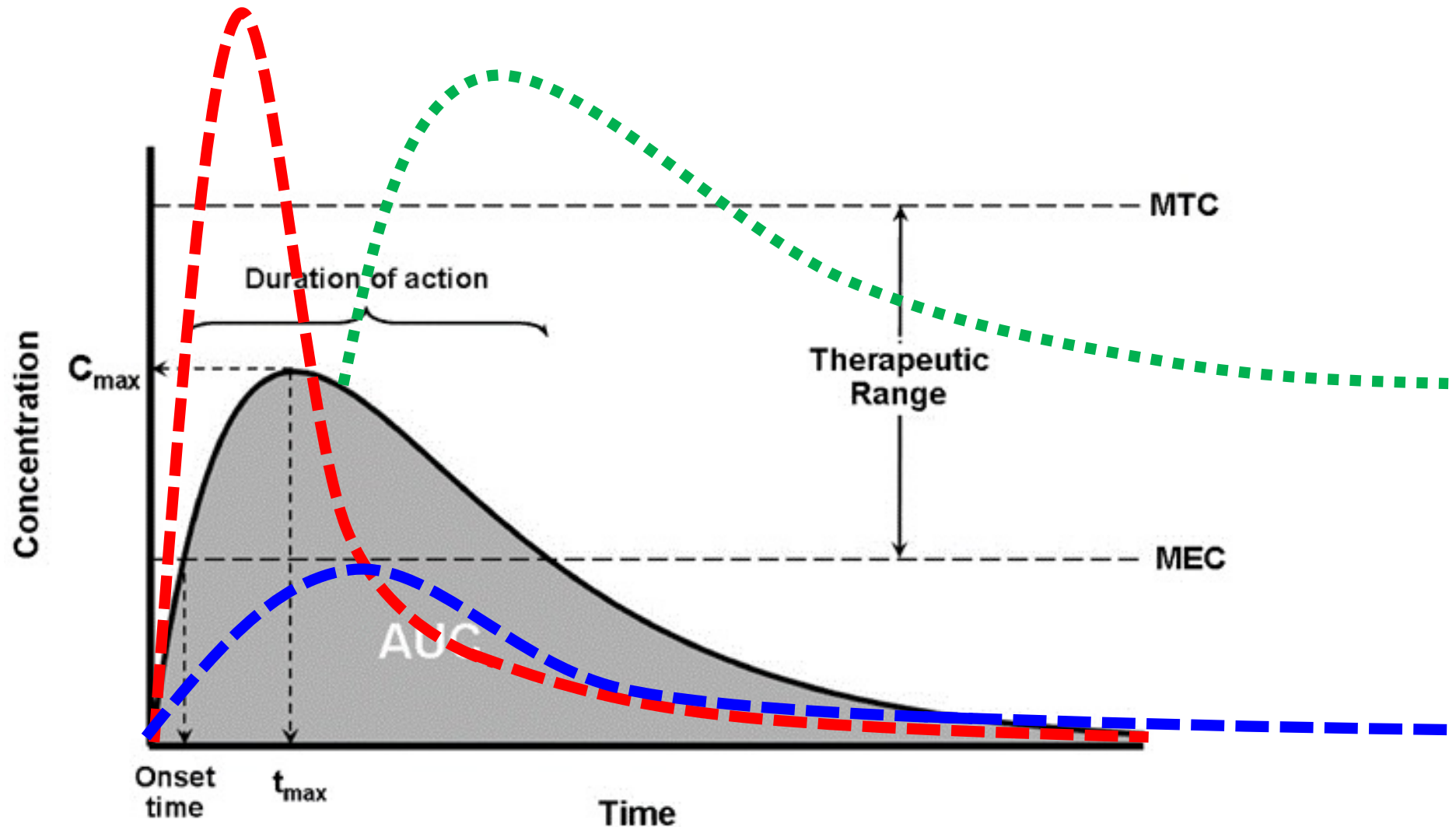
Therapeutic area	Rate of efficacy with standard drug treatment
Cancer (all types)	25%
Alzheimer's disease	30%
Incontinence	40%
Hepatitis C	47%
Osteoporosis	48%
Rheumatoid arthritis	50%
Migraine (prophylaxis)	50%
Migraine (acute)	52%
Diabetes	57%
Asthma	60%
Cardiac arrhythmias	60%
Schizophrenia	60%
Depression	62%

For depression, the data apply specifically to the drug class known as selective serotonin reuptake inhibitors.

Source: Brian B. Spear, Margo Heath-Chiozzi, and Jeffrey Huff, "Clinical Application of Pharmacogenetics," *Trends in Molecular Medicine* (May 2001).



