Innovative Sensors based on Silicon technologies for Health and Automotive Applications

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11 Settembre 2020
"IUNET days

Outline

- ✓ Intro: Silicon Material and Related Technologies
- ✓ Innovative Sensors for Automotive Application
- ✓ Novel Sensors for Health Application

1. INTRO

WHY SILICON IS SO ATTRACTIVE FOR INNOVATIVE SENSING….

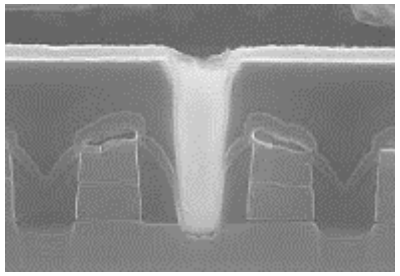
Si Physical Aspects for sensing

- low heat capacity
- good thermal conductivity
- can be made porous to increase the surface-area and reaction efficiency
- electrical conduction….

WHY SILICON IS SO ATTRACTIVE FOR INNOVATIVE SENSING….

Technology Aspects:

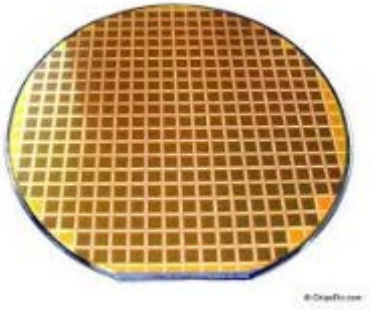
-**consolidated Production technologies** and industrialization processes



- **technologies able to combine multiple functions** to achieve a complete analysis solution, including fluid management, amplification, hybridization or affinity binding, and detection.

-**integration of electrodes** to the chip, as well as "*intelligence on board*" with microelectronics circuitry

-**high-volume production**



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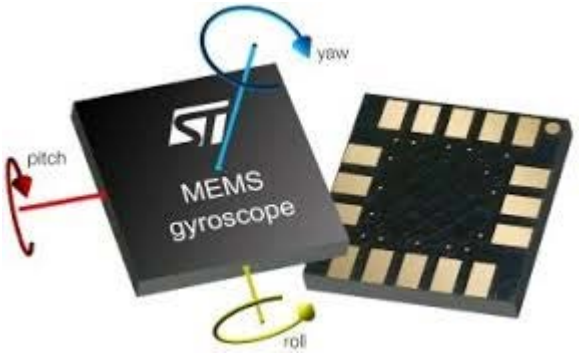
SILICON ENABLE A PLETORA OF SENSOR PRODUCTS

Pressure Sensor (piezoresistive sensor)

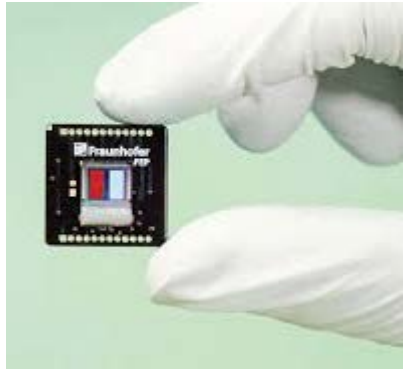
Temperature Sensor

Gyroscope Sensor



Irradiance Sensor

Light Sensor



Time-of-Flight Proximity Sensor

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2. Innovative Sensors For Automotive

How we can use Silicon for Innovative Sensors in Automotive?

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Ministero dell'Istruzione, dell'Università e della Ricerca

ADAS+

Sviluppo di Tecnologie e Sistemi Avanzati per la Sicurezza dell'Auto mediante piattaforme Advanced Driver Assistance System General

PON ARS01_00459

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RESEACH CONTEXT

https://www.digitaltrends.com/cars/the-future-of-car-tech-a-10-year-timeline/

ADVANCED DRIVER ASSISTANCE SYSTEMS

Tesla driver assistance system may reduce accidents due to negligence and fatigue from long term driving (*Epstein, Zach (2016-07-21). "Tesla Autopilot Crash Avoidance Model S Autopilot saves man's life". BGR. Retrieved 2016-08-26)*

What is ADAS??

ADAS (**A**dvanced **D**river **A**ssistance **S**ystem) Program

International Strategic Alliance of major car makers

….and not only….

http://www.dadss.org/ ; http://optics.org/press/3265

Great interests: Automotive Coalition for Traffic Safety (ACTS), U.S. Department of Transportation's National Highway Traffic Safety, Administration's(NHSA), Car makers, Tech companies, etc..

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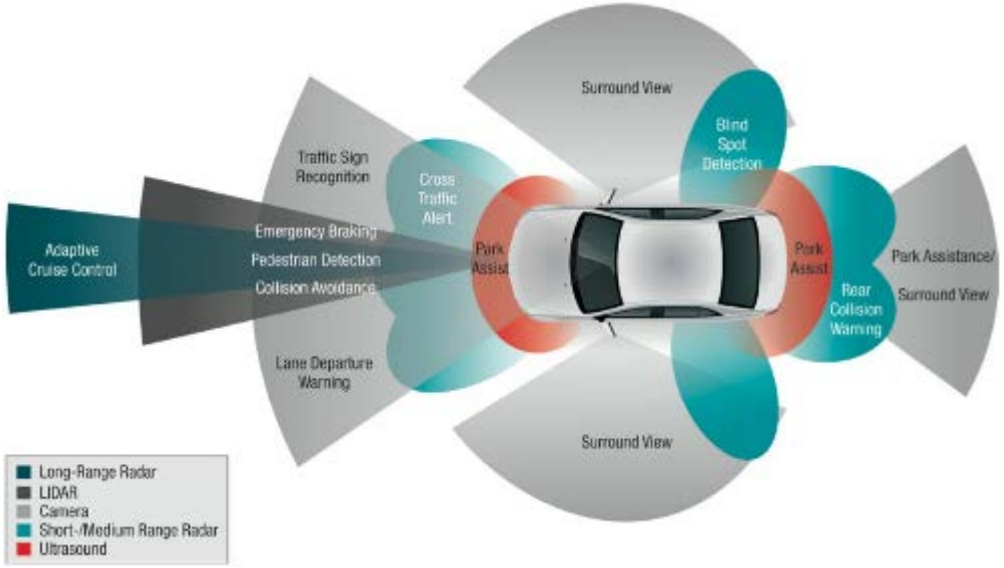
STATE OF ART

CURRENT ADAS SYSTEMS they base their control functions mainly on data coming from sensors outside the passenger compartment (Radar and LiDAR), computer vision and networking systems.

THERE ARE NOT **FUNCTION OF CONTROL** USING **DATES COMING FROM DIRECT ACTION OF DRIVER**



Benchmarking Sensors for Vehicle Computer Vision Systems
Mitchigan Technology Reasearch Institute

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NEXT GENERATION ADAS SYSTEMS

ADAS +

….not only car direction control….

but also

Driver drowsiness

sobriety, psycho-physical state

Car environment

Smart Sensor Platfom for Driver Health

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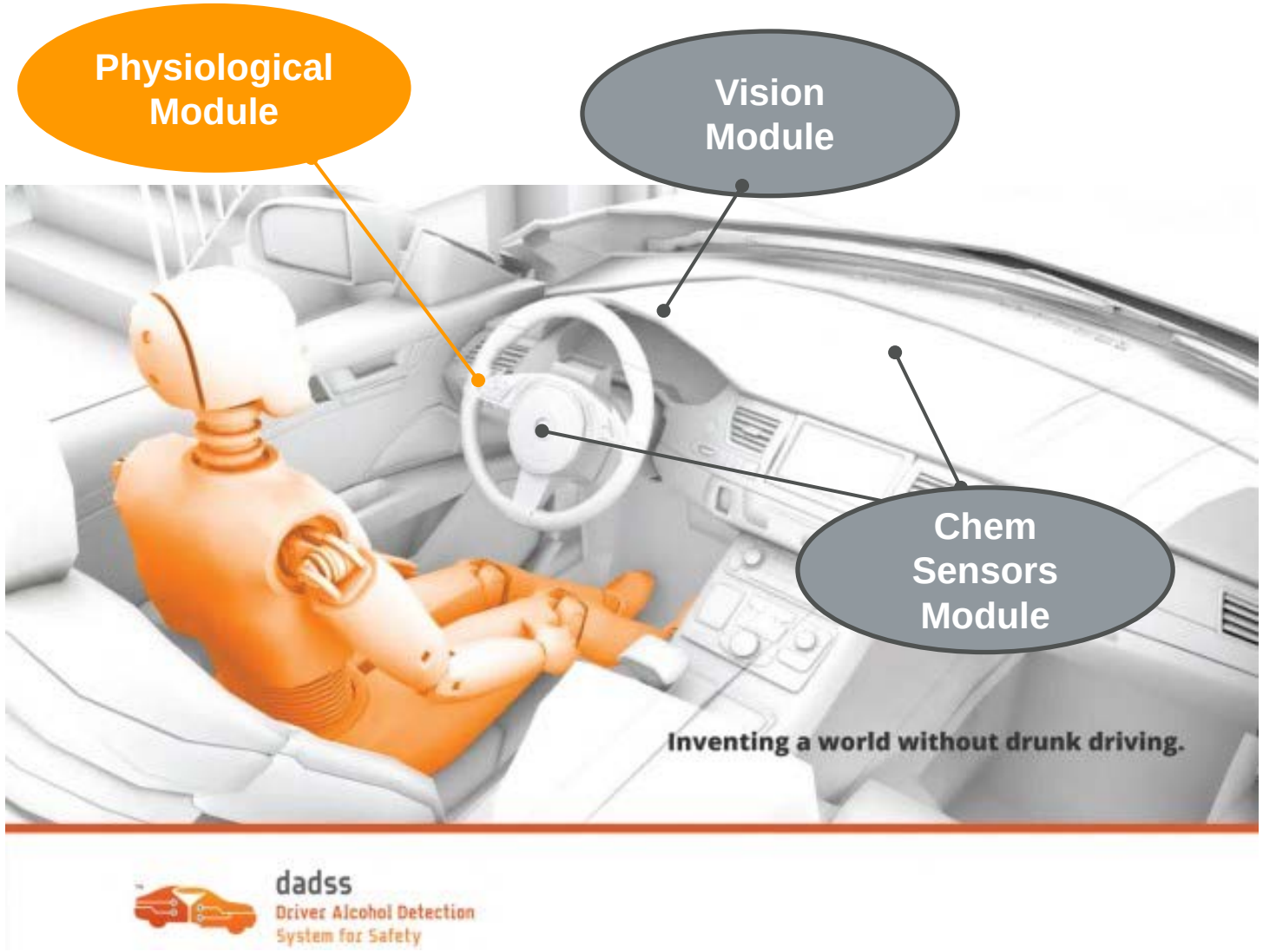
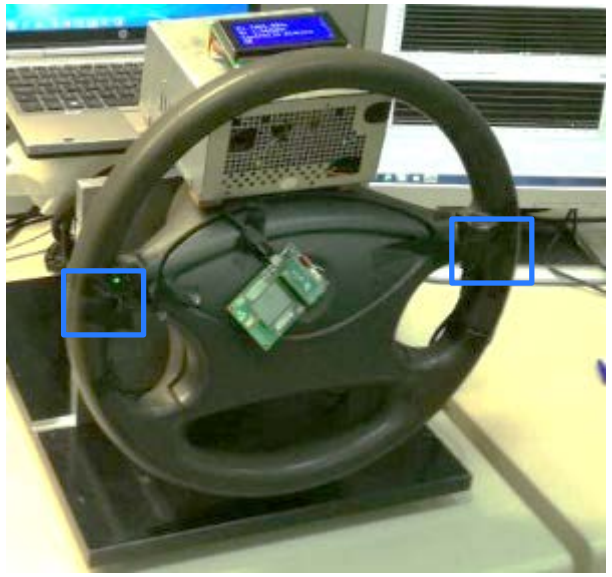
ADAS+ Platform:
3 Technological Modules



