CMOS Pixelated Capacitive Sensor platform for biosensing and many other applications

Frans Widdershoven

Smart sensors NEREID workshop
21st October 2016

SECURE CONNECTIONS
FOR A SMARTER WORLD

CMOS integration victory: radio

Vacuum tubes

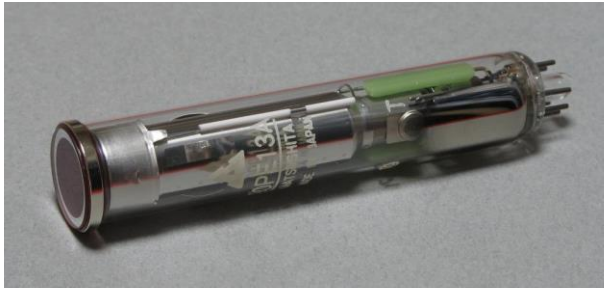
Transistors

Bipolar analog
radio IC

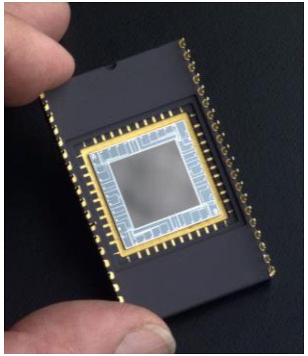
CMOS digital radio IC
(software-defined radio)

CMOS integration victory: camera

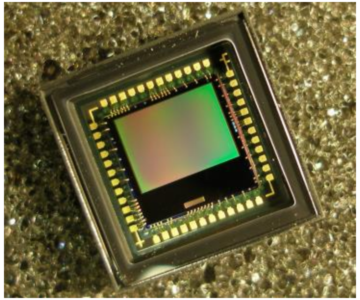
Film



Vacuum tube (Vidicon)



Charge-coupled device (CCD)



CMOS image sensor (CIS)

CMOS integration victory: storage

CMOS-based solid-state drive (SSD)

Hard disk

Magnetic tape

Ticker tape

Widdershoven’s 3 laws of IoT

1) Only non-trivial data need be transmitted

2) Autonomous devices need sensors to generate non-trivial data

3) What can be sensed by CMOS will be sensed by CMOS

Examples:

Voltage, current, power, temperature, RF spectrum, ambient light, magnetic field, images, radar, information, uniqueness (Physically Unclonable Functions), …

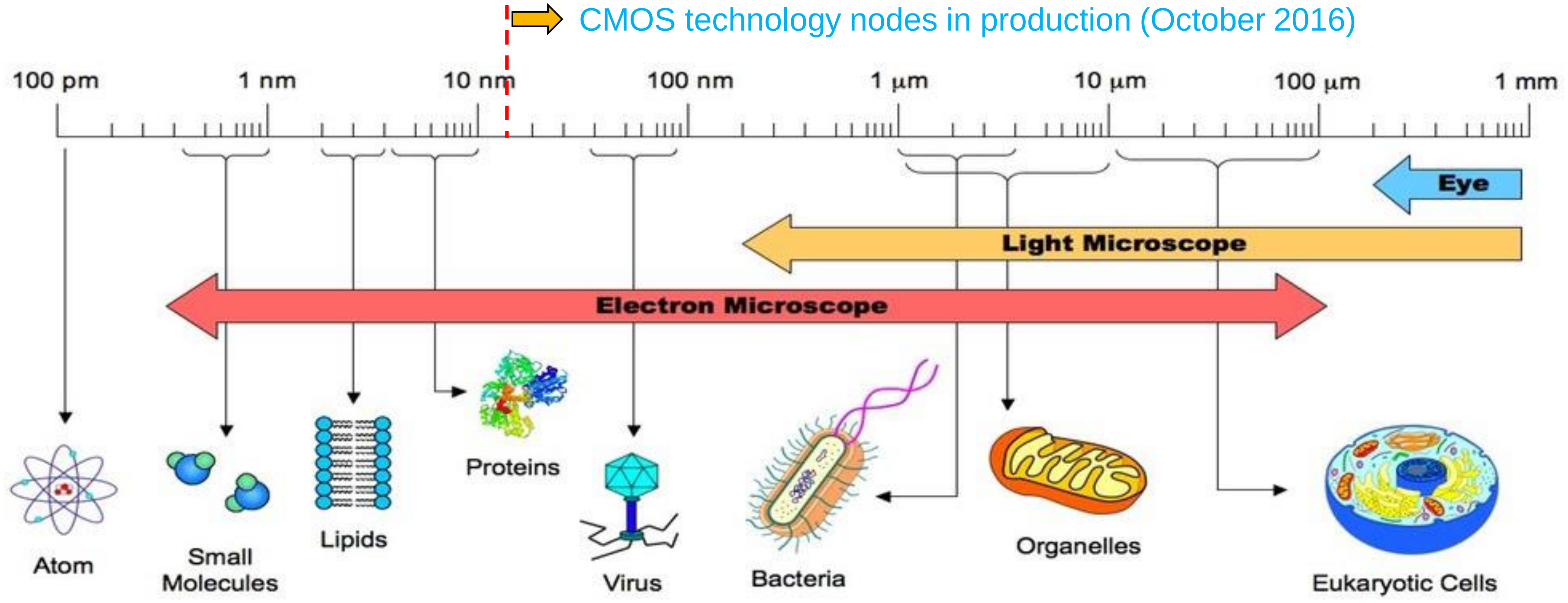
… and this trend continues!

Extend the CMOS integration victory to biosensing?

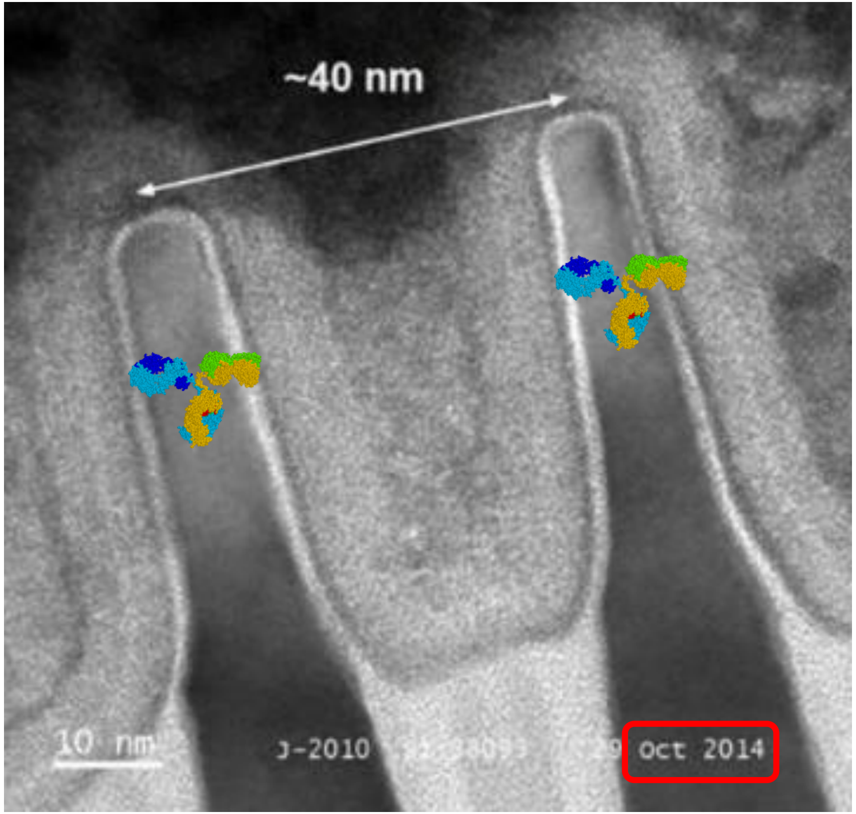
Maybe, but only if we stay close to “standard” CMOS