# Patients' metabolism drive the Drugs effect in time!



# Course Motivation: From Labs to Hands



- 100.000 \$ (machinery)
- 1.000 \$ the single  $\mu$ -array

Labeled



Label-Free

- 50 \$ (machinery)
- 0.05 \$ the single strip



Bayer HealthCare

# Next step: the future already begun



Glucose Personal Diagnostics on our iPhones

(c) S.Carrara

# Next step: the future already begun

How to use the FreeStyle Libre System



1. Apply sensor with applicator

2. Scan sensor using FreeStyle Libre Reader

3. Get reading on the reader

FOR FULL INSTRUCTIONS  
[www.freestylelibre.co.uk](http://www.freestylelibre.co.uk) >

OVERVIEW

HOW TO USE

FIND OUT MORE

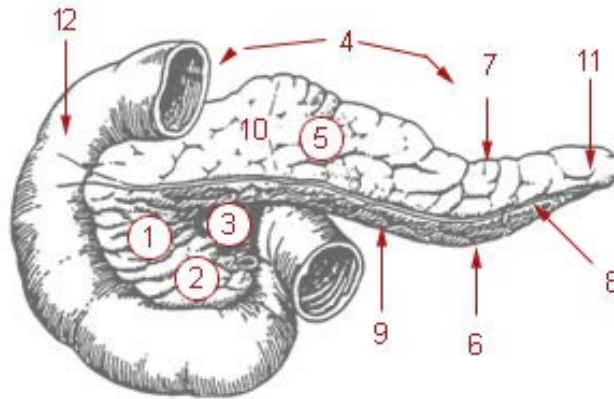
Glucose Personal Diagnostics on our Skin



# The Pancreas Functions

## IN-put Signals

Bile acids →  
pH →  
Syrinic proteases →  
Glucose →  
Glycagone pancreatic →  
.....



## OUT-put Signals

→ insulin  
→ Lipase  
→ Fospholipase A  
→ Cholesterol esterase  
→ Endopeptidase  
→ Esopeptidase  
→ Elastase  
→ Ribonuclease  
→ Enterochinase  
.....

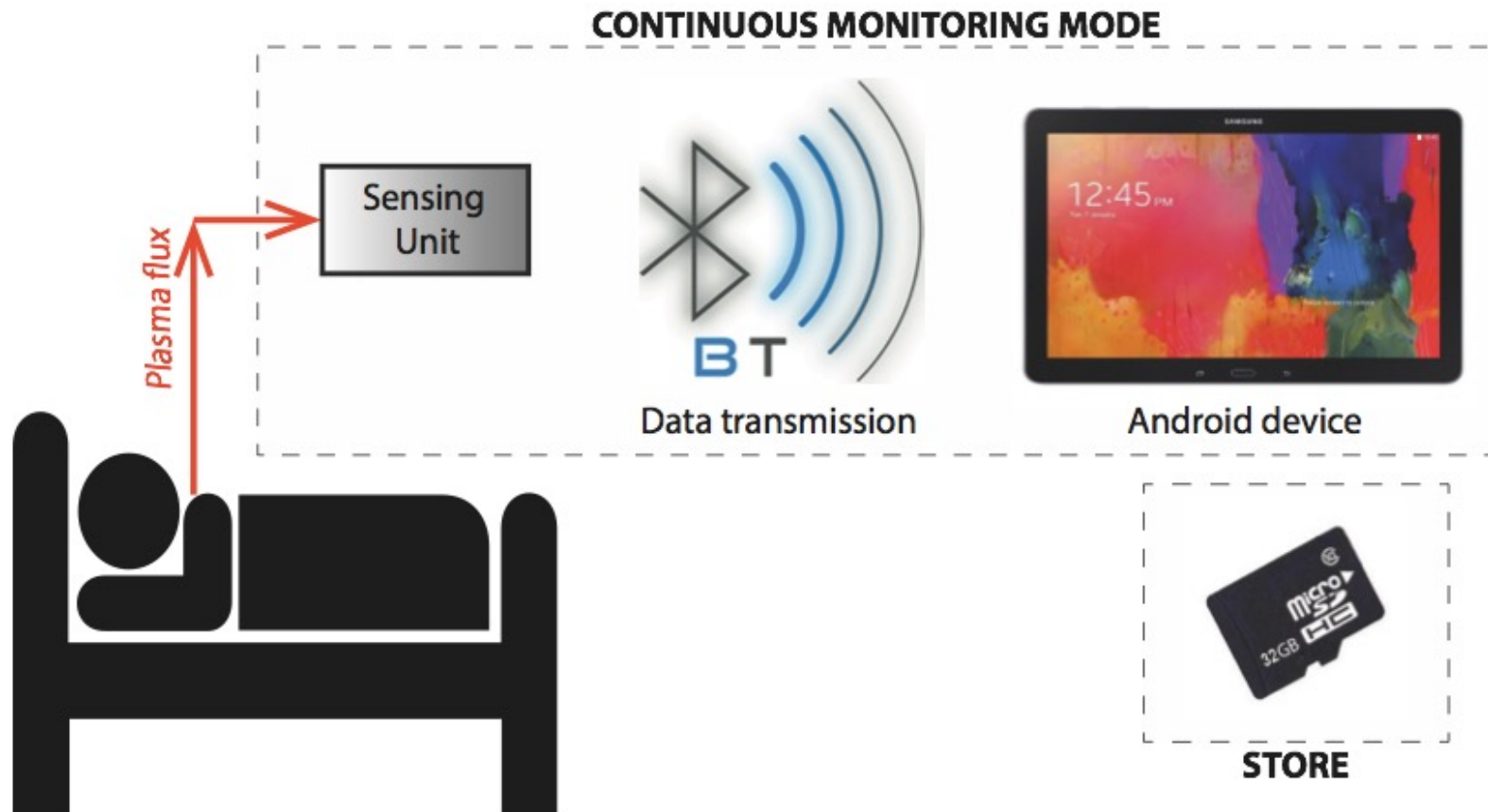
# Intensive-Care-Units (ICU) Monitoring



The present monitoring scenario foresees lot of independent devices and input/output interfaces