Physiological Module

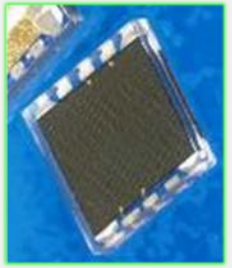
Integrated
Physiological
Sensor

Physiological Module

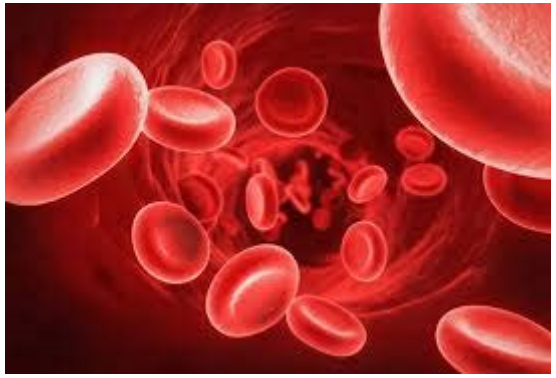


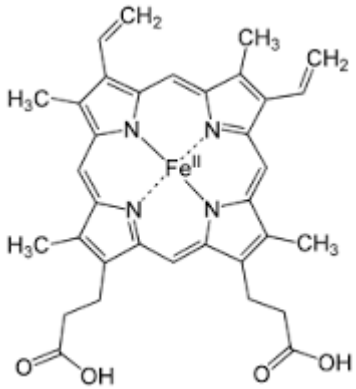
Physiological Probe

IR LED



Silicon photomultiplier **SiPM**



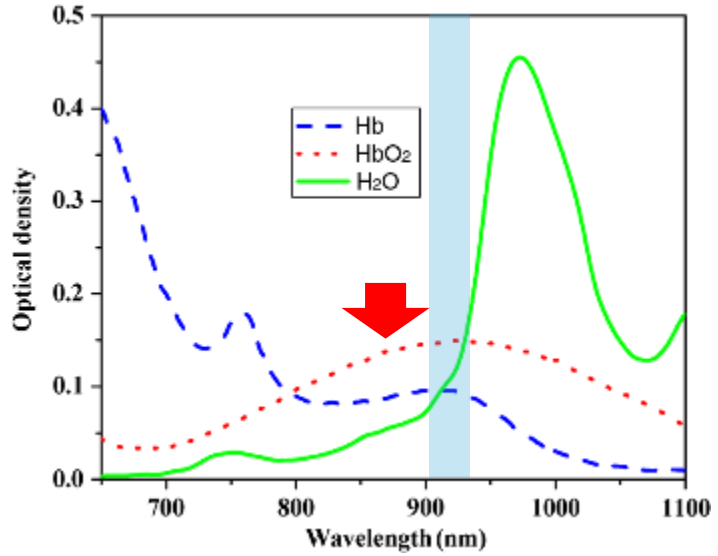


Emoglobina

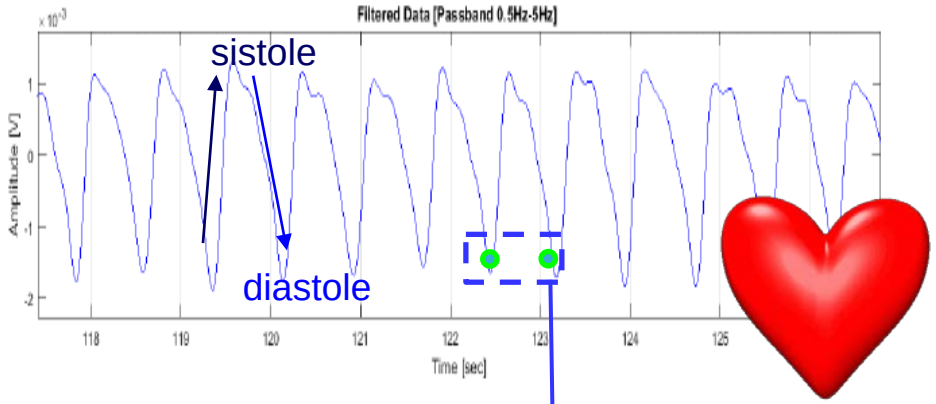
Backscattered IR Light (SiPM)

IR Light (LED)

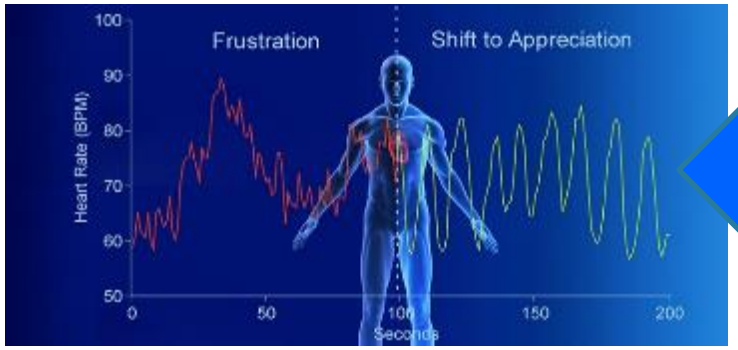
Physiological Module

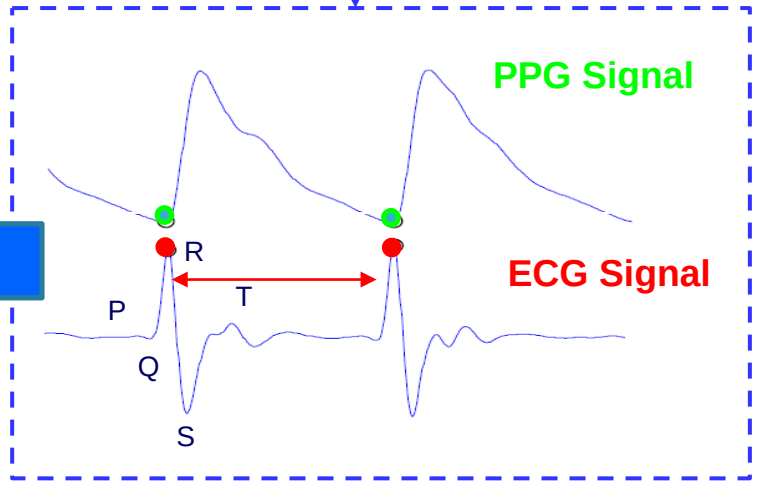


PhotoPlethysmoGraphy Signal



Heart Rate Variability (HRV)



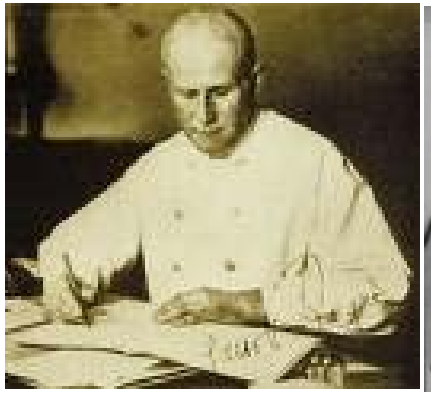


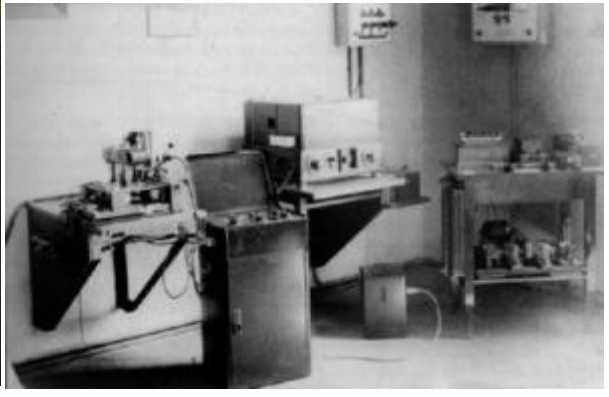
McCraty R., Shaffer F, *Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health risk*, Glob Adv Health Med. 2015 Jan;4(1):46-61. doi: 10.7453/gahmj.2014.073.

Are a PHYSIO Probes really able to measure the drowsiness reliably?

Prince Method for Drowsiness Detection

EEG: Electro-EncephaloGram



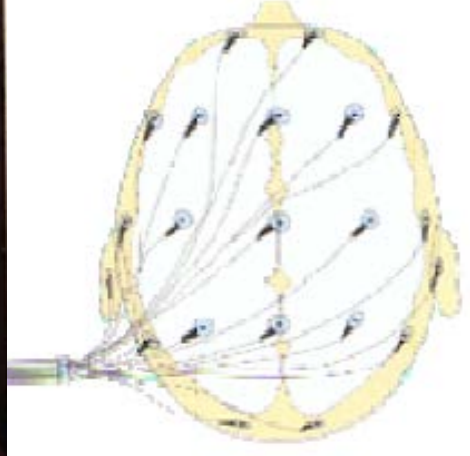


HANS BERGER (1873-1941)

First recordings of electro-cortical activity

Electrodes (16-24) secured on the scalp by means of a conductive paste (to ensure a low resistance connection)

relatively simple non-invasive painless



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Typical EEG Waveforms

EEG consists of waves with different

- ✓ frequency
- ✓ amplitude

} **Rhythms**

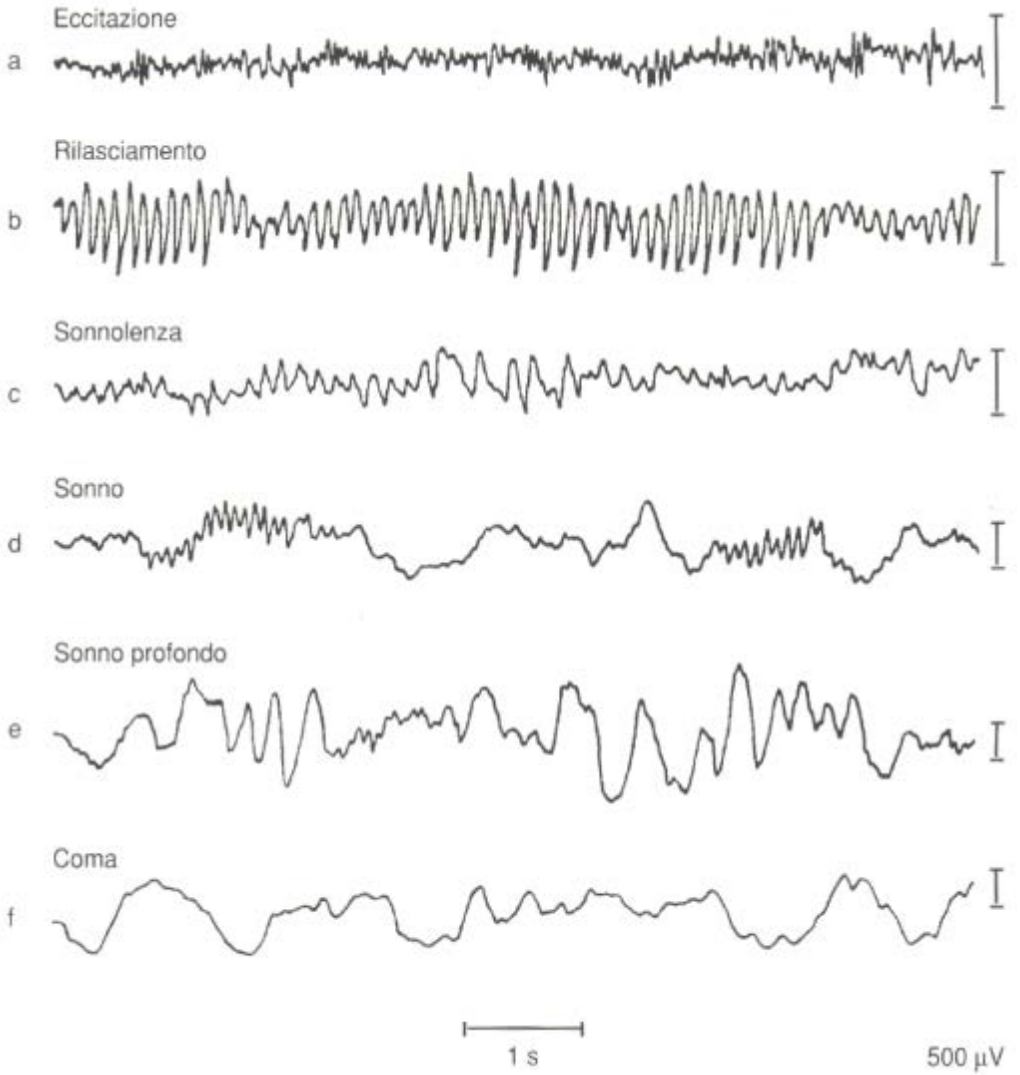
indicated by Greek letters:

α, β, δ, θ

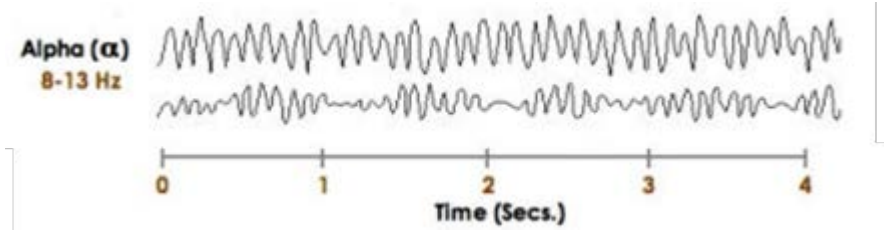
The variation in amplitude of such waves correlates specifically to:

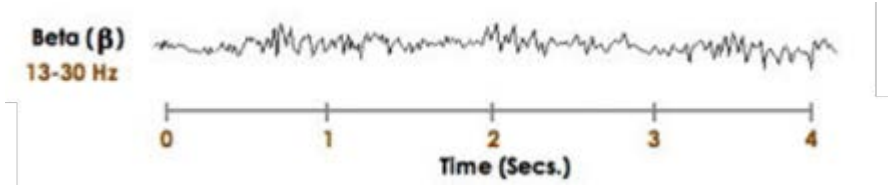
- physiological events
(sensory stimulation, sleep, etc.)

