Alternative Use of Silicon

Edoardo Charbon	TU Delft
Alex Dommann	EMPA
Pantelis Georgiou	Imperial College London
Bruno Murari	ST Microelectronics
Roland Thewes	TU Berlin

Chair: Giovanni De Micheli, EPFL

Centre SI Integrated Systems Centre

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Alternative Use of Silicon

Do we need to understand Quantum Mechanics, fully?

E. Charbon

TU Delft

Some opinions (at this symposium)

- Marco Gilli (polito) – students should learn the basics of science and engineering when they are fresh (men).
- Alberto Sangiovanni-Vincentelli (UCB) – one must learn the fundamentals first and then everything else.
- Marco Casale Rossi (Synopys) – Universities should teach how to learn.

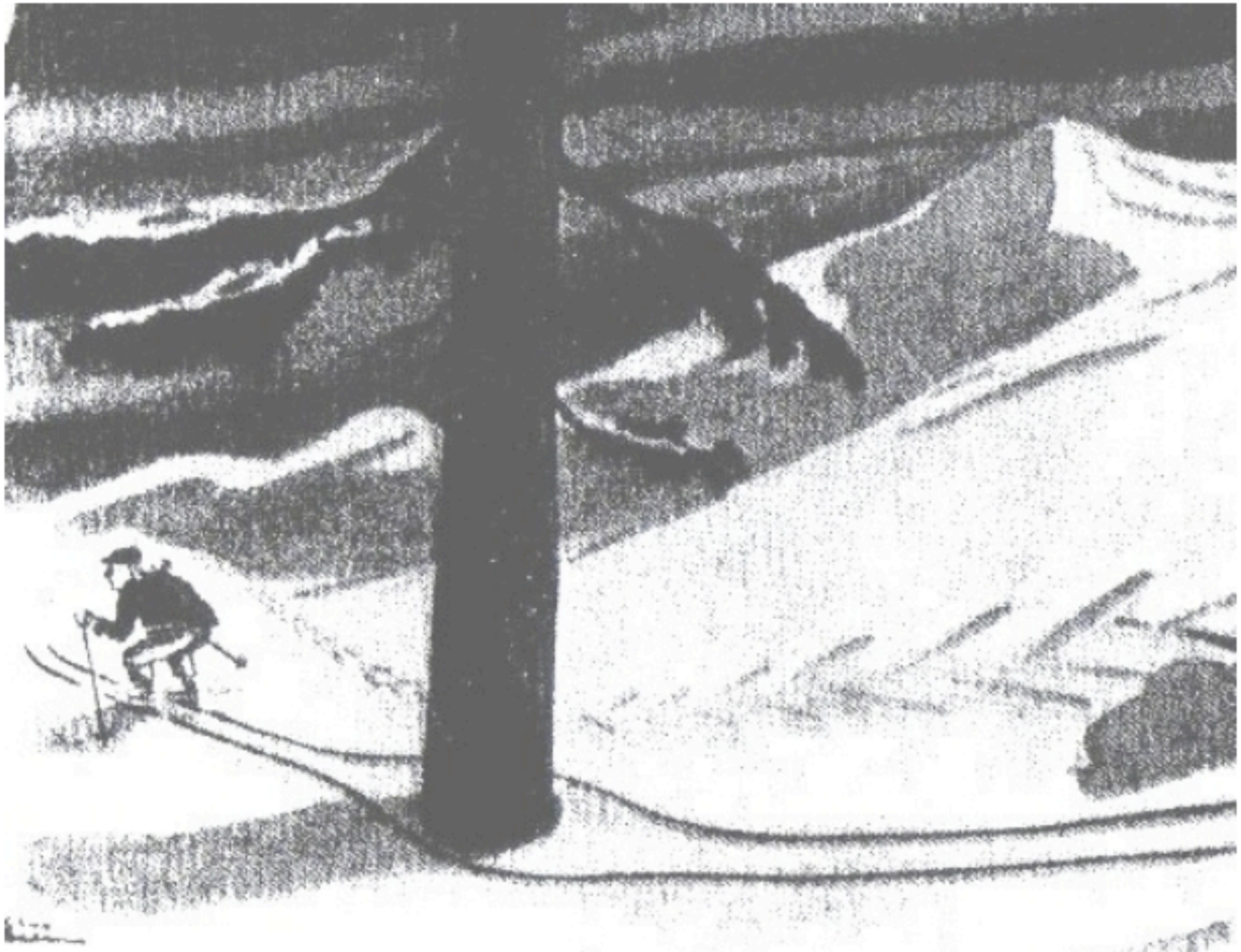
2014 Nobel Prize in Chemistry

Stefan W. Hell

for his contributions to Super-Resolution Microscopy

Made possible, in great part, by photon counting cameras

Quantum Mechanics

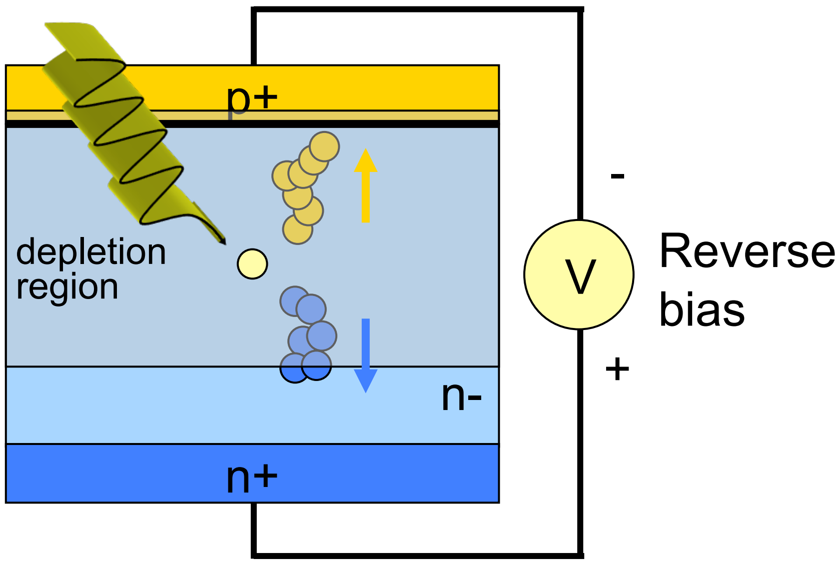


Source: Neil J. Gunther

… Actually…

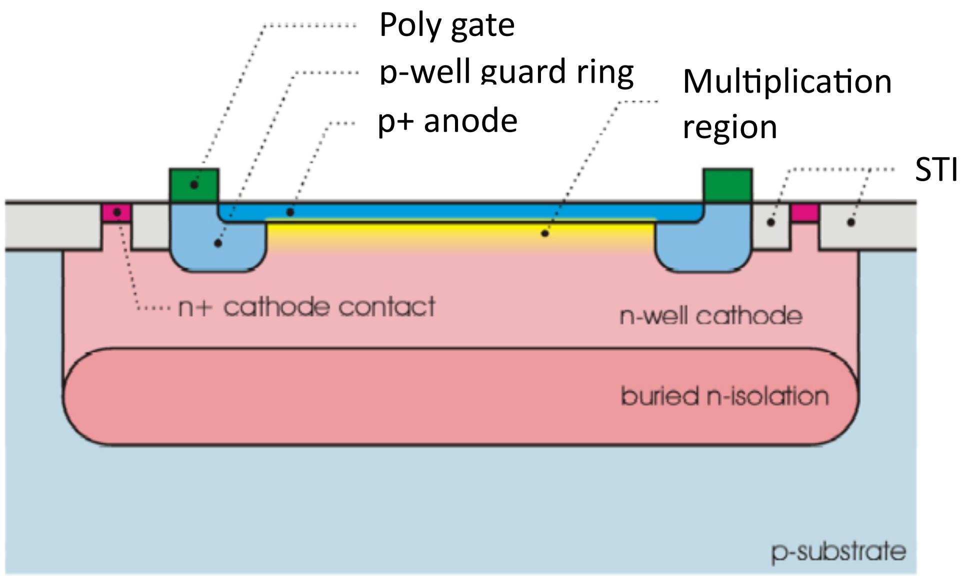
- Quantum Mechanics is at the core of electronics, but quantum effects could be more or less ignored until recently
- Examples of trend:
  - **tunneling FET**, a major player in sub-10nm CMOS
  - **single-photon avalanche diodes (SPADs)**, a new photonic sensor for photon counting in CMOS

Single-photon avalanche diodes (SPADs) for photon counting



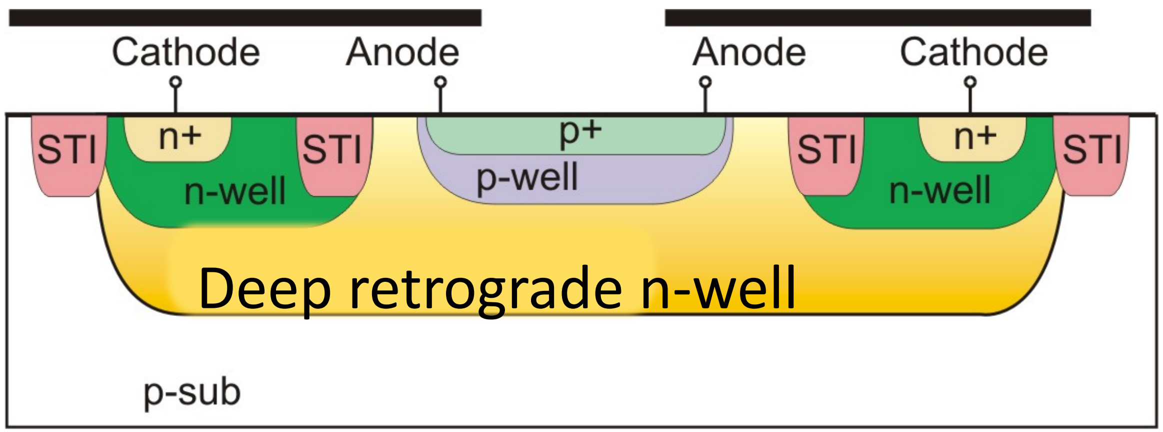
In CMOS

CMOS photon counting



2004 (EPFL)

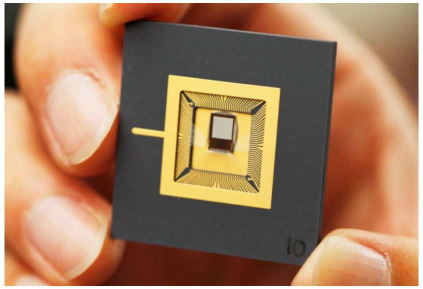
Today (STM)

