



EDMI Microsystems and Microelectronics

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

Lecture #8

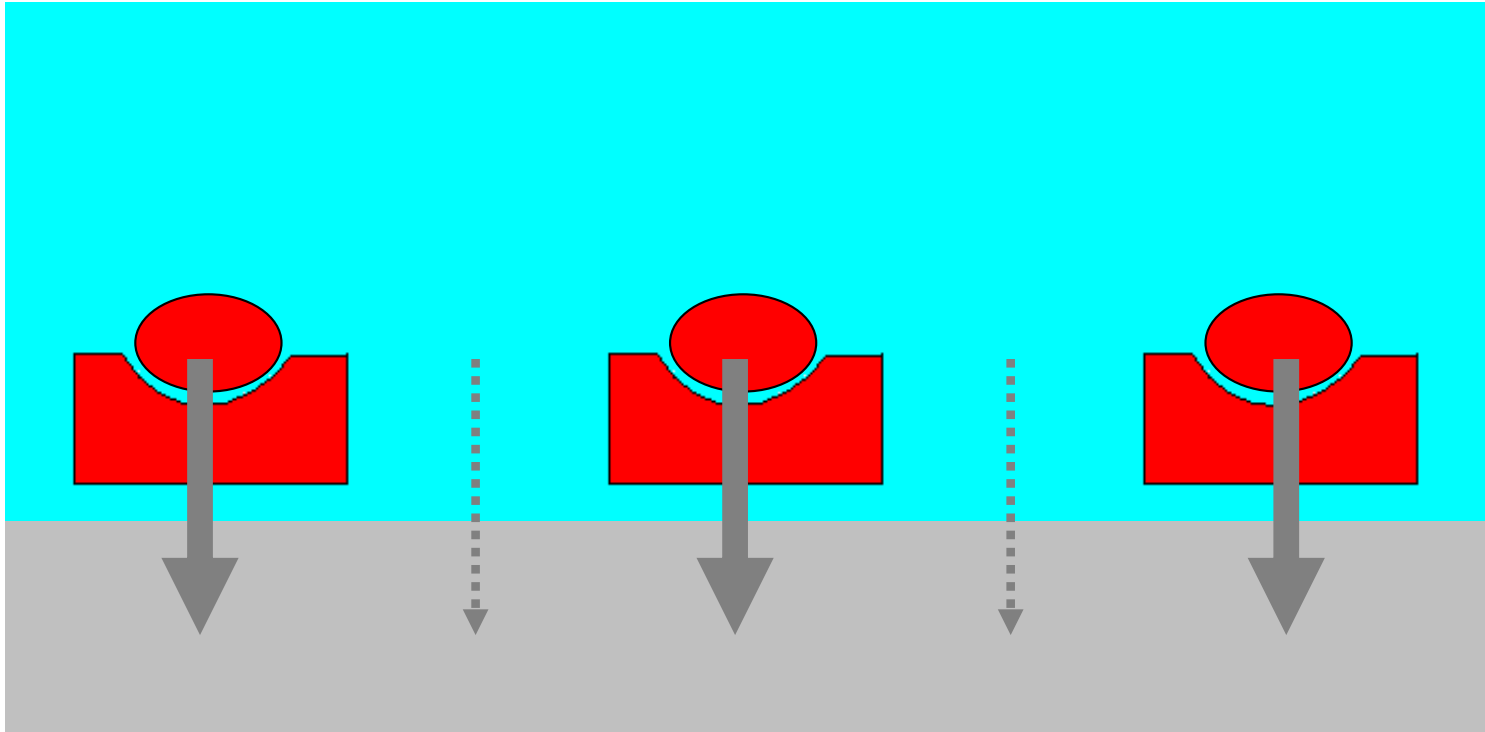
Nanotechnology to prevent Electron Transfer

Lecture Outline

(Book Bio/CMOS: Chapter' paragraphs § 6.3-8)

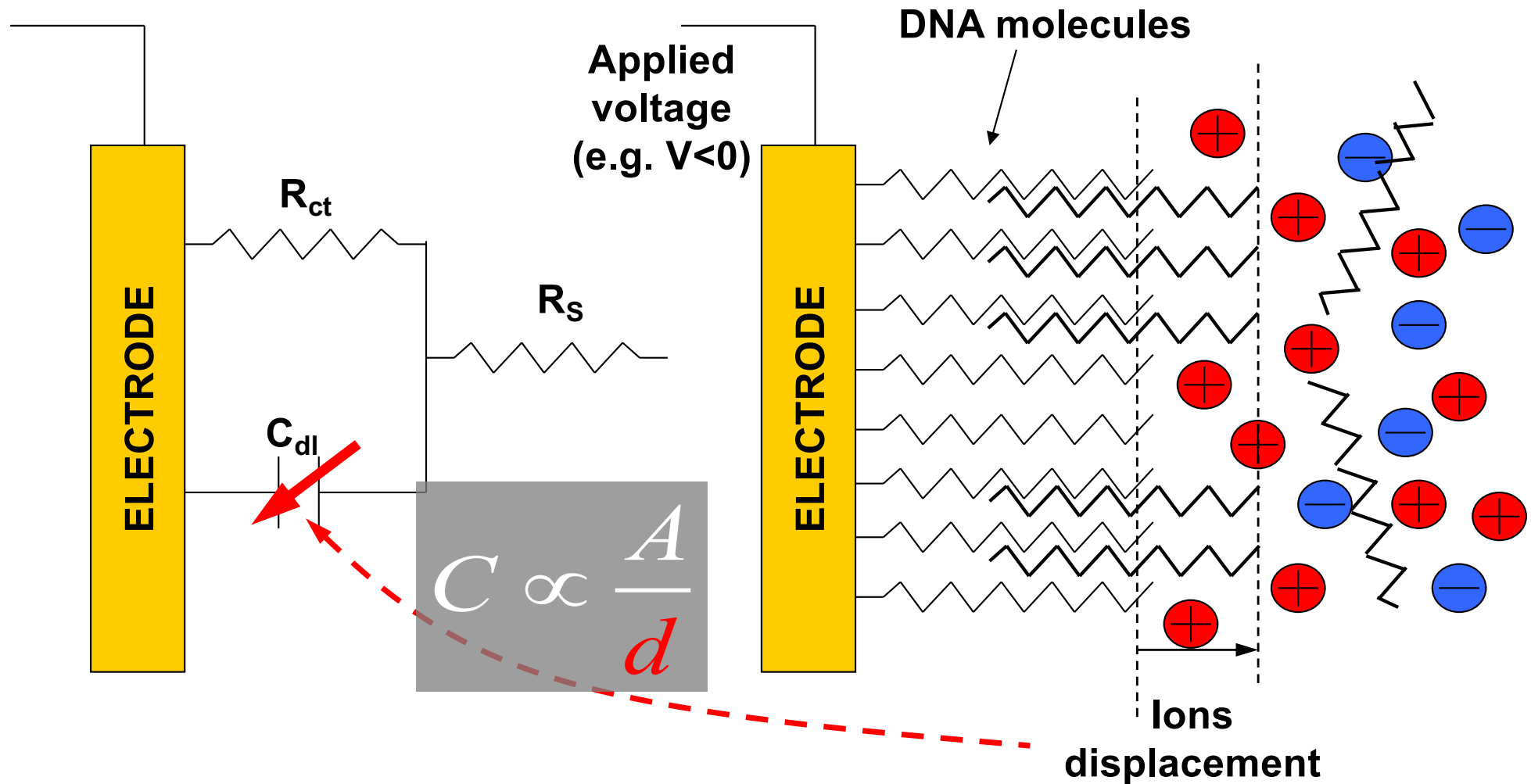
- Electrical behavior of DNA at the interface
- Nanoscale properties of DNA films
- Blocking agents
- Precursor films
- Electrical behavior of Antibodies

CMOS/Sample interface



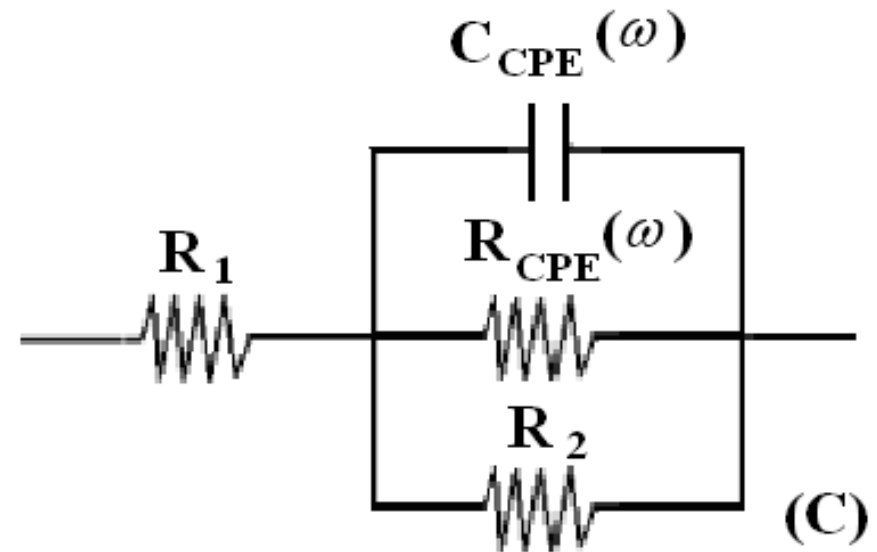
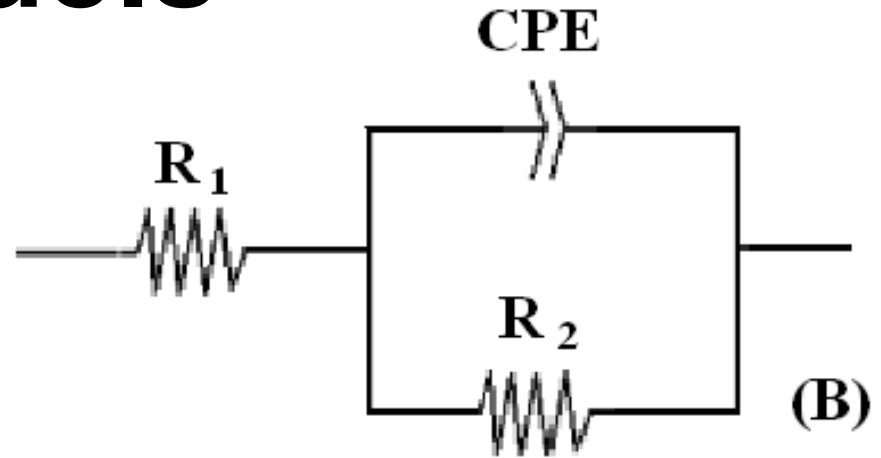
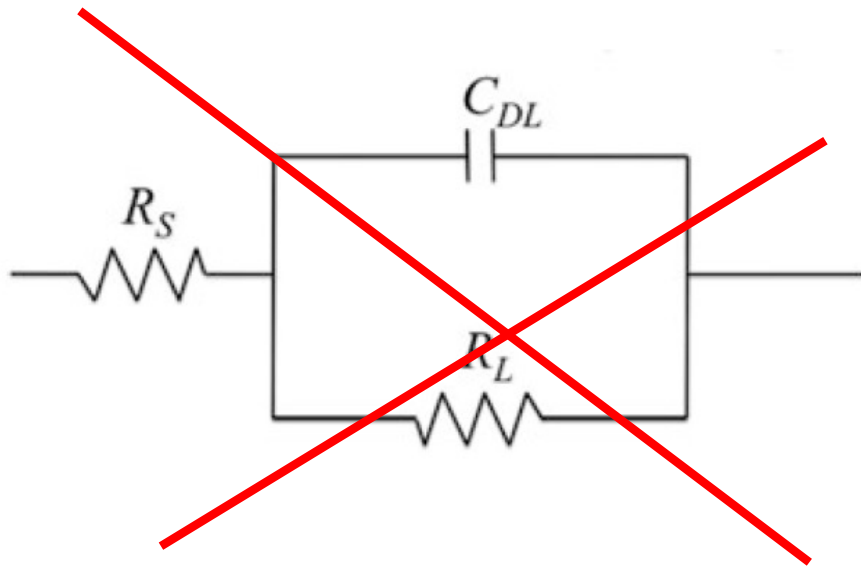
The interface between the CMOS circuit and the bio-sample needs to be deeply investigated and organized

The Capacitance DNA Detection



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

Interface models



Equivalent circuits of DNA Bio/CMOS interface

CPE element

$$Z_{CPE} = \frac{1}{C_p(j\omega)^\alpha} = \frac{\cos\left(\frac{\pi}{2}\alpha\right)}{C_p\omega^\alpha} - j\frac{\sin\left(\frac{\pi}{2}\alpha\right)}{C_p\omega^\alpha}$$

$$Z_{CPE} \cong \frac{1}{\omega^\alpha C_p} \sqrt{1 - \alpha^2} + \frac{1}{j\omega^\alpha C_p} \alpha$$

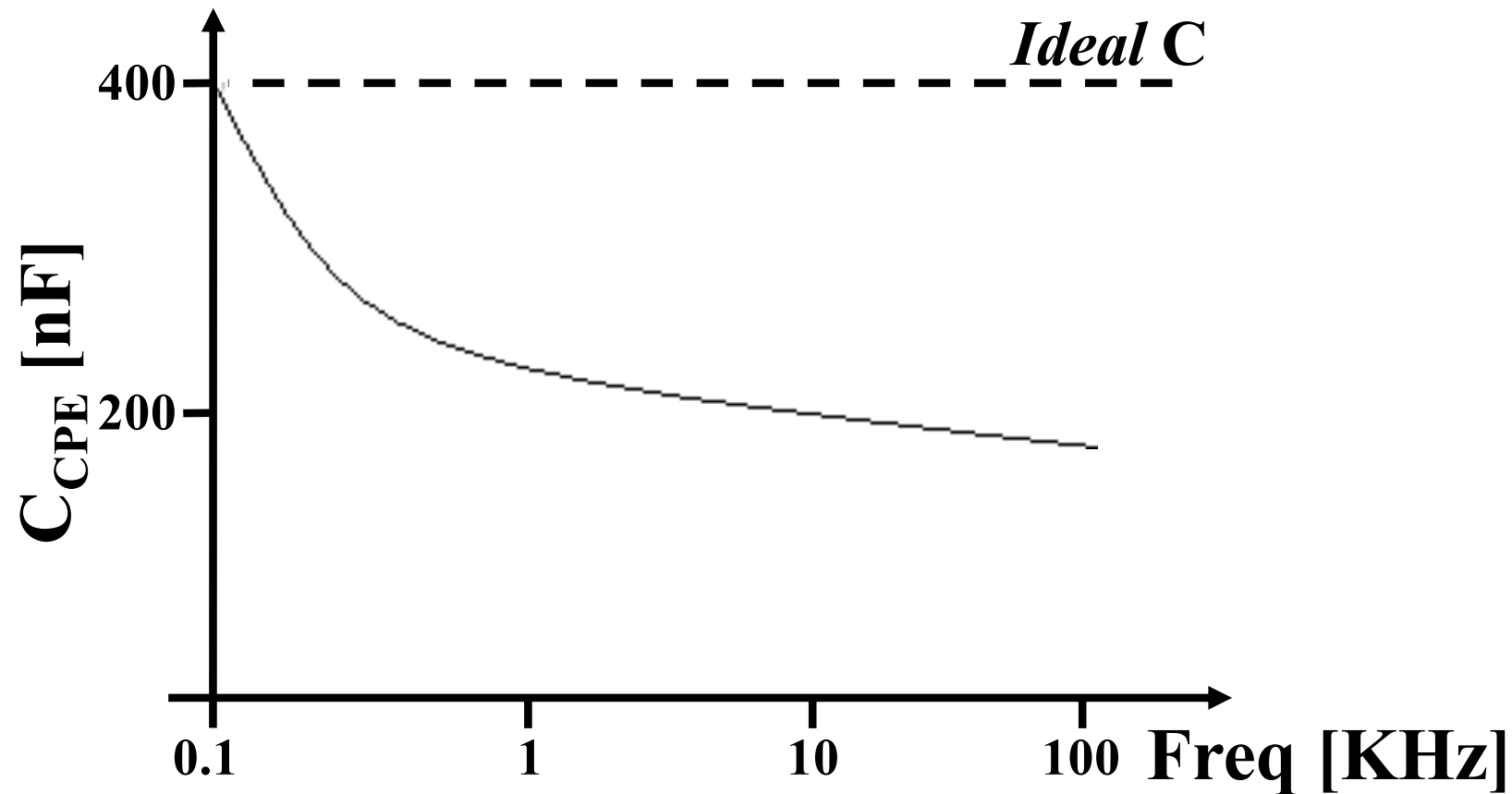
CPE element

$$Z_{CPE} \begin{cases} R_{CPE} \cong \frac{1}{\omega^\alpha C_p} \sqrt{1 - \alpha^2} \\ X_{CPE} \cong \frac{1}{\omega^\alpha C_p} \alpha \end{cases}$$

