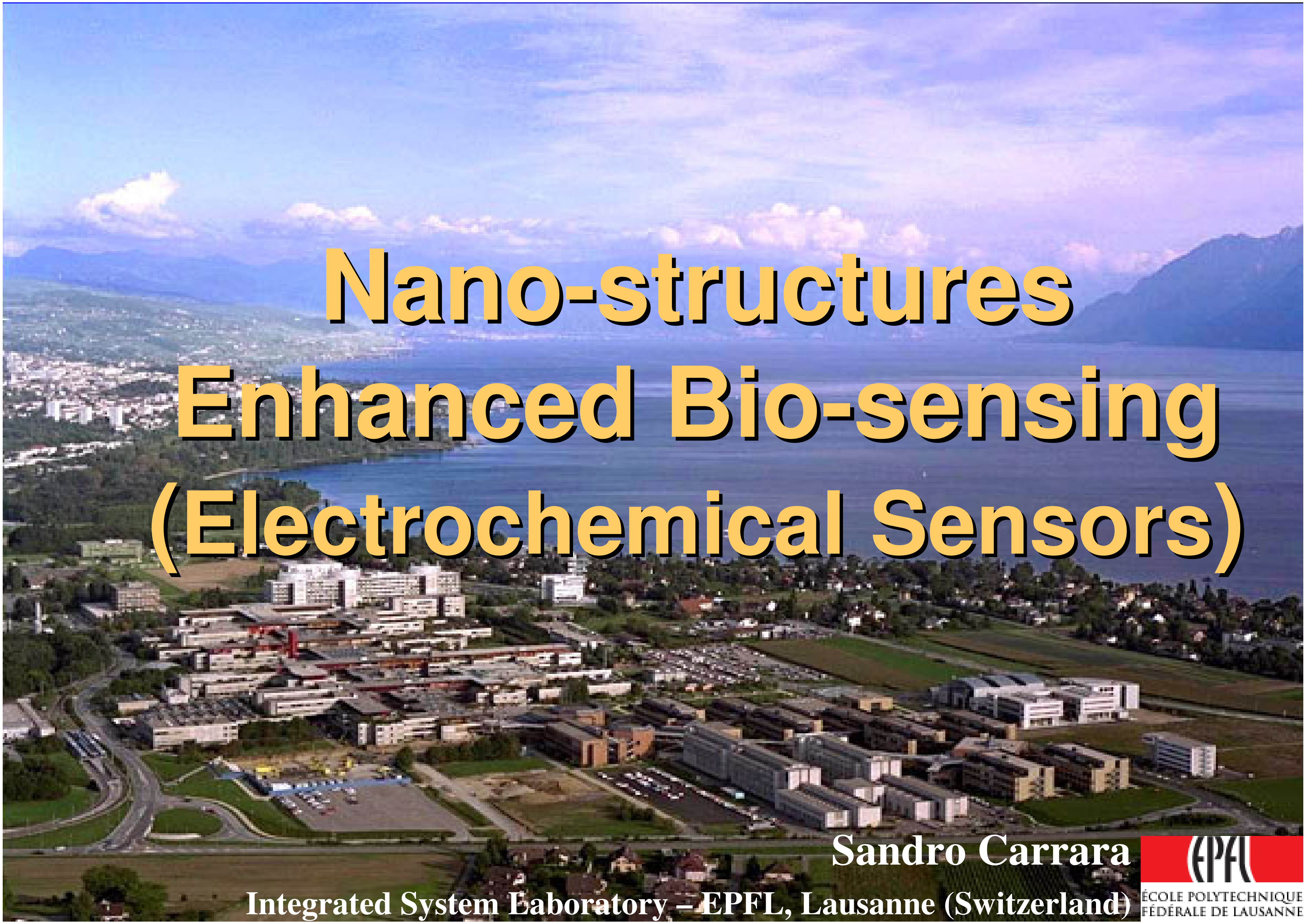


Nano-structures Enhanced Bio-sensing (Electrochemical Sensors)

Sandro Carrara

Integrated System Laboratory – EPFL, Lausanne (Switzerland)

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

What is Nanotechnology?

"Biology is not simply writing information; it is doing something about it. A biological system can be exceedingly small. Many of the cells are very tiny, but they are very active"

R.P.Feynman

Bio-inspired, so:

Nano-BIO-technology

Plenty of Room at the bottom, MIT lesson, Dec. 1959

The Motivation

- 100.000 $ (machinery)
- 1.000 $ the single μ-array

for DNA

for Glucose

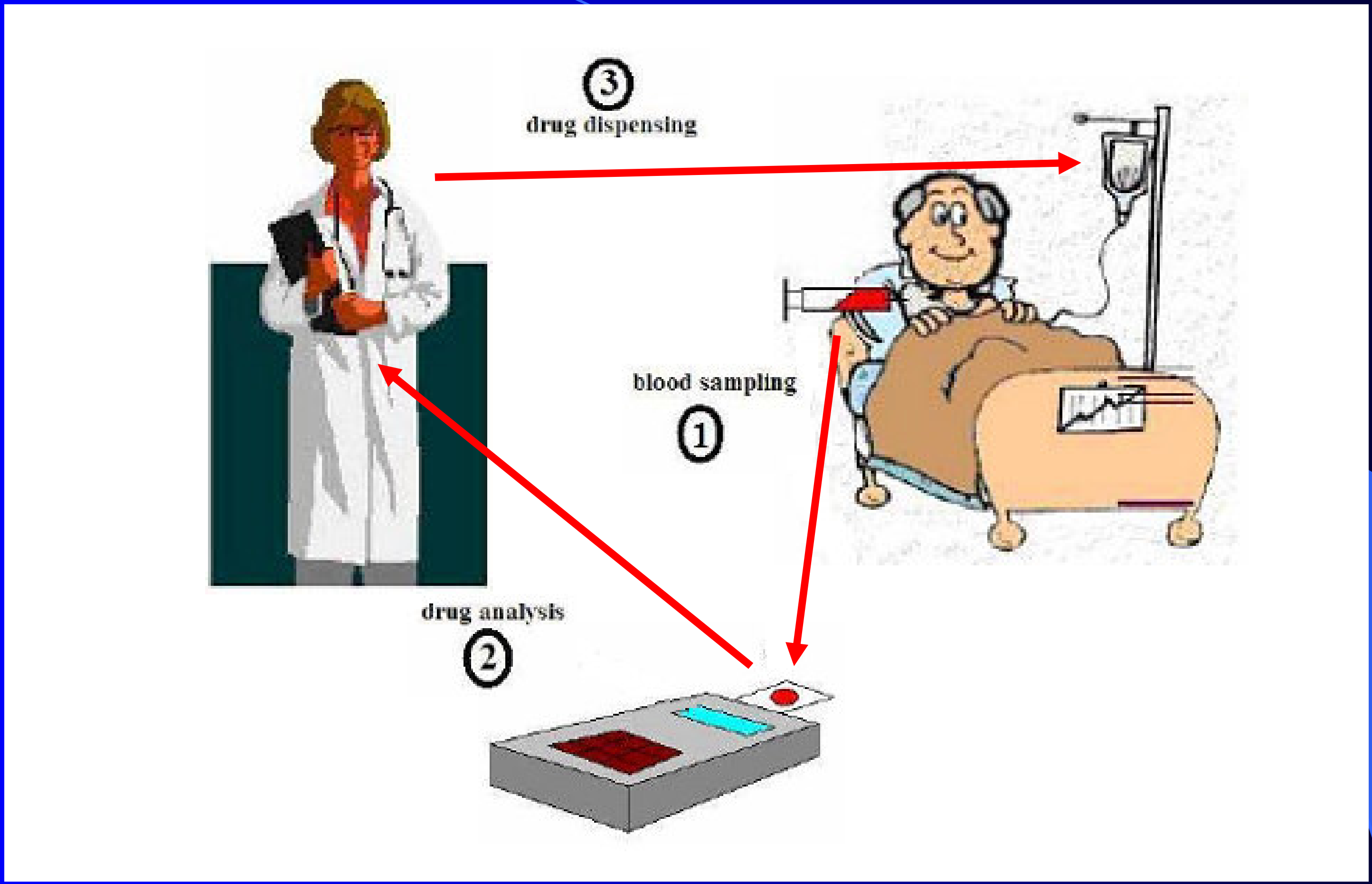
- 50 $ (machinery)
- 0.05 $ the single strip

The Motivation

for DNA

- 0.08 $/mm^2 the single on-board CMOS bio-chip

Point-of-Care in Personalized Therapy



New systems for Drugs Monitoring in personalized therapies are an important frontier challenge

Which are the building blocks?

"the science of objects with smallest dimensions ranging from a few nanometers to less than 100 nanometers"

G.M.Withesides

Small 1(2005) 172-179

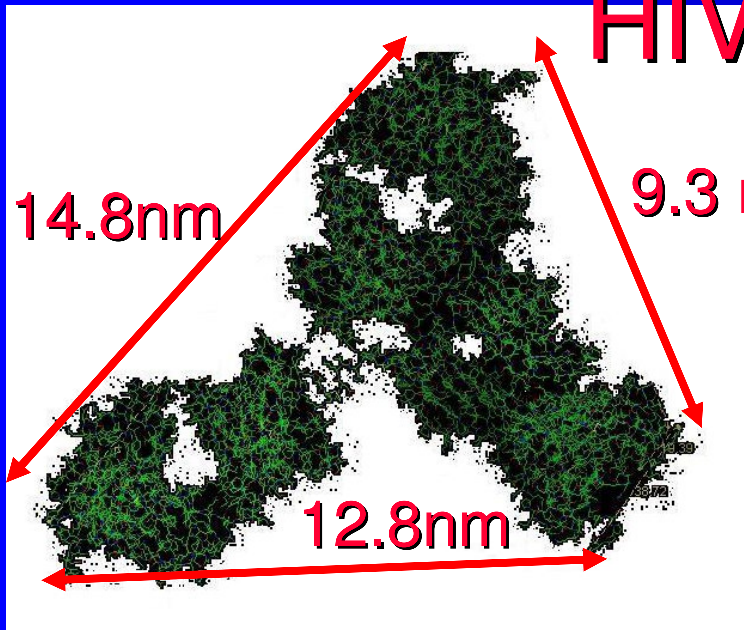
Building blocks under 100 nm size

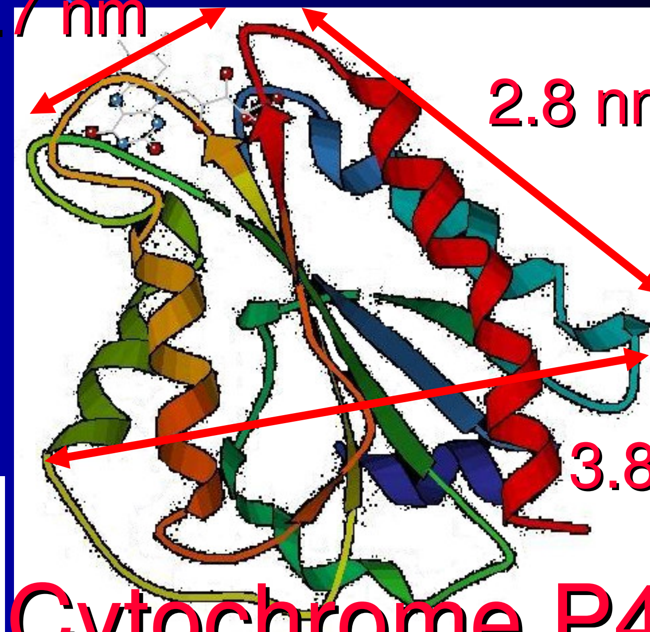
OJBECT	TYPICAL SIZE
Cell	10 micron
Bacteria	2 micron
Chromatid	840 nm
Chromatin	10 nm - 300 nm
Proteins	50 nm
Virus	90 nm
Nanotubes	Length =micron, Thickness =10-50 nm
Nanoparticles	3-15 nm
DNA	L = 2 m, Thickness = 2 nm
Simple molecules	2 nm
Atoms	0.2 nm

Whitesides definition!

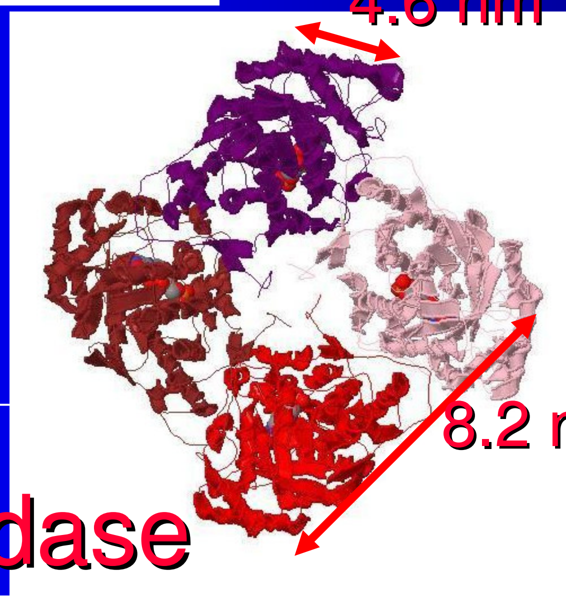
The proteins size

HIV antibody





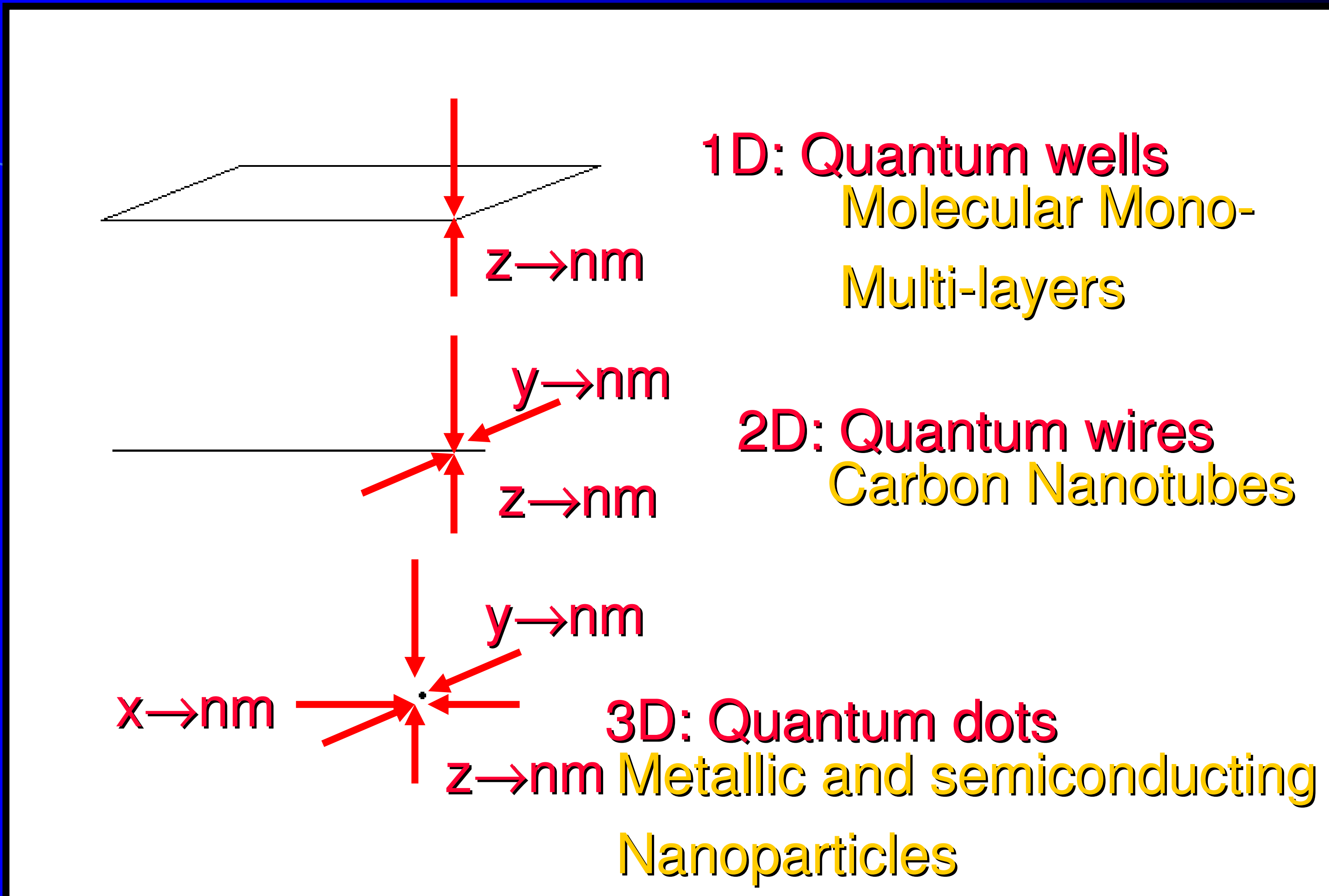
Cytochrome P450



Lactate Oxidase

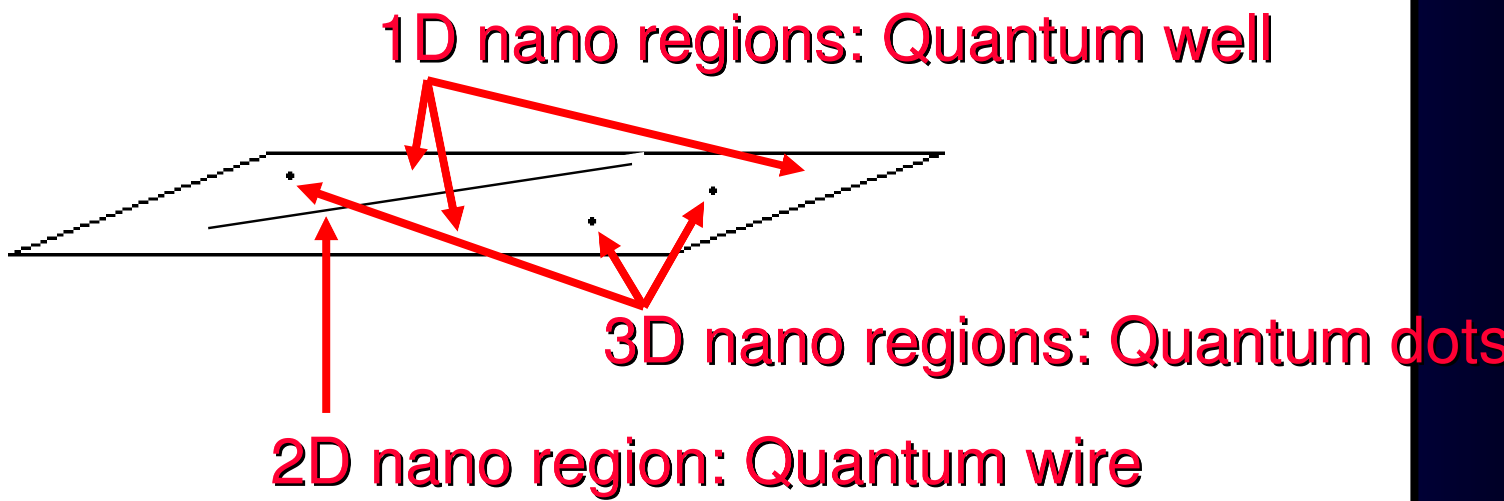
ne

How nano?



The dimension drives the phenomena

How nano?



polymer's layers + Carbon Nanotubes

Protein's layers + metallic nanoparticles

Arachidate layers + semi-conducting nanoparticles

The dimension drives the phenomena

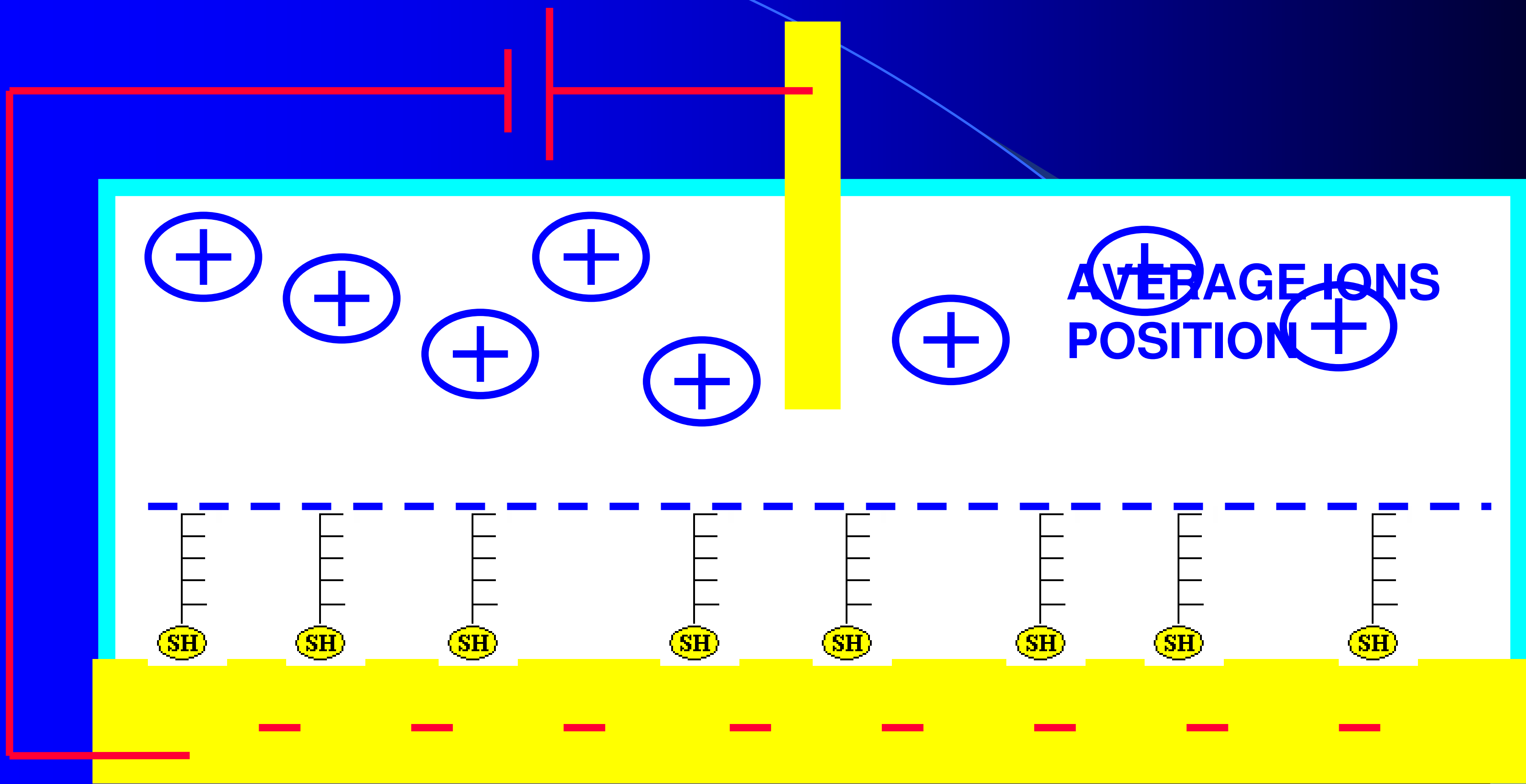
Examples of Nano-Bio-sensing?

- DNA biosensors enhanced by 1D nanostructures.
- Enzymes biosensors enhanced by 2D nanostructures.
- Enzymes biosensors enhanced by 3D nanostructures.

1-D Nanostructures for DNA detection

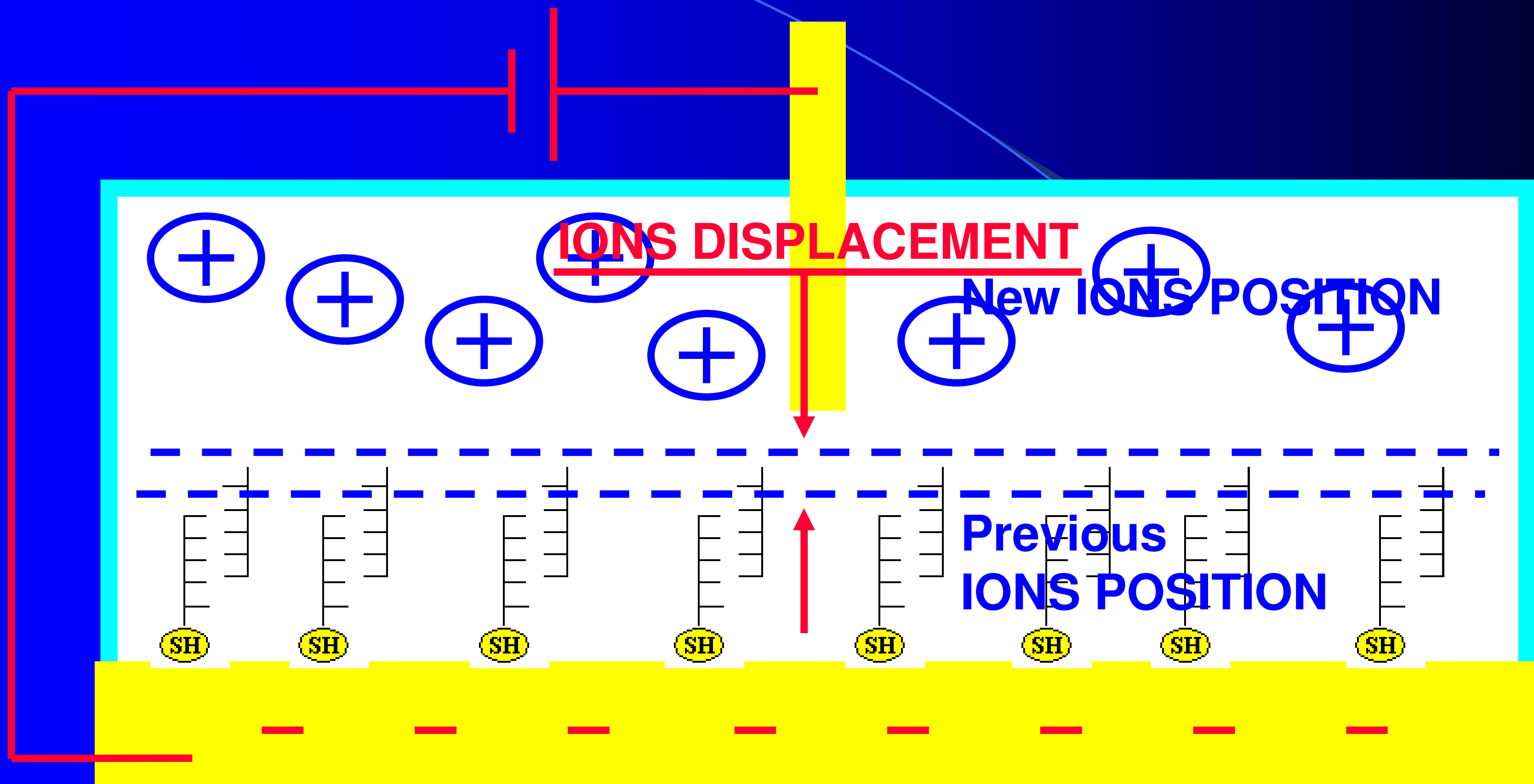
- Surface Wettability
- Surface Electrical Properties

Electrochemical Interface



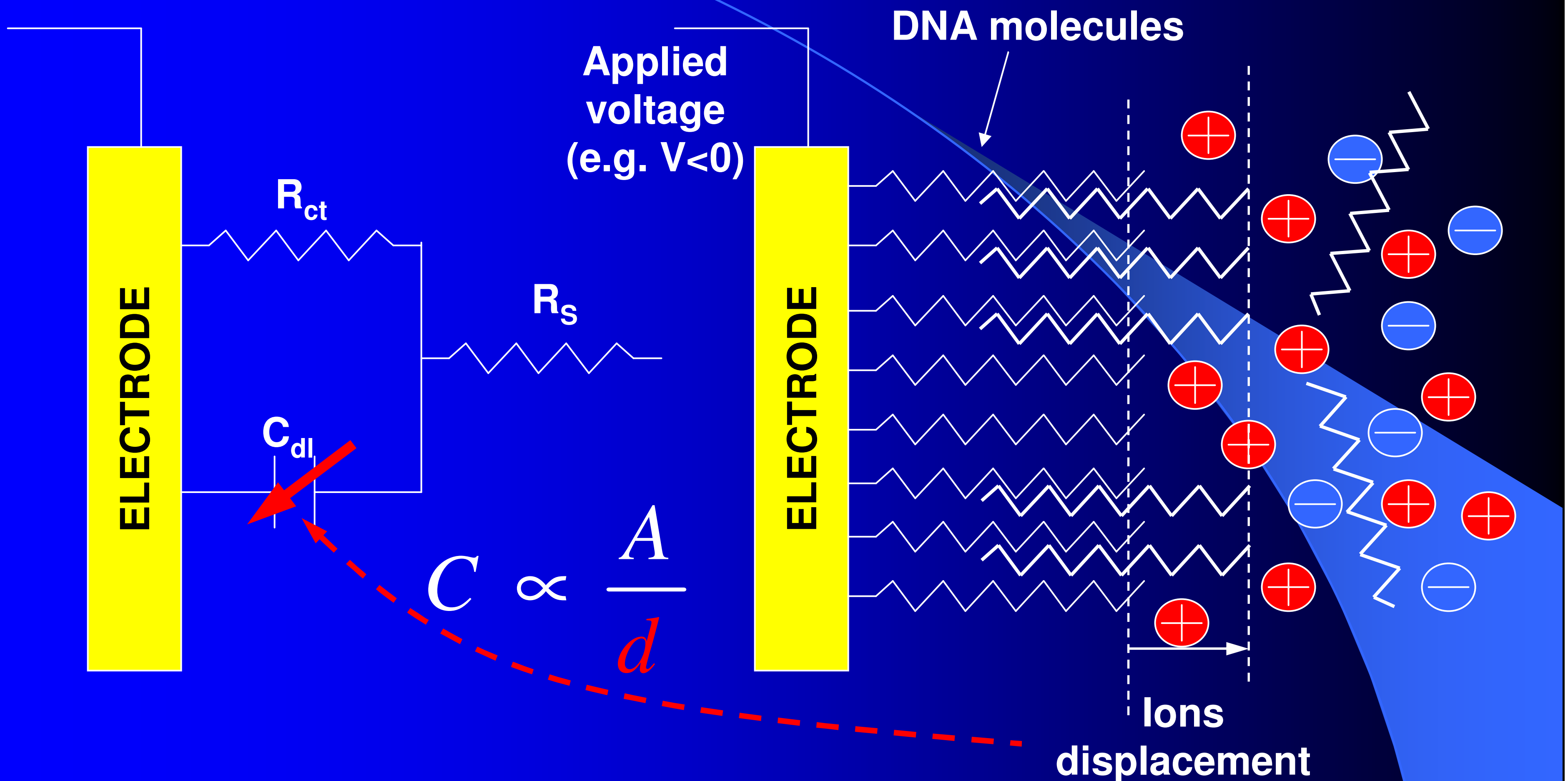
Ion planes are formed at the interface when electrodes immersed in solution are polarized

Electrochemical Interface



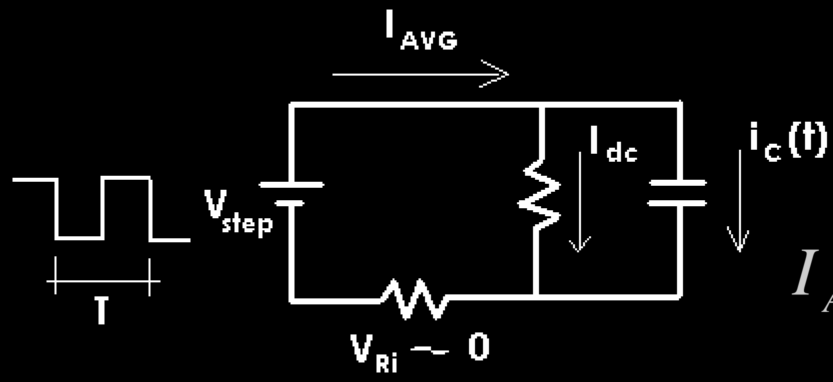
Ion planes are formed at the interface when electrodes immersed in solution are polarized

The DNA Detection Principle



Unlabeled ssDNA may be detected with capacitance measurements as due to charge displacement

Current Based Capacitance Measurement (CBCM)



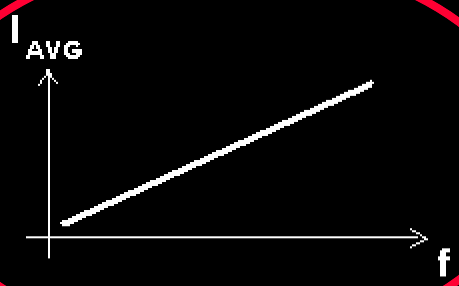
$$i(t) = I_{dc} + i_C(t)$$

Frequency!

$$I_{AVG} = \frac{I_{dc}}{2} + \frac{1}{T}\int_0^{T/2} i_C(t)\,dt$$

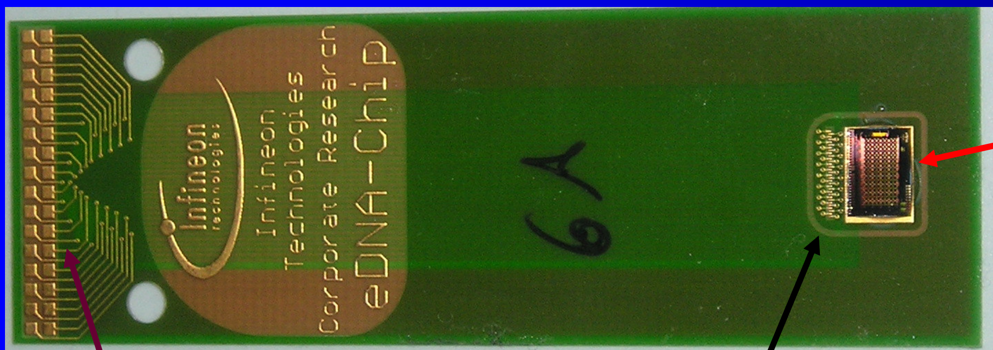
$$I_{AVG} = \frac{I_{dc}}{2} + CV_{step}f$$

THE CAPACITANCE !