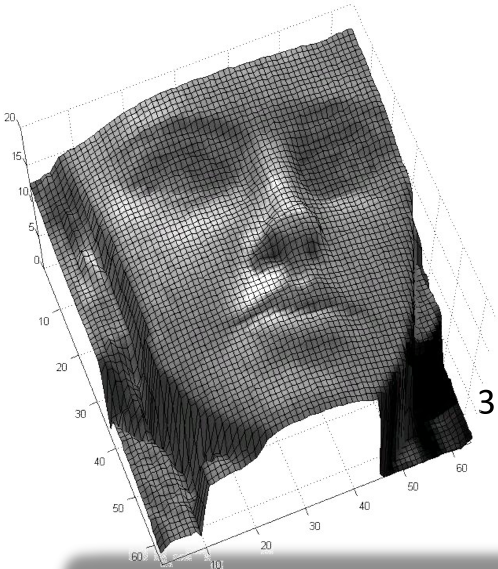


Drawing: D. Stoppa

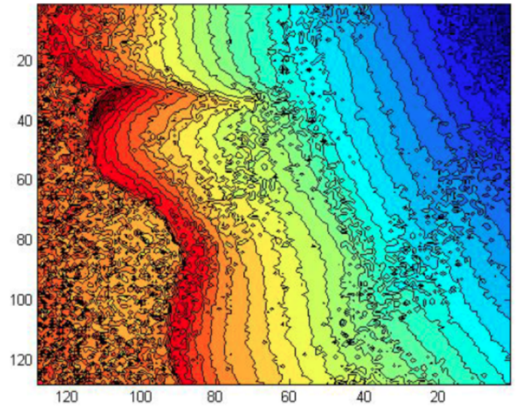
Why bother with photon counting?

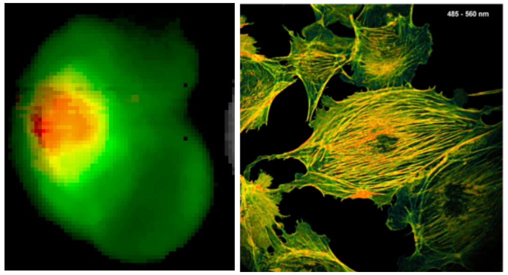
Lots of applications


Quantum Security


3D Vision

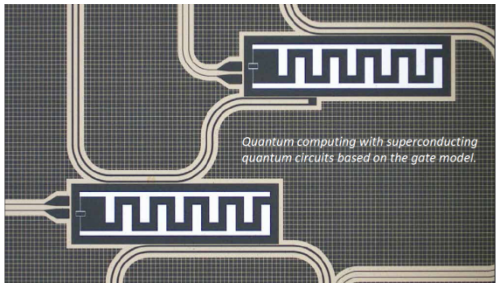
Near Infrared Imaging (NIRI)



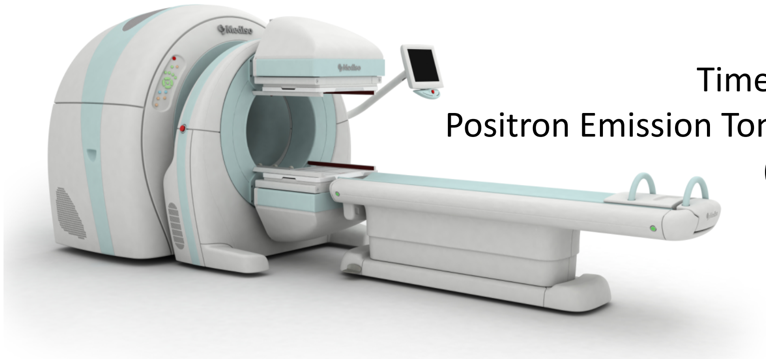

Fluorescence Lifetime Imaging Microscopy (FLIM) and super-resolution microscopy (STED, STORM, GSDIM, PALM, etc.)


Super-resolution Microscopy

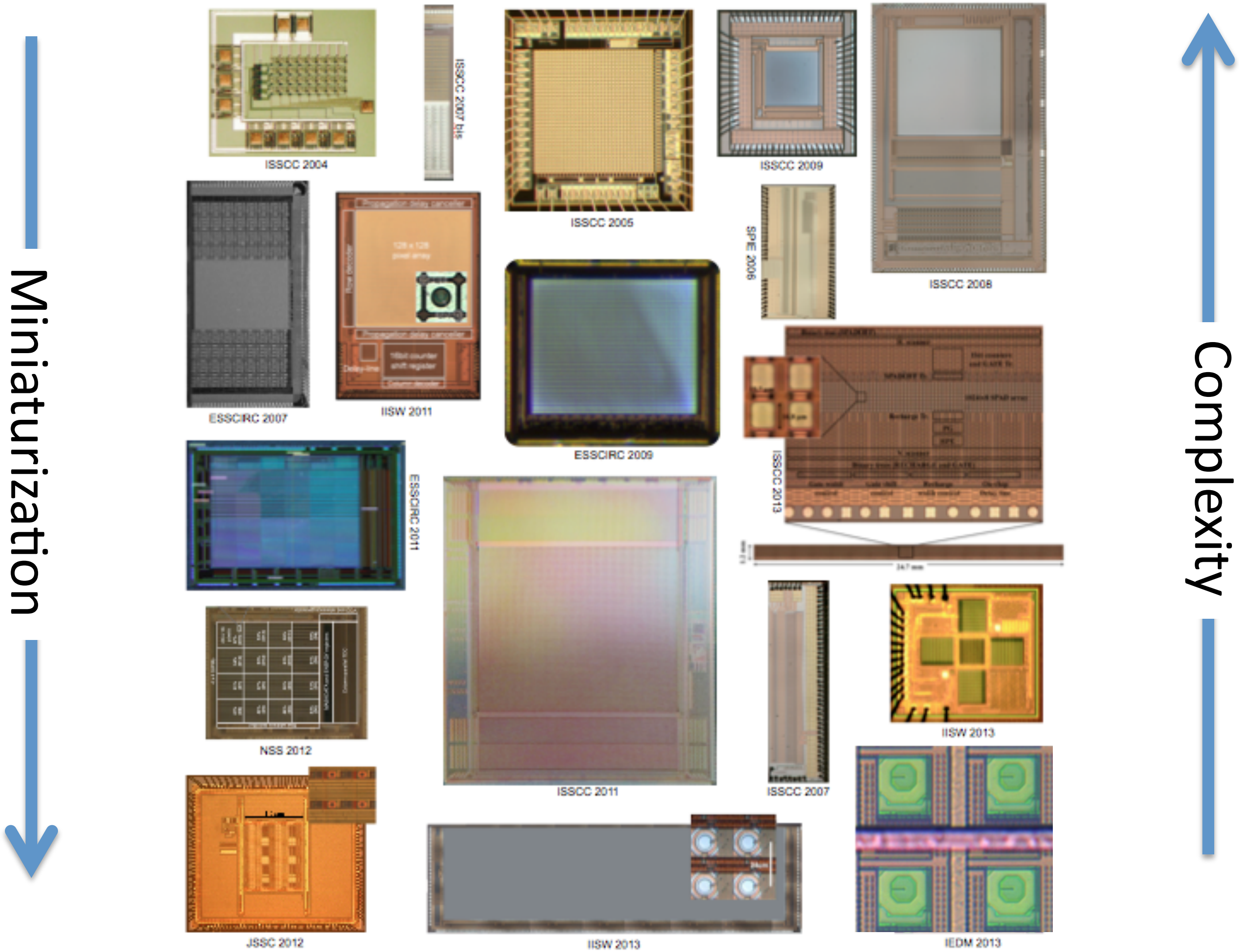

Time-resolved Raman Spectroscopy



Electronics for Quantum Computing


Time-of-Flight Positron Emission Tomography (TOF PET)

CMOS Single-Photon Imagers (2004-14)



Latest…

11.4 A 67,392-SPAD PVTB-Compensated Multi-Channel Digital SiPM with 432 Column-Parallel 48ps 17b TDCs for Endoscopic Time-of-Flight PET

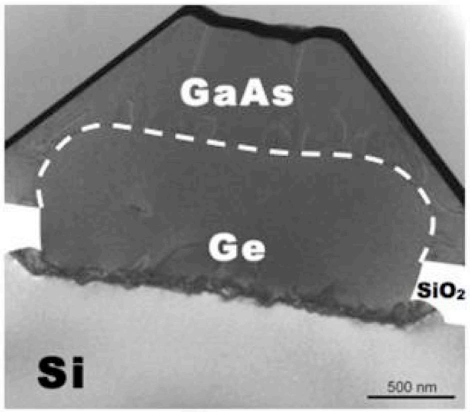
Augusto Carimatto, Shingo Mandai, Esteban Venialgo, Ting Gong, Giacomo Borghi, Dennis R. Schaart, Edoardo Charbon

Delft University of Technology, Delft, The Netherlands

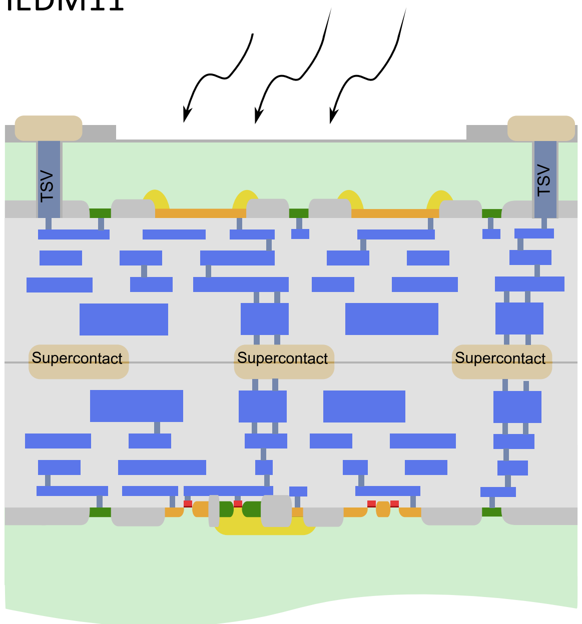
ISSCC 2015

Other trends

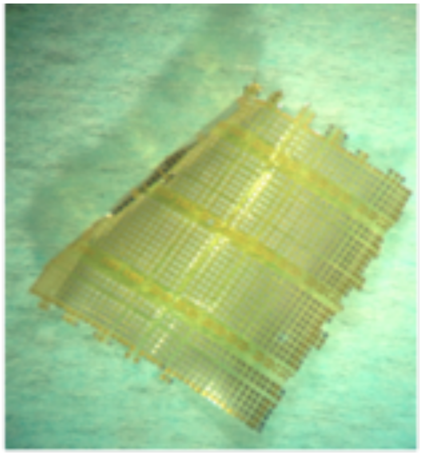
- 3D IC
- Sub-65nm CMOS
- New Materials
- Flexible