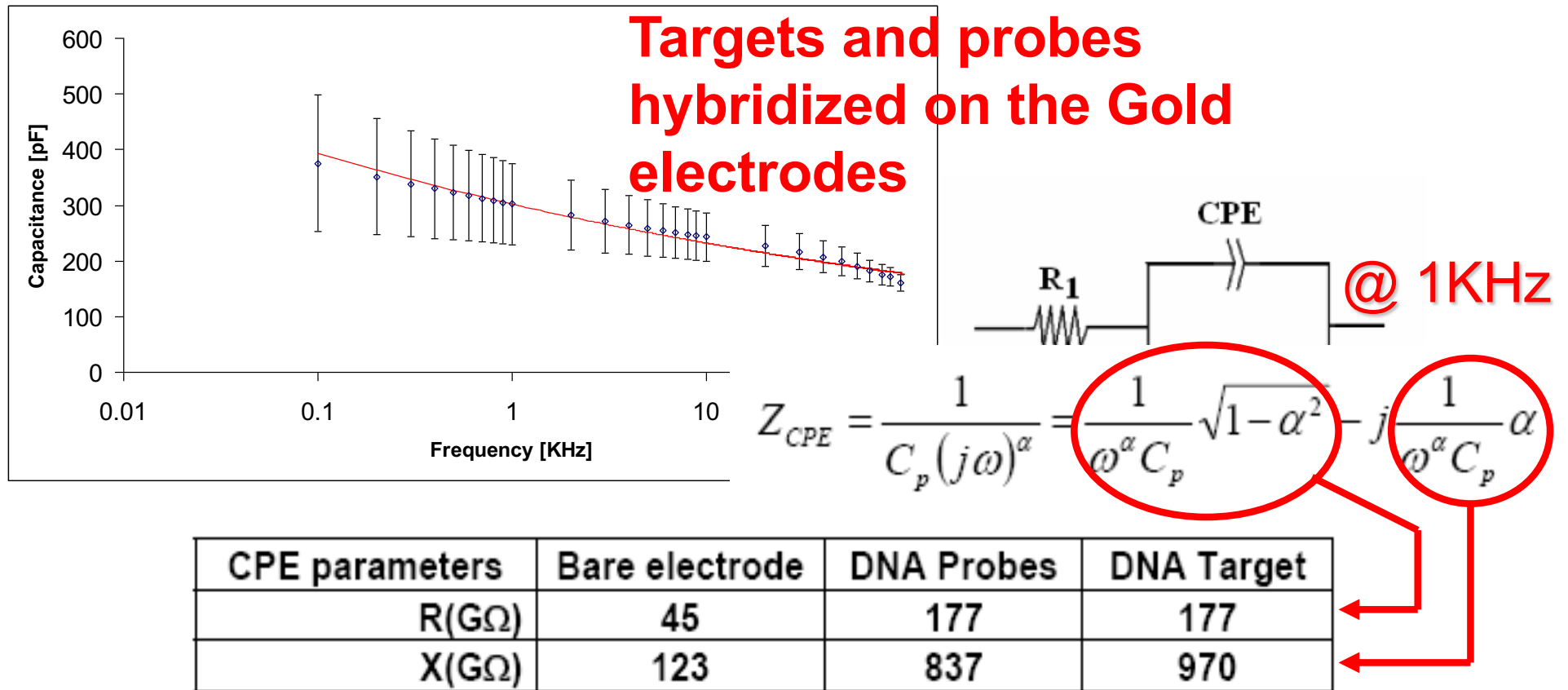
$$|X_{CPE}| \cong \frac{1}{\omega^\alpha C_p} \alpha = \frac{1}{\omega^{\alpha-1} \omega C_p} \alpha = \frac{1}{\omega \left(\frac{C_p}{\alpha \omega^{1-\alpha}} \right)}$$

$$C_{CPE} \cong \frac{C_p}{\alpha \omega^{1-\alpha}}$$

Equivalent Capacitance vs frequency



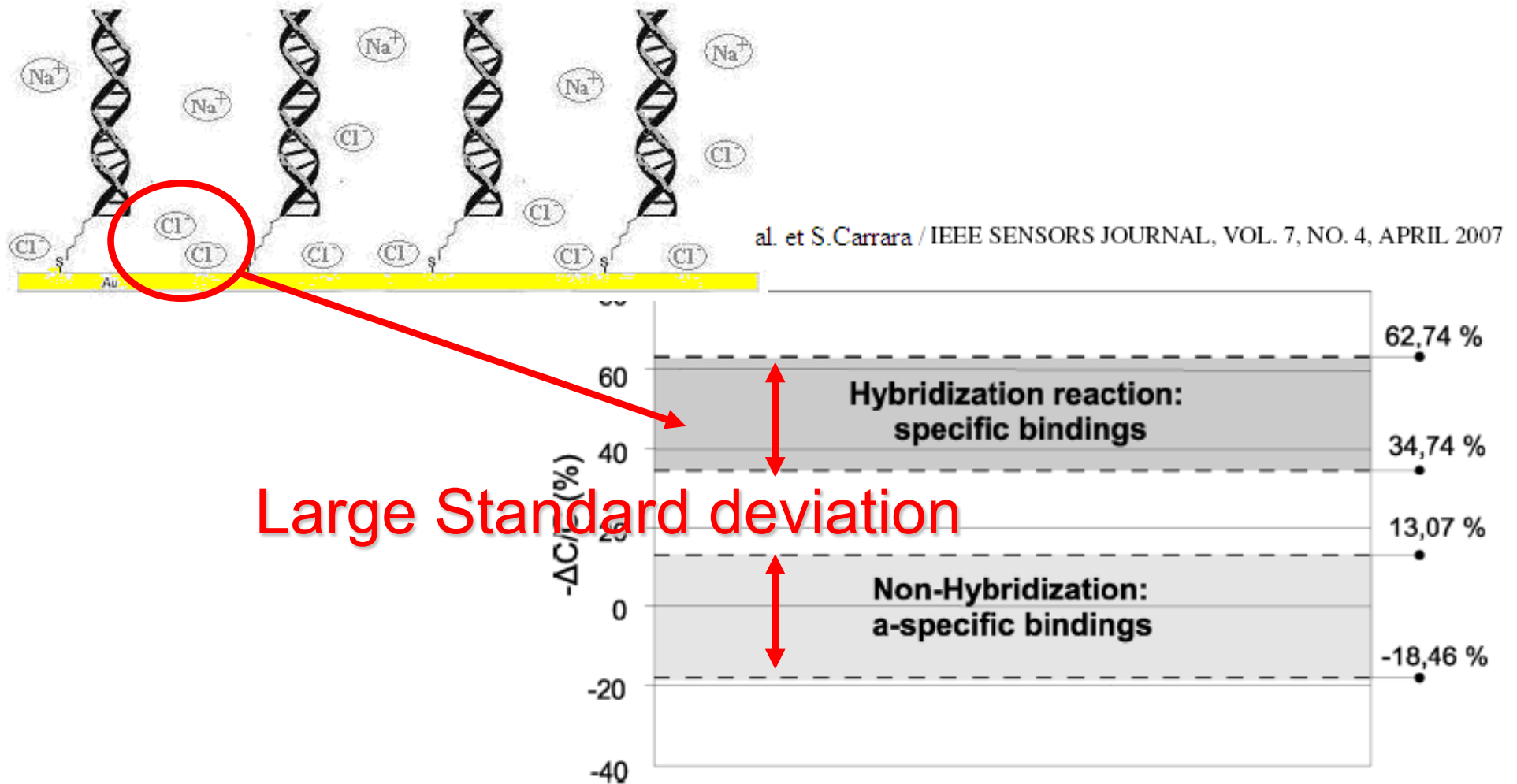
Equivalent Capacitance vs frequency



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 bio-layer

Nano-aperture in the probes film



Solution ions in free contact with electrodes surface results in very large standard deviations

The problem of time instability

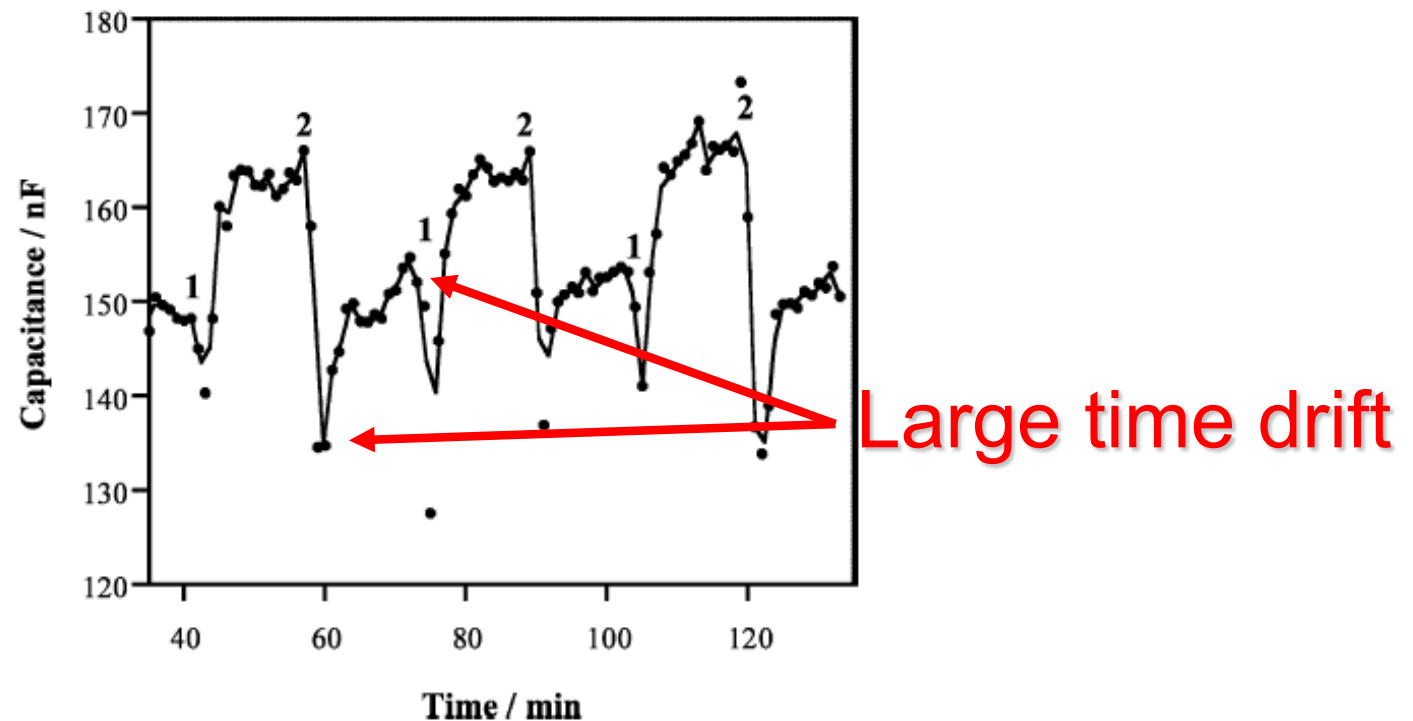
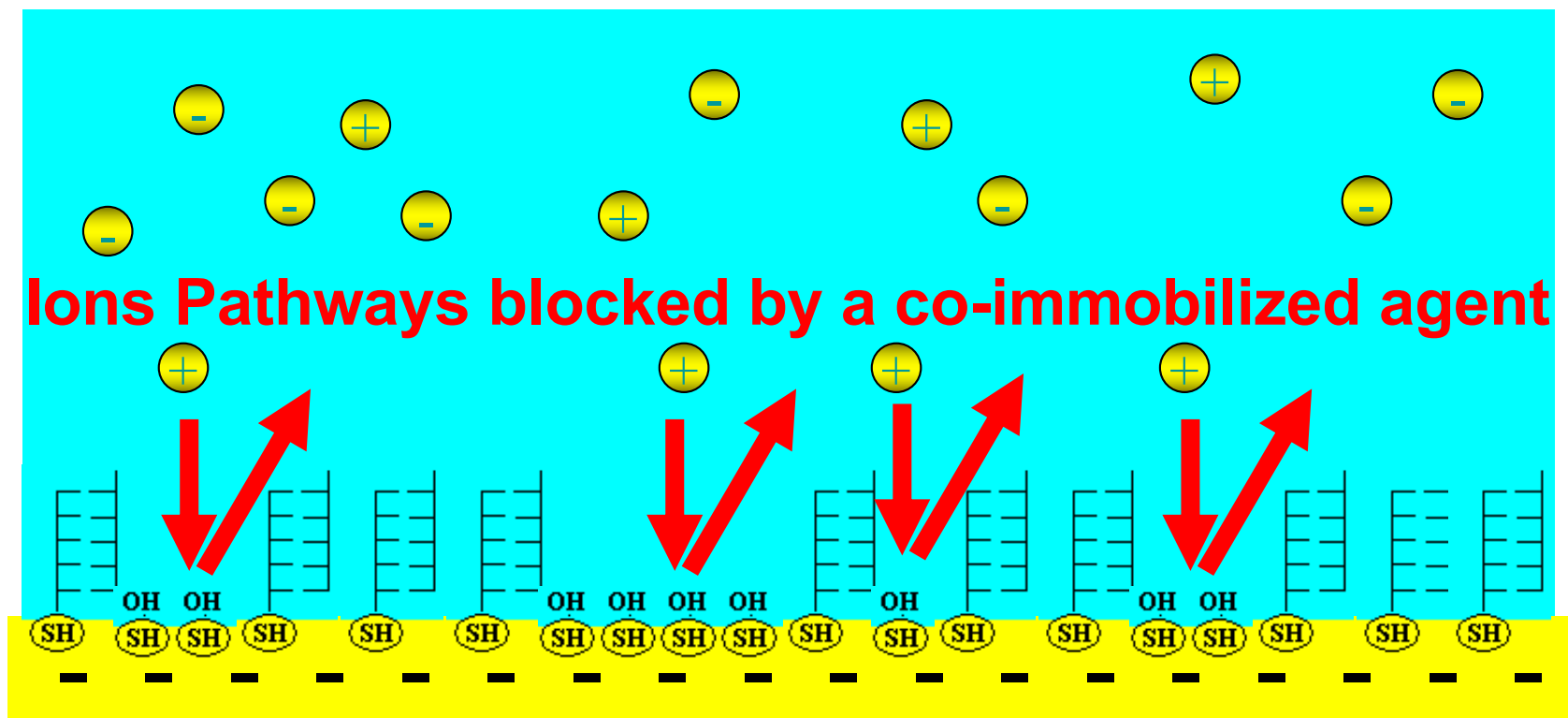


Fig. 7. Regeneration of the EC20 modified electrode with (1) 1 mM EDTA after injections of (2) 100 μM Zn^{2+} . Other experimental conditions are as in Fig. 5.