Method for a precise Capacitance measurement

Liquid Measurement set-up

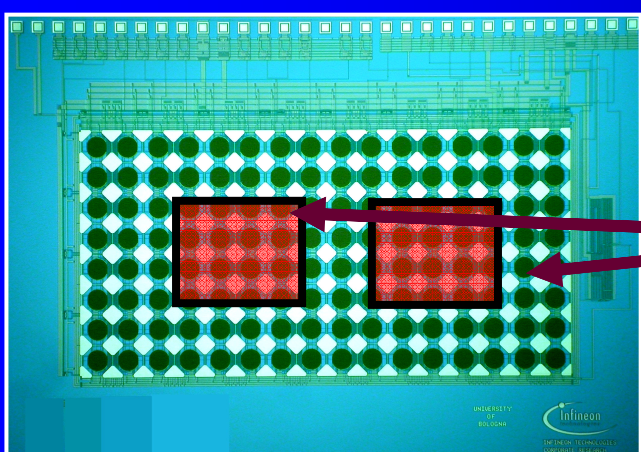


Chip is glued on a PCB

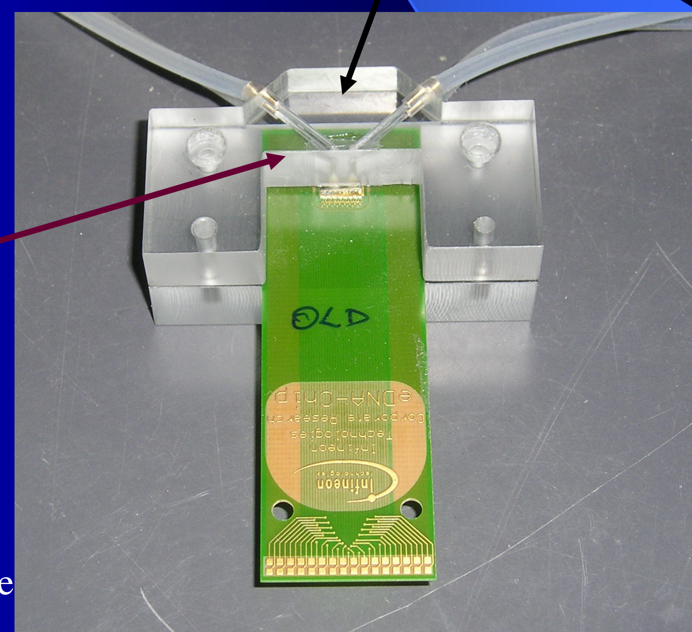
Output PCB pads

Bonding wires

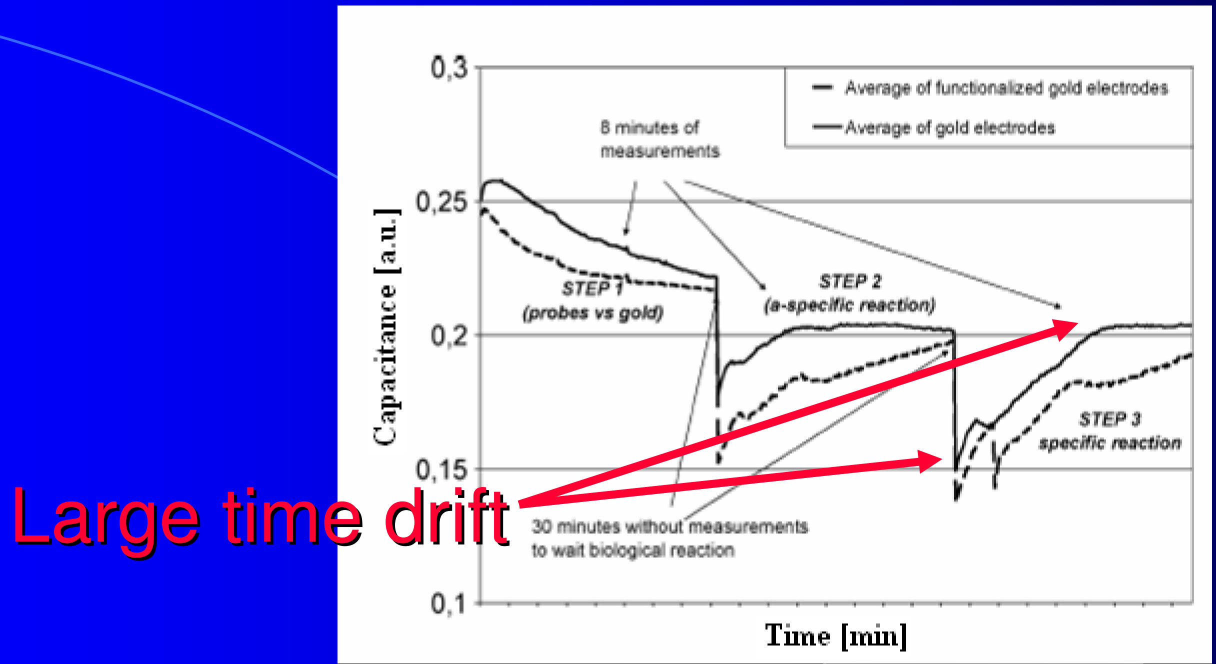
Fluidic cell



Two different Chambers 1mmX1mm



The problem of time instability



al, et S.Carrara, IEEE J.Solid State Circuit 41 (2006) 2956-2964

Capacitance variation during DNA hybridization

The problem of time instability

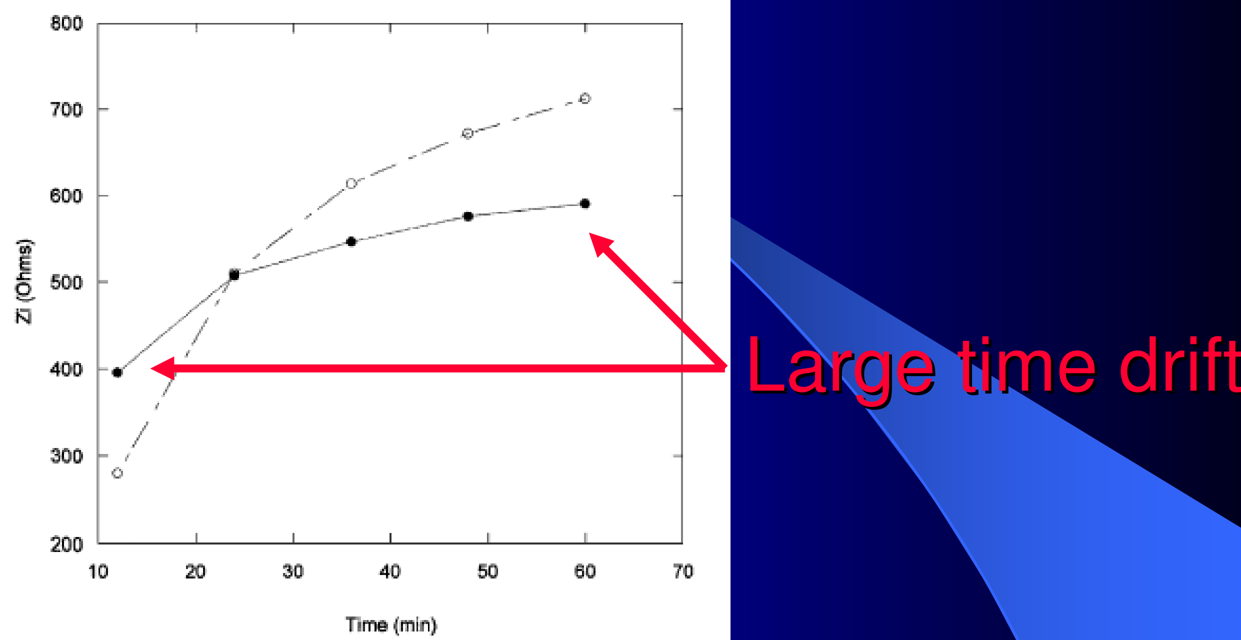


Figure 10. Imaginary impedance variations at 1.1 V for immobilization (closed circle), and 1.0 V for hybridization (open circle), as a function of time.

A. Macanovic / *Nucleic Acids Research, 2004, Vol. 32, No. 2*

Detection of DNA sequences by using peptide nucleic acid as probe molecules immobilized on Silicon with silane linkers

The problem of largely scattered data points

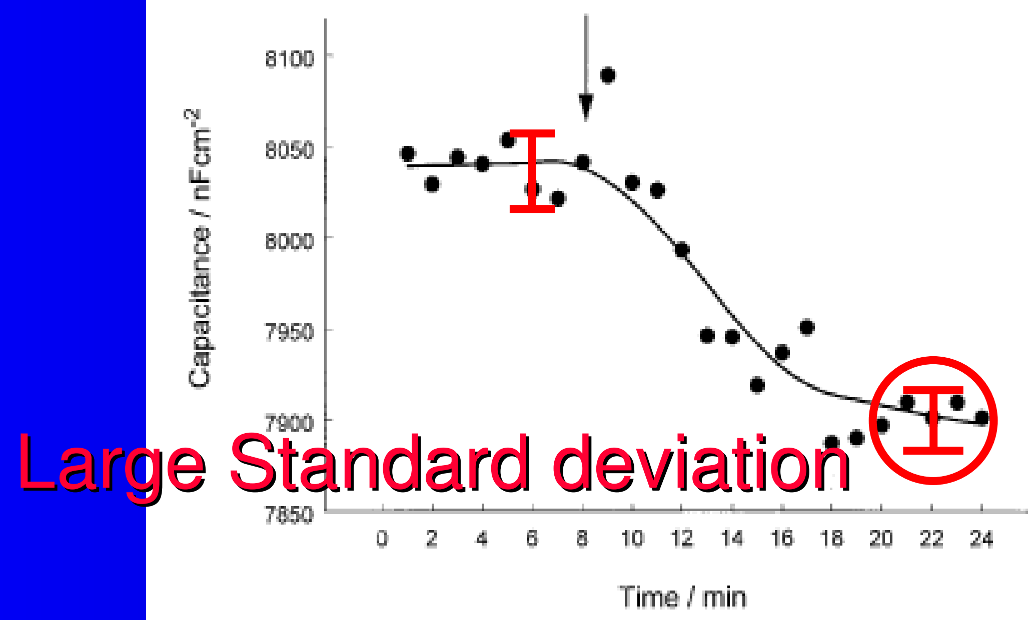
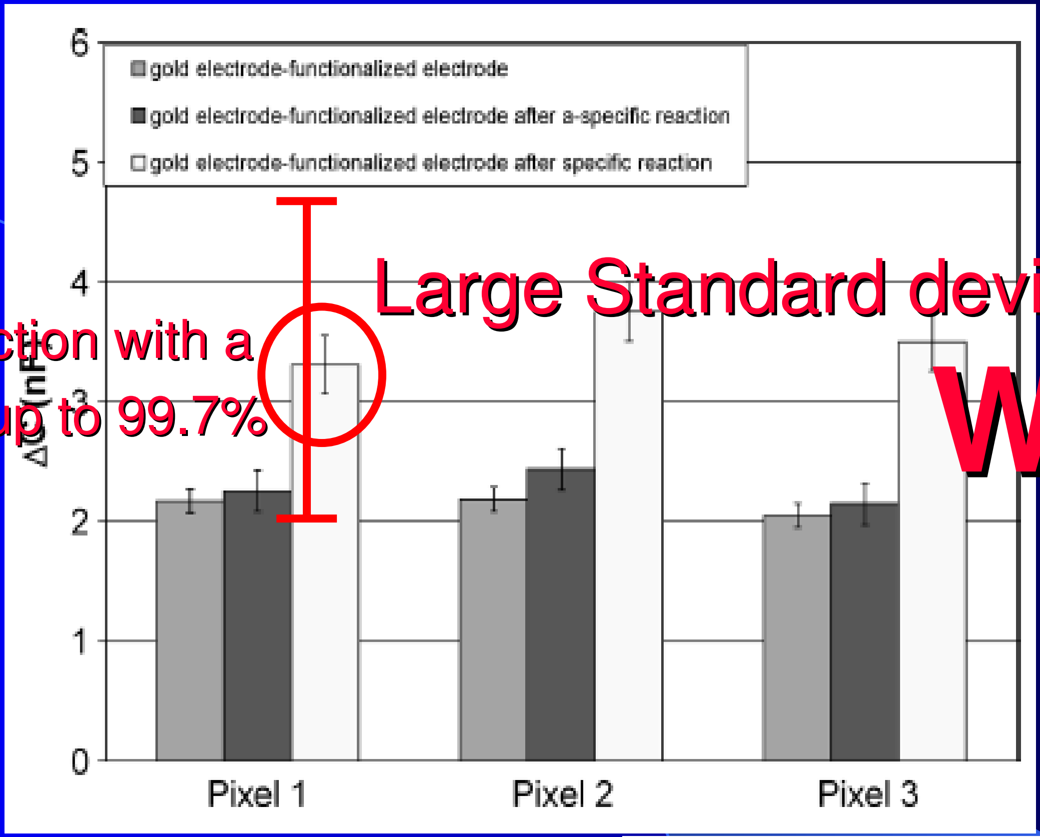


Fig. 5. A typical response signal for an electrode with self-assembled CMV-SH upon injection of a CMV sample at a concentration of 10^{-1} molecules /μL. The carrier was an aqueous solution containing 0.9 g/L sodium-azide, 0.5 g/L Tween 20 at a flow rate of 0.5 mL/min.

C. Berggren et al. Electroanalysis **1999**, 11, No. 3

Capacitance variation during DNA hybridization

The problem of large errors in detection



Large Standard deviation

3 σ: no detection with a confidence level up to 99.7%

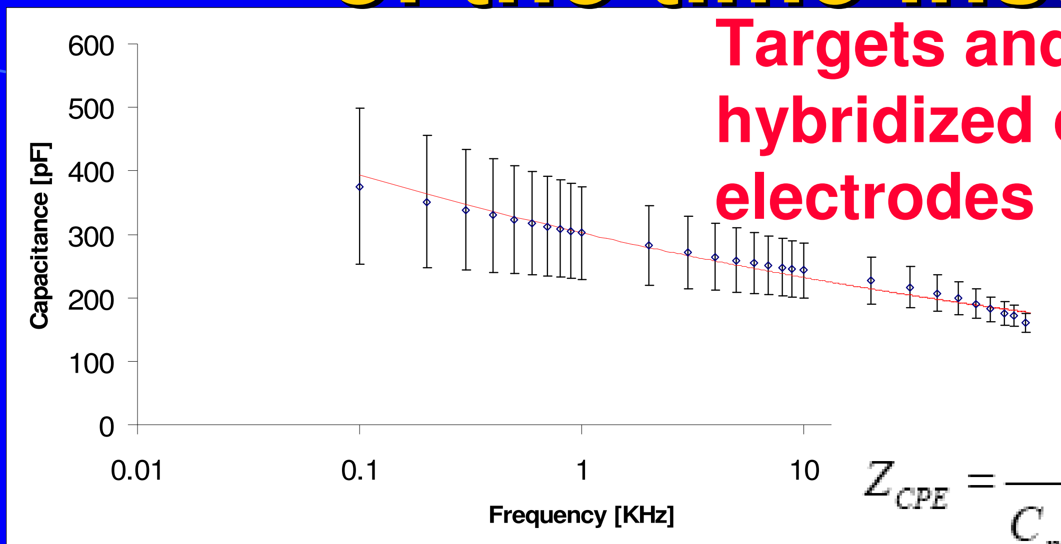
Why?

al, et S.Carrara, IEEE J.Solid State Circuit 41 (2006) 2956-2964

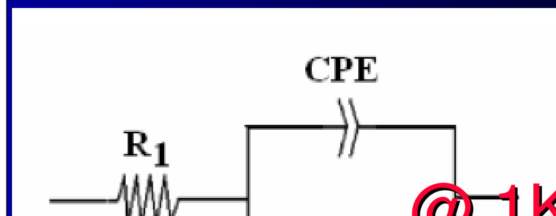
The Average Capacitance Drift in time

Results in a too large standard deviations on the DNA detection

How to understand the reason of the time instability?



Targets and probes hybridized onto Gold electrodes



@ 1KHz

$$Z_{CPE} = \frac{1}{C_p (j\omega)^{\alpha}} = \frac{1}{\omega^{\alpha} C_p}\sqrt{1-\alpha^2} - j\frac{1}{\omega^{\alpha} C_p}\alpha$$

CPE parameters	Bare electrode	DNA Probes	DNA Target
R(GΩ)	45	177	177
X(GΩ)	123	837	970

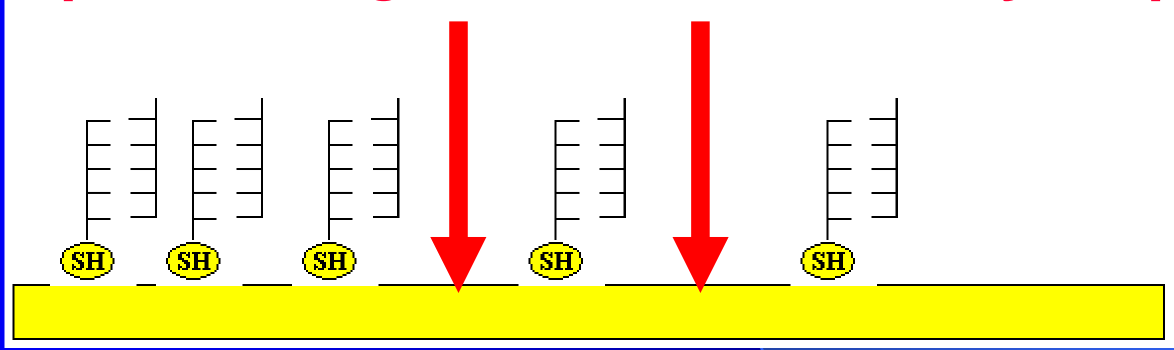
S.Carrara et al., Sensors and Transducer Journal 76 (2007) 969-977

Charge transfer pathways through the DNA layer affect the ideal Capacitance behavior of the layer at interface with the solution sample

The average capacitance upon the frequencies may shows as the DNA interface layer behavior

Charge transfer pathways through the probe layer

Ions transport through nanometer size layer apertures

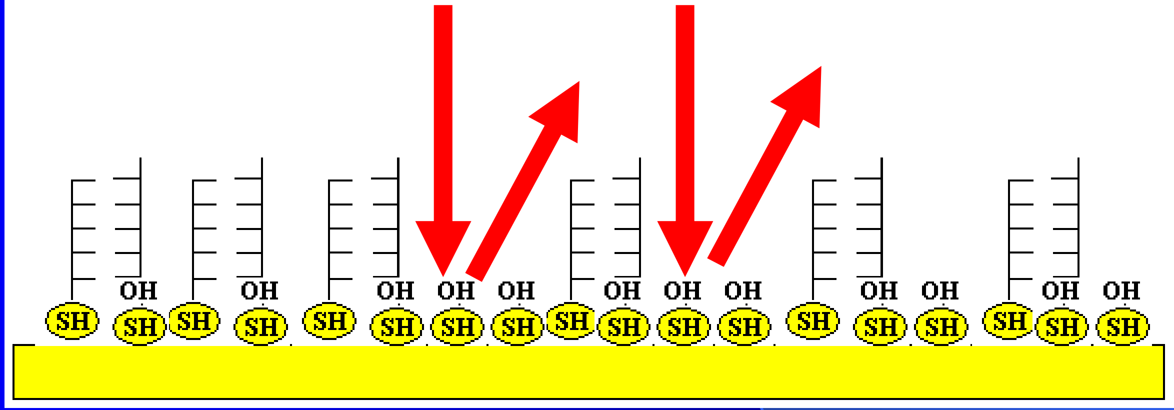


The frequency and time dependence of the Average Capacitance are similar to those observed on clean electrodes

Co-immobilized Thiols as Pathway Blockers

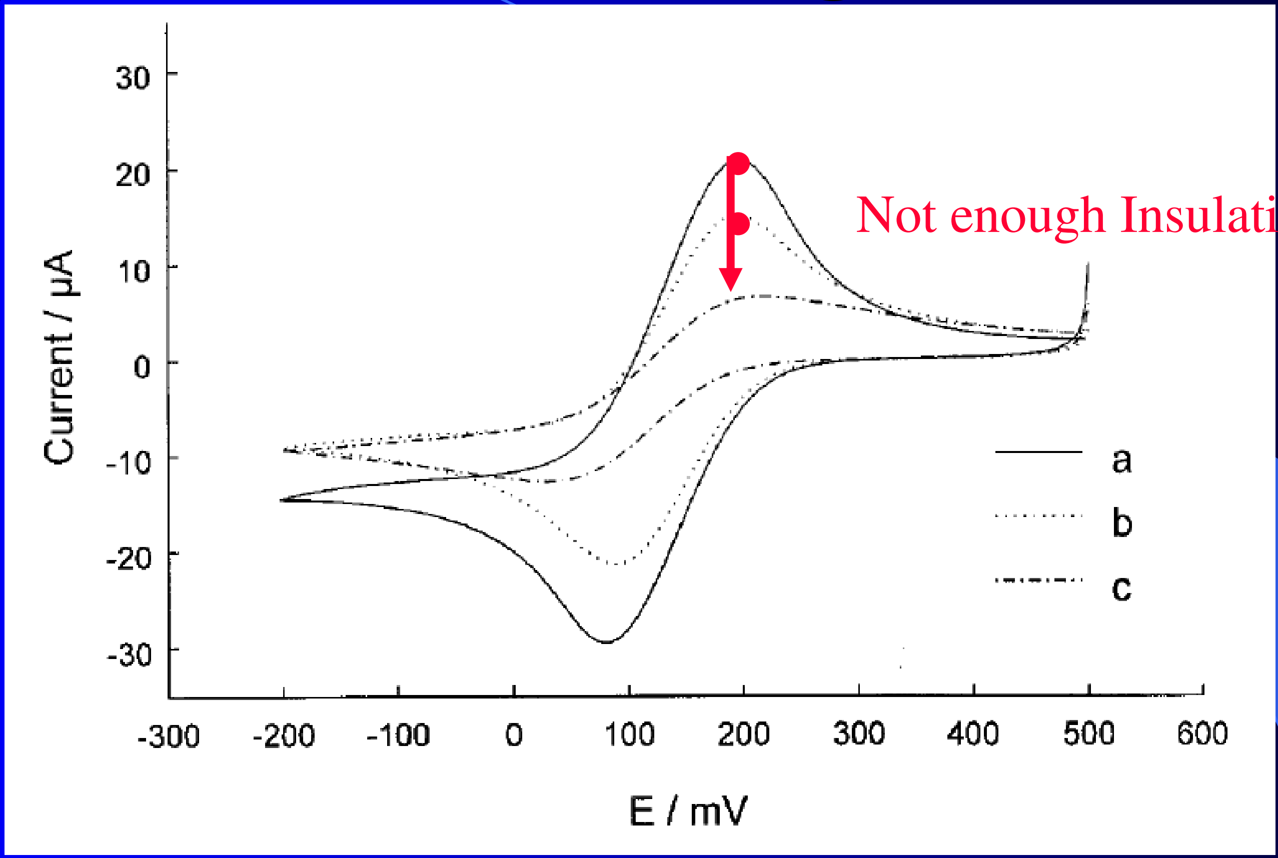
Mercapto-Hexanol

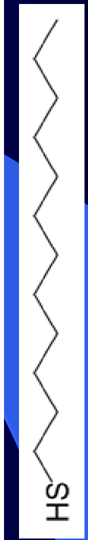
No layer apertures of direct access of the bare gold



Repelling molecules may be used to improve the interface behavior of Hybridized DNA mono-layers

Improved insulating behavior





C. Berggren et al. Electroanalysis 1999, 11, No. 3

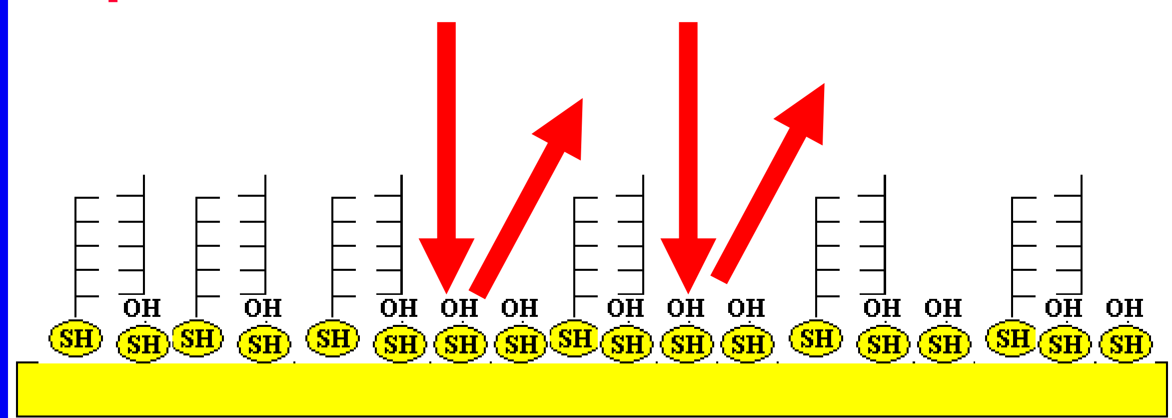
Redox reaction of K3Fe(CN)6 on gold electrode (a),
ss-DNA onto gold (b) and ss-DNA + 1-dodecanethiol onto gold (c)

Further Thiols as Pathway Blockers

Lipa-DEA molecule 

Mercapto-Hexanol 

No layer apertures of direct access of the bare gold

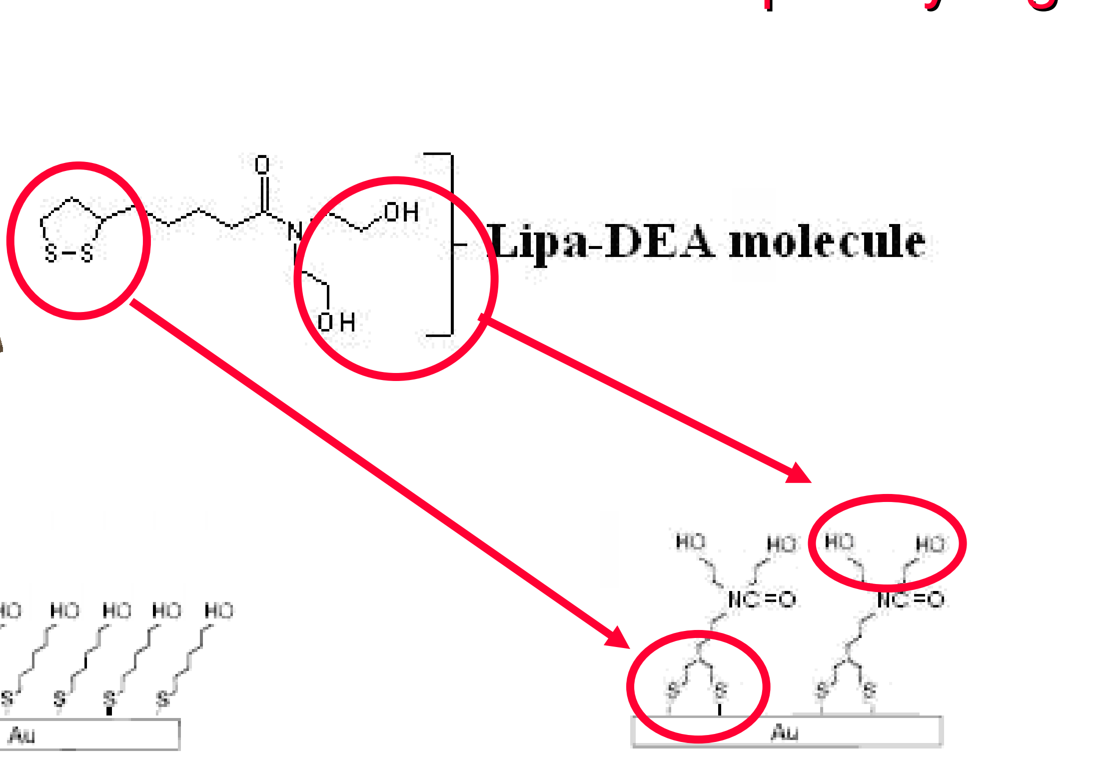


Other repelling molecules may be used to improve the interface

Behavior of Hybridized DNA mono-layers

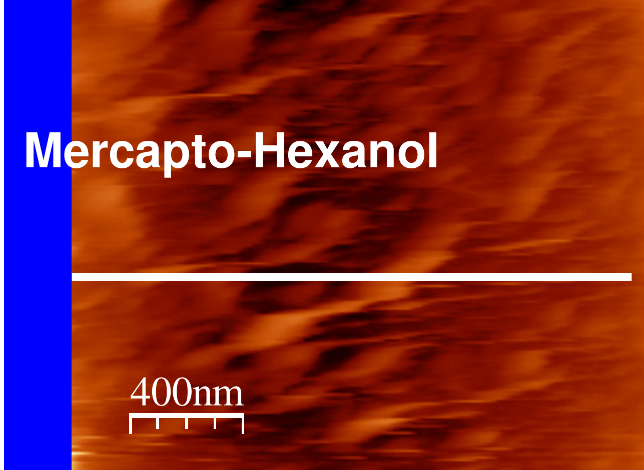
Lipa-DEA blockers

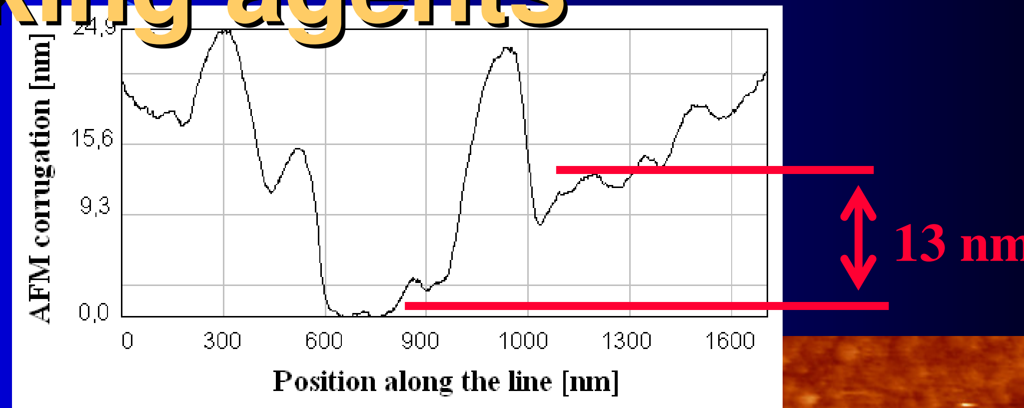
Different kind of thiols developed by Inger Vikholm