- pathological event
(epilepsy, coma, etc.)



EEG Rhythms for Drowsiness





Asleep (Drowsiness)

Awake

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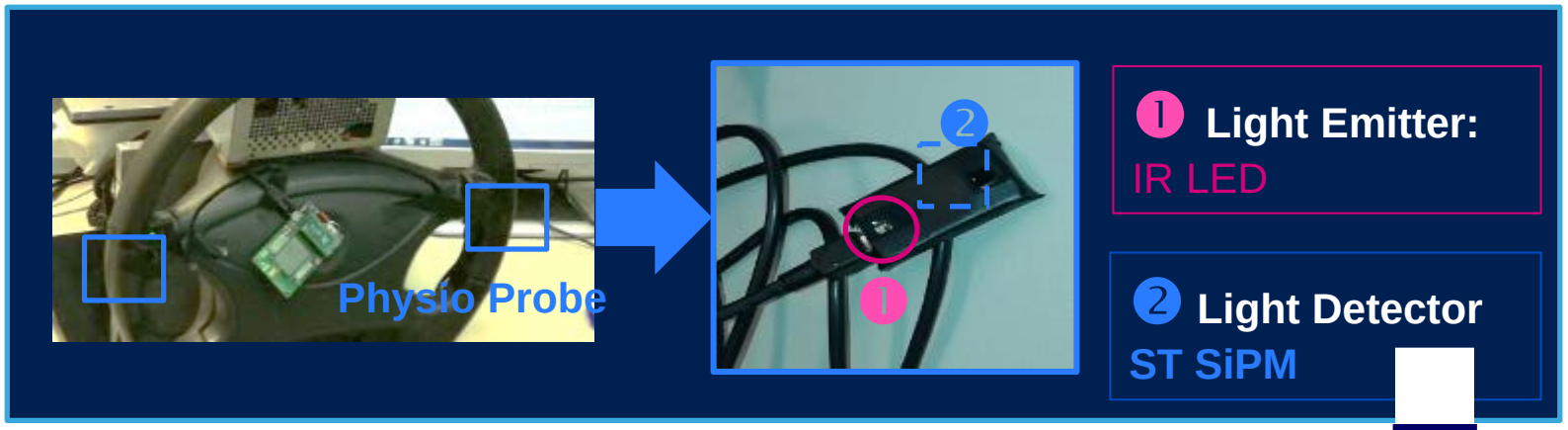
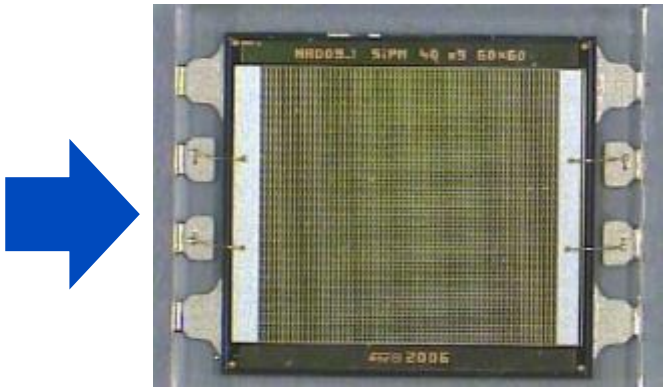
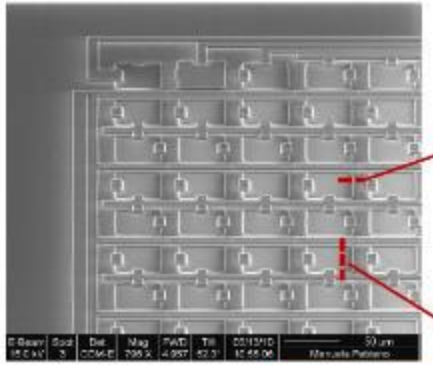
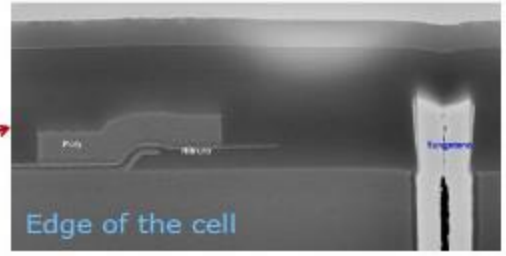
ST Drowsiness Probe



Silicon Photo Multiplier







Array of Photodidodes
~ 4400 cells (60x60um each)

Technological Details

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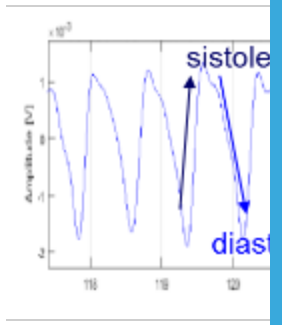
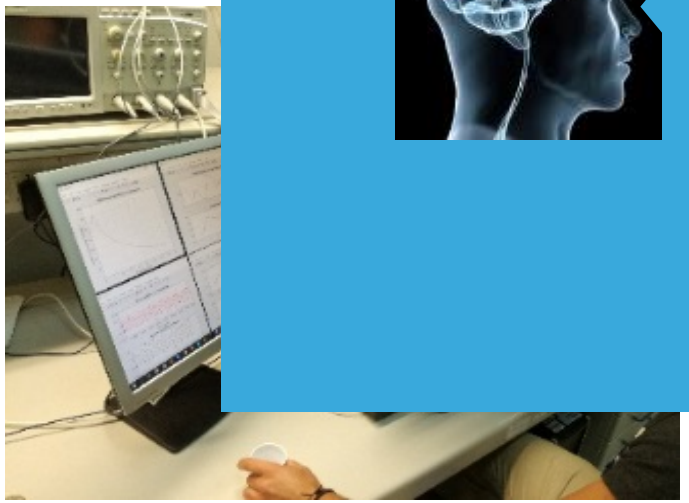
The Drowsiness Approach

Is there a correlation between

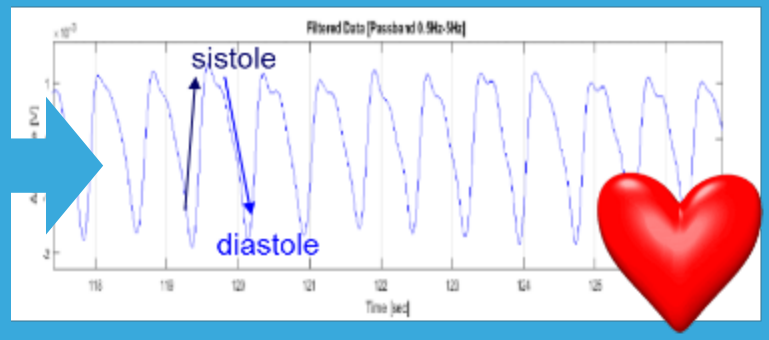
PPG Signal

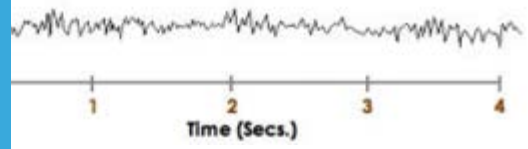
Photo

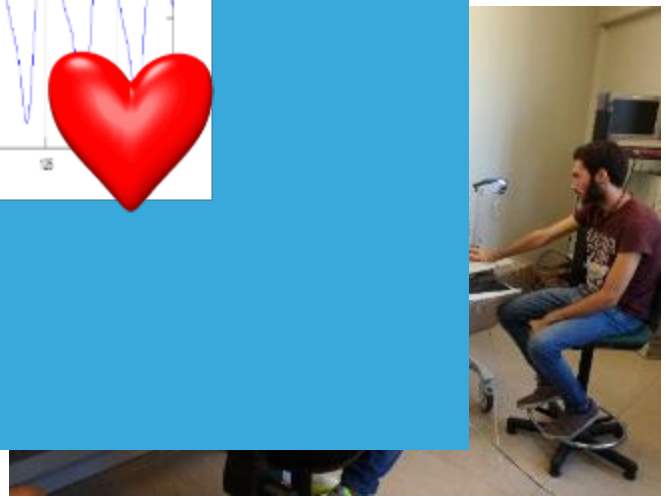




PhotoPlethysmoGraphy Signal







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Study Experimental Plan

> 70 Volunteers Recruited
~ 5 months of data collection
~ 3 months for data elaboration

For each volunteers

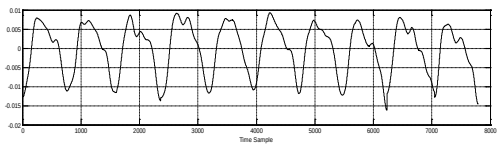
both PPG and EEG

have been collected!

Short List of Valid Volunteers

Age Range	Sex		TOTAL by Age
	F	M	
20-30	13	9	22
31-40	7	3	10
41-50	5	3	8
51-60	3	5	8
>60	6	2	8
TOTAL	**34**	**22**	**56**

How the Algorithm Works…



PPG Filtering

Patent 102017000081018

Normalization

LM MLP Neural Network System 1

Pre-trained Levenberg-Marquadt

Mathematical HF features

LM MLP Neural Network System 2

Multi-Layer Motor Map Neural Network

μ(Autocorr)
σ (EEG)
μ(EEG)

