EDMI Microsystems and Microelectronics

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

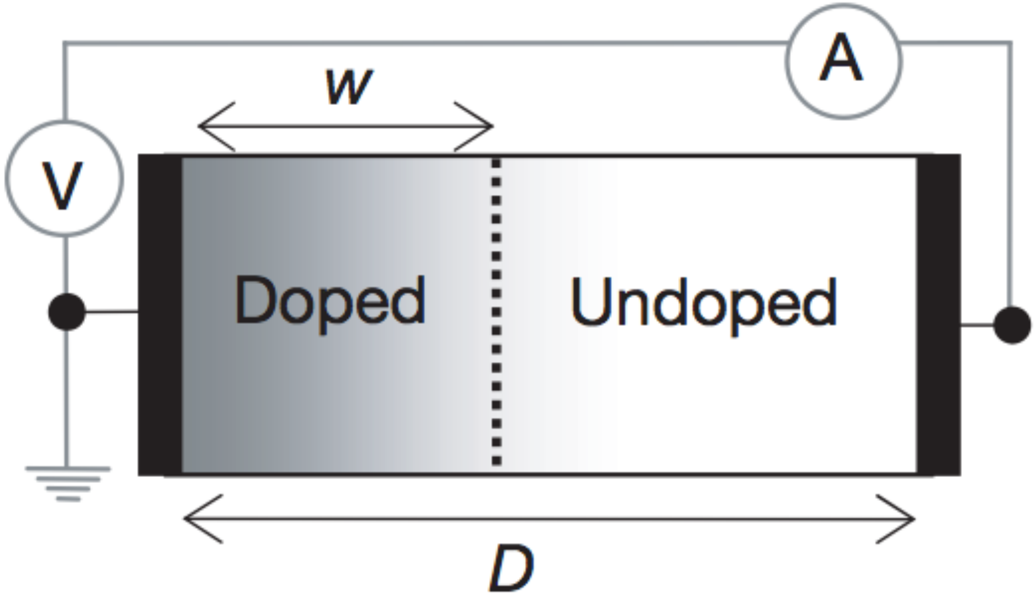
Lecture #14

CMOS for Sensing (and computing!) with Memristors

Memristive Sensors Milestones

2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018

Strukov & Williams



w-state model

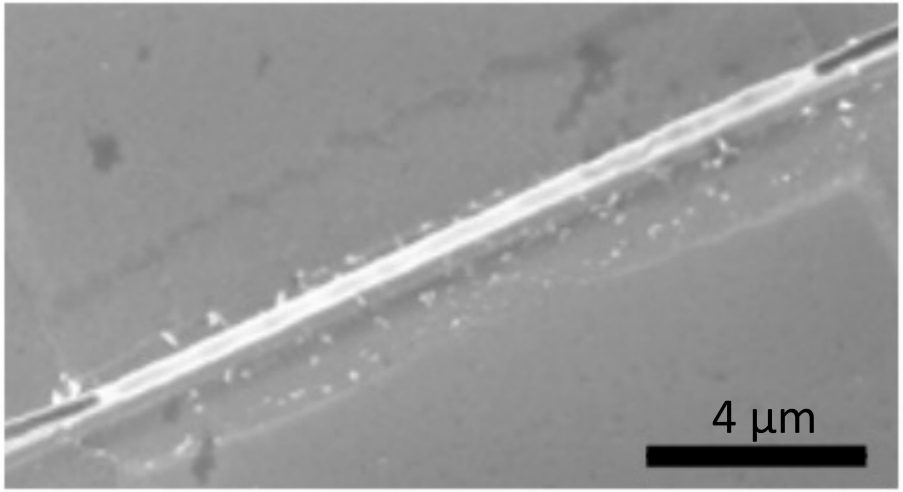
D.B. Strukov, al et S. Williams, Nature 2008

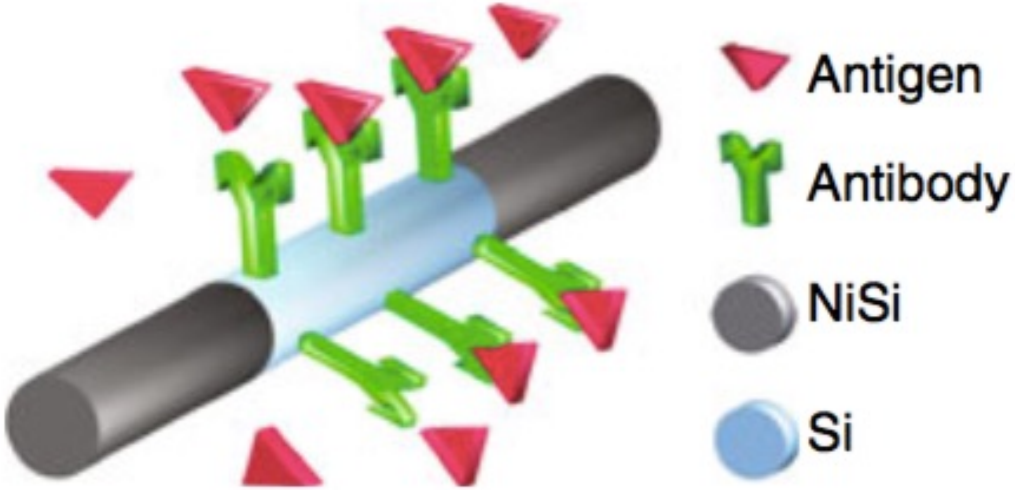
Memristive Sensors Milestones

2008 › 2009 › 2010 › 2011 › 2012 › 2013 › 2014 › 2015 › 2016 › 2017 › 2018

AntiRabbit

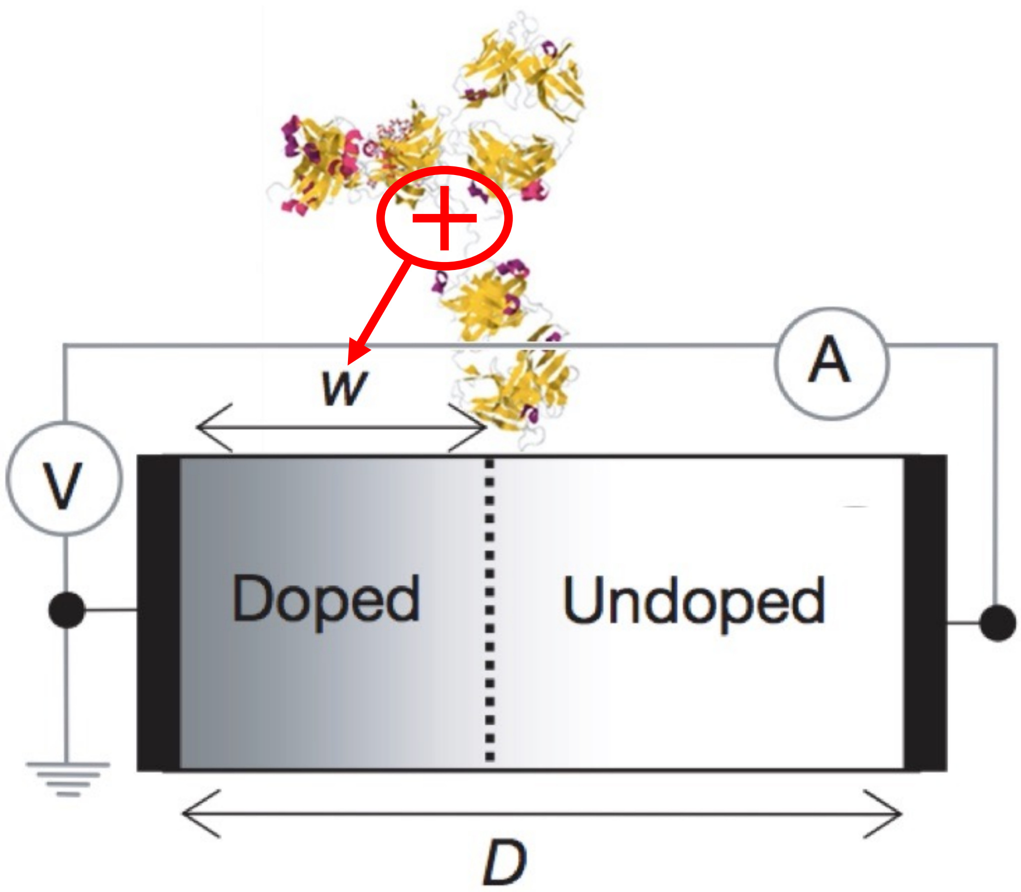
D. Sacchetto et al. / BioNanoSci. 1 (2011) 1–3





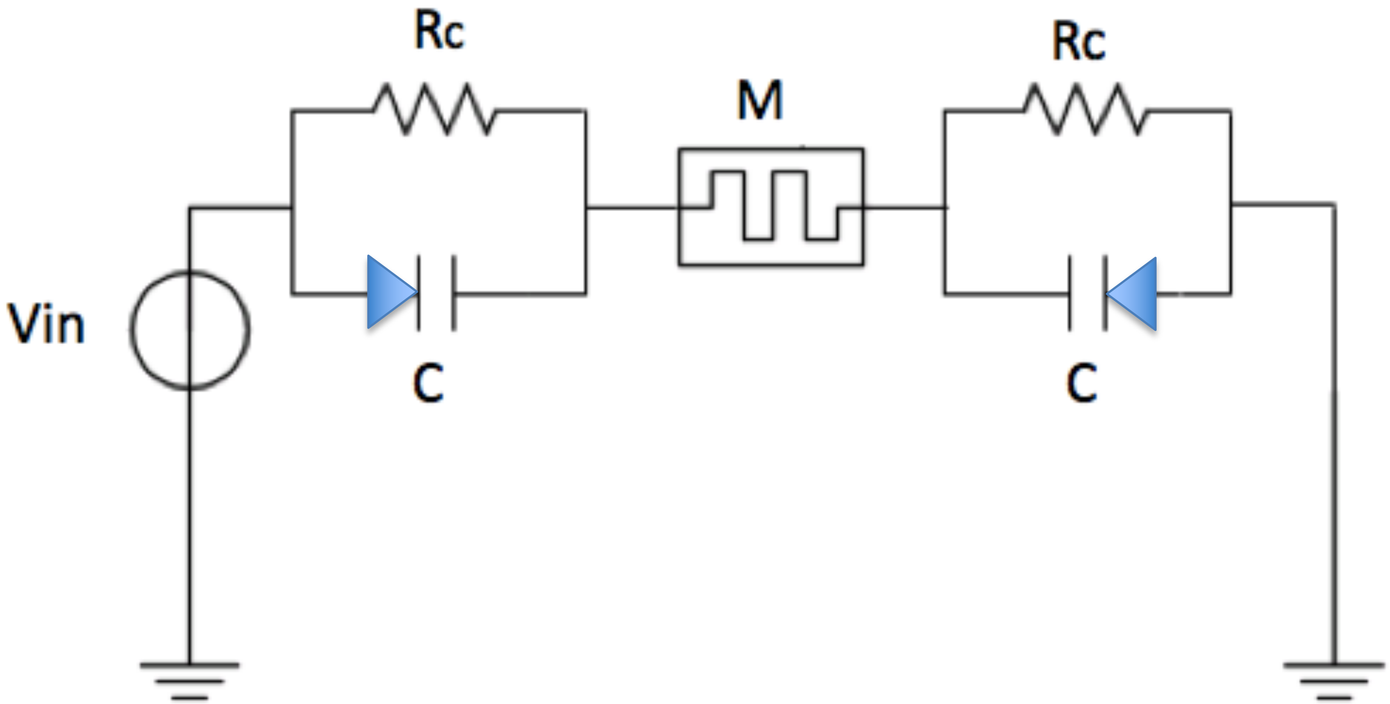
Suspended functionalized silicon nanowire with NiSi regions
Bio-functionalized with Antibodies

Why the Voltage Gap appears in Memristive Biosensors?



Biomolecules affect the w-state of the device

Memristive Model



The Non-pinched Hysteresis is initially modelled by the capacitance of the two Schottky Barriers

Memristive Model

I. Tzouvadaki, al et S. Carrara, *IEEE Sensors Journal 15(*2014) 6208-6217

Antigen concentration [fM]	Voltage gap [Volts] *Experimental values* [9]	Capacitance (C) [nF]	Voltage gap [Volts] *Simulation values*
0	0.84	36	0.844
5	0.56	24	0.563
10	0.37	15	0.362

Typical values of the excess capacitance reported in literature are **around 43nF**. It is the combination of the space charge capacitance characterizing the diode and of the diffusion capacitances due to the carriers injection

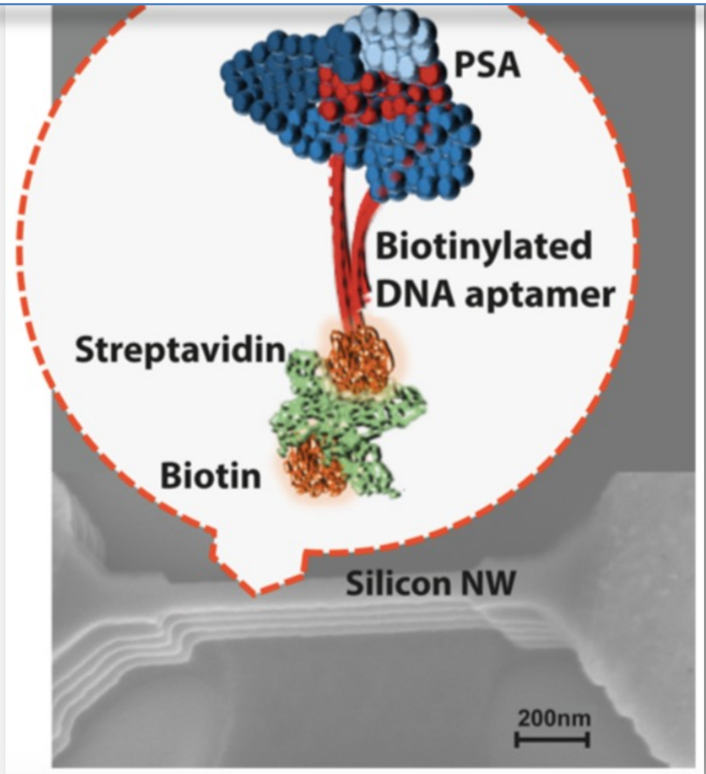
J. Werner, et al., *Phys. Rev. Lett.*, 1988, **60**, 53-56

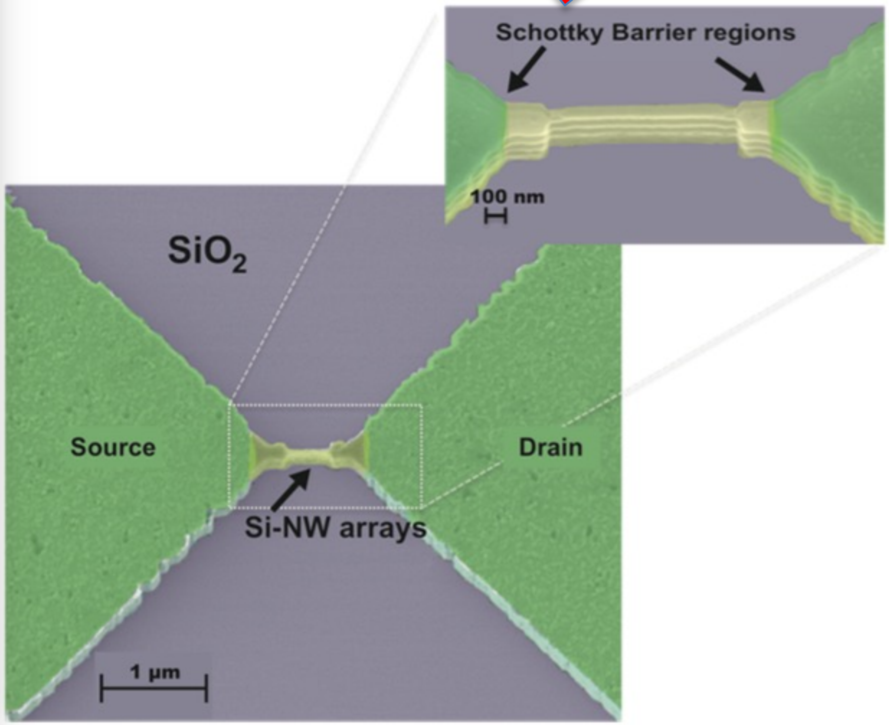
While typical capacitance values concerning only contributions by the depletion area are in the range of pF

M. Bleicher & E. Lange, *Solid State Electron.*, 1973, 16, 375-380

Memristive Sensors Milestones

I. Tzouvadaki et al. / Nano Lett. 16(2016) 4472−4476





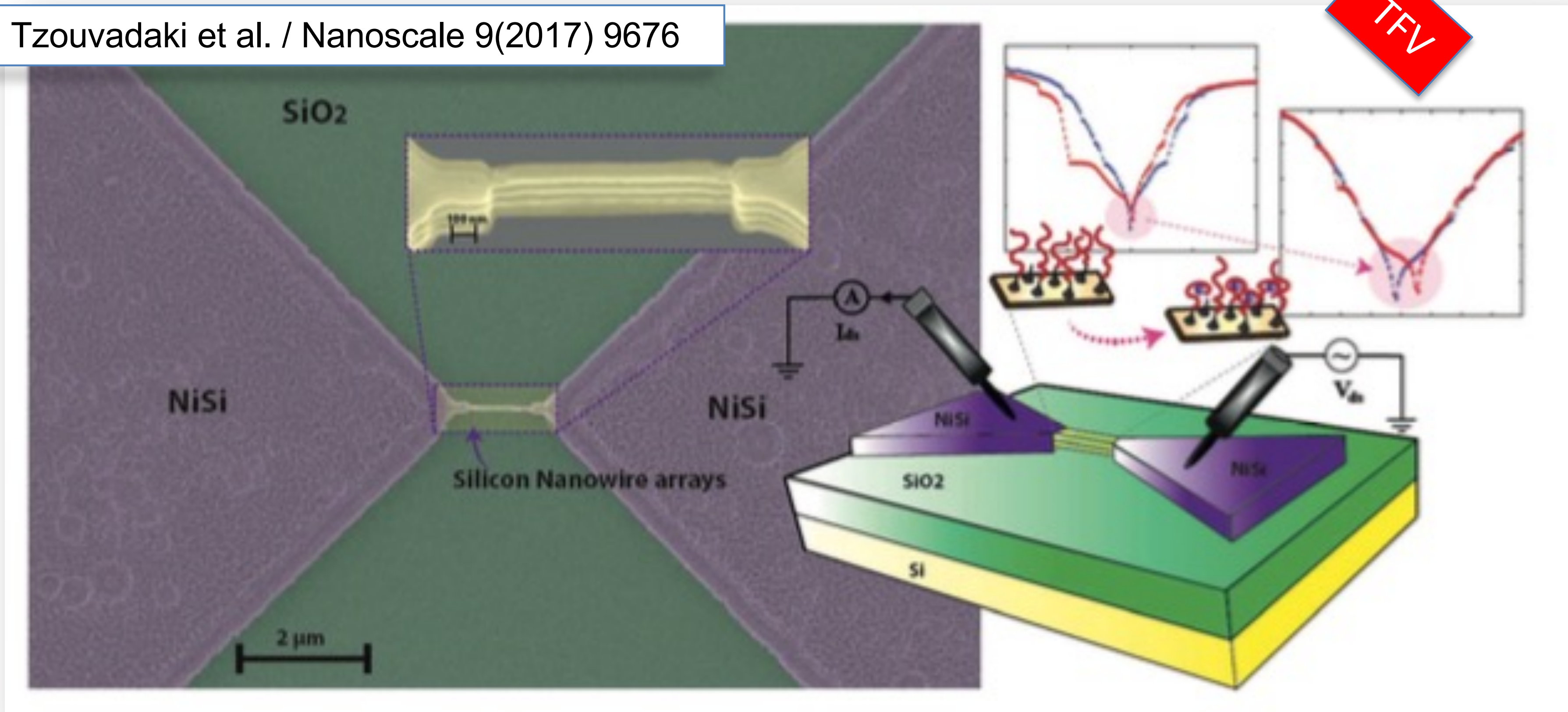
Very first worldwide ever-reported electrochemical biosensor based on a memristive effect and DNA aptamers

Memristive Sensors Milestones

2008 › 2009 › 2010 › 2011 › 2012 › 2013 › 2014 › 2015 › 2016 › 2017 › 2018

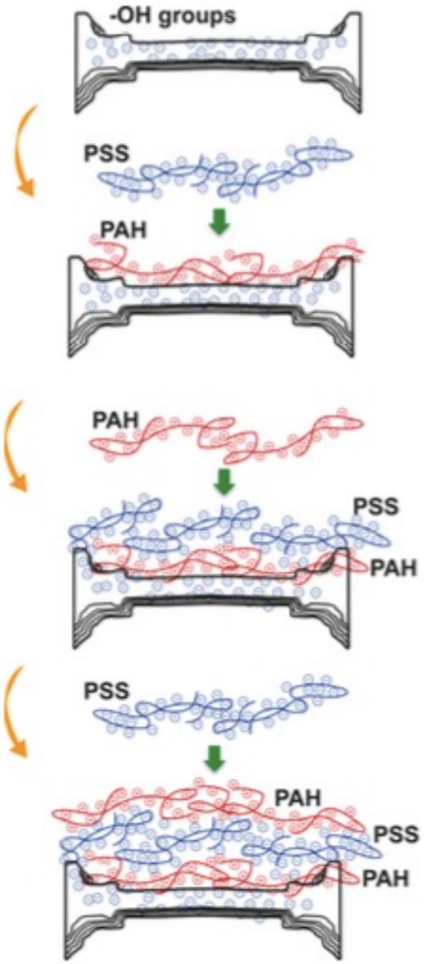
TFV

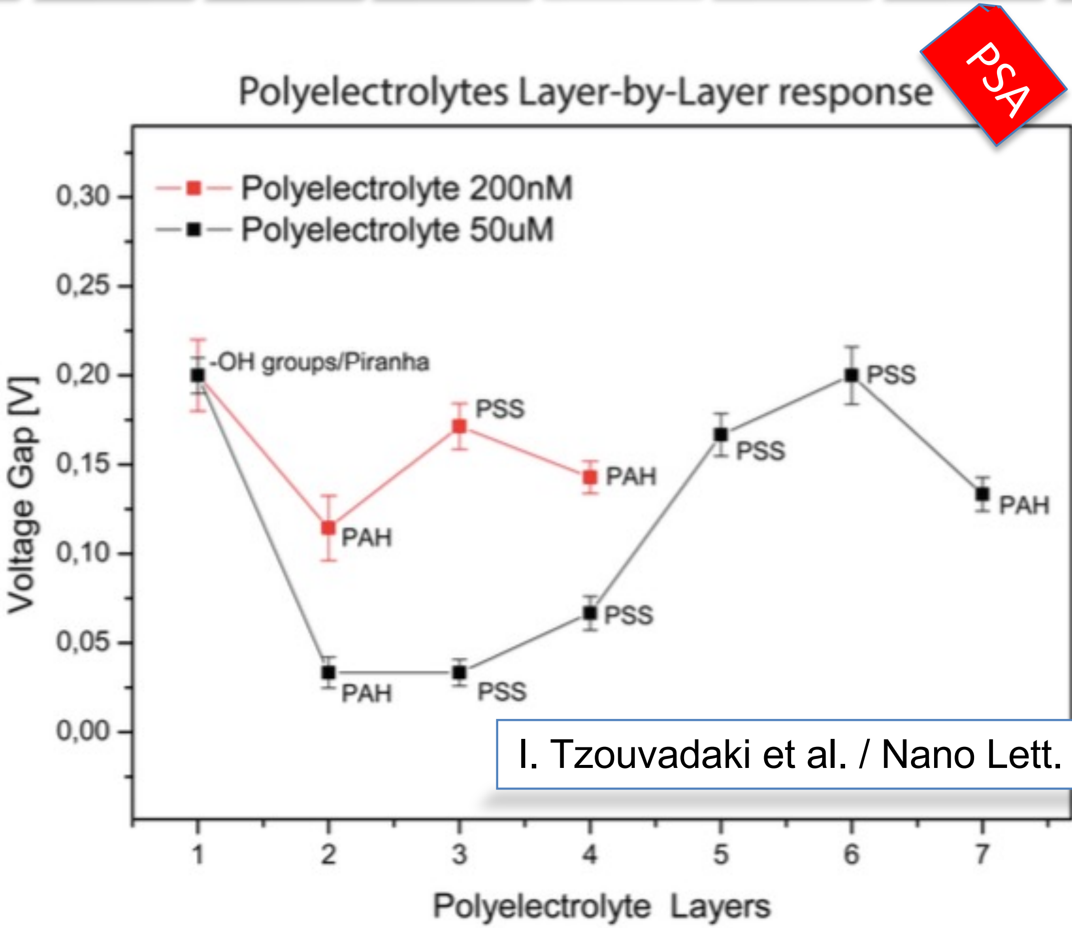
I. Tzouvadaki et al. / Nanoscale 9(2017) 9676