Sammak, Aminian, Charbon, Nanver, IEDM11

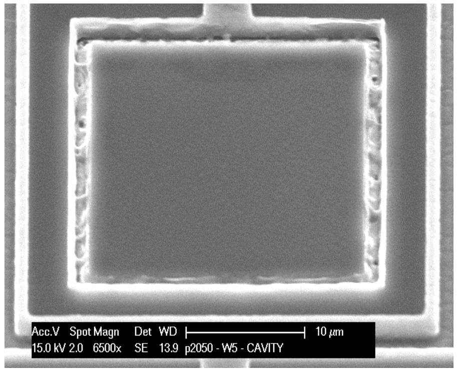


Mata Pavia, Wolf, Charbon, NSS14



Sun, Ishihara, Charbon, JSTQE, 2014

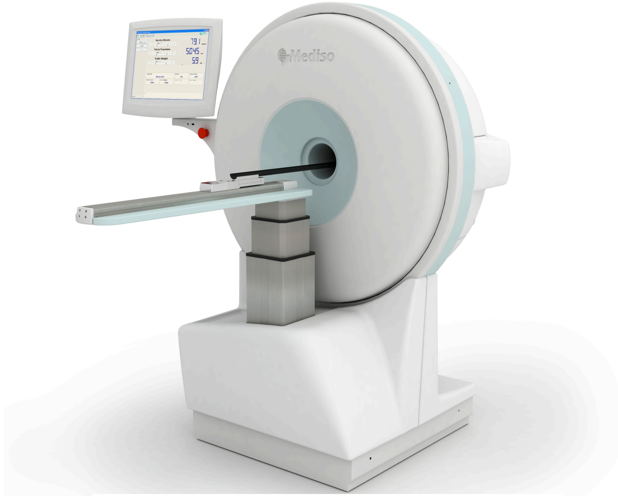
Sammak, Aminian, Charbon, Nanver ECS14



What about products, effect on society?

Industrial/Consumer Acceptance

forimtech
fiber optic radiation imaging technologies



Mediso

Fastree 3D
imagers

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EPFL
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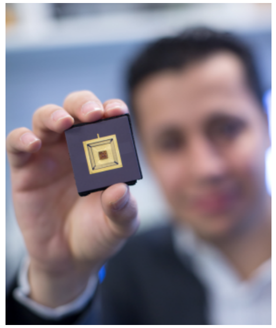
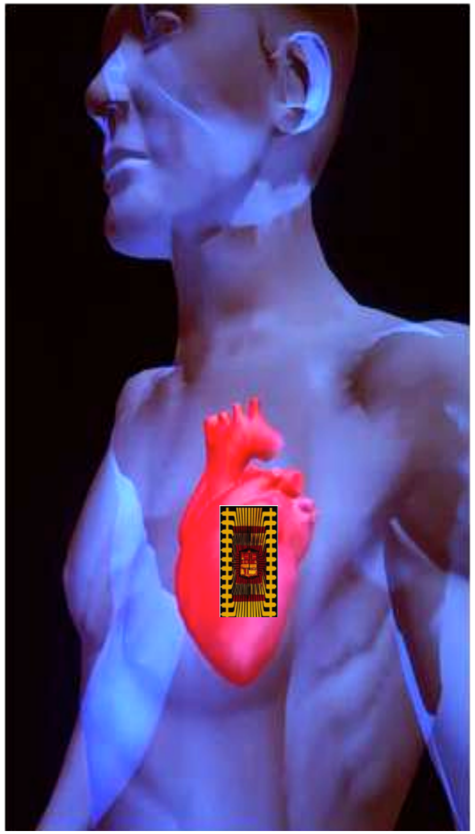
Bio-inspired Semiconductors for Healthcare

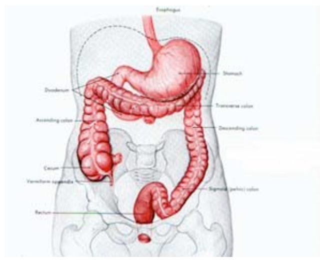
Imperial College London

Dr. Pantelis Georgiou (pantelis@imperial.ac.uk)
Centre for Bio-inspired Technology,
Institute of Biomedical Engineering,
Department of Electrical and
Electronic Engineering



Alternative uses of Silicon
Symposium on Emerging trends in Electronics
2nd December 2014



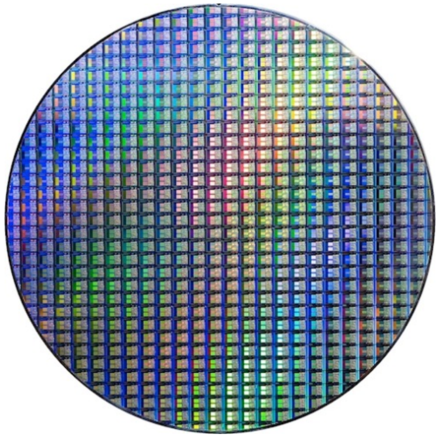


Imperial College London

Can we leverage on $1 trillion investment in Microelectronics to create more affordable healthcare?

Needs of Modern Healthcare

- Health services originally designed to manage acute illness (i.e. infections and injury)
- Today, however 70-78% of health budget expenditure is on Chronic Disease!



CMOS Opportunities

- Scalable
- Repeatable
- Low cost
- Miniaturization
- System Integration
- Dedicated performance (low noise, low power)

Personalised Healthcare

- Technology from Hospital to the Home - New Wave Lifestyle
- Medical devices towards consumer devices

Imperial College London

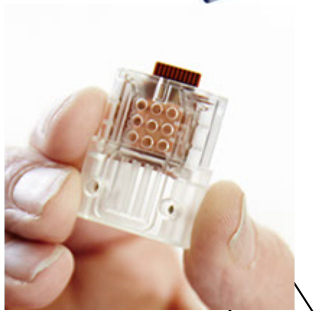
DNA Testing Today

Min. 2 weeks

Healthcare Application

- Point-of-Care Diagnostics
- Sequencing Technology of the Future

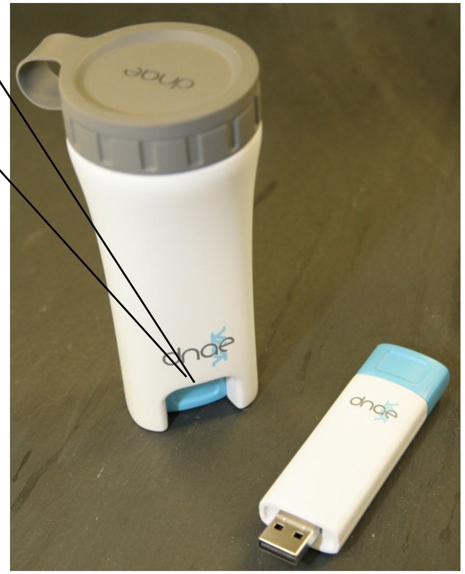
SNP Chip



DNA Testing at Imperial: No Lab

15 – 20 mins

To read your DNA



Source: DNA electronics website (www.DNAe.co.uk)

Combined DNA Amplification and Detection in CMOS

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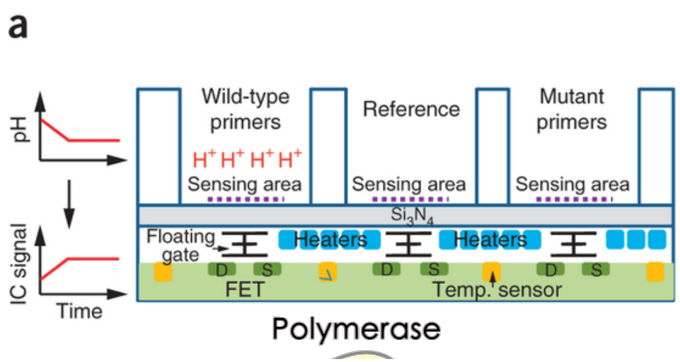
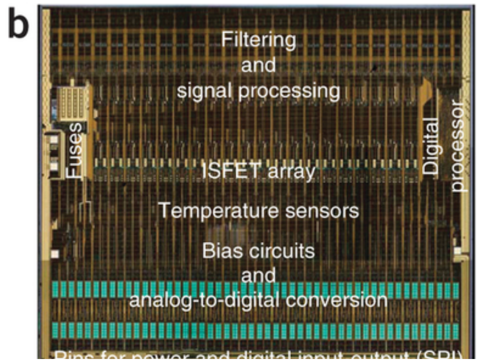
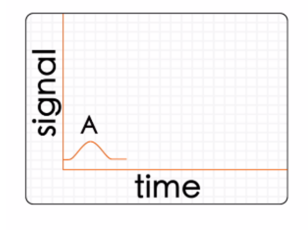


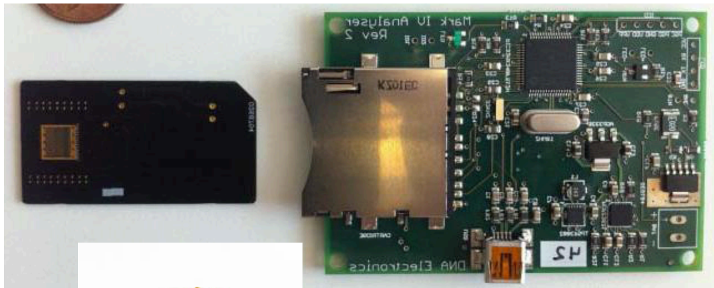


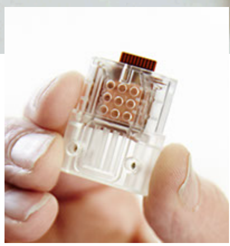


CMOS is cheap, integration is expensive, how do we break this barrier of co-design?

Features

- Fully unmodified CMOS
- Detect Hydrogen ions using Ion-sensitive Field Effect Transistors.
- Can use heating to amplify DNA through PCR (polymerase chain reaction)
- Use a reference chamber to do differential measurement and cancel out chemical drift.