- It’s the result of a multi-B$ world-wide aligned development effort, so don’t mess it up!
- Exploit its strengths:
  - Small feature sizes
  - High speed & low power
  - Embedded signal conditioning, A/D conversion, programmability,…
  - Low-cost and high-yield volume production
  - …

Biological length scales



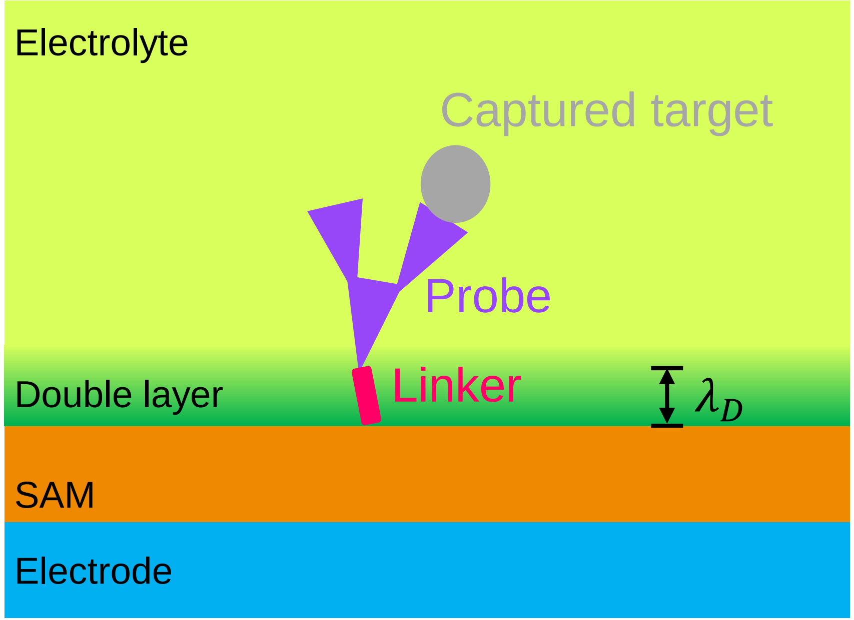
IgG antibody compared to 14-nm finFET



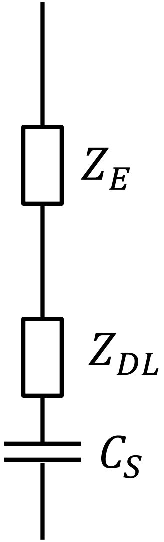
TEM cross-section through 2 fins (Intel)

“Capacitive” sense electrode

Cross-section:

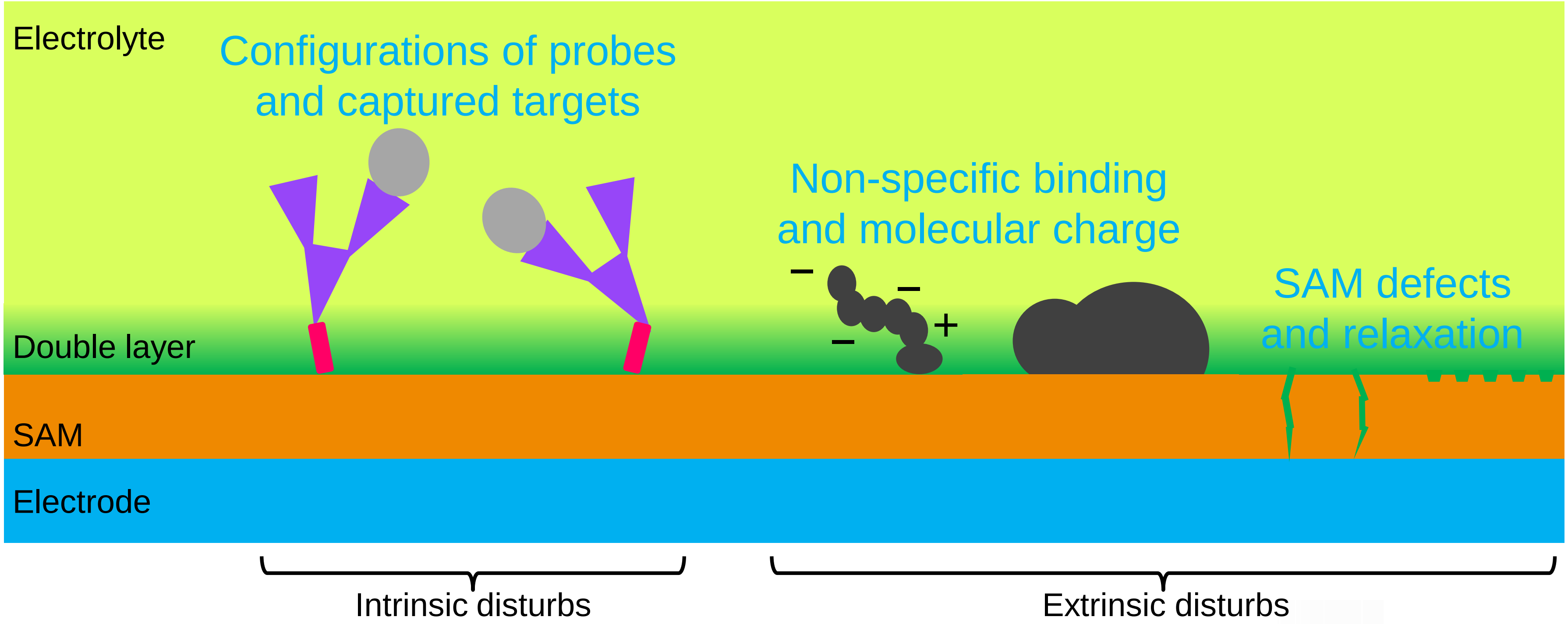


Equivalent circuit:



λ_D: Debye length (~0.8 nm at 150 mM salt concentration)

Disturbs



Electrolyte
Configurations of probes and captured targets
Non-specific binding and molecular charge
SAM defects and relaxation
Double layer
SAM
Electrode
Intrinsic disturbs
Extrinsic disturbs

Sensitivity scaling

$$Z_1 = \frac{h_1}{A_1 \sigma_1}$$

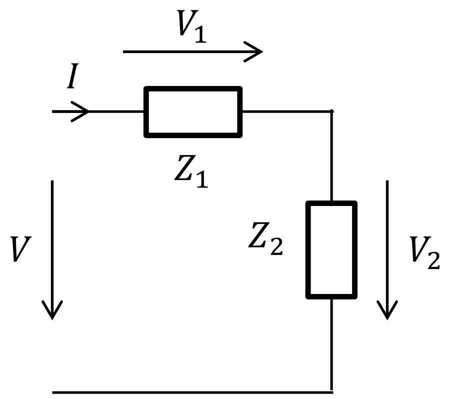
h_1, A_1, σ_1: height, area and complex conductivity of element 1