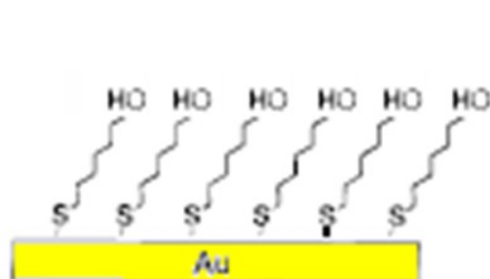
Heavy metal ion capacitance detection by using phytochelatine as probe molecule

Nano-aperture blocked in the probes film

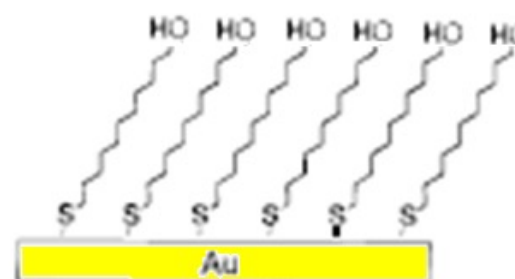


Ion Pathways blocked at the nanoscale

Blocking Agents



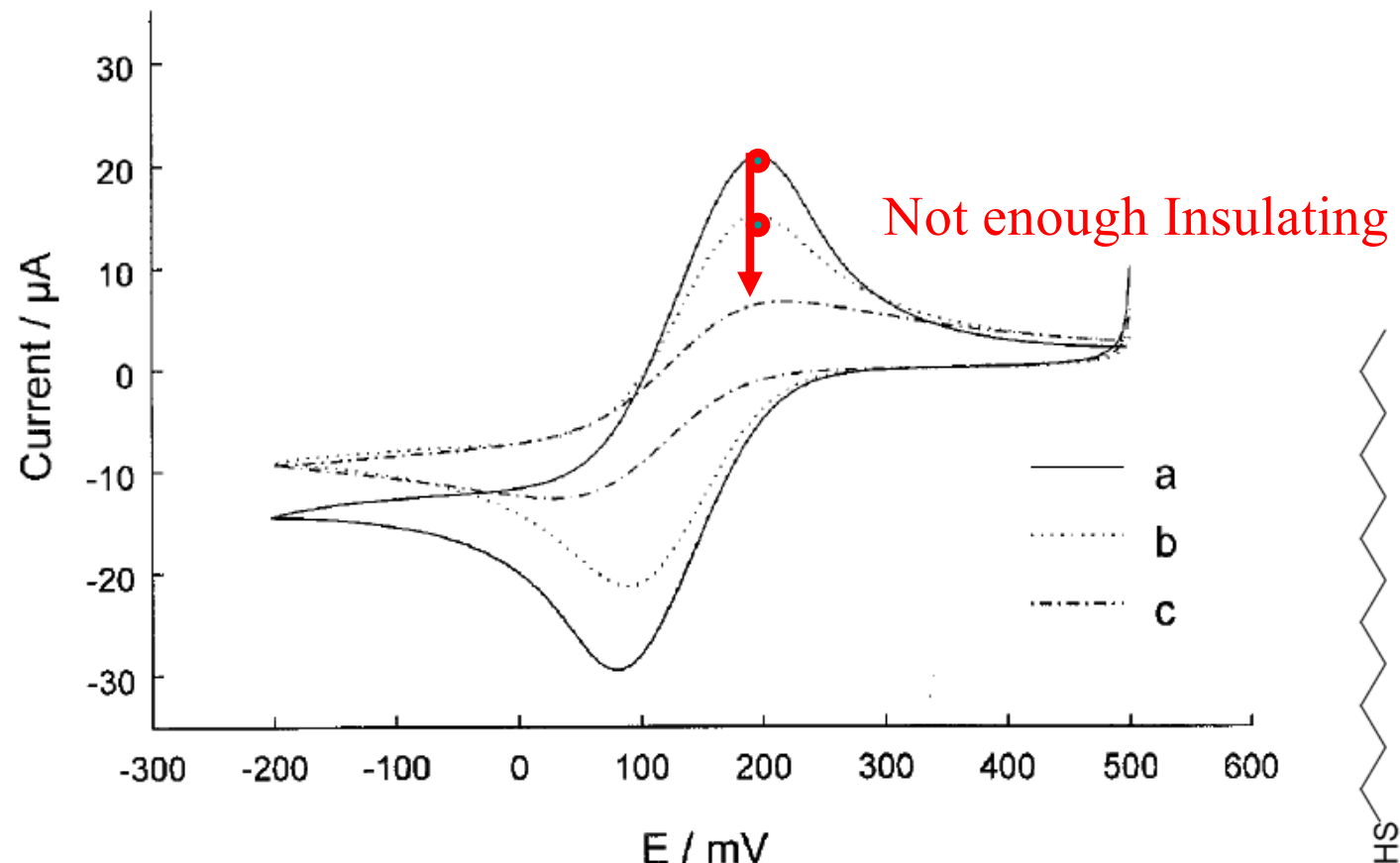
Mercapto-Hexanol



Mercapto-Undecanoic Acid

Increased stability by using mercapto-hexanol
or longer thiols

Improved insulating behavior



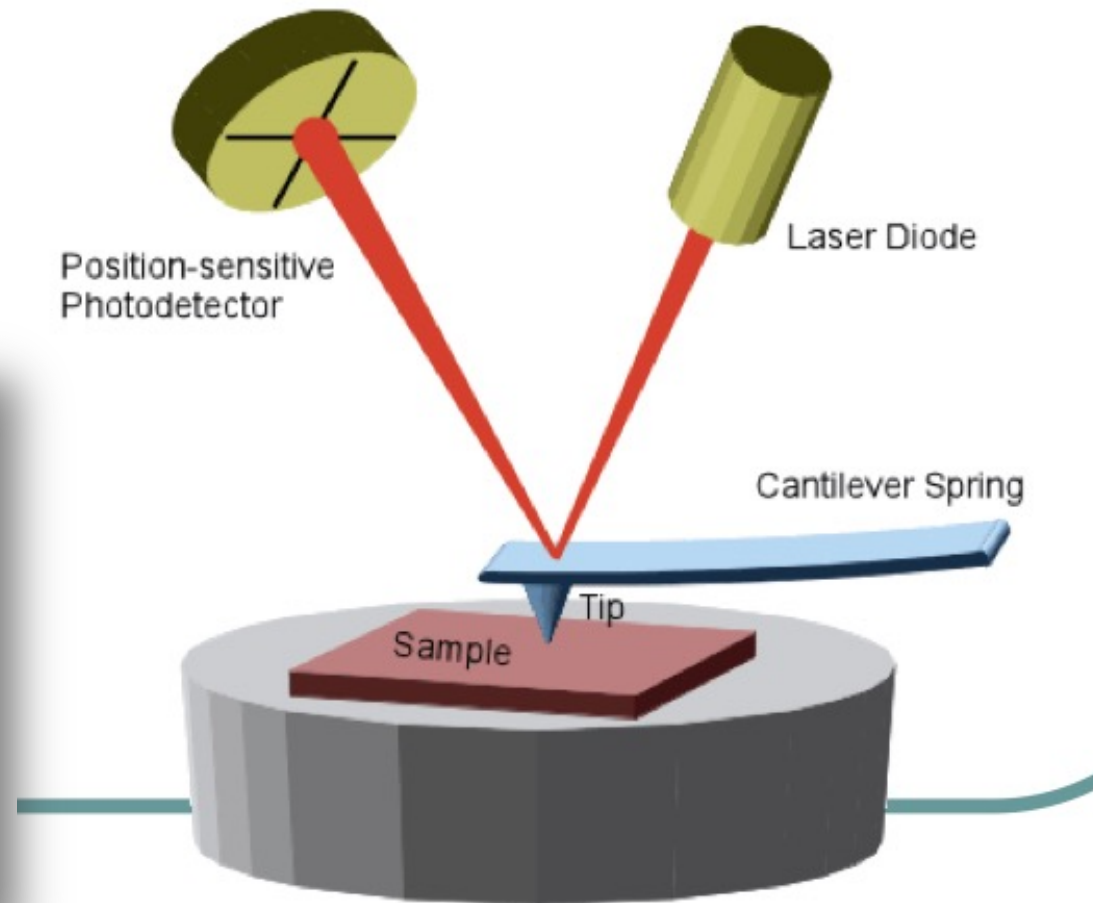
C. Berggren et al. Electroanalysis 1999, 11, No. 3

Redox reaction of $\text{K}_3\text{Fe}(\text{CN})_6$ on gold electrode (a),
ss-DNA onto gold (b) and ss-DNA + 1-dodecanethiol onto gold (c)

AFM: Working principle

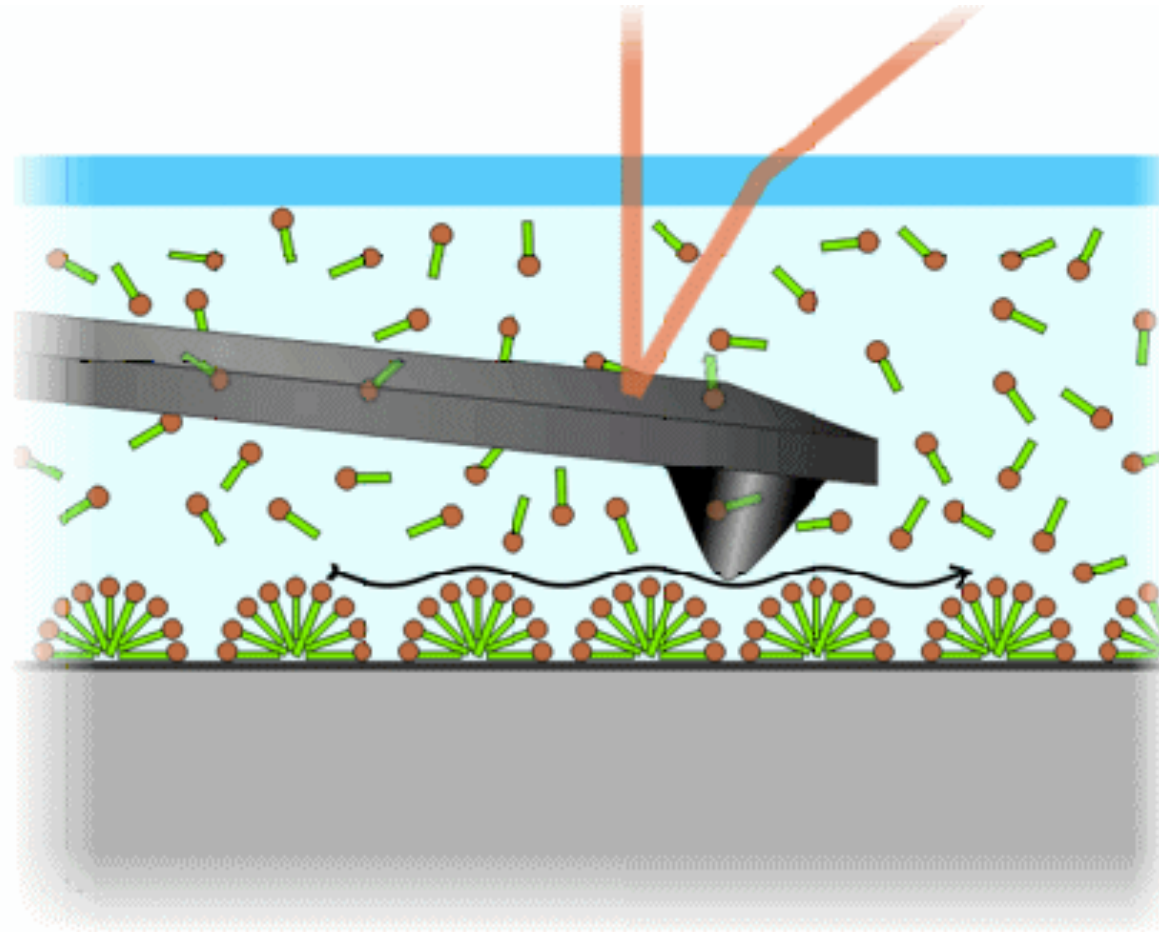
3 major abilities:

1. force measurement between probe-sample
2. imaging from forces that sample imposes on probe (3D, pseudocolor)
3. manipulation use forces to change sample properties



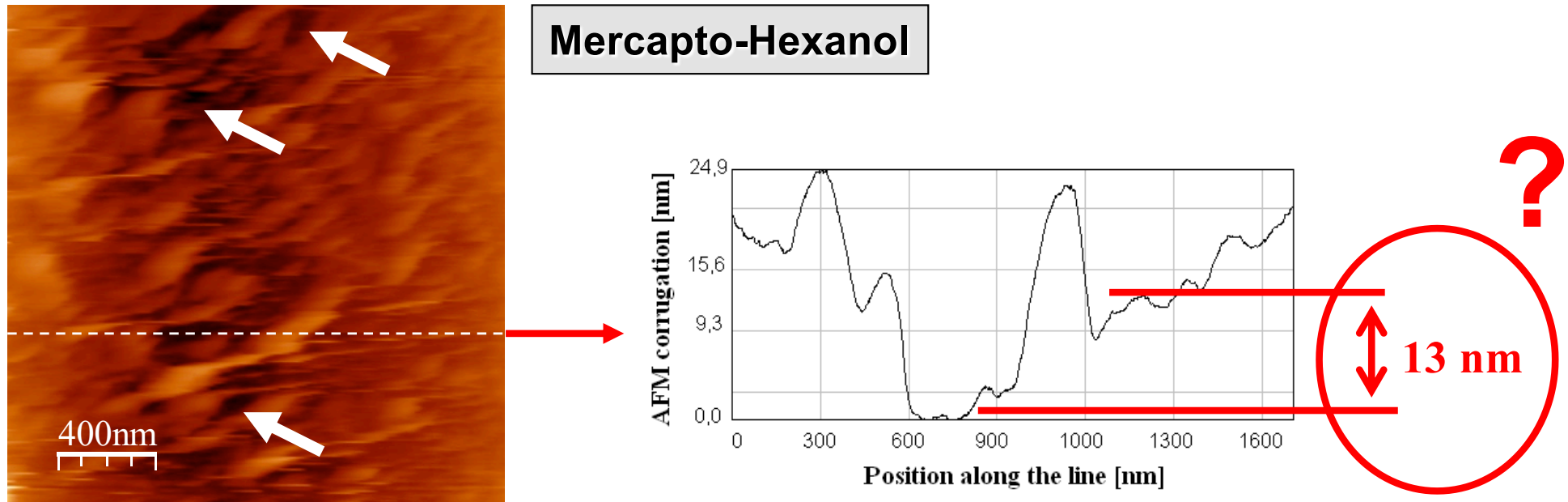
AFM detection principle by monitoring the bending of the cantilever that host the tip

AFM in liquid



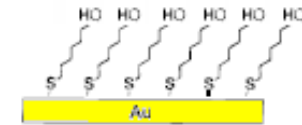
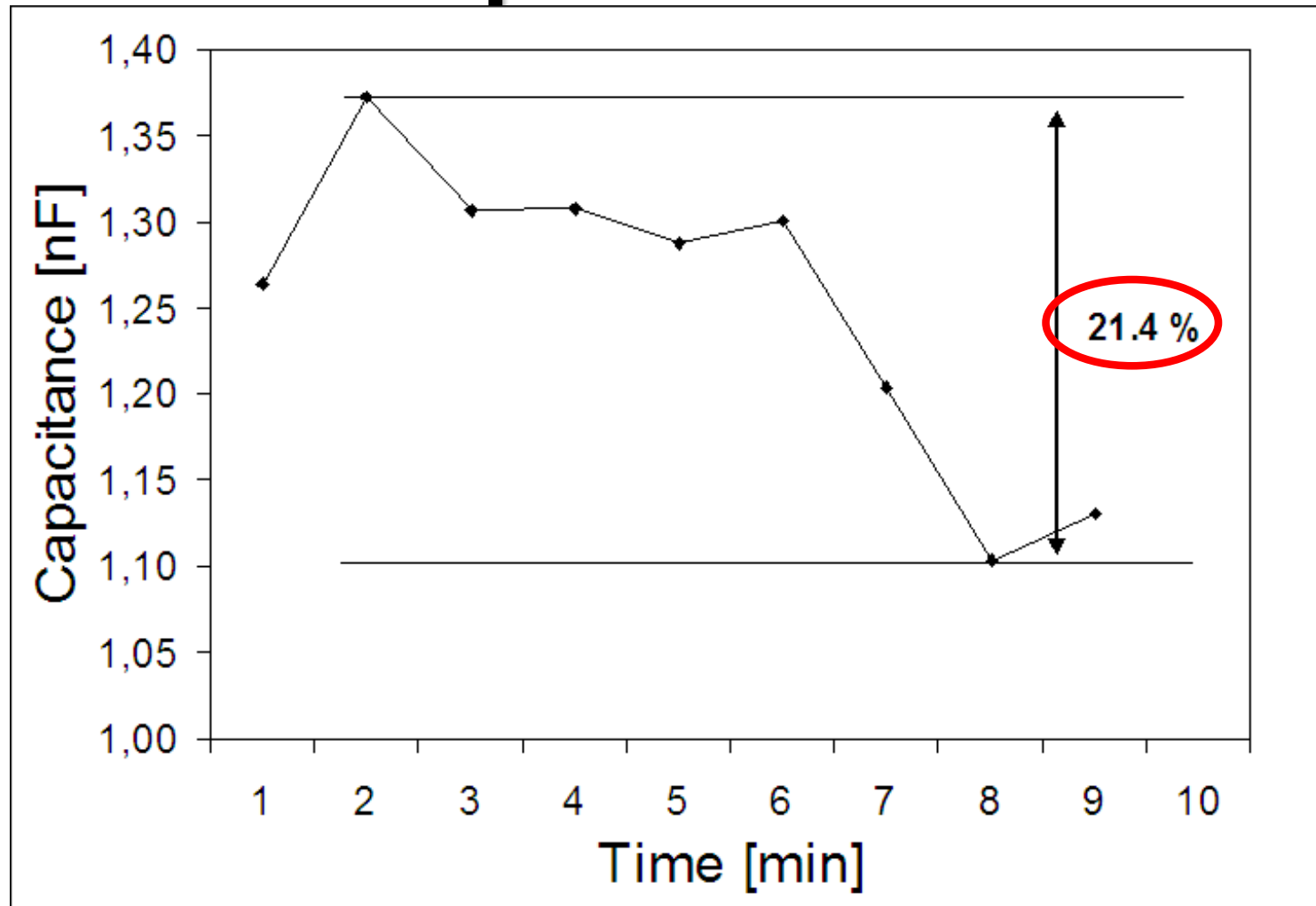
AFM is also used fully in water for imaging typically biological systems in their native environments