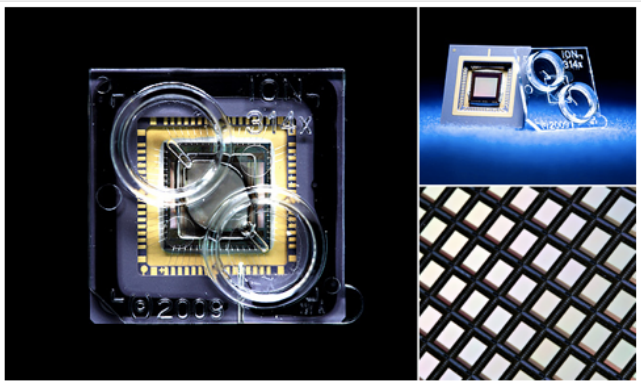


$$V_{chem} = \gamma + 2.3 \cdot U_t \cdot a \cdot pH$$

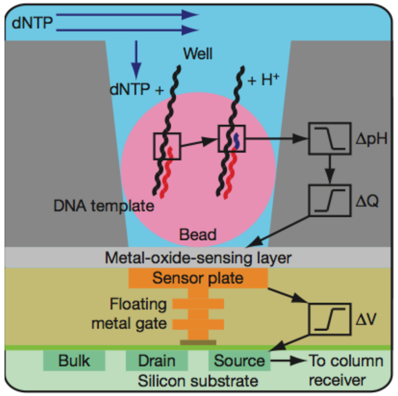
C.Toumazou, et al.,"Simultaneous dna amplification and detection using a pH-sensing semiconductor system," Nature methods, 2013.

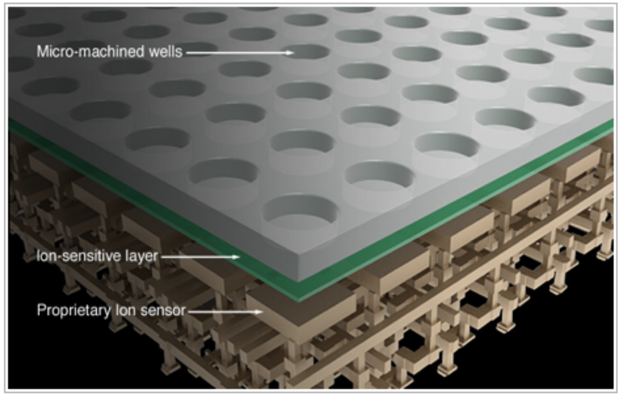
Semiconductor DNA sequencing

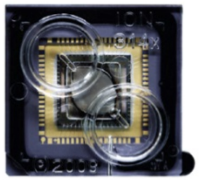
- Moores law has already found its way to DNA sequencing using ISFETs!



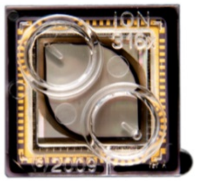
Reading DNA: Ion Torrent's chip, built using semiconductor technology, can read DNA sequence directly, without the optical systems used by other sequencing machines. Credit: Ion Torrent



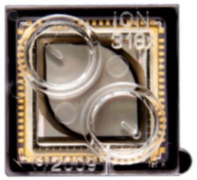




Ion 314



Ion 316

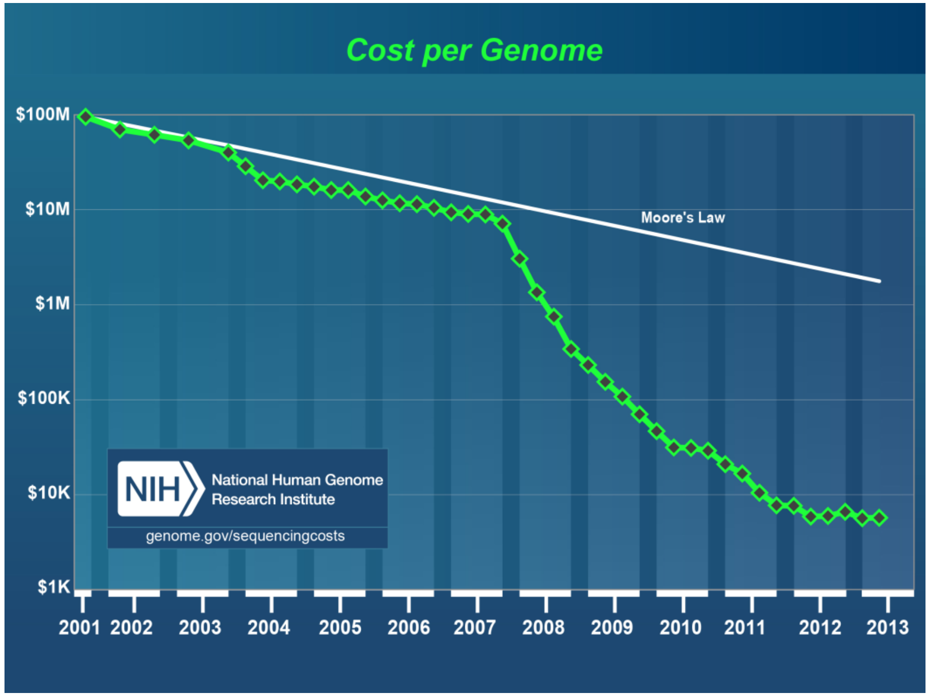


Ion 318

Ion Semiconductor Sequencing Chip	Output	Read Length		Total Sequencing Time
		2011	2012	
314	> 10Mb	> 200bp	> 400bp	< 2 hours
316	> 100Mb			
318	> 1Gb			
Accuracy:	>99.99% consensus accuracy and >99.5% raw accuracy.			

Source: ion Torrent website (www.iontorrent.com)

Whole Genome Sequencing Costs



How can we scale CMOS sensors and fluidics reliably to exploit Moore?

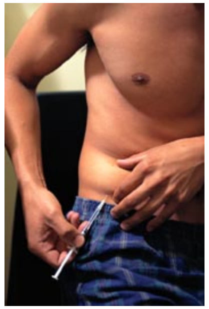
The $100 Genome?

- When is Moore enough?
- Challenges:
  - Things difficult to detect at smaller volumes
  - Noise, mismatch
  - Reliability of sensors
  - Micro-fluidic integration
  - Data Bandwidth
  - Bio-informatics, Big data

Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP)

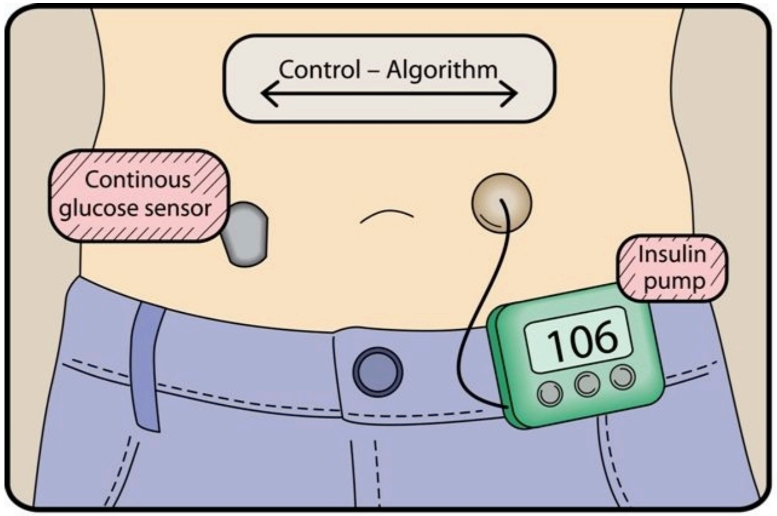
Diabetes

Current Treatment

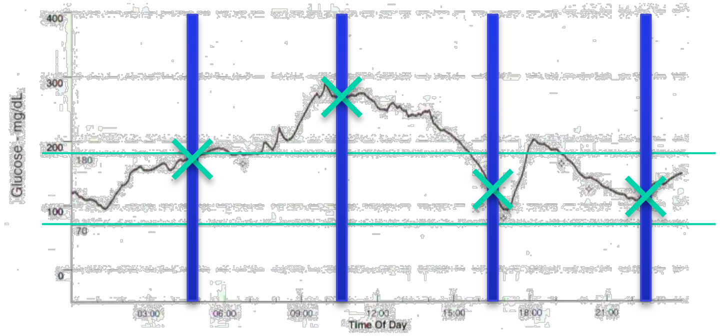


Glucose measurement *Insulin injection*

Artificial Pancreas



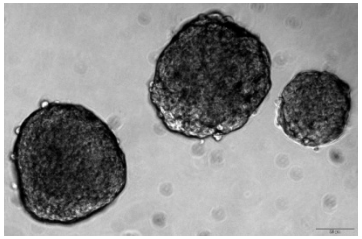
Sub-optimal treatment



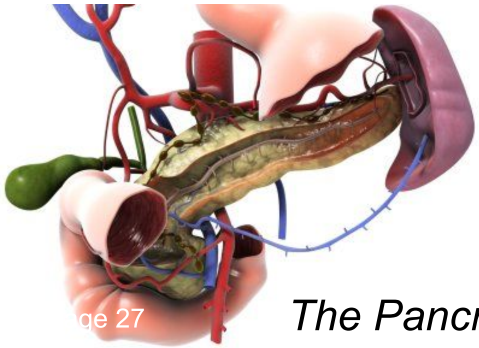
Can we use a Bio-inspired Approach?