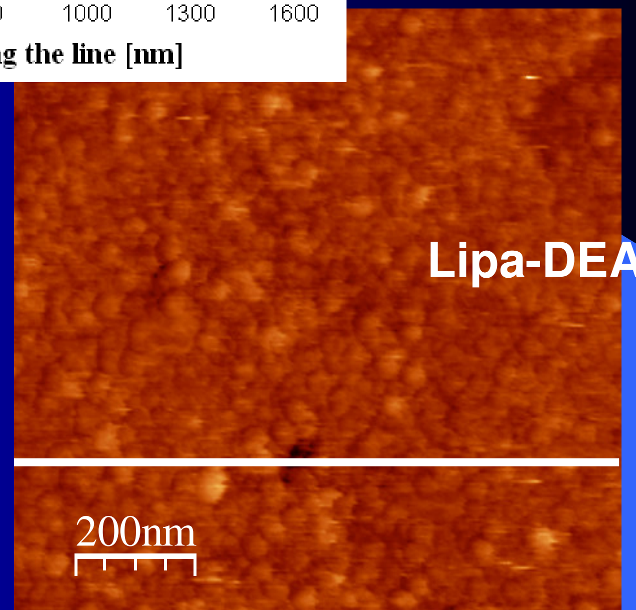


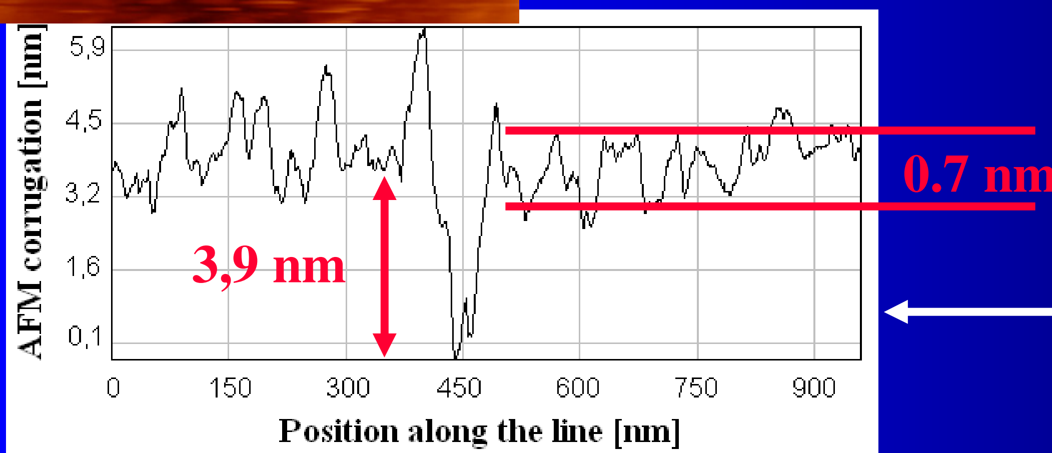
N,N-bis(2-hydroxyethyl)-α-lipoamide (Lipa-DEA) may be used as more efficient blocking agents

ssDNA Mono-layers with blocking agents



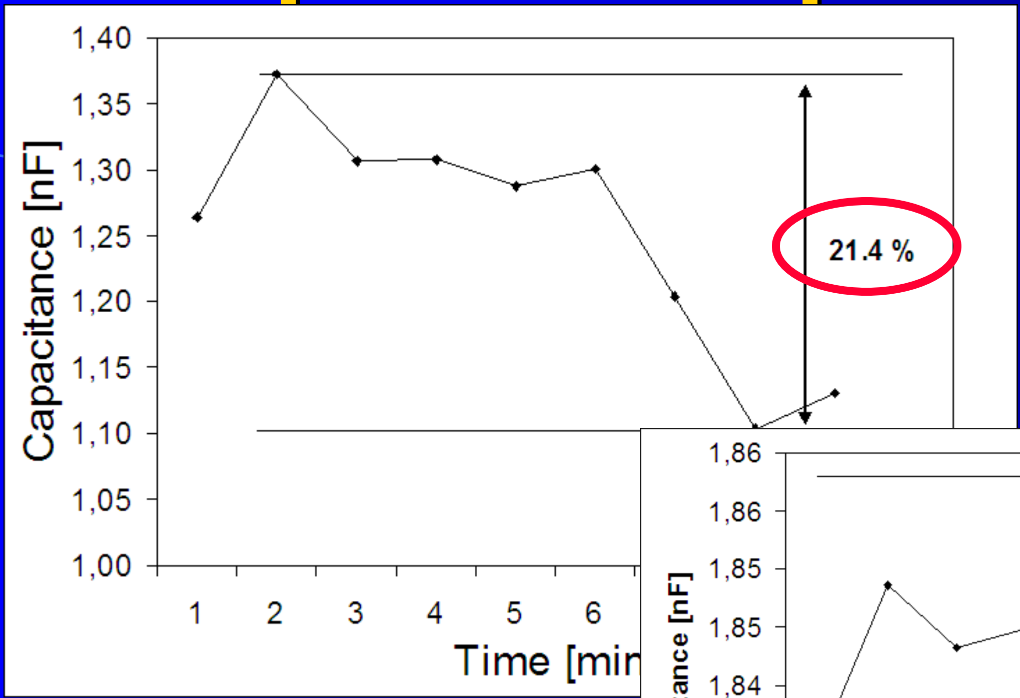


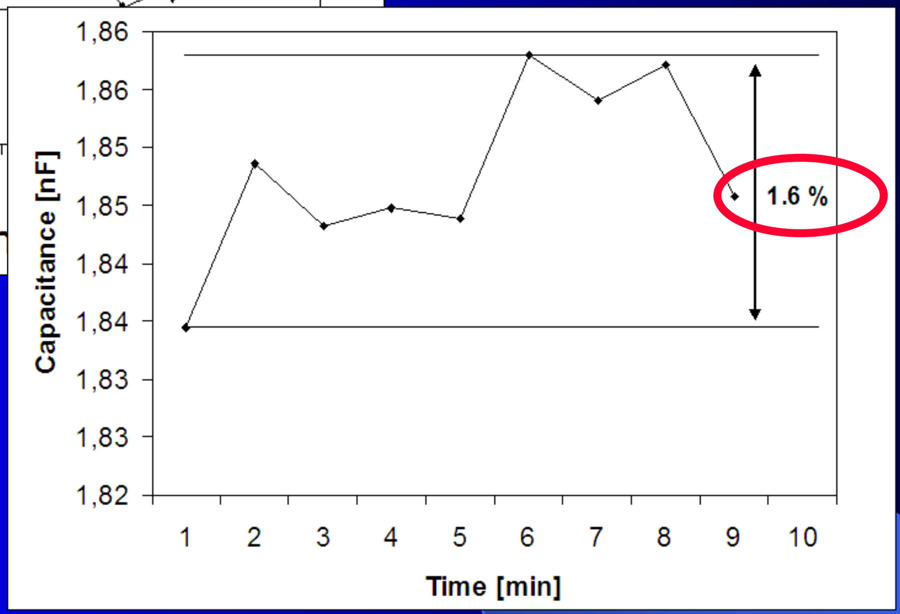


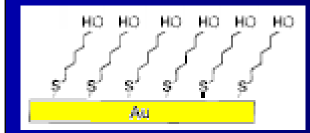


Monolayer of ssDNA with blocking agents still present deep groves crossing the film

Improved Capacitance Stability

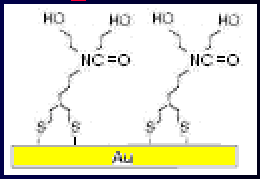






Mercapto-Hexanol

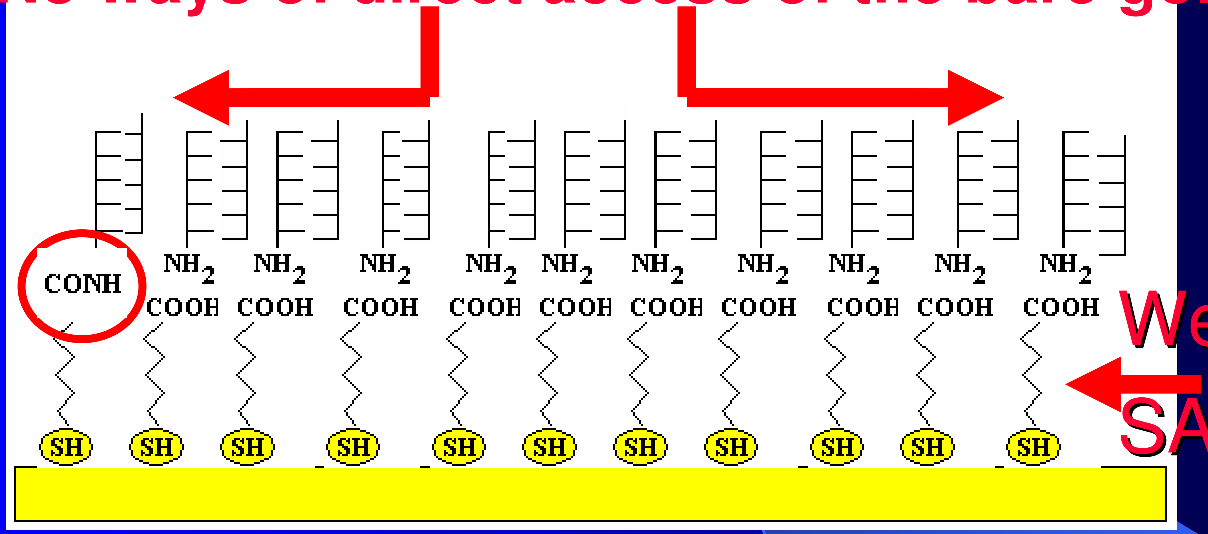
Lipa-DEA



Increased stability by using Lipa-DEA as blocking agent

Improved surface for capacitance detection

No ways of direct access of the bare gold



Covalent binding

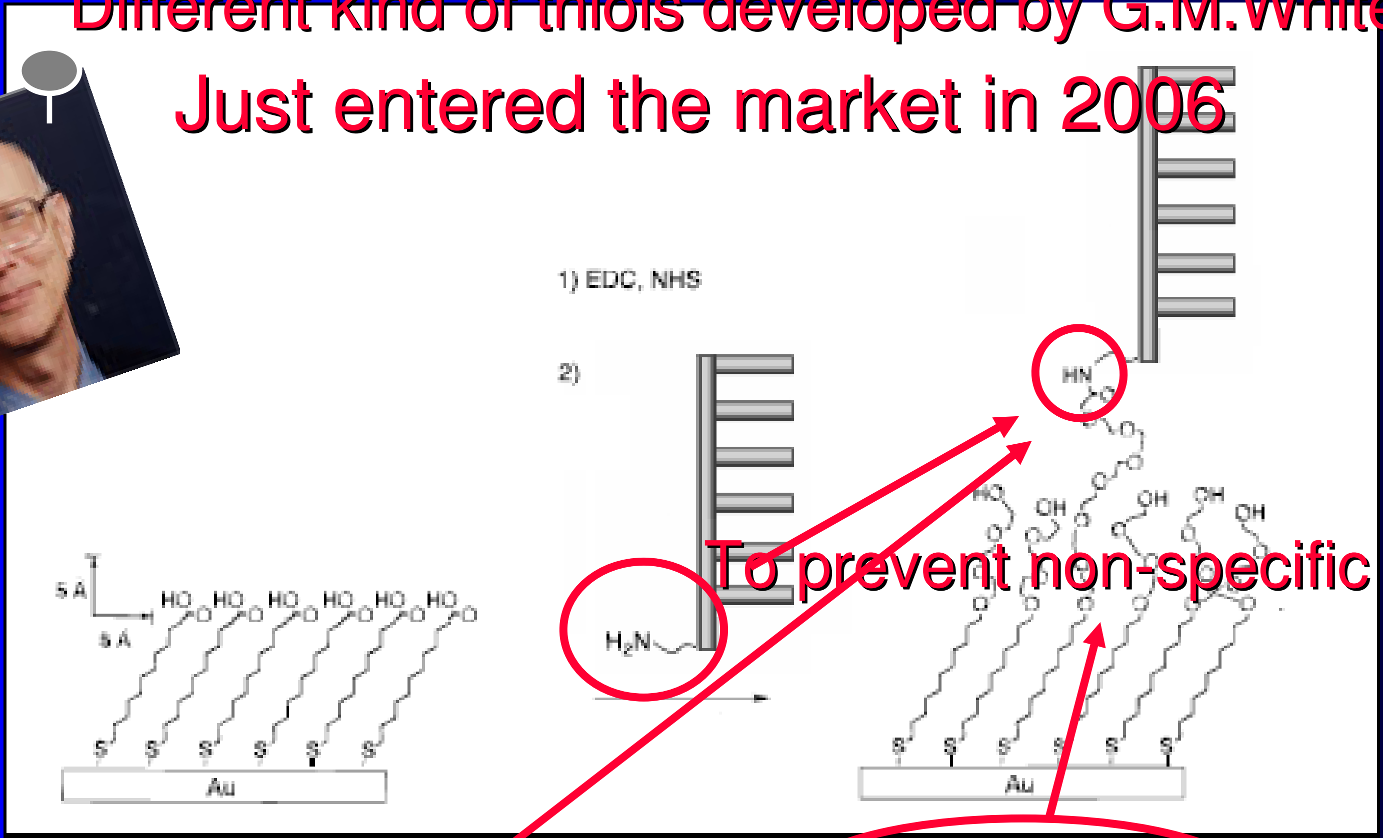
Well formed SAM

Highly packed thiols monolayer may be used to improve the DNA detection capability

Ethylene-Glycol Blockers

Different kind of thiols developed by G.M.Whitesides

Just entered the market in 2006

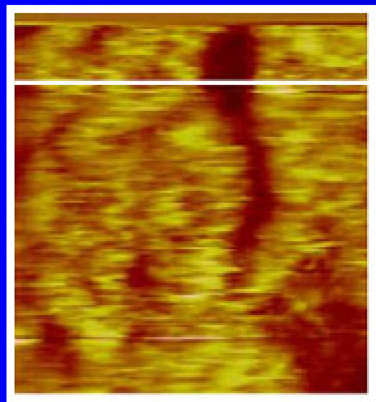


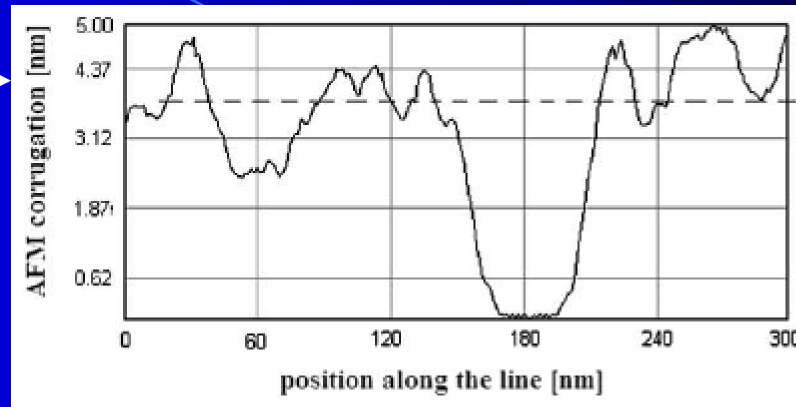
Covalently linked by using Ethylene-Glycol carboxyl terminated alkyl Thiols

Ethylene-glycol Mono-layers

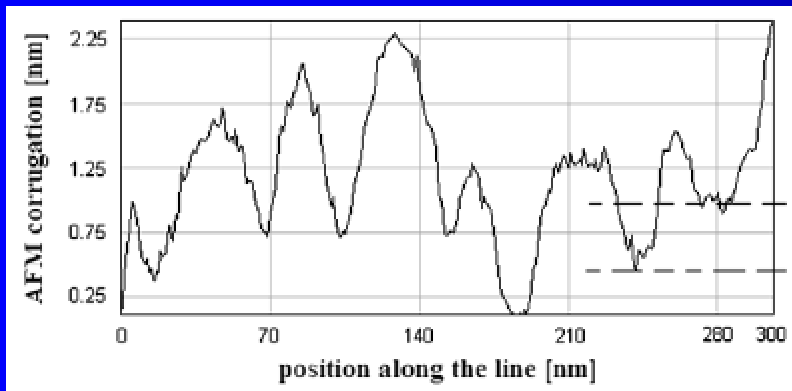
S. Carrara et al./Surface Science xxx (2009) xxx–xxx

Non-EG

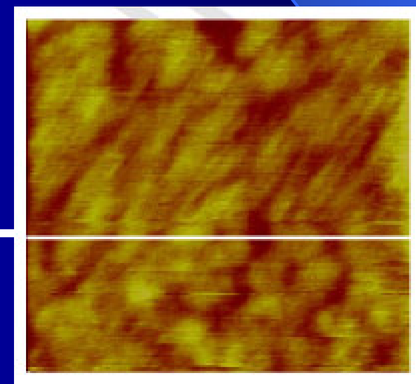




3.75 nm



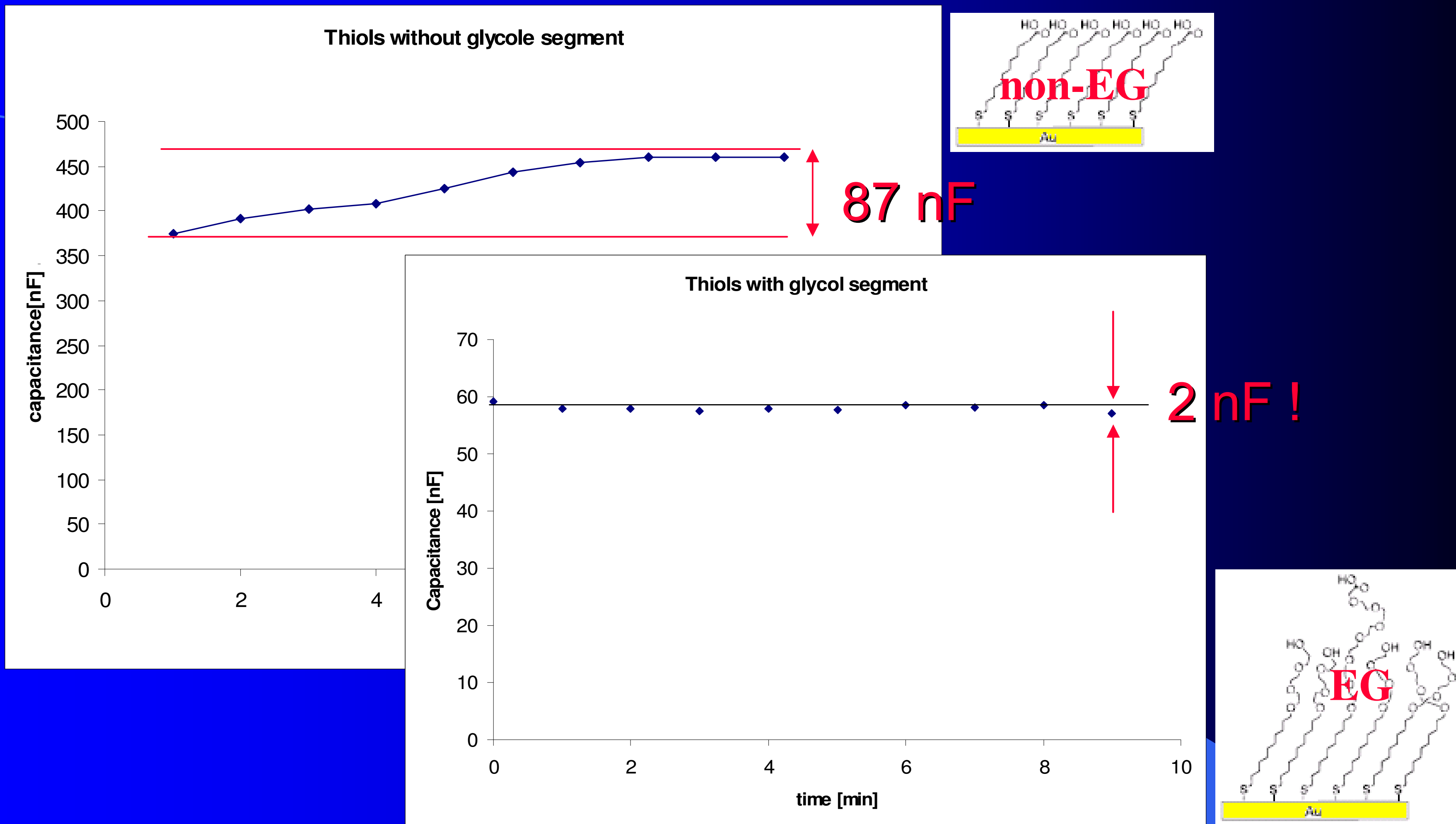
0.5 nm



EG

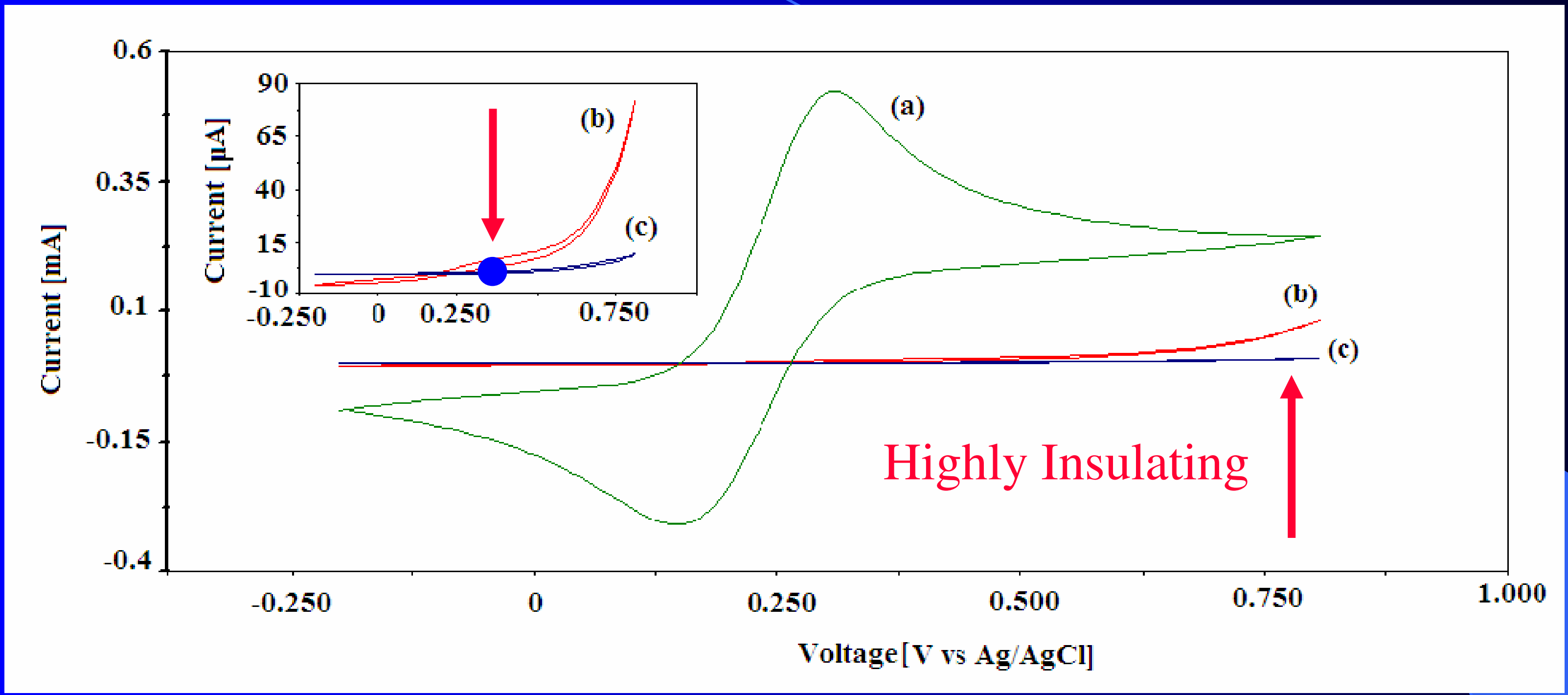
Monolayer of alkanethiols with ethylene-glycol chains does not present deep groves crossing the film

Improved Capacitance Stability



Increased stability by using Ethylene-Glycol thiols

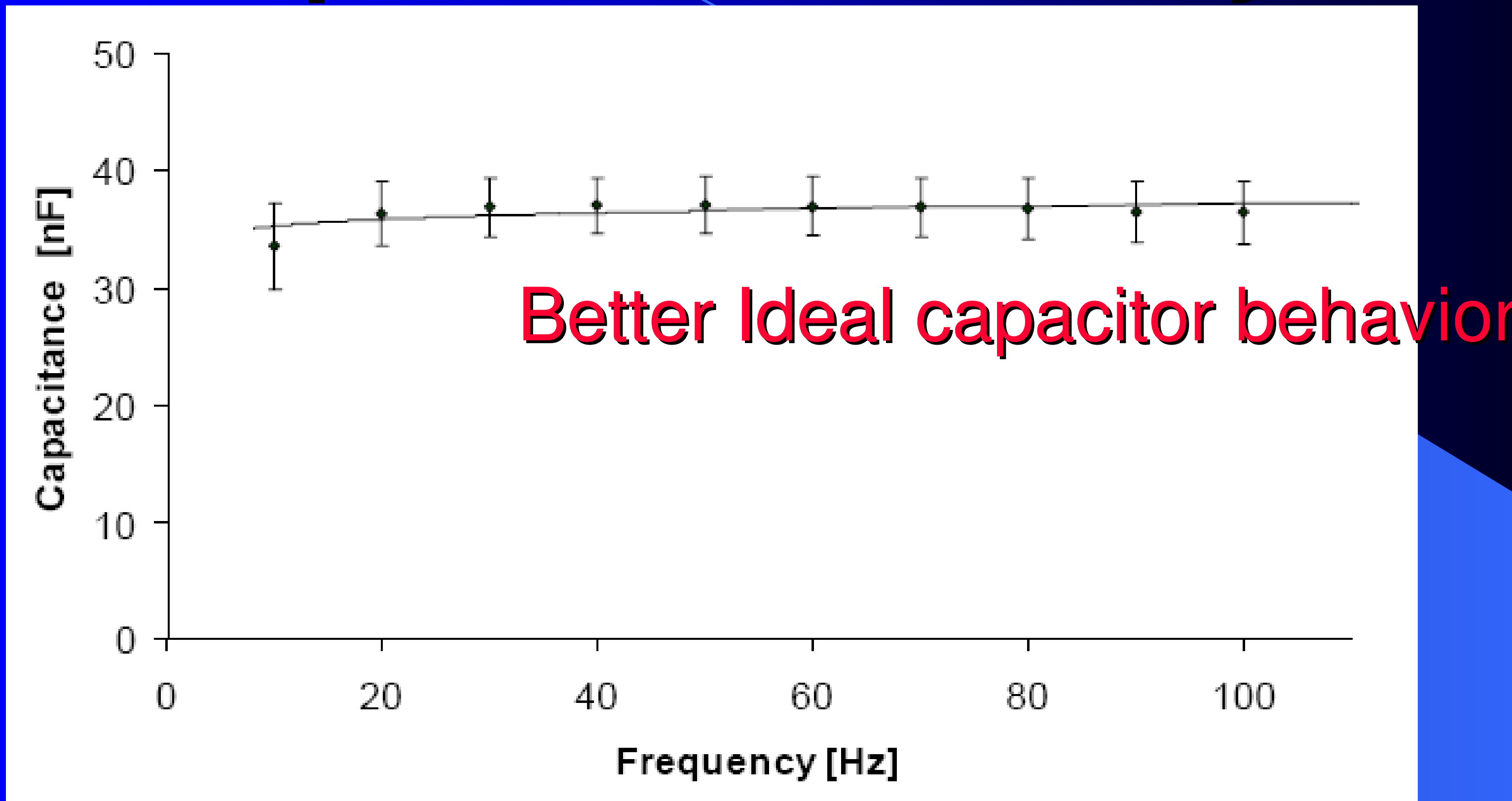
Improved insulating behavior



S. Carrara et al. / Sensors and Actuators B 136 (2009) 163–172

Redox reaction of K3Fe(CN)6 on gold electrode (a), non-EG-thiols film (b) and EG-thiols film (c)