Nano-scale Apertures



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

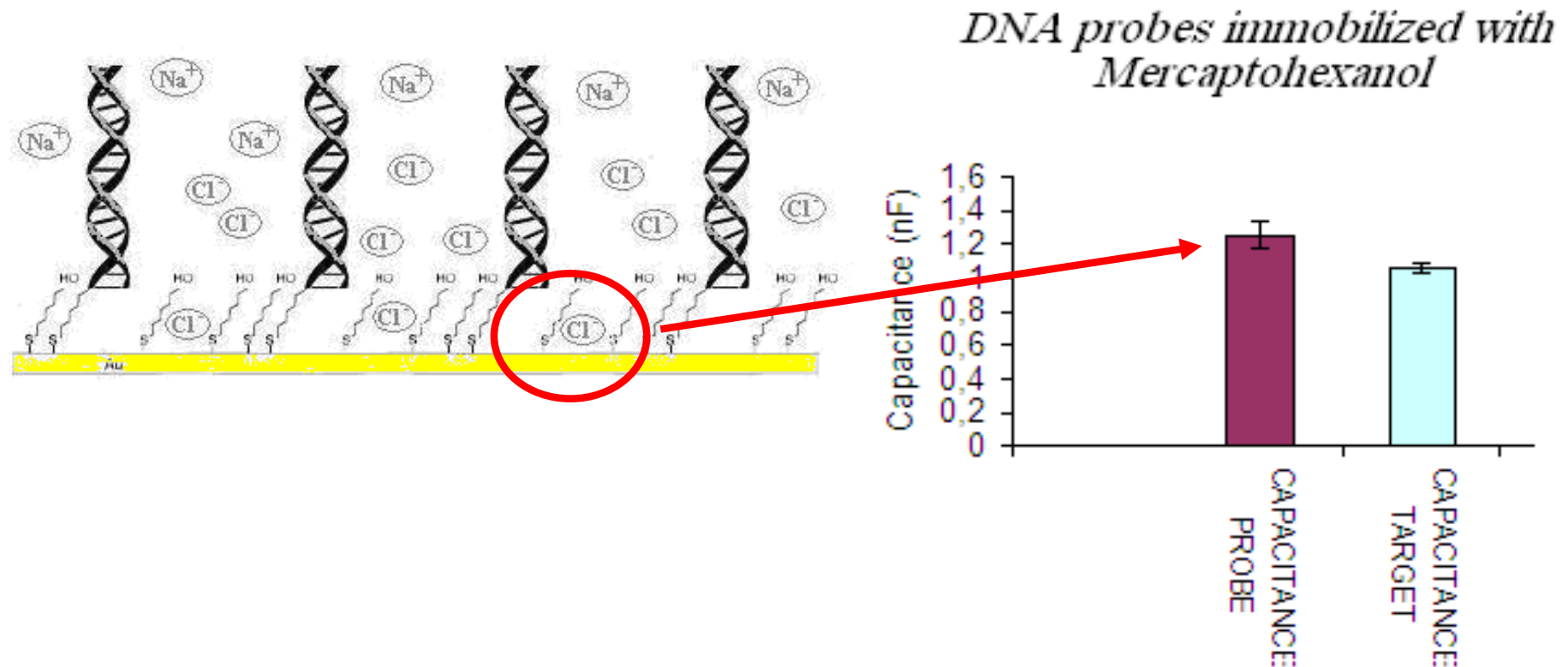
Capacitance Instability



Mercapto-Hexanol

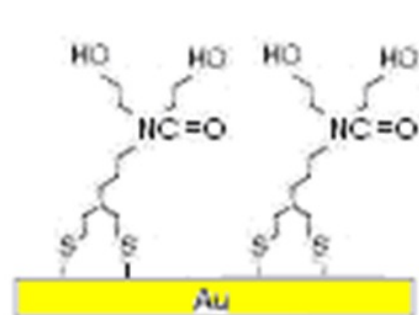
Mercapto-Hexanol is not enough as blocking agent

Mercapto-Hexanol partially block

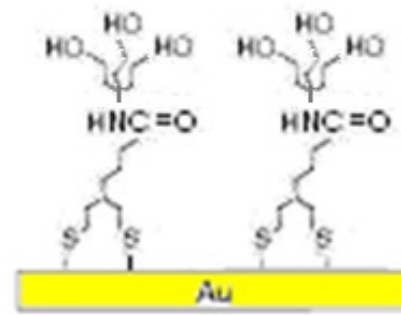


The presence of mercapto-hexanol partially prevent the solution ions in free contact with electrodes and results in a reduction of the standard deviations

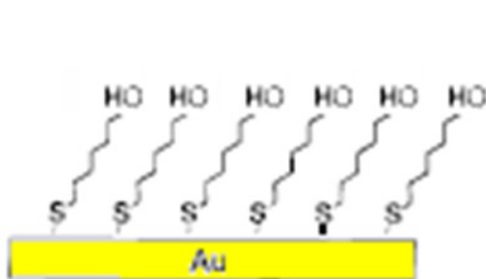
More Effective Blocking Agents



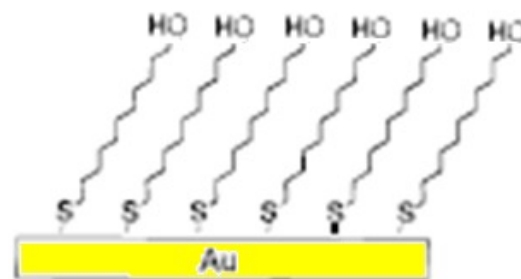
Lipa-DEA



Lipa-Tris



Mercapto-Hexanol

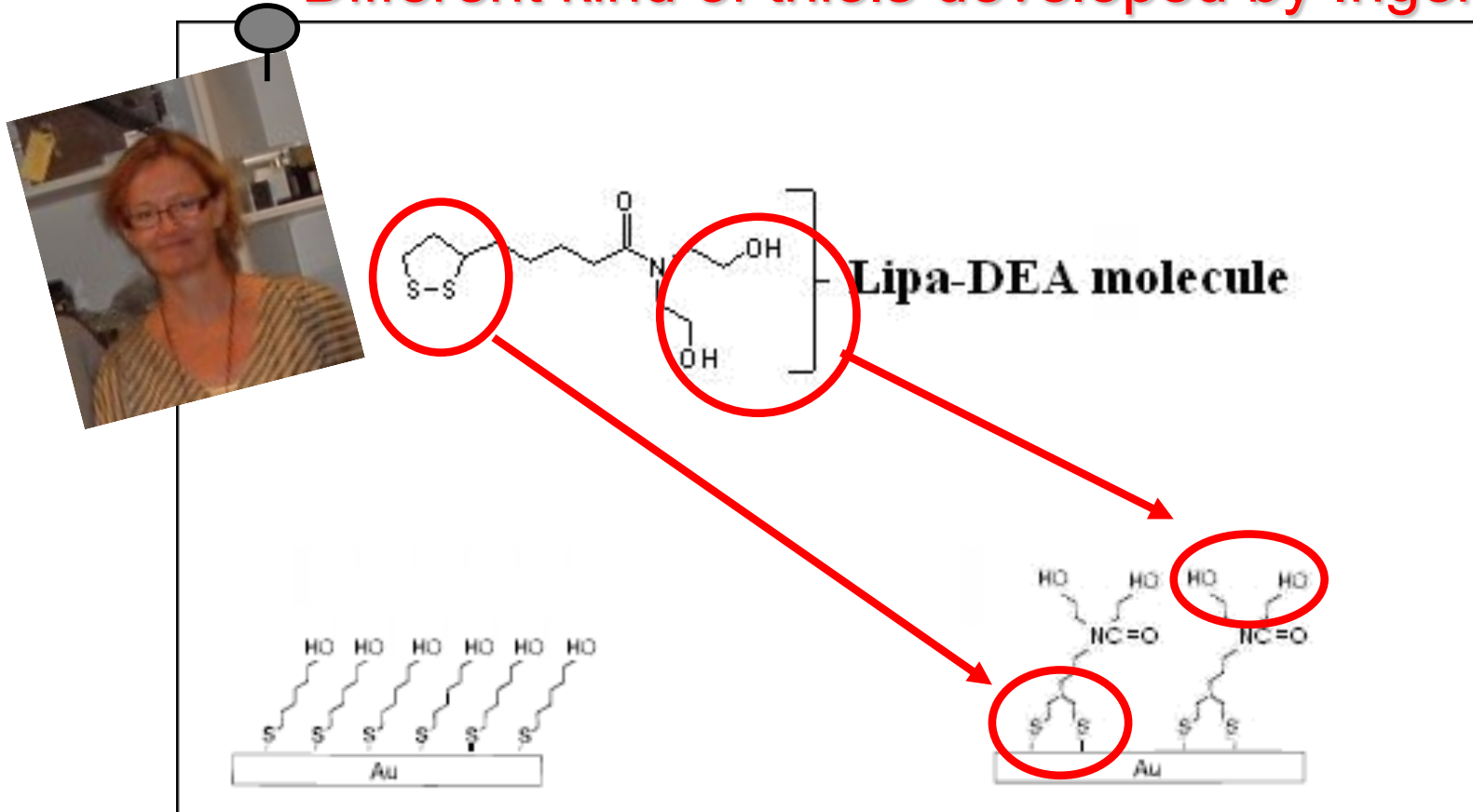


Mercapto-Undecanoic Acid

Increased stability by using Lipa-DEA
as blocking agent

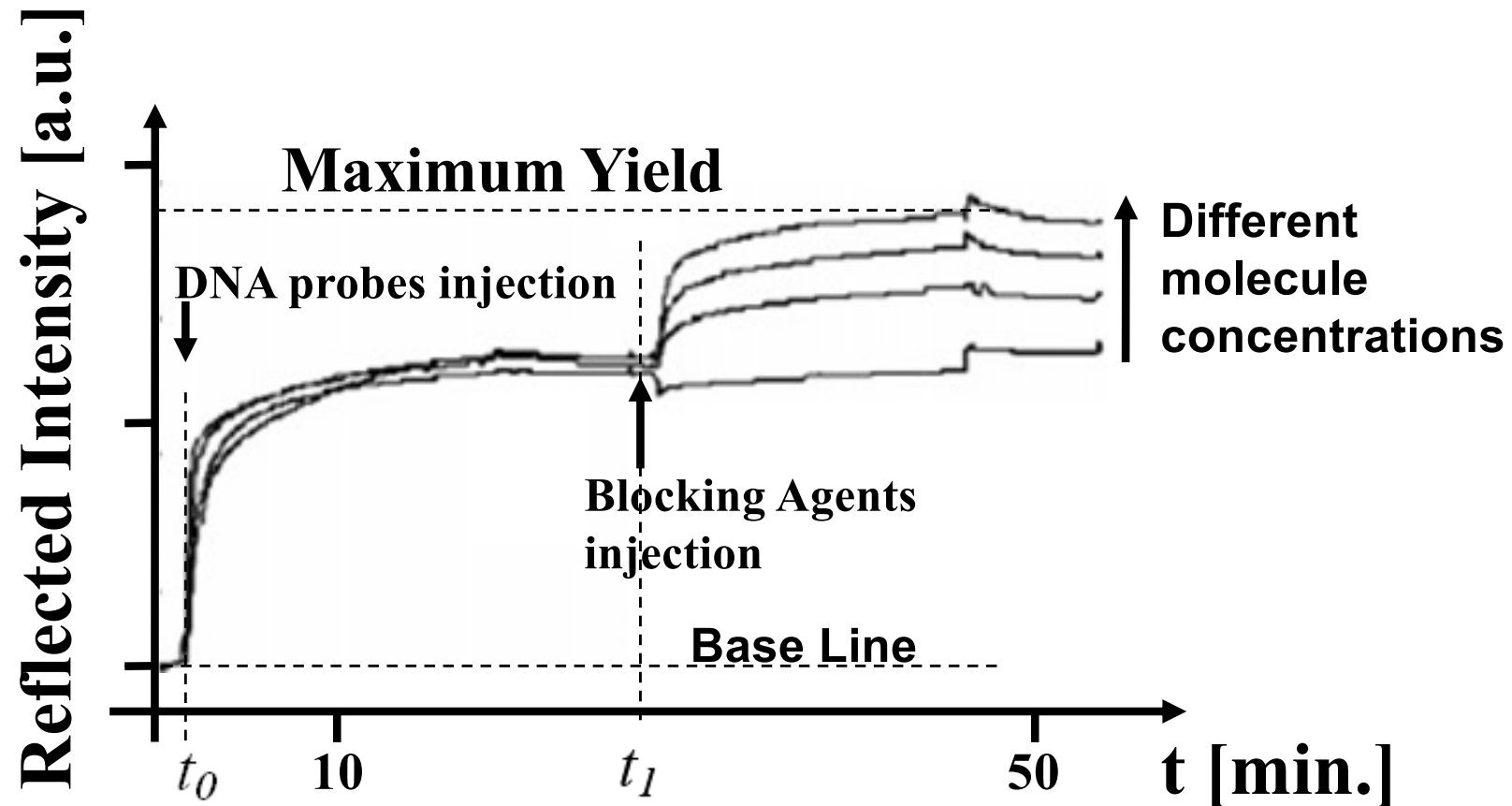
Lipa-DEA blockers

Different kind of thiols developed by Inger Vikholm



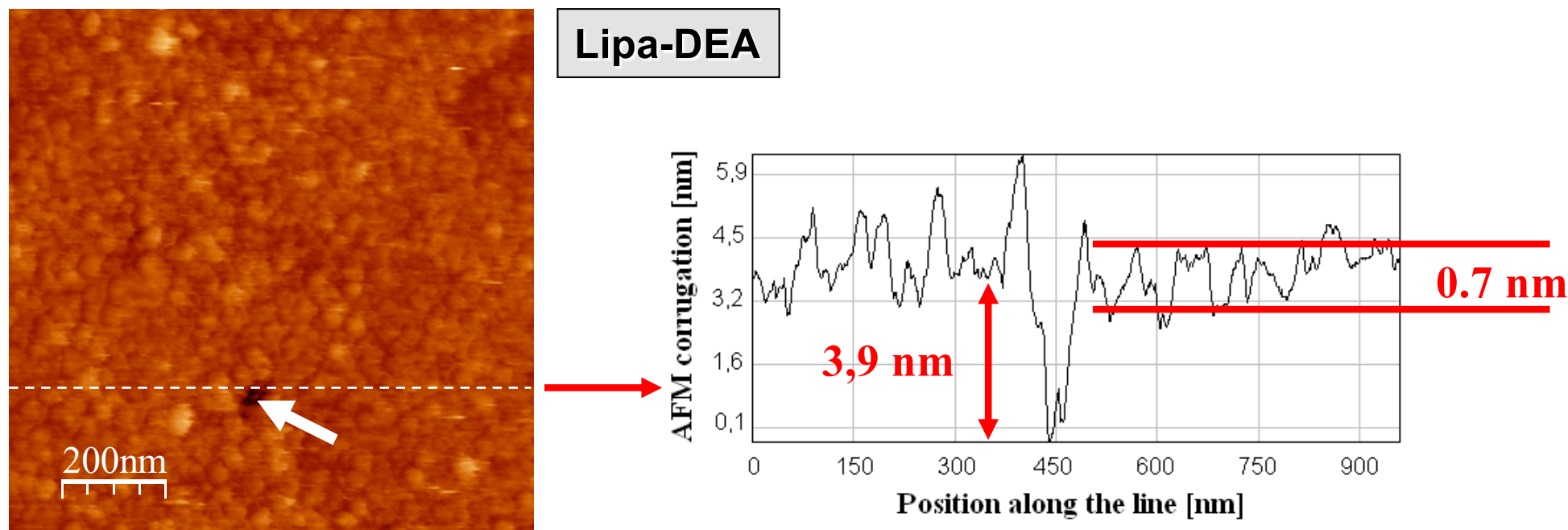
N,N-bis(2-hydroxyethyl)- α -lipoamide (Lipa-DEA) may be used as more efficient blocking agents