(c) S.Carrara

# Lab-on-a-chip for ICUs



F. Stradolini, *et al.*, *IEEE Sensors Journal* 16(2016) 3163 - 3170

Monitoring scenario where the main parameters of the patient are continuously displayed on an Android mobile device

(c) S.Carrara

# The full connected system



The whole system with the Android™ interface that allows connectivity too



# One Interface for Remote Monitoring of Patients in Intensive Care Units



Image / *Bam Labs*

The whole system with the Android™ interface that allows connectivity too

S.Carrara (C)

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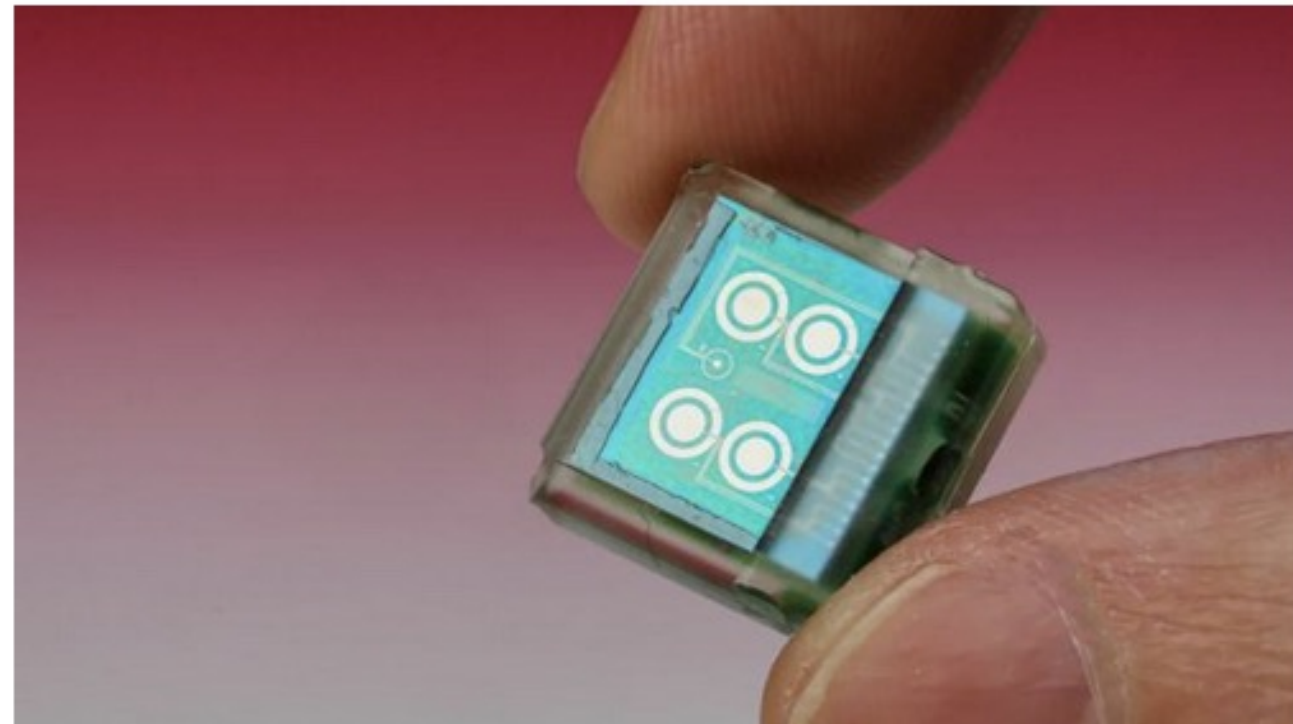
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# A subcutaneous biosensor chip to revolutionize tomorrow's medicine

May 29, 2015 9:26 AM

[Relaxnews](#)