$$Z = Z_S + Z_B = \frac{V}{I} = \frac{V}{A_1 J_1} = \frac{V}{A_1 \sigma_1 E_1}$$

$$Y = \frac{1}{Z}$$

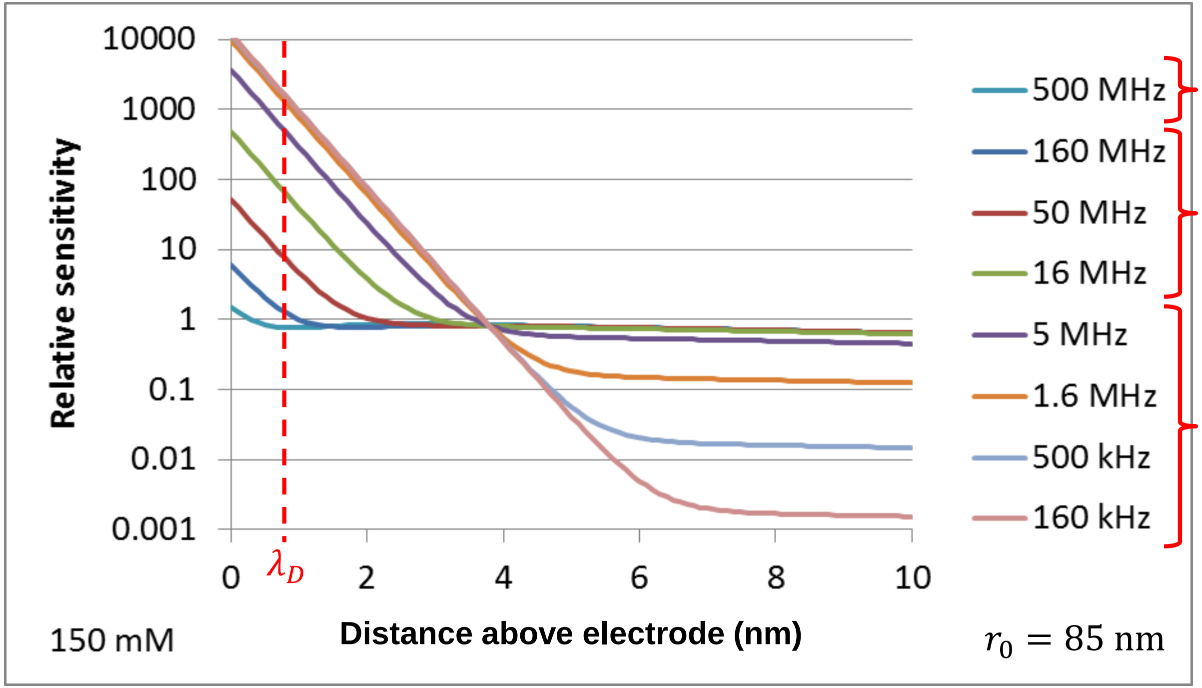
$$\Delta Y \approx \Delta \sigma_1 \frac{\partial Y}{\partial \sigma_1} = \Omega_1 \Delta \sigma_1 \left(\frac{E_1}{V}\right)^2$$

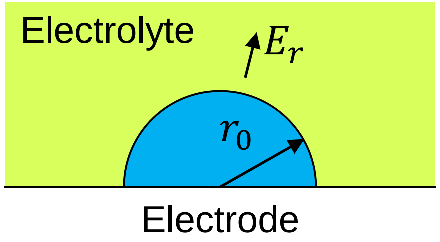
$\Omega_1 = h_1 A_1$ (volume of element 1)



→ Sensitivity is proportional to the square of the local electric field strength!

Model system: semi-spherical metal nanoelectrode





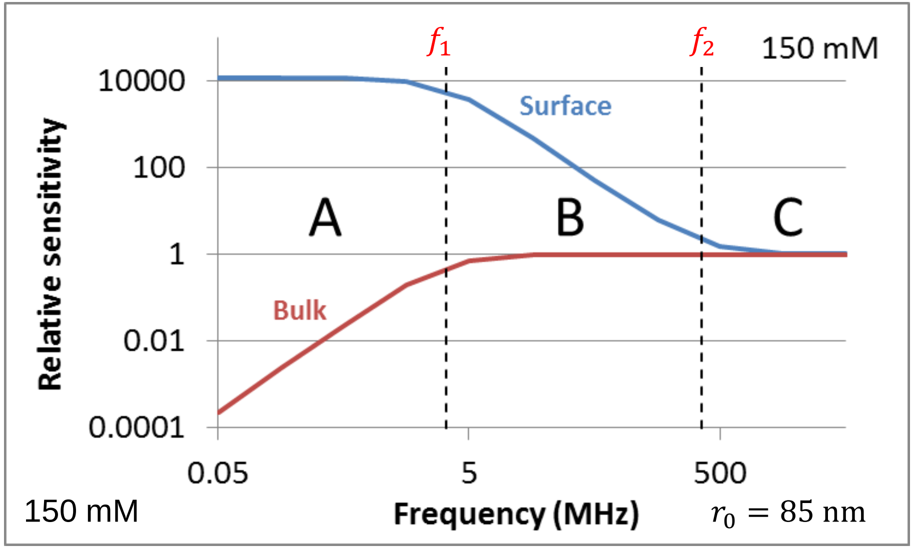
$$\text{Relative sensitivity} = \left|\left(\frac{r_0 E_r}{V}\right)^2\right|$$

Frequency ranges

$$f_2 = \frac{\sigma_{E,DC}}{2\pi\epsilon_E}$$

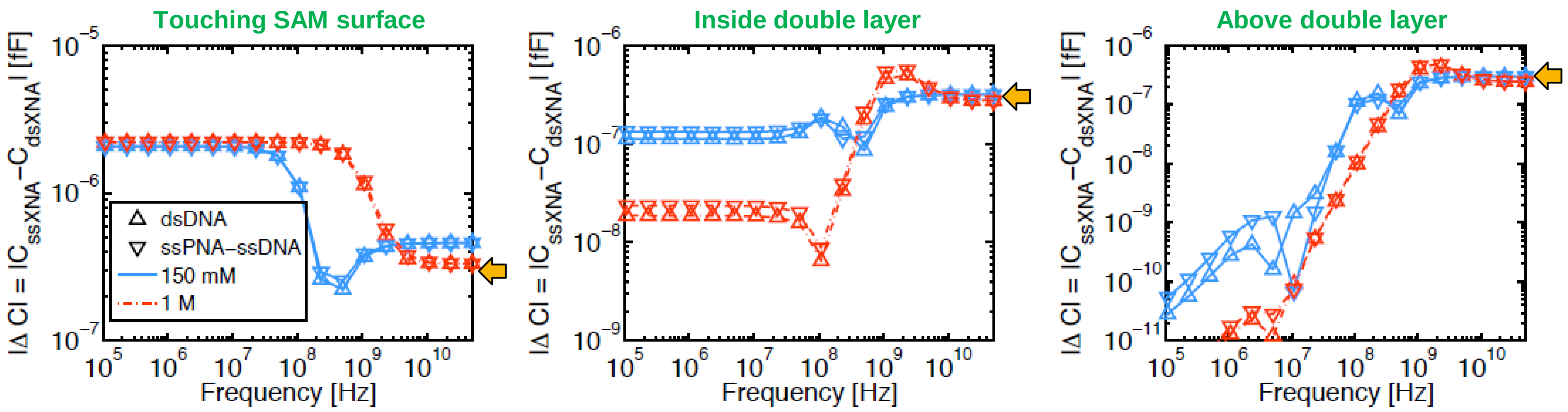
$$f_1 \approx \frac{f_2}{1 + \frac{r_0}{\lambda_D}}$$

Semi-spherical nano electrode ($r_0 = 85\ \mathrm{nm}$) and 150 mM salt concentration:
$f_1 \approx 3.3$ MHz, $f_2 = 360$ MHz



Frequency range	Bulk sensitivity	Surface sensitivity
A (< 3.3 MHz)	**Low** (“blocking” double layer)	**High** (saturated at low-frequency level)
B (3.3 – 360 MHz)	**Nominal** (“transparent” double layer)	**High** (still exceeding bulk sensitivity)
C (> 360 MHz)	**Nominal** (“vanished” double layer)	**Nominal** (same as bulk sensitivity)

Validation by numerical simulations



(d) $d = 0$ nm; $r_{ss} = r_{ds}/\sqrt{2}$ (e) $d = \lambda_D/2$; $r_{ss} = r_{ds}/\sqrt{2}$ (f) $d = h_{mol}$; $r_{ss} = r_{ds}/\sqrt{2}$

Figure 4: Absolute value of the change in capacitance due to the ssPNA-ssDNA or dsDNA hybridization ~~for the different models and~~ at different heights of the molecule from the SAM. The sharp cusps at intermediate frequencies are caused by sign changes.