SPR on successive deposition of Blocking Agents



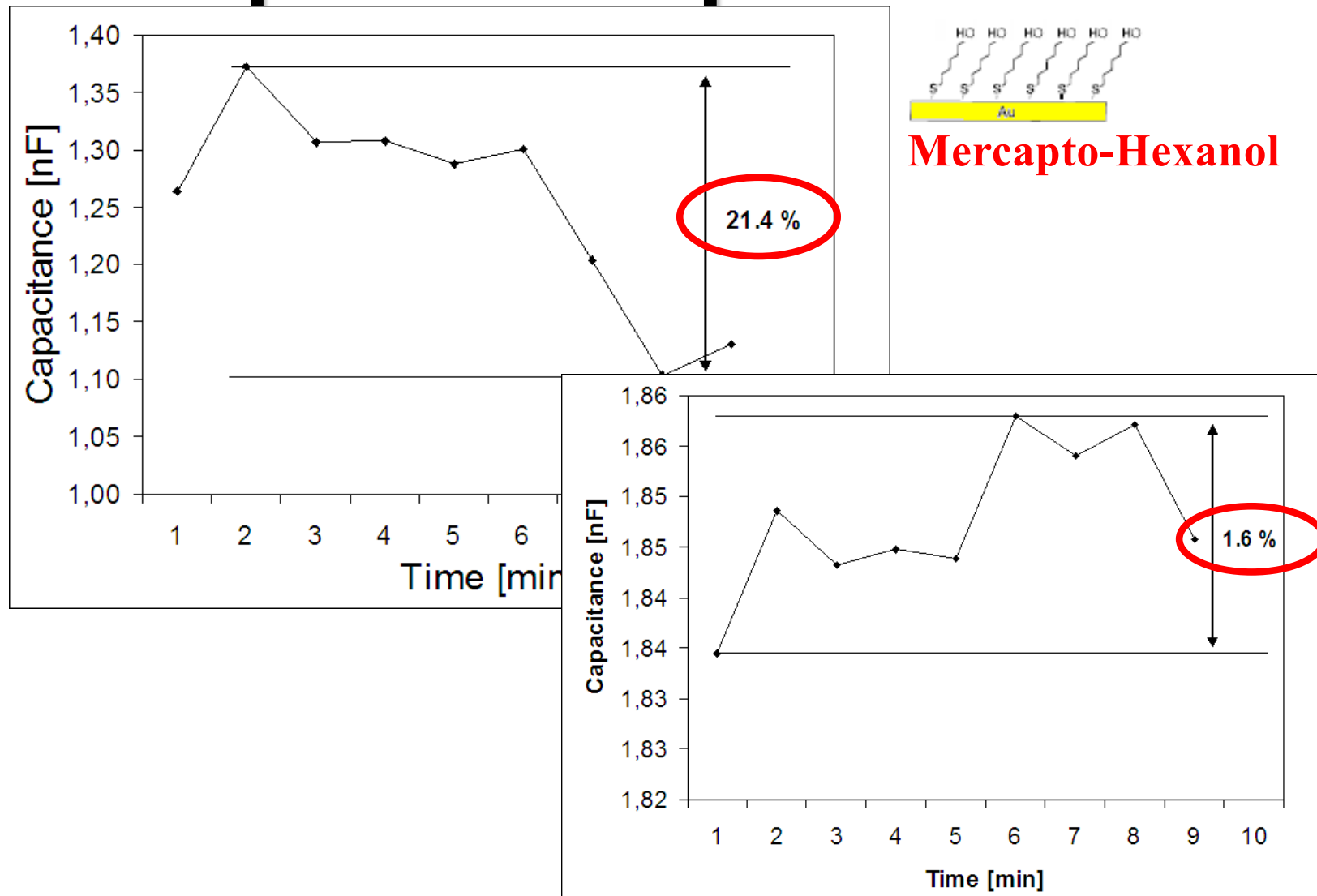
I. Vikholm-Lundin et al. / Biosensors and Bioelectronics 22 (2007) 1323–1329

Nano-scale Apertures



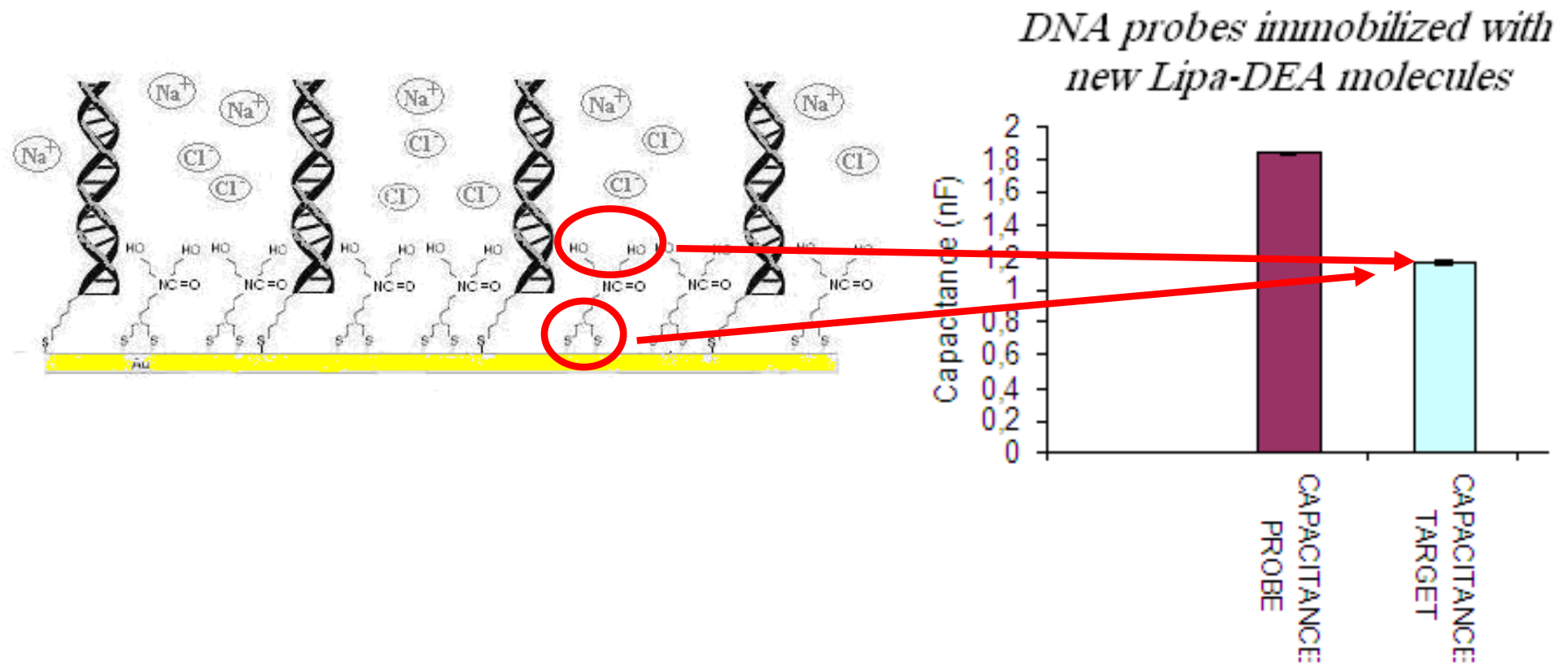
Monolayer of ssDNA with blocking agents still present deep groves crossing the film

Improved Capacitance Stability



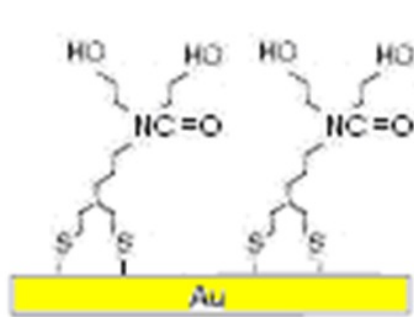
Increased stability by using Lipa-DEA as blocking agent

Lipa-DEA further improves

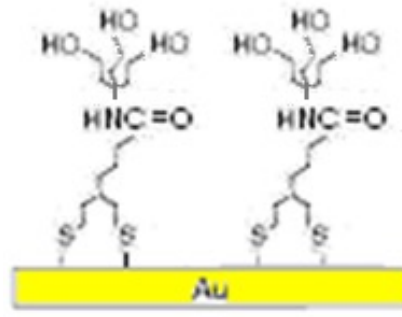


The presence of Lipa-DEA further prevent the solution ions in free contact with electrodes and results in a strong reduction of the standard deviations

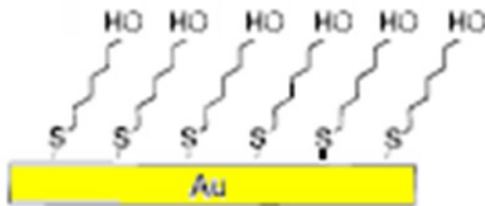
Precursors Monolayers



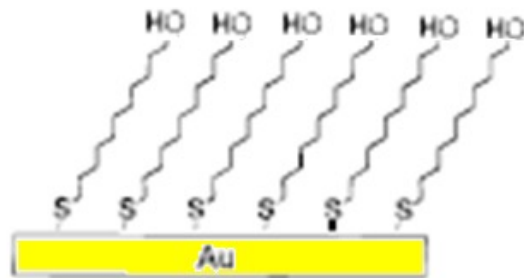
Lipa-DEA



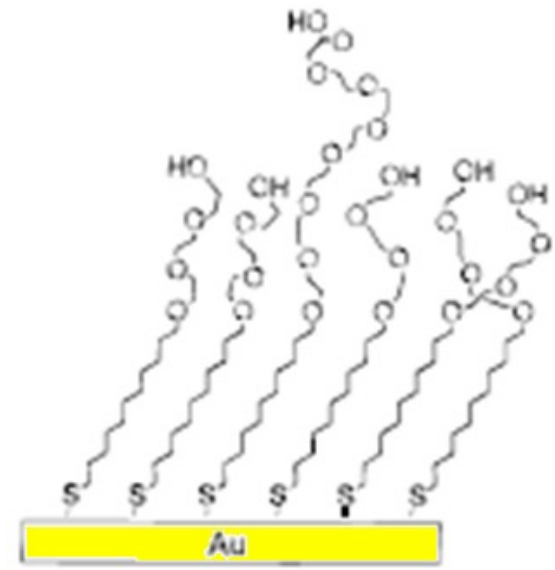
Lipa-Tris



Mercapto-Hexanol



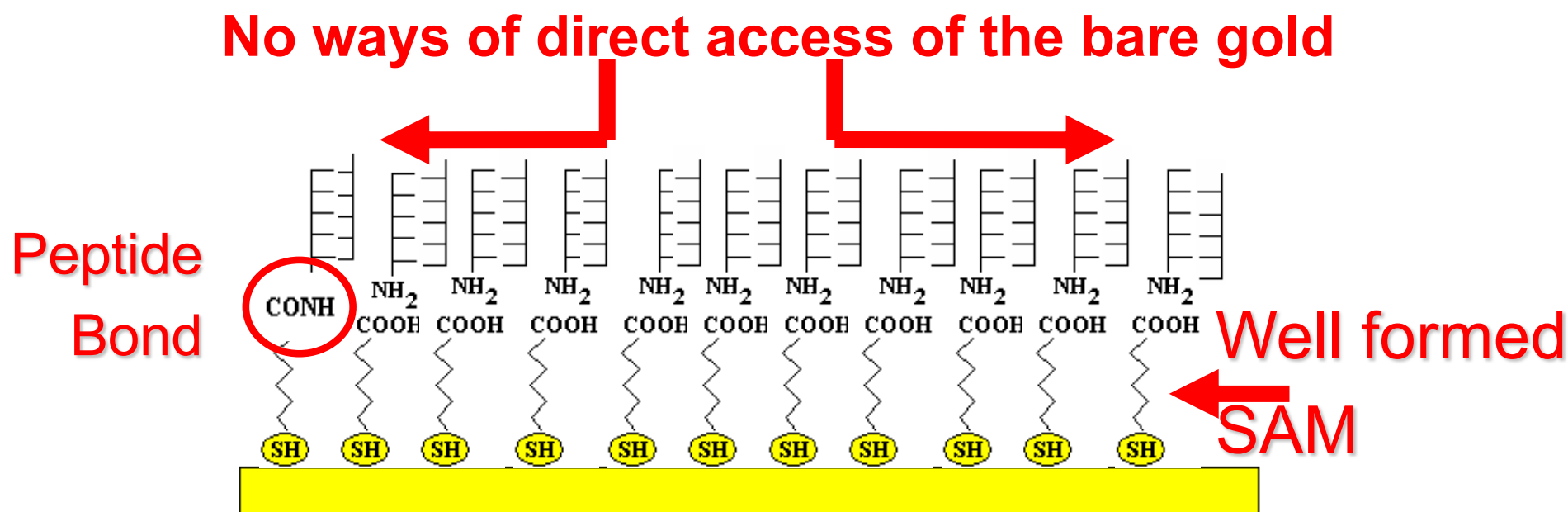
Mercapto-Undecanoic Acid



Ethylene-Glycol Thiols

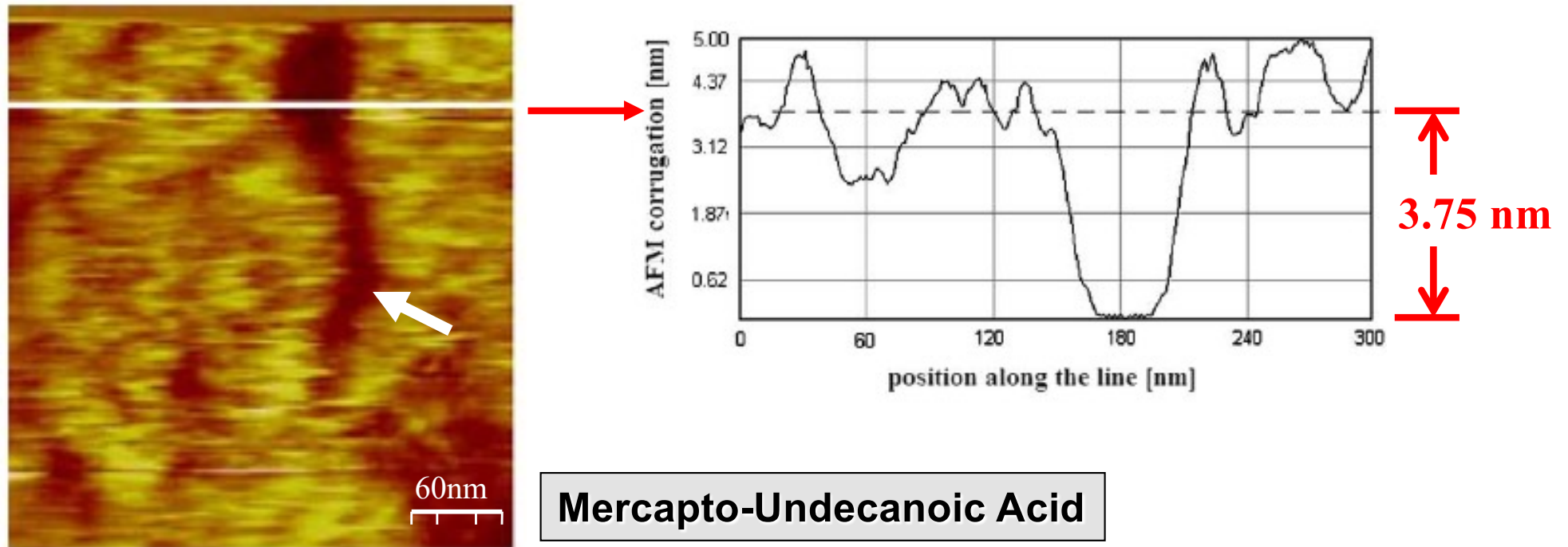
Increased stability by introducing precursors monolayers with Ethylene-Glycol function