(c) S.Carrara

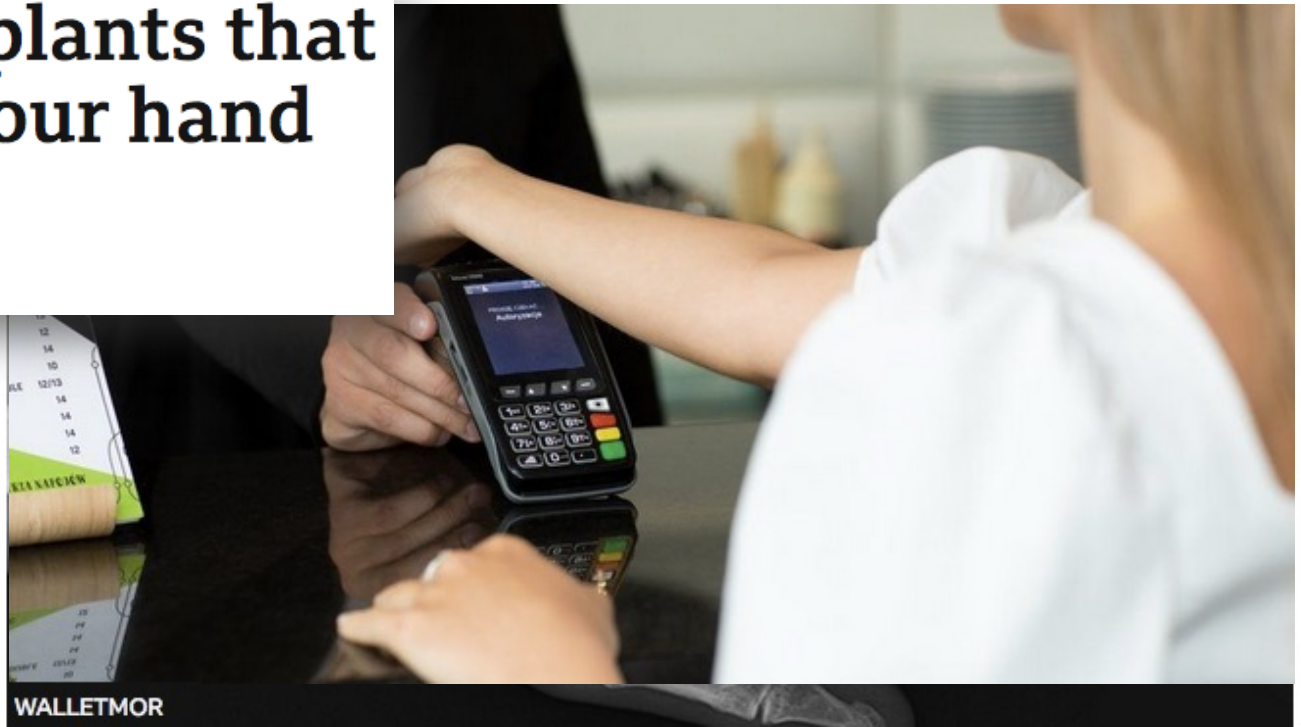
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# The microchip implants that let you pay with your hand

By Katherine Latham  
Business reporter

© April, 11th, 2022



An x-ray showing a Walletmor implant, which are injected into a person's hand after a local anaesthetic

For many of us, the idea of having such a chip implanted in our body is an appalling one, but a 2021 survey of more than 4,000 people across the UK and the European Union found that 51% would consider it.



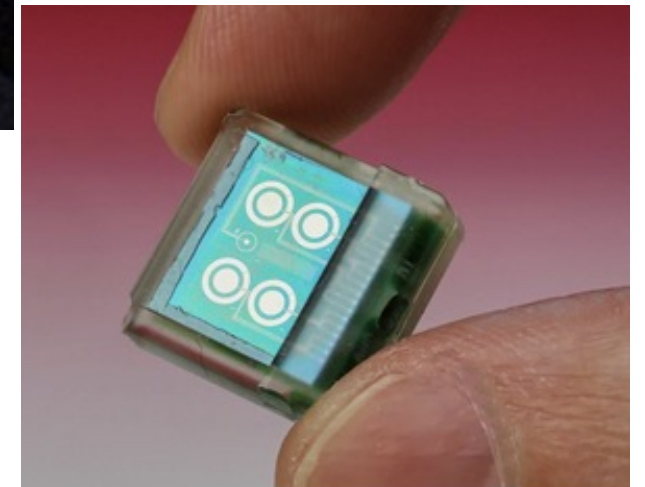
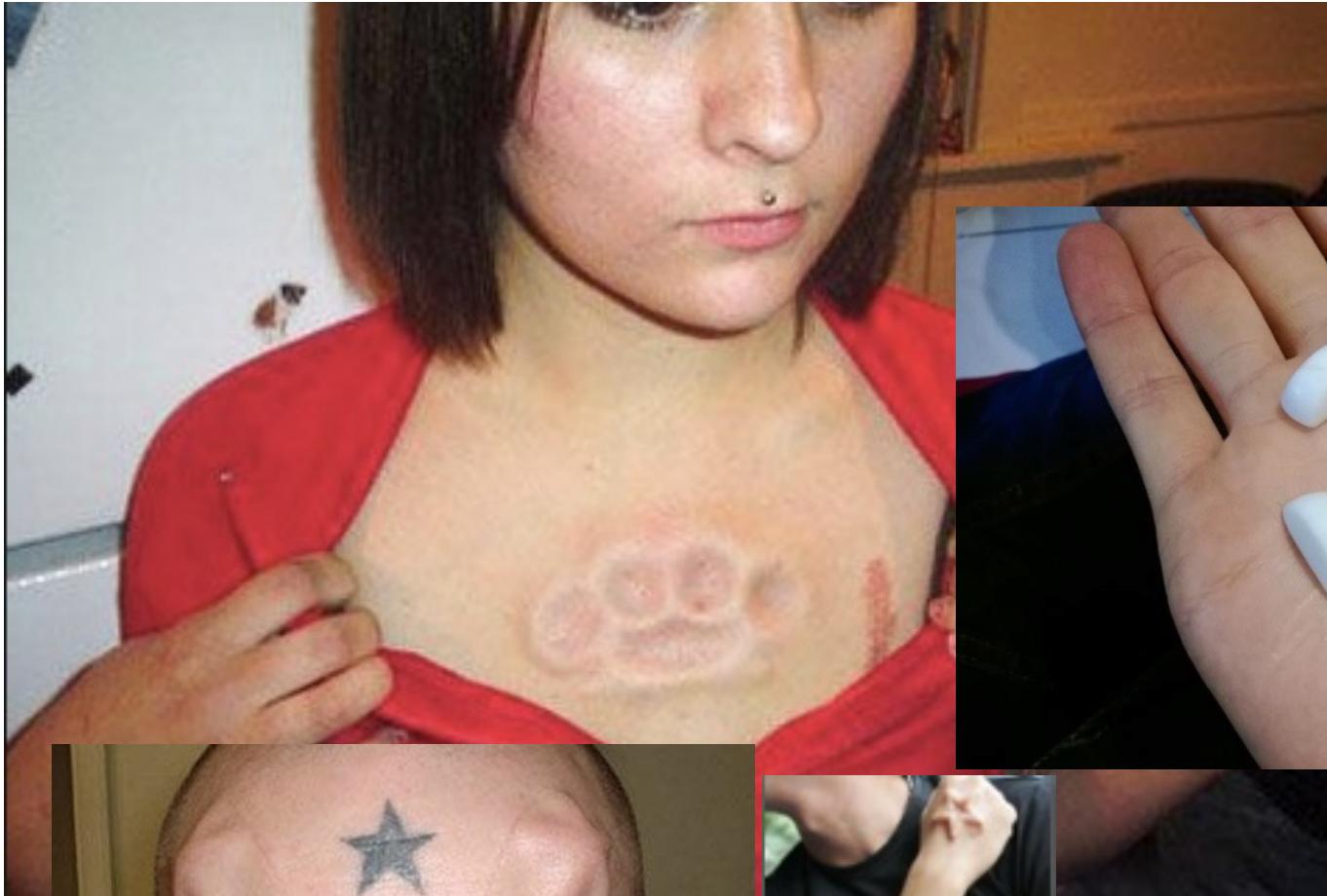
# **Chips under the skin? See video on Moodle!**