SAM: 2.5 nm thick; PNA/DNA: 13.2 nm long (40-bp)

Federico Pittino, Federico Passerini, Luca Selmi, Frans Widdershoven, Microelectronics Journal 45 (12), December 2014

Issues

Probe molecules

- Typically much larger than λ_D (e.g. largely extending above double layer)
- Should not stick directly to SAM surface (to avoid denaturing and to keep capturing sites accessible for target molecules)

Other molecules

- May stick directly to SAM surface (non-specific binding)

Issue

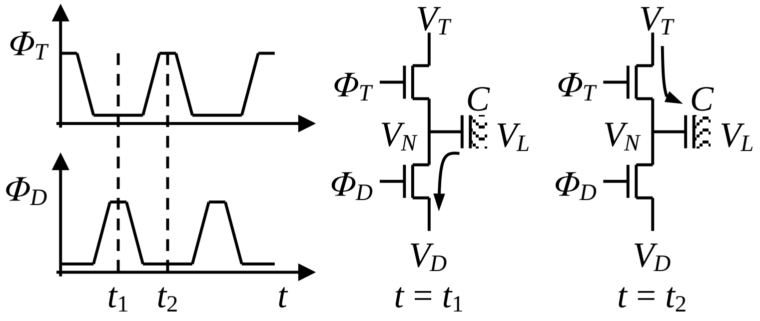
- At frequencies below f_2 the sensitivity for non-target molecules and/or SAM surface damage is much higher than for target molecules

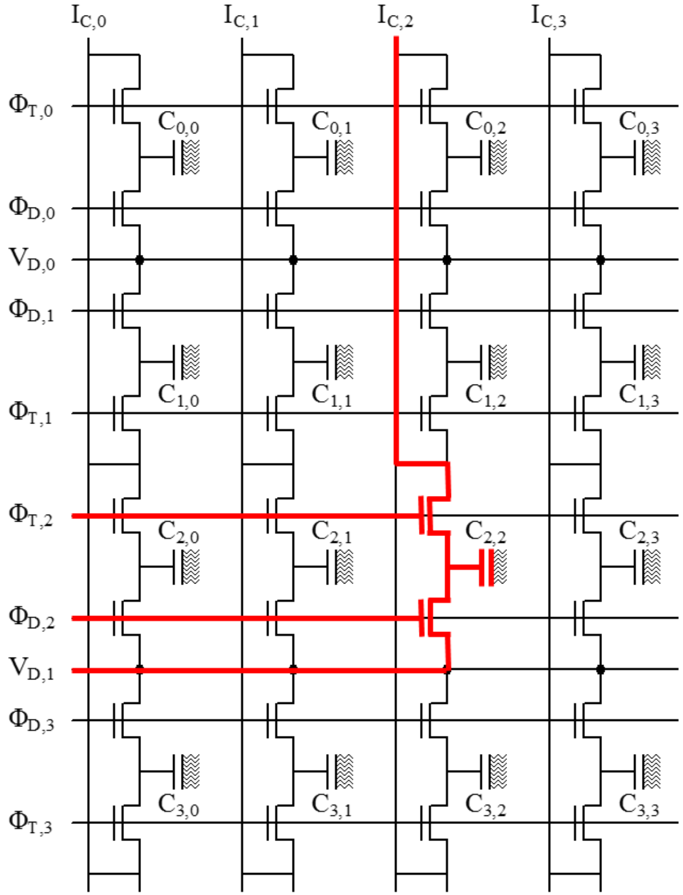
Solution

- Use modulation frequencies $\geq f_2$ (or at least as high as possible)*

* You won't find this experimentally by searching for the frequency that gives the highest response

NXP's CMOS Pixelated Capacitive sensor chip





$$Q = L_0(V_T - V_D)(C + C_P)$$

$$\Delta Q = L_0(V_T - V_D)\Delta C$$

L_0: number of charge/discharge cycles
C_P: parasitic capacitance (~0.4 fF)

Typically operated at 1 – 50 MHz (runs up to 320 MHz)

Intrinsic SNR of single sensor cell

Cumulative reset noise 2 switch transistors: ${\sigma_Q}^2 = 2Nk_BT(C + C_P)$

… and no 1/f noise (at least in principle)

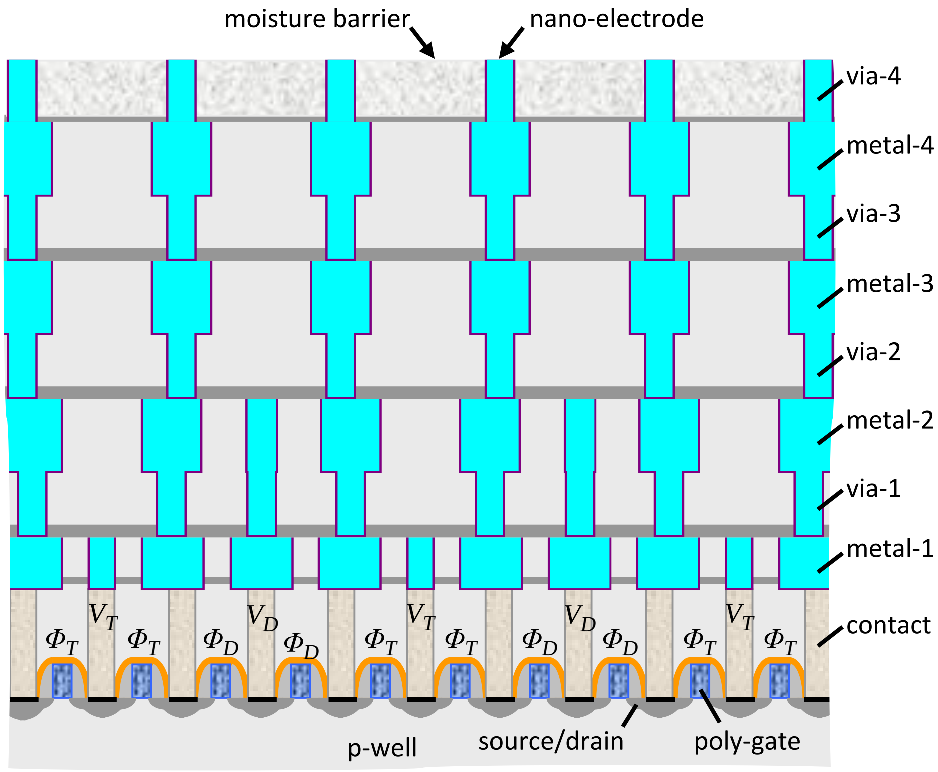
Intrinsic signal/noise ratio (SNR):

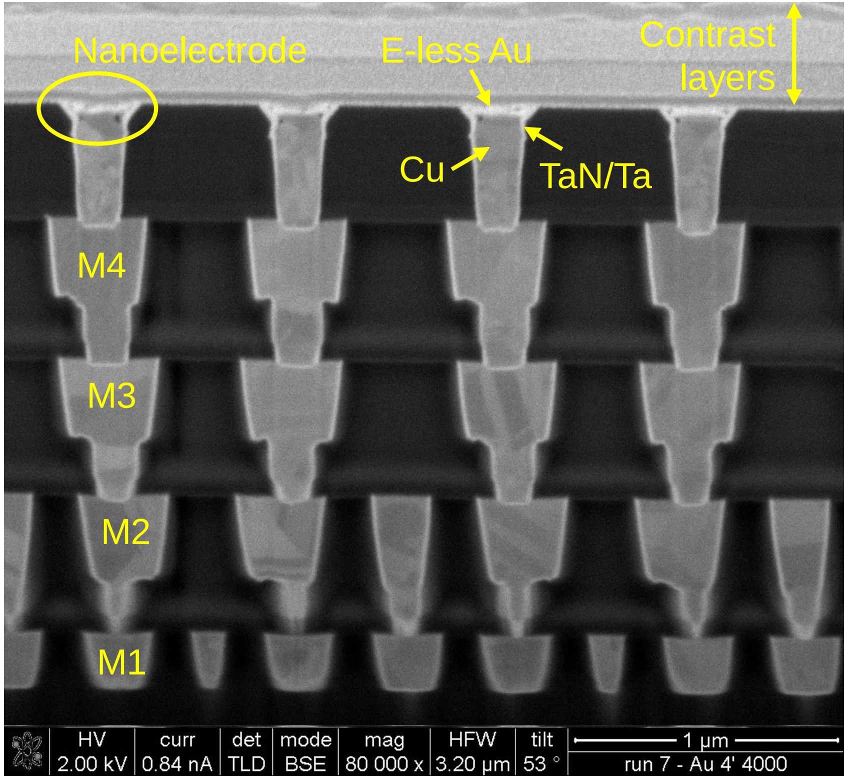
$$SNR_0 = \frac{(\Delta Q)^2}{{\sigma_Q}^2} = \frac{N(V_T - V_D)^2(\Delta C)^2}{2k_BT(C + C_P)}$$