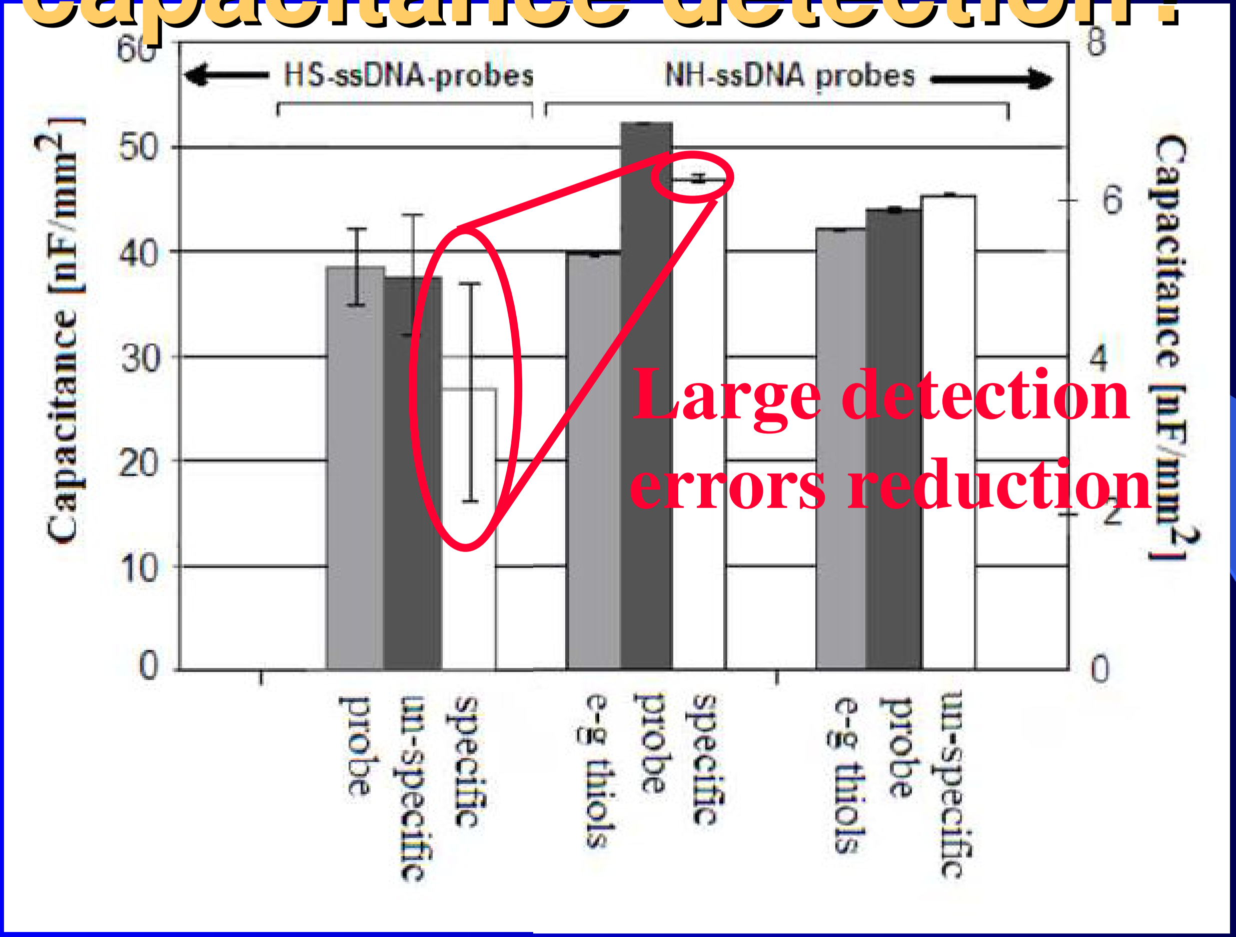
Improved DNA array



S.Carrara et al. / Sensors & Transducers Journal 88 (2008) 31-39

Capacitance vs frequency of NH_2-terminated ss-DNA immobilized onto EG-Thiols precursor layer

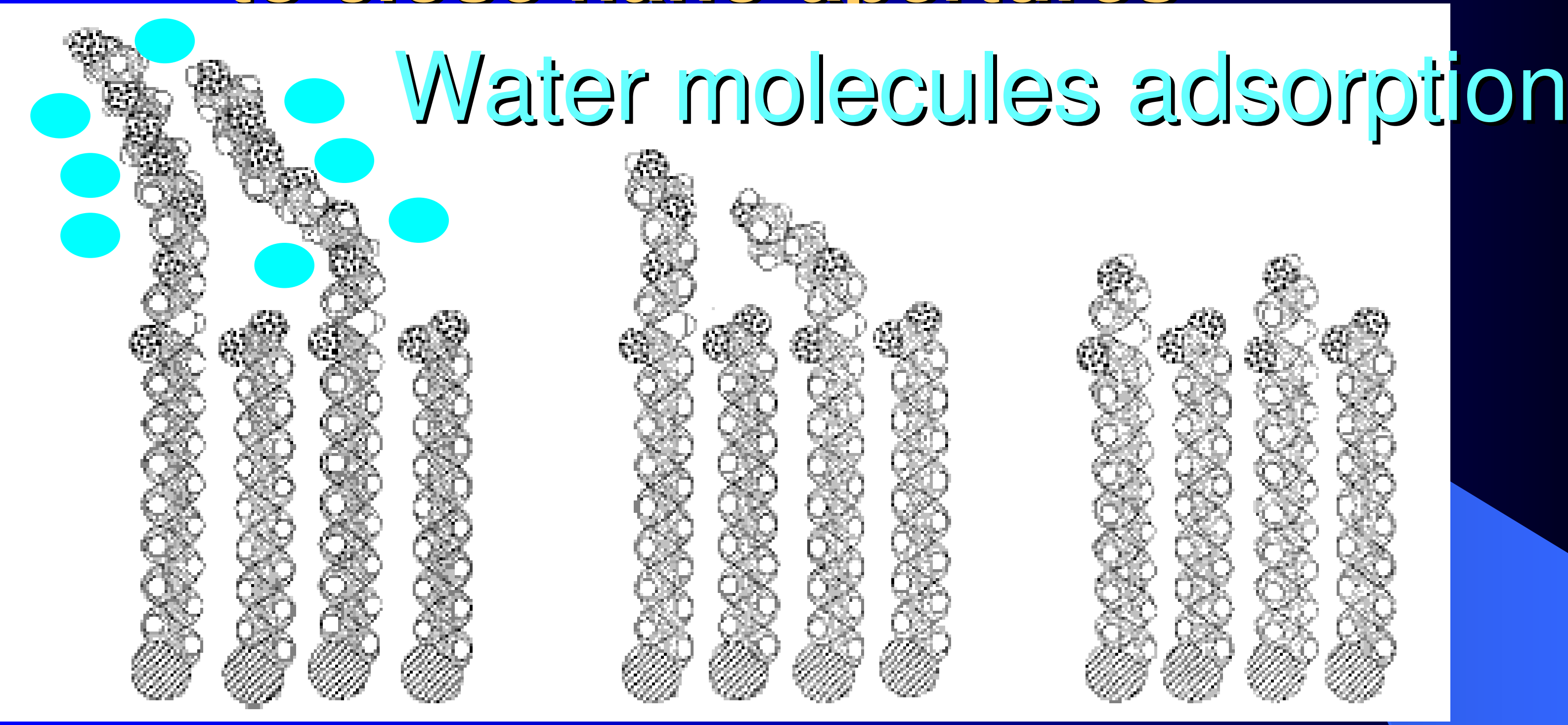
Why the EG-Thiols improve the capacitance detection?



S. Carrara et al. / Biosensors and Bioelectronics xxx (2008) xxx–xxx

DNA detection based on ss-DNA-SH terminated directly immobilized onto gold and ss-DNA-NH_2 terminated immobilized onto EG-Thiols

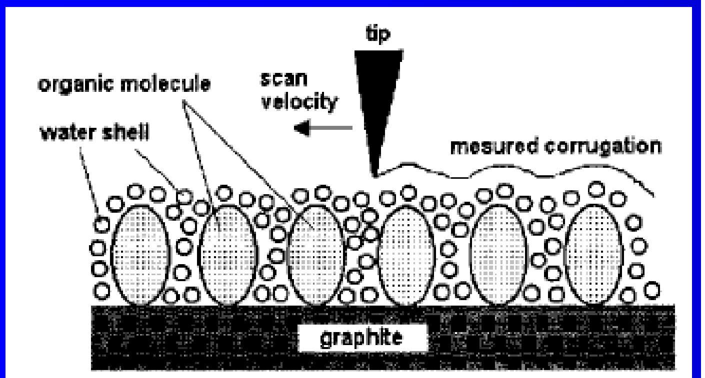
Space filling of the EG thiols to close nano-apertures



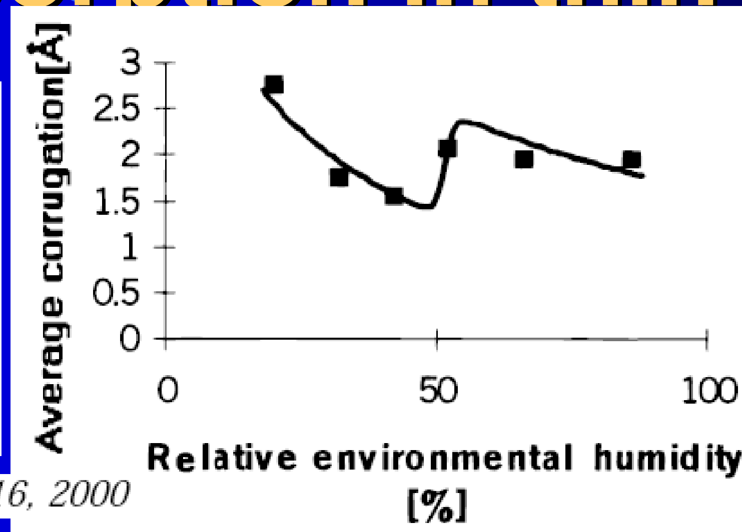
Chapman et al./ Langmuir, Vol. 16, No. 17, 2000

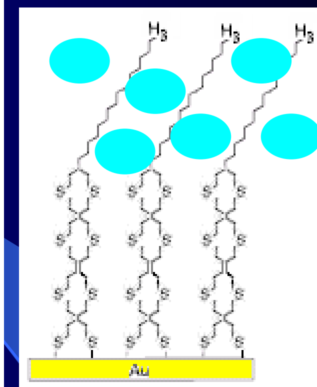
Space filling molecular model illustration of EG-thiols film presenting a 1:1 mixture of -CON(CH2CH2O)*n*H (*n*) 1, 3, or 6) and O2H/CO2- groups.

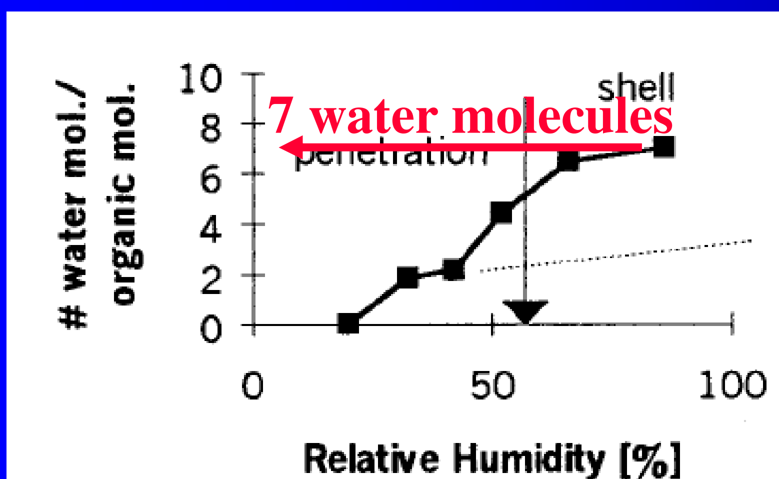
Water Adsorption in thin films

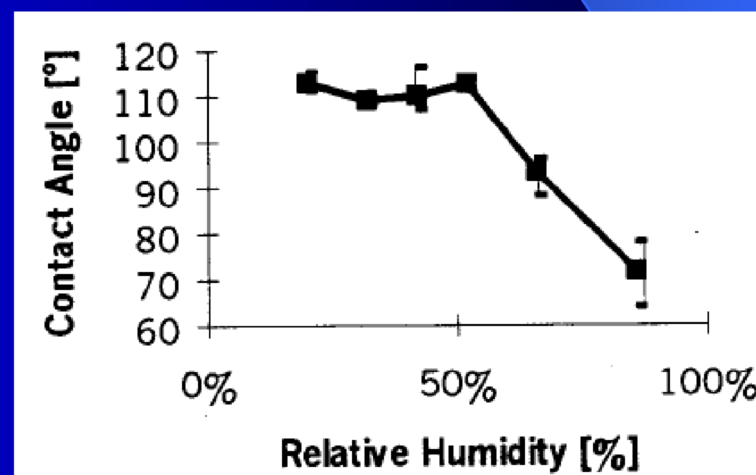


Carrara et al. / Langmuir, Vol. 16, No. 16, 2000



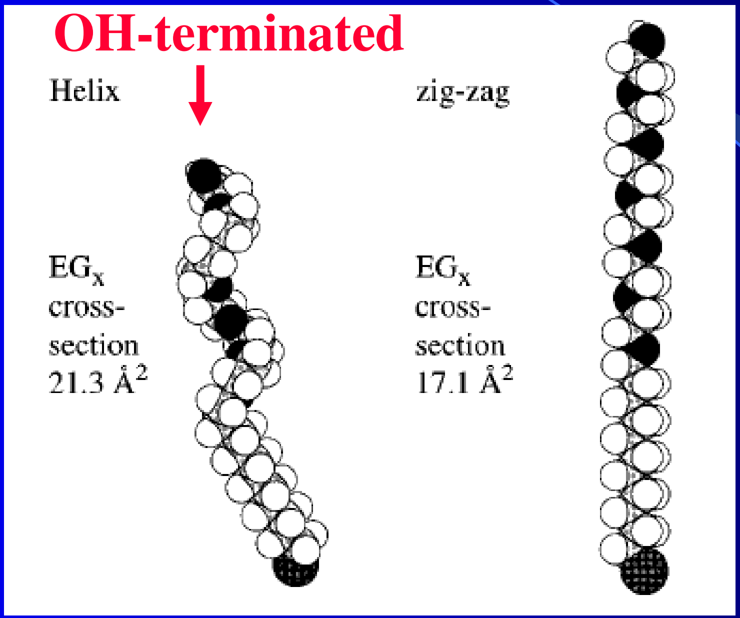






Film Water adsorption on alkyl thiol film chains

Water Adsorption in thin films

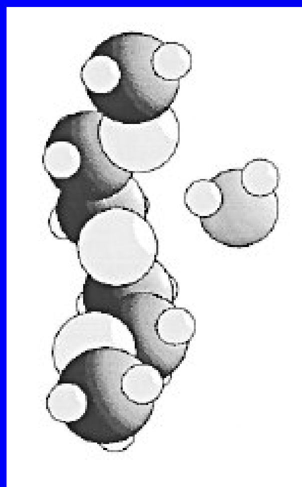


Harder et al. / *J. Phys. Chem. B, Vol. 102, No. 2, 1998*

Infrared spectroscopy demonstrates that ethylene-glycol chains in the methoxy-terminated monolayer are mainly in great disorder, while the hydroxyl-terminated monolayer chains are in a crystalline helical phase (Harder et al 1998)

Molecular conformations driven by terminal groups in EG-thiols

Water Adsorption in thin films



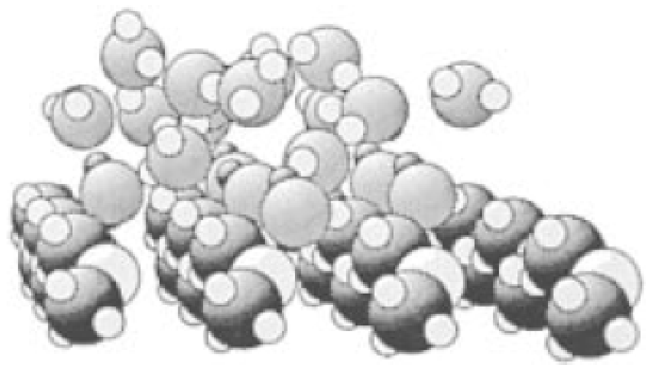
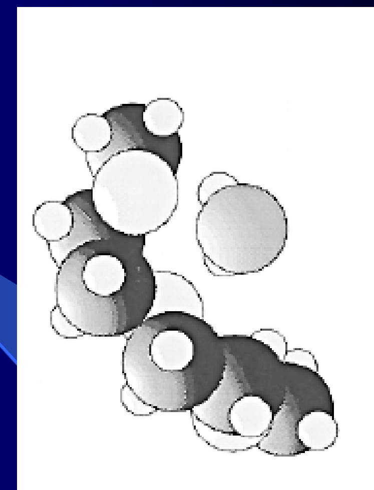


Figure 7. 20 water molecules form three adsorption layers on a hexagonal cluster of a helical OEG film with lattice constant 5 Å consisting of 3 × 4 helical OEG strands.

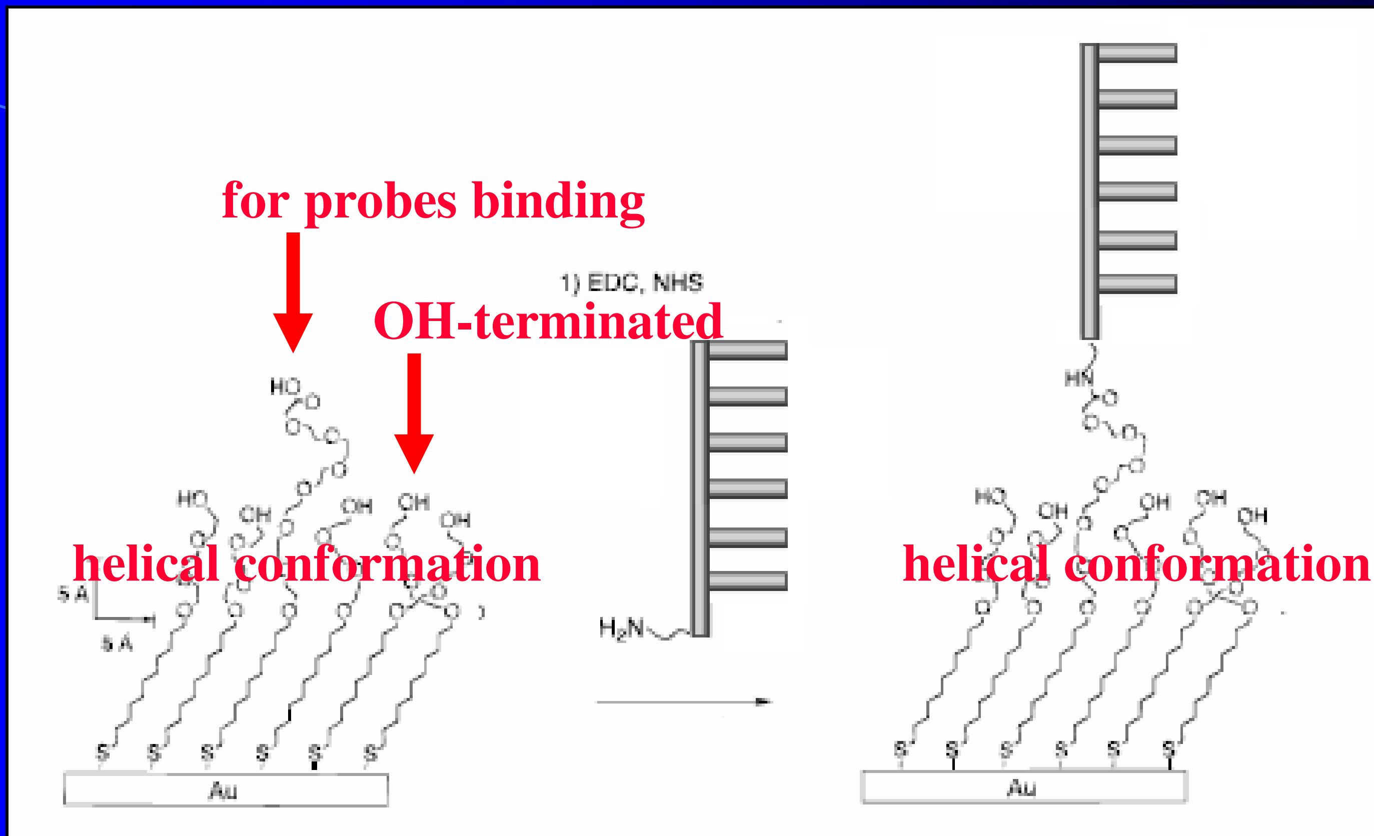


Wang et al. / *J. Phys. Chem. B, Vol. 101, No. 47, 1997*

We conclude the following: OEG in its helical conformation, but not in its "all-trans" form, is amphiphilic with respect to water. The stability of the water interface with helical OEG prevents proteins and other molecules from adsorbing irreversibly on the OEG surface.

Water adsorption and Molecular conformation in EG-thiols Film

Water Adsorption in thin films



Covalently linked by using three-glycol carboxyl terminated alkyl Thiols

Water Adsorption in thin films

Mass change	# of water molecules/EG-molecules
0,14 ng/mm^2	16

The estimated mass changing correspond to 16 water molecules each ethylene-glycol alkanethiol. Up to 7 water molecules for each organic molecules may be fund in dried alkyl chains film (Carrara et al. 2000). The other water molecules are strongly coordinated by ethylene-glycol chains in our film

S. Carrara et al. / Biosensors and Bioelectronics xxx (2008) xxx–xxx

QCM measurements on dried EG-thiols film conditioned with water buffer

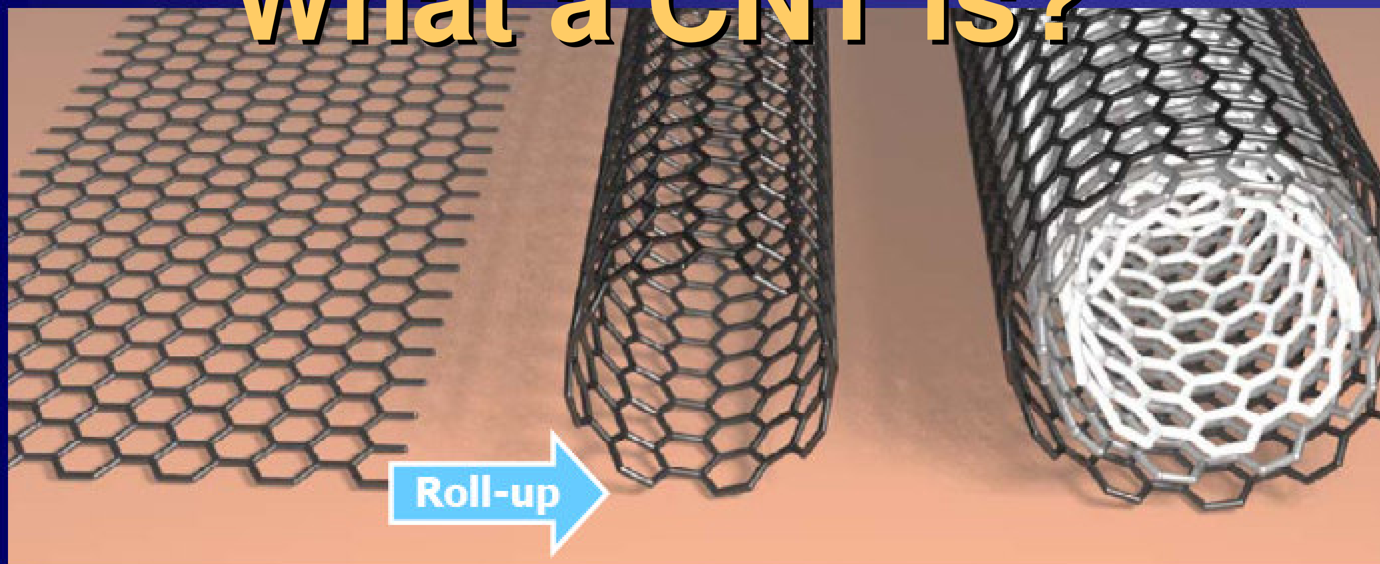
Examples of Nano-Bio-sensing?

- Antibodies and DNA biosensors enhanced by 1D nanostructures.
- Enzymes biosensors enhanced by 2D nanostructures.
- Enzymes biosensors enhanced by 3D nanostructures.

2-D Nanostructures for Enzymes bio-sensing

- Surface Polarization
- Surface charging
- Electron Transfer Efficiency

What a CNT is?

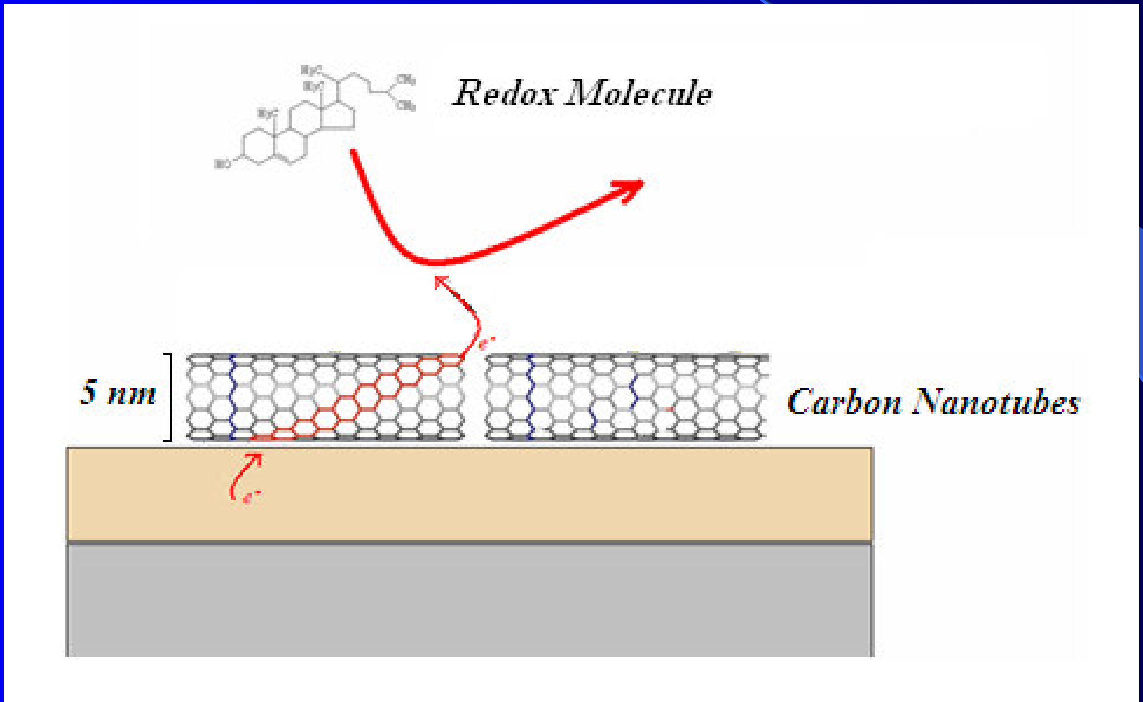


Graphene (sp² hybridized) | Single-Walled Nanotube (SWCNT) | Multi-Walled Nanotube (MWCNT)

Courtesy: K. Banerjee/California Univ.

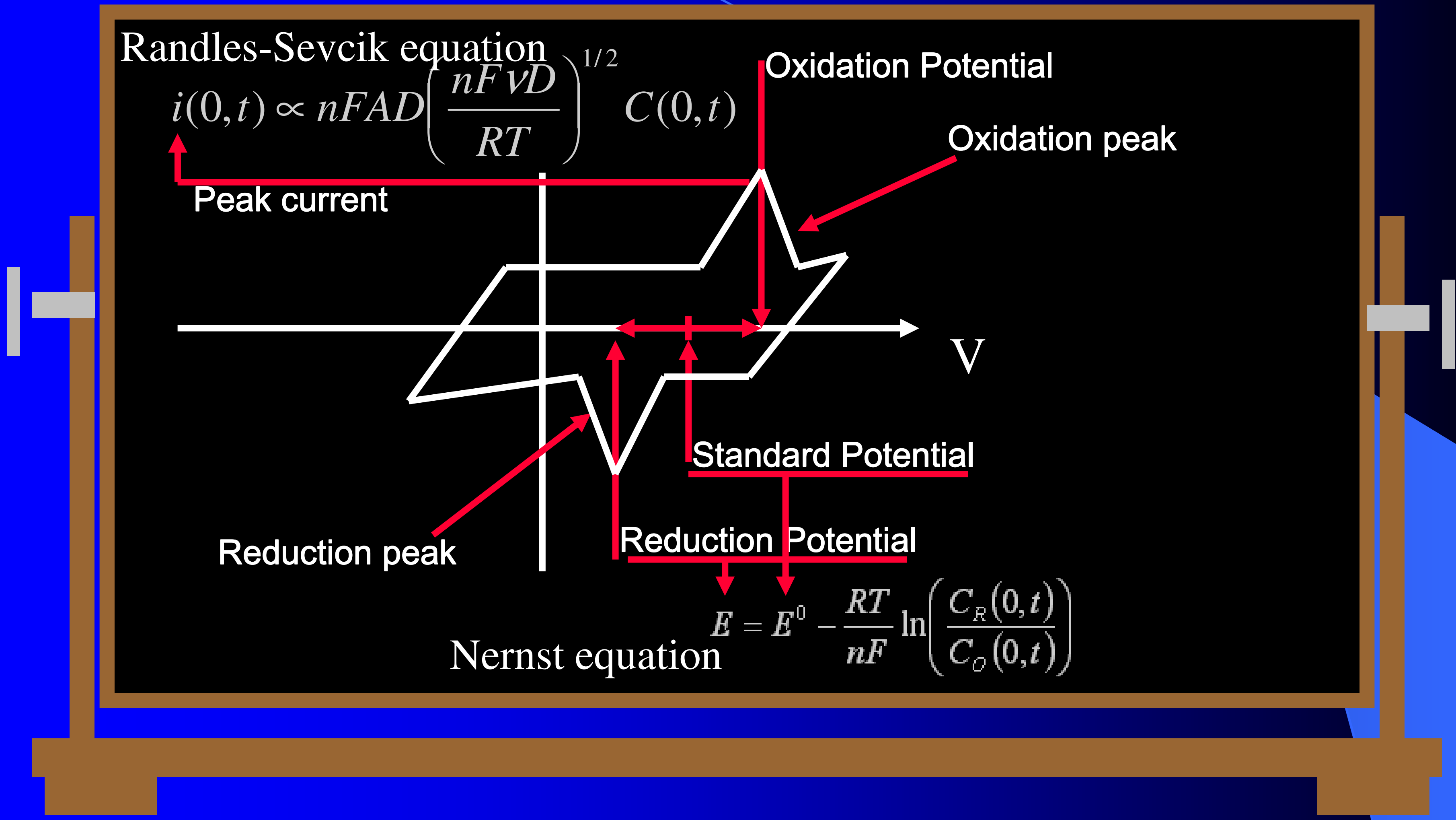
	Cu	SWCNT	MWCNT
Max current density (A/cm^2)	<1x10^7	>1x10^9 Radosavljevic, et al., *Phys. Rev. B*, 2001	
Thermal conductivity (W/mK)	385	5800 Hone, et al., *Phys. Rev. B*, 1999	3000 Kim, et al., *Phys. Rev. Let.*, 2001
Mean free path (nm) @ room temp	40	>1,000 McEuen, et al., *Trans. Nano.*, 2002	25,000 Li, et al., *Phys. Rev. Let.*, 2005

Electron Transfer Mediated by 2D nanostructures

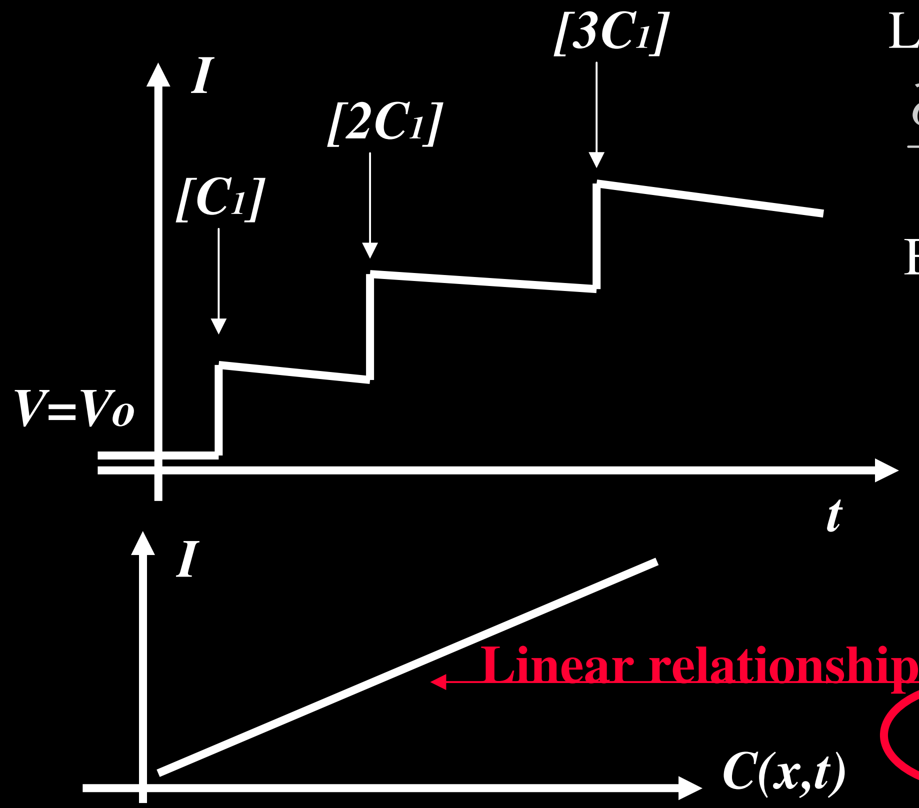


Carbon Nanotubes may be used in Electrochemical Interfaces

Redox reactions from Voltammetry



Redox reactions from Amperometry



Linear diffusion equation

$$\frac{\partial C(x,t)}{\partial t} = D\frac{\partial^2 C(x,t)}{\partial x^2}$$

Boundary conditions

$$\begin{cases} C(x,0) = C_o \\ \lim_{x\to\infty} C(x,t) = C_o \\ C(0,t) = 0, t \to \infty \end{cases}$$