Ultrasensitive label-free Aptamer-based memristor to monitor therapeutic compounds

Memristive Sensors Milestones

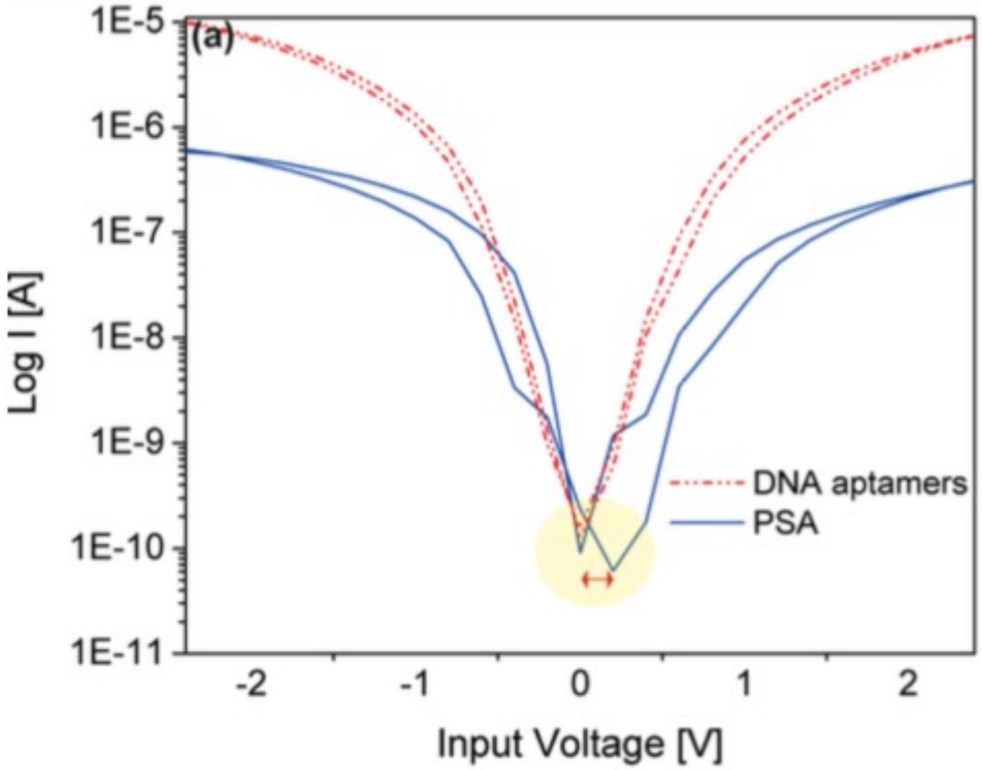


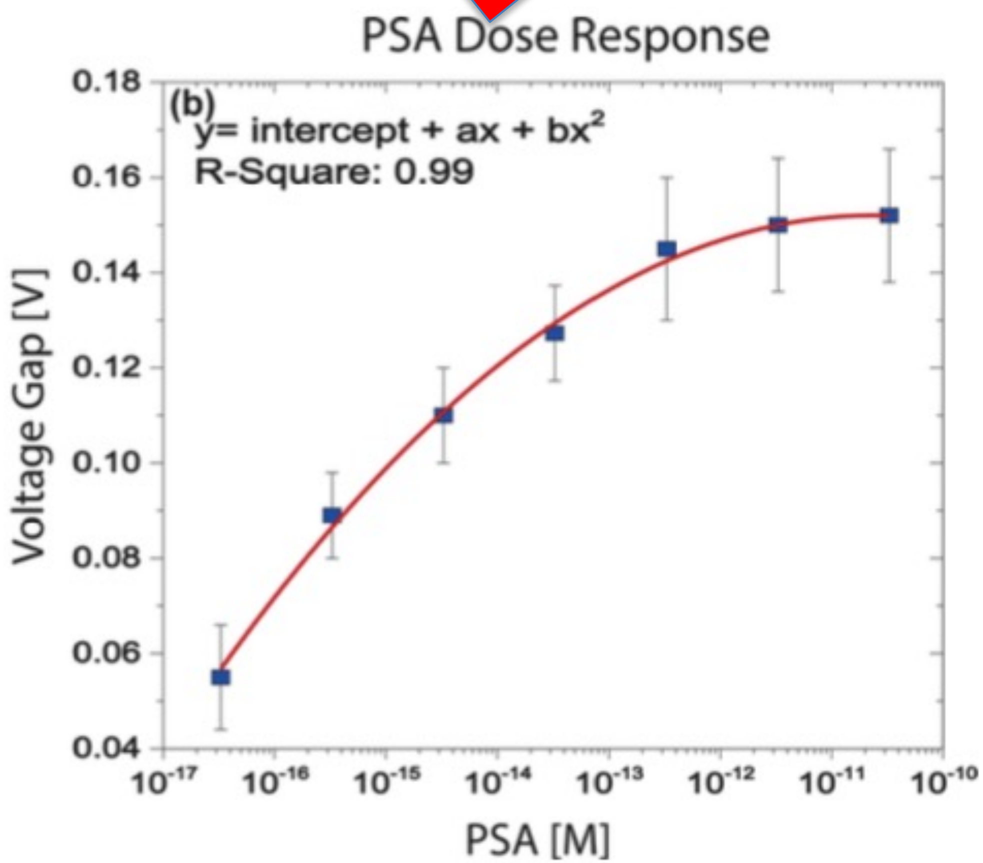


I. Tzouvadaki et al. / Nano Lett. 16(2016) 4472−4476

Memristive Sensors Milestones

I. Tzouvadaki et al. / Nano Lett. 16(2016) 4472−4476

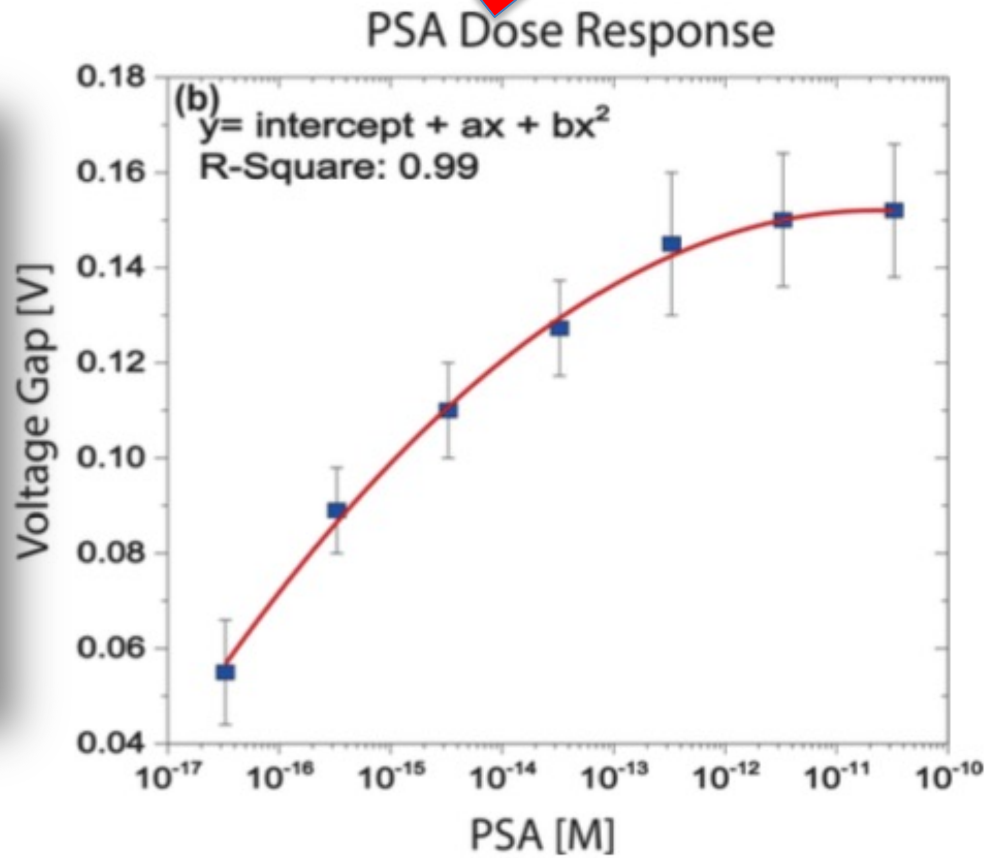




Memristive Sensors Milestones

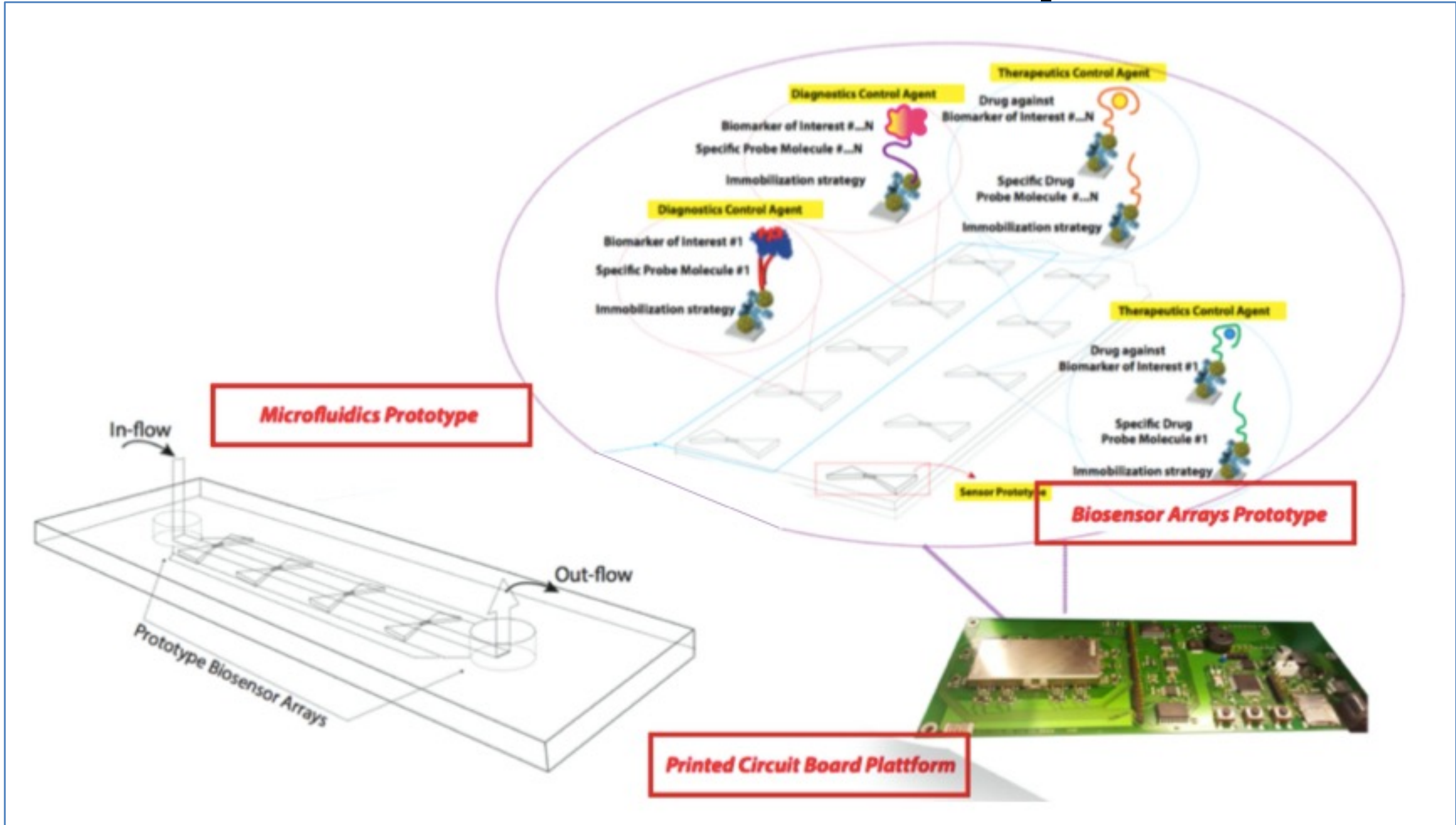
I. Tzouvadaki et al. / Nano Lett. 16(2016) 4472−4476

electrode surface	LOD	reference
gold electrodes	37 nM	Formisano et al.[14] (2015)
GCE	pM range	Souada et al.[15] (2015)
gold electrodes	30 pM	Jolly et al.[16] (2015)
glassy carbon electrode (GCE)	7.6 pM	Liu et al.[17] (2012)
GCE	0.15 pM	Kavosi et al.[18] (2015)
gold electrodes	fM range	Yang et al.[19] (2015)
gold electrodes	30 fM	Jolly et al.[20] (2016)
GCE	300 aM	Kavosi et al.[18] (2015)
Si-nanowires	23 aM	present work



Best Ever Biosensors for Cancer Markers by Aptamers

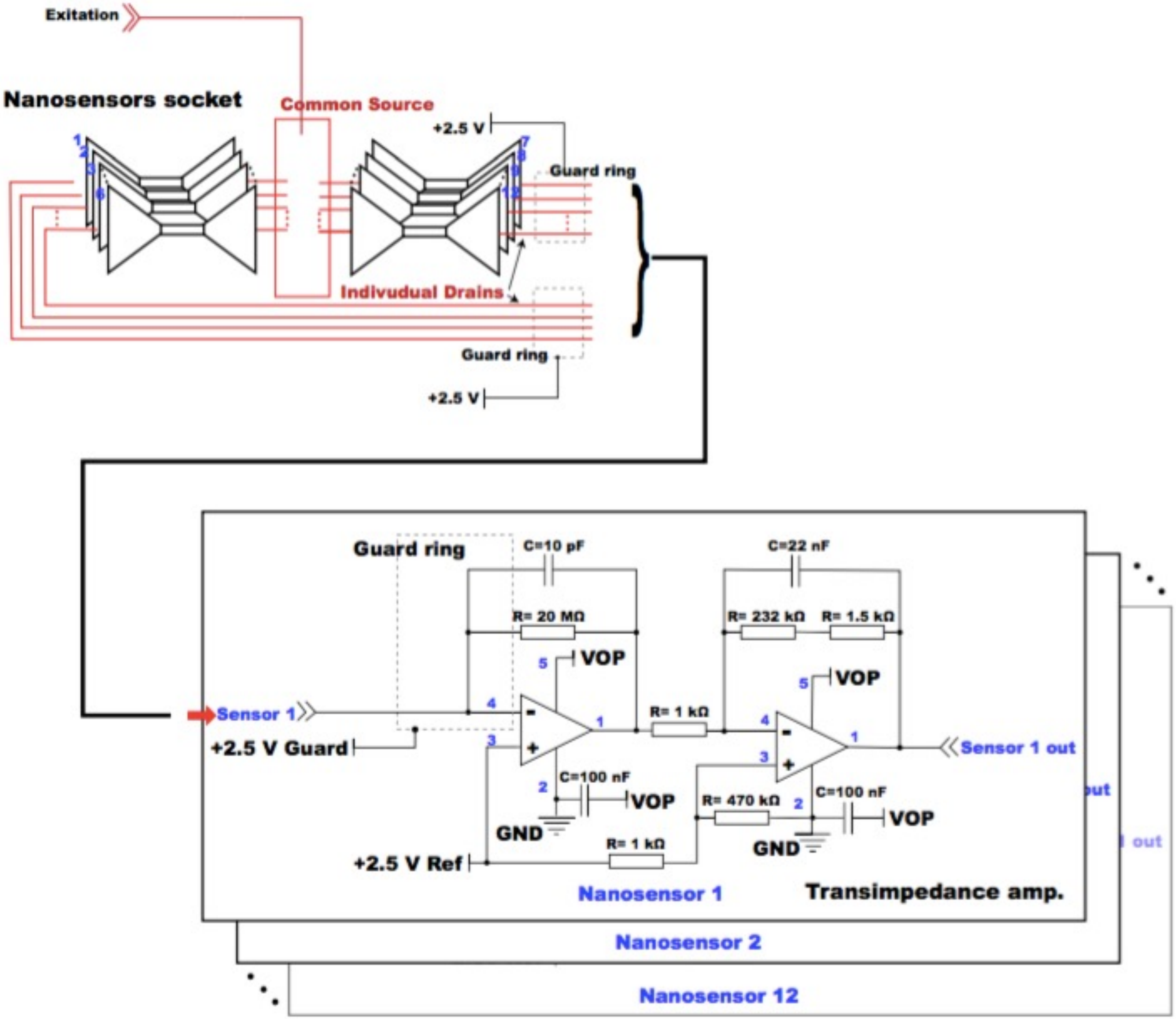
Multi-Panel on Chip



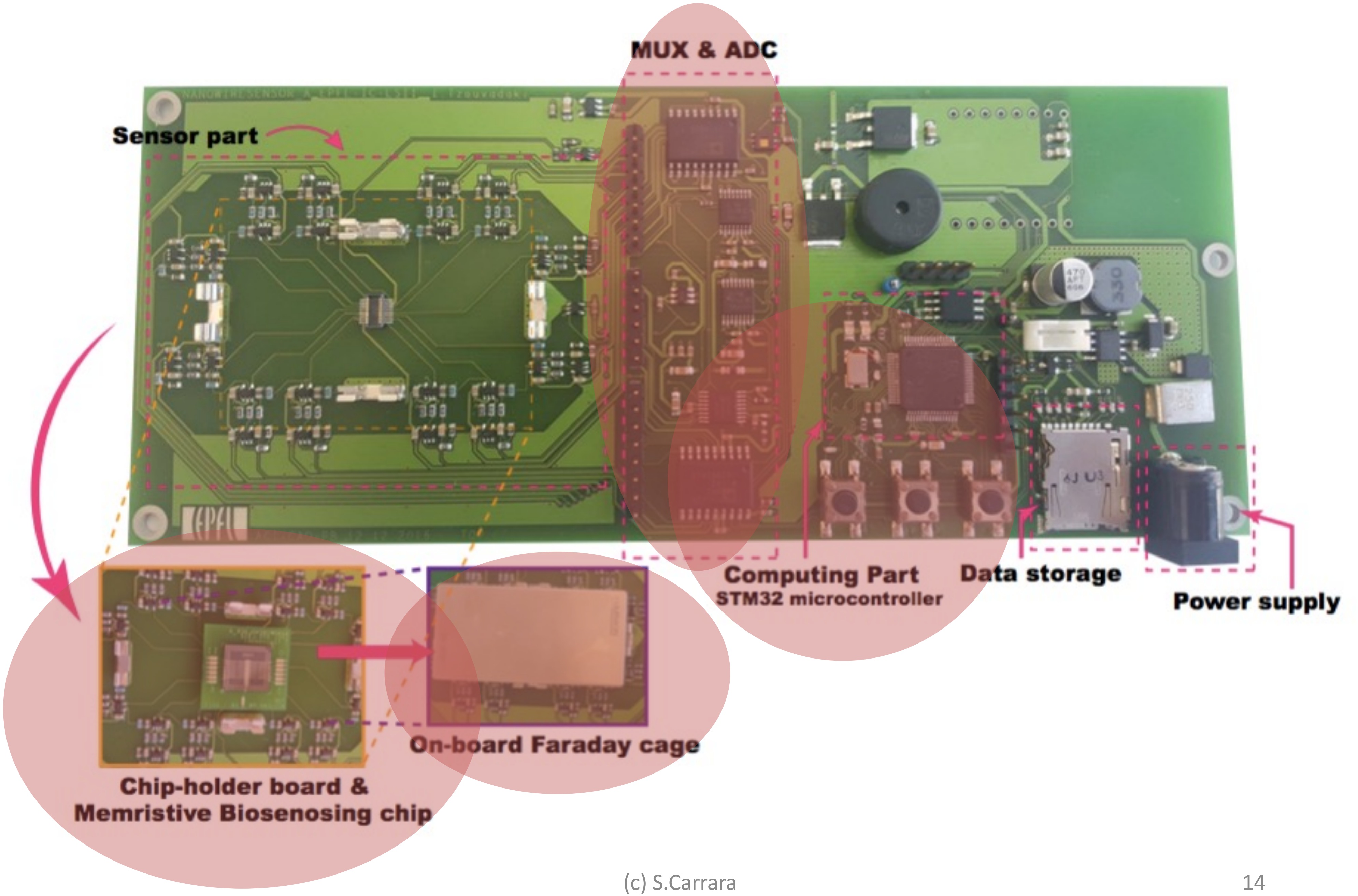
I. Tzouvadaki et al. / IEEE Sensors Journal 14(2019) 5769–5774