Reason for using nanoelectrodes

Reason for using advanced CMOS

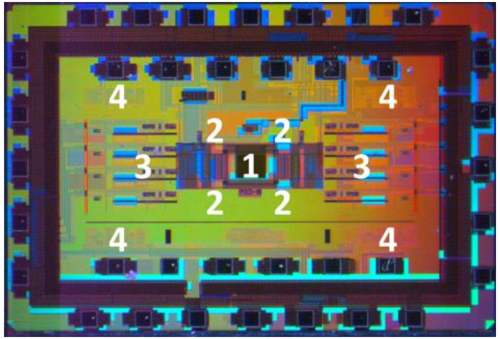
Cross-section (90-nm CMOS)





Early example with e-less Au nanoelectrodes (not used anymore)

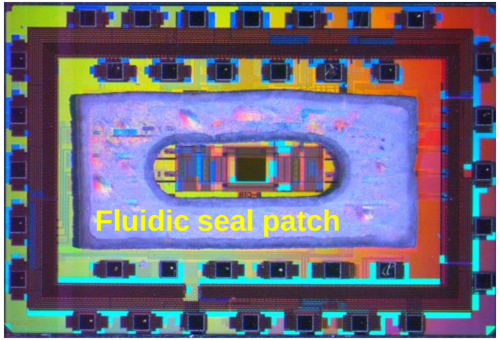
NXP's CMOS Pixelated Capacitive sensor chip (2)



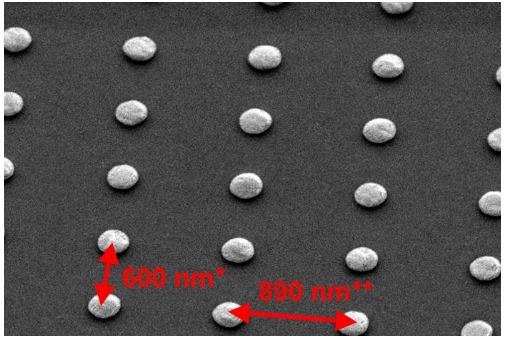
3.2 mm × 2.1 mm in 90-nm CMOS (TSMC)

Chip features:

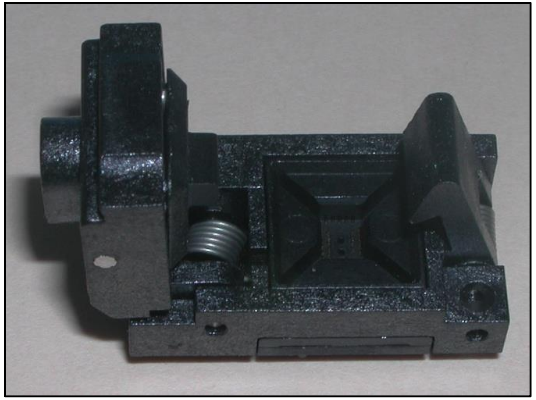
1) 256×256 (= 65,536) nanoelectrodes
2) 4 temperature sensors
3) 8 A/D converters
4) 256 digital data accumulators



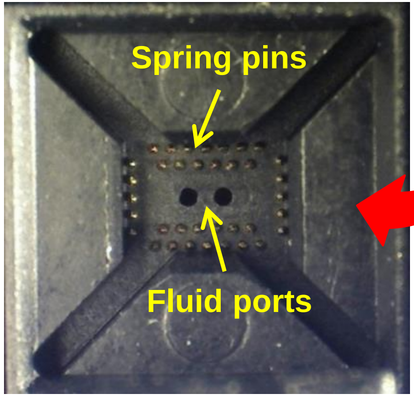
Flip over



Current process: Au-rich AuCu nanoelectrodes, made "the CMOS way"

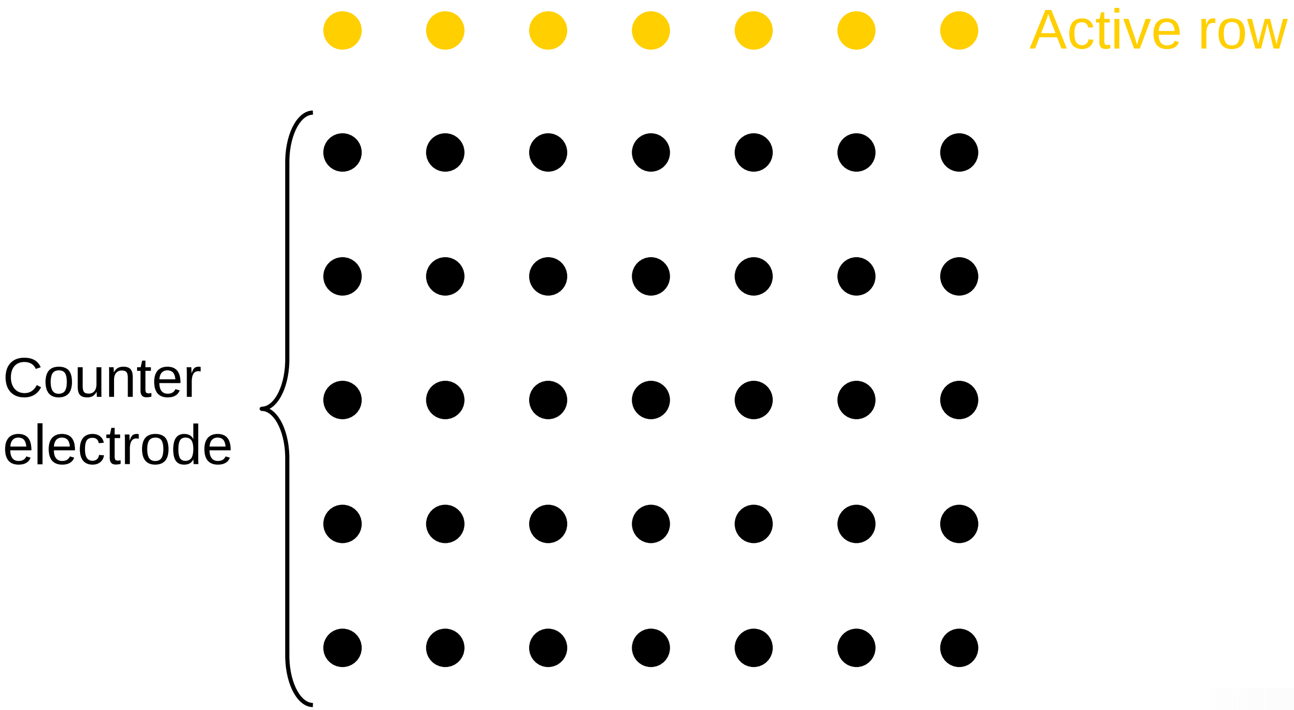


Modified CSP test socket
(Aries Electronics part number A1924-314-23)