[EuroNews, June 2015]



# Under the skin for body sculpting

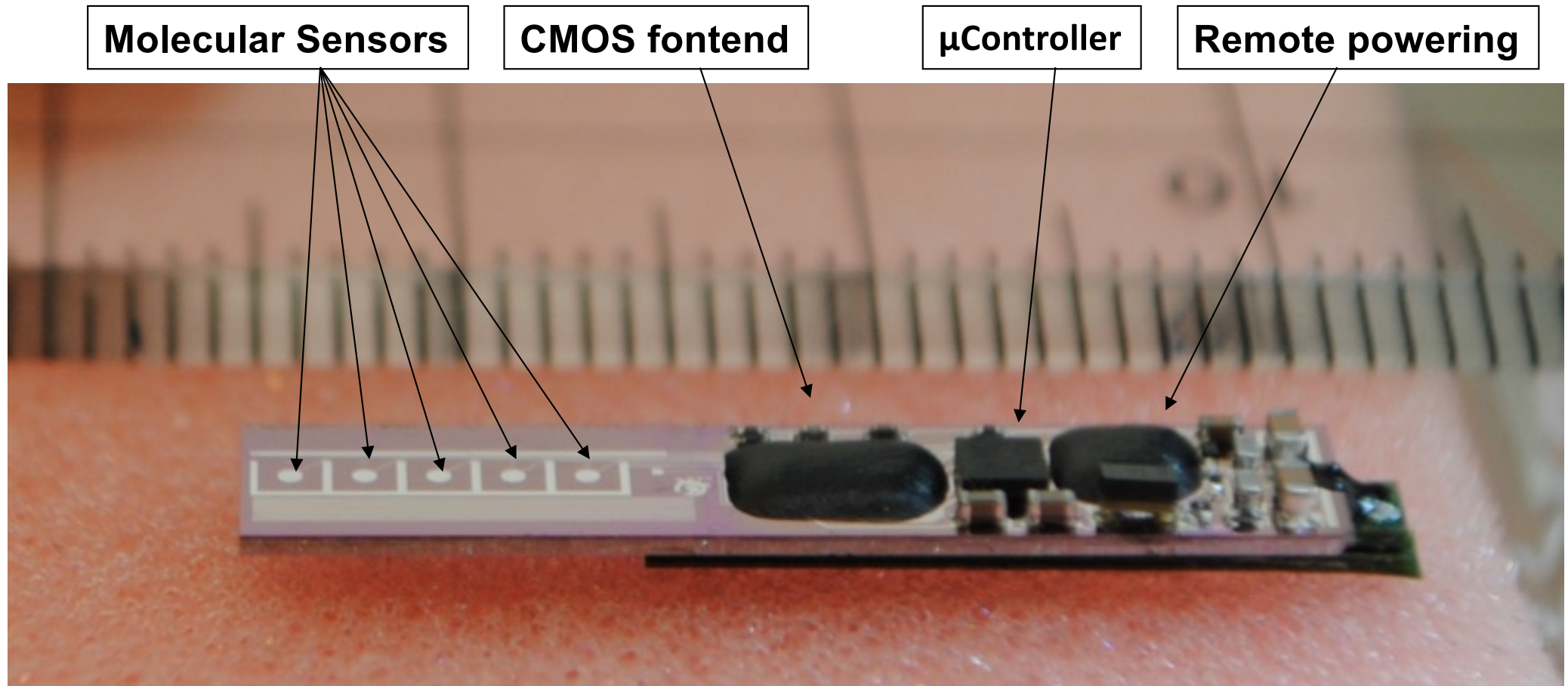


(c) S.Carrara

# Enhancing human being



# Size and Shape to be injectable as a Needle?



The IC has been fabricated in UMC 0.18 technology and interfaced to the passive multi-panel platform