Imperial College London

Pancreatic Beta Cells

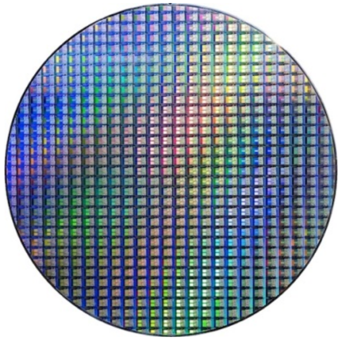


Biology



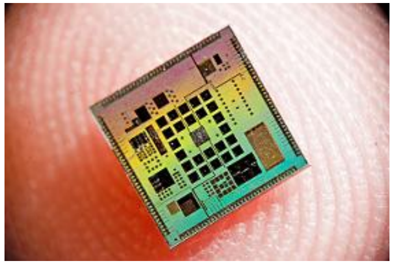
The Pancreas

Semiconductor technology



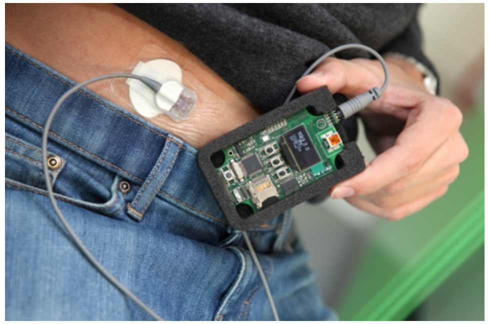
Low-cost

Microchips



Miniature, Low-power

Novel Medical Devices



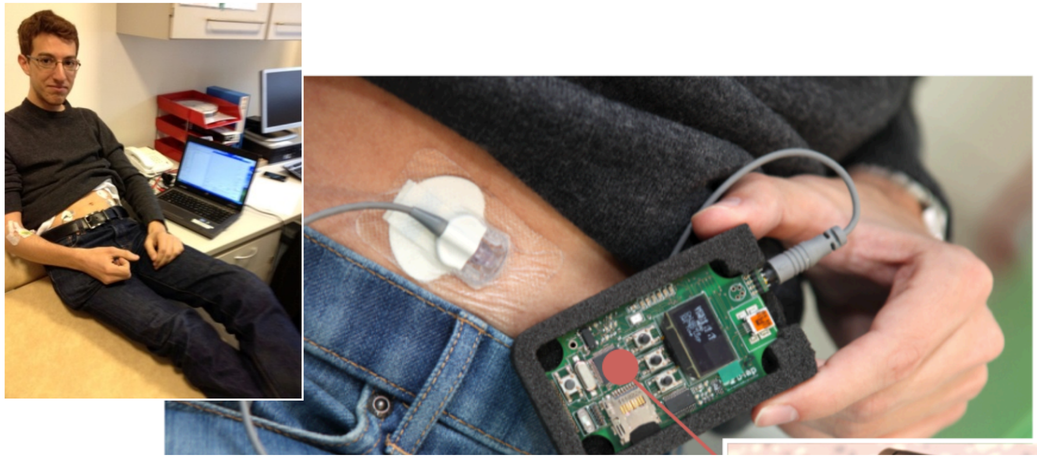
Therapy

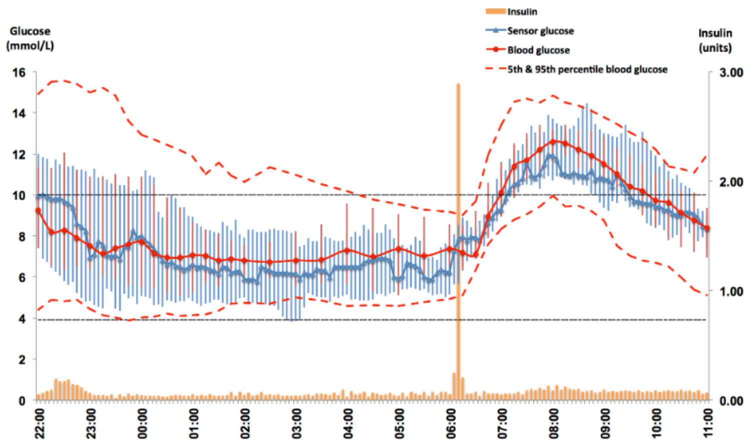
b·iap
bio inspired artificial pancreas

Imperial College London

The Bio-inspired Artificial Pancreas

A Wellcome Trust funded initiative to create the world's first Bio-Inspired Artificial Pancreas for blood glucose Control





- **Co-integration with wireless devices is currently difficult.**
- **Need to think about common wireless standards and security.**
- **Needs a patient pull rather than an technological push!**
- **Design for Regulation!**
- **Need to guarantee safety! Built in self test, redundancy**

Herrero P, Georgiou P, Oliver N, Johnston DG, Toumazou C, "A bio-inspired glucose controller based on pancreatic b-cell physiology". J. Diabetes Sci.Technol.6,606–616. 2012

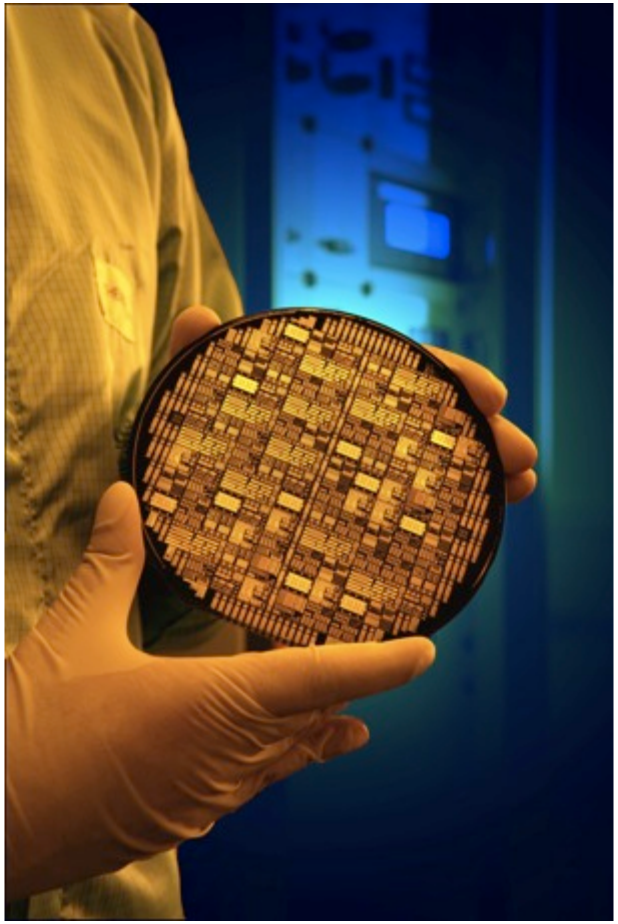
To conclude

Semiconductors for Healthcare

- Disruptive technology
    - Leveraging on the $1 trillion investment over the past 4 decades
    - Realising medical systems like consumer devices
    - Good for **robust, low-cost, high density, low power and high performance miniature systems**

Bio-Inspired Technology

- Implementing biology in modern technology to replace biology
    - Applications in chronic disease management
    - Improved quality of life



"The future has already arrived. It's just not evenly distributed yet"

William Gibson

Bruno Murari

ST Microelectronics

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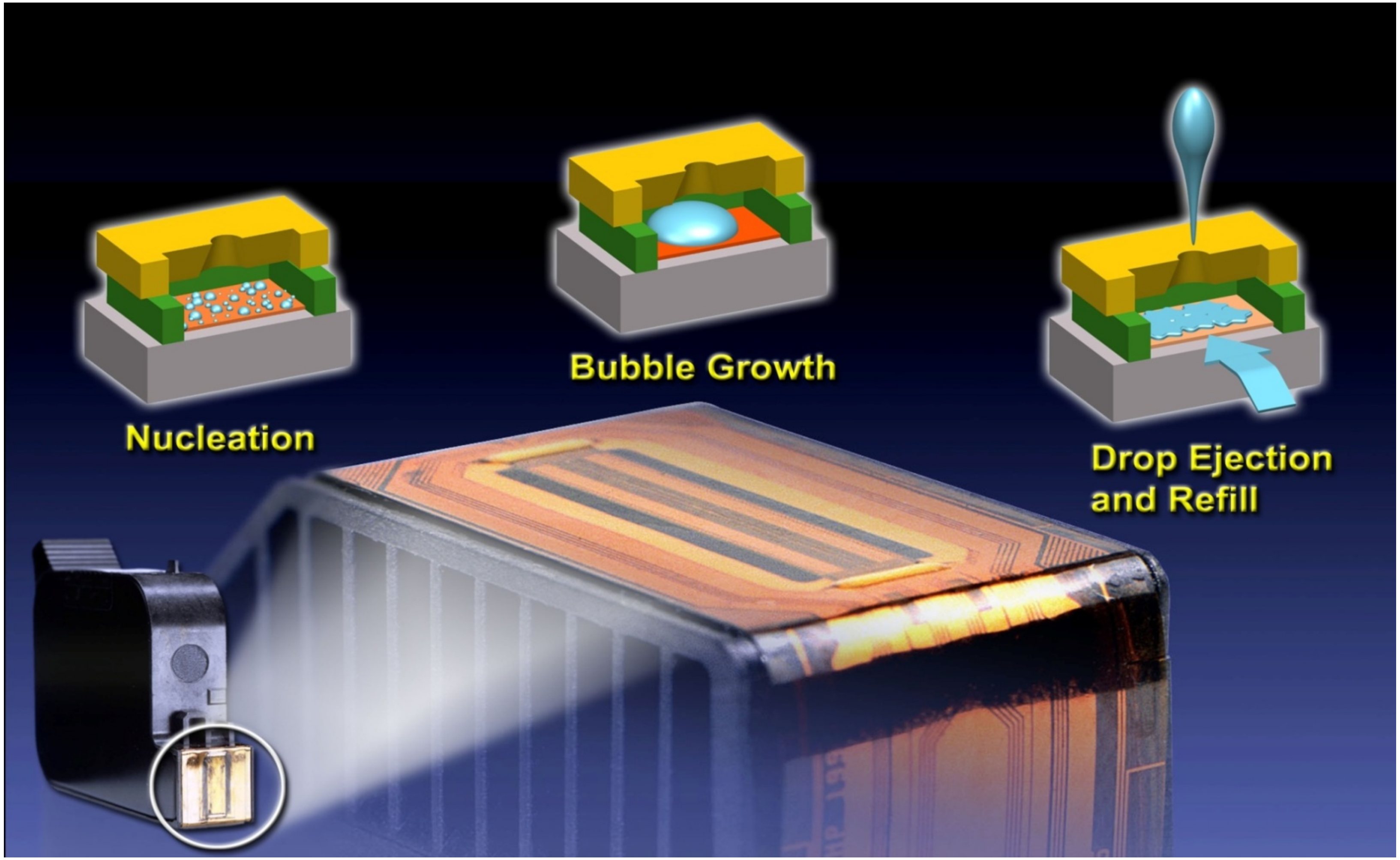
Alternative use of Silicon