Memristive Multipanel Platform for Theragnostics with Microfluidics

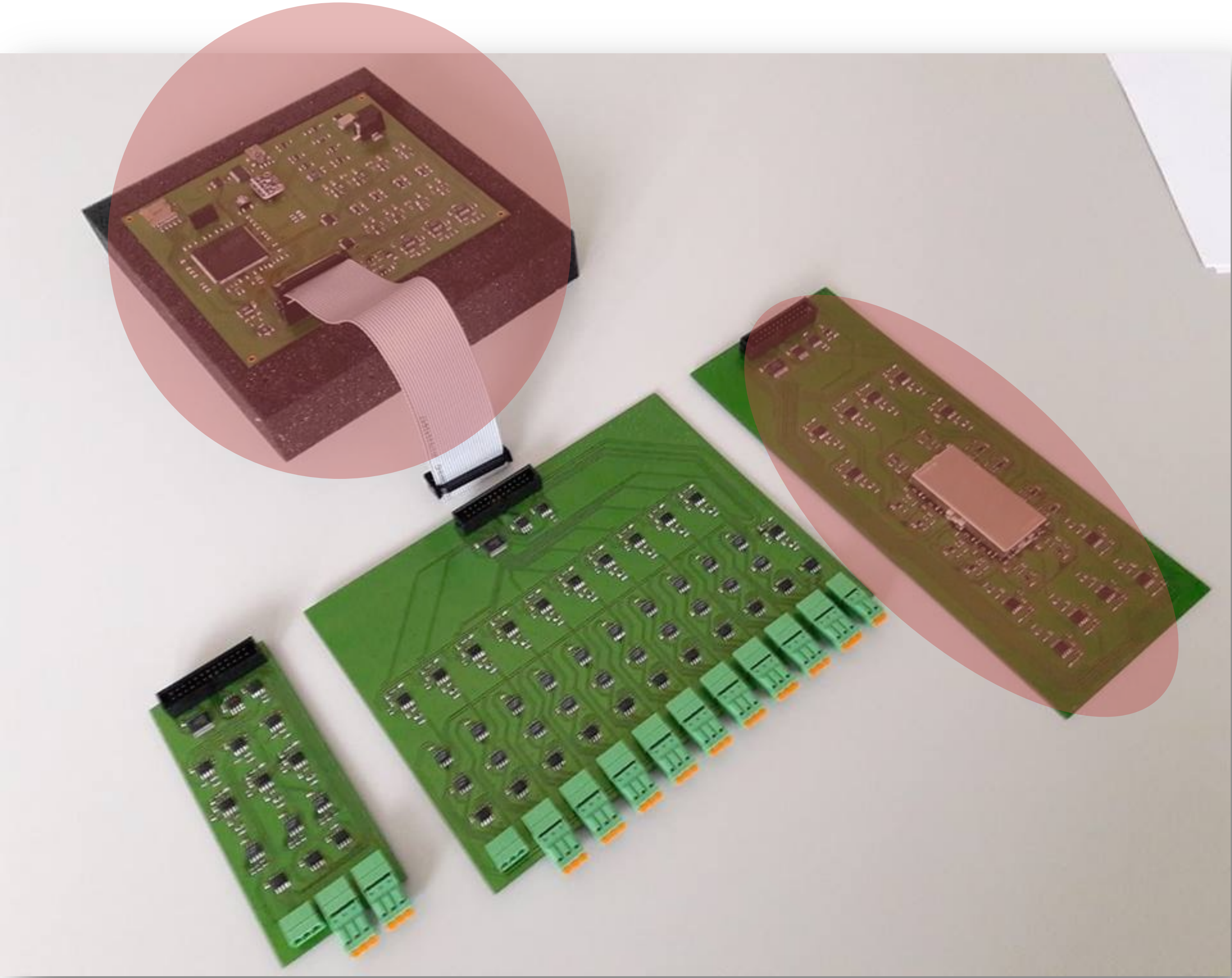
CMOS interface to Memristive Sensors



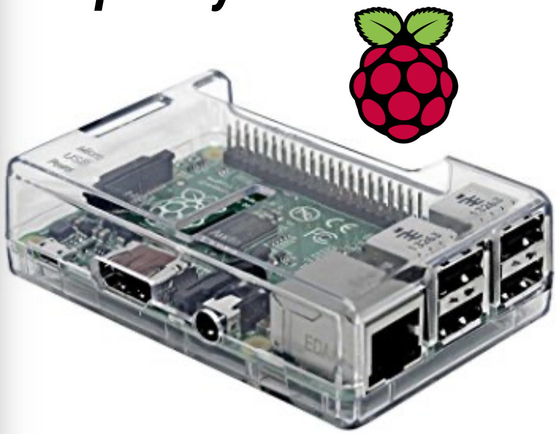
Sensor frontend on PCB



Sensor frontend for Respberry Pi

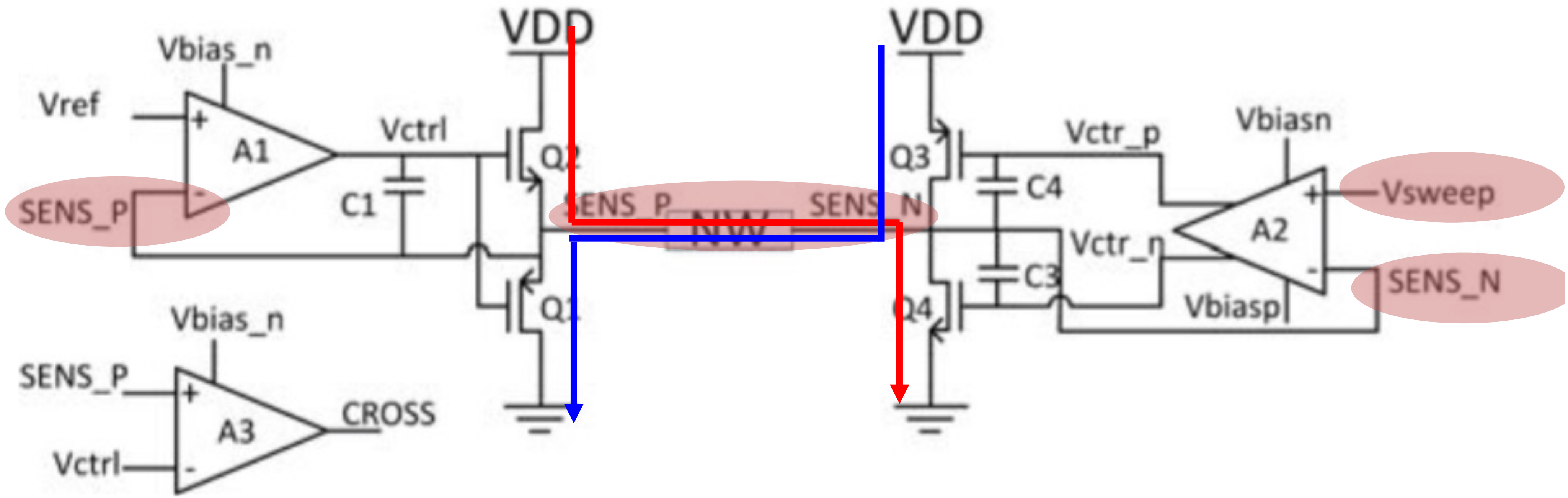


TDM core:
Raspberry Pi 1



CMOS design for V_{gap}

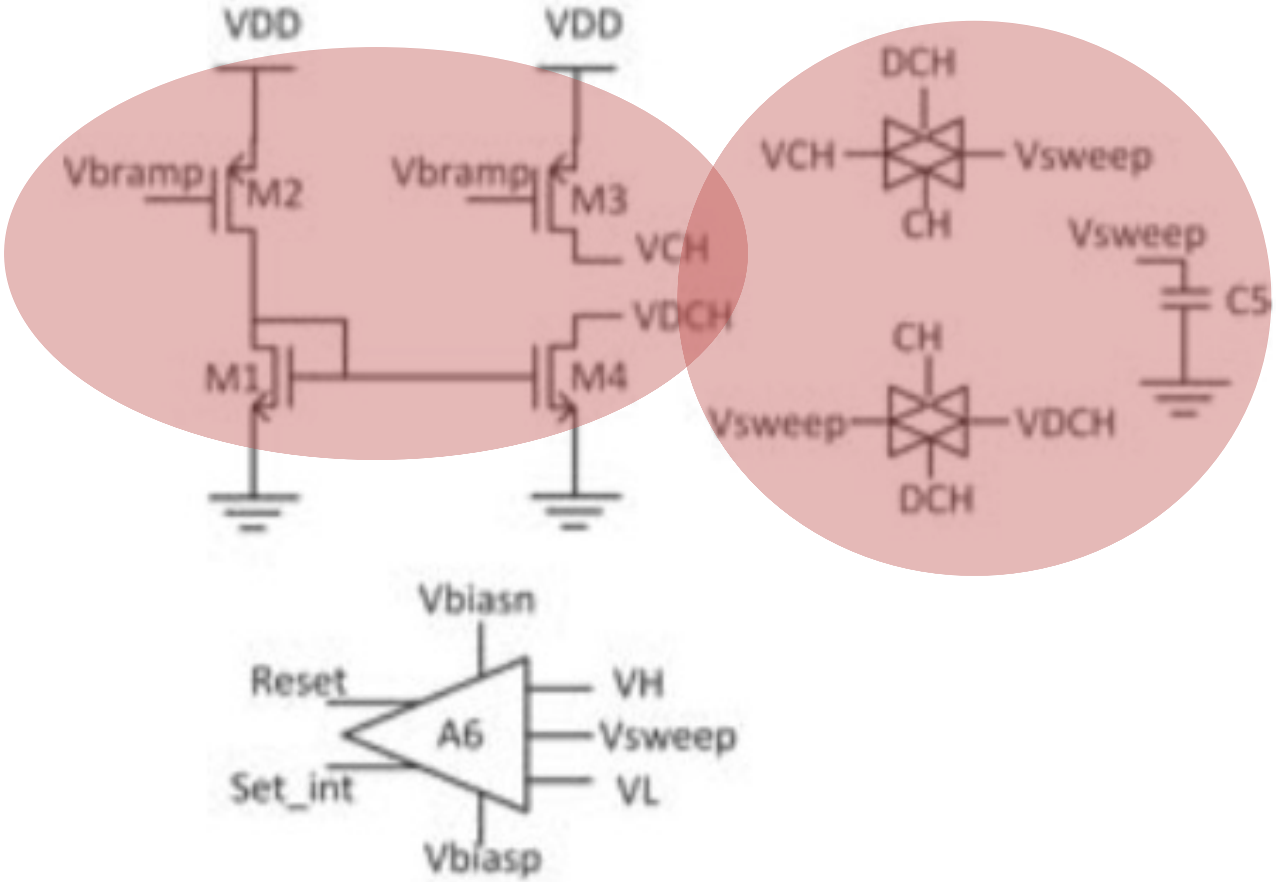
Ali Zaher, al. et S.Carrara, IEEE BioCAS 2014



COSM circuit for automatic acquisition of the V_{gap}

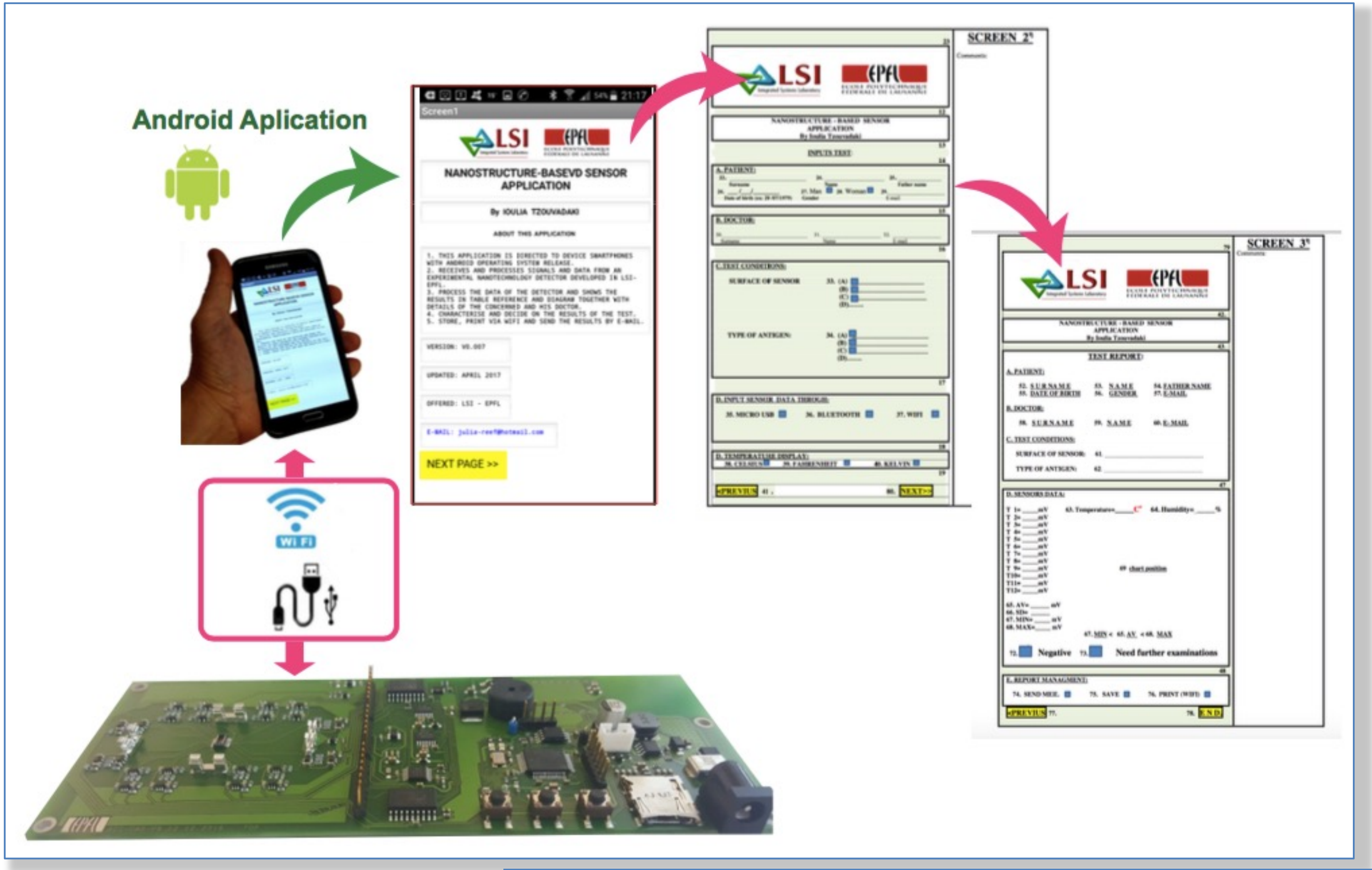
CMOS design for V_{gap}

Ali Zaher, al. et S.Carrara, IEEE BioCAS 2014



COSM circuit for automatic acquisition of the V_{gap}

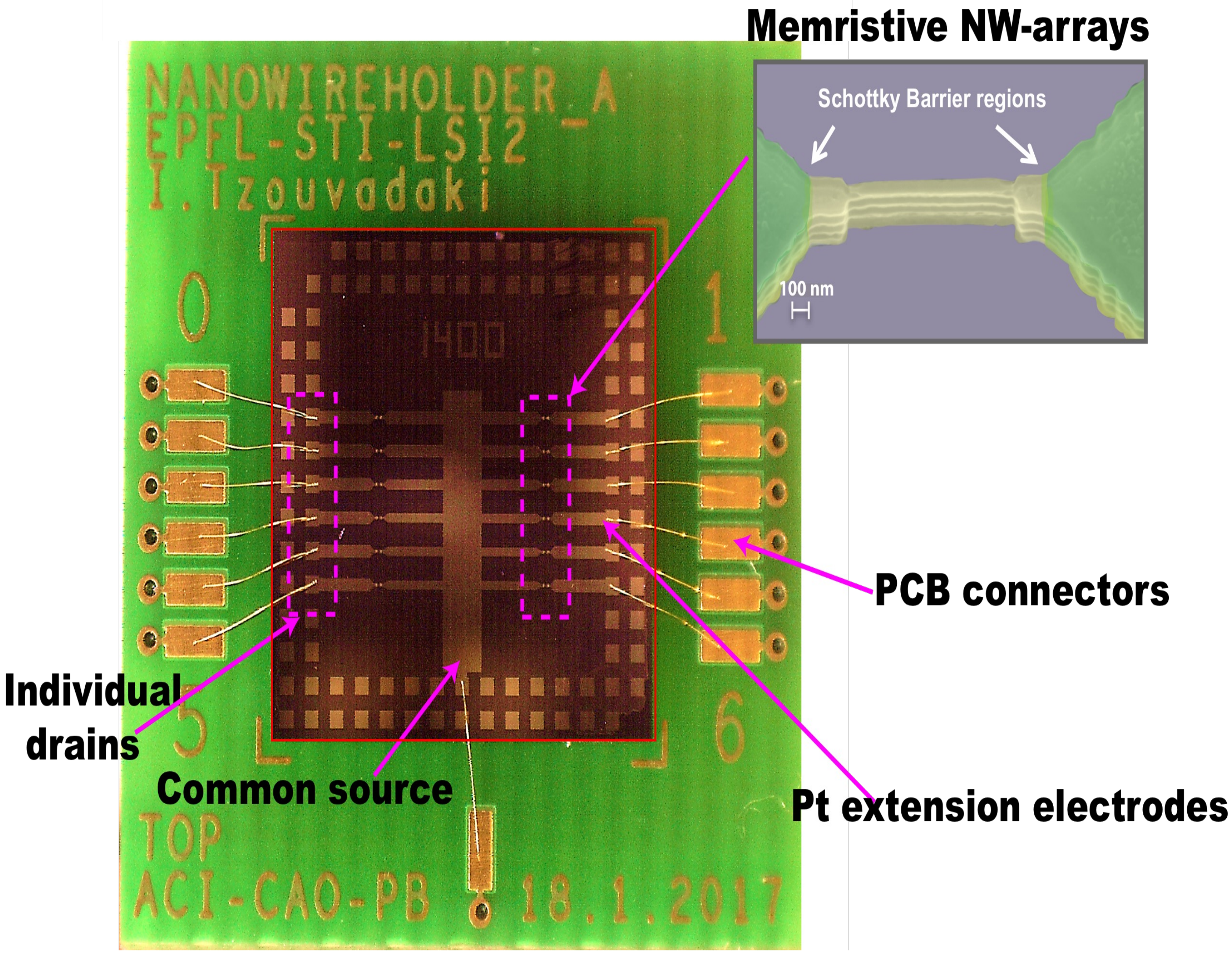
Android Application



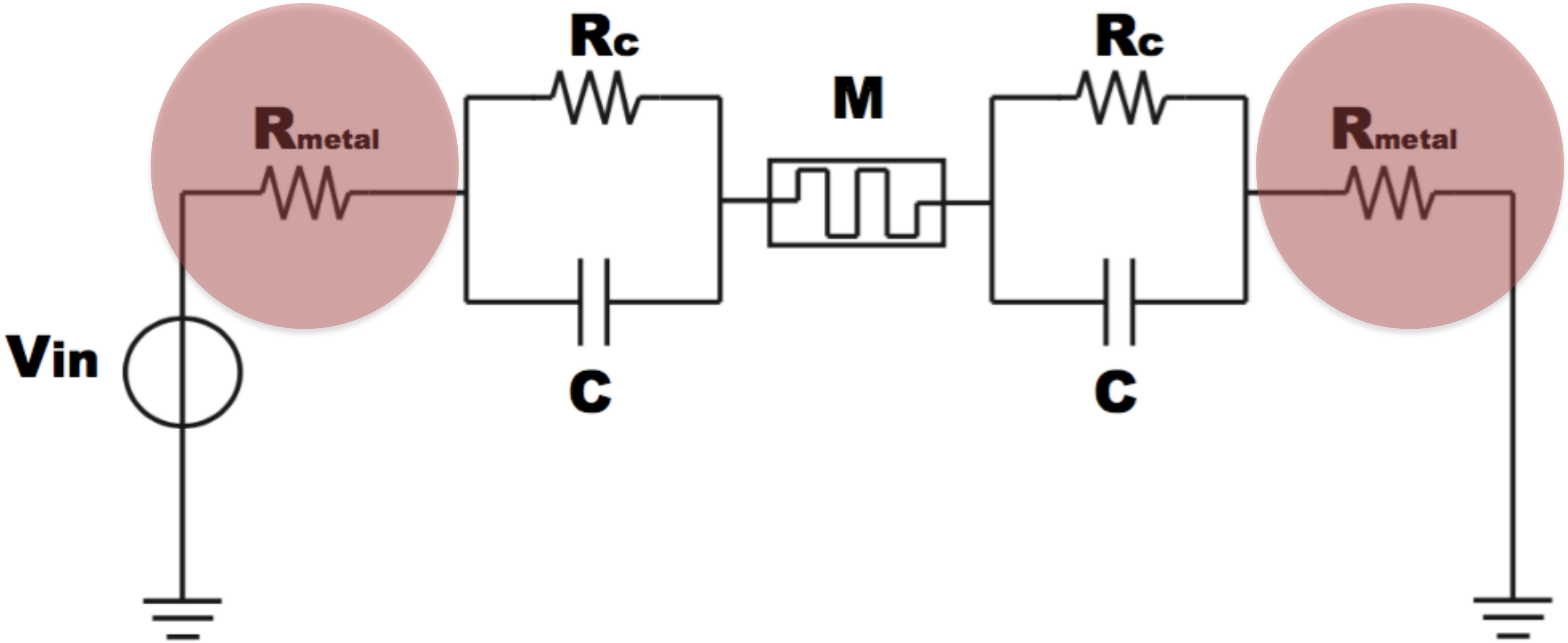
I. Tzouvadaki et al. / IEEE Sensors Journal 14(2019) 5769–5774