# ECG monitoring by Medtronic



Mark Phelps by Medtronic, and the Reveal LINQ™ system

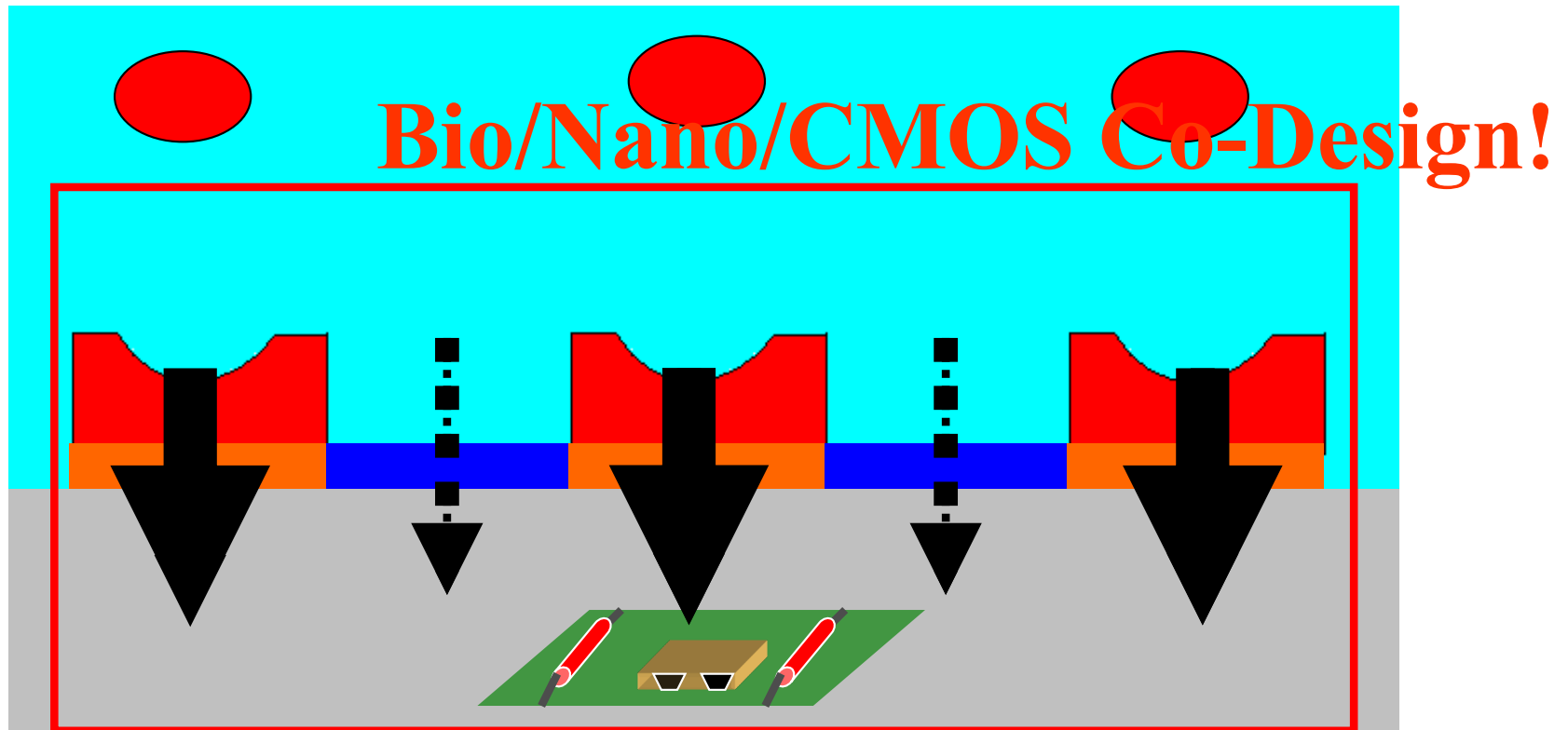


# Toward Ultrasensitive Biosensors:

1. Fully integration of **Bio**molecules to assure specificity
2. Fully integration of **Nano**-structures to assure sensitivity
3. Proper **CMOS** frontends to assure
  - (i) Correct Voltage driving
  - (ii) Precise Current measurements,
  - (iii) Reliability in Temperature and pH