Cottrell equation

$$i(x,t) = \frac{nFAD^{1/2}C(x,t)}{\pi^{1/2}t^{1/2}}$$

Carbon Nanotubes contribute to Redox Reactions Efficiency

Nernst equation

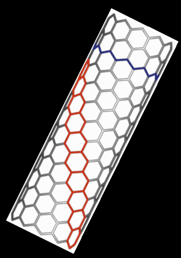
$$E = E^0 - \frac{RT}{nF}\ln\left(\frac{C_R(0,t)}{C_O(0,t)}\right)$$

Randles-Sevcik equation

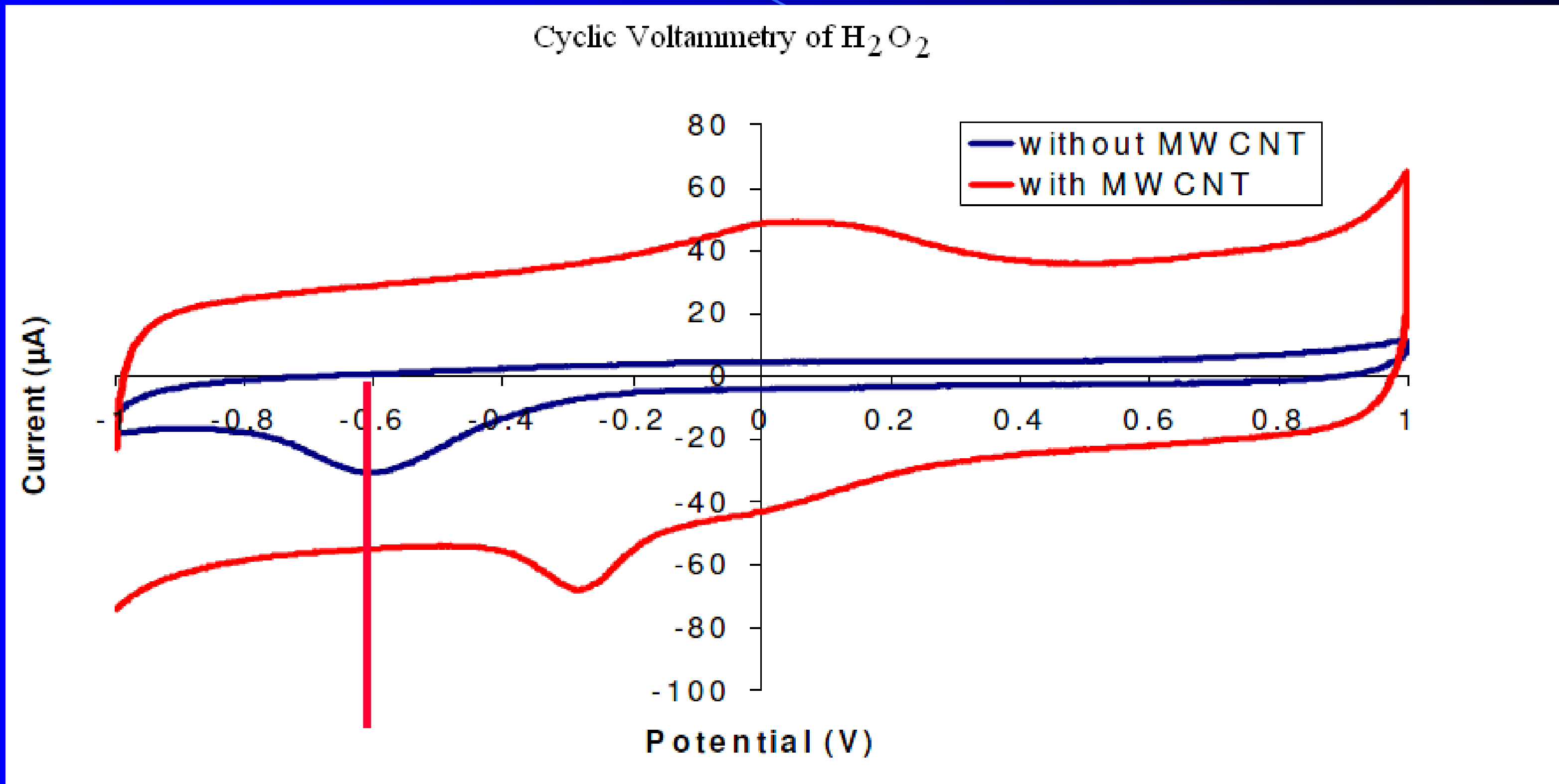
$$i(0,t) \propto nFAD\left(\frac{nF\nu D}{RT}\right)^{1/2} C(0,t)$$

Cottrell equation

$$i(x,t) = \frac{nFAD^{1/2}C(x,t)}{\pi^{1/2}t^{1/2}}$$

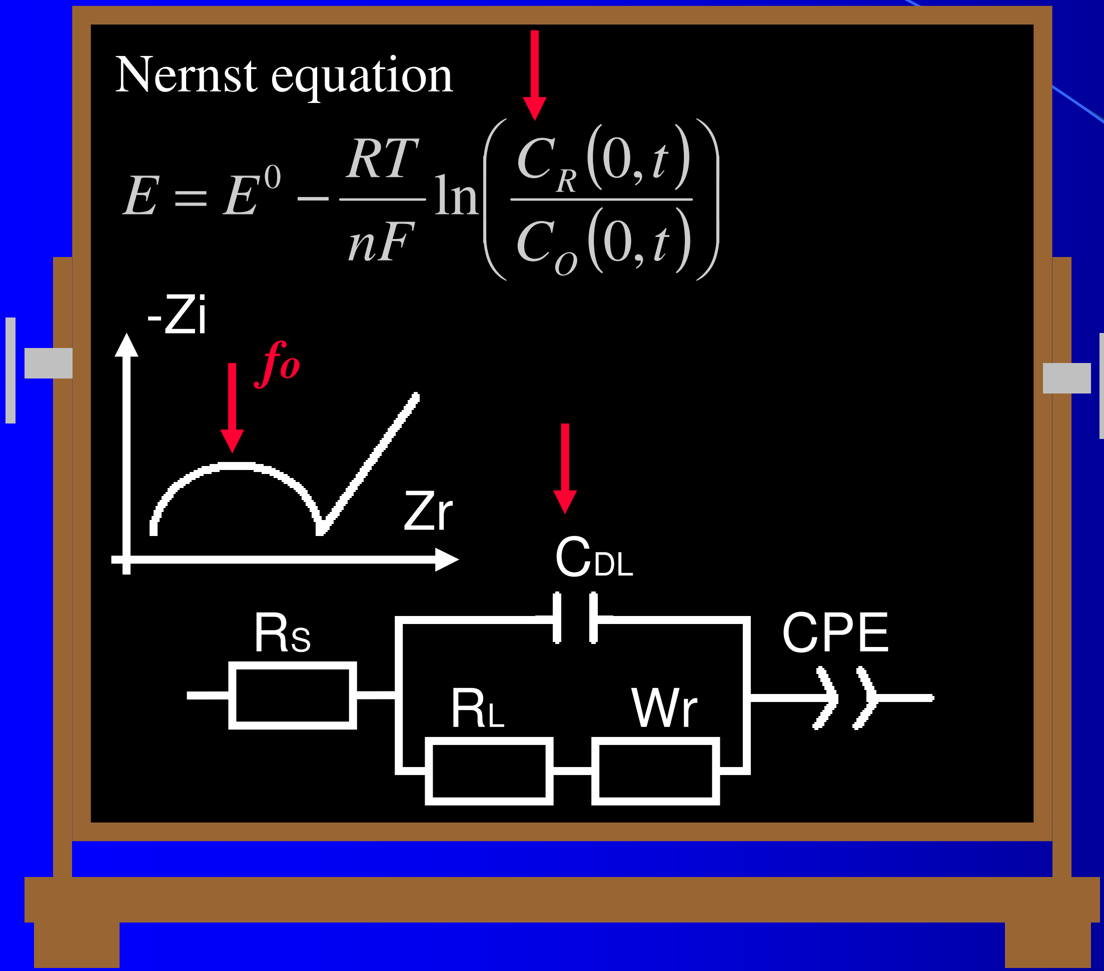


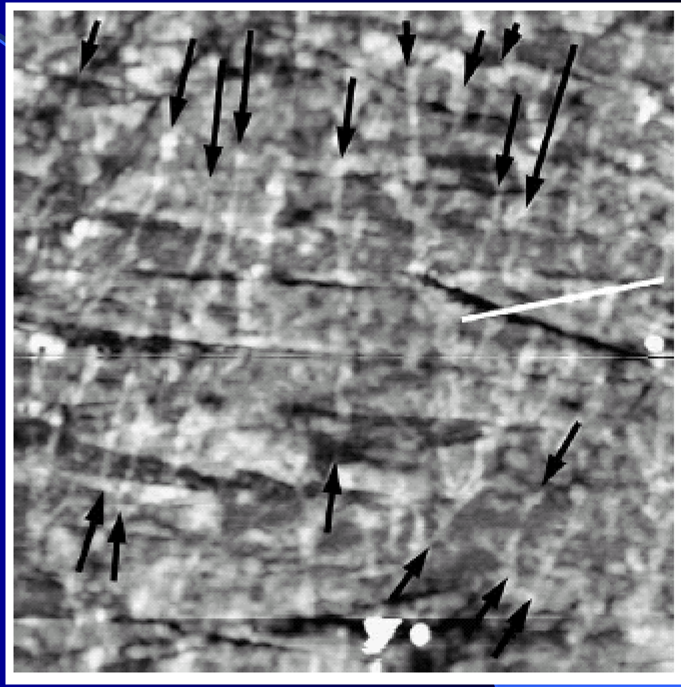
Nernst Effect on Electrochemical H_2O_2 detection with Nano-structured Electrodes



The peak potential is shifted toward lower potentials in case of electrons-transfer is mediated by carbon nanotubes

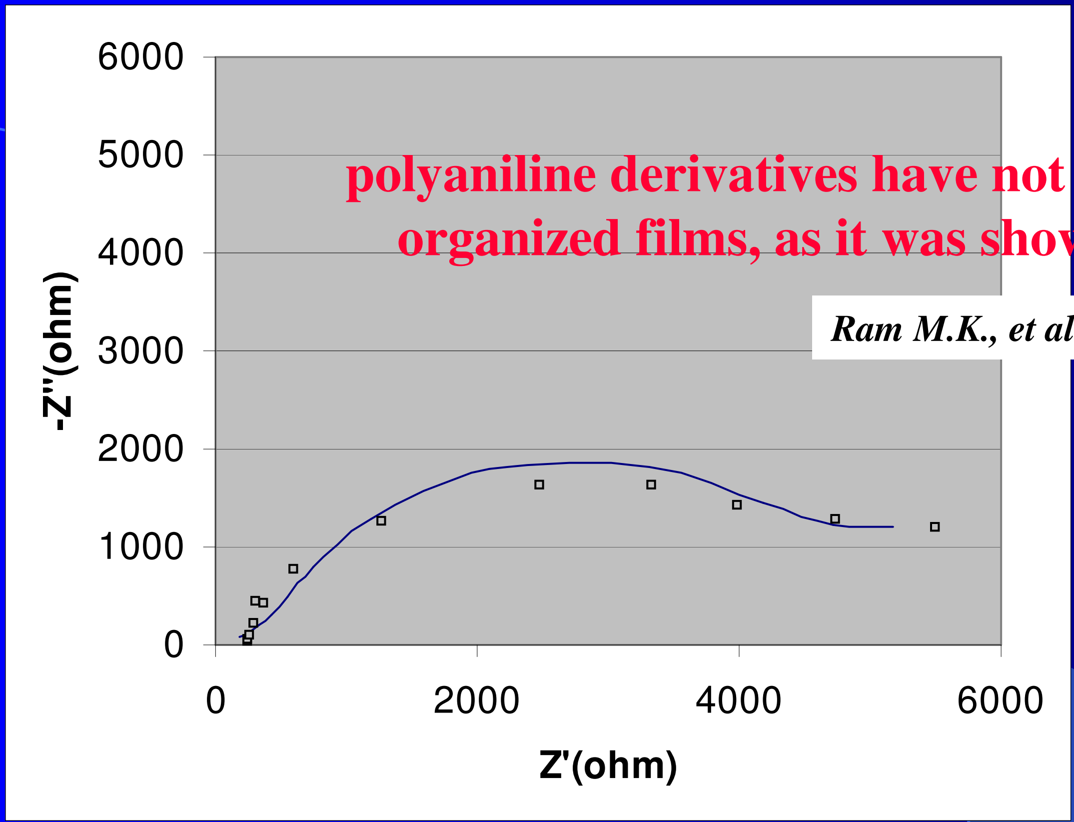
Carbon nanotubes contributions to Surface Concentration and Layering





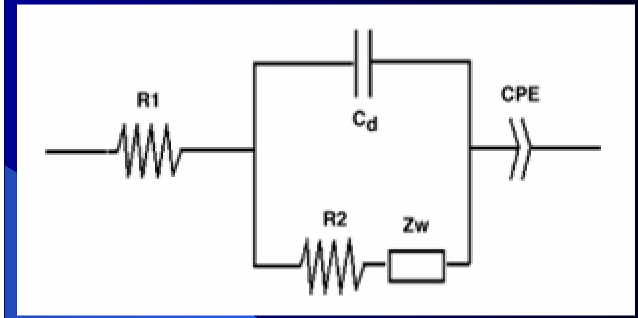
S. Carrara et al. / Sensors and Actuators B 109 (2005) 221–226

Poly-(ortho)-anisidine (POAS)



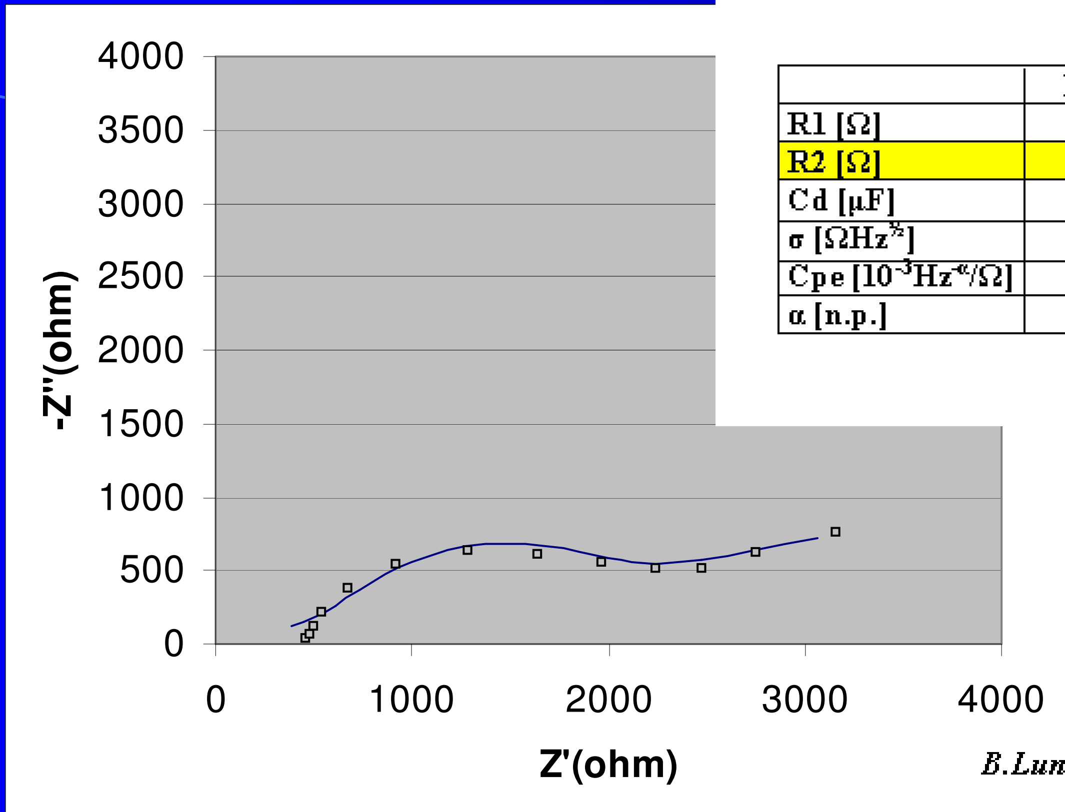
polyaniline derivatives have not the tendency to form well organized films, as it was shown by AFM microscopy

Ram M.K., et al., Synthetic Metals 100(1999) 249-259



Nyquist impedance diagram of a POAS film. Experimental data are showed by boxes. Data are acquired in the frequency range from 100 mHz up to 1KHz. The solid line shows the best fitting

Conducting Polymer + Carbon Particles



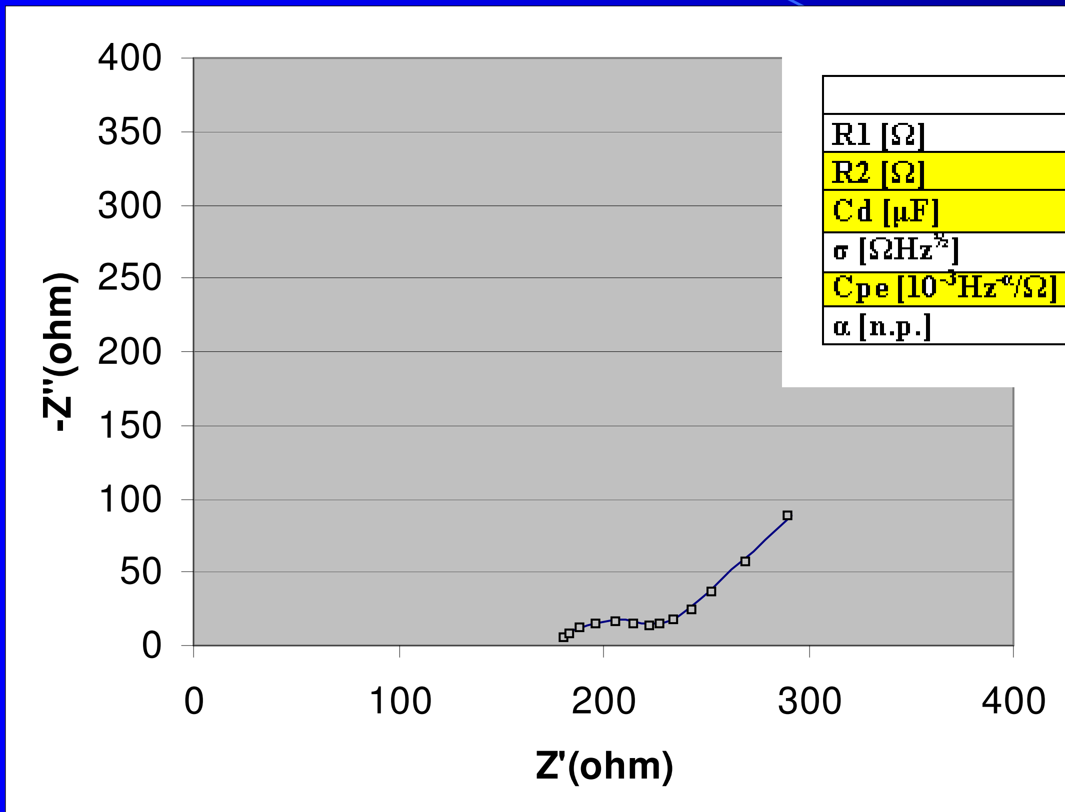
	POAS	POAS+CB
R1 [Ω]	46	64
R2 [Ω]	3165	869
Cd [μF]	32.7	23.3
σ [$\Omega Hz^{½}$]	353	252
Cpe [$10^{-3} Hz^{\alpha}/\Omega$]	0.57	0.49
α [n.p.]	0.298	0.207

Charge transfer resistance coherently decreases with the Lundberg Theory of conducting mixtures

B.Lundberg, B.Sundqvist / J.Appl.Phys 60 (1986) 1074-1079

Nyquist impedance diagram of a POAS film. Experimental data are showed by boxes. Data are acquired in the frequency range from 1KHz down to 100mHz. The solid line shows the best fitting

Conducting Polymer + Multi Walled CNTs



	POAS	POAS+NT
R1 [Ω]	46	173
R2 [Ω]	3165	50
Cd [μF]	32.7	117.1
σ [$\Omega Hz^{1/2}$]	353	215
Cpe [$10^{-3} Hz^{-\alpha}/\Omega$]	0.57	11.68
α [n.p.]	0.298	.575

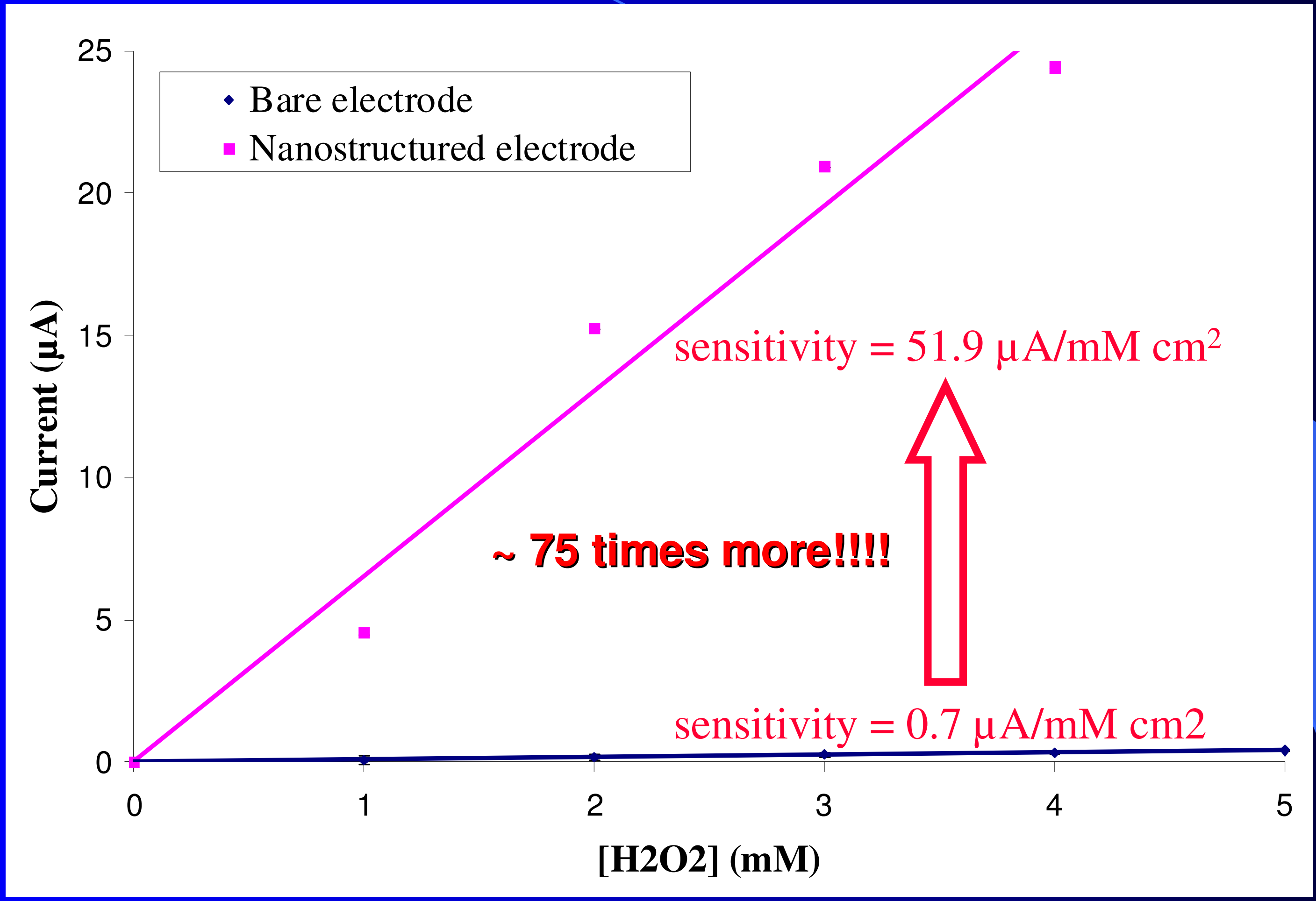
S.Carrara et al., Sensors and Actuators B: Chemicals 109 (2005) 221-226

Pure electrostatic attraction in the double layer and faradic reaction are responsible for the super-capacitance phenomena in Carbon Nanotube structures

Pan et al., Chem. Mater., Vol. 19, No. 25, 2007

- Nyquist impedance diagrams of a POAS film synthesized with Carbon Nanotubes. Experimental data are showed by boxes. Data are acquired in the frequency range from 1KHz down to 100 mHz. The solid line shows the best fitting

Cottrel Effects on H_2O_2 detection with Nano-structured Electrodes



Peroxide Detection

TABLE I

SENSITIVITY VALUES FROM LITERATURE

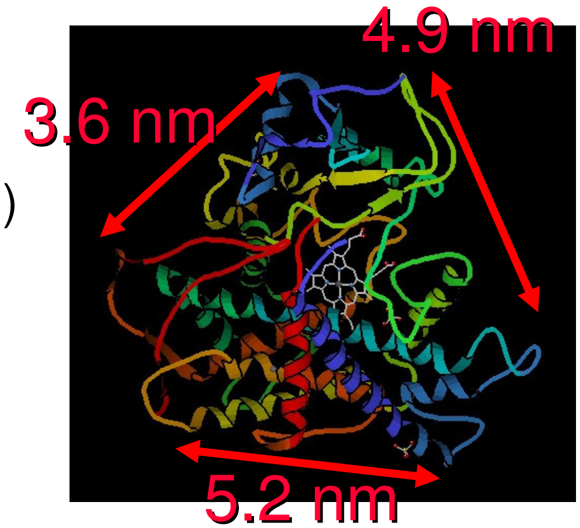
Methods	Sensitivity
Au-Nafion®- TNTs [11]	0.24 μA mM^{-1} cm^{-2}
Polypyrrole - polyanion/PEG [12]	0.[illegible]5 μA mM^{-1} cm^{-2}
MWCNT-chitosan [13]	8[illegible]3 μA mM^{-1} cm^{-2}
chitosan/PVI-Os/CNT [9]	19.7 μA mM^{-1} cm^{-2}

2 order of magnitude!!!

[9] X. Cui, *Biosensors and Bioelectronics*, vol. 22, pages 3288-3292, 2007
[11] M. Yang, *Nanotechnology*, vol. 19, page 075502, 2008
[12] W.J. Sung, *Sensors and Actuators B*, vol. 114, pages 164-169, 2006
[13] Y. Tsai, *Sensors and Actuators B*, vol. 125, pages 474-481, 2007

The peroxide detection is highly improved by using carbon nanotubes

P450 for Drugs Monitoring



RH (e.g. benzphetamine)

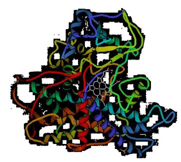
O_2

From electrode

$2e^-$

$NADPH + H^+$

Drugs detection !