Multipanel Platform with Wireless Communication to Android

Memristive Biosensors holder PCB: the disposable sensing modules

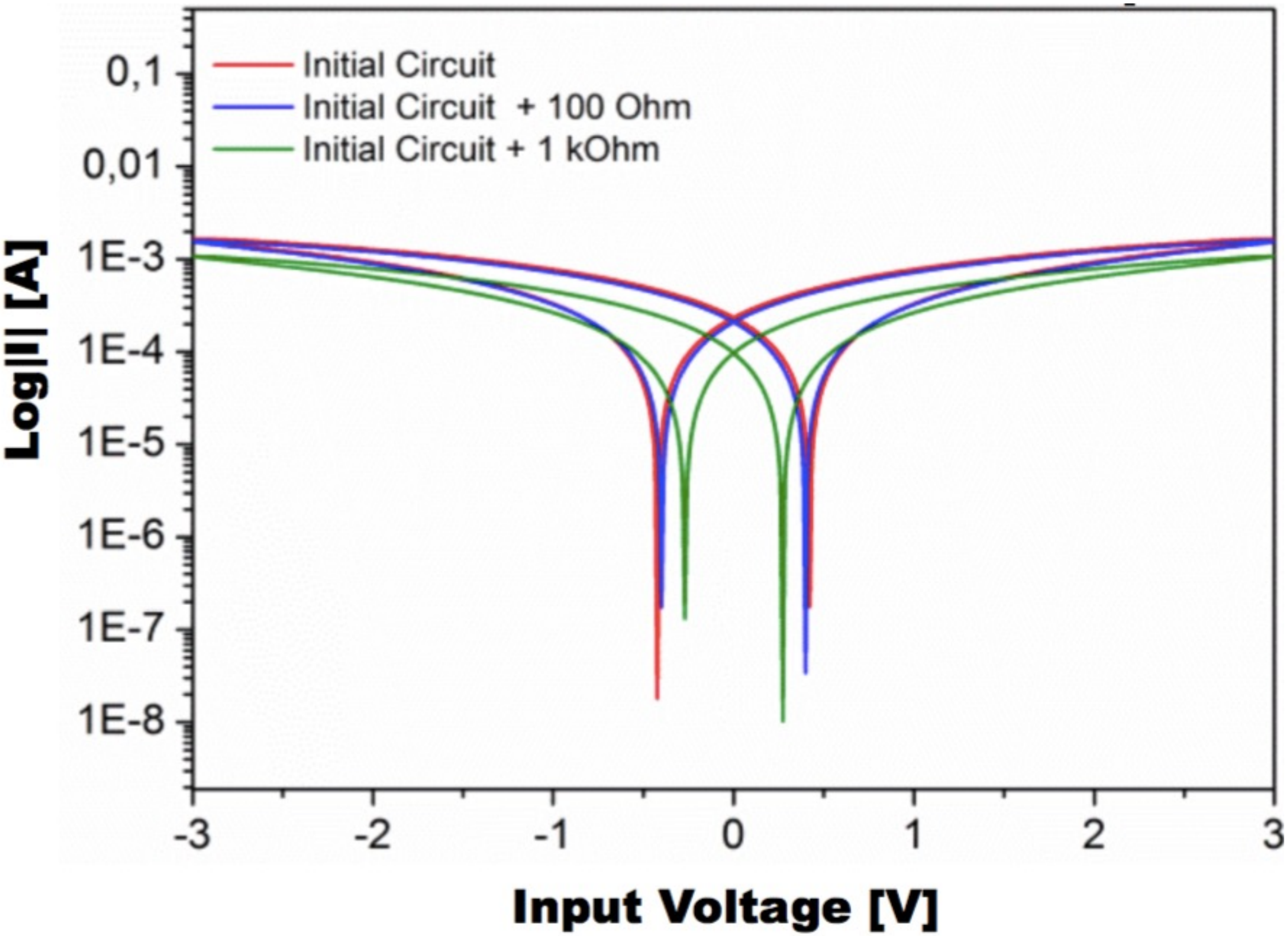


Bio/CMOS interface: issues on connections

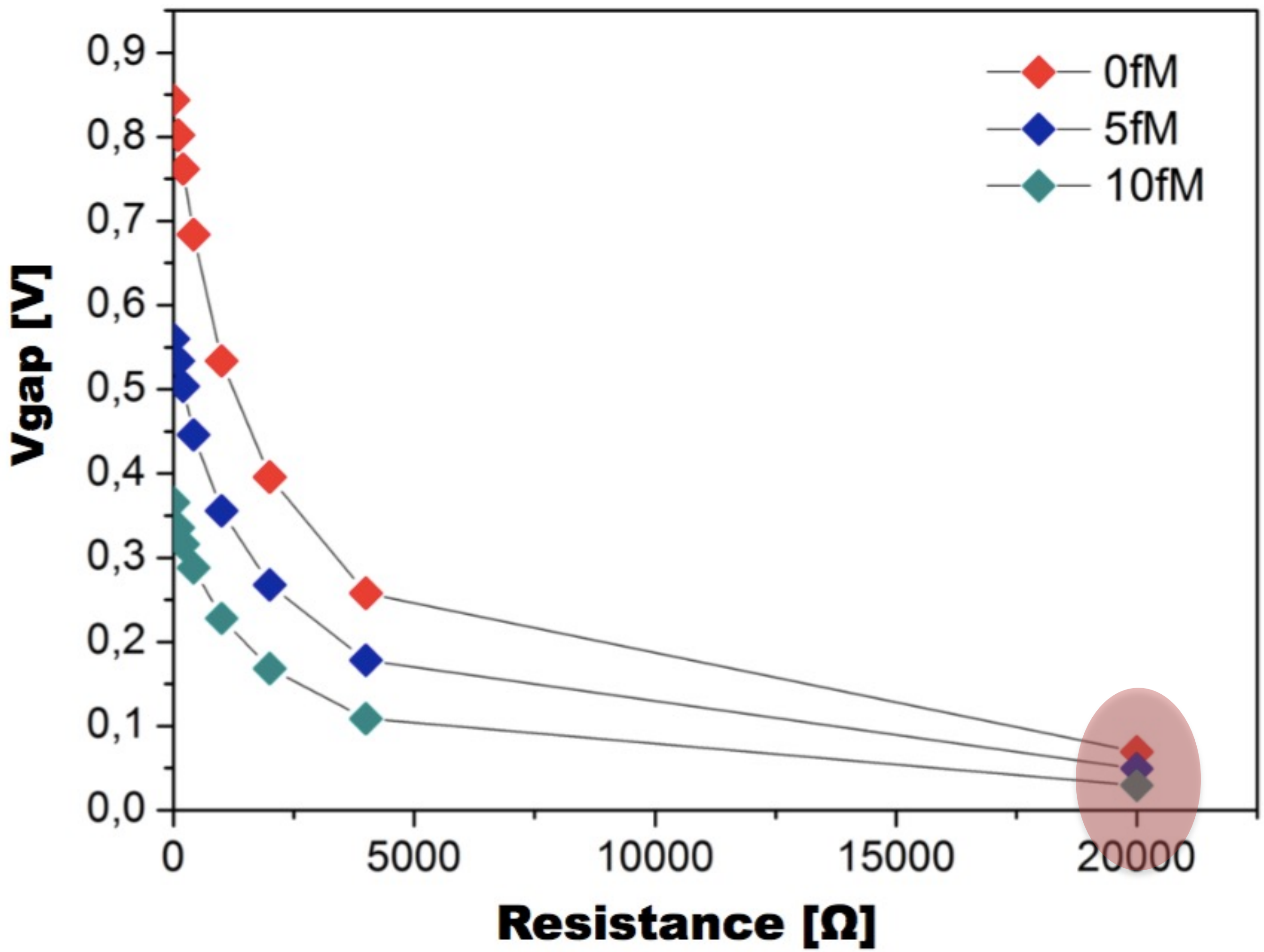


Bio/CMOS interface: the connections

I. Tzouvadaki & A.Vallero, al et S. Carrara, IEEE *ISCAS* 2016



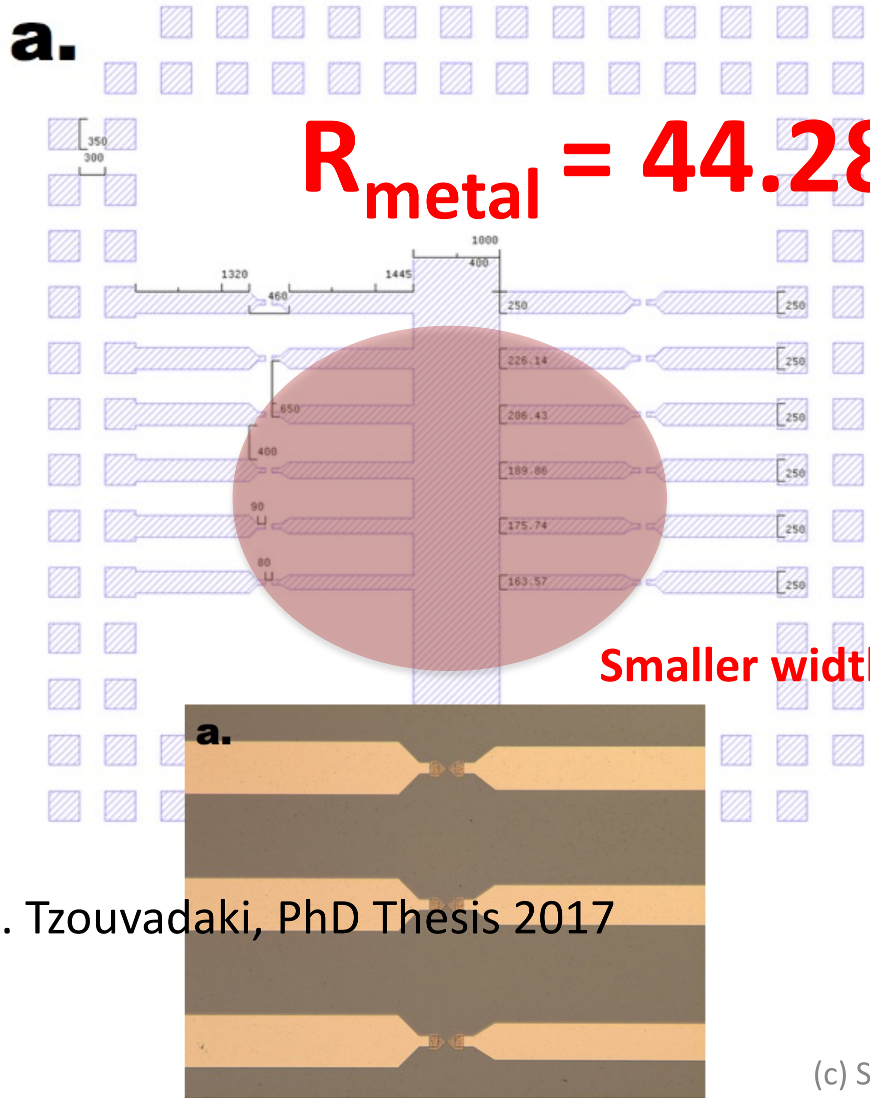
Bio/CMOS interface: the problem of connections



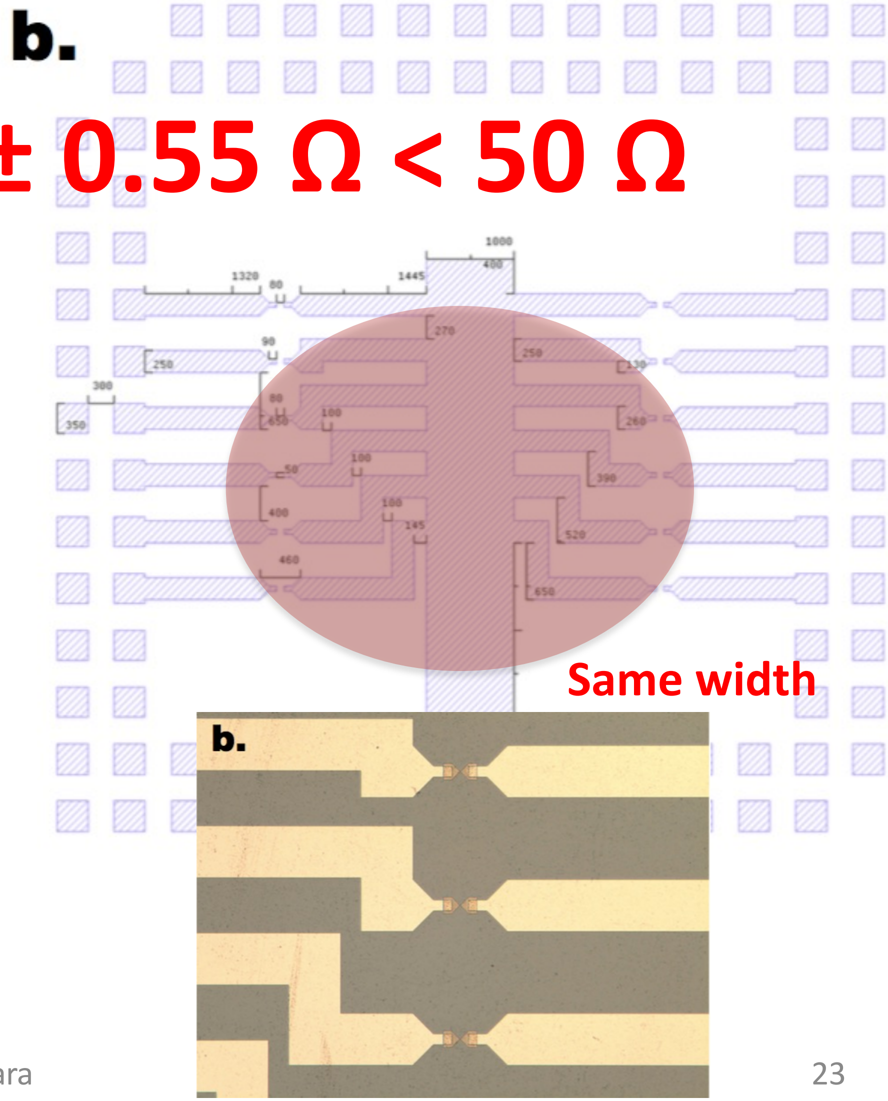
I. Tzouvadaki & A.Vallero, al et S. Carrara, IEEE *ISCAS* 2016

Bio/CMOS interface: Proper design of connections

$$R_{metal} = 44.28 \pm 0.55\ \Omega < 50\ \Omega$$



Smaller width



Same width

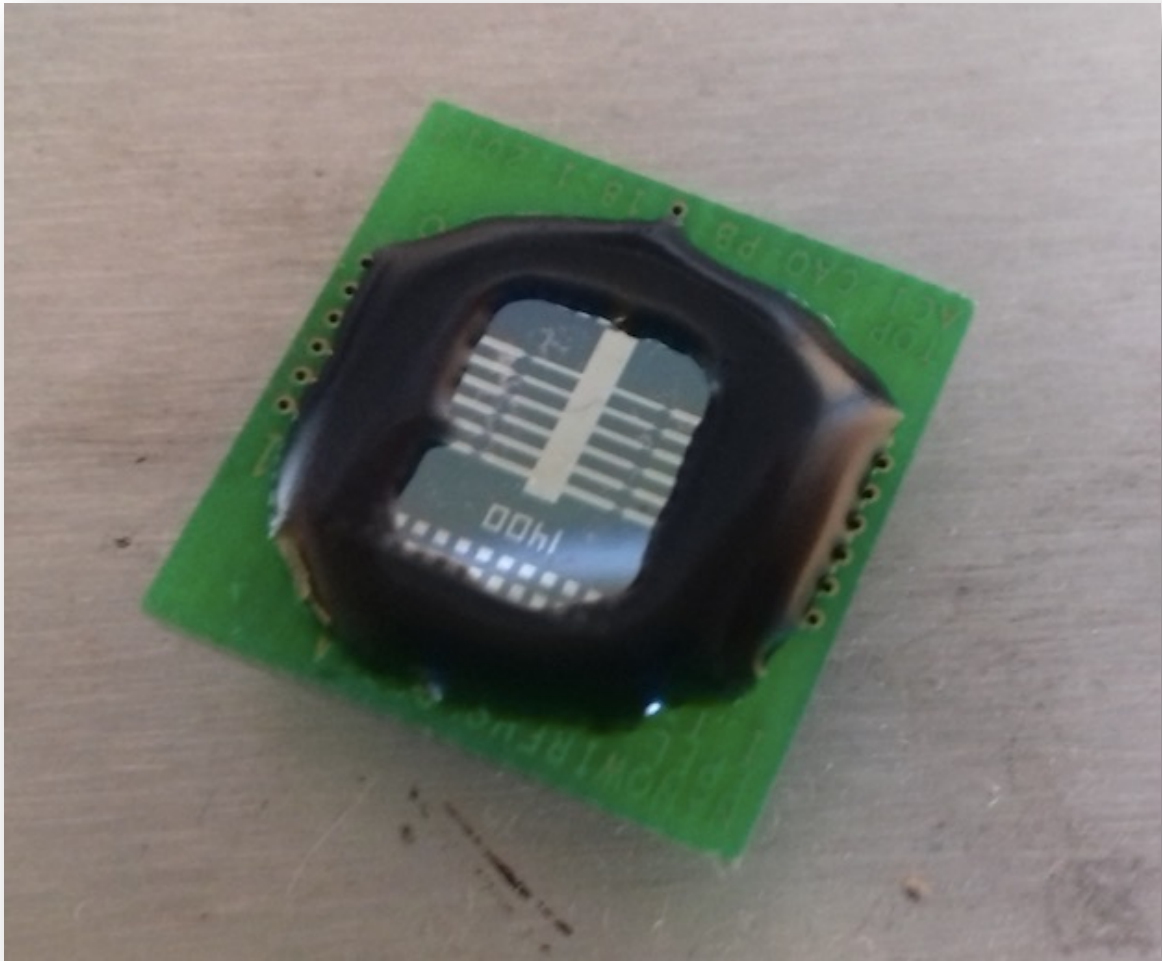
I. Tzouvadaki, PhD Thesis 2017

Memristive Sensors Milestones

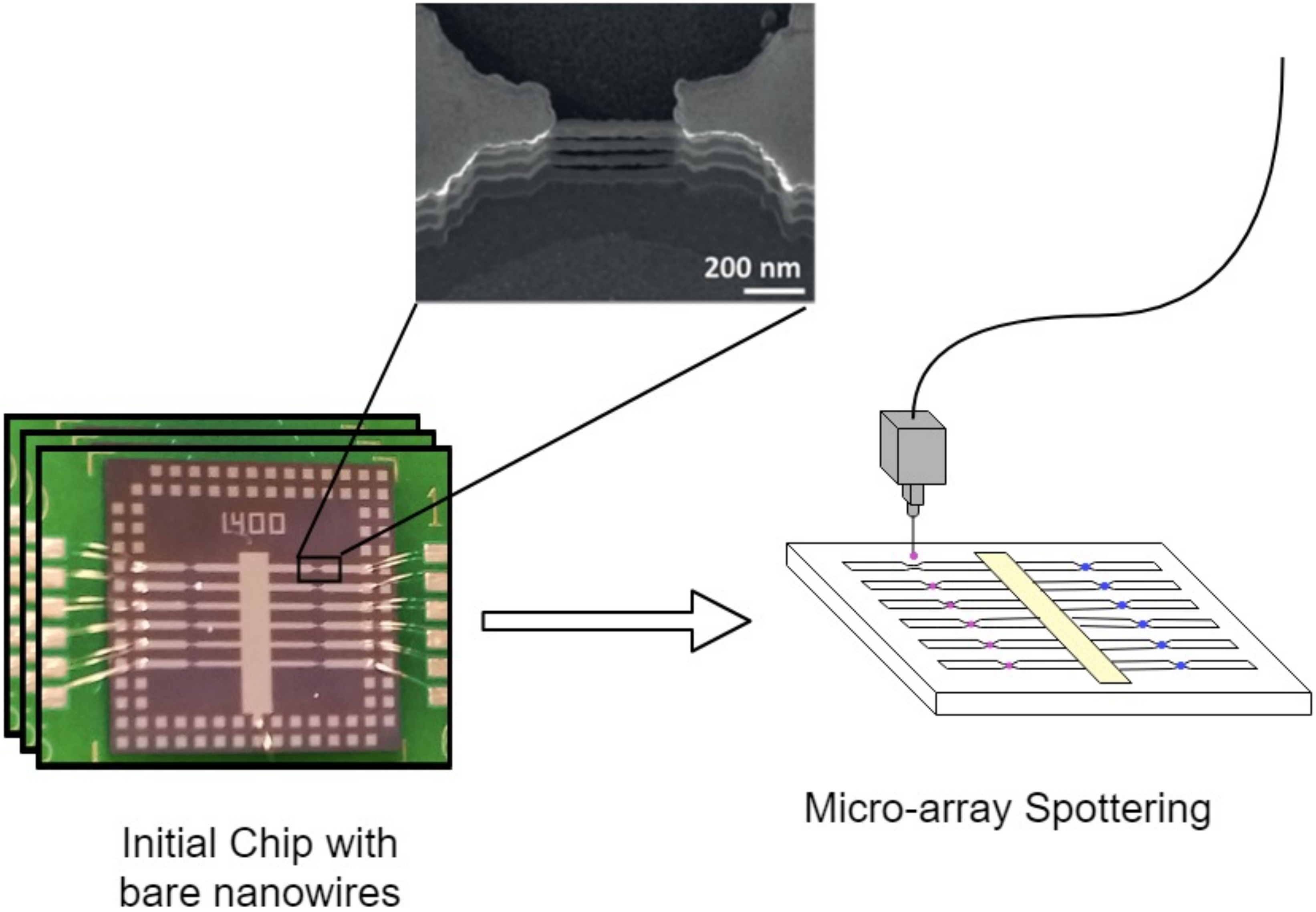
2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020