**Bio/Nano/CMOS Co-design !**

# CMOS/Sample interface

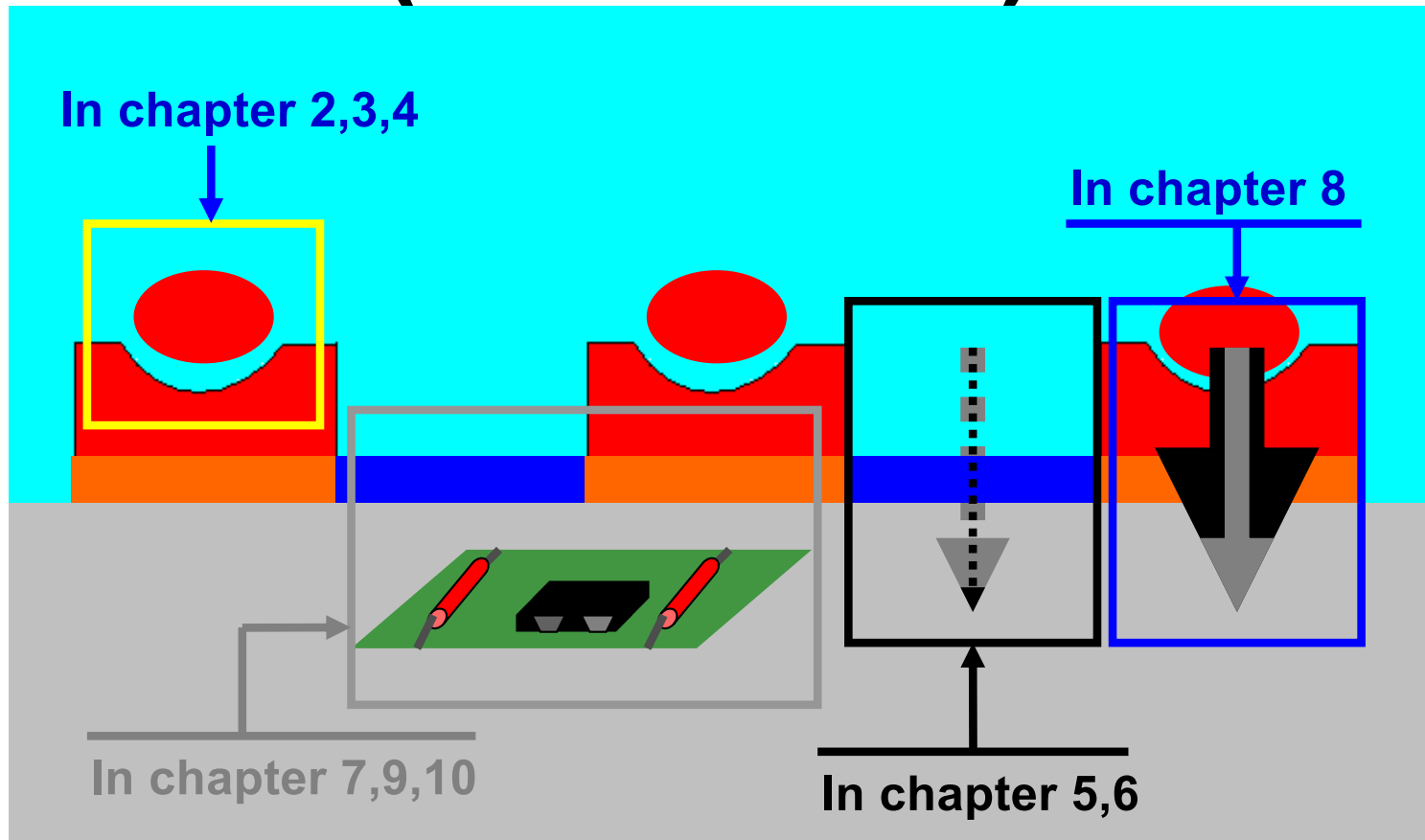


The interface between the CMOS circuit and the bio-sample needs to be deeply investigated and organized

# Get you copy of the Textbooks

The image shows a screenshot of a web browser displaying the Springer Link website. The browser's address bar shows the URL `link.springer.com/book/10.1007/978-1-4614-4690-3`, which is circled in red. The website header includes the Springer Link logo, a search bar, and navigation links. The main content area displays the book **Bio/CMOS Interfaces and Co-Design** by Sandro Carrara. The book cover is shown on the left, and the right side features a 'Download Book (7,900 KB)' button, which is also circled in red. Below the download button, there is a 'Table of contents (10 chapters)' section. On the right side of the page, there is a 'MyCopy Softcover Edition' for 24.99 EUR/USD/GBP/CHF, with a 'Buy Now' button circled in red. The EPFL logo is visible in the top right corner of the website.