Cytochrome
P450 2B4

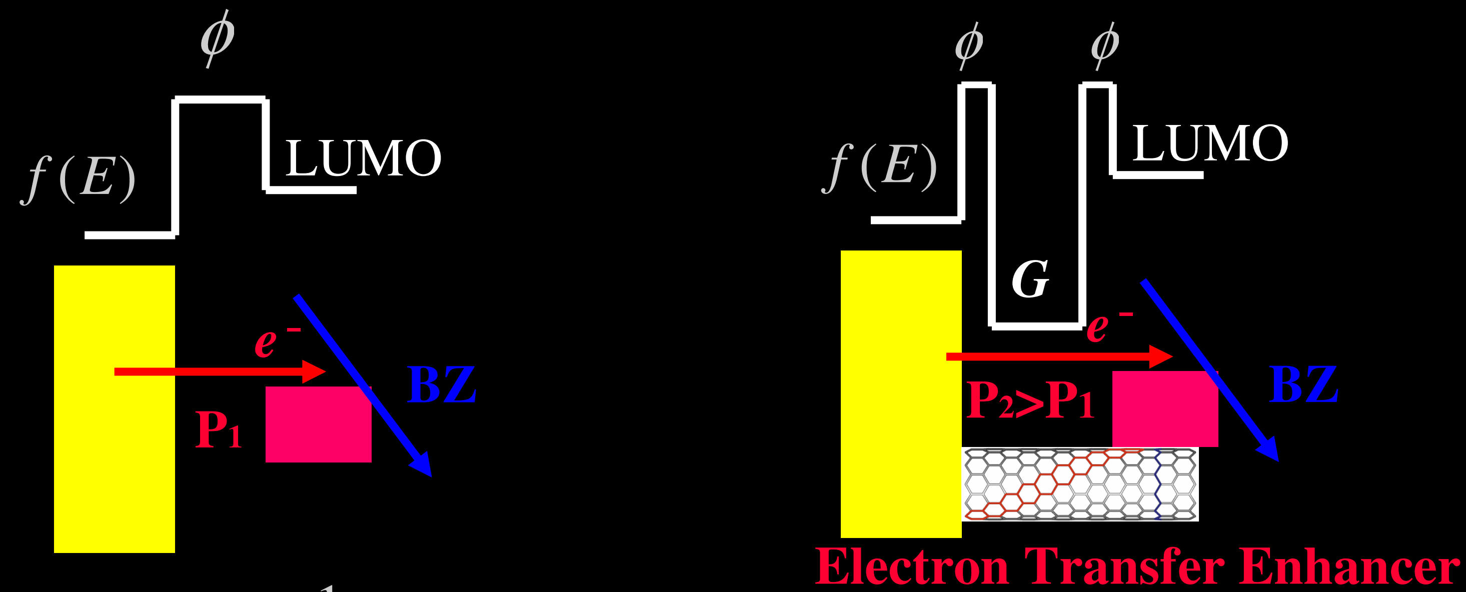
NADP

H-O-H

R-OH Oxidized form

more soluble
then
faster secreted

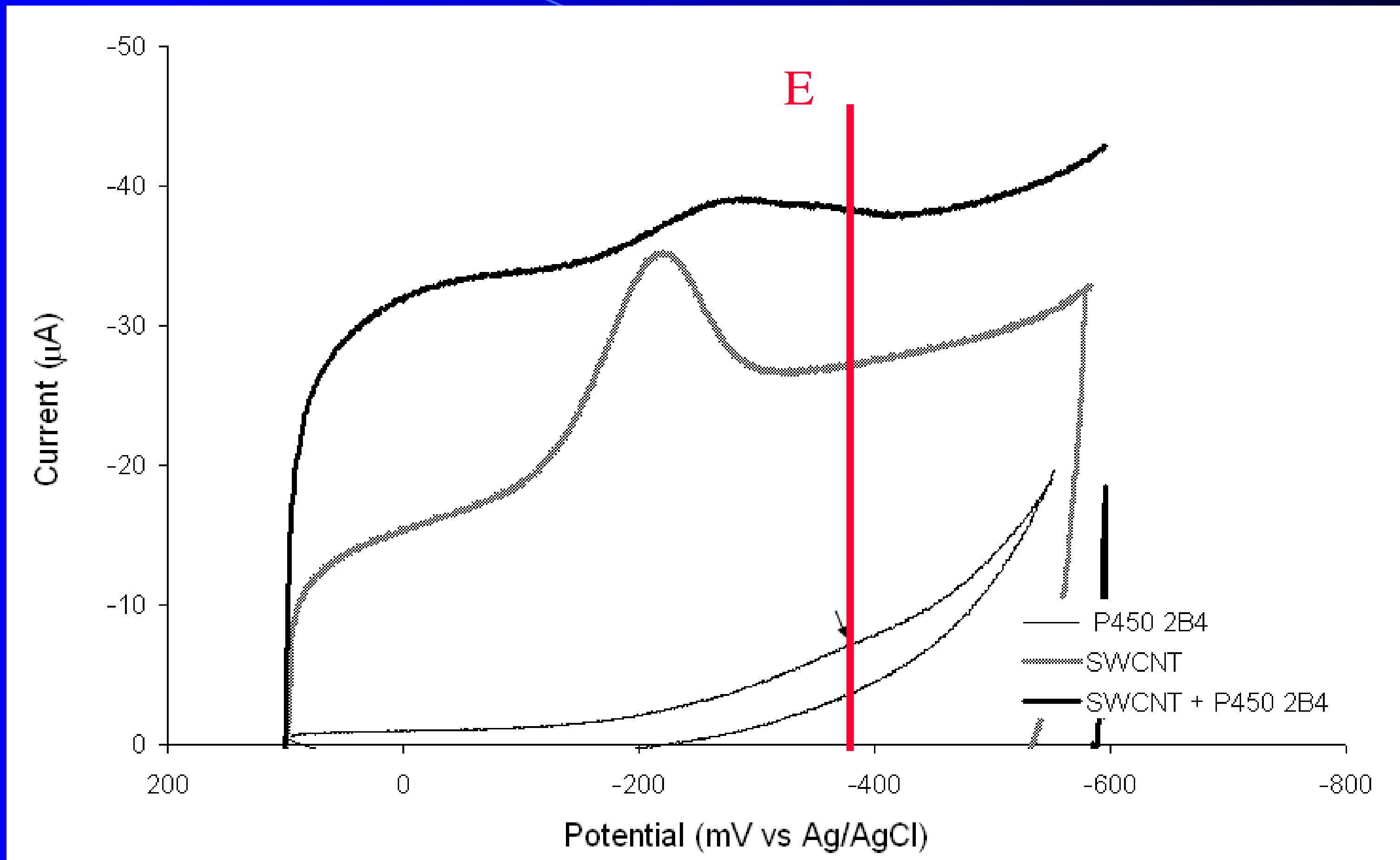
An improved P450/Electrode coupling by Ballistic Nanotubes



$$f(E) = \frac{1}{1 + e^{\frac{E - E_F}{K_B T}}}$$

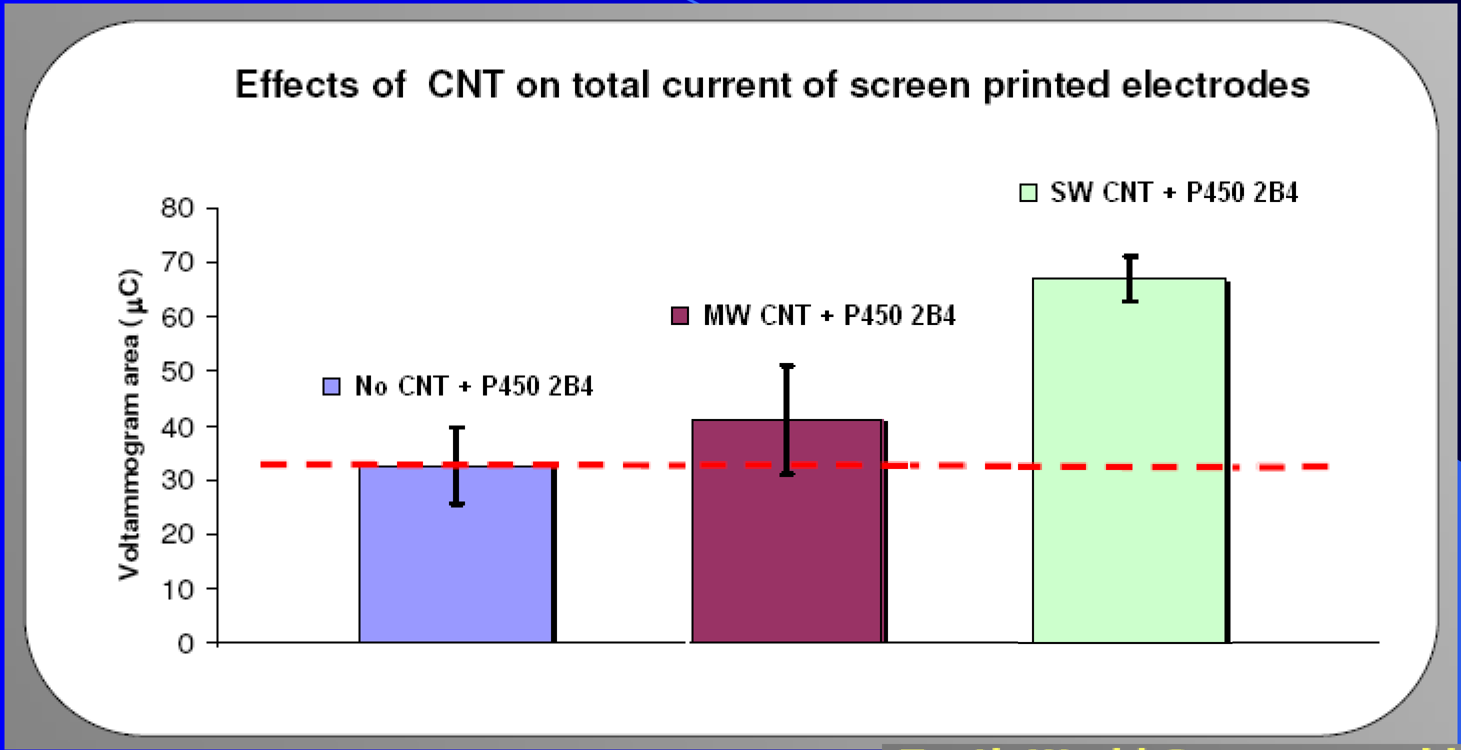
$$G = nG_0 = n\left(\frac{e^2}{2\hbar}\right)$$

Nernst Effect



A shift in the Peak Potential is observed when the P450 Activity is mediated by Single Walled Carbon Nanotubes

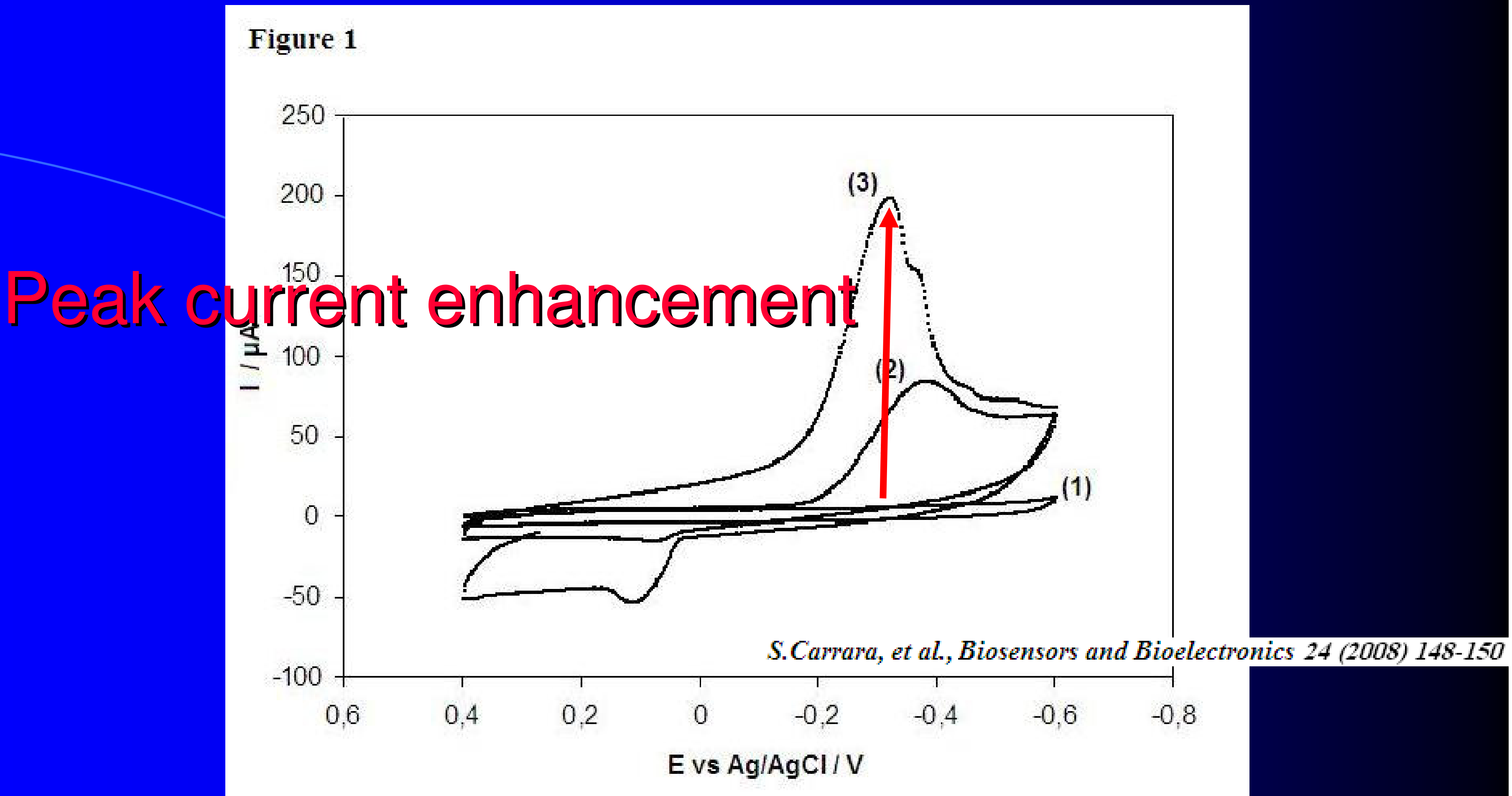
Layering affects total Charging



Tenth World Congress on biosensors
Shanghai – May 14,16 2008

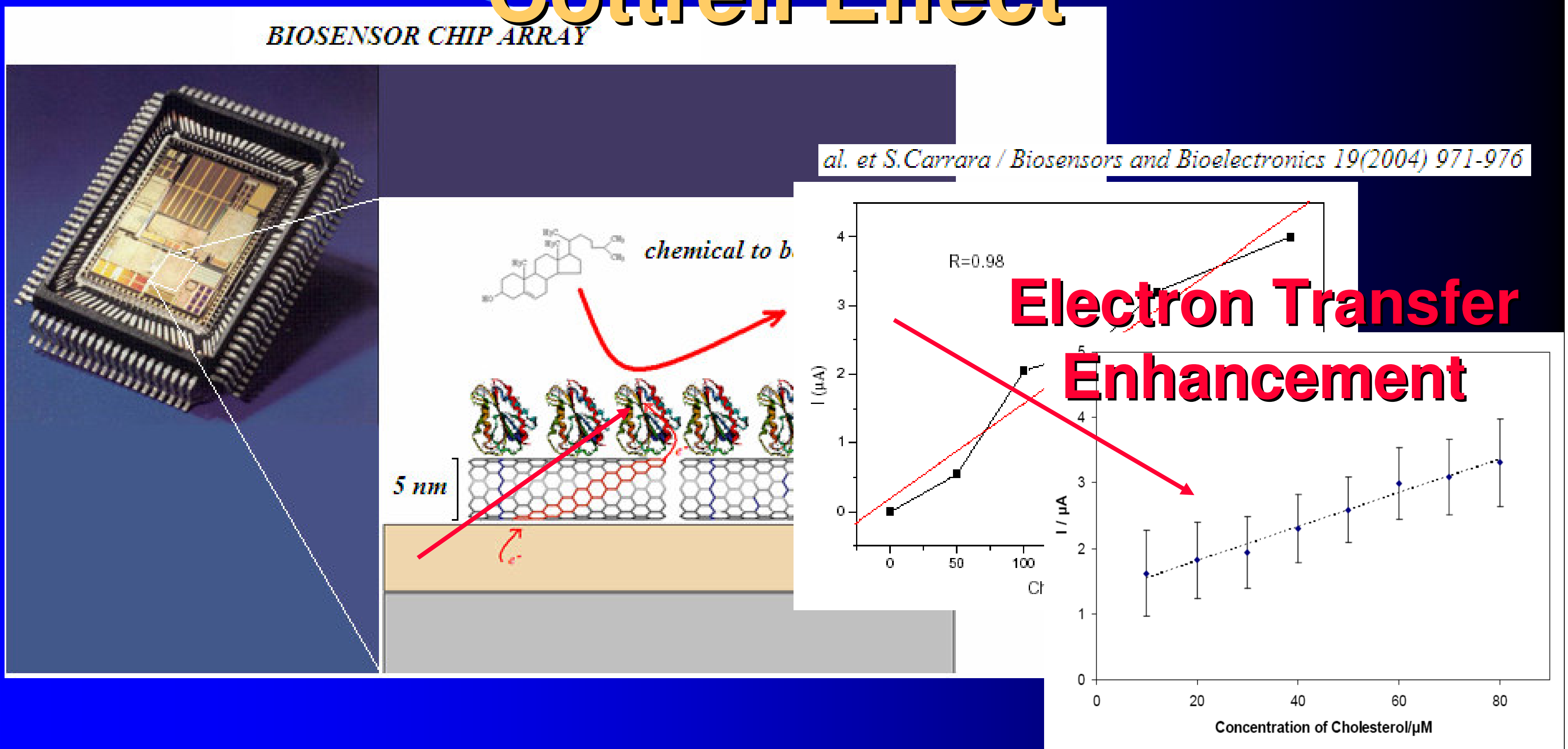
Different Total Charges as calculated from Cyclic Voltammetry with electrodes not structured and structured by using SW or MW Carbon Nanotubes

Randles Effect



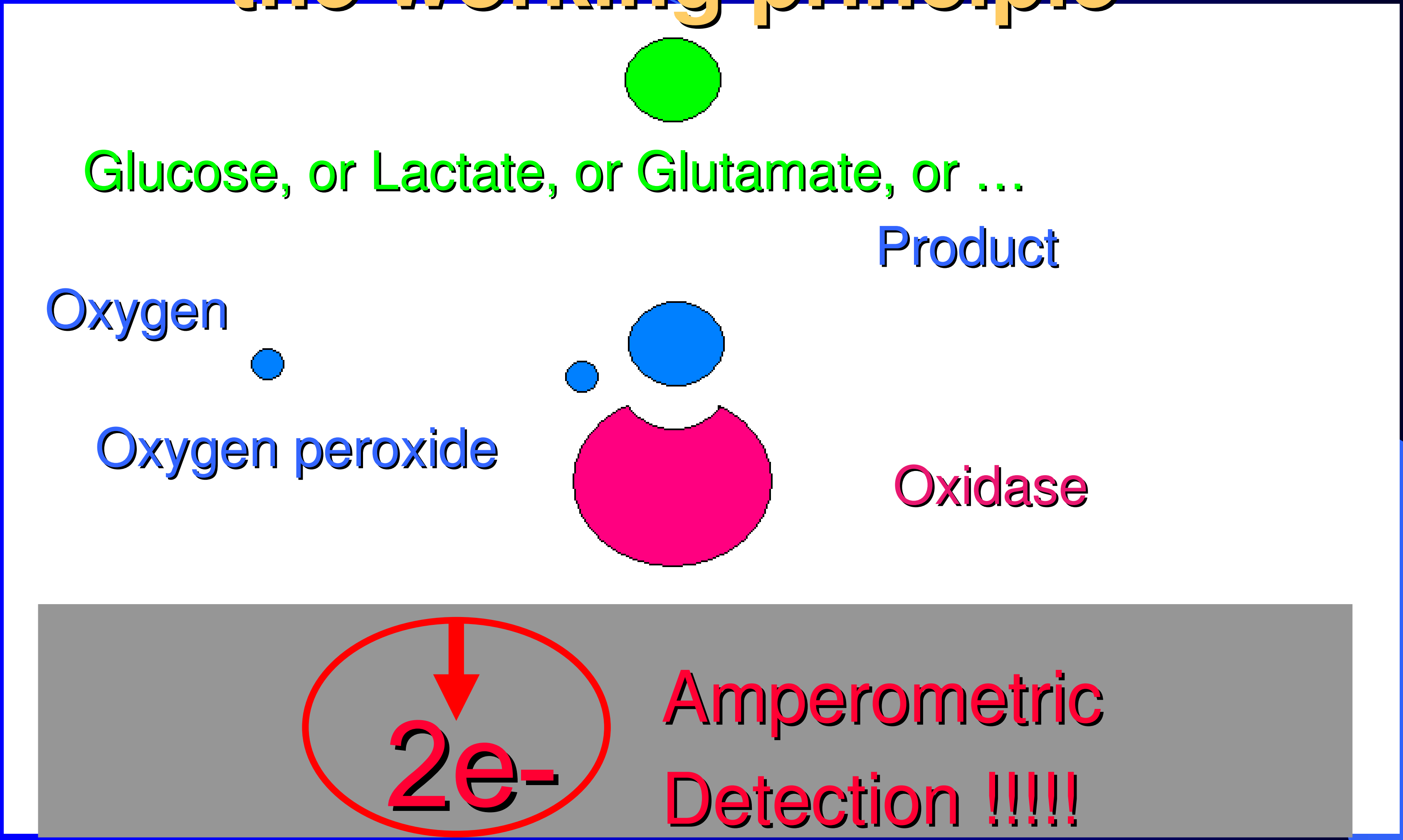
The Peak Current is larger when the P450 Activity is mediated by Multi Walled Carbon Nanotubes

Cottrell Effect

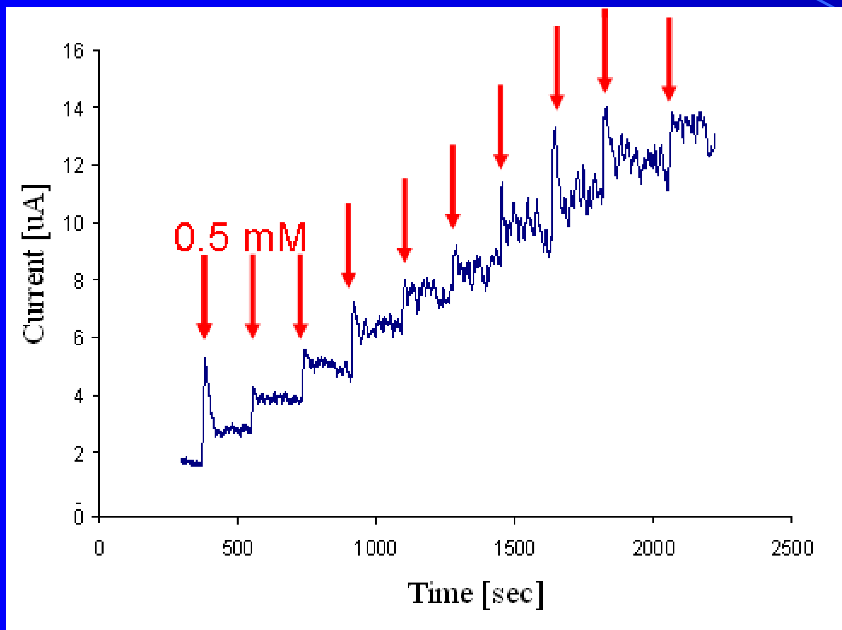


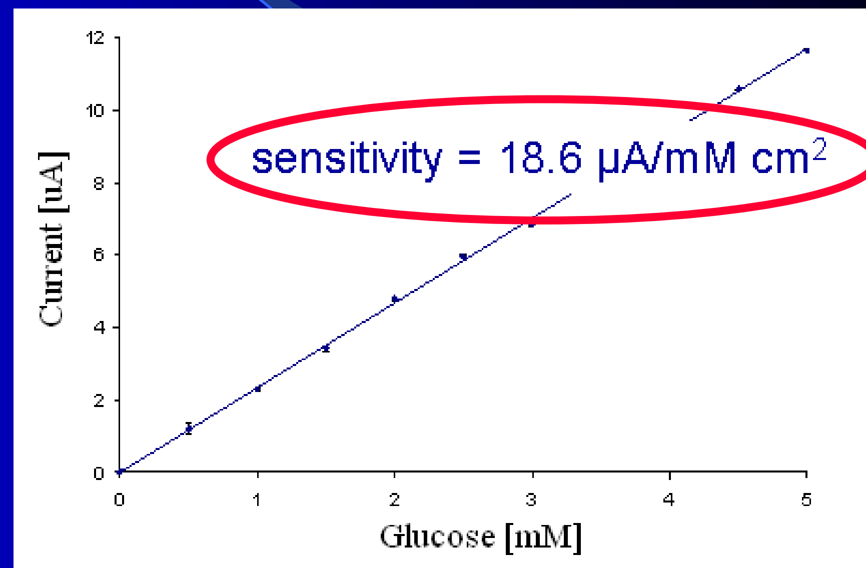
The Sensitivity is enhanced when the P450 Activity is mediated by Multi Walled Carbon Nanotubes

Oxidases based detection: the working principle



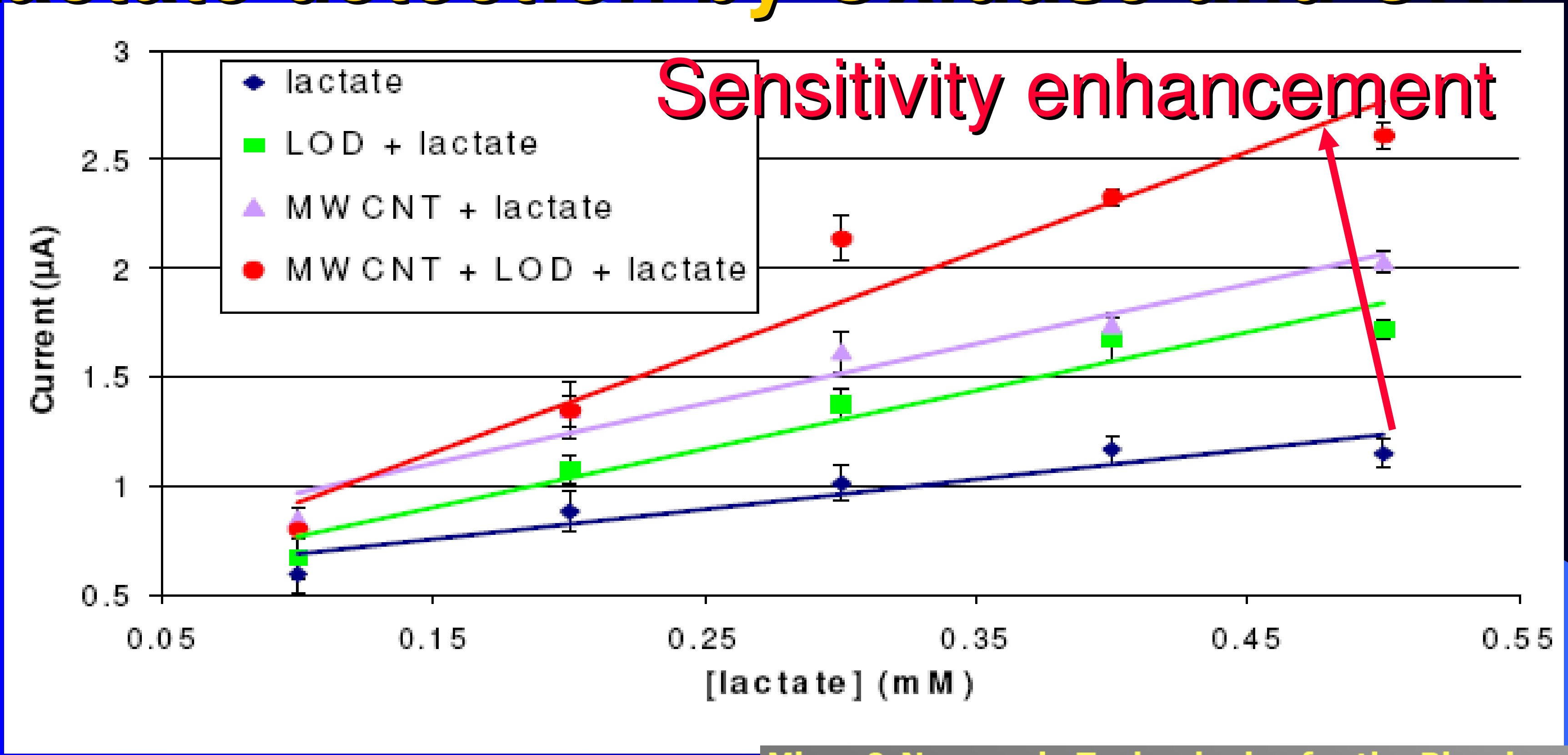
Glucose detection by Oxidase and CNT





Sensitivity Enhancement in Glucose detection by using GOD immobilized onto Multi Walled Carbon Nanotubes

Lactate detection by Oxidase and CNT



Micro & Nanoscale Technologies for the Biosciences
Montreux – November 17-19, 2008

Sensitivity Enhancement in Lactate detection by using LOD immobilized onto Multi Walled Carbon Nanotubes

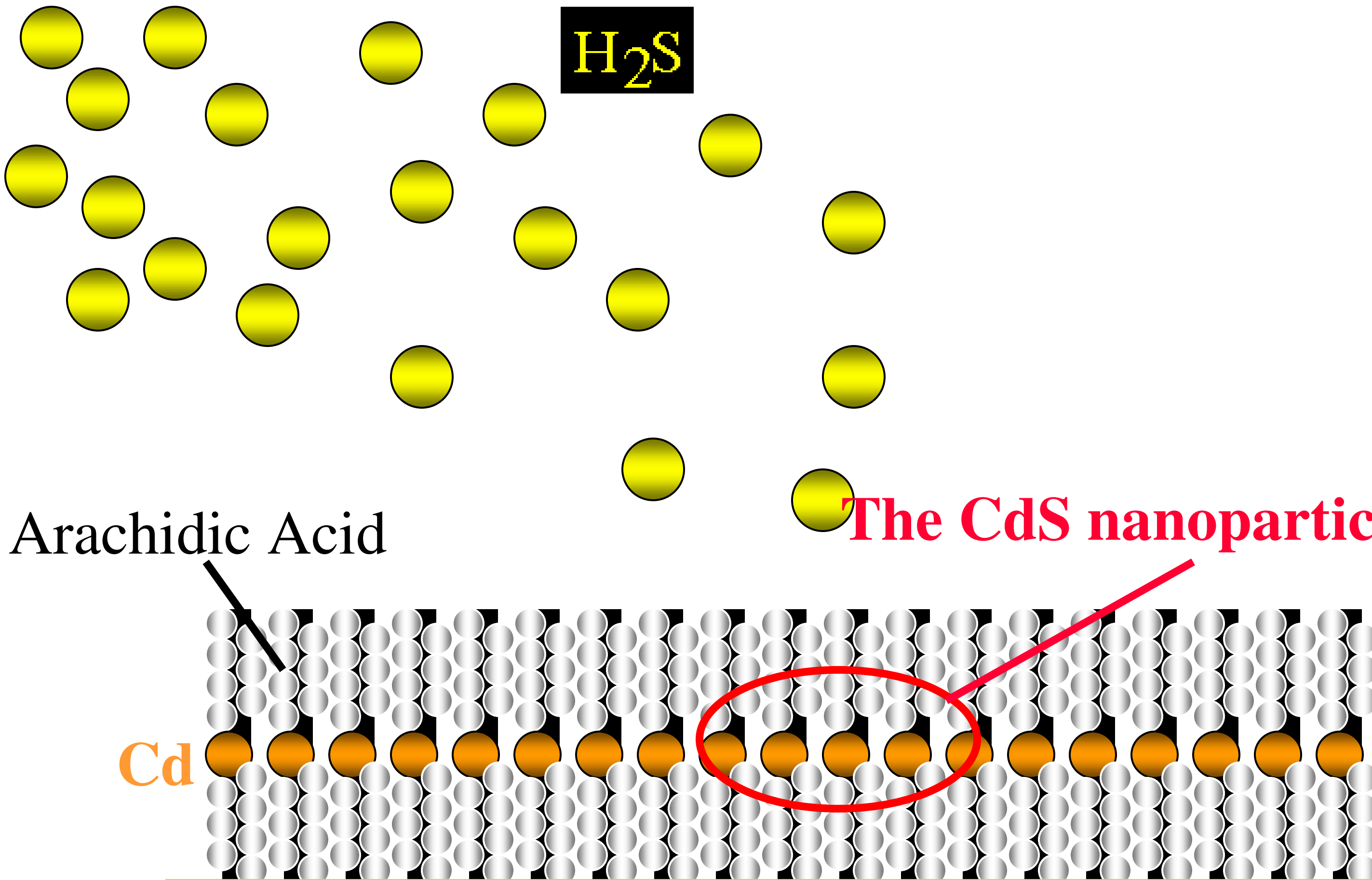
Examples of Nano-Bio-sensing?

- Antibodies and DNA biosensors enhanced by 1D nanostructures.
- Enzymes biosensors enhanced by 2D nanostructures.
- Enzymes biosensors enhanced by 3D nanostructures.

3-D Nanostructures for Enzymes bio-sensing

- Single Electron Trapping
- Electron Transfer Efficiency

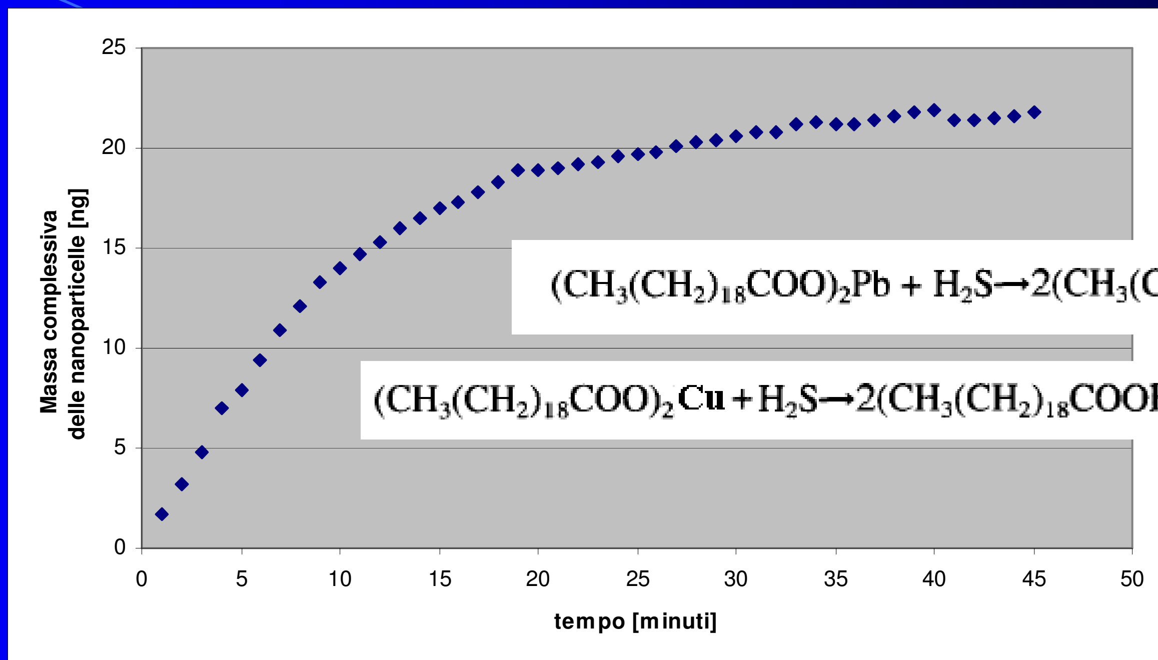
Semiconducting particles fabrication in Thin Solid Films



The final particle is surrounded by a insulating barrier also in case of other formation techniques!