Gramzyme

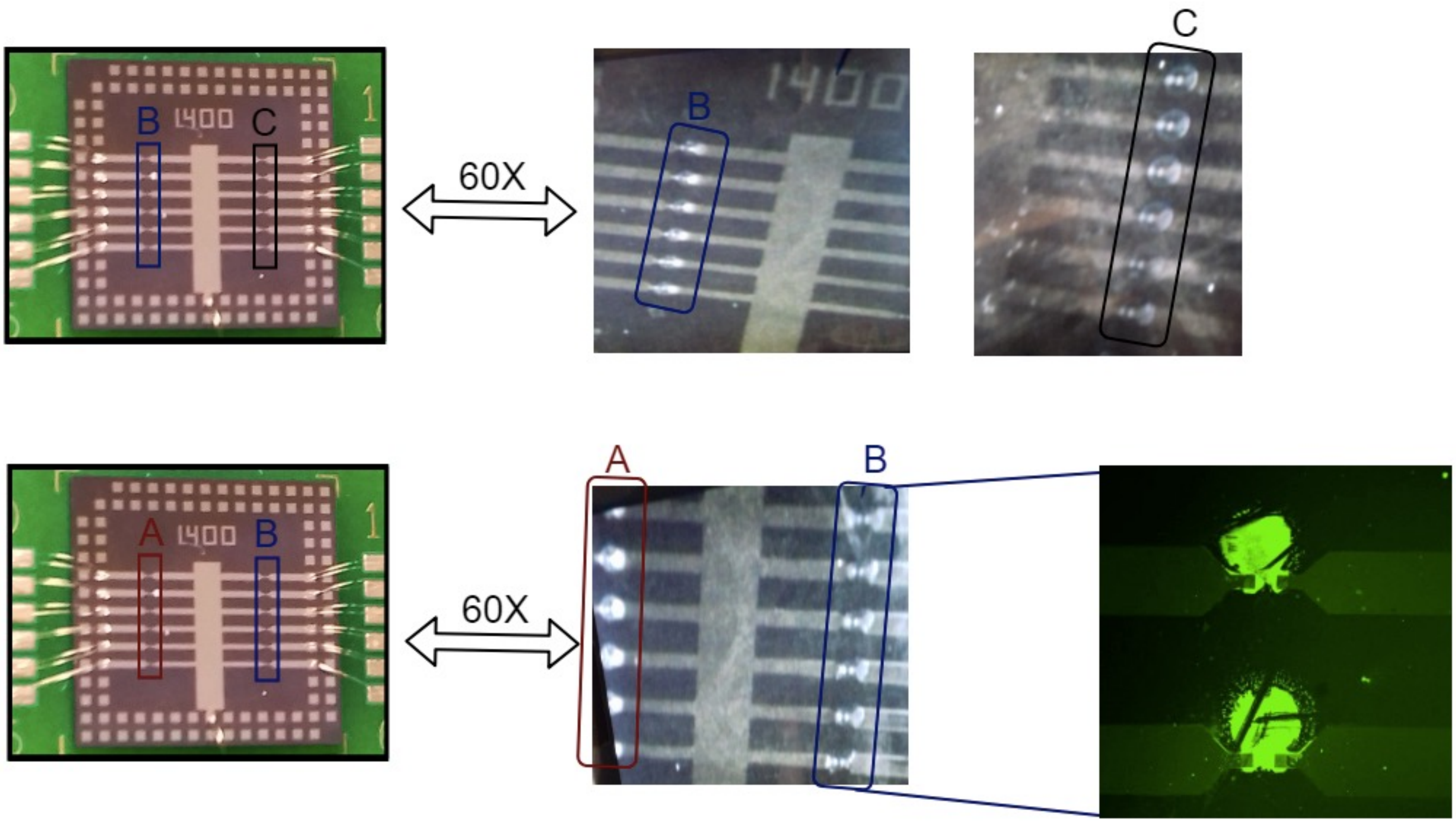
Interferon-γ



Automated Spotting for Multiplexing

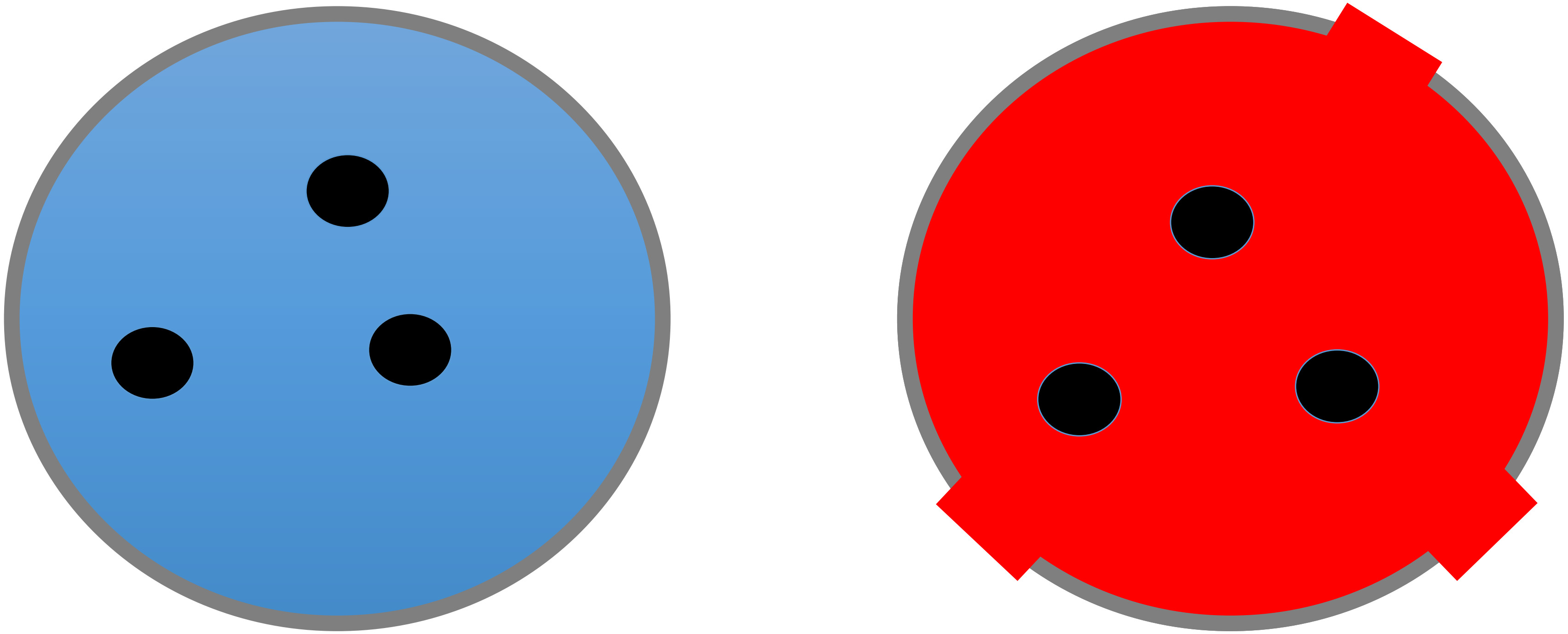


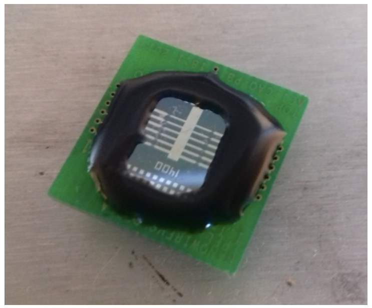
Multiplexing for Specific Cancer Markers



A: Granzyme B: Ifn-y C: Gelatine

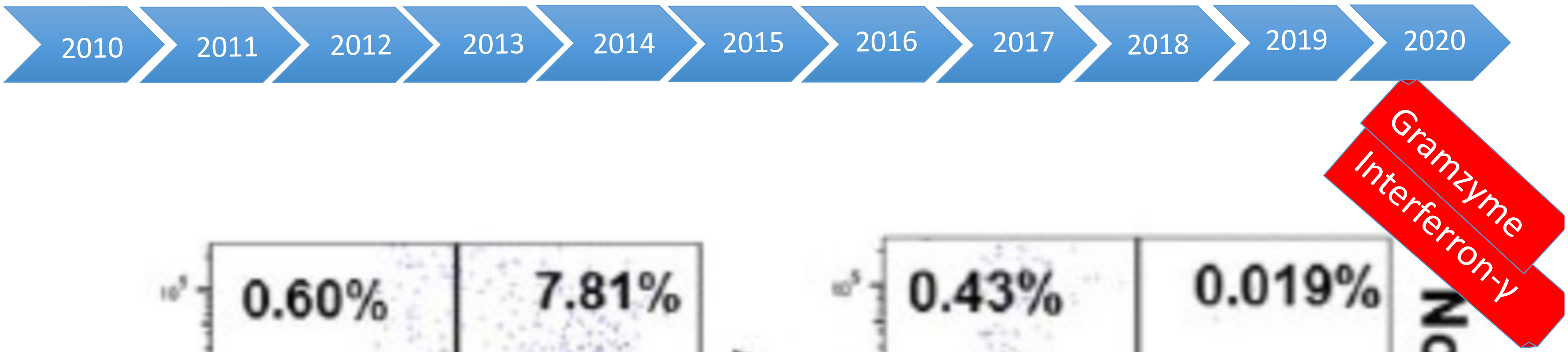
Non-Activated versus Activated CD8 T Cells

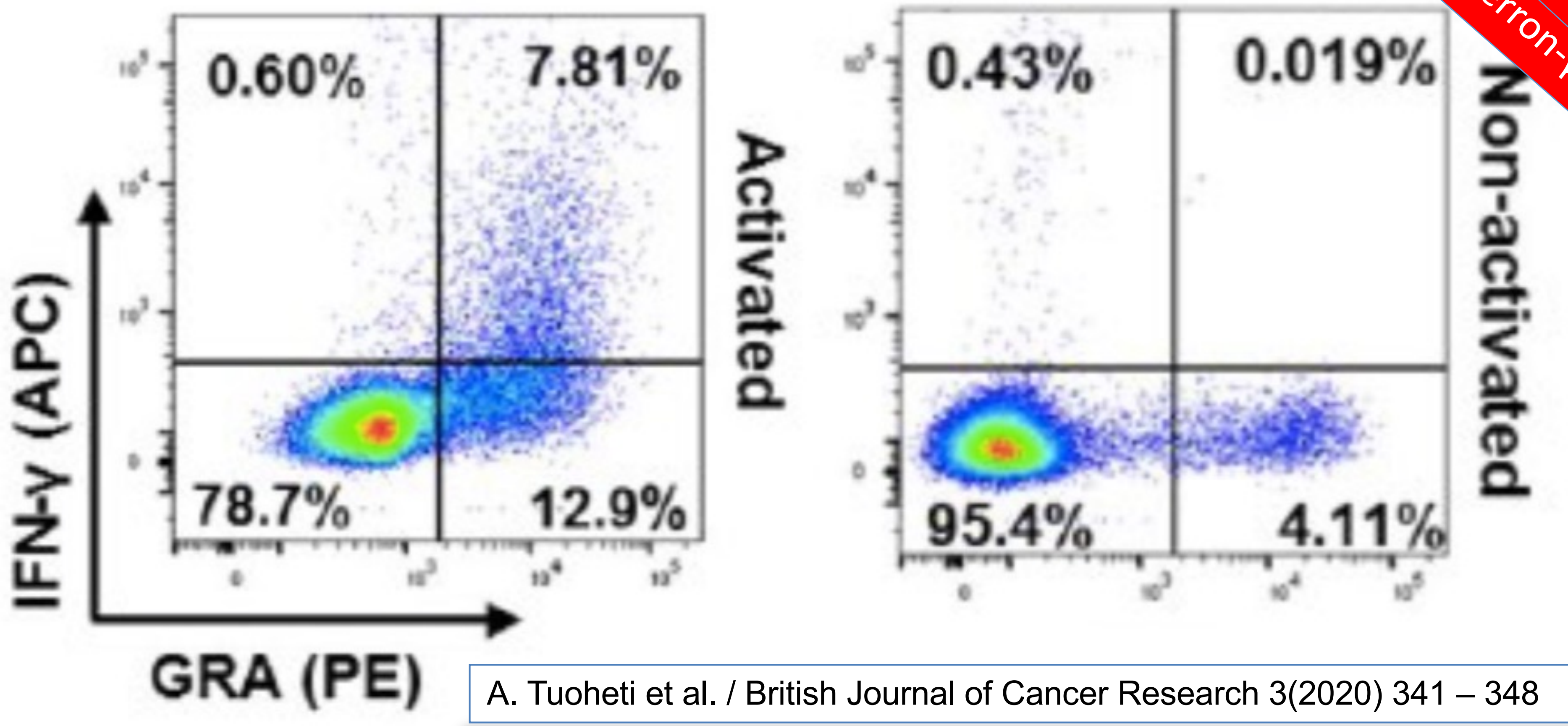




→ **Detection!**

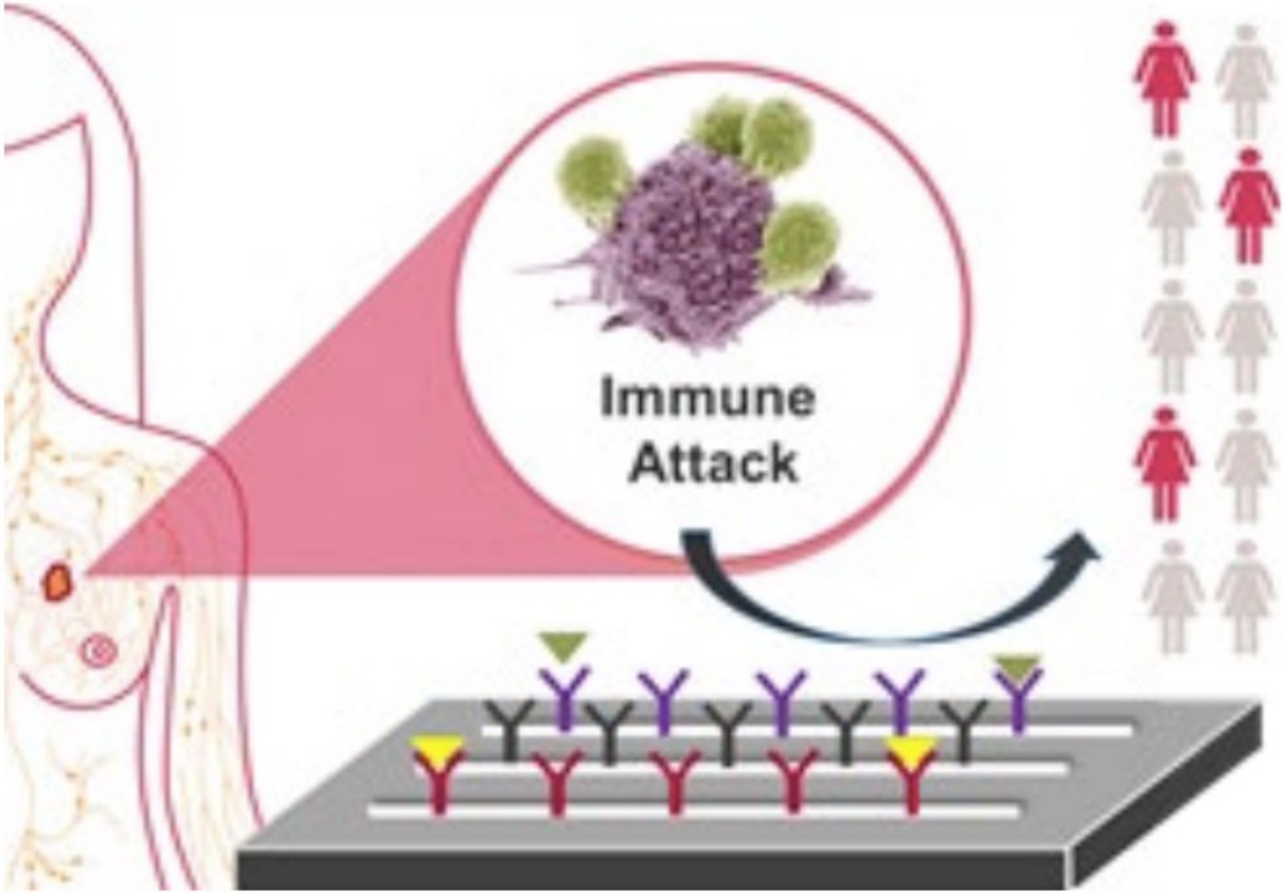
Non-Activated versus Activated CD8 T Cells





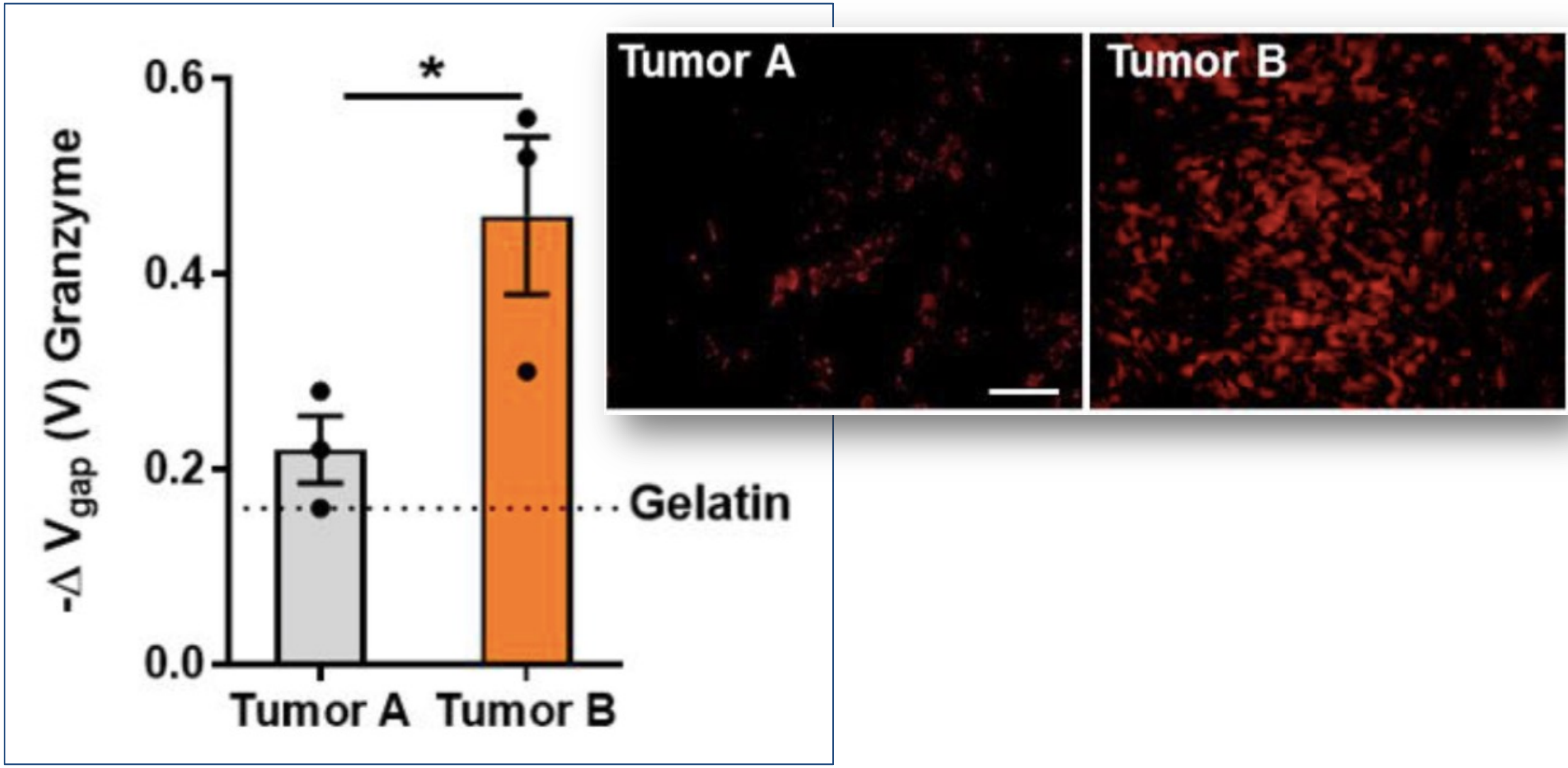
A. Tuoheti et al. / British Journal of Cancer Research 3(2020) 341 – 348

Brest Cancer Patients Stratification with Memristive Biosensors



A. Tuoheti et al. / British Journal of Cancer Research 3(2020) 341 – 348

Differentiating kind of Tumour with Memristive Biosensors

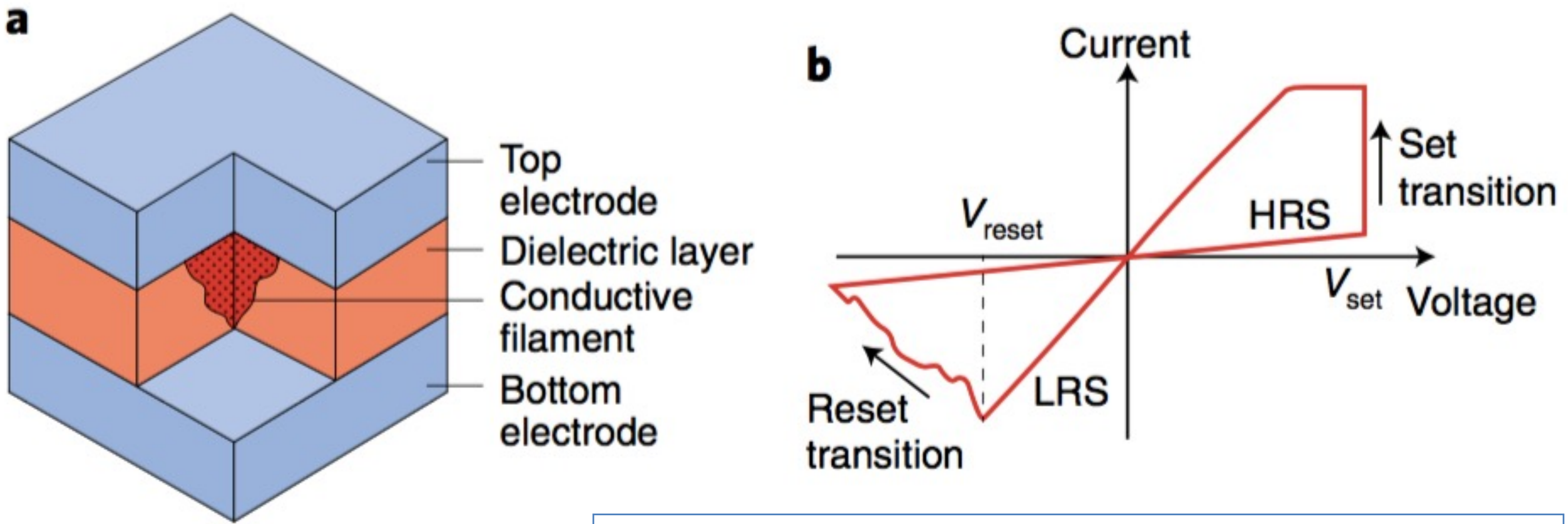


A. Tuoheti et al. / British Journal of Cancer Research 3(2020) 341 – 348

Key Messages:

- Measurements with **Memristive Biosensors** are much away more powerful than with conventional devices.
- To diagnose correctly Cancer, we definitely need measure **multiple cancer markers**.
- To correctly stratify Cancer Patients, we definitely need to **compute probability indexes** on a set of multiple cancer biomarkers.