Bruno Murari
STMicroelectronics Scientific Advisor

Montreux 2 dec. 2014

Inkjet cartridge



Sensors are Changing the World

Smart City

Reduce traffic congestion

Better use of resources

Improve security

Smart Car

Reduce emissions

Increase safety

Save fuel

Smart Home

Make entertainment more interactive and immersive

Increase comfort

Save energy

Smart Me Healthcare

Empower patients

Help physicians monitor and diagnose remotely

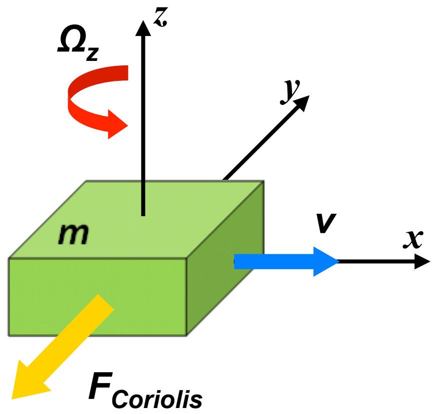
Smart Me Fitness & Wellness

Help to lead healthier lives

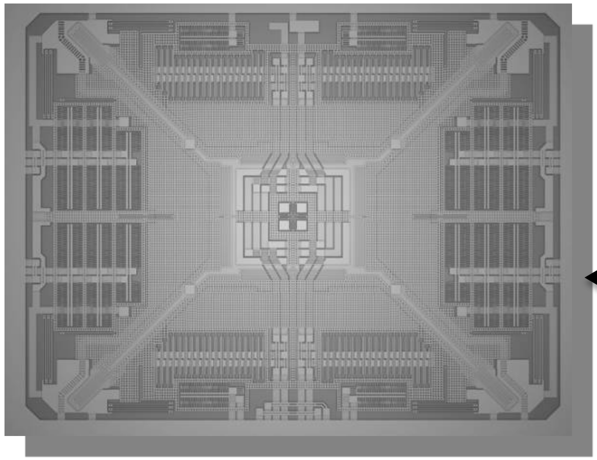
Optimize sports performance

Early warning of illness

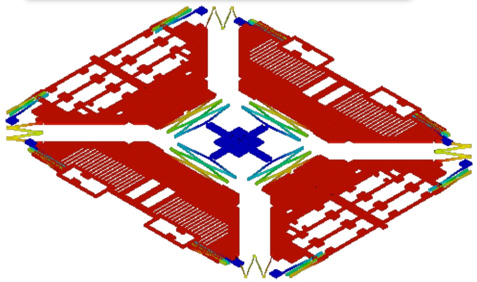
The Most Advanced MEMS Gyroscope



$$F_{Coriolis} = -2m\Omega_z \Lambda v$$

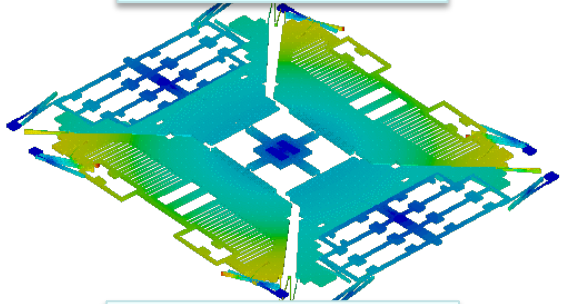


Drive mode

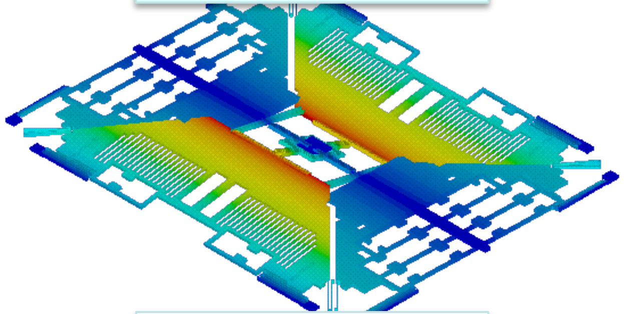


SINGLE DRIVING MASS

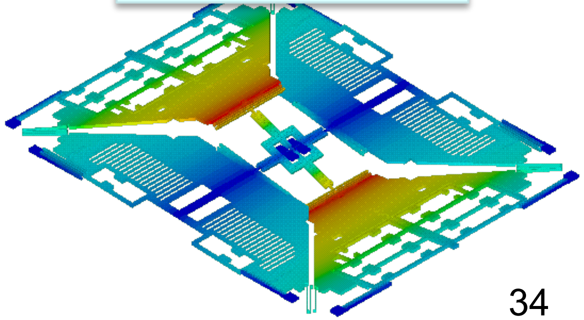
Yaw mode

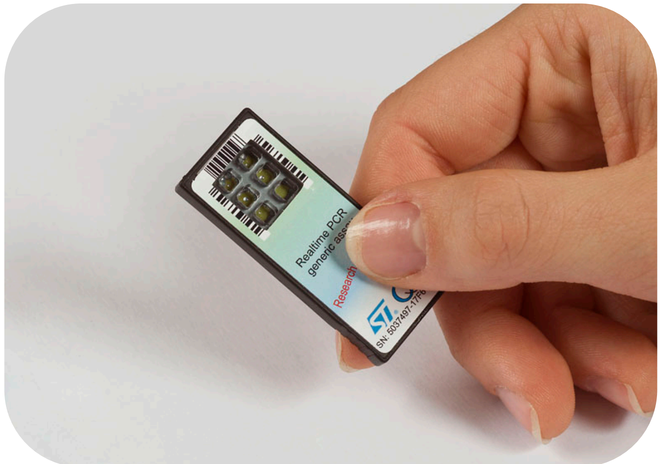


Pitch mode



Roll mode



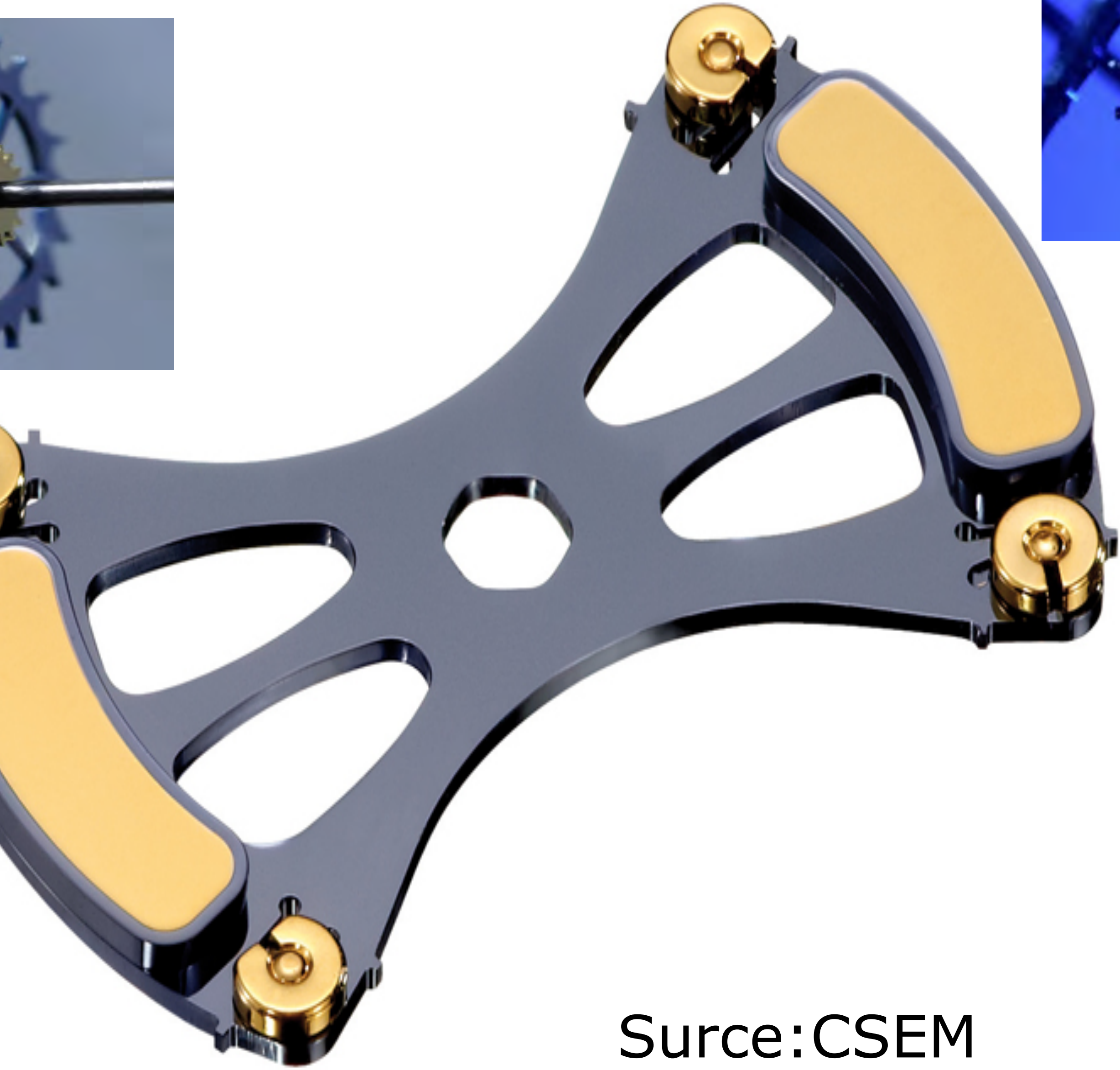


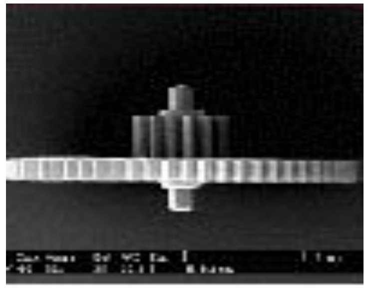
AST Molecular Biology

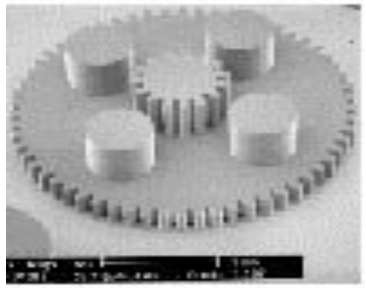
Dynamic structural monitoring

life.augmented

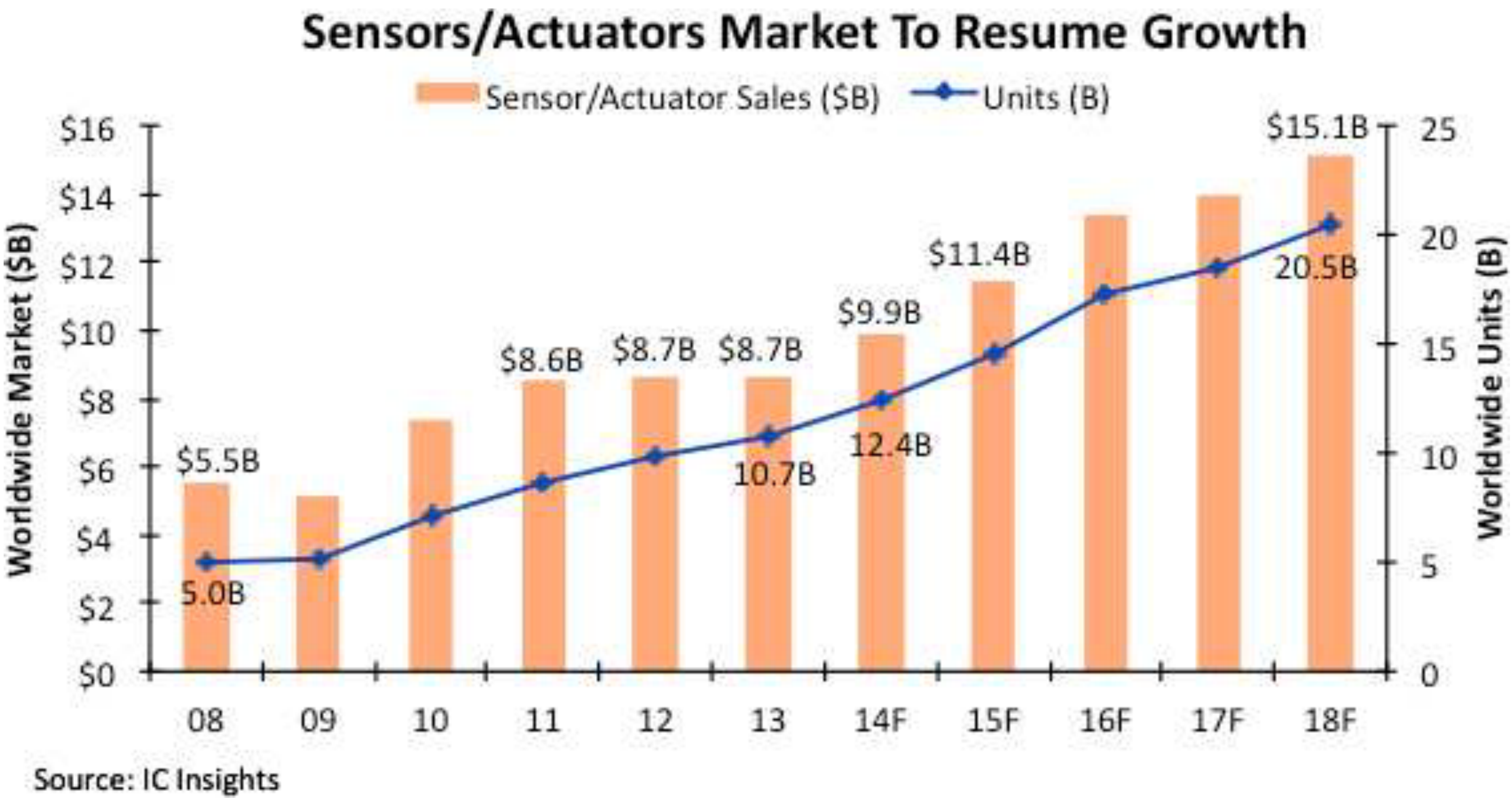
More than MEMS or Macro MEMS ?







Surce:CSEM


Sensors/Actuators Market To Resume Growth
Sensor/Actuator Sales ($B)
Units (B)
Worldwide Market ($B)
Worldwide Units (B)
$16
$14
$12
$10
$8
$6
$4
$2
$0
25
20
15
10
5
0
$5.5B
$8.6B
$8.7B
$8.7B
$9.9B
$11.4B
$15.1B
5.0B
10.7B