Level of Driver Drowsiness Detection

0-0.5 -> Drowsy Driver

0.51…1.00-> Wakeful Driver

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Results

RULES

	Drowsy	Awake
Real Case:	0	1
ADAS Algo	0-0.50	0-51-1.00

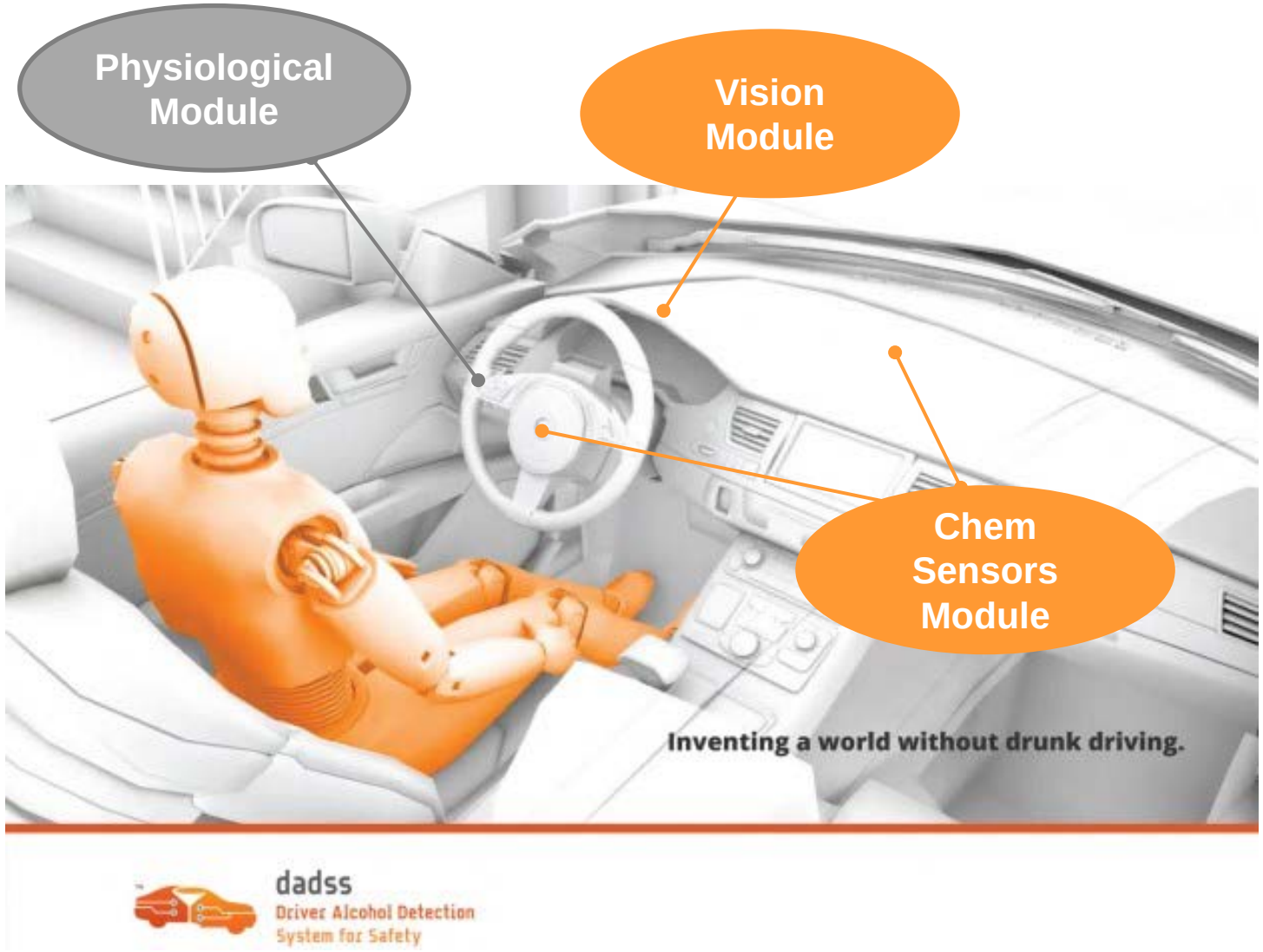
ALL OK!

Case	Real	Algorithm Output (5min PPG trace)
1	0	0.242
2	0	0.345
3	0	0.112
4	1	0.654
5	1	0.801
6	1	0.675
7	0	0.432
8	0	0.234
9	0	0.199

F. Rundo and S.Conoci “An electrophysiological signal processing method, corresponding system, computer program product and vehicle” IT Patent N. **102019000005868**

F. Rundo, PG Fallica, S.Conoci, R.Parenti, V. Perciavalle, *A Method Of Processing Electrophysiological Signals, Corresponding System, Vehicle And Computer Program Product* - **IT 82720893**

ADAS+ Platform:
3 Technological Modules



MODULO VISION

4 SENSORS:

- ✓ **AMBIENT LIGHT CAMERA** (INSIDE THE CAR CABINET)
- ✓ **IR CAMERA IR** (INSIDE THE CAR CABINET)
- ✓ **RADAR SENSOR** (OUTSIDE)
- ✓ **LIDAR SENSOR** (OUTSIDE)

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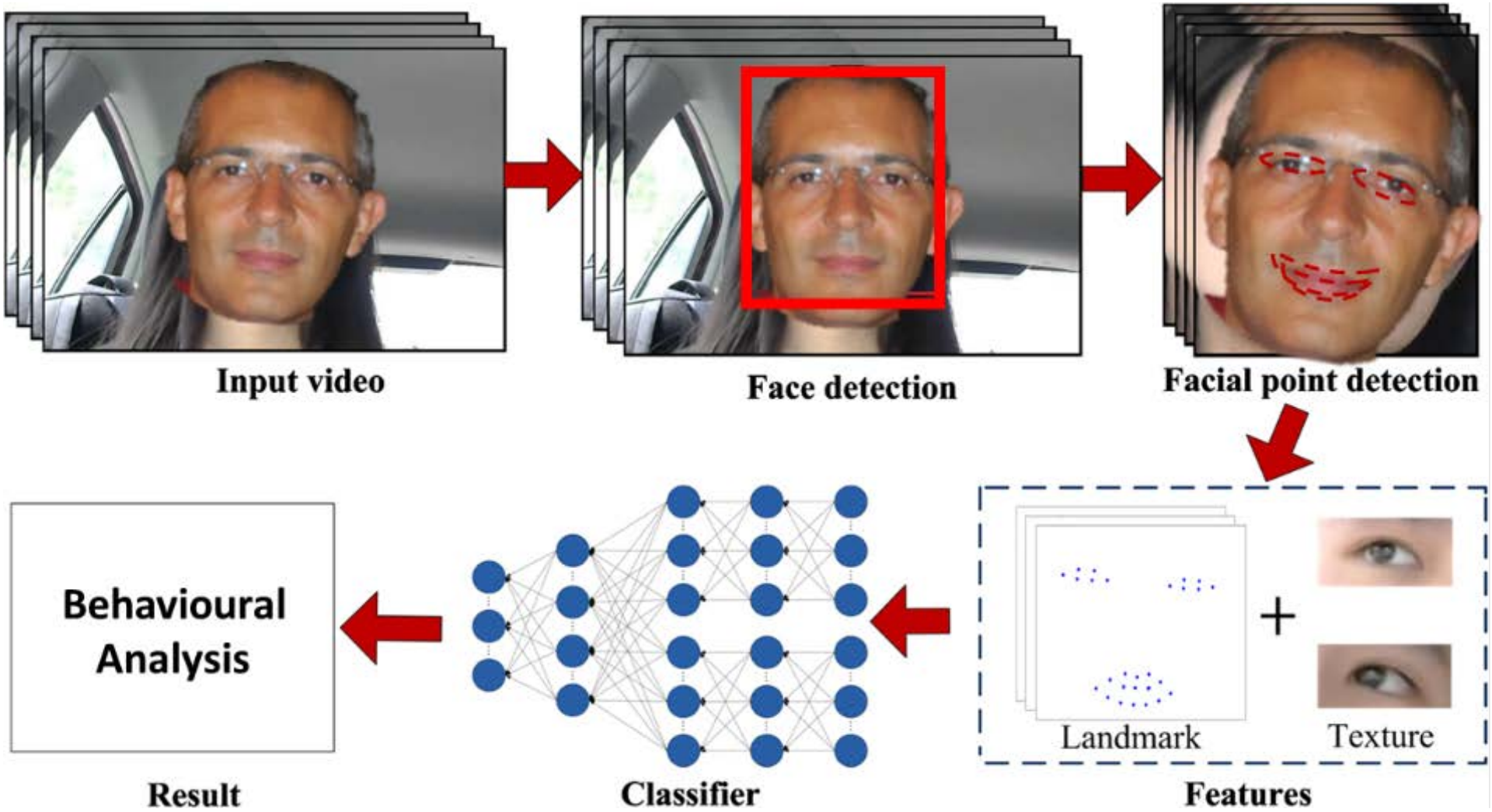
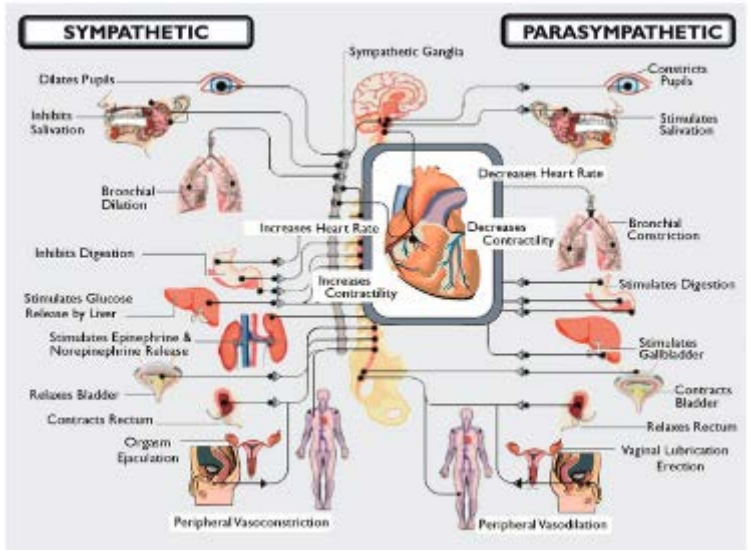
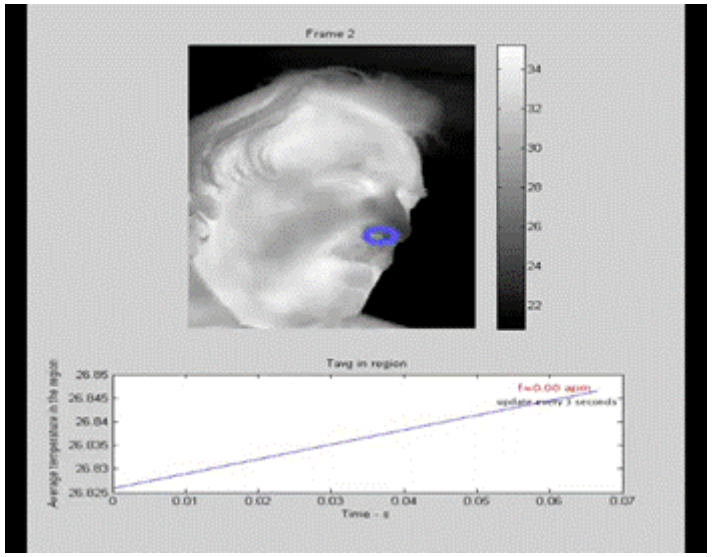
Ambient Light Camera

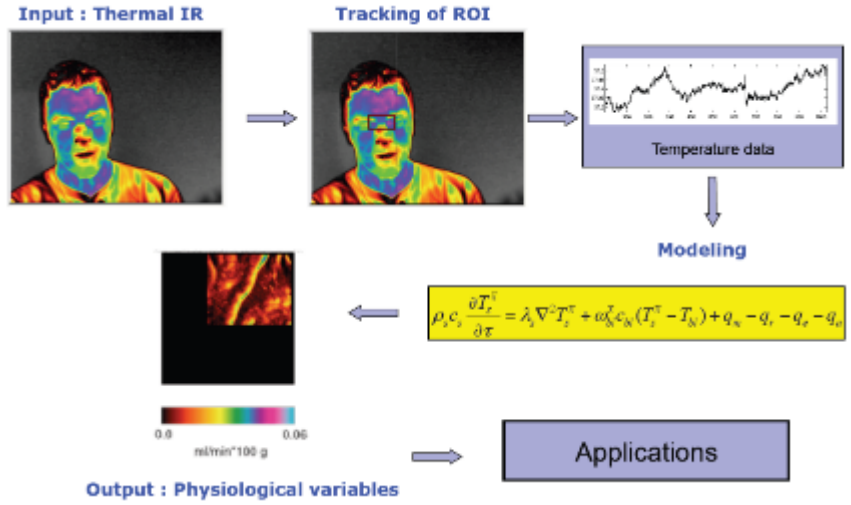
Overall Flow



Contact-Less Monitoring of Psychophysiological States







Merla, Frontiers in Psychology 2014

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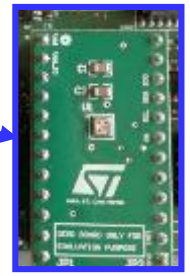
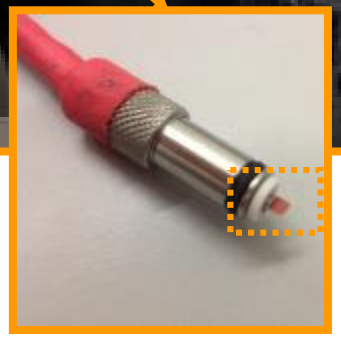
Sensor Module



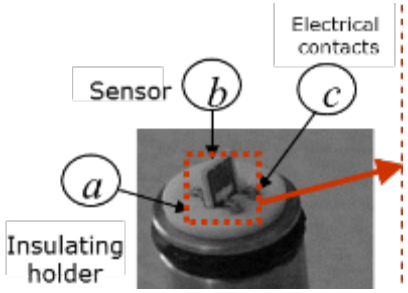
GHT25S
Air Quality Sensor



Ethanol Sensor
(Breath Test)