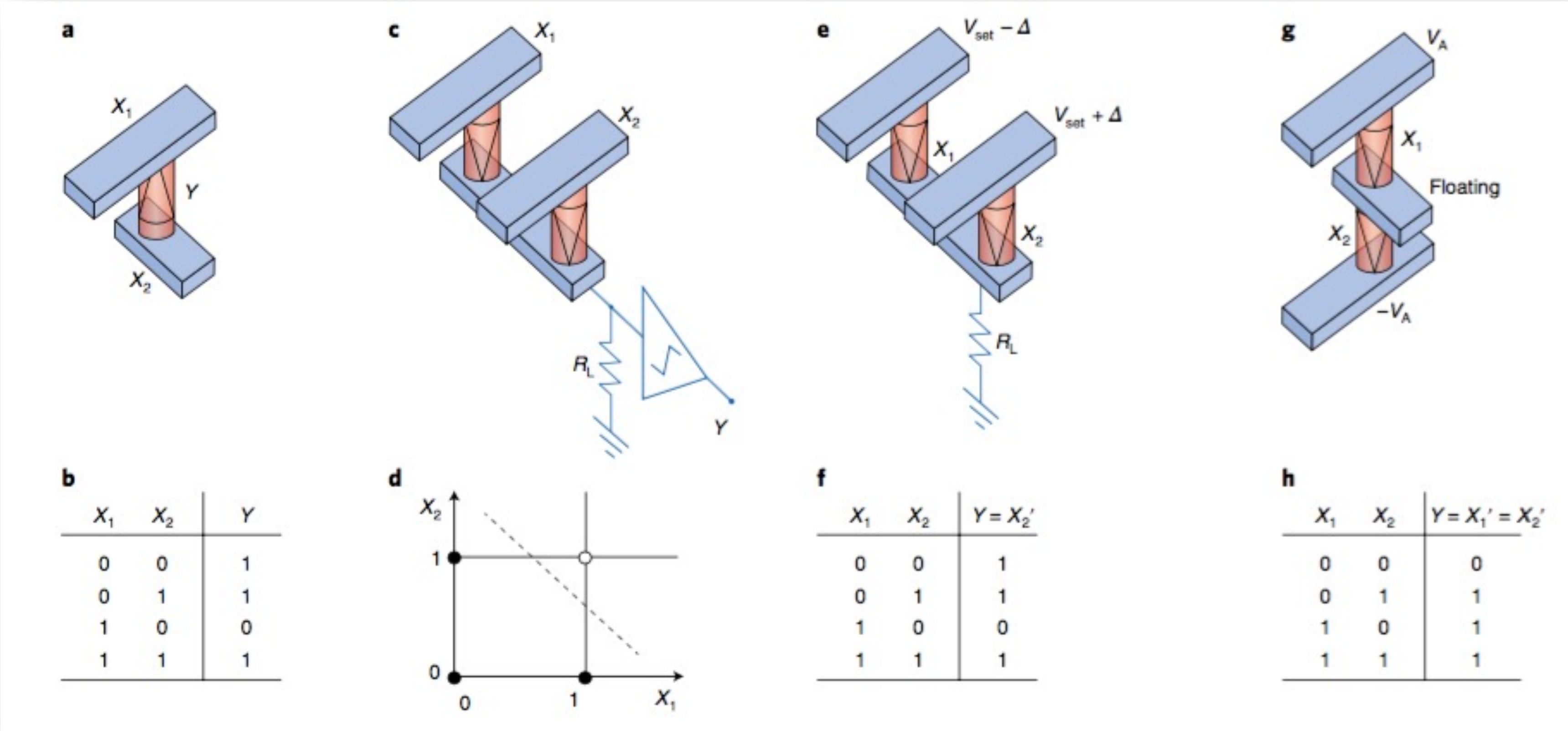
In-Memory Computing Device



D. Ielmini and H.-S.P. Wong, Nature Electronics 1(2018) 333-343

Computational RRAM memory devices

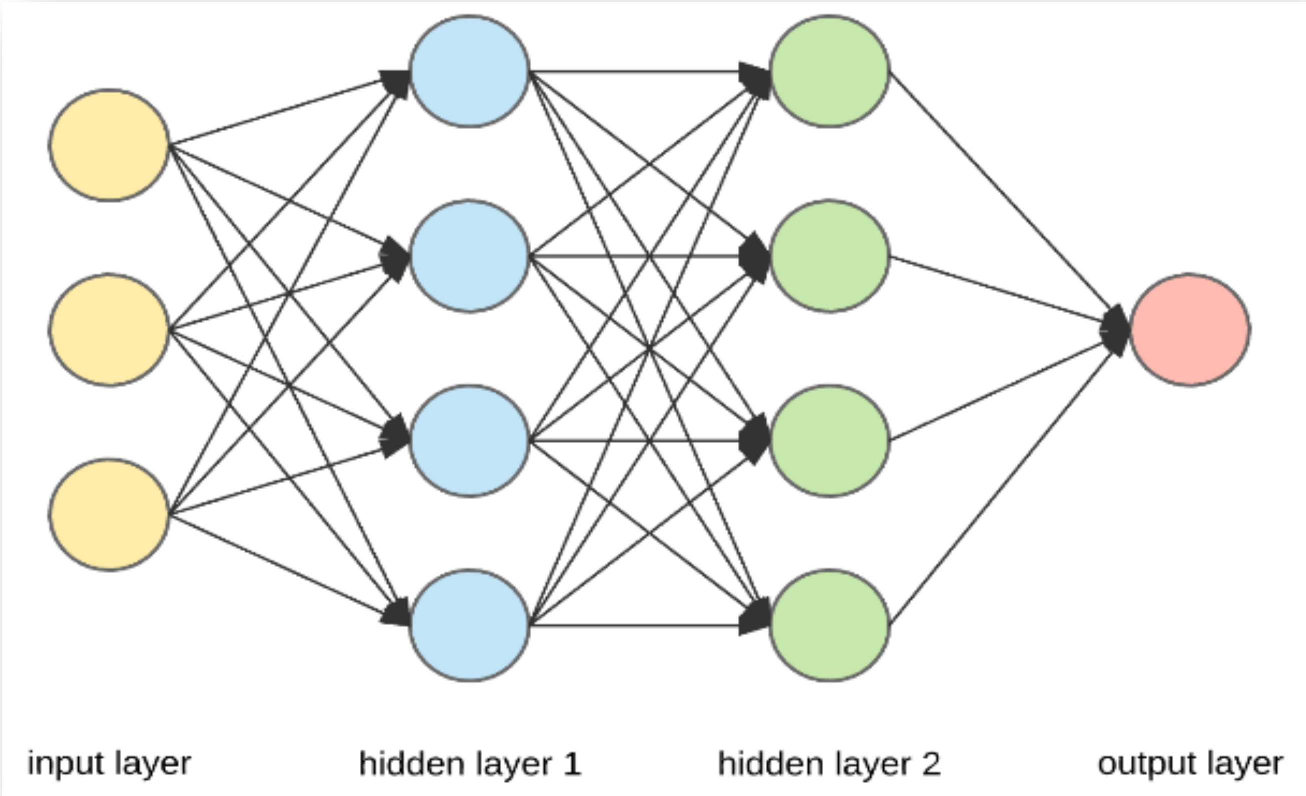
In-Memory Computing



D. Ielmini and H.-S.P. Wong, Nature Electronics 1(2018) 333-343

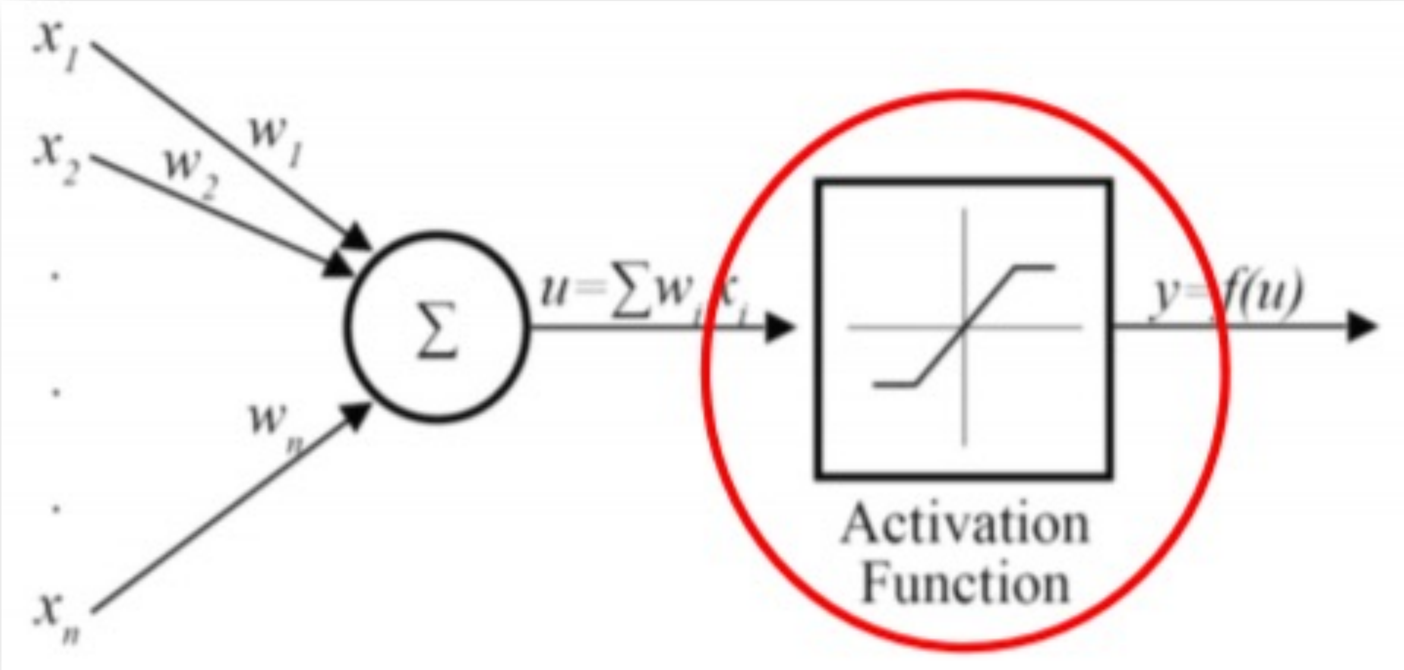
In-Memory Computing with RRAM-based digital logic gates

Artificial Intelligence by Deep Learning



Neural networks are multi-layer networks of neurons that Compute by classify things, make predictions, etc.

Key device for Deep Learning



Deep learning is based on « neurons » (artificial), which typically "learn" on inputs by an Activation Function that changes their "transmitting state"

Artificial Intelligence in Hardware

J. Fingas / www.engadget.com on Sept, 26°, 2021

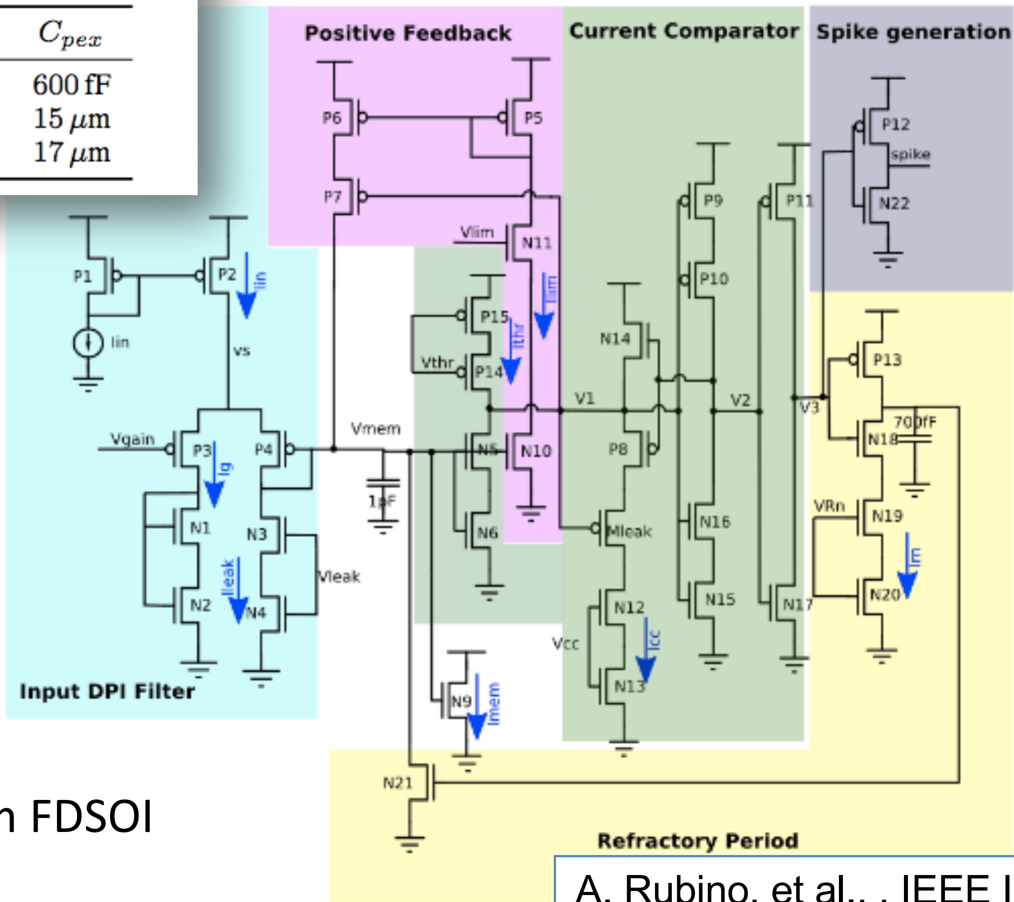
Image credit
VICTOR HABBICK VISIONS/SCIENCE PHOTO LIBRARY via Getty Images

Neuromorphic chips need for roughly 100 billion neurons

Complexity of Computing Chips

CAPACITANCE VALUES AND SIZES USED IN THE DESIGN

	C_{mem}	C_{ahp}	C_{ref}	C_{pex}
Value	1 pF	2 pF	700 fF	600 fF
Width	20 μm	28 μm	16 μm	15 μm
Length	20 μm	30 μm	19 μm	17 μm



@22nm FDSOI

A. Rubino, et al., , IEEE ICECS, 2019, 458-461

How many transistors do we need for realizing a single CMOS neuron?

Supersize AI on Whole Wafer!

	WSE 2	WSE	Nvidia A100
Size	46,225 mm^2	46,225 mm^2	826 mm^2
Transistors	2.6 trillion	1.2 trillion	54.2 billion
Cores	850,000	400,000	7,344
On-chip memory	40 gigabytes	18 GB	40 megabytes
Memory bandwidth	20 petabytes/s	9 PB/s	155 GB/s
Fabric bandwidth	220 petabits/s	100 Pb/s	600 gigabytes/s
Fabrication process	7 nm	16 nm	7 nm

IEEE Spectrum, issue on July, 2021

Cerebras's wafer-size chip boasts 2.6 trillion transistors

Costs of Computing Chips

MIT Technology Review

Sign in

COMPUTING

A $2 Billion Chip to Accelerate Artificial Intelligence

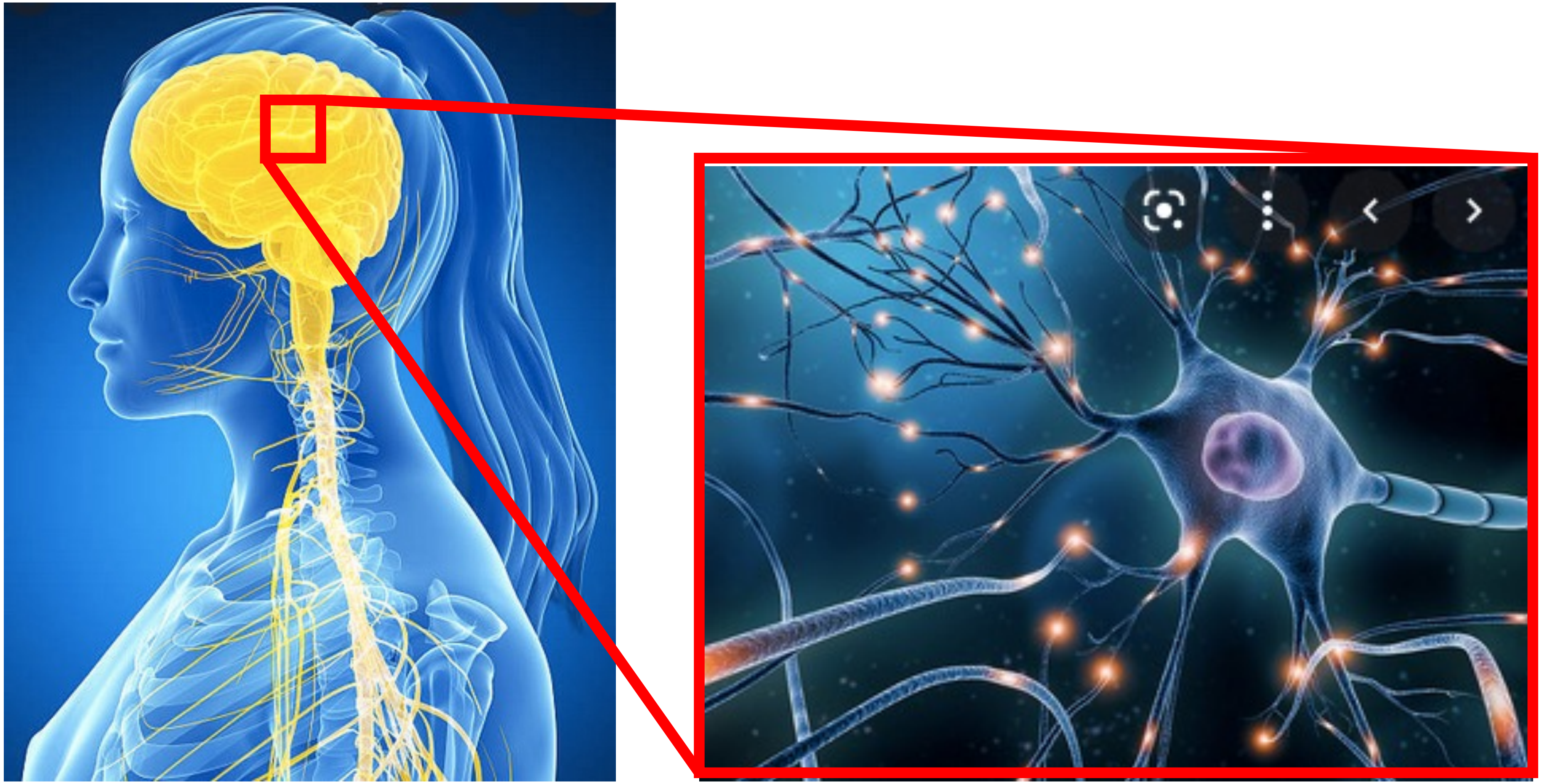
A new chip design from Nvidia will allow machine-learning researchers to marshal larger collections of simulated neurons.

By Tom Simonite

April 5, 2016

Billion neurons may cost Billion $

Biological Computation



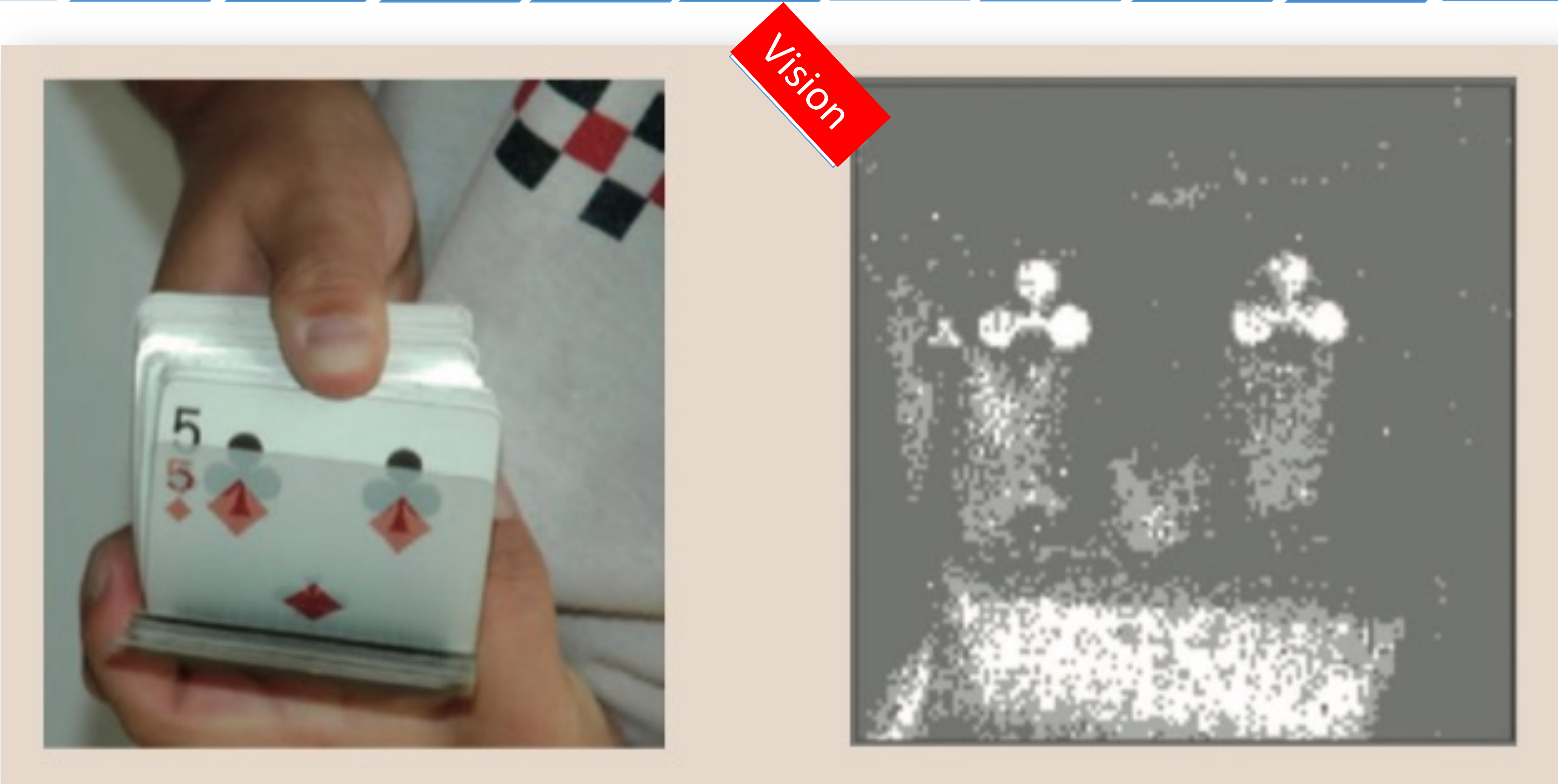
Biological neuron (natural) are « single devices » which change Activation Function « by leaning », so from their past, which means coding the past in a different state!

In-Memory Computing

So, If we succeed in getting a device that works like natural neurons we may develop machines computing like human brain !