12.4B
20.5B
08
09
10
11
12
13
14F
15F
16F
17F
18F
Source: IC Insights

Roland Thewes

TU Berlin

Symposium on Emerging Trends in Electronics
Panel: Alternative Use of Silicon

After the Gold Rush –
Low Volume Biomedical CMOS Devices
Creating Great Value?

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TU Berlin, Berlin, Germany

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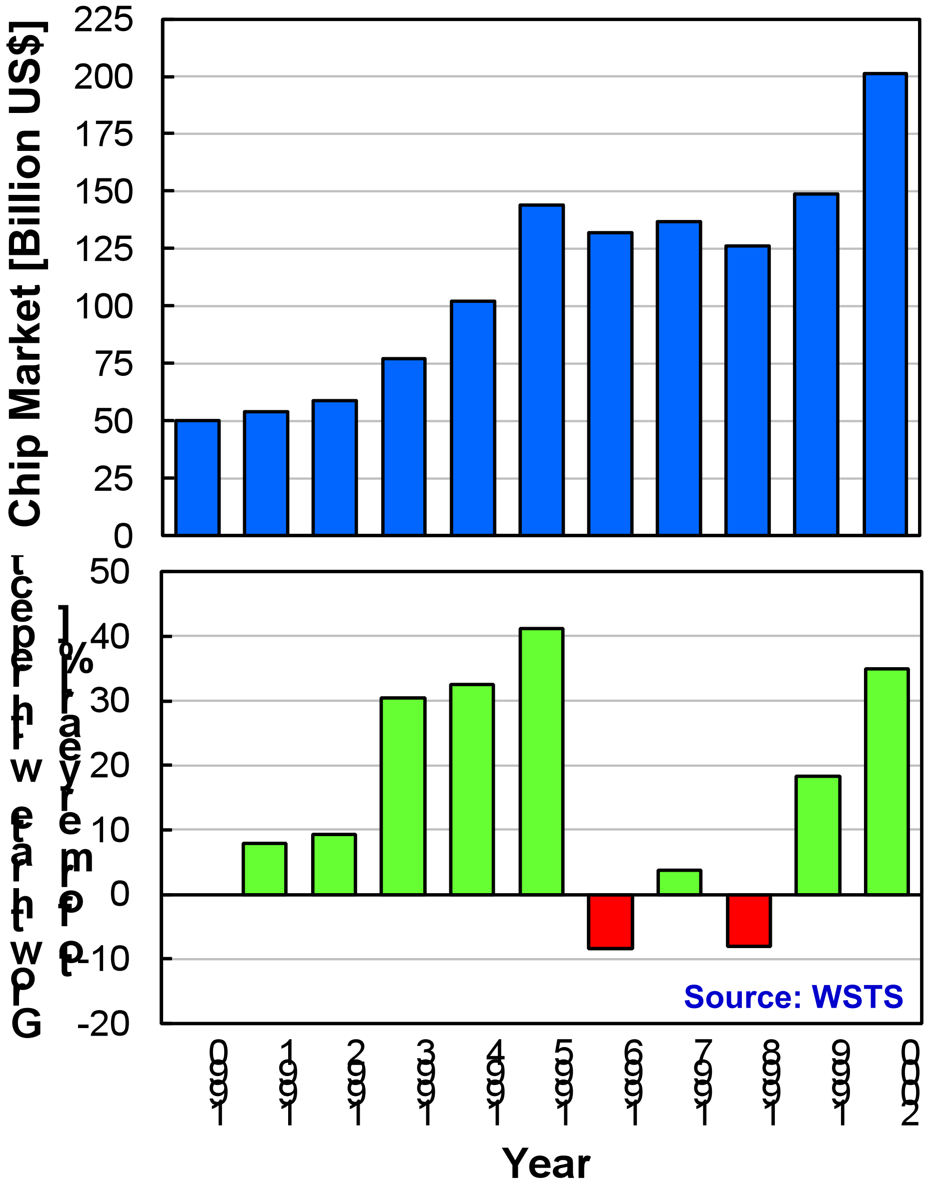
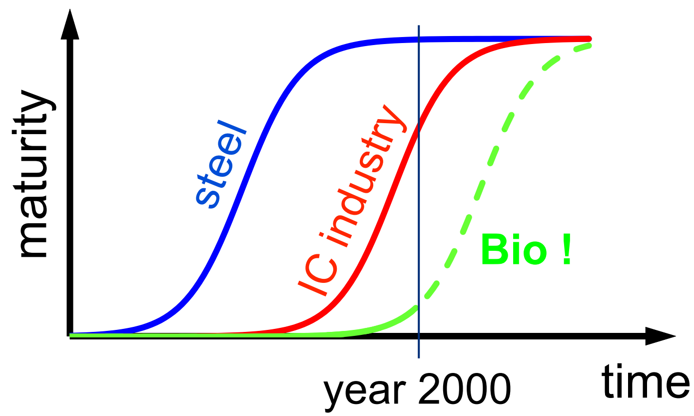
Montreux, Switzerland
December 1 - 2, 2014

Semiconductor Industry in the Year 2000:
The “Next Big Thing”?



Year 2000:

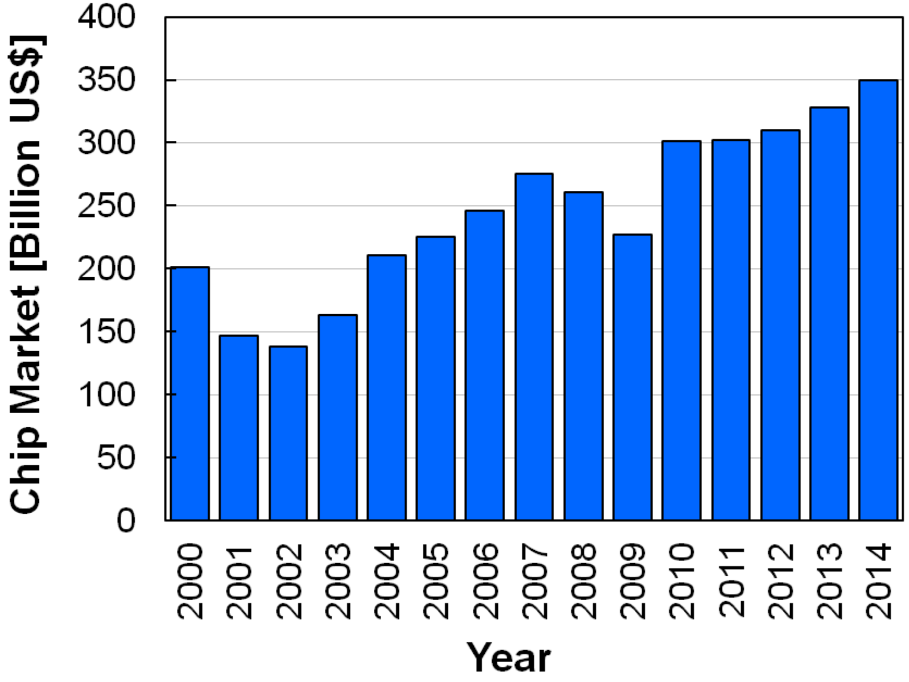
- 200 billion US$ chip market frontier exceeded for the first time
- “.com bubble”
- Huge growth of the amount of biotech companies and startups
- Business developers in semiconductor industry speculated that bio could be “the next big thing” also for the chip industry:



Semiconductor Industry in the Year 2014:
The "Next Big Thing"?

- Today:
  Total medical semiconductor revenue > 4 billion US$.

- However, most important segments are:
  - Home care including health and wellness applications (blood pressure, heart rate, and glucose monitoring, …)
  - Clinical including medical imaging (portable medical electronics as portable ultrasound devices, portable ECG devices, …)



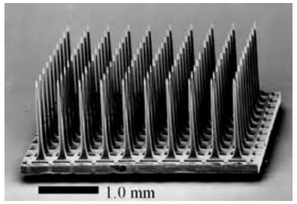
Sources: WSTS, IC insight

- This includes many "standard ICs" – possibly somewhat optimized for biomedical purposes – such as processors and memory.