SOBRIETY SENSOR (BREATH TEST)

✓ **SENSORE PER DRIVER SOBRIETY** (INTEGRATED IN THE STEEL)



MULTICHIP

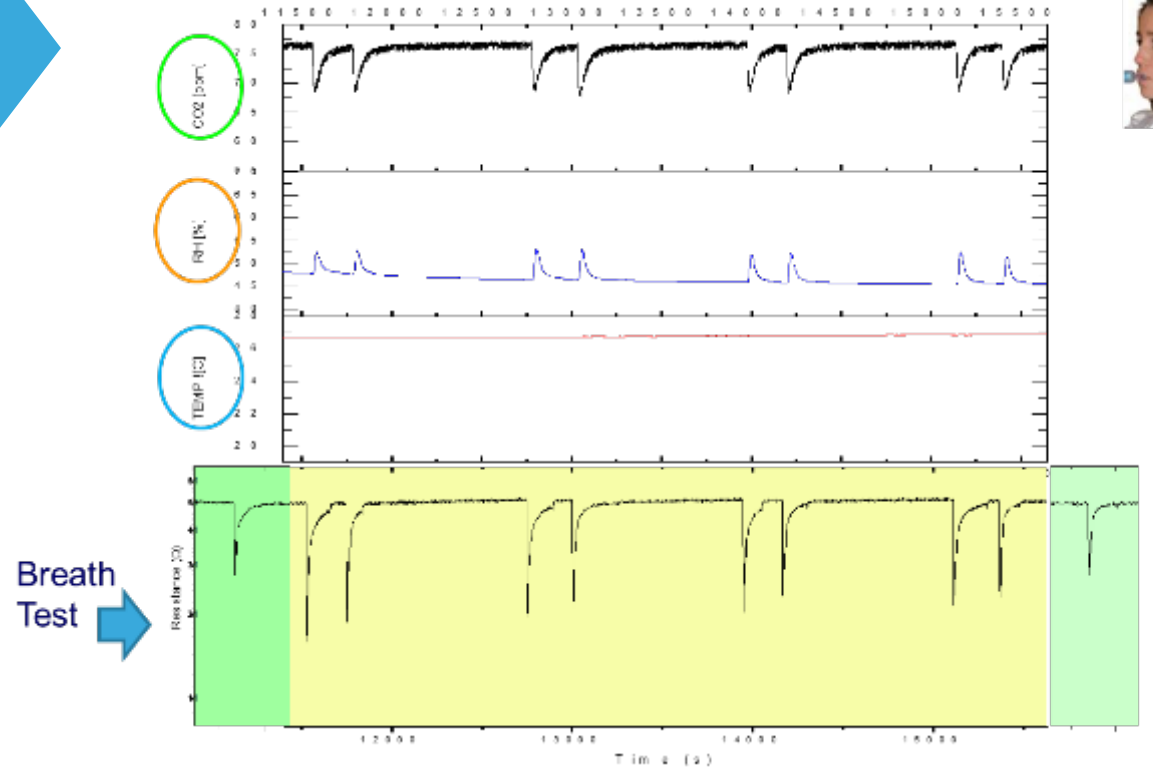
ETOH SENSOR

+

HUMIDITY SENSOR

+

CO2 SENSOR



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Air Quality Test

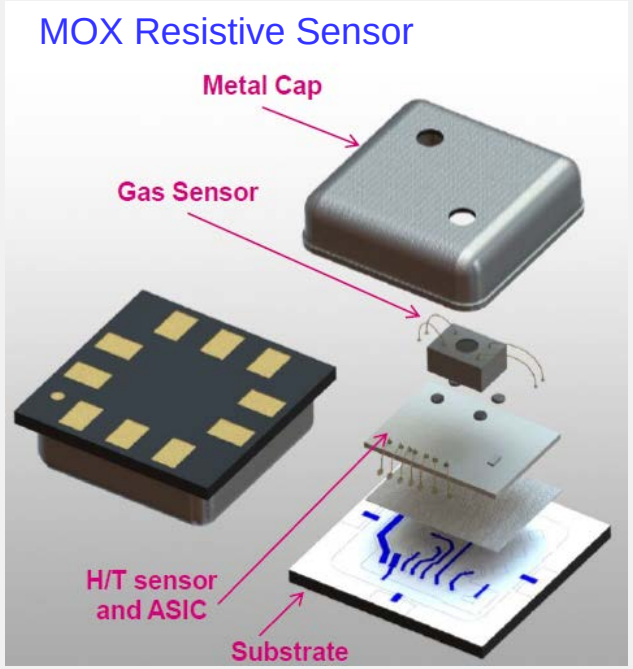
GHT25S

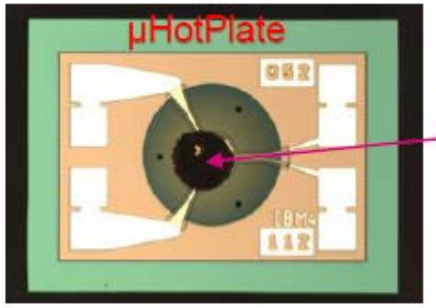
Air Quality Sensor Demo Board

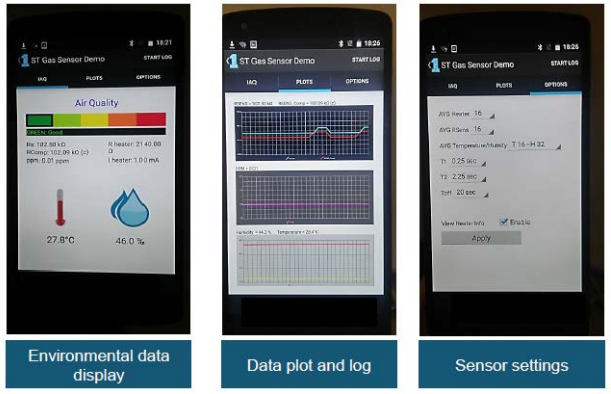
Humidity Sensor

Temp Sensor

Voc (CO, EtOH, HCHO..)







Graphical Interface

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Final Output

ADAS+ car control unit integrating Sensor Platform

Validation on Car Test

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2. Innovative Sensors For Health:
A particular Case: BioChip for DNA Analysis

How Silicon can be Innovative?

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Intro:
The Context

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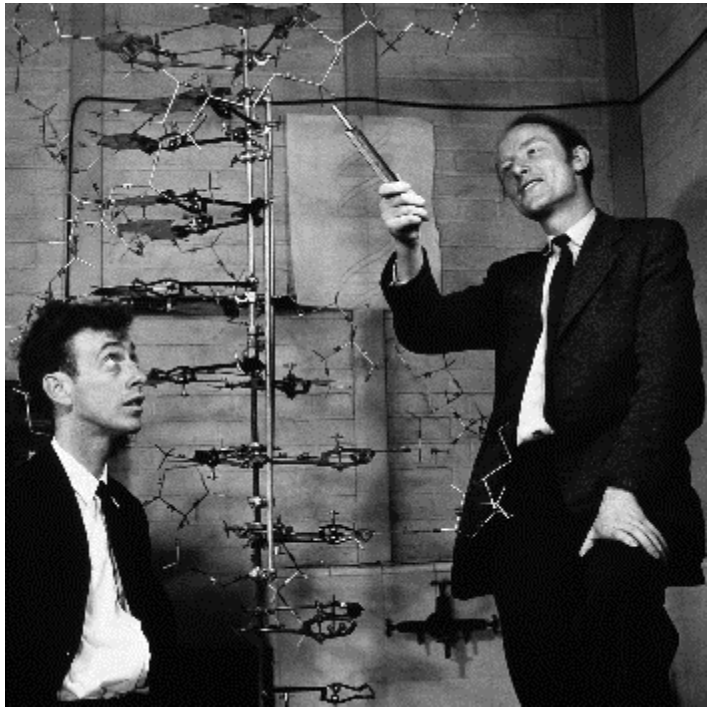
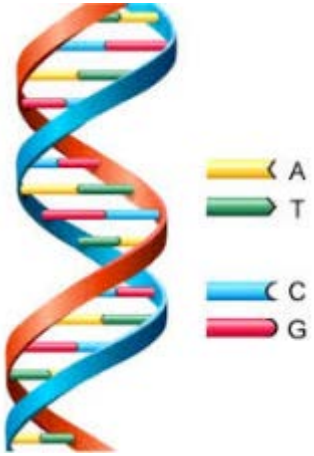
Genetic Analysis Technologies
The Pillars

1 – DNA structure Discovering



1953 *Francis Crick and James Watson*
figured ou ad a
double-he



1962, Nobel Prize in Physiology or Medicine "*for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material*".

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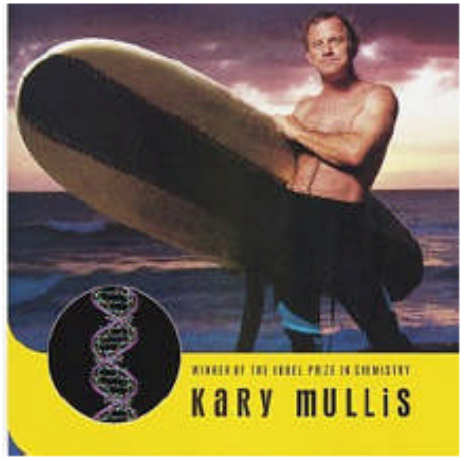
Genetic Analysis Technologies
The Pillars

2 - DNA amplification Method Discovering

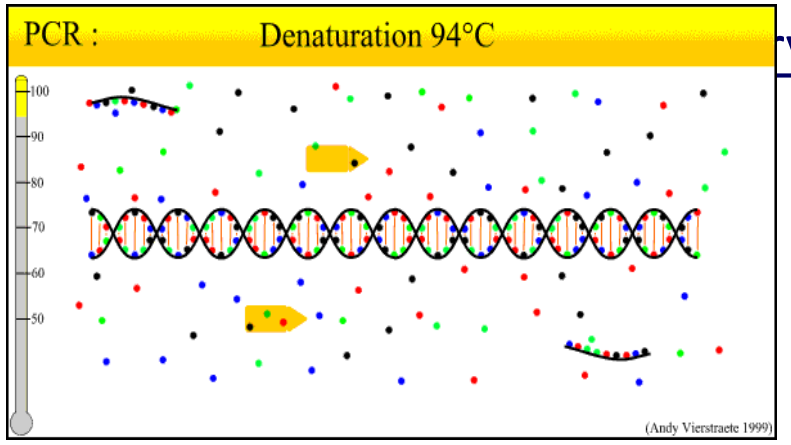
Polymerase Chain Reaction (**PCR**) (1983)

"DNA photocopier"



« Sometimes a good idea comes to you when you are not looking for it »

- 1983 *Kary Mullis* discovers the PCR
- [y]



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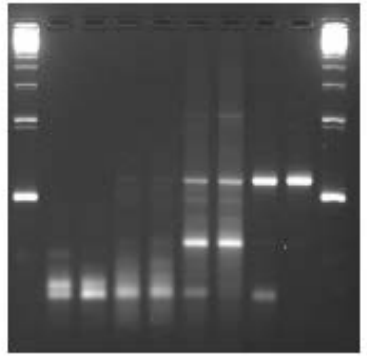
Genetic Analysis Technologies
The Pillars

2 - DNA amplification Method Evolution

Real Time **PCR**

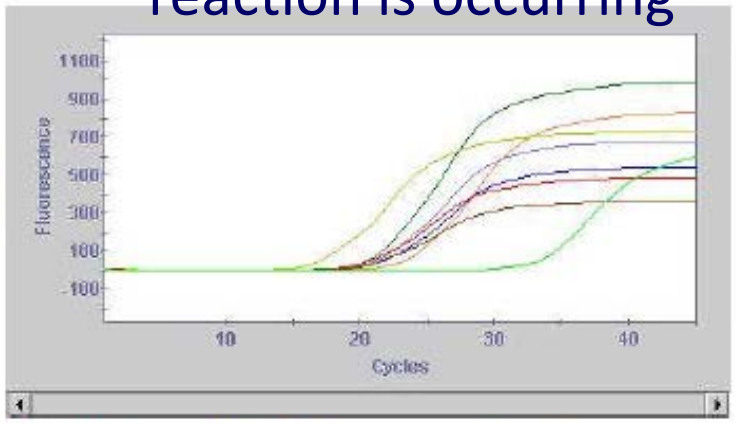
(Roche early 1990Ys)