Film precursors below probes



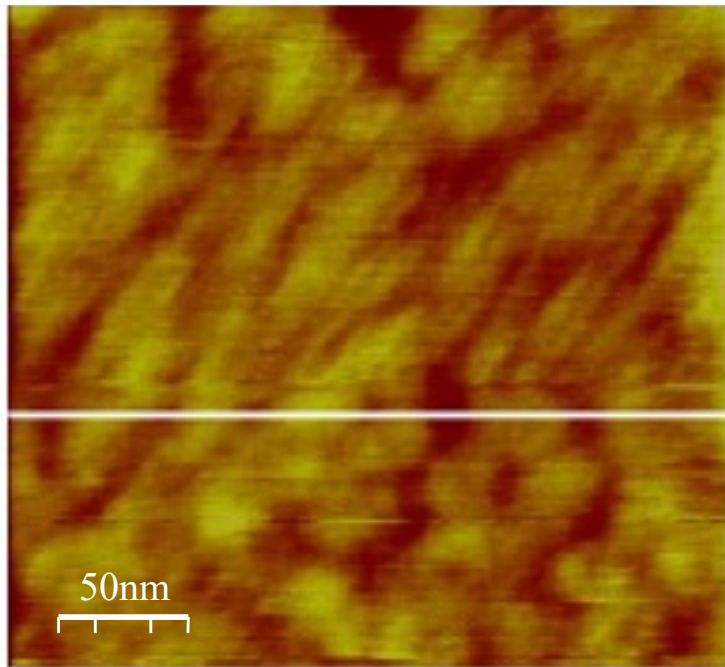
Highly packed thiols monolayer may be used
to improve the DNA detection capability

Nano-scale Apertures

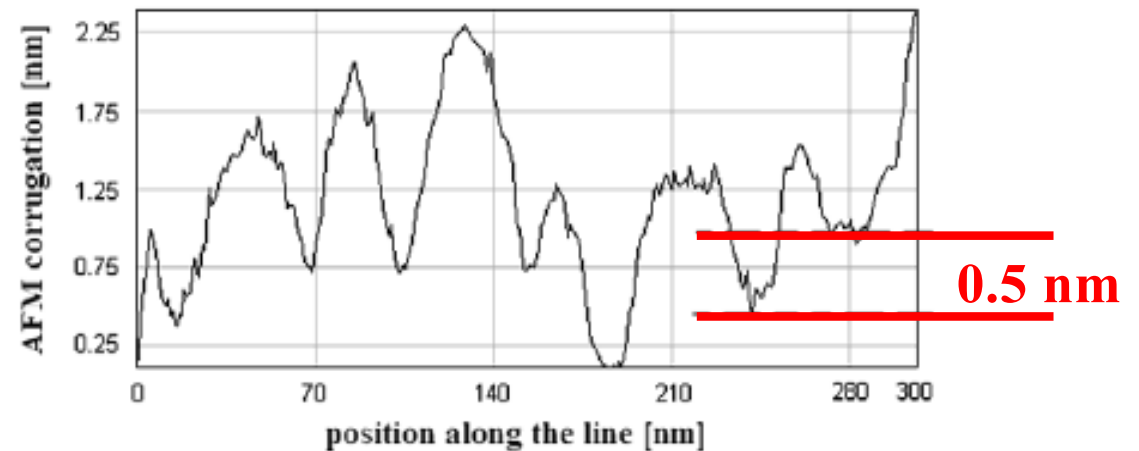


Monolayer of alkanethiols with ethylene-glycol chains does not present deep groves crossing the film

Absence of Nano-scale Apertures

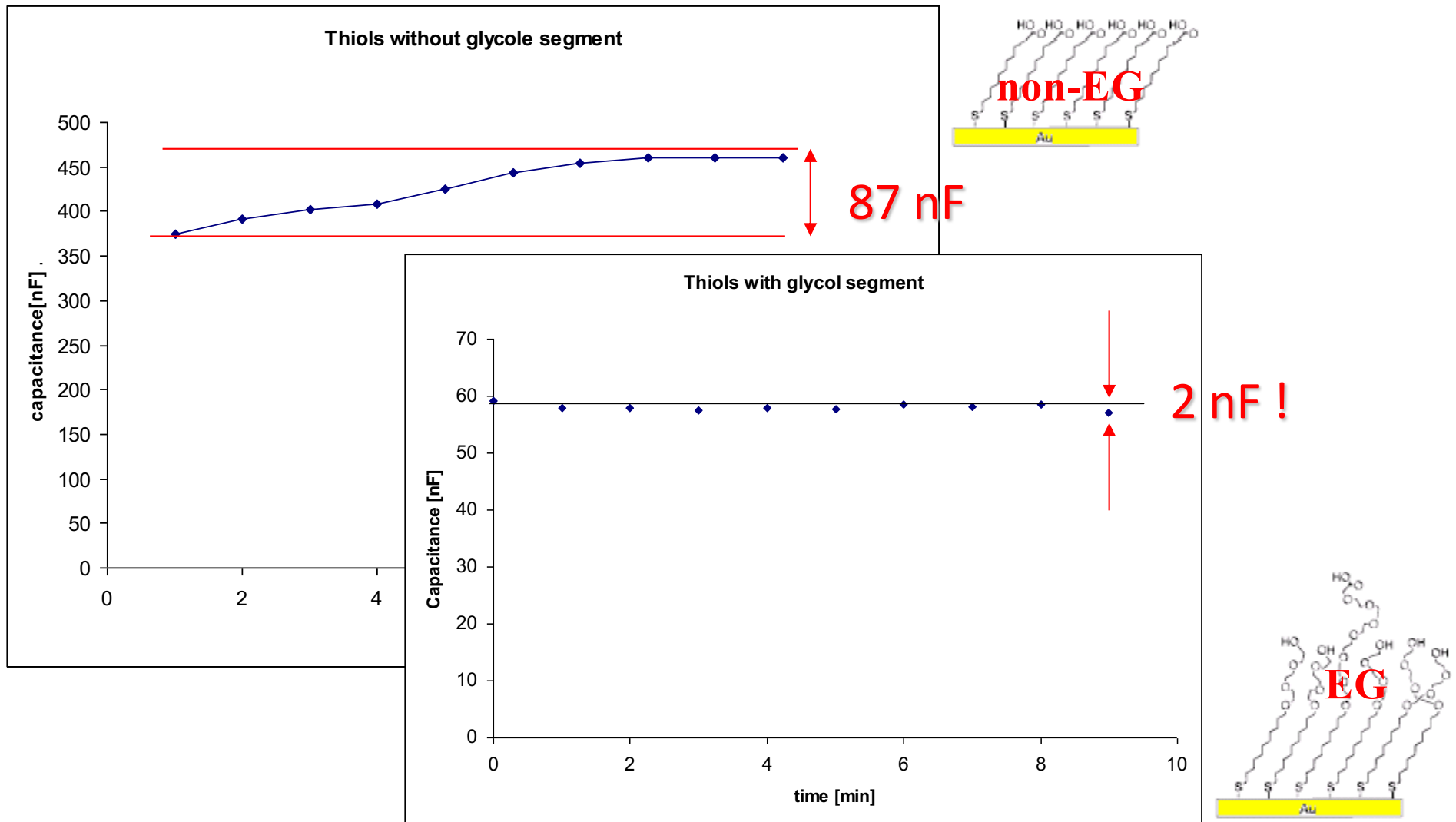


Ethylene-Glycol Film



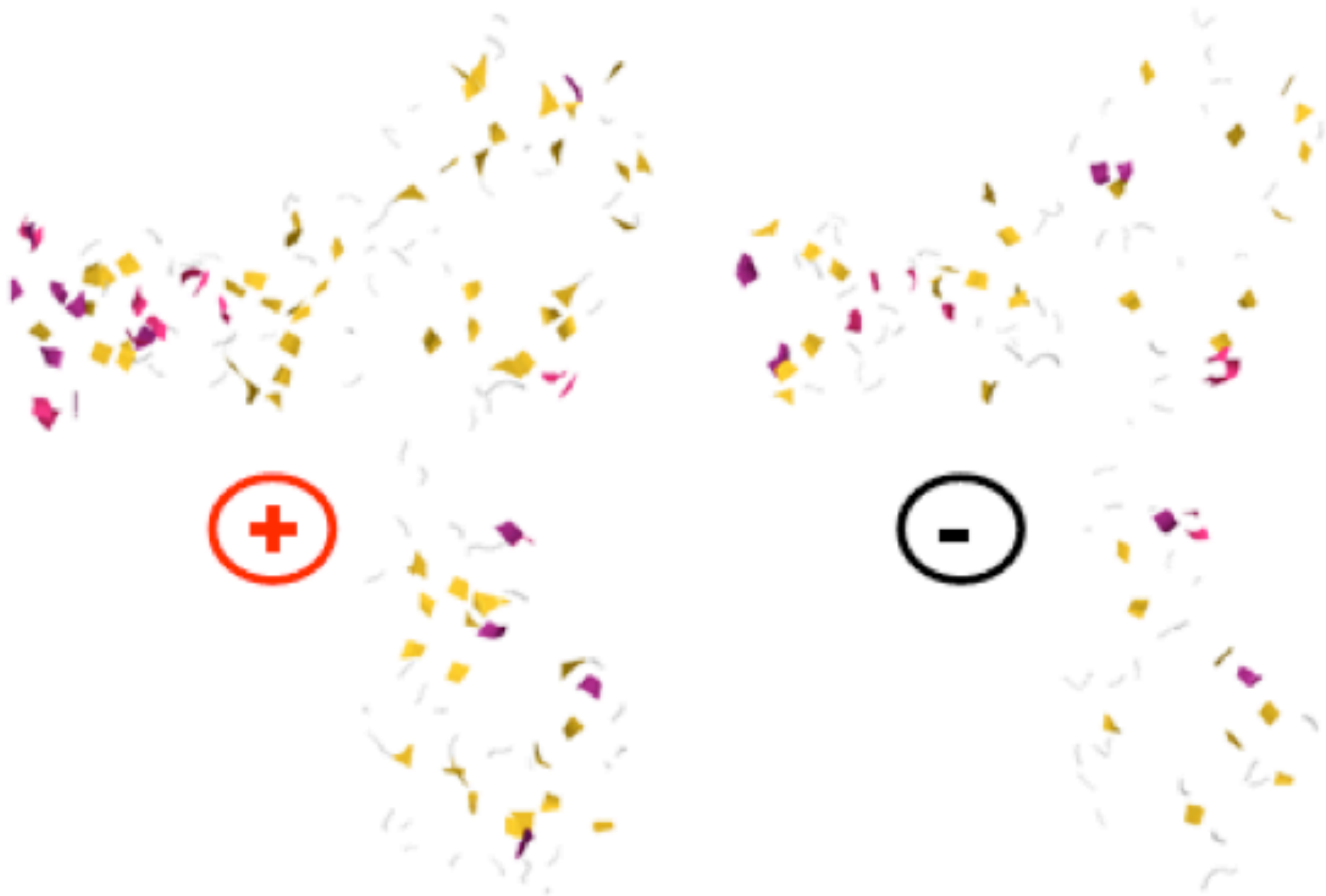
Monolayer of alkanethiols with ethylene-glycol chains
does not present deep groves crossing the film

Improved Capacitance Stability



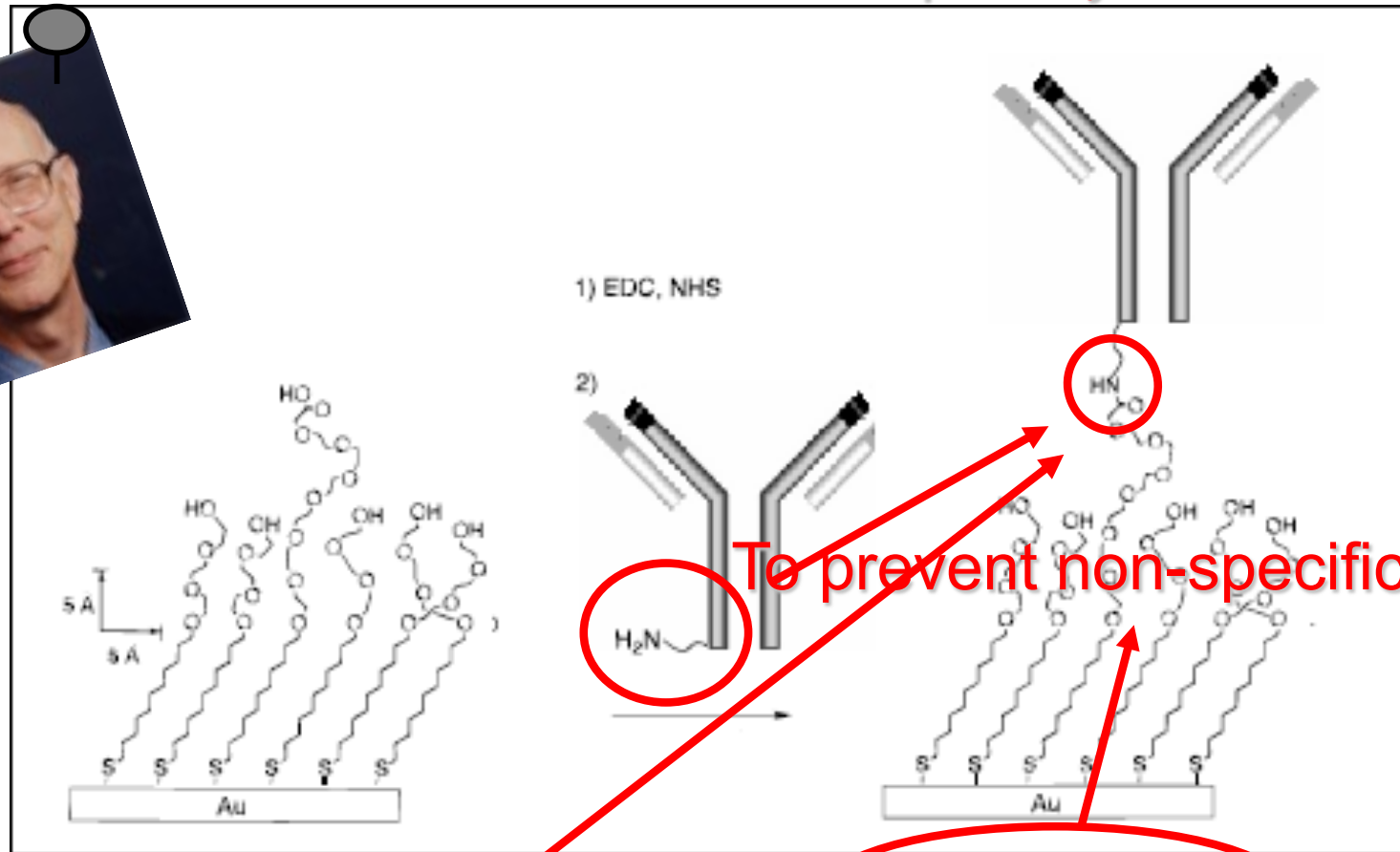
Increased stability by using Ethylene-Glycol thiols