- So, where and how do customized CMOS biochips contribute?

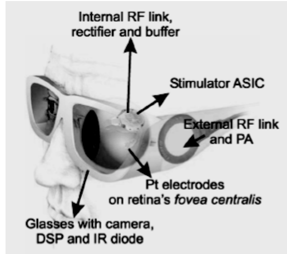
CMOS Devices for Biomedical Purposes
Devices and Applications

Pace maker,
Zarlink



Utah BMI

Deep brain stimulator, Medtronic
(fig. right from www.nature.com)

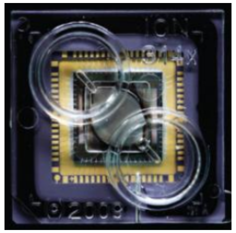


Retinal implant (from
M. Ortmanns, JSSC 2007)

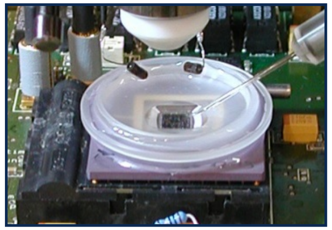
Blood glucose
meter, Bayer

Ultrasound machine,
portableultrasounds

Wearable EEG headset,
IMEC

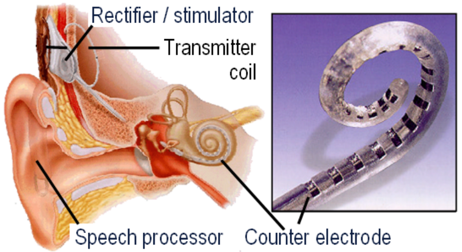


DNA sequencing
chip, Ion Torrent

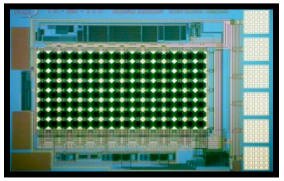


"Neurochips",
Max-Planck Society

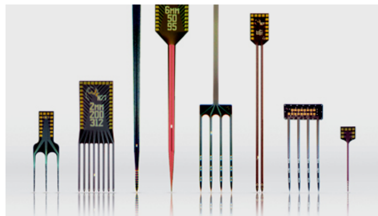
Hearing aid, Phonak



Cochlear implant
(from K. Wise, IEDM 2002)



DNA microarray,
Siemens

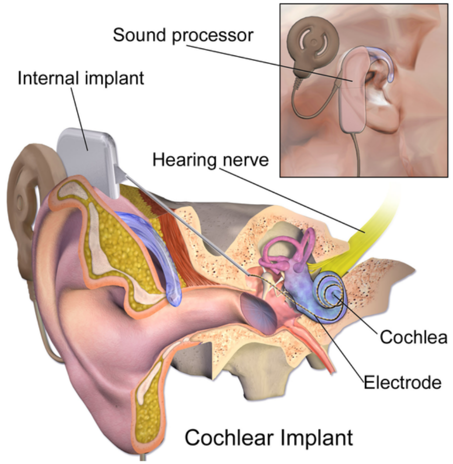


Next generation DBS and BMI
devices, Neuronex

today's volume (?) product emerging devices / fields under development

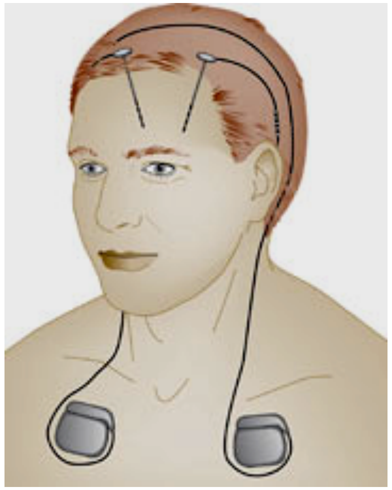
Where does Innovation Come from?
Two Established Applications …

- **Cochlear Implants**
  - restoring hearing to the profoundly deaf by means of auditory nerve stimulation
  - Internal devices: array of electrodes wound through the cochlea to stimulate the auditory nerve, receiver, stimulation circuitry. External devices: microphone(s), speech processor, power / data transmitter
  - Development since more than 30 years
  - Volume: 300,000 worldwide on December 31, 2011.



http://commons.wikimedia.org/wiki/File:Blausen_0244_CochlearImplant_01.png

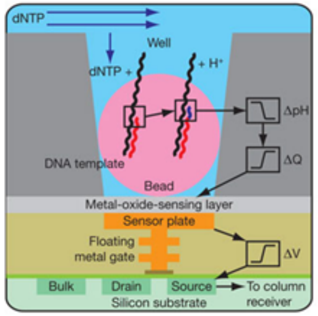
- **Deep Brain Stimulation**
  - The device implanted in the brain stimulates the brain and is controlled by the device implanted underneath the skin within the thorax region.
  - Approved for human therapies since 2009.
  - Closed loop systems under development
  - Volume: (S. Oesterle, Medtronic, Plenary Talk ISSCC 2011): "… worldwide 1 device every 30 minutes …"



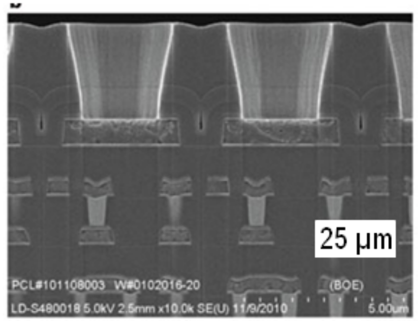
www.nature.com

What Do CMOS Chips Contribute?
Consider CMOS Chip Based DNA Sequencing …

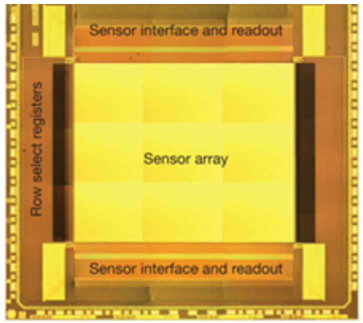
- DNA sequencing: determination of the order of the four DNA bases (A, T, C, G)
- Human DNA: 3.2 10^9 base pairs
- Market estimation for 2015: 2 billion US$
- Next generation sequencing (NGS): faster + cheaper
- Ion-Torrent: CMOS chip with ISFET array, “sequencing-by-synthesis”



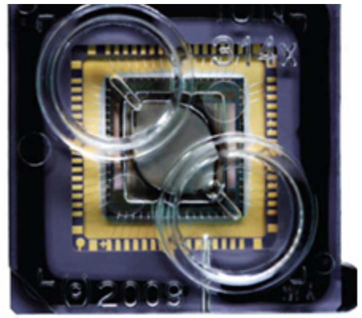
Principle



Cross section



Chip photo



Packaged device

J. M. Rothberg et al, Nature 475, 348–352 (21 July 2011)

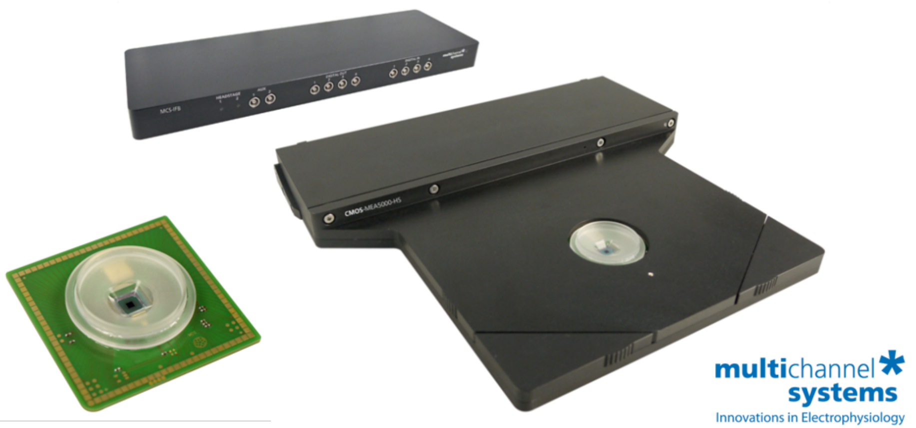
- **What else is left to do?**
  1. Purification of Genomic DNA from cells (lysis, breaking the cells’ nuclei, …)
  2. Fragmentation (random process: fragments must “overlap”, length up to 1 kb)
  3. Amplification (fragments serve as “vectors”, vectors are cloned, …)
  4. Determination of sequence of bases, i.e.: fragment-based sequencing **(CMOS!)**
  5. Determination of the entire strand sequence by overlapping fragment data

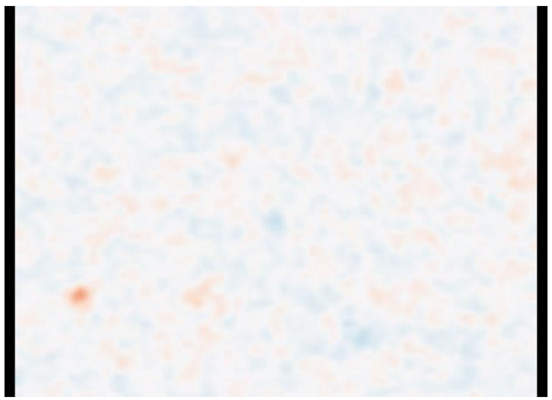
Biomedical CMOS Chip Properties
… Considered from the User's Standpoint

- Users and customers (who are not electronic engineers) do not care what is inside the chip
- However, they appreciate functionality which is not available using other tools or technologies

⇨ CMOS technology, appropriate and innovative circuit design, assembly techniques, software, … are enablers!

- Example "Neurochips" with high spatiotemporal resolution:
  - *first publications roughly 10 years ago*
  - *commercialization: started recently and is on-going*
  - *discussed volumes: few 1000 devices per year*





Summary
Low Volume Biomedical CMOS Chips

- Create value in an ethical, societal, and commercial sense although related applications are niches.
- Related business models must be identified to make technical opportunities successful in real-life applications.
- As engineers we need to try to understand the entire application chain, and not to develop solutions and then try to identify the problem.
- Scaling helps in that sense that older technologies get affordable to create a business case. Many customized biomedical chips rely on technologies with > 100 nm feature size.
- Electronics can be an inevitable enabler (but only one piece of the entire puzzle).

Alternative Use of Silicon

Edoardo Charbon	TU Delft
Alex Dommann	EMPA
Pantelis Georgiou	Imperial College London
Bruno Murari	ST Microelectronics
Roland Thewes	TU Berlin

Chair: Giovanni De Micheli, EPFL

Centre SI
Integrated Systems Centre

EPFL
ÉCOLE POLYTECHNIQUE
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