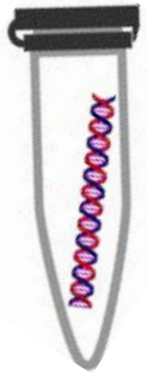
PCR → Detection *end*



EF gel

RT PCR → Detection while the reaction is occurring





Quantitative

Closed System

Molecular Diagnostic

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Genetic Analysis Technologies
The Pillars

3 – Completion of Genome Sequencing

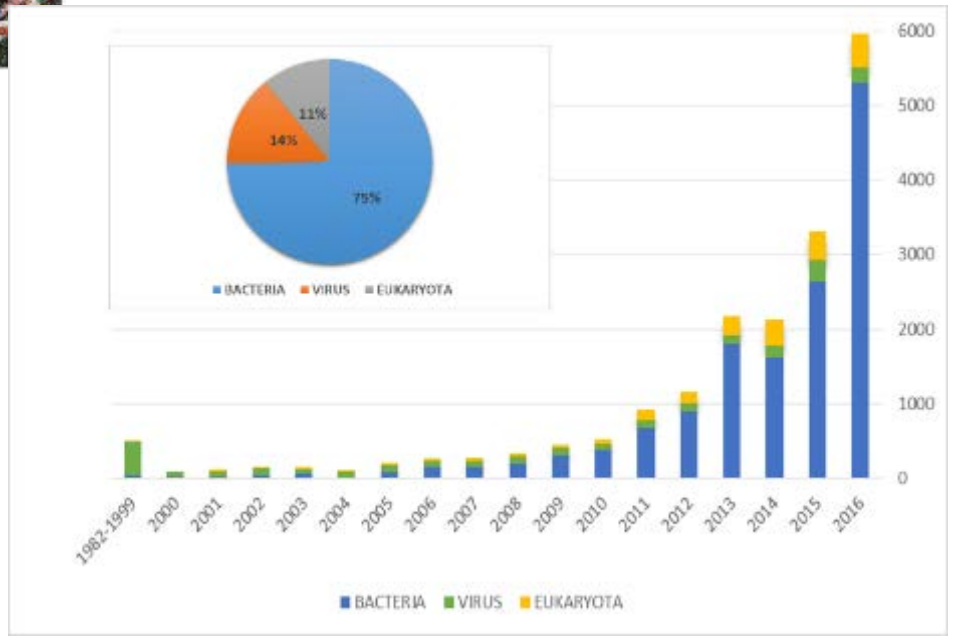
1976 – Bacteriophage MS_2 Genome

2001 –Human Genome

Initial sequencing and analysis of the human genome
Nature 2001

YTD –Sequenced Genomes

Source: GeneBank
https://www.ncbi.nlm.nih.gov/nucgss/



More than
14.000
genomes!

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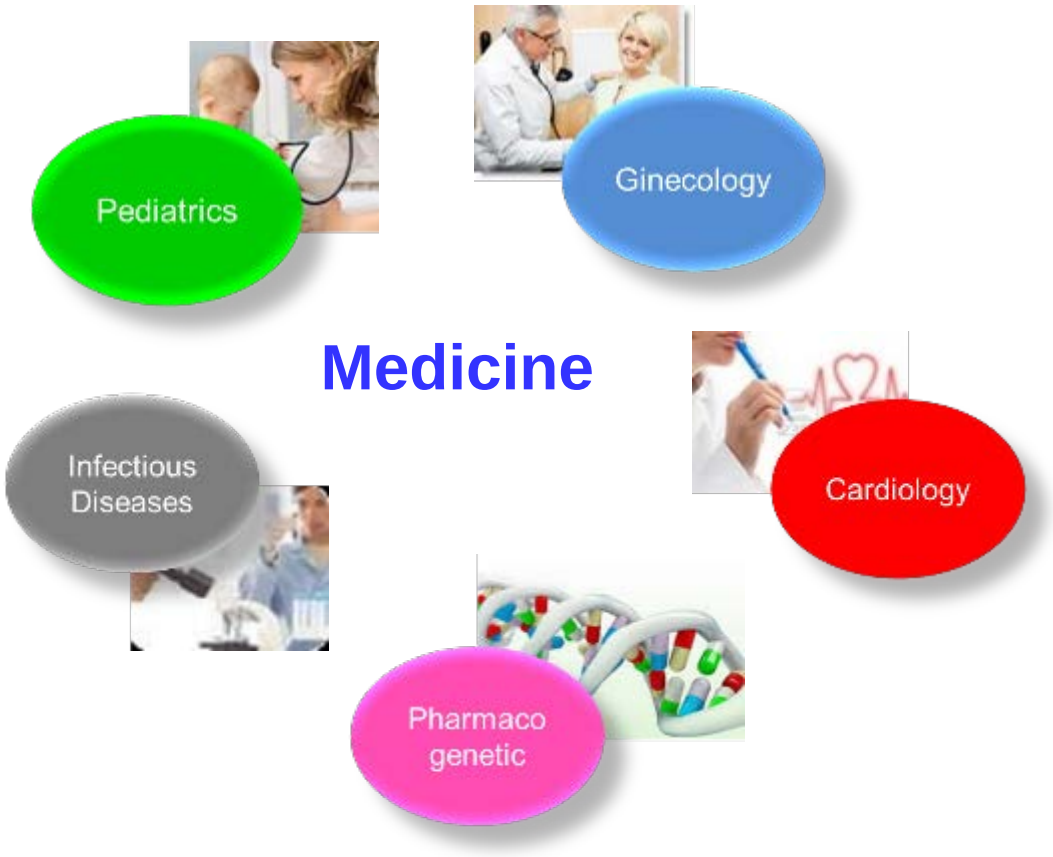
S Petralia and S Conoci, **ACS Sensor,** *2017, 2, 876-891*

Genetic Analysis Applications



Forensic

Short Tandem Repeat (**STR**) Profiles

Food

Species Identification, OGM...

Important Advancements in Heathcare, Forensic and Food...

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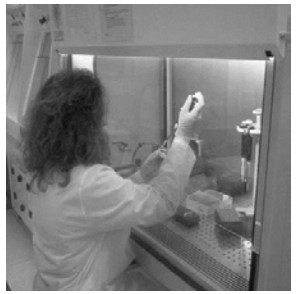
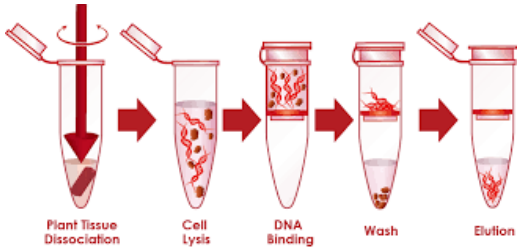
How Genetic Analysis Works

1- Sample Preparation

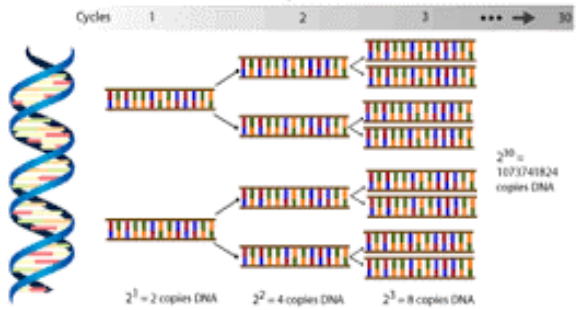
Nucleic Acid Extraction





2- PCR

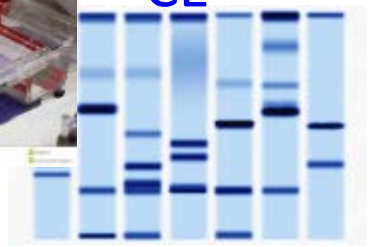
Nucleic Acid Amplification



3- EF/RT-PCR….

Nucleic Acid Detection

CE



RT-PCR

TIME: 2 - 10 h

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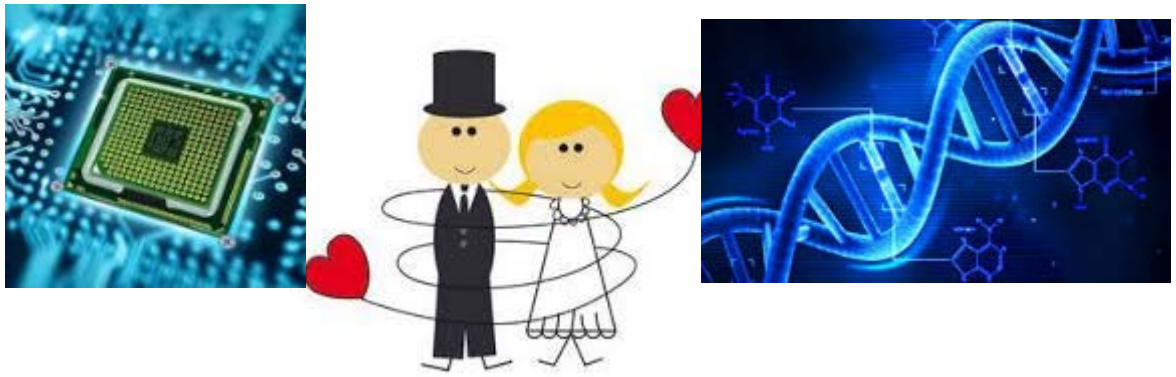
....the late ’80...microtechnologies appears in the genetic analysis....

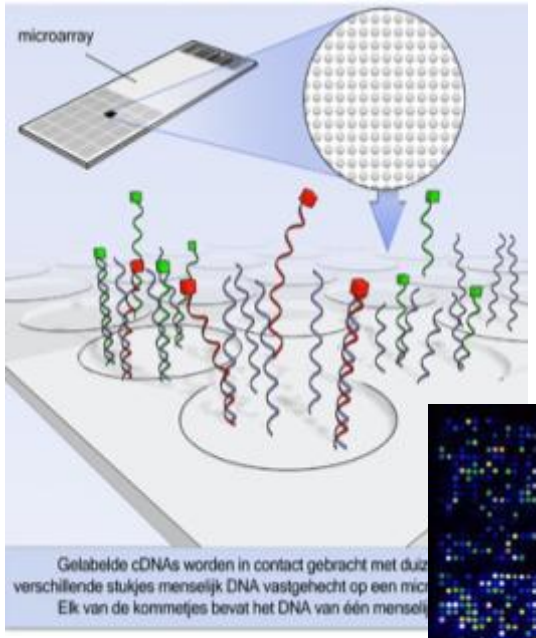


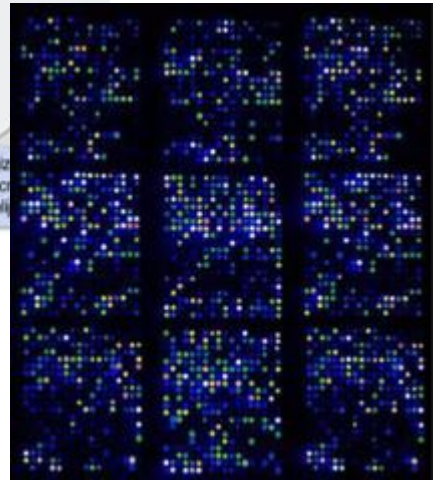
Genetic Analysis MicroTechnologies

Biochips

Microarray

(1st microsystem)





microsystems

with

***tailored surface properties* for life sciences applications**

which typically offer *high parallelization of analysis*

- 1989: First Affymetrix Genechip Prototype
- 1994- First cDNAs are developed at Stanford.

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What socially going in Healthcare....