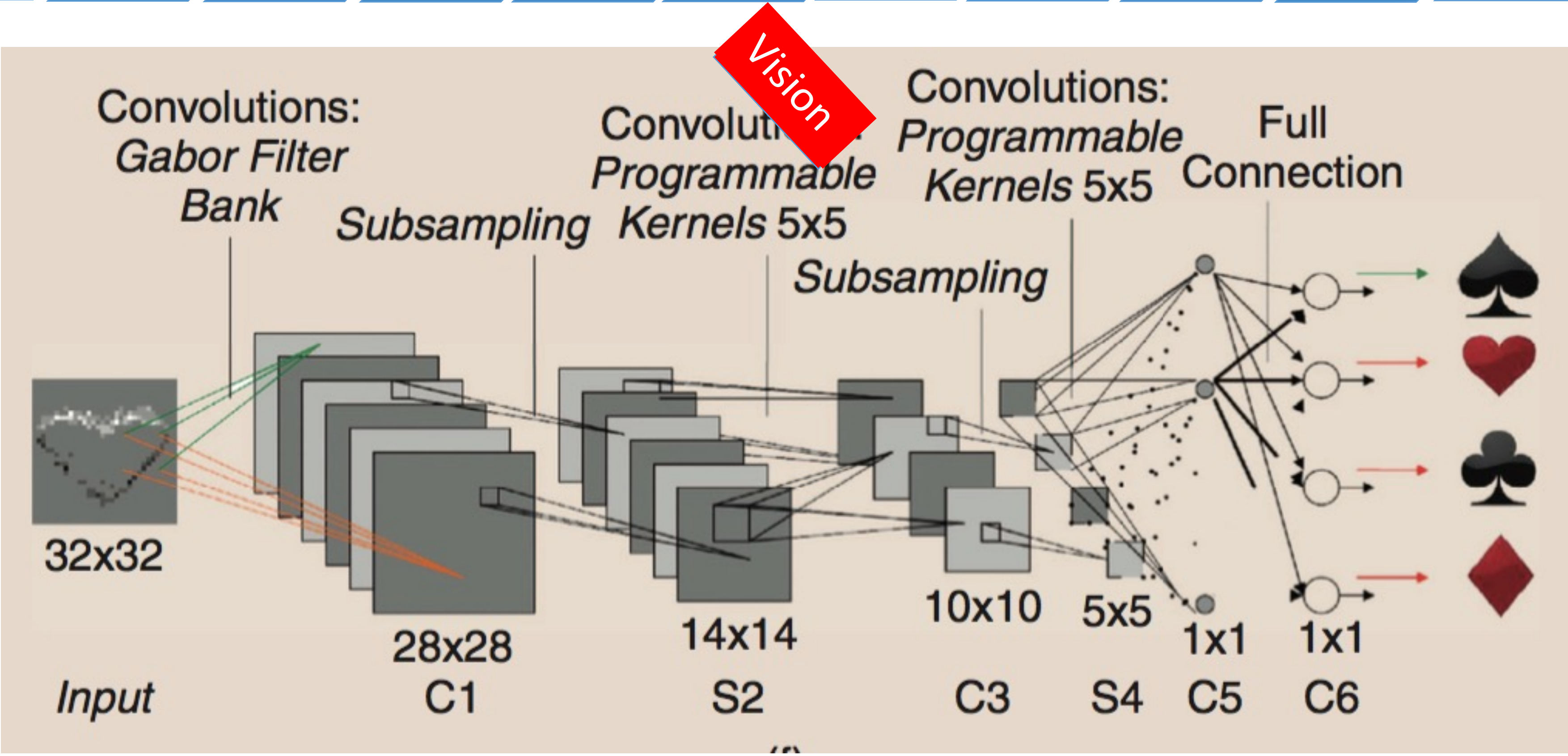
Memristive Sensors Milestones

2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018



T. Serrano-Gotarredona, et al. / IEEE CAS Mag. 13 (2013) 74-88

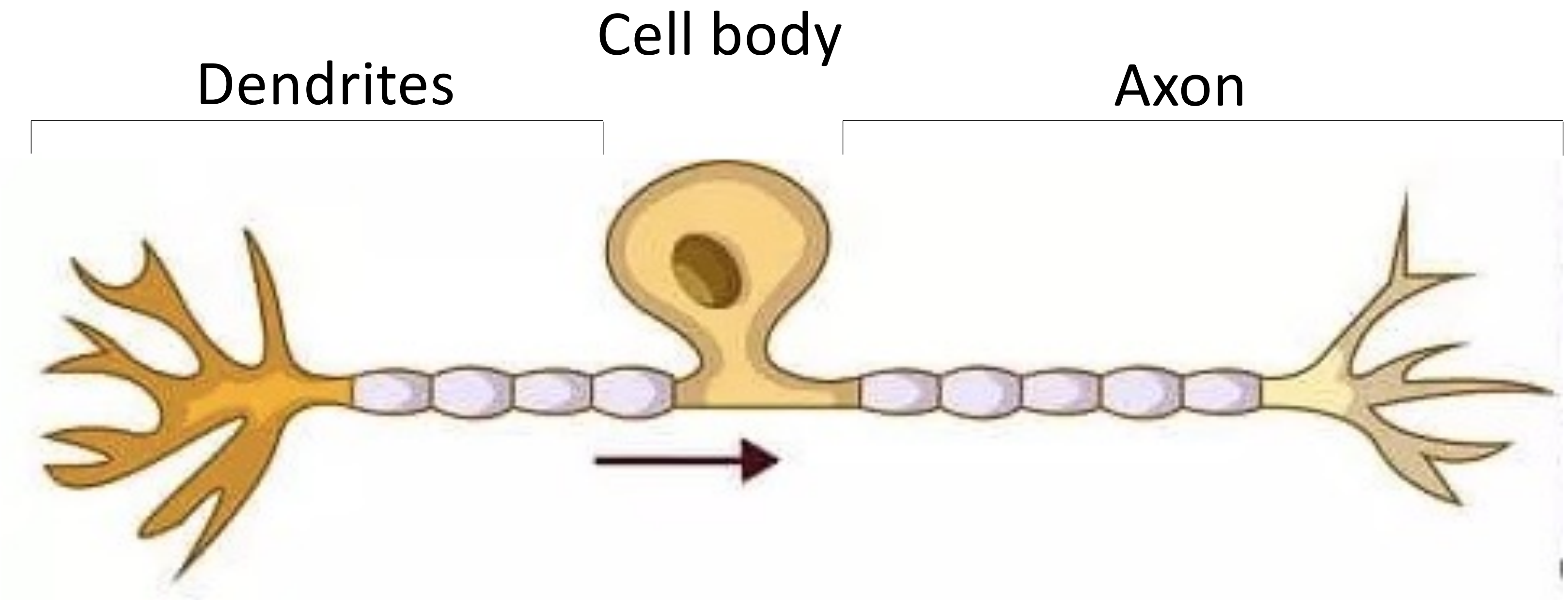
Memristive Sensors Milestones



Event-driven sensing and classification by CMOS/memristors integrated in an artificial retina

T. Serrano-Gotarredona, et al. / IEEE CAS Mag. 13 (2013) 74-88

Biological Sensing

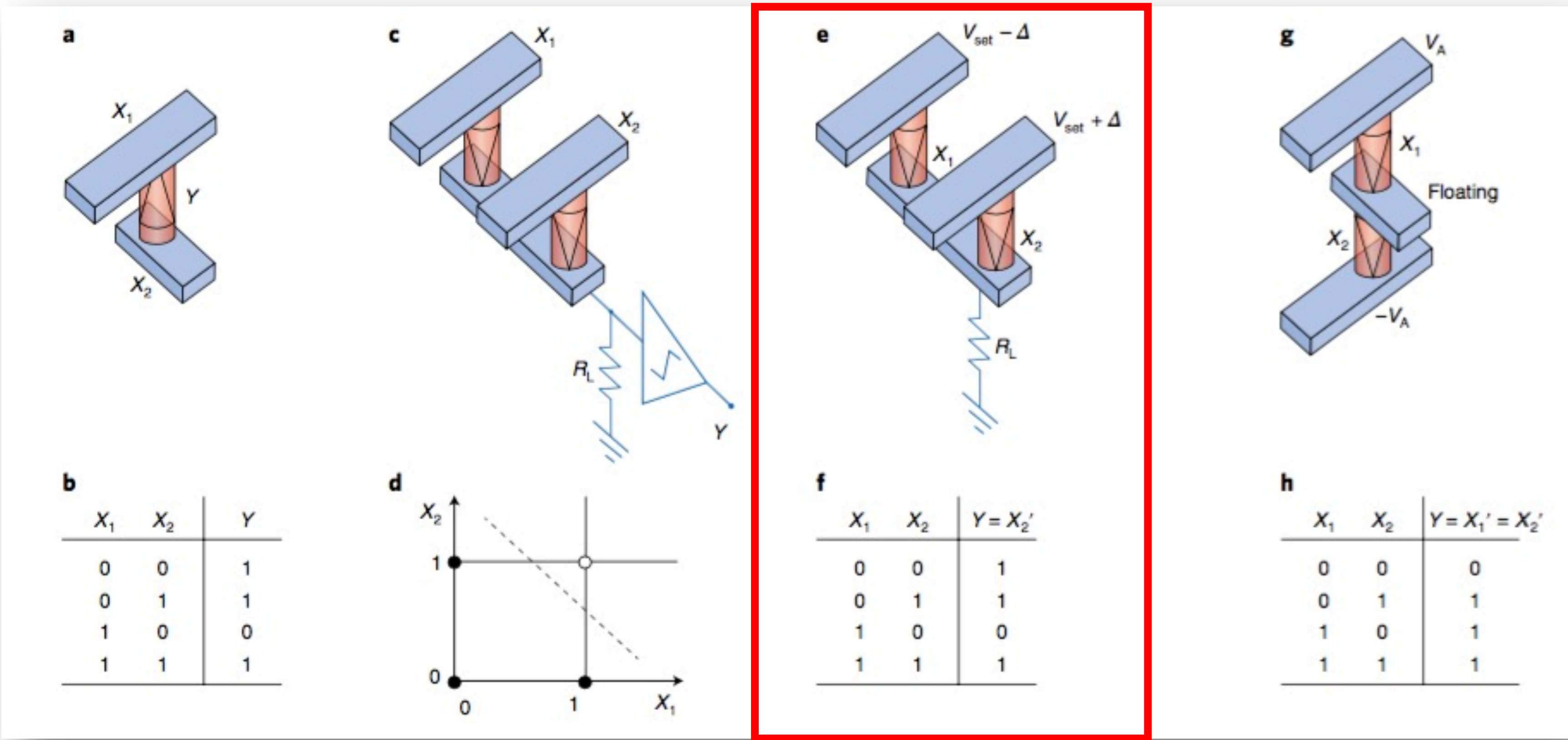


Human nervous system contains several kind of neurons, including sensory neurons

In-Memory Sensing

So, If we succeed in getting a device
that works like natural neurons we may
develop machines computing like
human brain and...
…like human peripheral nervous
sensing system,
we may also develop machines to
SENSE & COMPUTING !!!

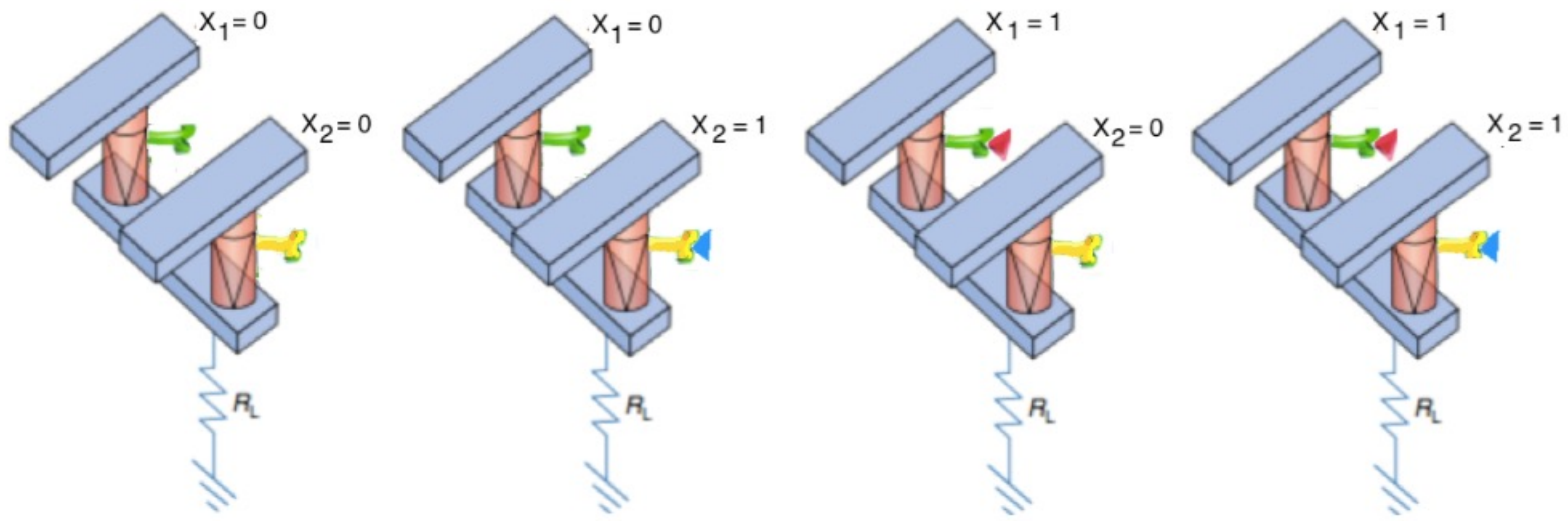
In-Memory Computing



D. Ielmini and H.-S.P. Wong, Nature Electronics 1(2018) 333-343

In-Memory Computing with RRAM-based digital logic gates

In-Memory Sensing & Computing



Cancer Markers: PSA, PSMA

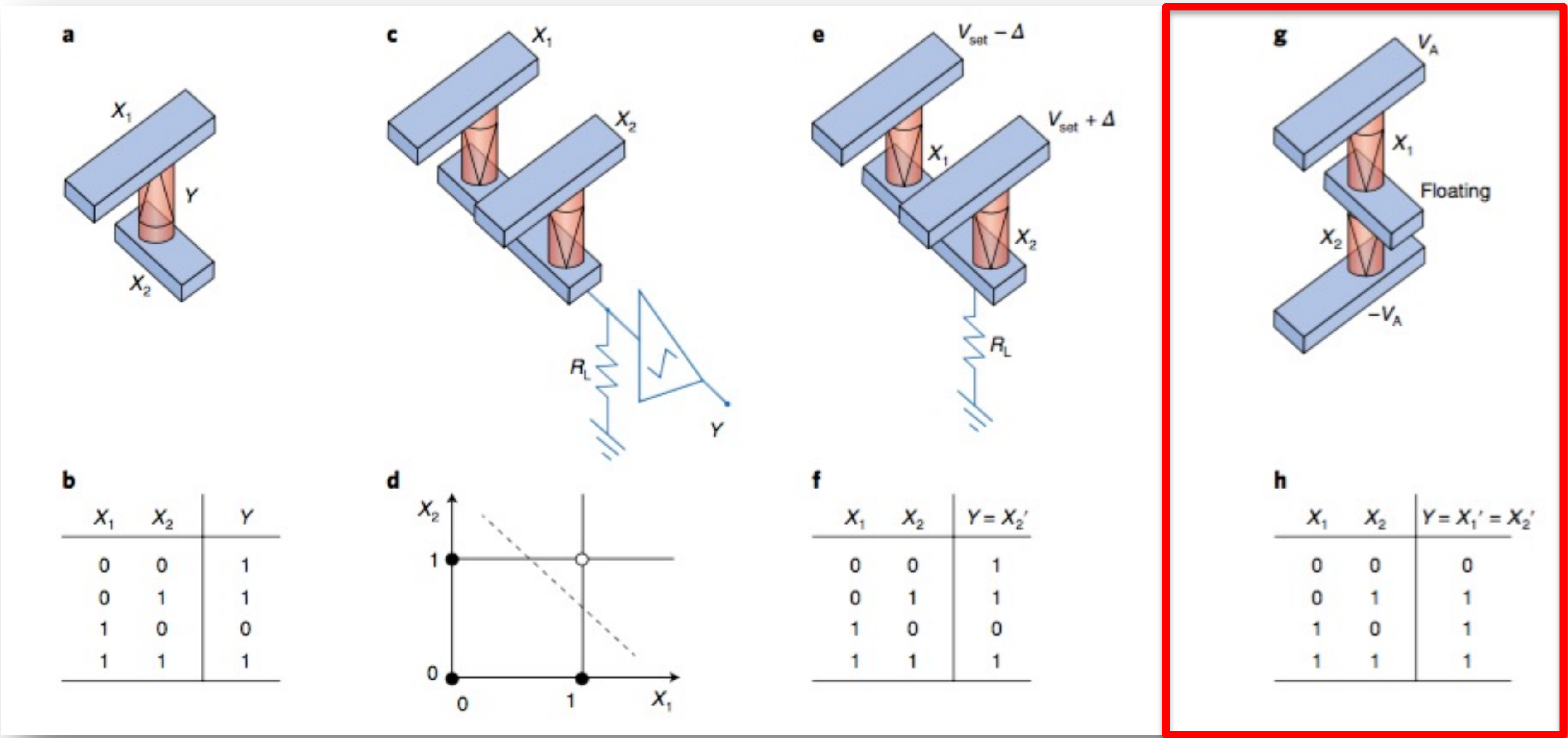
Chemical to Sense: PSA, PSMA

X_1 (PSA)	X_2 (PSMA)	$Y = X_2'$	Computing output
0	0	1	No Cancer
0	1	1	No Cancer
1	0	0	Cancer
1	1	1	No Cancer

S.Carrara, et al., SNF Grant, 2021

In-Memory Sensing with RRAM-based sensing digital logic gates

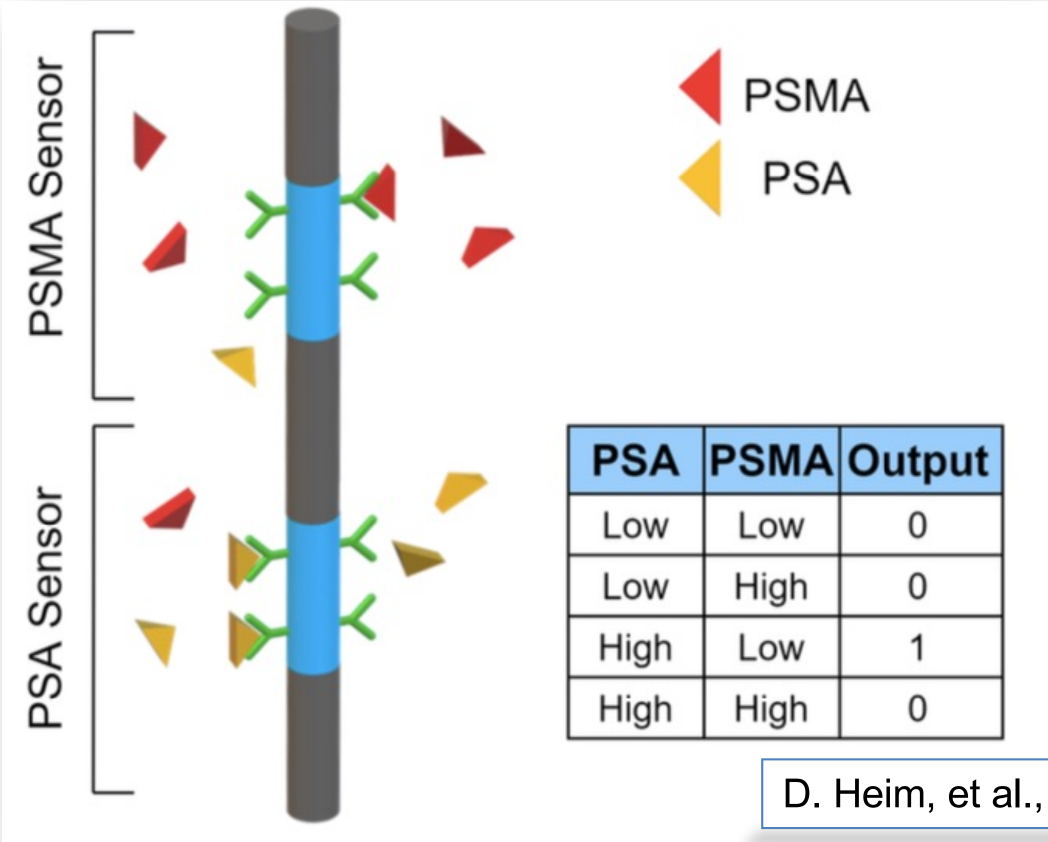
Back to Several Architectures



D. Ielmini and H.-S.P. Wong, Nature Electronics 1(2018) 333-343

In-Memory Computing with RRAM-based digital logic gates

Novel Approach in Edge Computing In-Memory Sensing of Cancer Markers

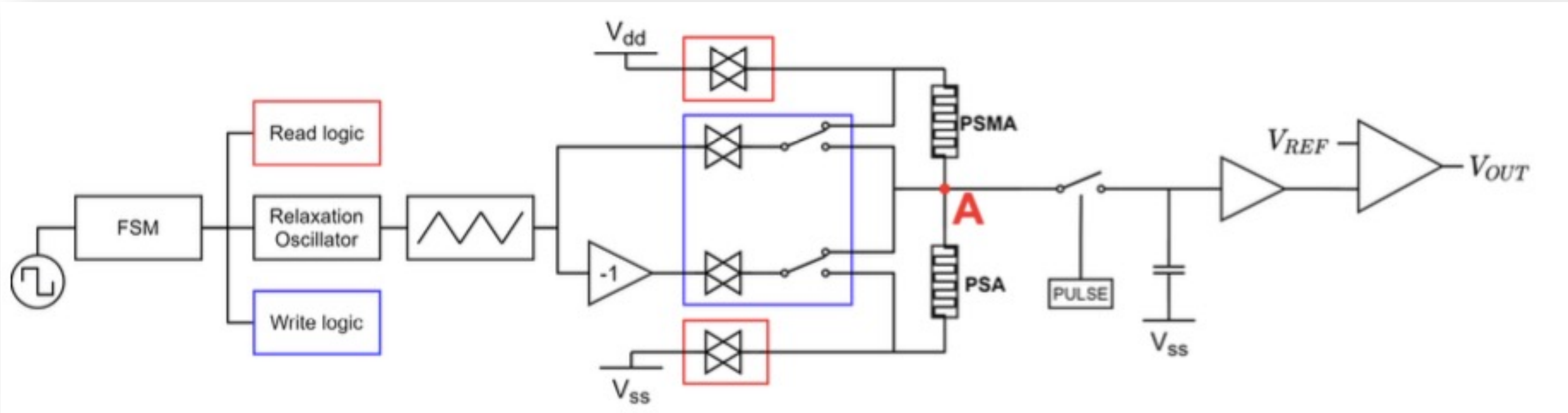


PSA	PSMA	Output
Low	Low	0
Low	High	0
High	Low	1
High	High	0

D. Heim, et al., IEEE ISCAS 2022

Two sensors interact with each other to perform a logical operation already at the sensor node

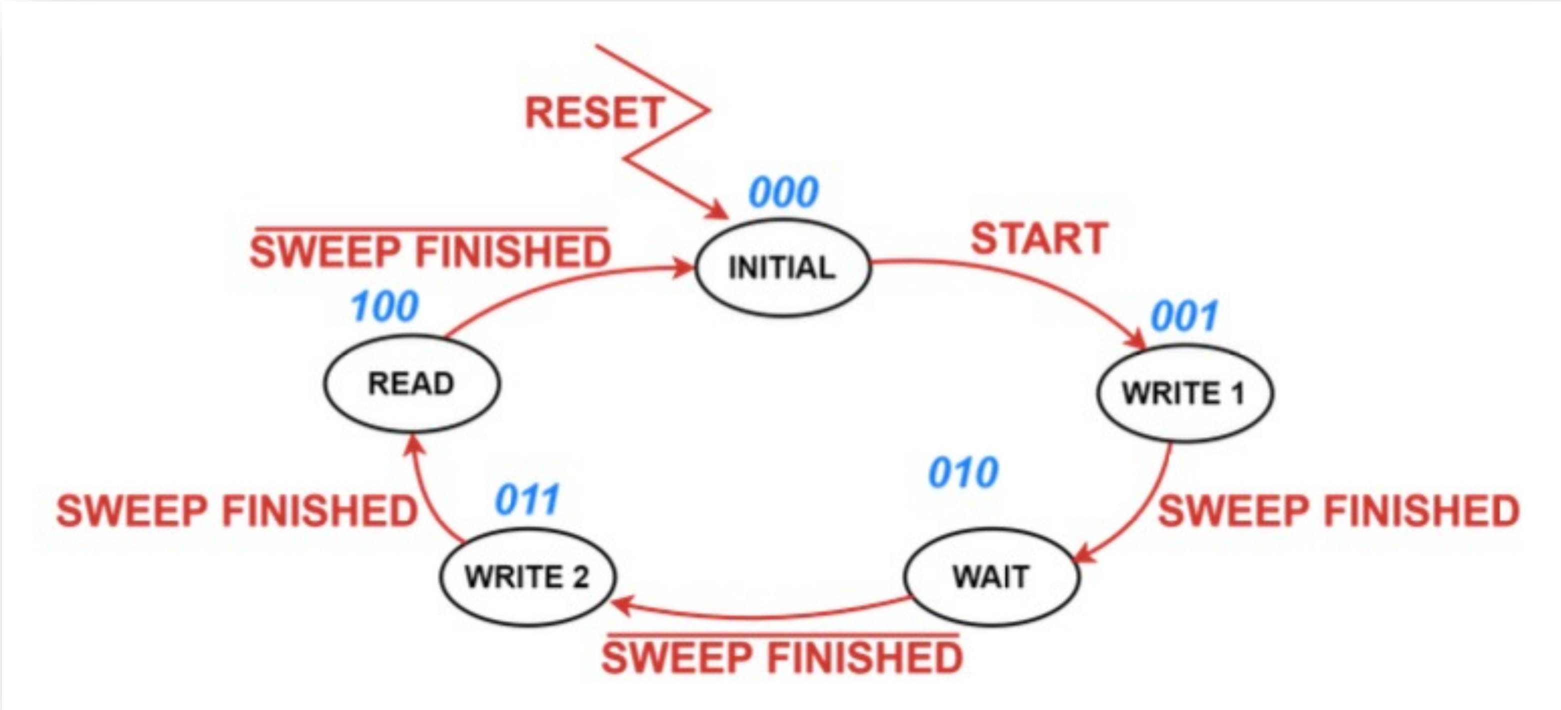
Novel Approach in Edge Computing In-Memory Sensing of Cancer Markers