Charges on an Antibody



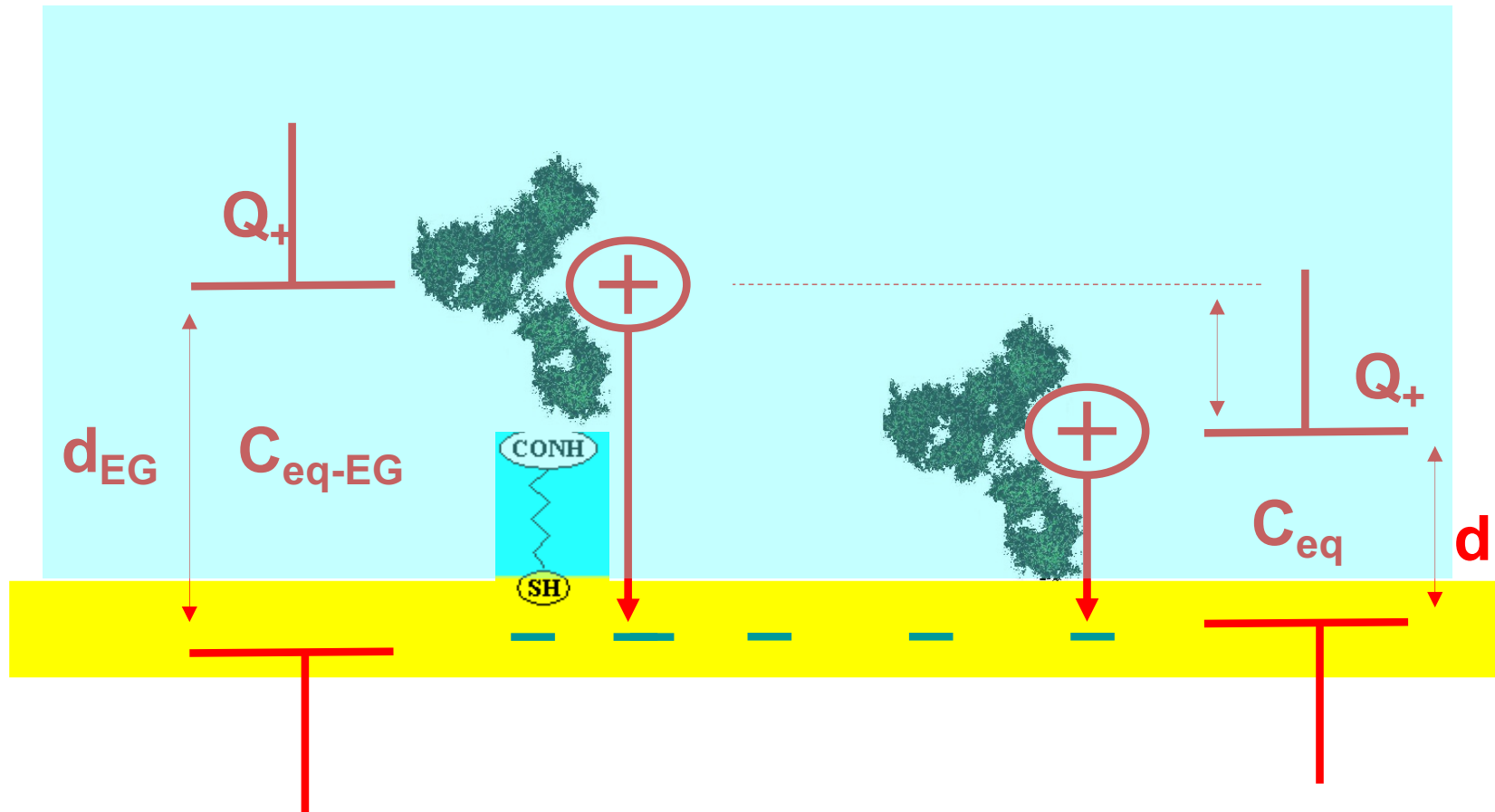
Ethylene-Glycol Blockers

Different kind of thiols developed by G.M. Whitesides



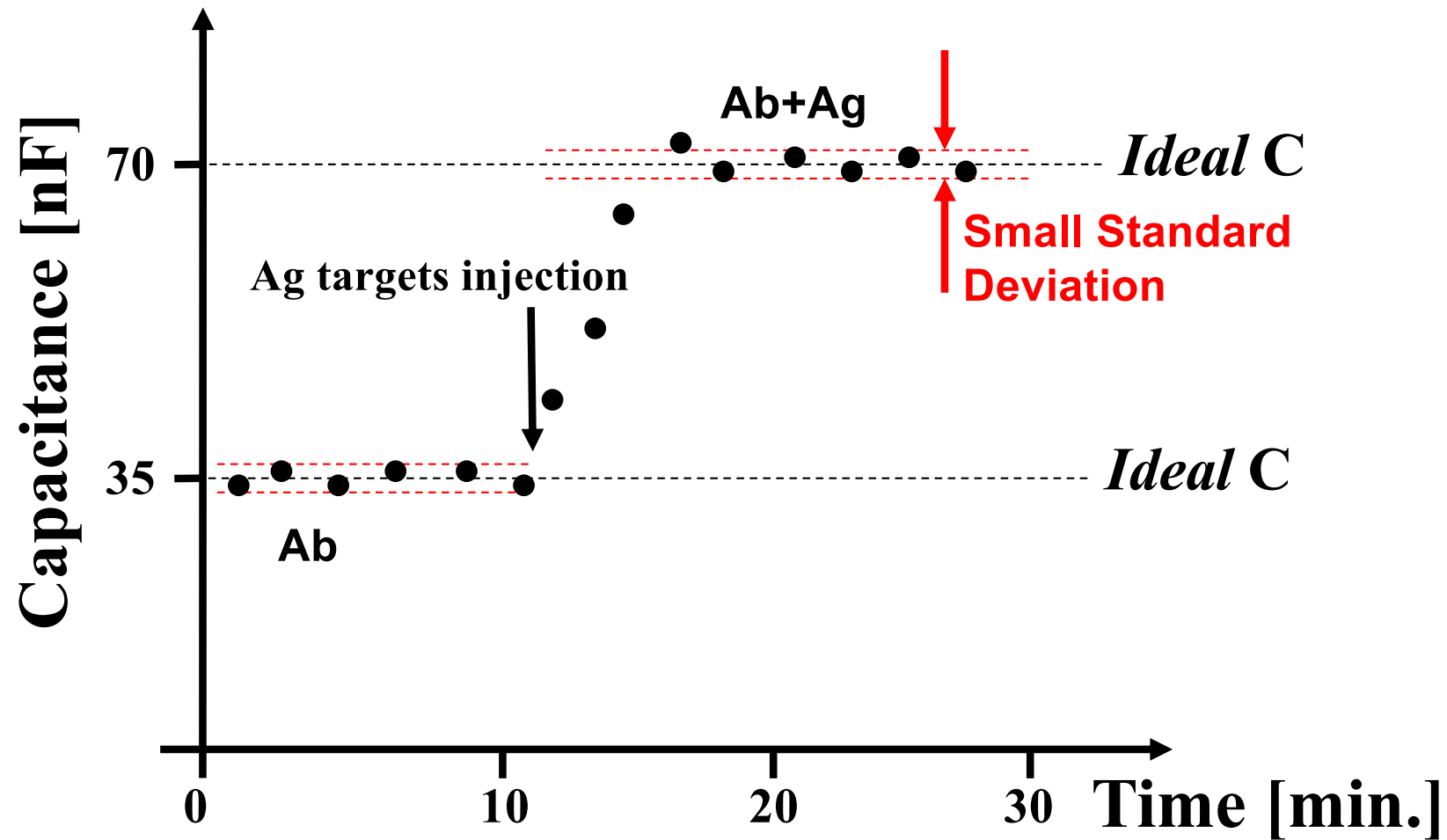
Covalently linked by using Ethylene-Glycol
carboxyl terminated alkyl Thiols

Capacitive detection

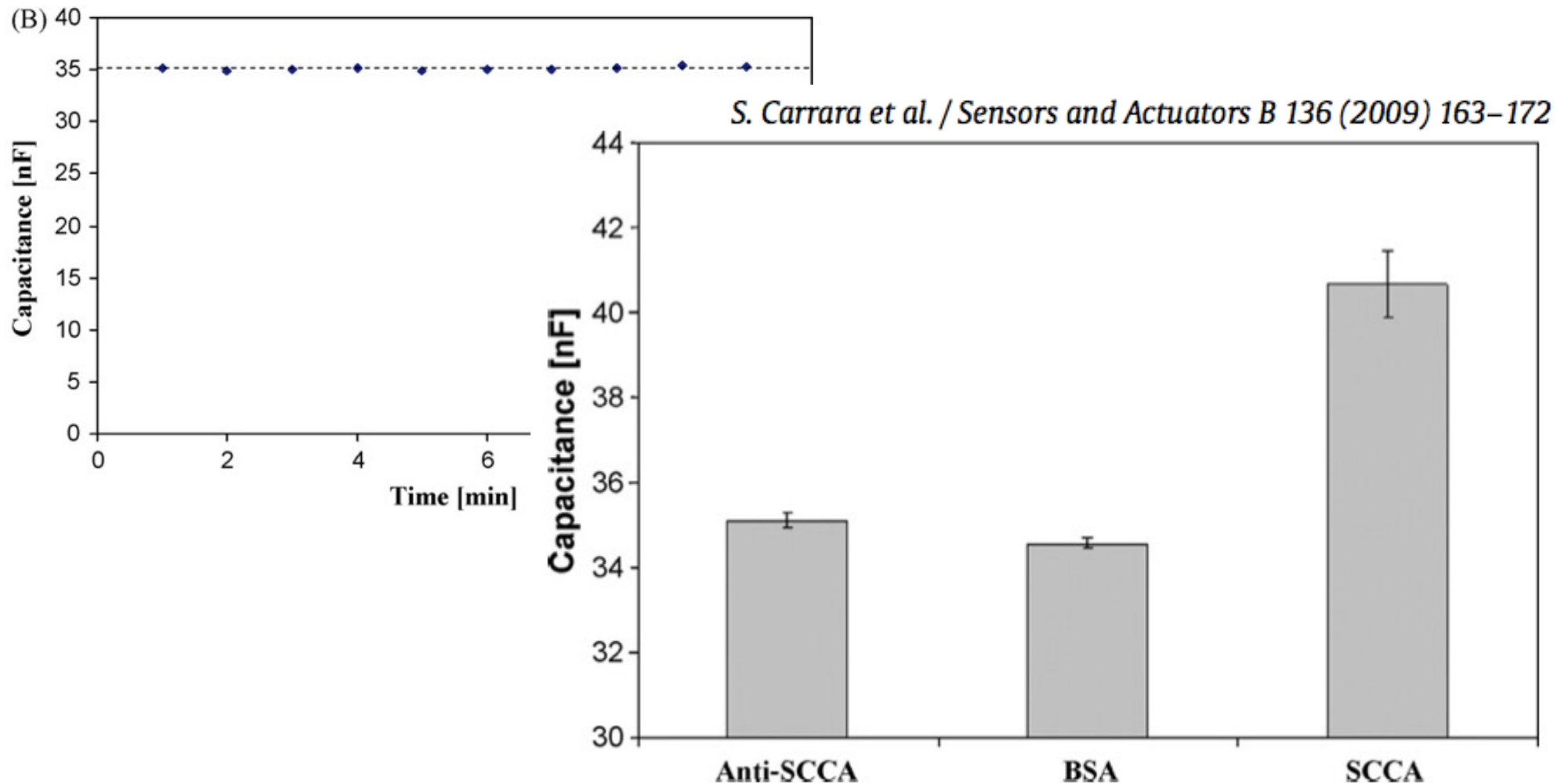


Charged residues of the antibody may affect charge carriers in the electrode

Reduced scattered-data

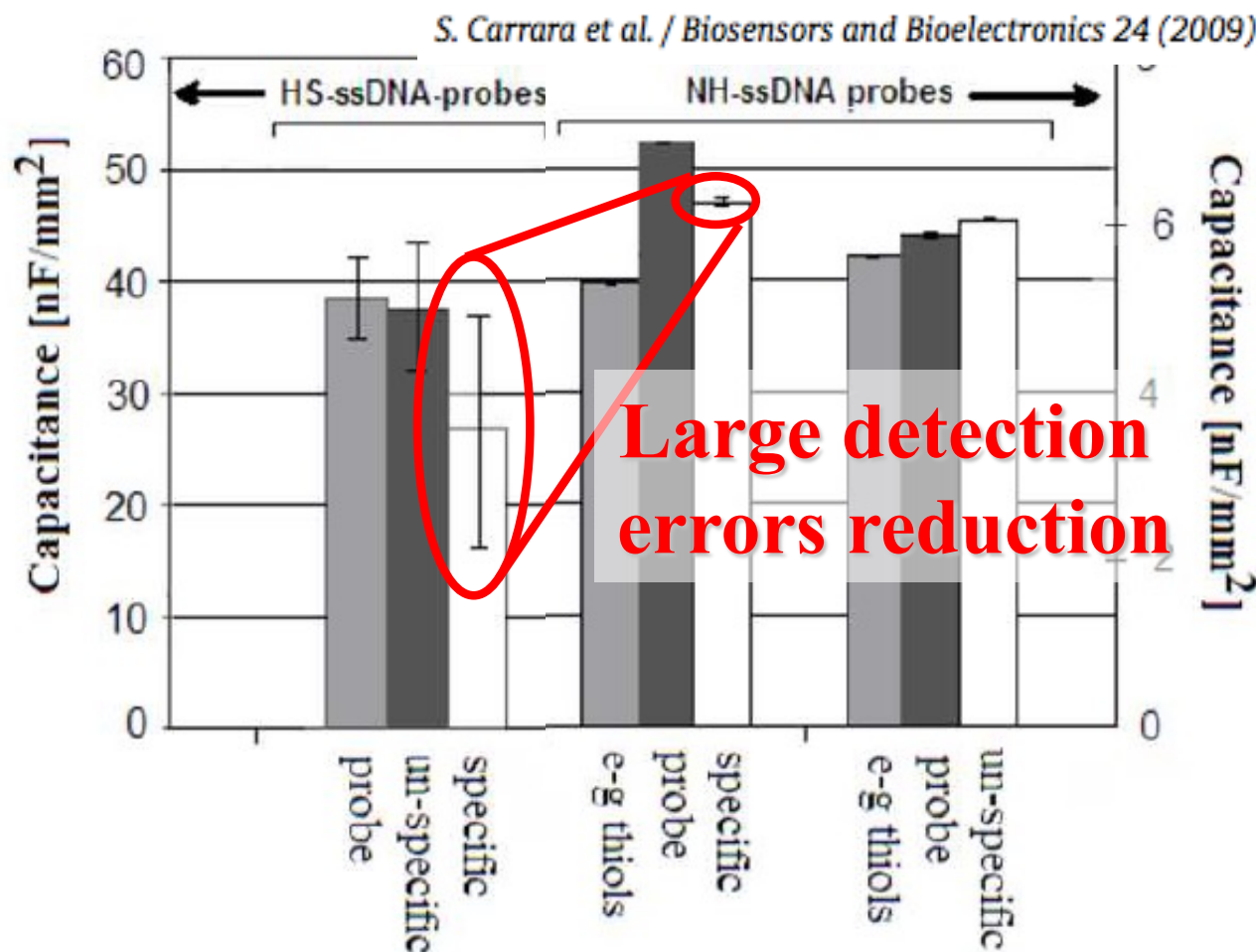


Cancer Marker Capacitance Detection



Highly reproducible Capacitance detection of the cancer-marker protein SCCA by immobilizing the antibodies onto EG-Thiols precursors

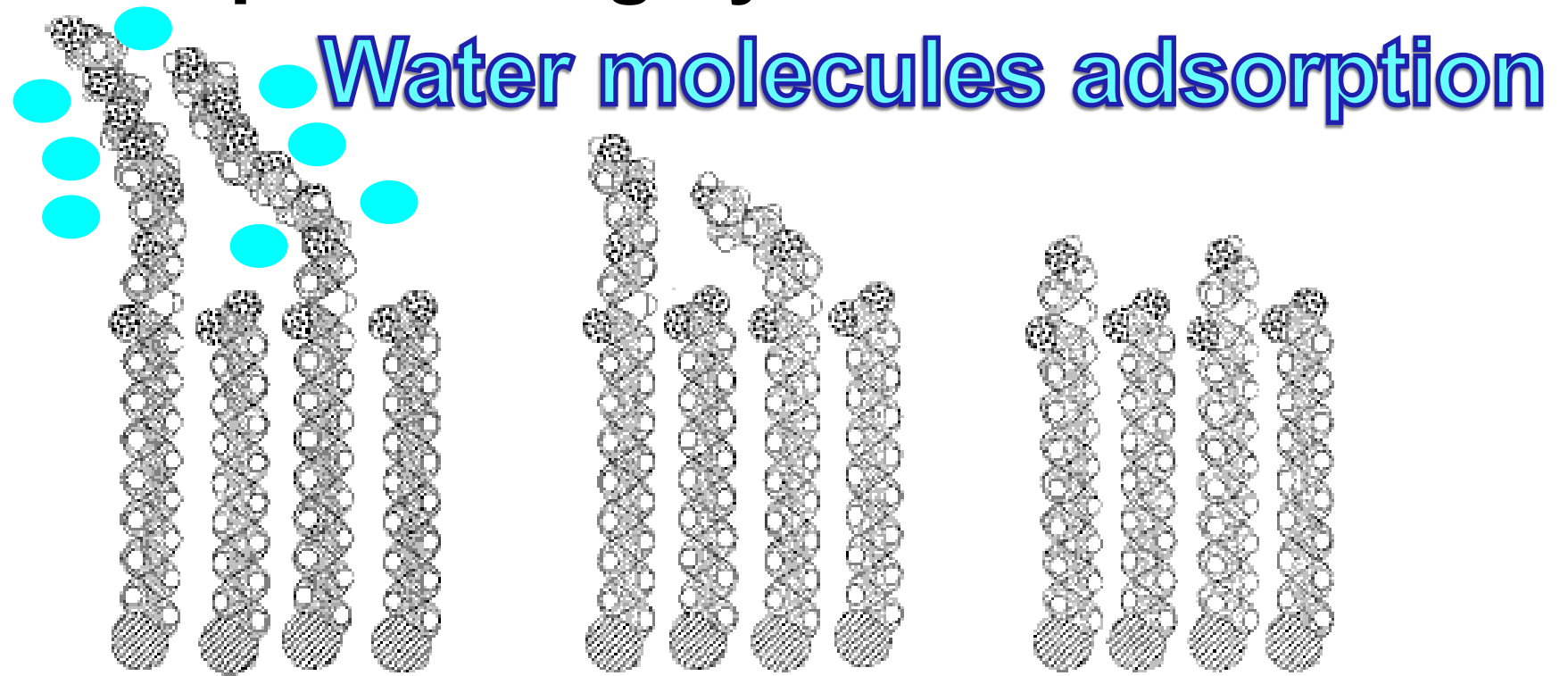
Capacitance detection of DNA



Highly –reproducible DNA detection based on ss-DNA-SH terminated directly immobilized onto gold and ss-DNA-NH₂ terminated immobilized onto EG-Thiols

Why it works so well to close nano-apertures?