The decentralization of healthcare

Advances in technology and strains on the current healthcare system are driving patient treatment to physician offices, rapid clinics, and homes

Scientia Advisors

Centralized ..... **Decentralized**

- The increasing migration of healthcare from centralized, core hospital locations to more point-of-care settings such as emergency rooms, outpatient clinics, rapid and urgent care clinics, and the home
- A Decentralized Healthcare system aims to improve overall implementation of healthcare programs, provide uniformity of healthcare standards across rural and urban areas and lower costs by moving to more streamlined and efficient programs

ICU: Intensive Care Unit
ER: Emergency Room
PO: Physician Office

Source: Scientia analysis

Advancements in technology promote decentralization

Small, easy-to-use, mobile devices allow for patient testing and monitoring in clinics and at home with little or no expert assistance

Scientia Advisors

TRADITIONAL EQUIPMENT

Large, stationary equipment that must be operated by healthcare professionals

SEMI-PORTABLE EQUIPMENT

Bench-top and handheld devices used in clinics and POs allowing for faster, on-site results

MOBILE EQUIPMENT

Small devices for clinical and in-home use requiring little to no professional assistance

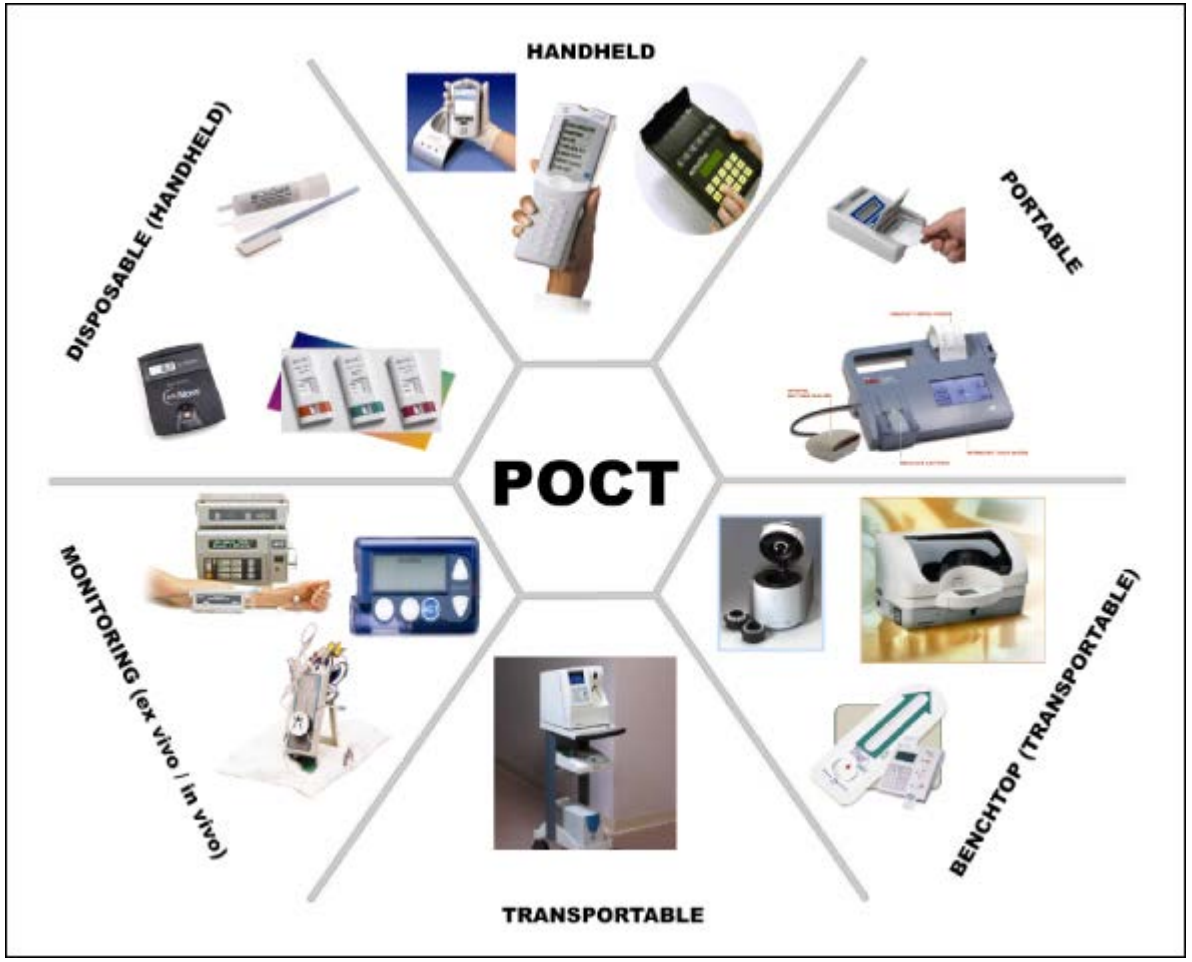
FUTURE?

Medical equipment is decreasing in size and becoming easier to use

Source: Scientia Analysis, Roche

Strategic Guidelines for the Next Generation of Genetic Analysis

- Miniaturization
- Integration
- Automation



Point of Care

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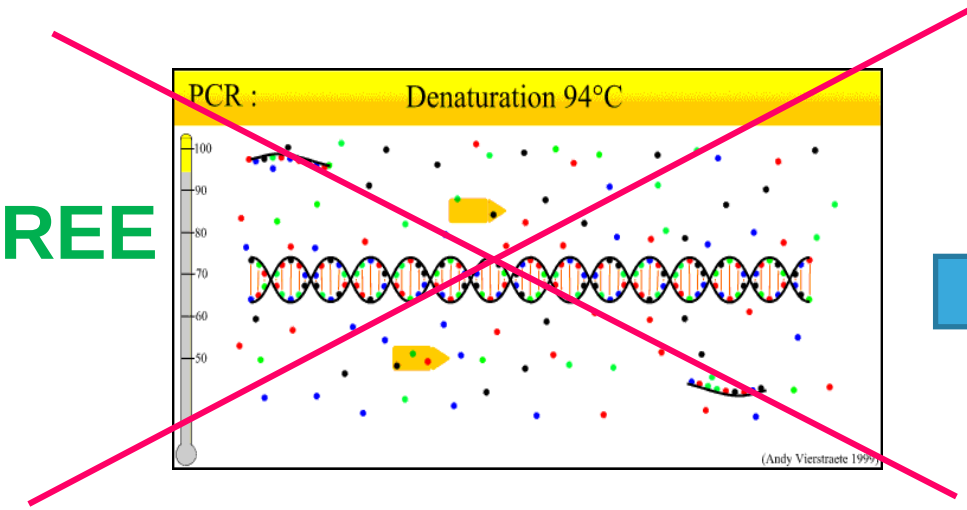
The Next Generation of Biotechnologies for DNA Analysis

PCR-FREE

NEW FRONTIER IN THE DNA DETECTION

PCR-FREE



Portable and
Easy-to-Use

GENETIC POINT-OF-CARE

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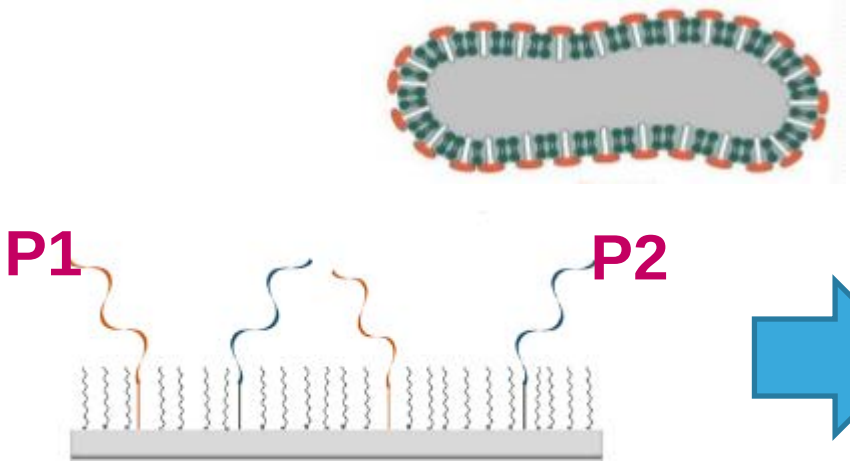
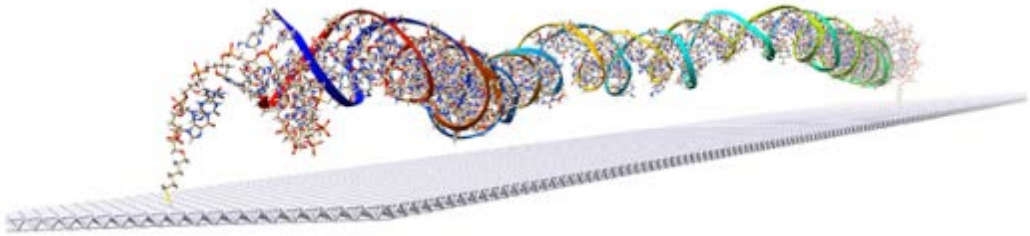
Biochemical Strategy Implementation for PCR-free Biotechnology

Surface Cooperative Hyb





Genome Anchoring to Surface

Once Genome is anchored to Surface Find an Effective Method for Transduction??

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First Approach

Intercalative Label for Cooperative Hybridization

STIMULUS

Signal

INSPIRATION CAME FROM….

United States Patent
Conoci et al.

(10) **Patent No.:** US 7,799,912 B2
(45) **Date of Patent:** Sep. 21, 2010

The stimulus on the Intercalative Label inside the whole Genome produces a Signal

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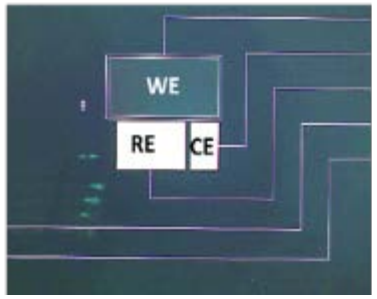
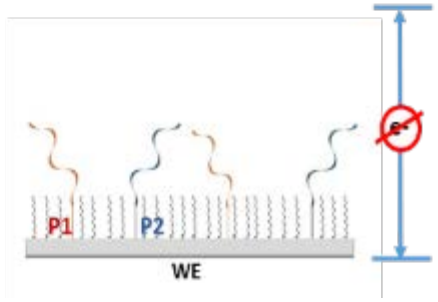
Detection Strategies 1st approach

Os Complex Redox Intercalative Probe

Miniaturised Electrochemical cell (2000 x 2000um)

Pt WE (1000x2000um)
Au RE (800x 500um)
Au CE (800x1250um)

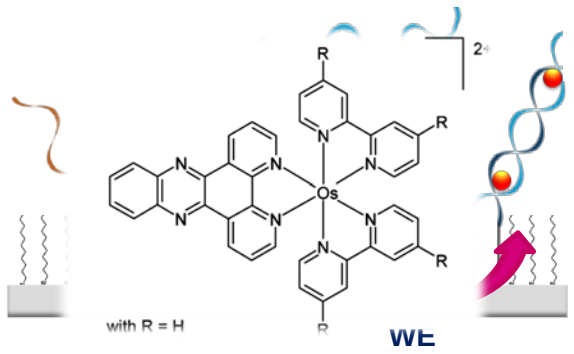




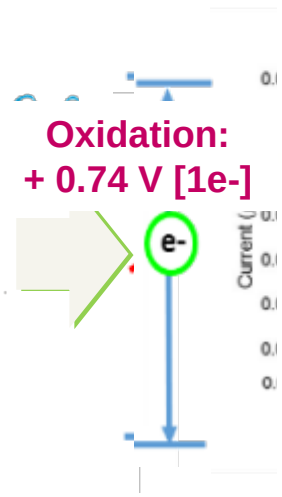
P1-P2 immobilized on Pt WE

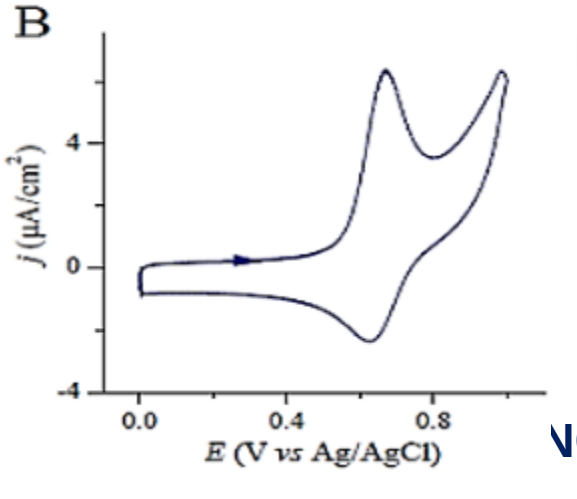
$[Os(byp)_2(dppz)]^{2+}$
5uM

Intercalative Redox active Os complex



Oxidation: + 0.74 V [1e-]