D. Heim, et al., IEEE ISCAS 2022

Block diagram of the entire circuit. A Finite State Machine (FSM) is used to control switches for writing and reading the biosensors states

Novel Approach in Edge Computing In-Memory Sensing of Cancer Markers



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Finite state machine diagram for writing and reading the biosensors states

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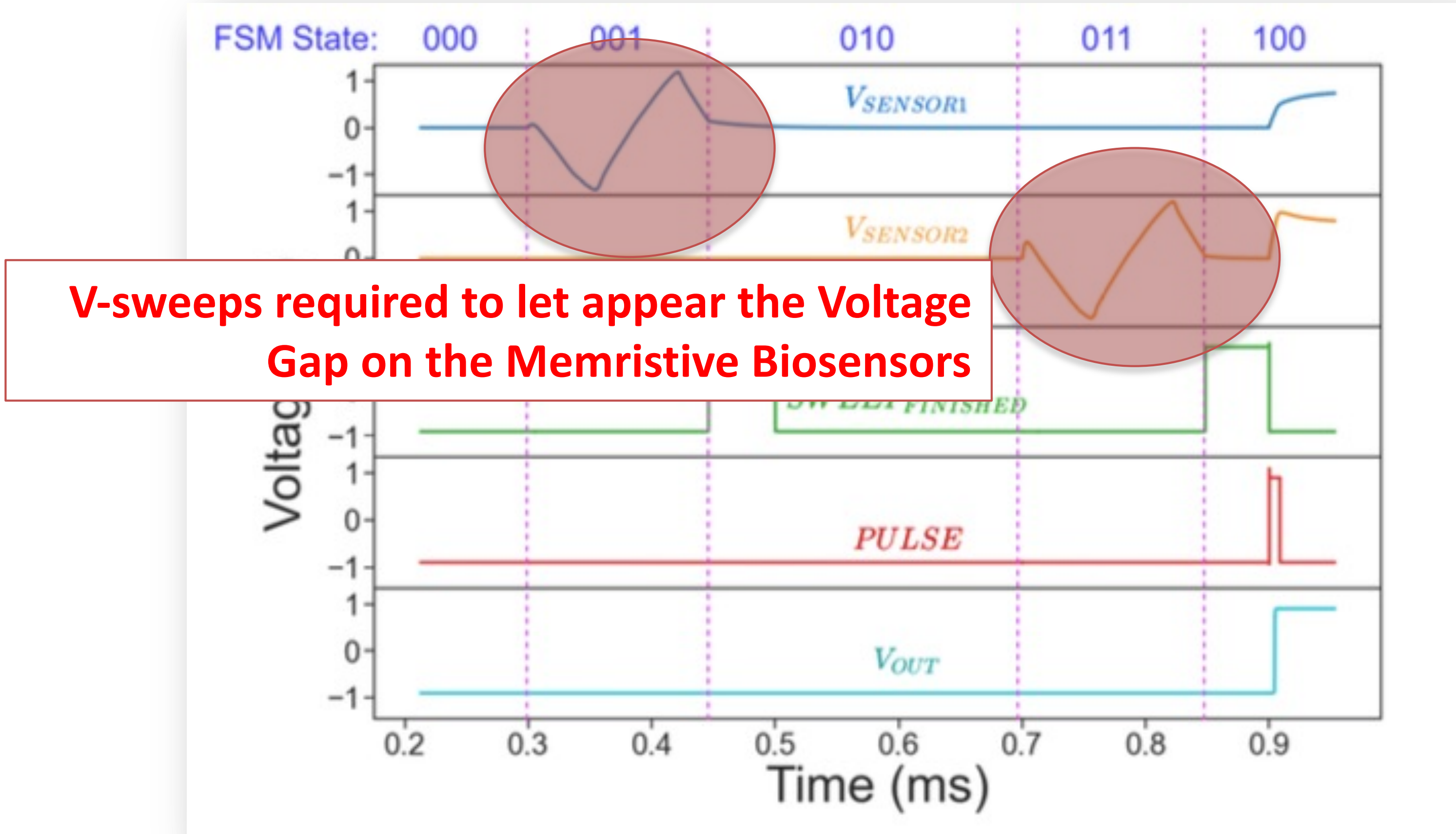
In-Memory Sensing of Cancer Markers



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Finite state machine states and main system signals

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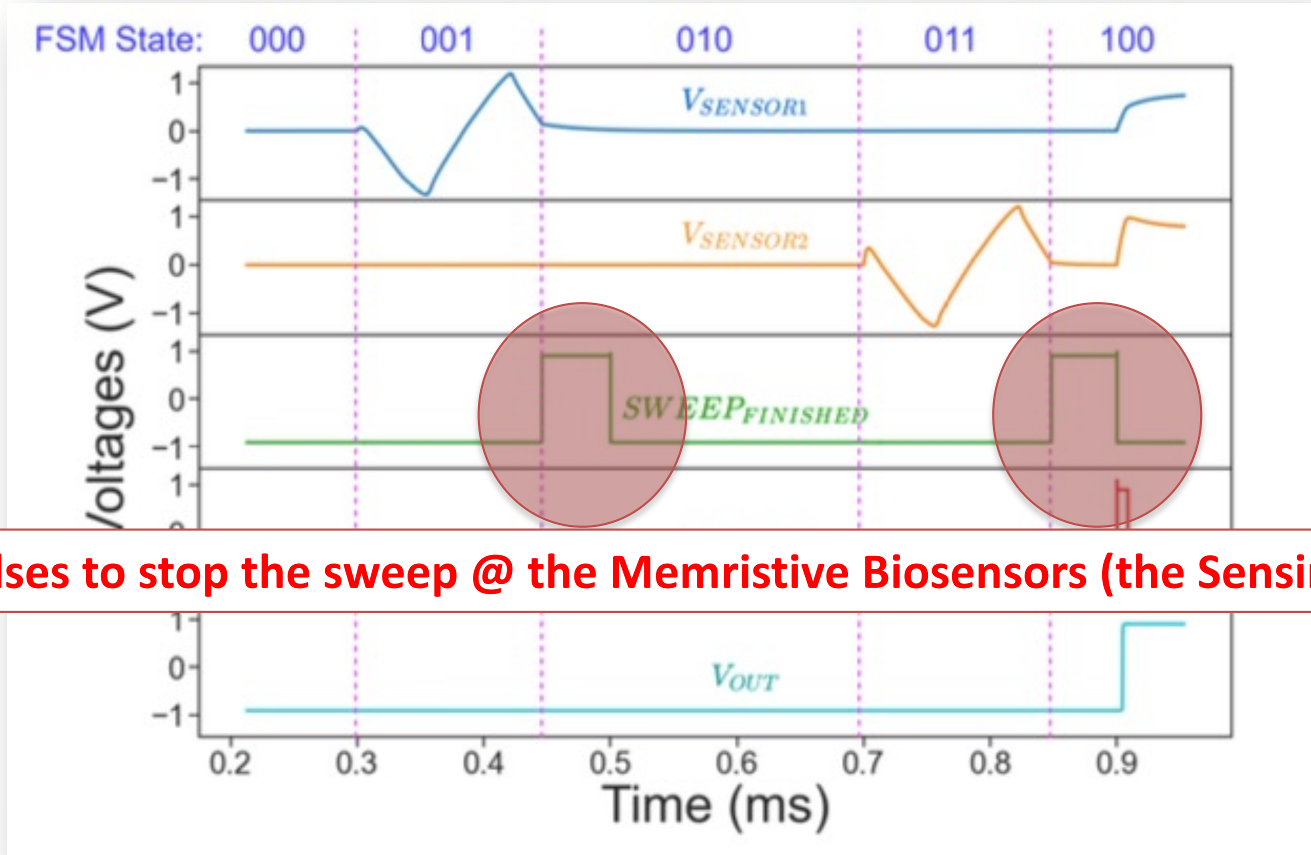

Pulses to stop the sweep @ the Memristive Biosensors (the Sensing!)

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Finite state machine states and main system signals

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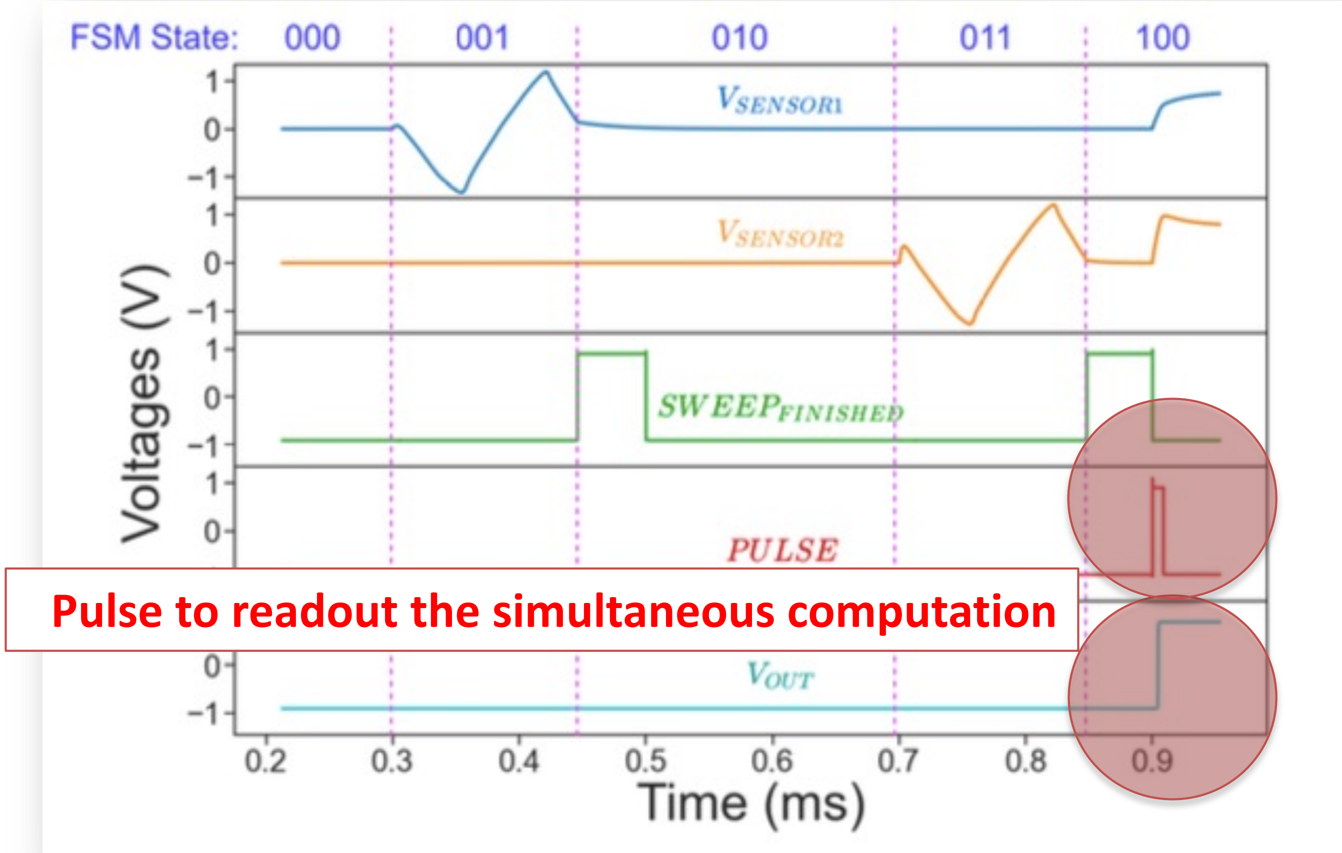

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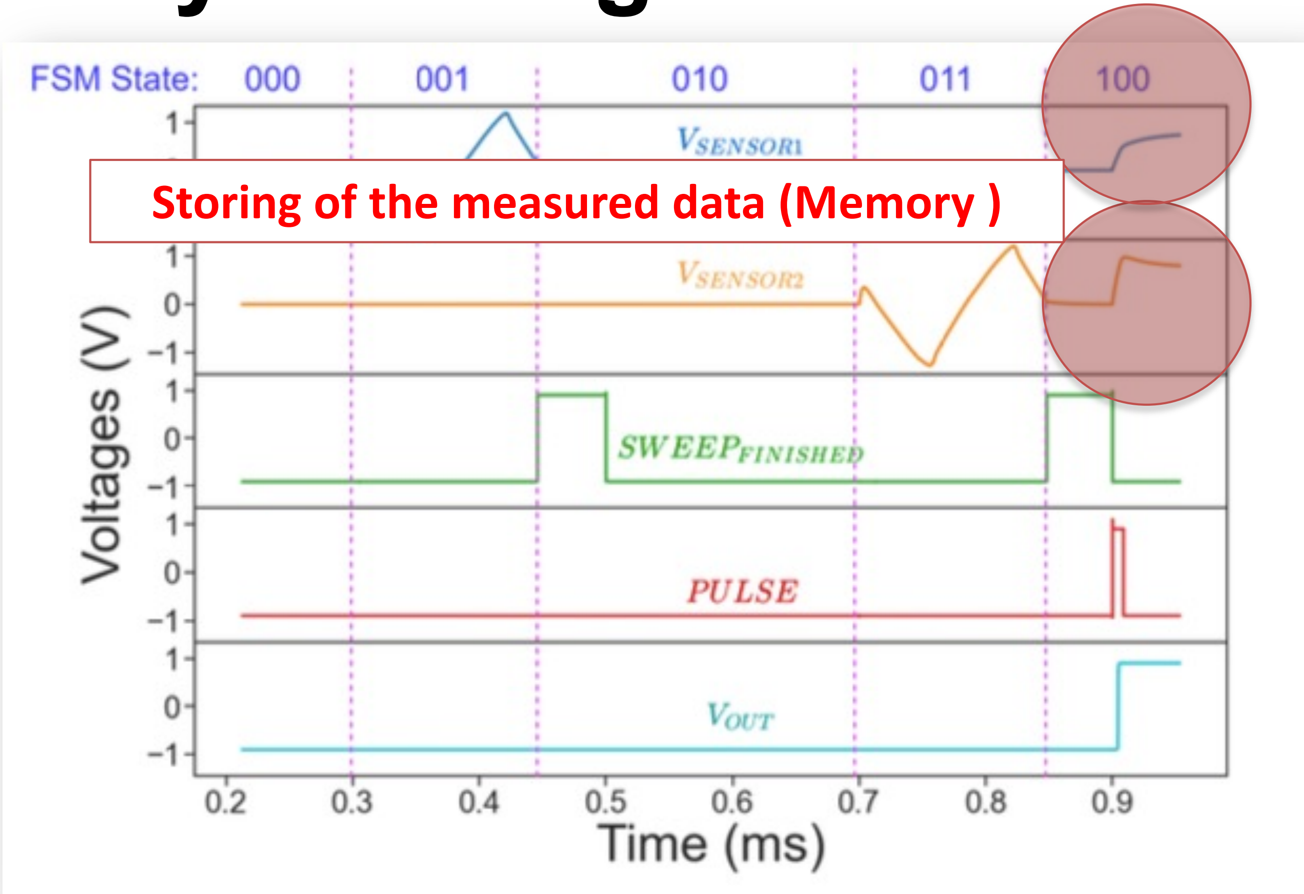

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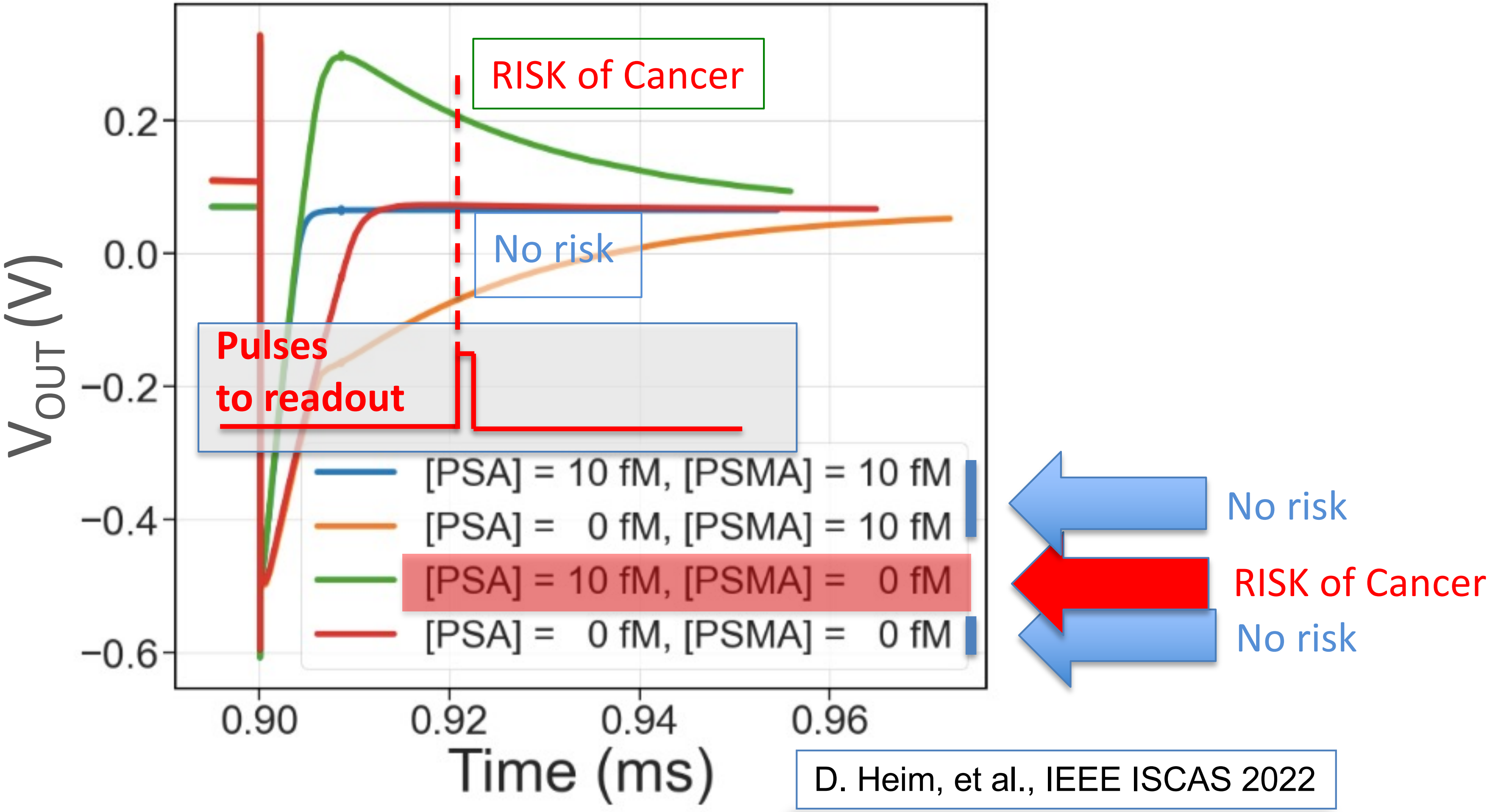

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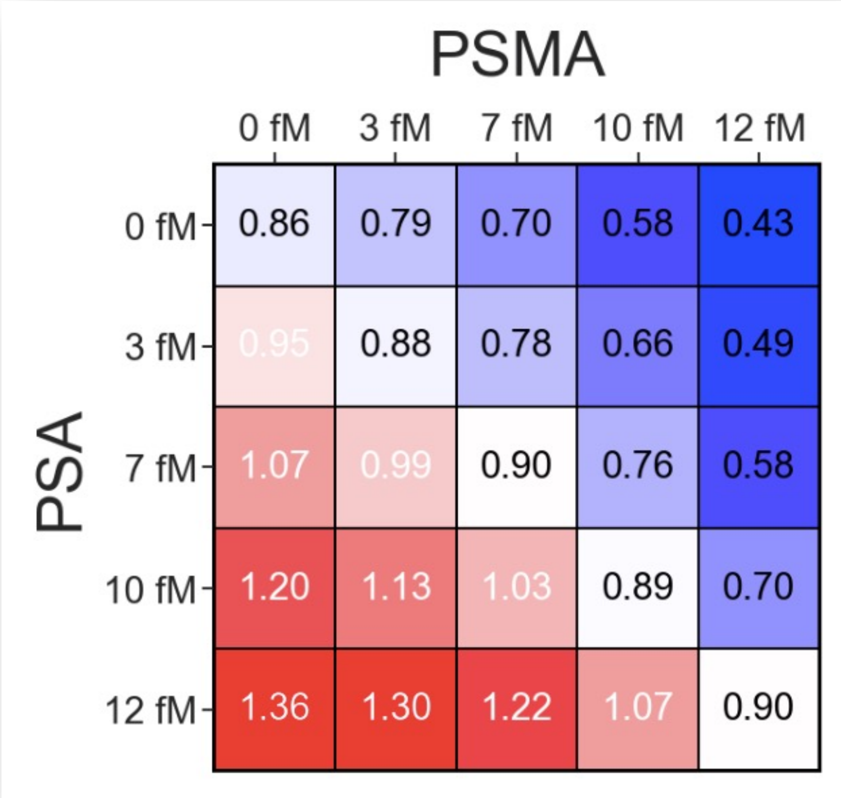

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Output Voltages directly as “Risk Probability for Cancer” for different concentrations of PSA/PSMA

Summary

- That's possible to realize artificial neurons with single devices: the Memristors!
- The development of Memristive devices for Sensing aims gave rise to the new field of Memristive Sensors.
- The coupling of Memristive Sensors with biomolecules gave rise to the new field of Memristive Biosensors.
- Coupling the capability of computational architecture based on memristors and memristive sensors we can realize new "**in-Memory Sensing & Computing**" machines.
- Case study: simultaneous computation of multi-biomarkers is really key to succeed in Cancer Diagnostics!