Sulfide based Nano-particles

$$(CH_3(CH_2)_{18}COO)_2Cd + H_2S \rightarrow 2(CH_3(CH_2)_{18}COOH) + CdS$$

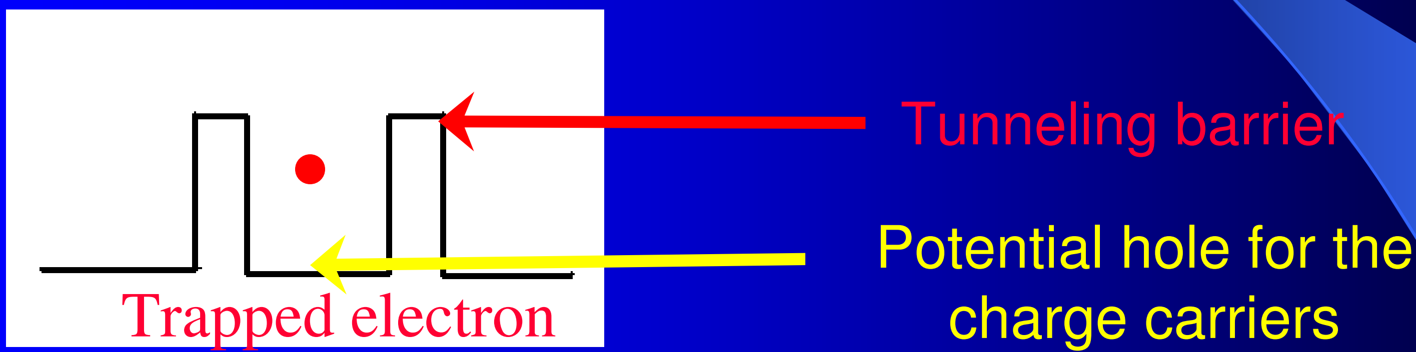


$$(CH_3(CH_2)_{18}COO)_2Pb + H_2S \rightarrow 2(CH_3(CH_2)_{18}COOH) + PbS$$

$$(CH_3(CH_2)_{18}COO)_2Cu + H_2S \rightarrow 2(CH_3(CH_2)_{18}COOH) + CuS$$

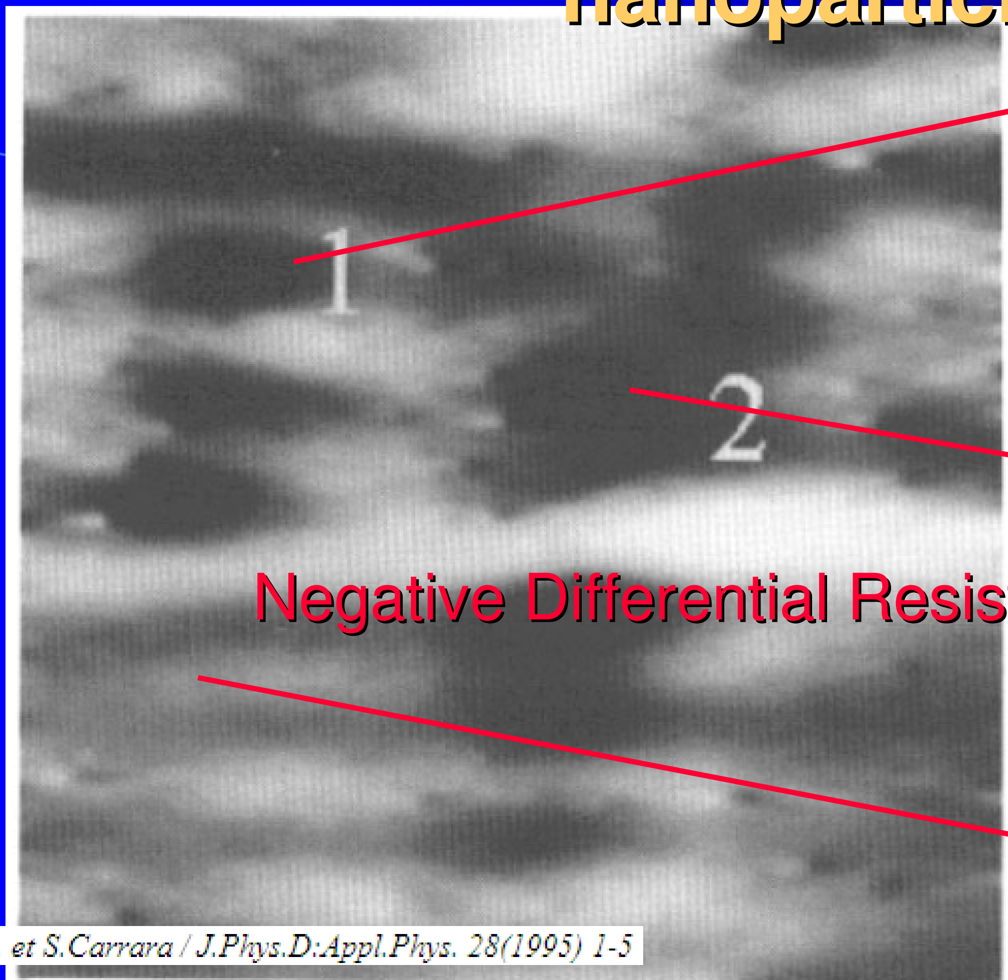
Mass variation during the grown of CdS nanoparticles in H2S atmosphere

The Two Barriers Systems

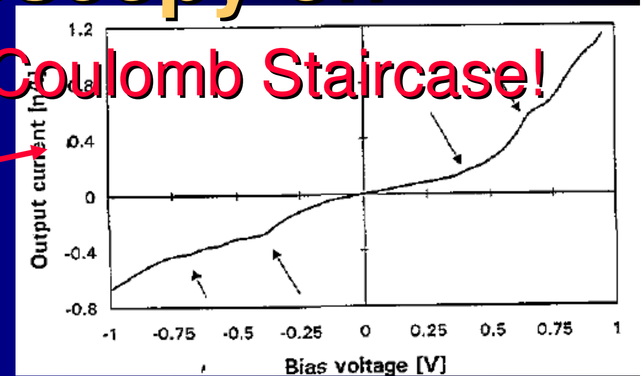


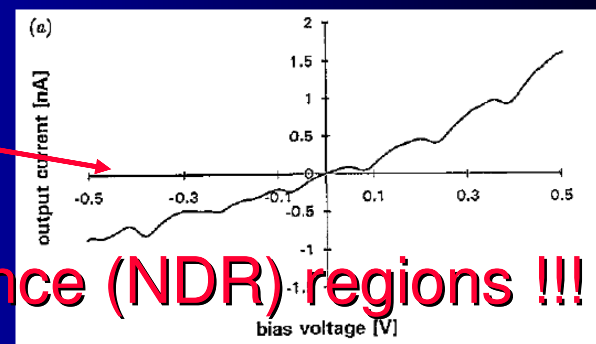
They act as electron-traps

STM imaging and spectroscopy on nanoparticles

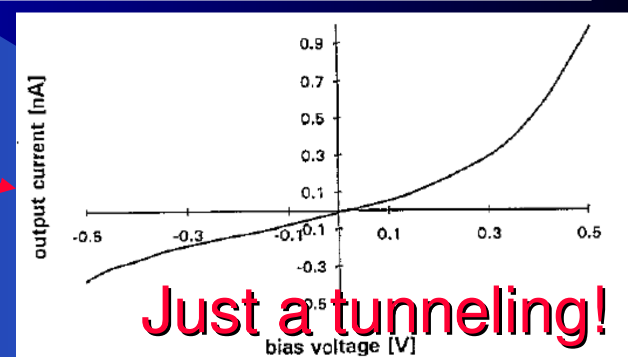


Coulomb Staircase!





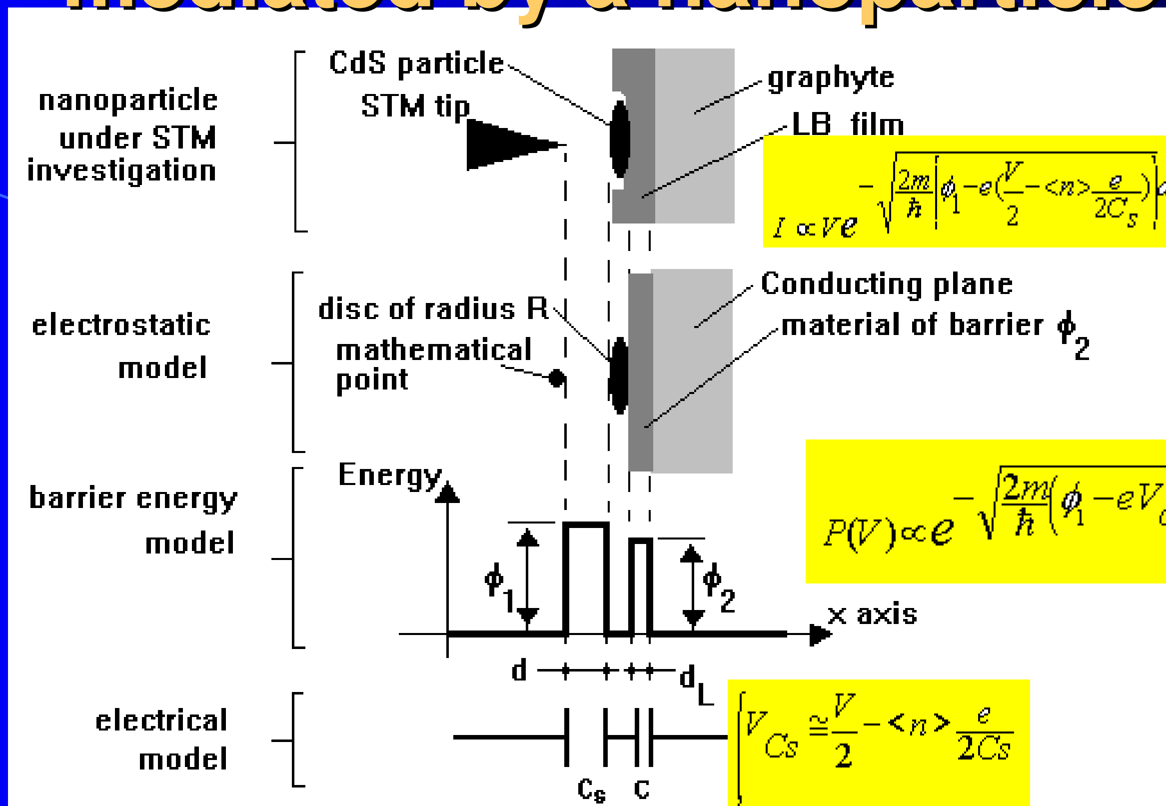
Negative Differential Resistance (NDR) regions !!!



Just a tunneling!

CdS nanoparticles (close to 5 nm in size) in Arachidic matrix

Single-electron conductivity mediated by a nanoparticle



$$I \propto V e^{-\sqrt{\frac{2m}{\hbar}\left[\phi_1 - e\left(\frac{V}{2} - \langle n \rangle \frac{e}{2C_s}\right)\right]}\,d}\; e^{-\sqrt{\frac{2m}{\hbar}\left[\phi_2 - e\left(\frac{V}{2} + \langle n \rangle \frac{e}{2C_s}\right)\right]}\,d_L}$$

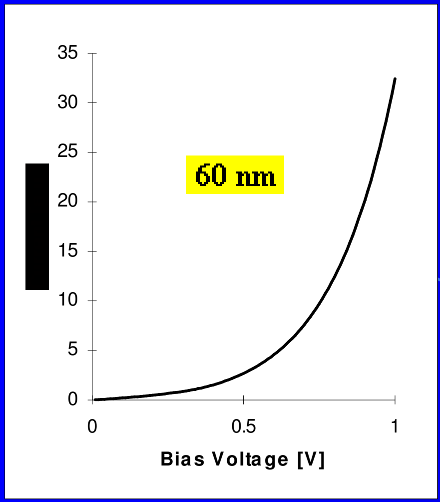
$$P(V) \propto e^{-\sqrt{\frac{2m}{\hbar}\left(\phi_1 - eV_{Cs}\right)}\,d}\; e^{-\sqrt{\frac{2m}{\hbar}\left(\phi_2 - eV_C\right)}\,d_L}$$

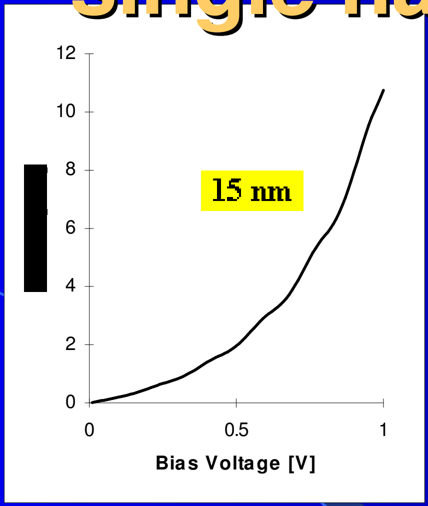
$$\begin{cases} V_{Cs} \cong \dfrac{V}{2} - \langle n \rangle \dfrac{e}{2Cs} \\ V_C \cong \dfrac{V}{2} + \langle n \rangle \dfrac{e}{2Cs}. \end{cases}$$

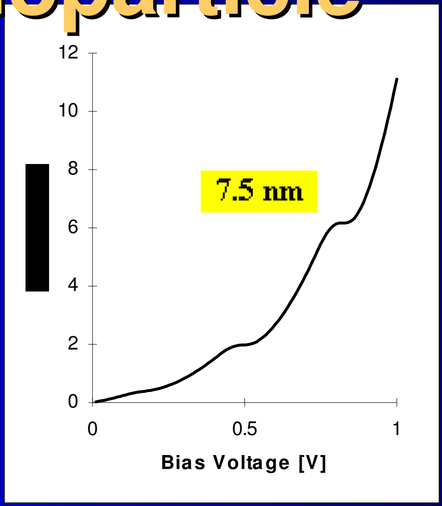
A semi-classical theory

S.Carrara, et al, in
J. H. Fendler and I. Dékány (eds.), Nanoparticles in Solids and Solutions, 497–503.
© 1996 *Kluwer Academic Publishers. Printed in the Netherlands.*

Single-electron conductivity on single nanoparticle

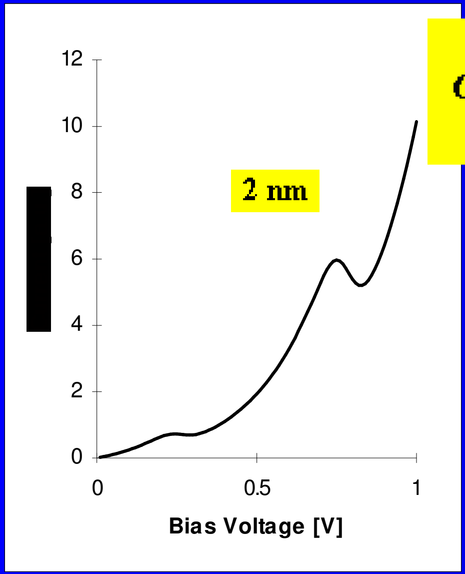






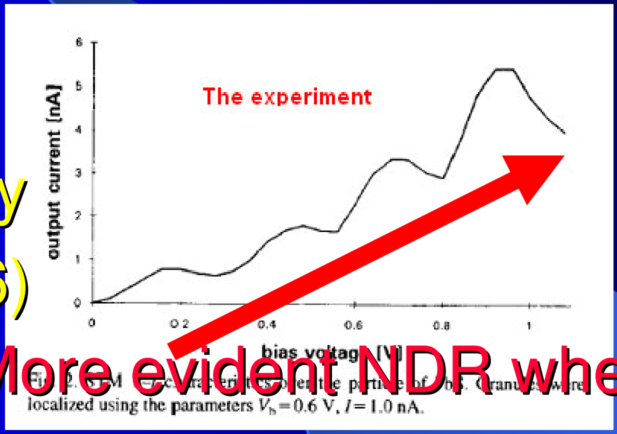
$$Cs < \frac{e^2}{2kT}$$

Likharev Theory Limit (1983)



$$Cs < \frac{ne^2}{\varphi}\sqrt{\frac{2m\phi d^2}{h^2}}$$

new Theory Limit (1996)

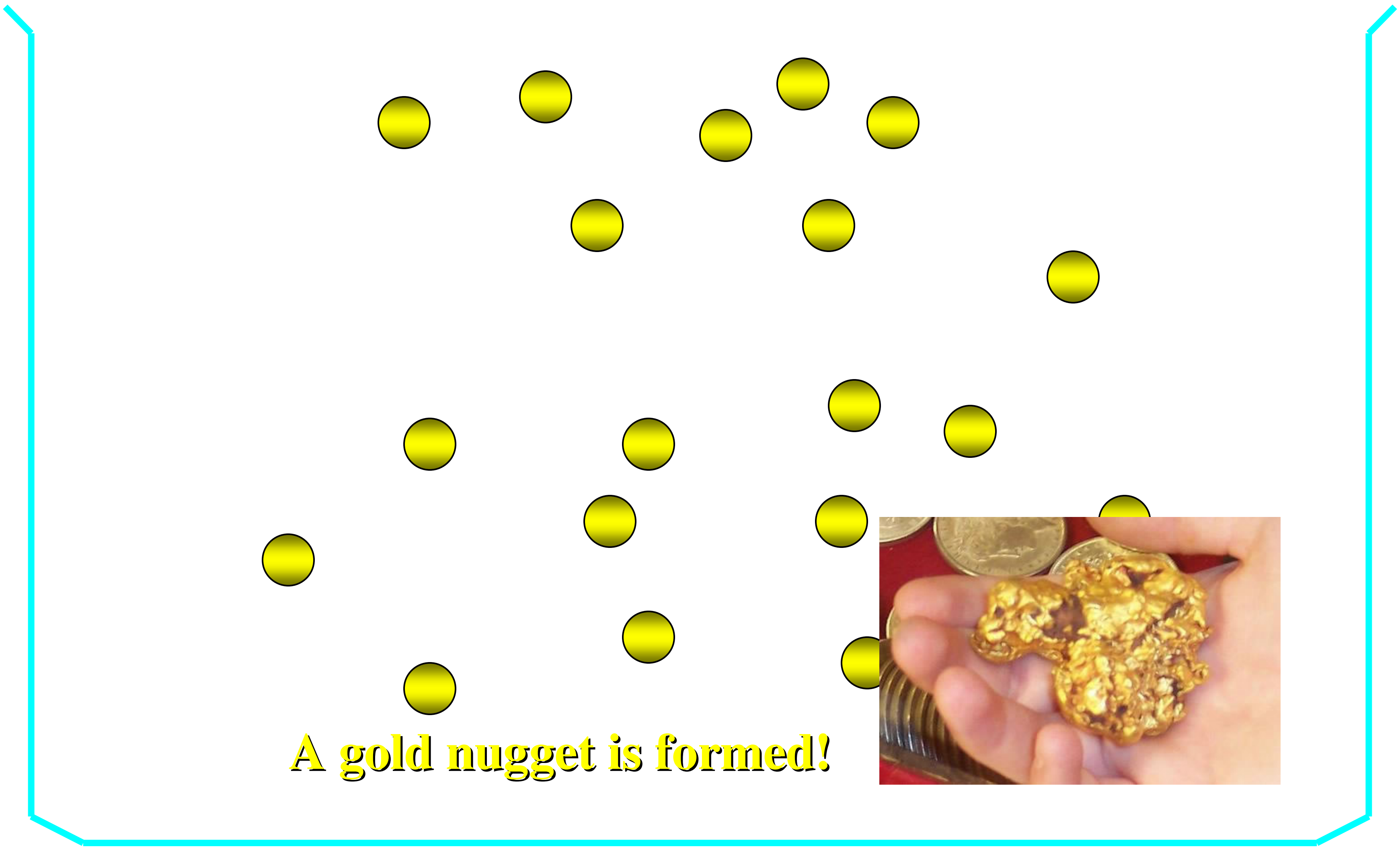


More evident NDR when n increase

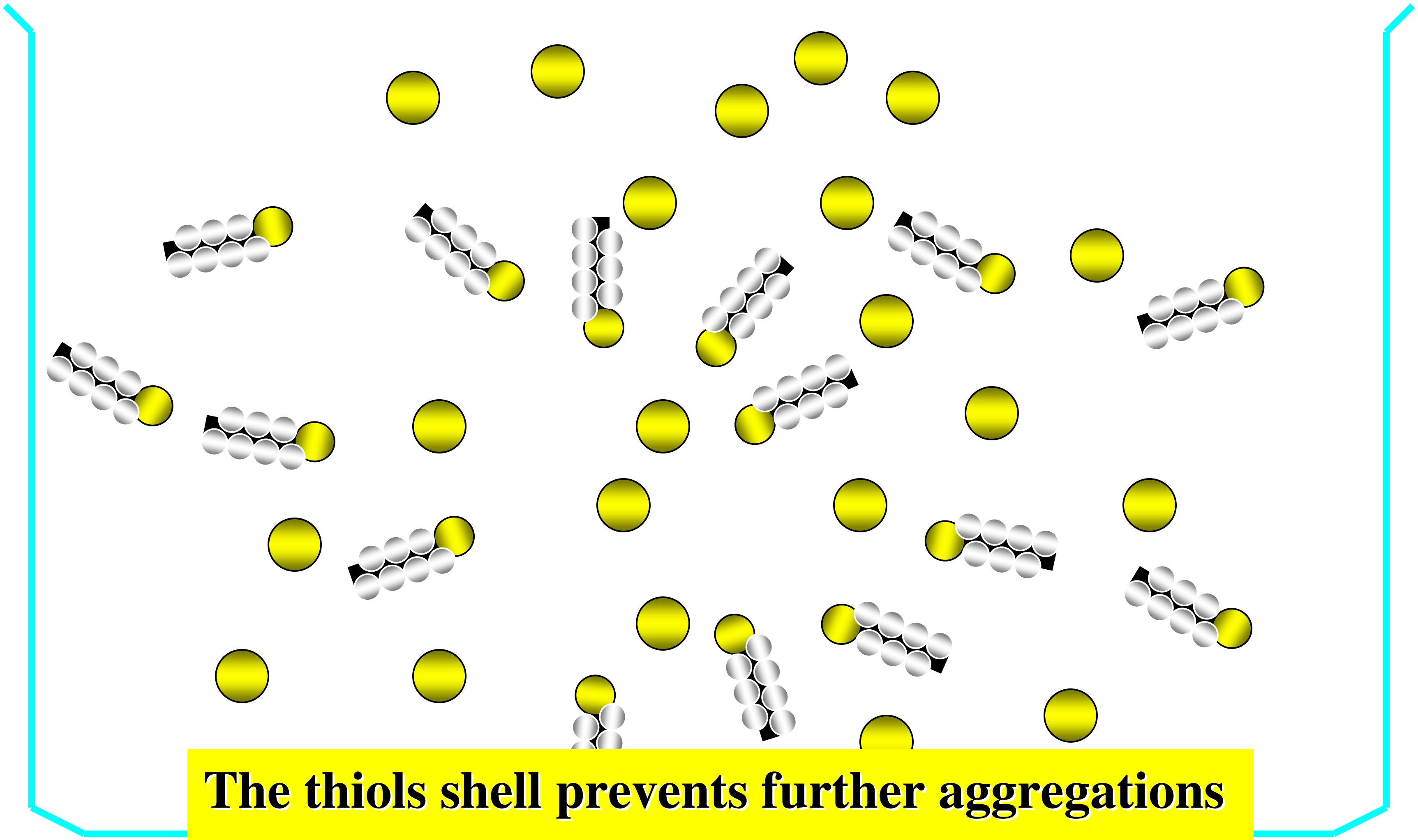
al. et S.Carrara / Thin Solid Films 284-285 (1996) 891-893

The size drives the phenomena !!!

Metallic particles fabrication in solution

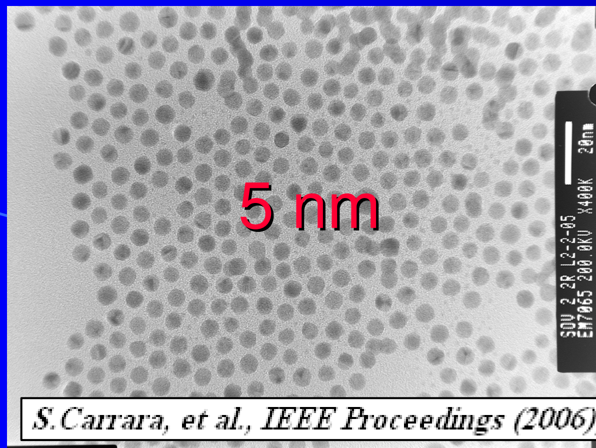


Metallic particles fabrication in solution



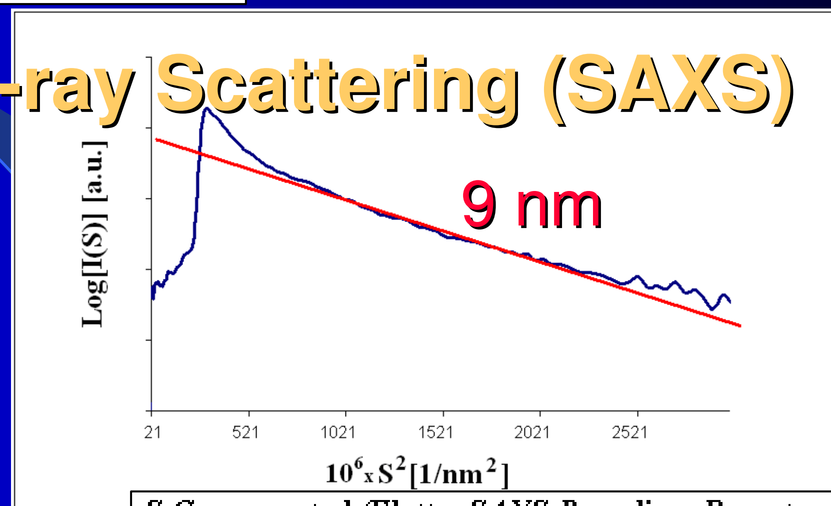
The thiols shell prevents further aggregations and this allows mono-disperse nanoparticles!