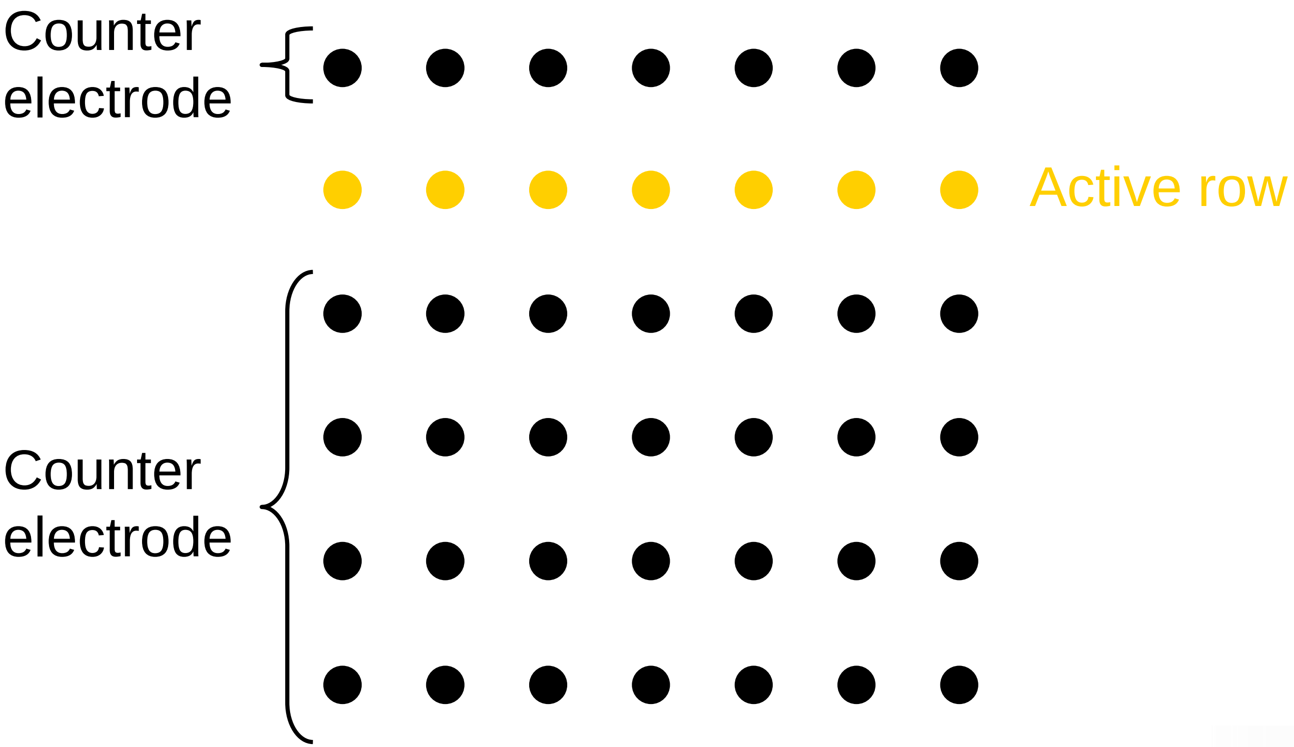


Thermal interface via backside of chip (not shown)