HBV

NO HBV

Analyst, 2017, 142, 2090–2093

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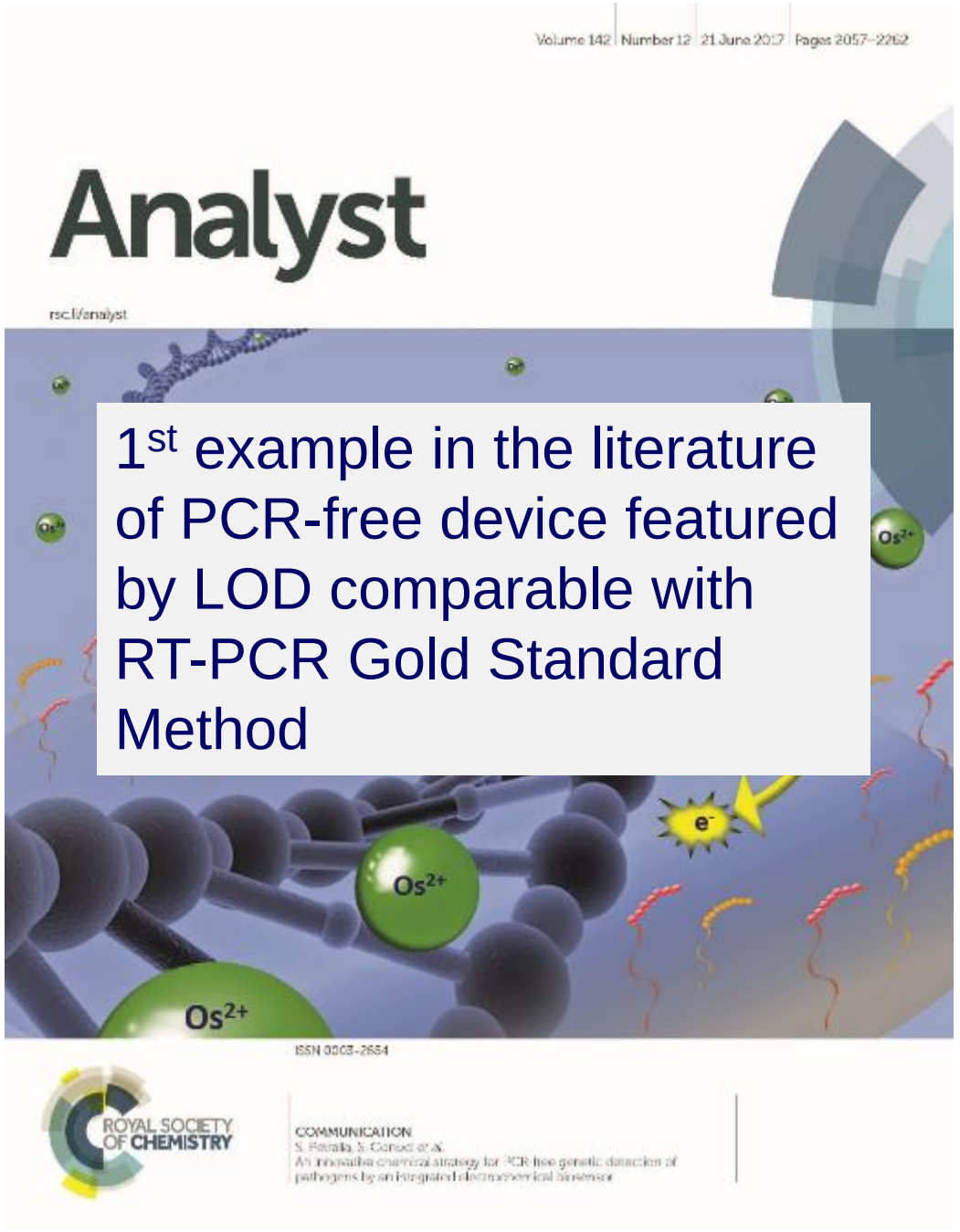
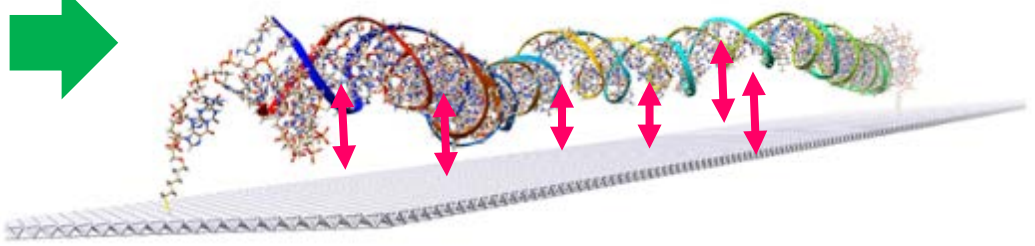

Volume 142 | Number 12 | 21 June 2017 | Pages 2057–2262
Analyst
rsc.li/analyst
1st example in the literature of PCR-free device featured by LOD comparable with RT-PCR Gold Standard Method
Os2+
e-
ISSN 0003-2654
ROYAL SOCIETY OF CHEMISTRY
COMMUNICATION

Principle of Detection Method

Second Approach

Label Free

STIMULUS



Signal

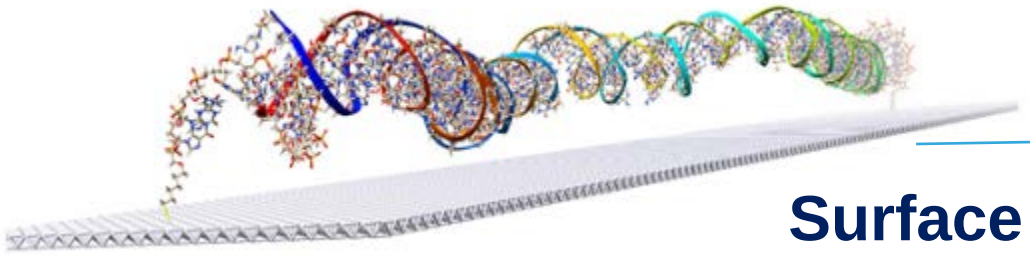
Upon a specific Stimulus the Interaction of the Whole Genome produces a Signal

Prof F.Priolo

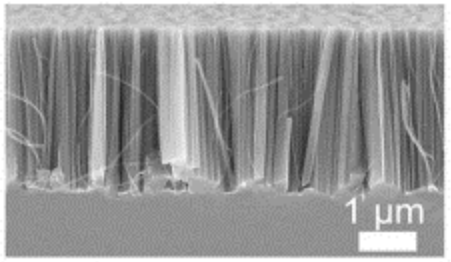
Detection Strategies

SECOND APPROACH

Label Free

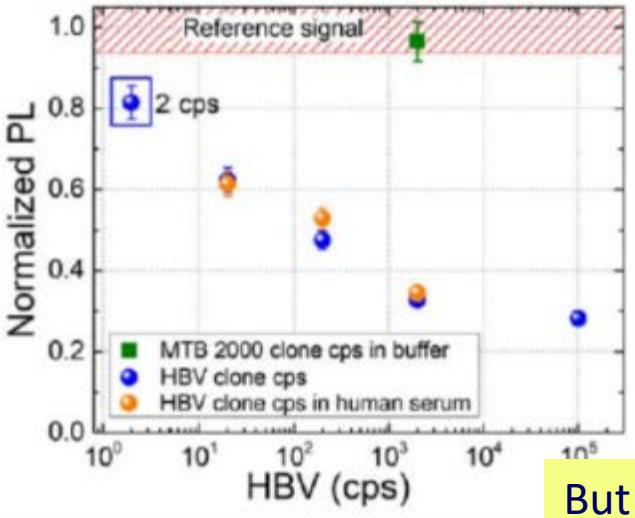


Surface



Silicon-NWs → able to emit light (quantum confinement effect) upon excitation @700nm

In presence of genome the emitted light intensities decreases



Direct genome detection without any amplification and label →

- ✓ **2 cps/reaction for analytical sample!**
- ✓ **20 cps/reaction for real sample (human serum)**

Overcome the **RT-PCR LOD**: 10 cps/reaction!

But Implementation on portable device not so easy!

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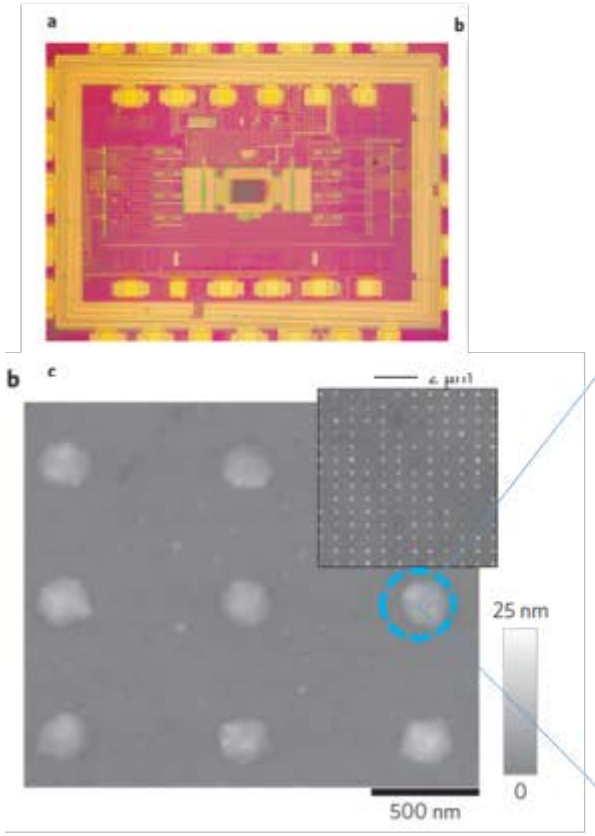
ACS Sensor, 2018,3, 1690

Prof L.Selmi

SECOND APPROACH

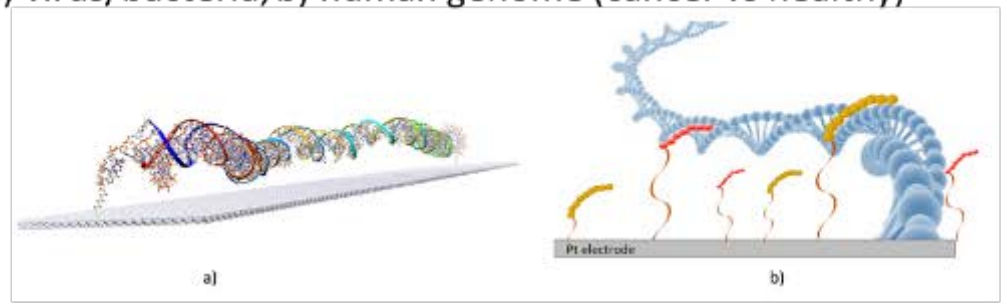
CMOS Nanocapacitor Array (256x 256 Nanoelectrodes)



C. Laborde et al, NATURE NANOTECHNOLOGY, 10, 2015 – 791-796

RNA/DNA Genome Fingerprint → *Impact: basic Knowledge of ocapacitive fingerprint of molecular recognition process; PCR Free detection*

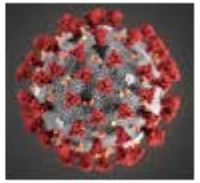
a) virus/bacteria; b) human genome (cancer vs healthy)



Cells fingerprint → *Impact: 1.basic Knowledge of capacitive cellular fingerprint; 2.Electrical Biopsy; 3. Personalized Therapy*

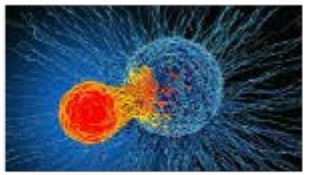
virus/bacteria

a)



cancer

b)



nervous

c)

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PCR-Free FUTURE PERSPECTIVE

MORE EXITING PERSPECTIVES

Molecular Analysis @ Not developed Countries

ACS Sensor, *2017, 2, 876-891*

SPECIAL THANKS TO….

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F Puntoriero

Prof F.Priolo
Prof. S.Battiato
Prof. V. Perciavalle

Dr. Cirino Vasi

Prof. Paolo Pavan
Prof Luca Selmi
Prof. Enrico Sangiorgi

Prof. Arcangelo Merla

Prof. Alessandro Busacca

Dr. Aldo Siciliano

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Thank you for your kind attention!