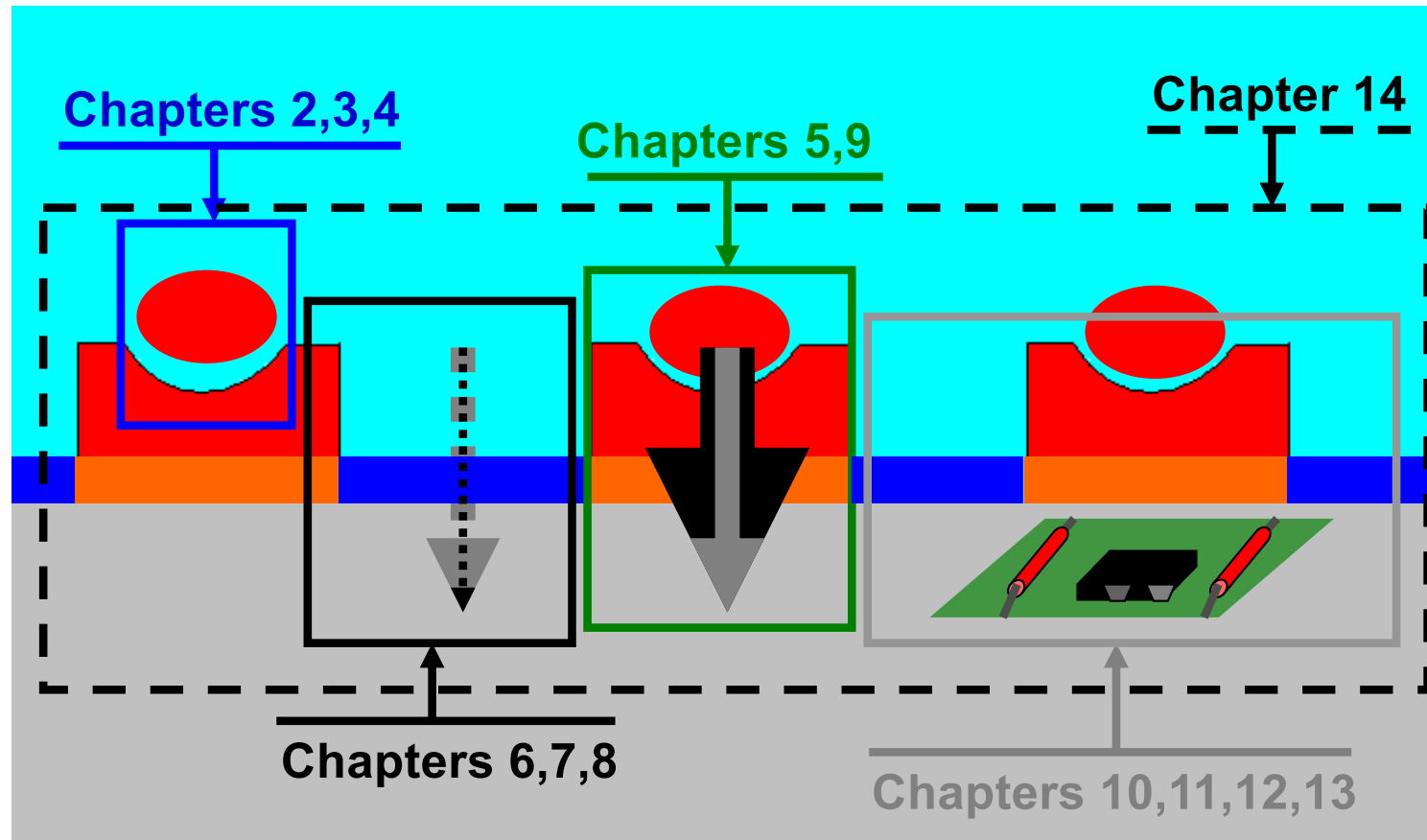
# Bio/CMOS interface book (1<sup>st</sup> Edition)



Introduction to Personal electronics, Distributed Diagnostics, and Bio/CMOS interfaces in Chapter 1



# Bio/CMOS interface book (2<sup>nd</sup> Edition)



Introduction to Personal electronics, Distributed Diagnostics, and Bio/CMOS interfaces in Chapter 1

**MICRO-614:** Electrochemical Nano-Bio-Sensing  
and Bio/CMOS interfaces

**Course outline**

1. Intro about Metabolism Monitoring
  2. Bio 1 metabolites, Peptides, Proteins & DNA
  3. Bio 2 Probes/targets interaction
  4. Bio 3 Detection principles
  5. Bio 4 Amperometric Biosensors
6. Nano 1 Functionalization: Methods & Models
  7. Nano 2 Characterisation by RM, SPR, SEM, AFM
  8. Nano 3 Preventing ET
  9. Nano 4 Enhancing ET
  10. Nano 5 Memristive Sensing
11. CMOS 1 in Constant Bias
  12. CMOS 2 in Scanning Voltage
  13. CMOS 3 for DNA: Capacitive & Amperometric
  14. CMOS 4 Memristive Sensing
  15. CMOS 5 Beyond implantable & wearable

**Bio**

**Nano**

**CMOS**

# To fruitfully follow the course

Meeting Information - Zoom × EDOC Teaching × Day-15th-June - Dropbox × Course: Electrochemical nano- ×

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**MICRO-614**

- 👤 Participants
- 📊 Grades
- 📁 General
- 📁 Day 1 - Bio: Probe/Target Molecular interactions
- 📁 Day 2 - Bio: Electrochemical Sensing
- 📁 Day 3 - Nano: Probes-layer for Targets Detection
- 📁 Day 4 - Nano/CMOS: Memristors and CMOS Analog4Bio

## Day 1 - Bio: Probe/Target Molecular interactions

- 📄 Bio/CMOS: present & future! (An introduction)
- 📄 Probe/Target interactions
- 📄 Sensing Principles with biomolecules
- 📄 APPENDIX 1: Building Blocks & Protein Structures
- 📄 APPENDIX 2: Binding Energy
- 📄 EuroNews about under-the-skin biochip

Read Chapter 2 in the Book for Conductive Solutions and the concept of pH, and Chapters 3 & 4 for Target/Probe biochemistry & interactions

Read also APPENDIX A in the Book for the concept of Molar Concentration

Solve the Exercise # 1 in page 28 of the Book (show computations)

Solve the Exercise # 9 in page 50 of the Book (justify the answer)

Solve the Exercise # 5 in page 85 of the Book (Solve the exercise by also