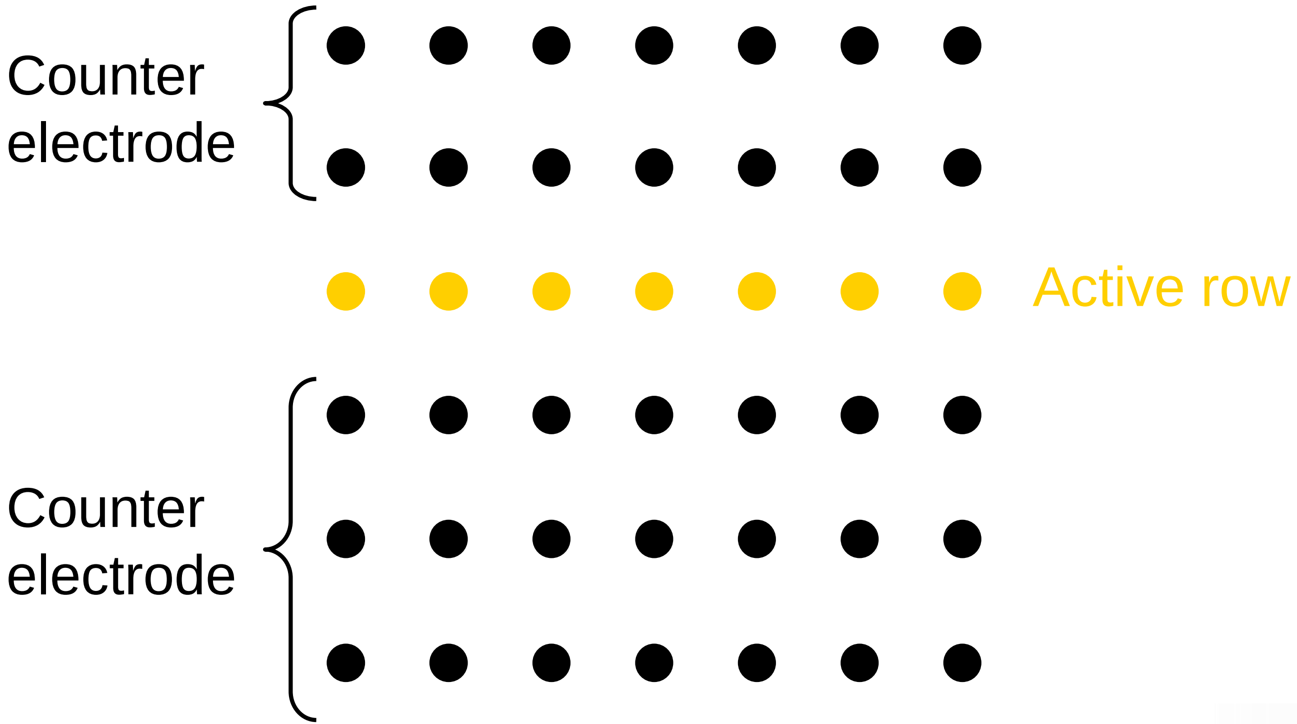
Reconfigurable counter electrode



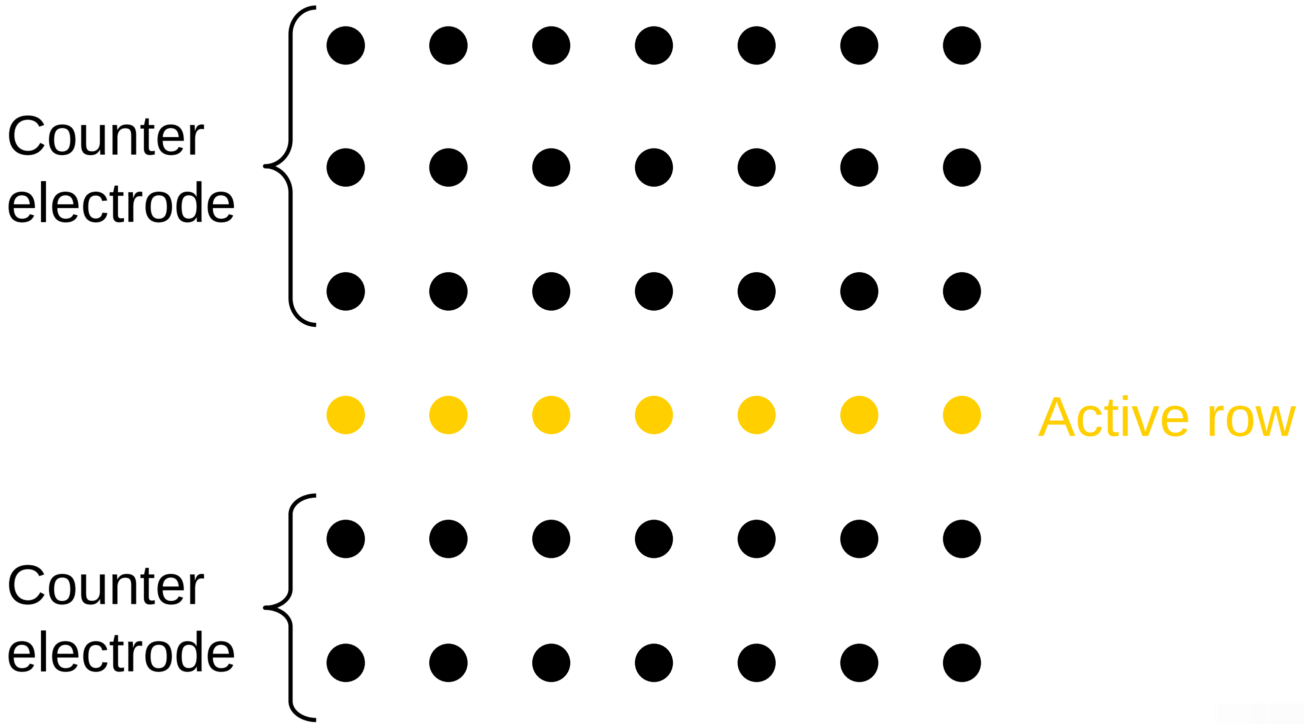
Reconfigurable counter electrode



Reconfigurable counter electrode



Reconfigurable counter electrode



Lower cut-off frequency (region A → B)

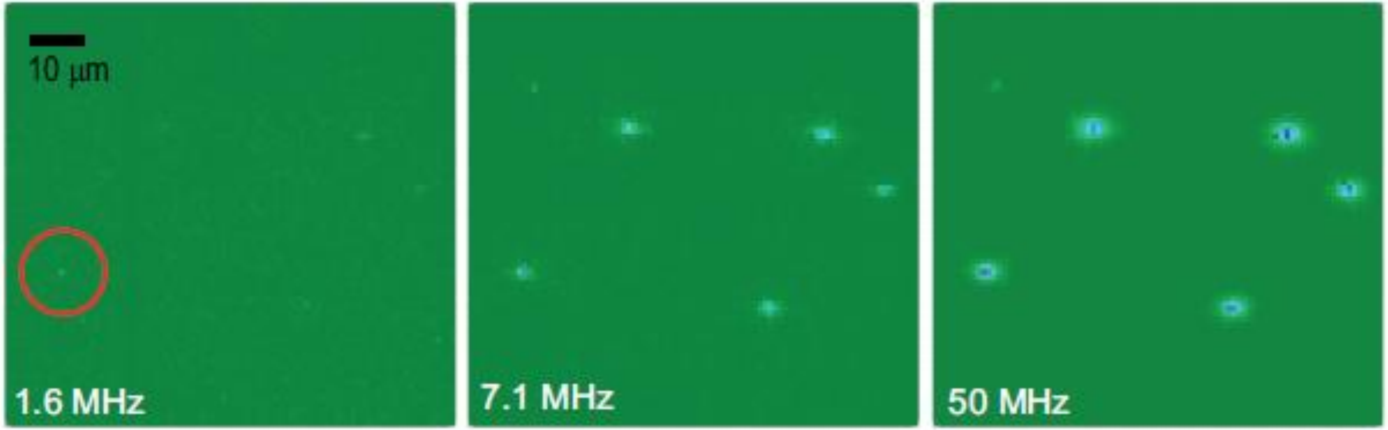


Figure 4.3: Spatial maps of the measured capacitance change (ΔC_{exp}) induced by the sedimentation of insulating 4.4-μm-radius particles at a salt concentration of 150 mM for frequencies of 1.6 MHz, 7.1MHz and 50MHz. Each pixel represents a nanoelectrode and each map was normalized to the maximum value of $|\Delta C_{\text{exp}}|$ over all the three pictures. The sensitivity to the presence of microparticles increases with increasing frequency.

Quantitative agreement with simulations

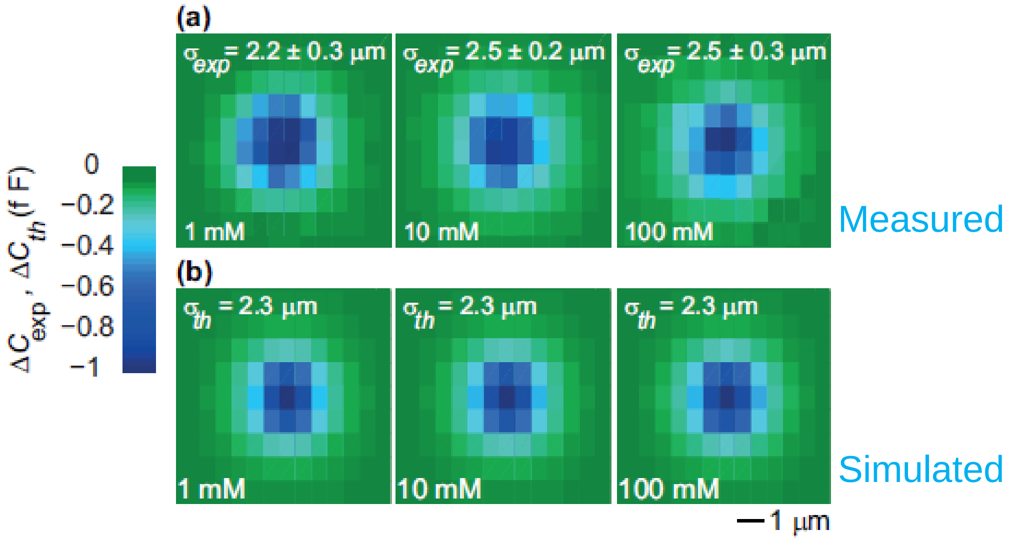


Figure 4.4: (a) Response to a single particle at salt concentrations of 1 mM, 10 mM and 100 mM and a frequency of 50MHz. The rectangular shape corresponds to the asymmetry in the pitch of the array. Apparent particle size σ is independent of ionic strength over two orders of magnitude. (b) Theoretical predictions (ΔC_{th}) for the same conditions as in (a).

Detection of particle conduction type

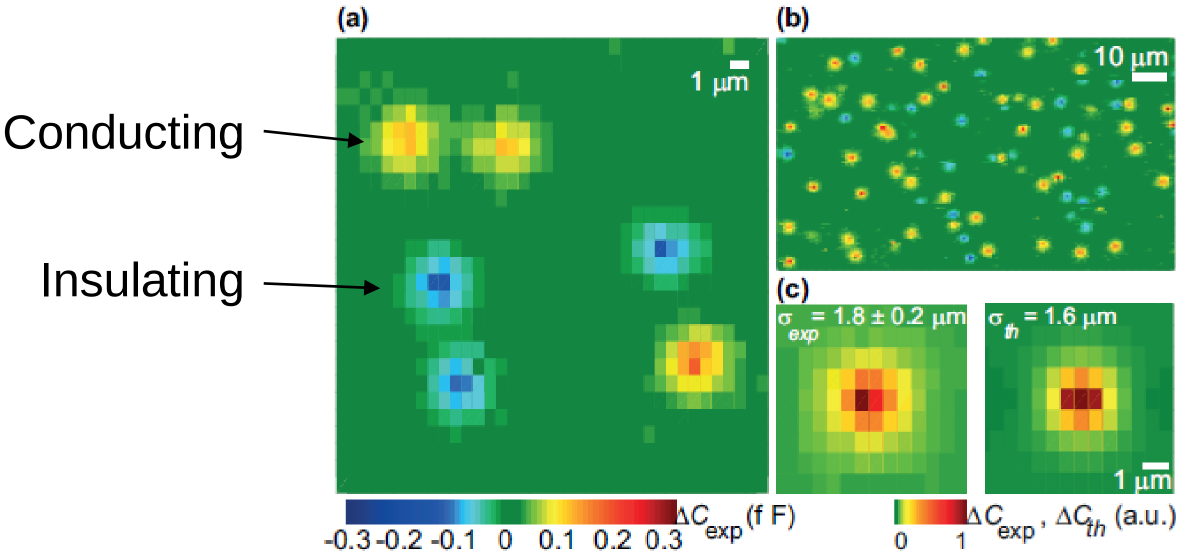


Figure 4.6: (a) Response of the array to a mixture of dielectric and conducting 2.5-μm-radius spheres. The signals have opposite polarities, demonstrating the ability to discriminate between two types of particle at high frequencies. (b) Zoomed-out view of (a), comprising 30% of the nanoelectrode array surface. (c) Comparison of experimental (left) and theoretical (right) capacitance maps of a conducting particle at 50 MHz and 100 mM salt.