Transmission Electron Microscopy



S.Carrara, et al., IEEE Proceedings (2006), ISBN 1-4244-0391-X

Small Angle X-ray Scattering (SAXS)



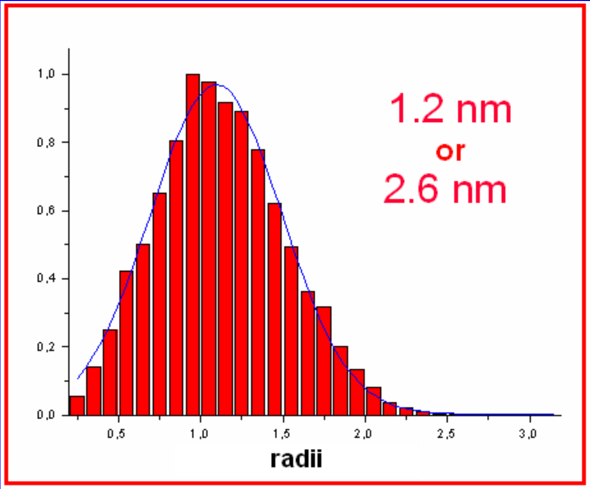
S.Carrara, et al./Elettra SAXS Beamline, Report activity 2005

TEM provides the metallic core size

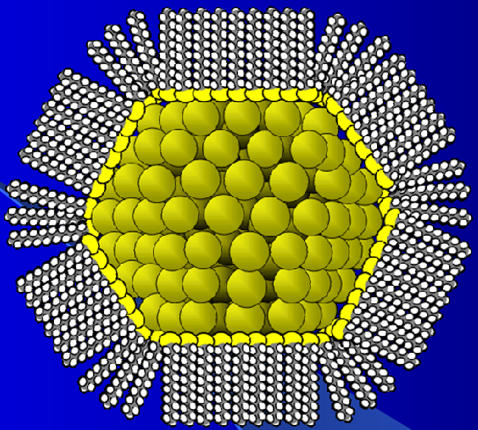
while SAXS provides the organic coating size

Gold Nanoparticles Size

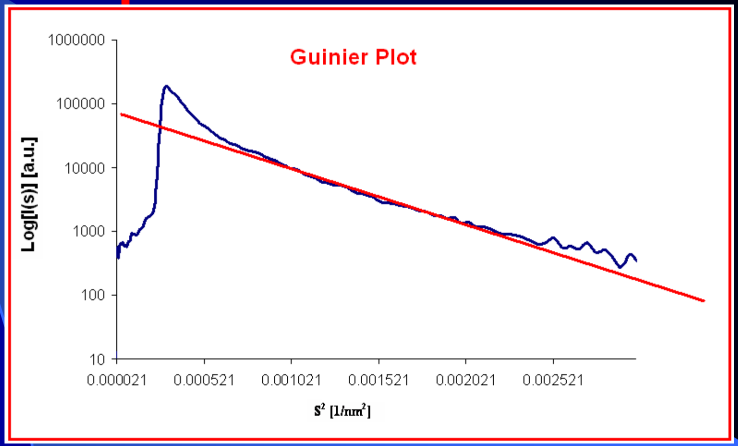
radius by TEM



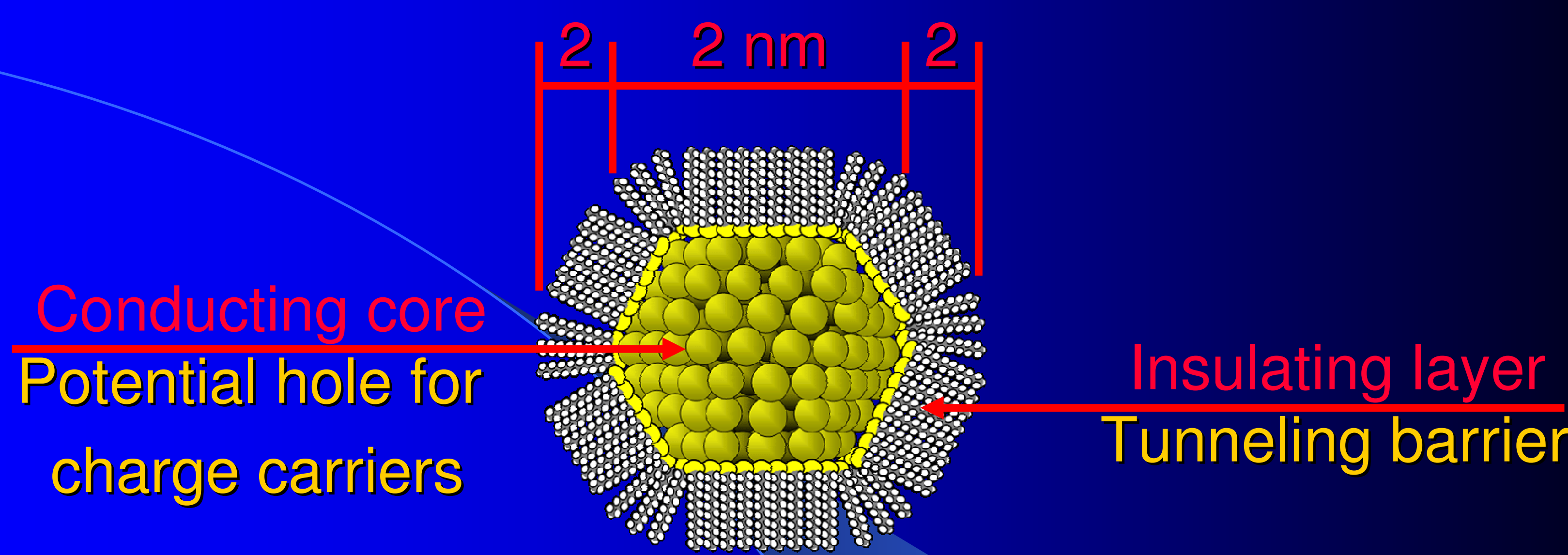
S.Carrara, et al., IEEE Proceedings (2006), ISBN 1-4244-0391-X



Radius by SAXS
= 3.1 nm
4.4 nm

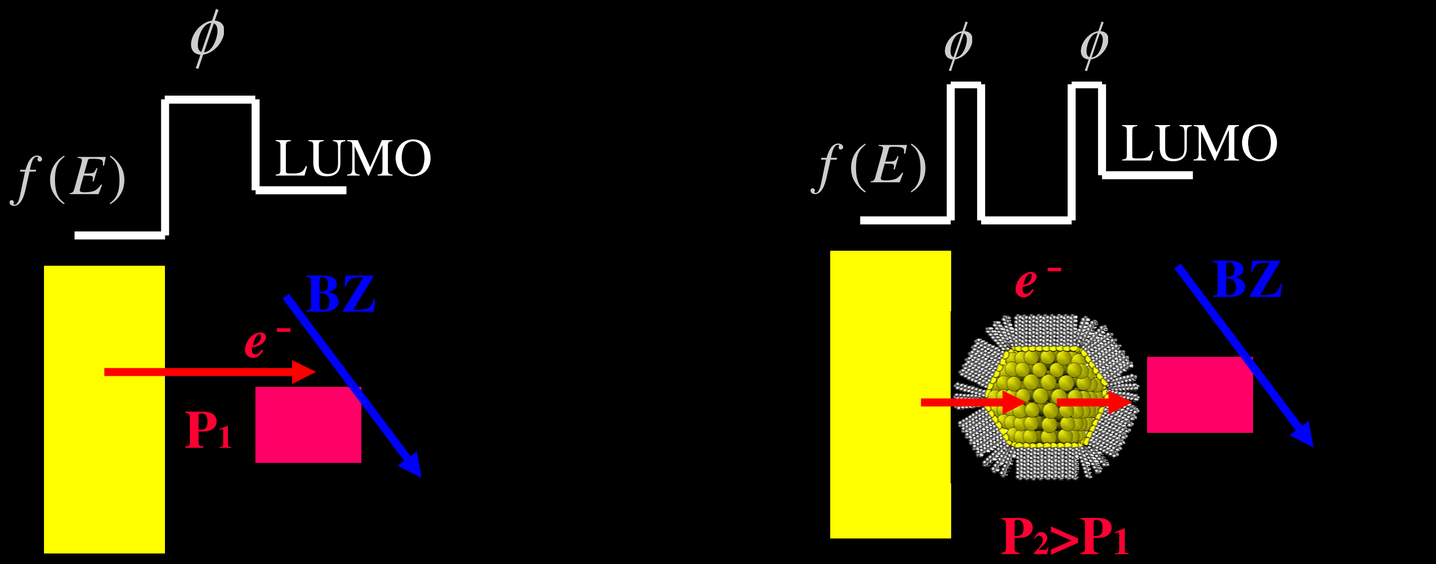


Gold nanoparticles as Quantum Dots



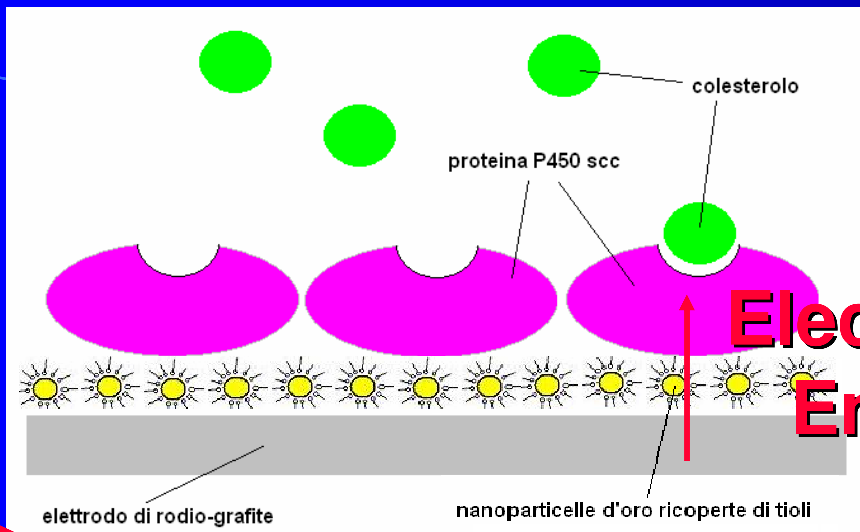
This nano-system is very useful
for quantum effects !!!

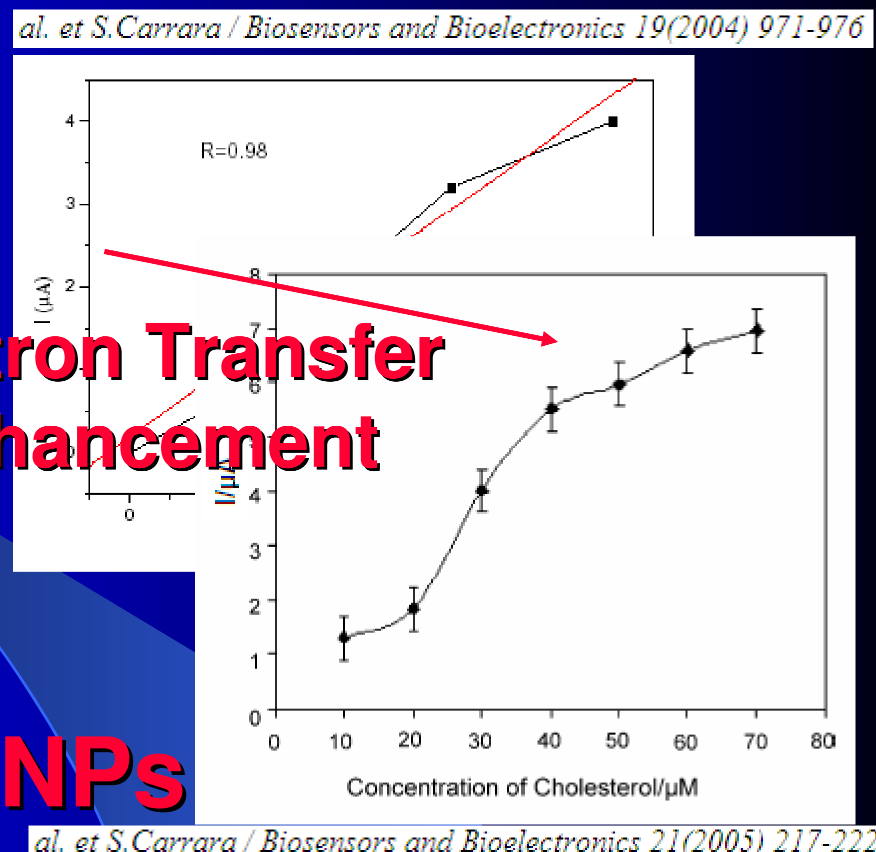
An improved P450/Electrode coupling by Quantum Dots



$$f(E)=\frac{1}{1+e^{\frac{E-E_F}{K_BT}}}$$

Cottrell Effect





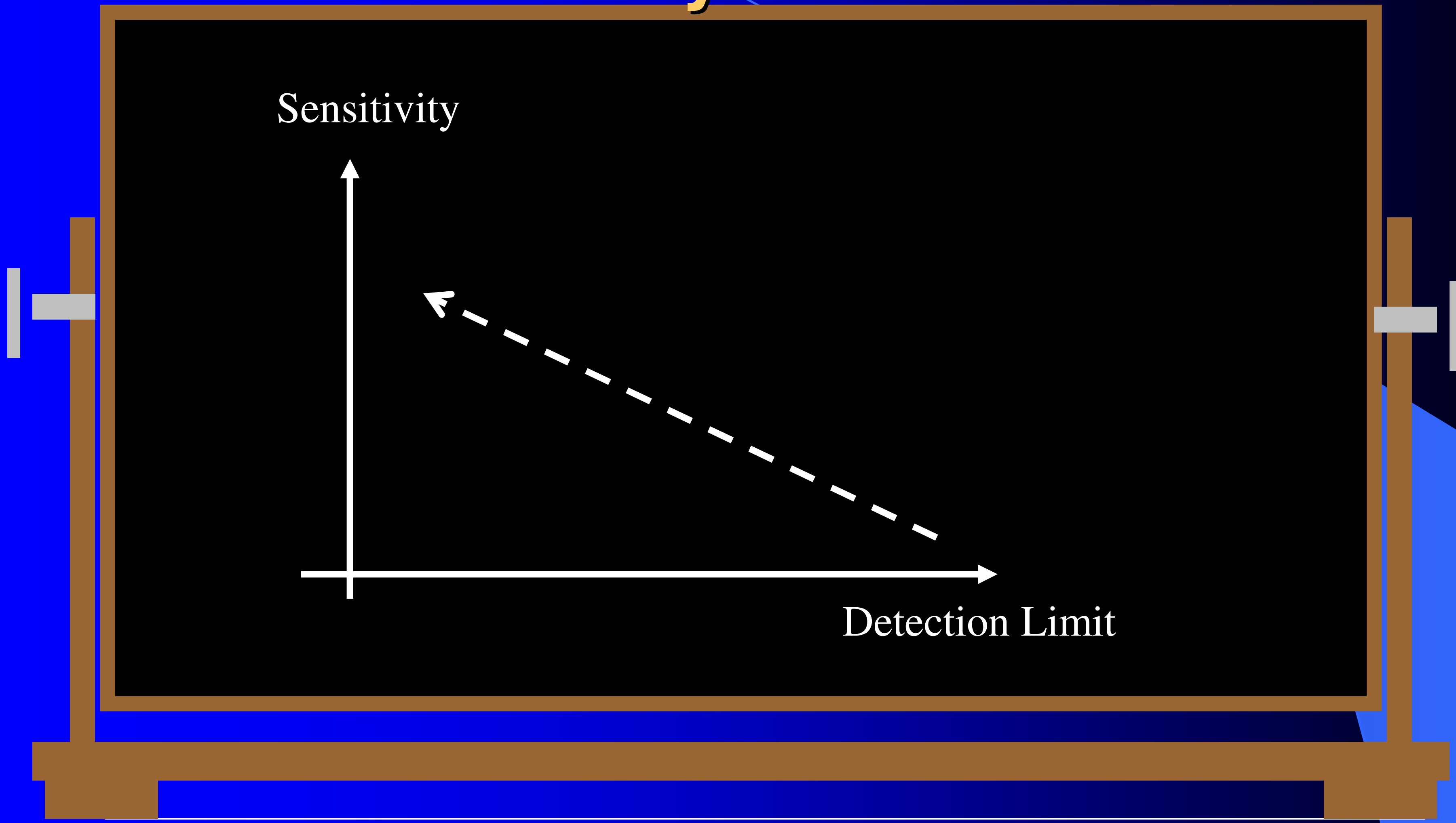
Electron Transfer Enhancement

~~P450+Riboflavin +phospholipids+ Albumine+ Glutaraldehyde~~

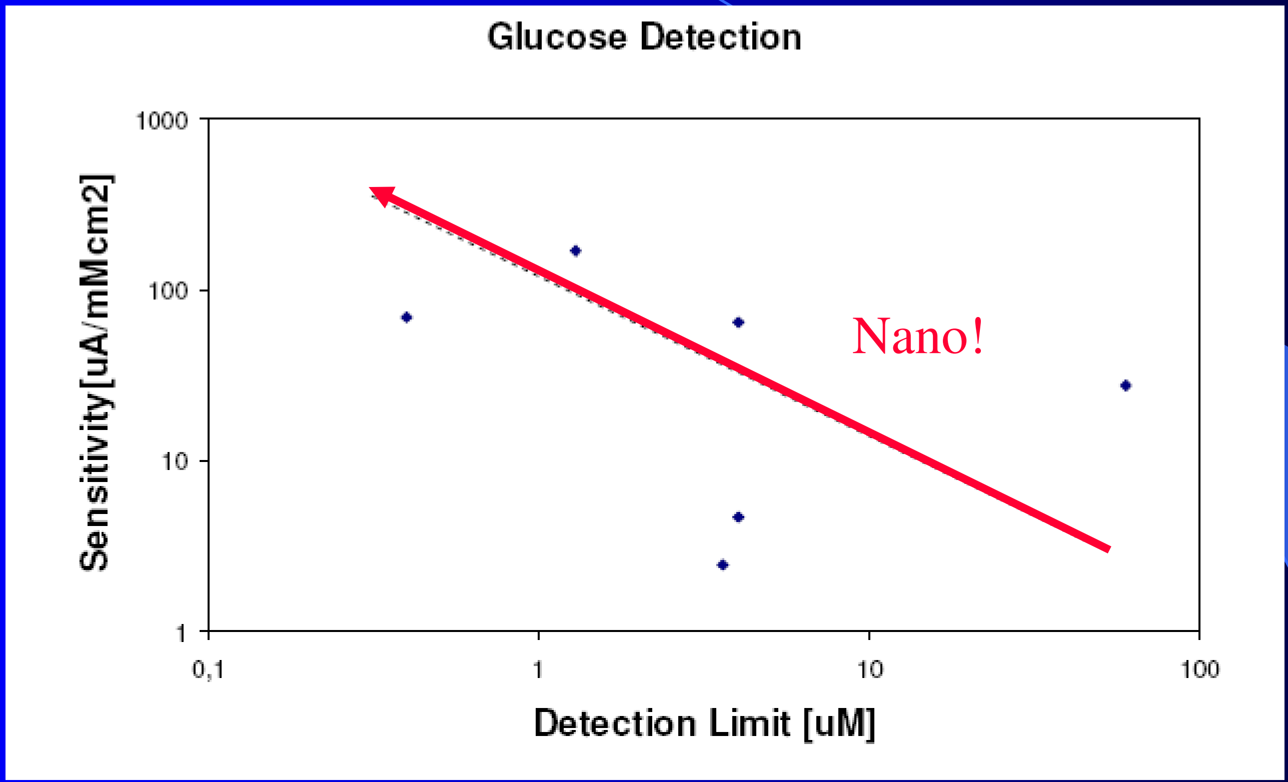
only NPs

The Sensitivity is enhanced when the P450 Activity is mediated by gold nano-particles

Nano affects Detection Sensitivity and Limit

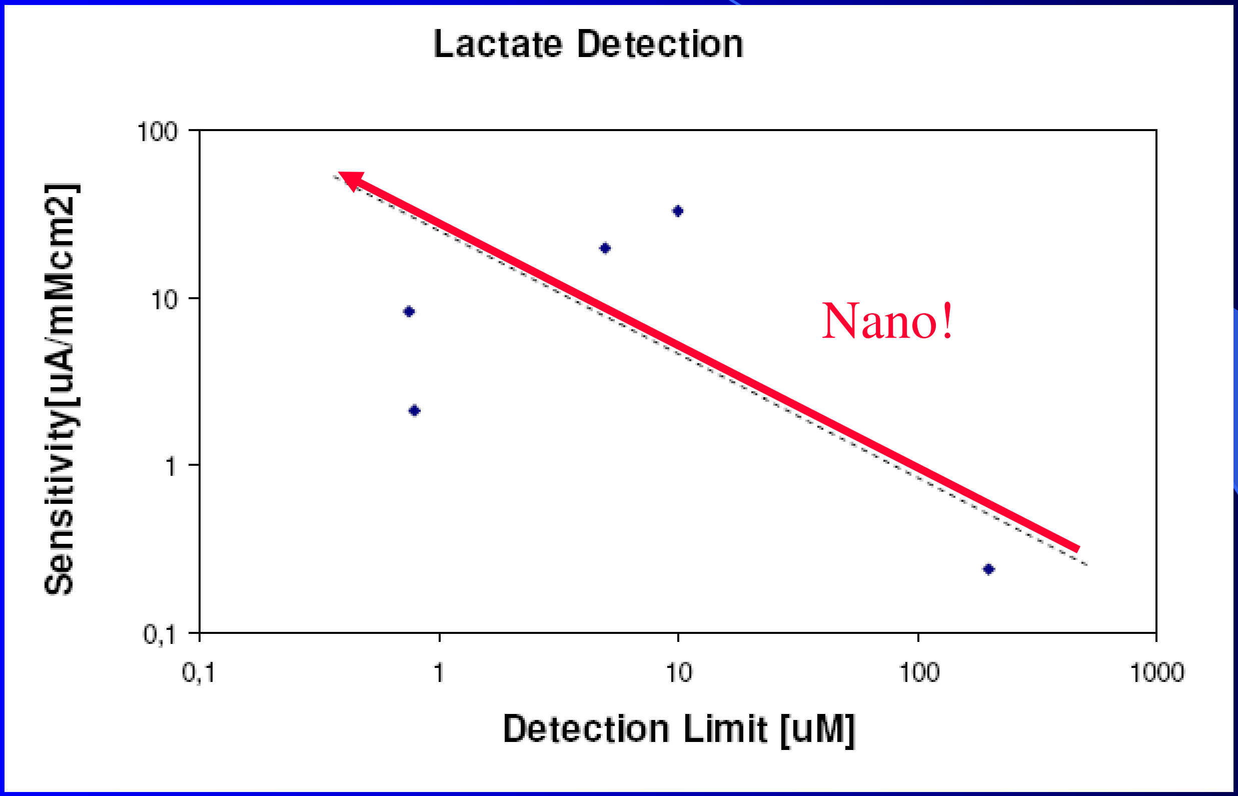


Sensitivity vs Detection limit



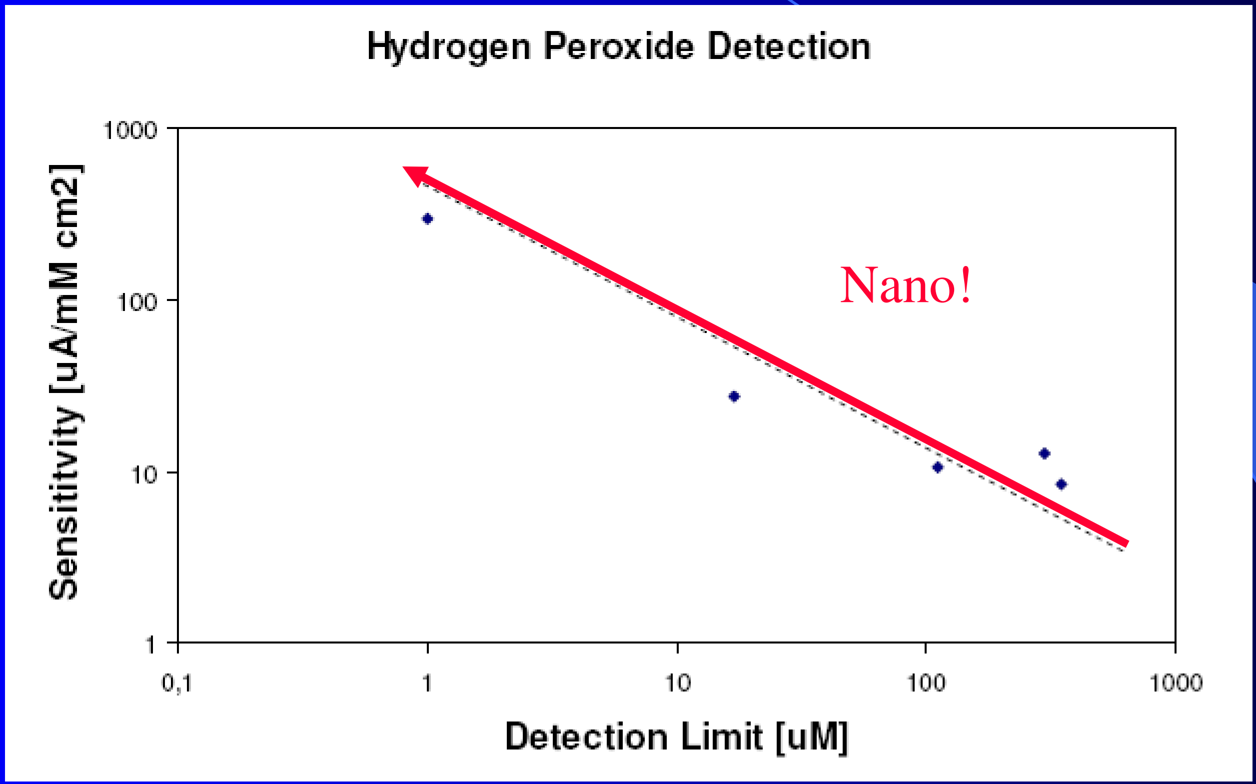
The case of Glucose

Sensitivity vs Detection limit



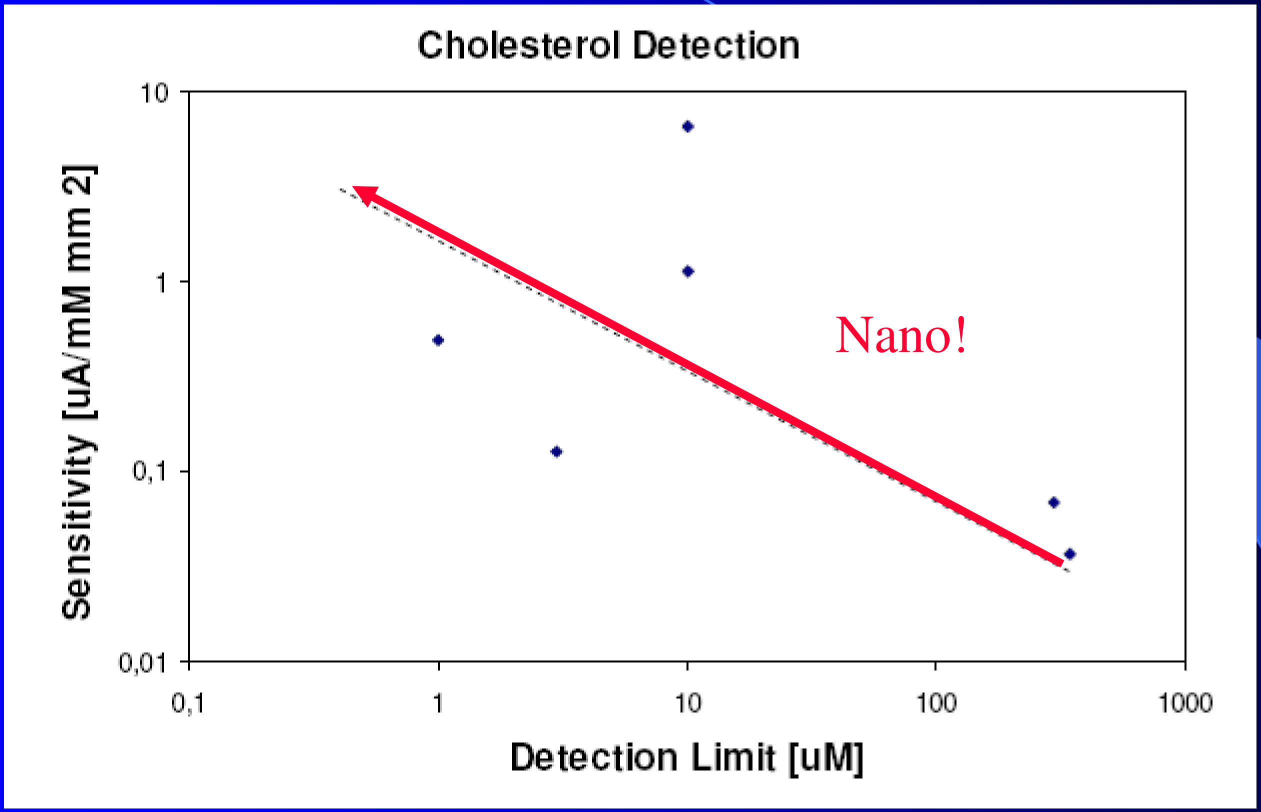
The case of lactate

Sensitivity vs Detection limit



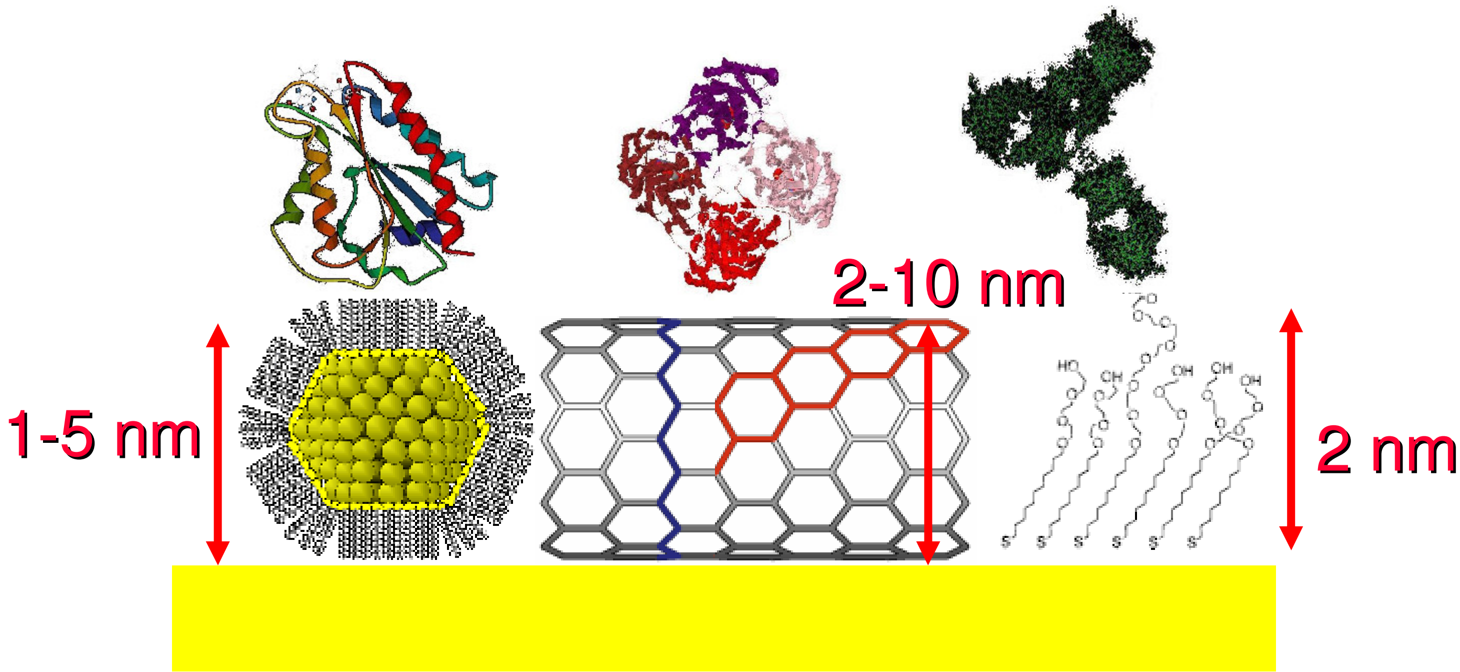
The case of Hydrogen Peroxide

Sensitivity vs Detection limit



The case of Cholesterol

Conclusions (1)

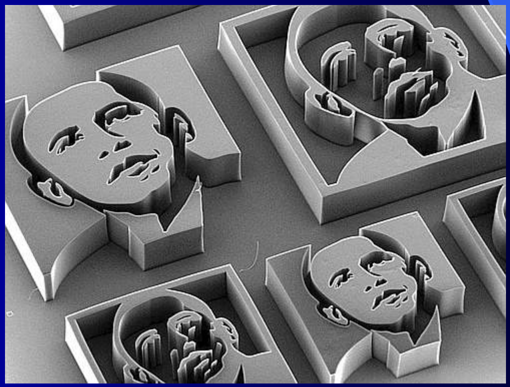


"Nano" Improves Bio-Sensing

Conclusions (2)

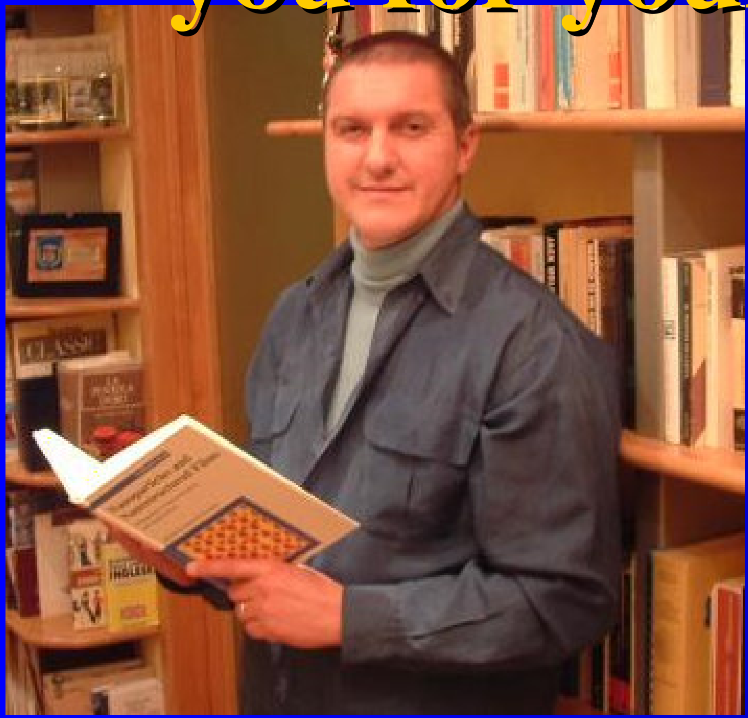
- 1D-nanostructures made by ethylene-glycol layers highly improve insulating property of electrochemical interfaces
- 1D-nanostructures made by ethylene-glycol mono-layers highly improve DNA label-free detection
- 2D-nanostructures by carbon nanotubes improve charging effect and electron-transfer in electrochemical interfaces
- 2D-nanostructures by carbon nanotubes improve sensitivity and detection limit in enzymes based bio-sensing
- 3D-nanostructures by metallic or semiconducting particles assure single-electron trapping
- 3D-nanostructures by metallic particles improve sensitivity and detection limit in enzymes based bio-sensing
- Nanotechnology is useful

  not only for Nanobama fabrication!!!



by **John Hart**, Michigan Univ., http://www.nanobama.com/

Thanks to all the peoples helping me on this research and thank to all of you for your kindly attention!



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Dedicated to Janos Fendler, a great pioneer in the field of Nano-particle technology