Detection of nanoparticle binding

- Nanoparticles captured by BSA layer on chip surface
- Independent verification with AFM

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Detection of … virus (one of the smallest viruses)

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Collecting statistics of captured nanoparticles

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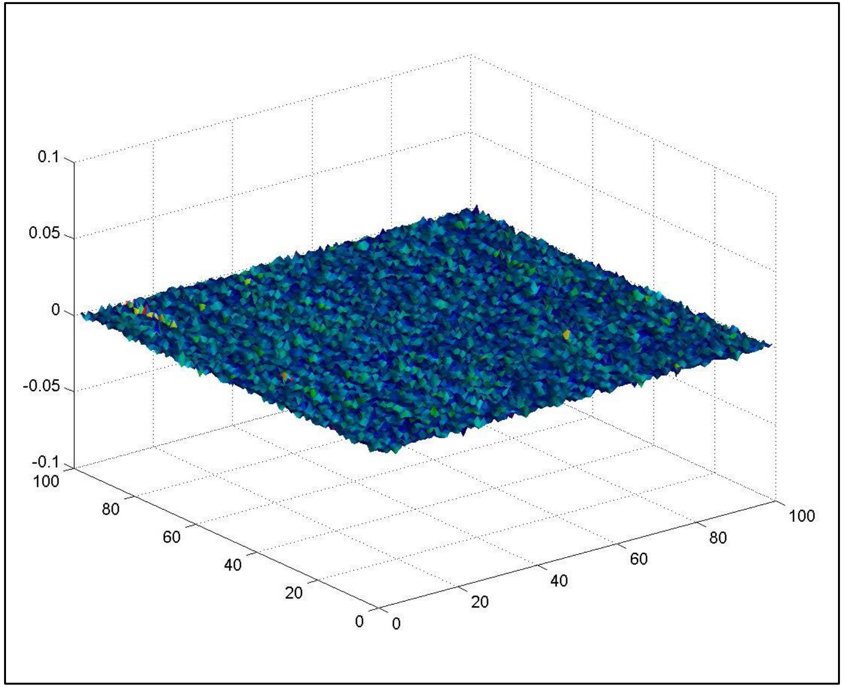
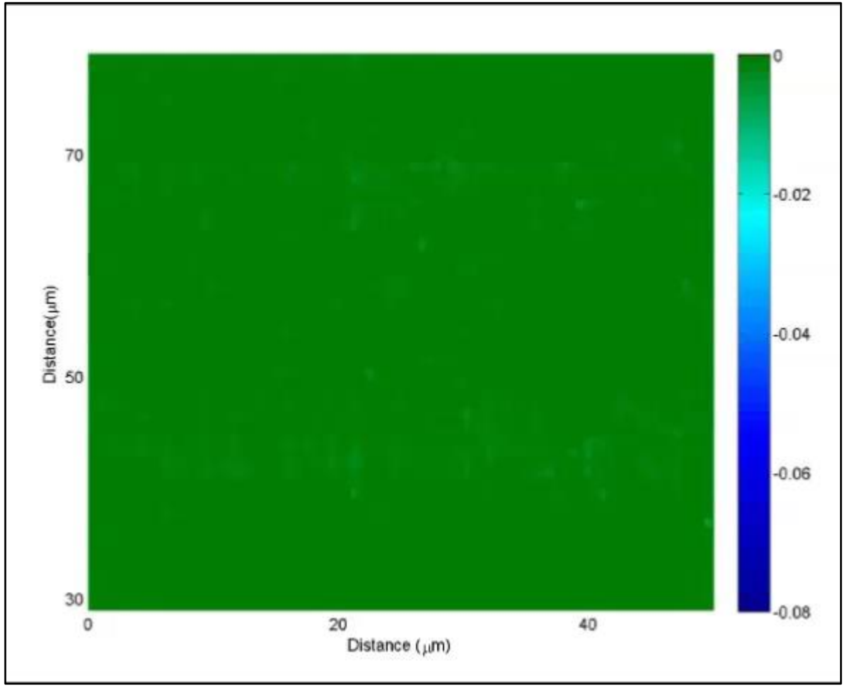
Counting of particles and imaging of living cells

1-µm dielectric particles in water (pH = 3)



MCF7 breast tumor cells in growth medium



Imaging of droplets in water-based emulsions

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Adding smartness: automatic particle tracking

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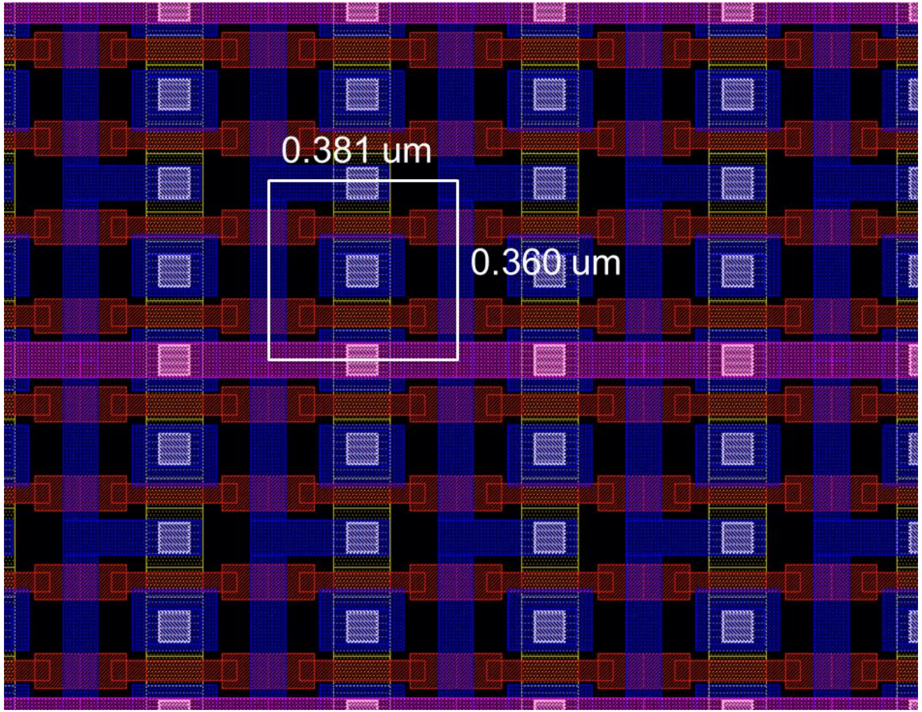
The future: surfing Moore’s Law?



40-nm CMOS design exercise

- 3 times cell area shrink
- Resolution comparable to that of optical microscopes

And what about 14-nm CMOS?

Thanks to my great collaborators!

Udine University (I)

- Luca Selmi, Federico Pittino, Federico Passerini, Pierpaolo Palestri, Andrea Bandiziol, Paolo Scarbolo, Andrea Cossettini

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