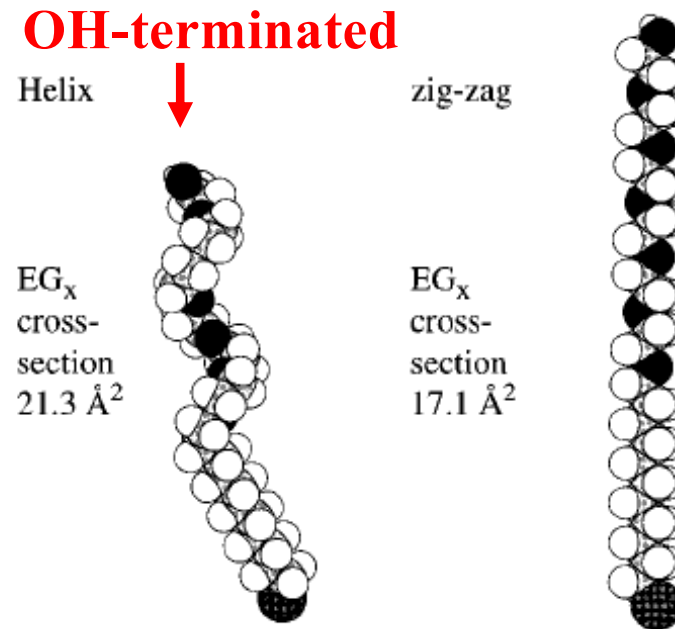
Space filling by EG thiols



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

Space filling molecular model illustration of EG-thiols film presenting a 1:1 mixture of $-\text{CON}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ ($n = 1, 3, \text{ or } 6$) and $\text{O}_2\text{H}/\text{CO}_2^-$ groups.

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

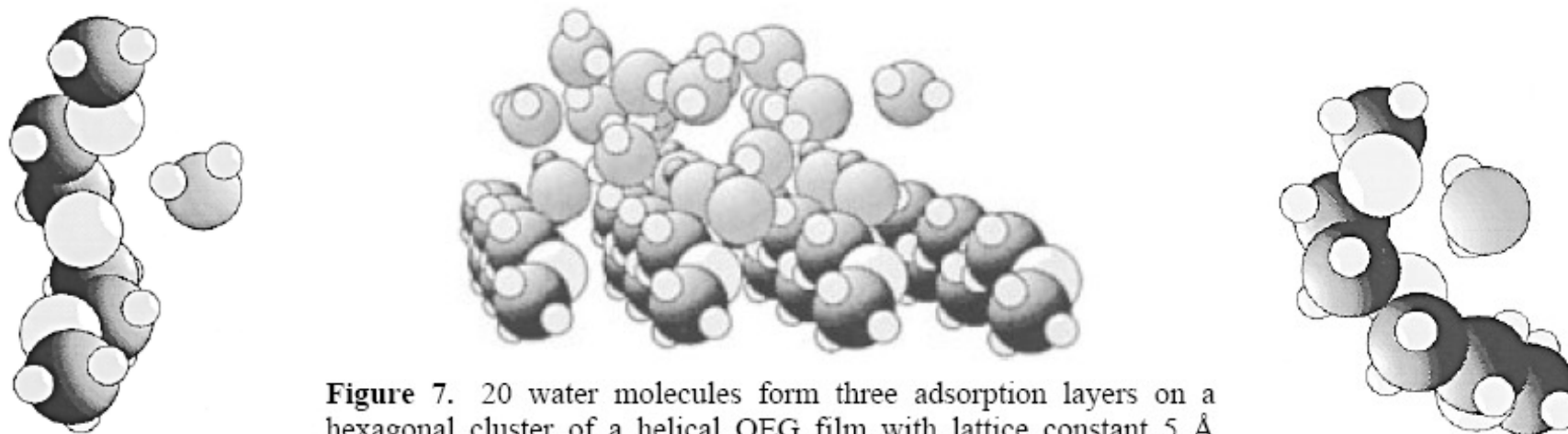


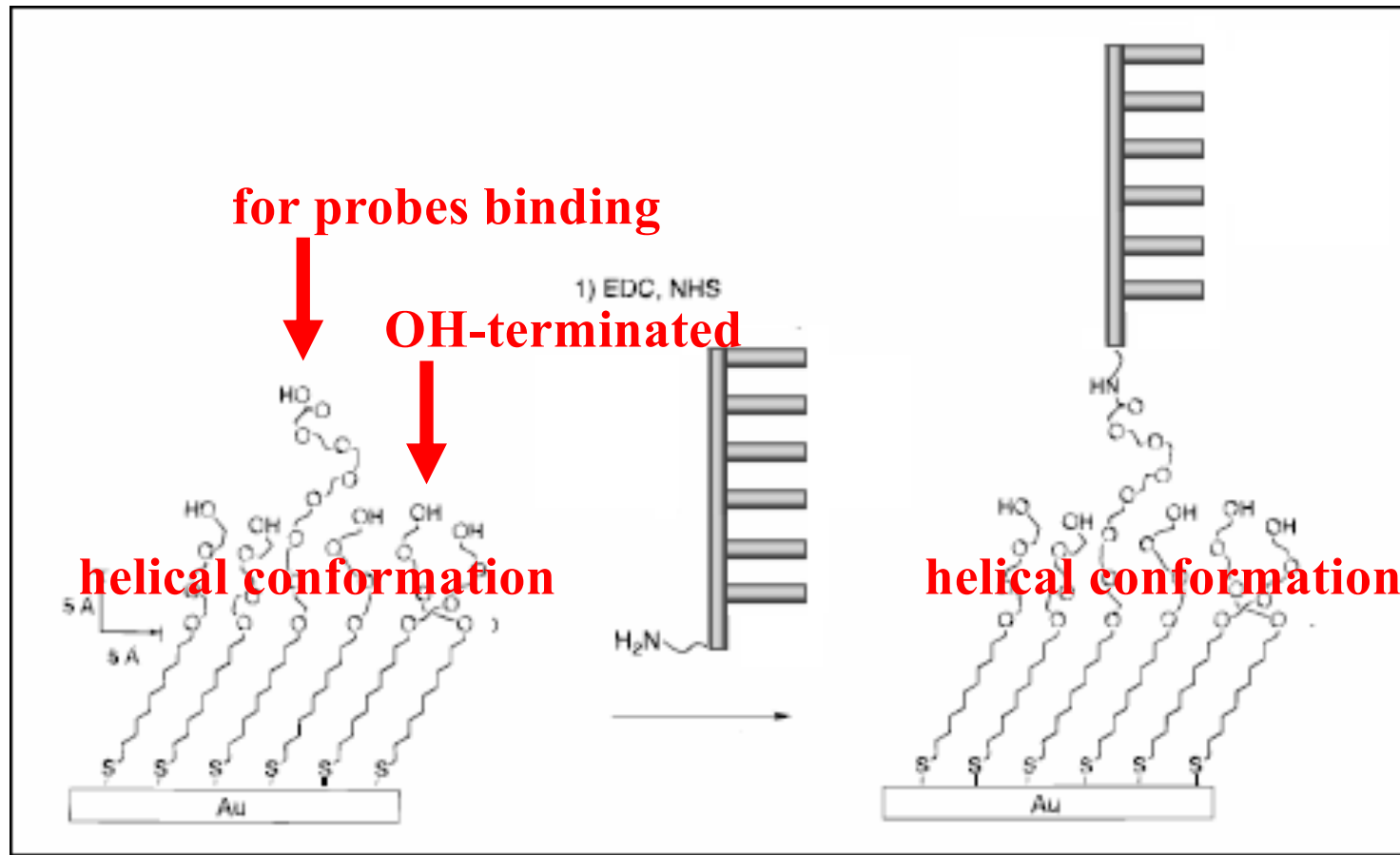
Figure 7. 20 water molecules form three adsorption layers on a hexagonal cluster of a helical OEG film with lattice constant 5 Å consisting of 3×4 helical OEG strands.

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.

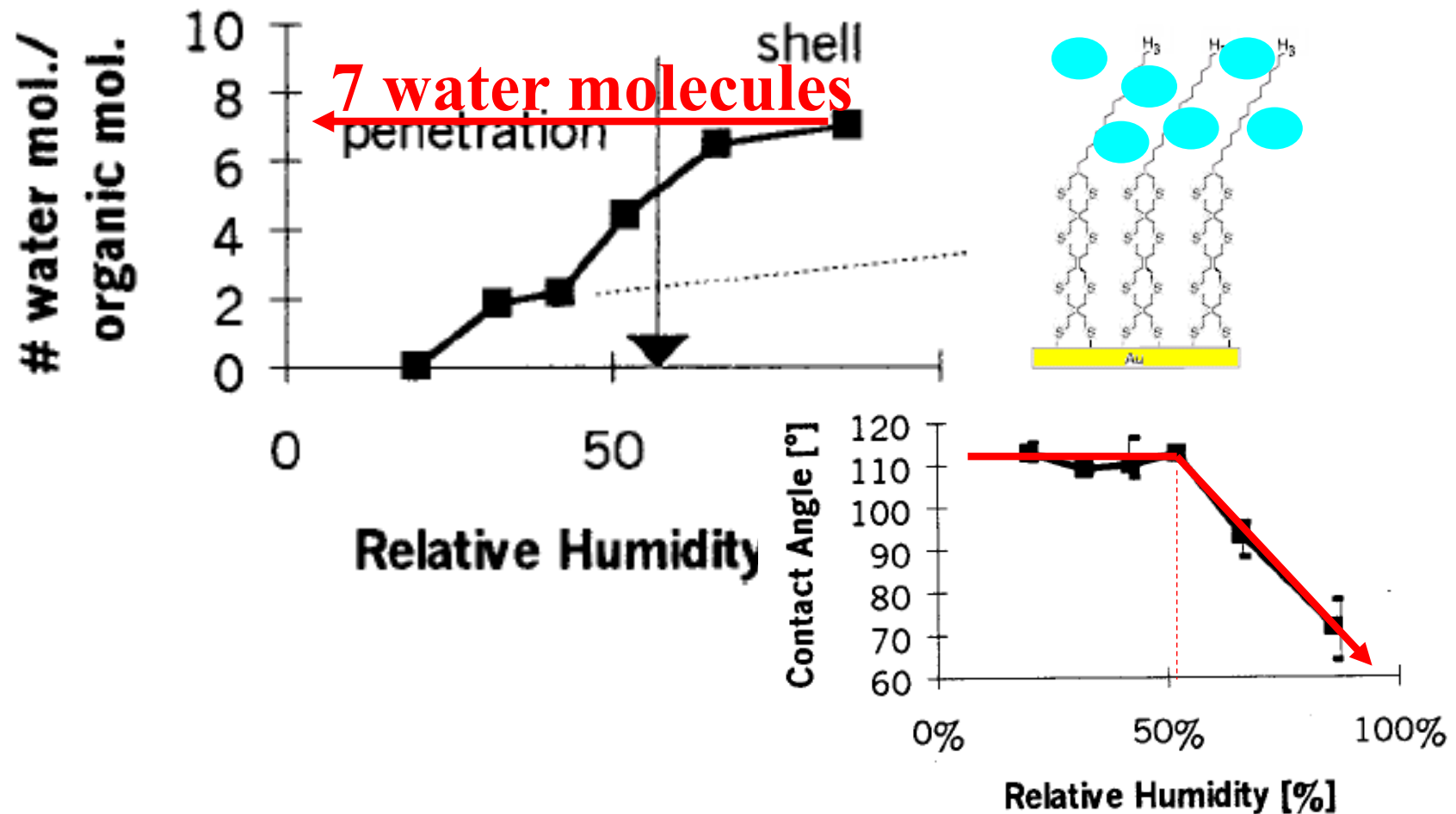
Water adsorption and Molecular conformation in EG-thiols Film

Water Adsorption in thin films



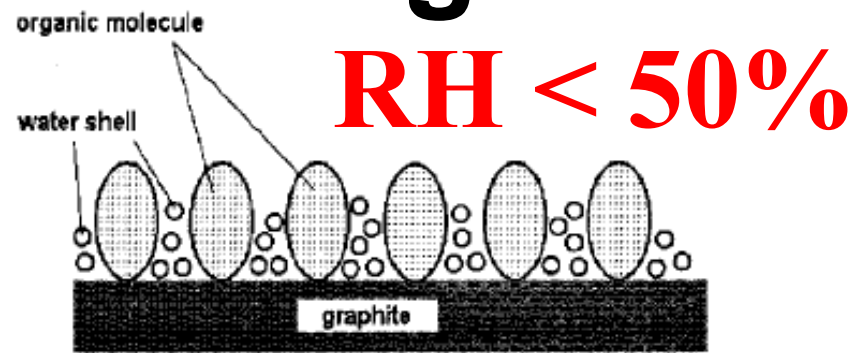
Covalently linked by using three-glycol
carboxyl terminated alkyl Thiols

Water Adsorption in thin films

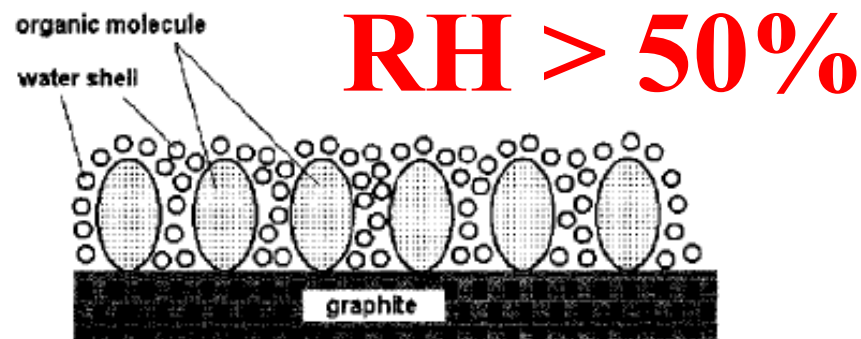


Film Water adsorption on alkyl thiol film chains

Water in Organic Films



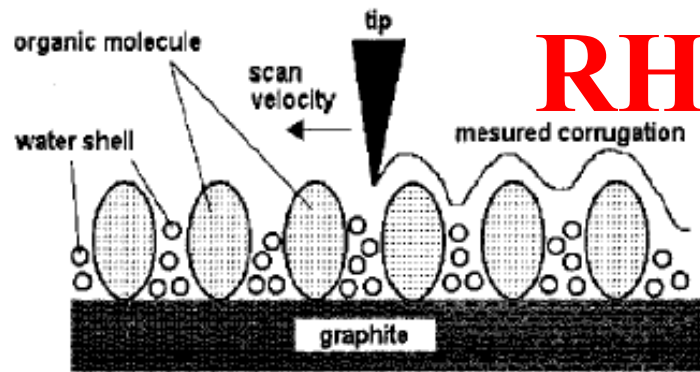
(A)



(B)

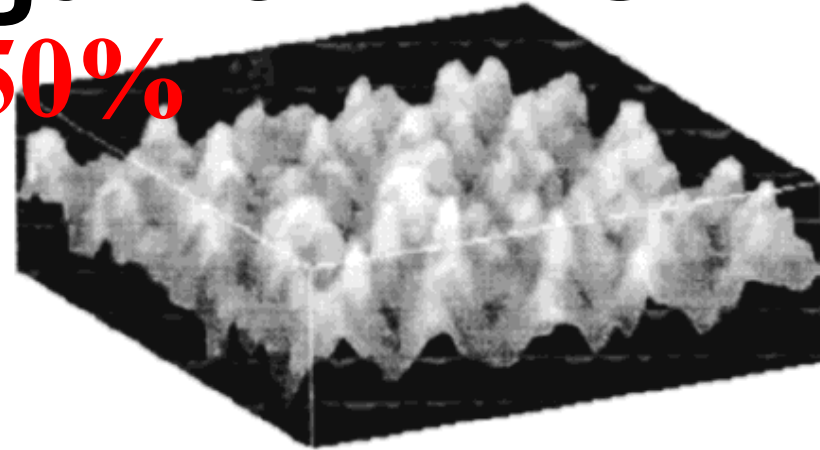
Water molecule are stored in the intra-molecular space in the thin film

Water in Organic Films

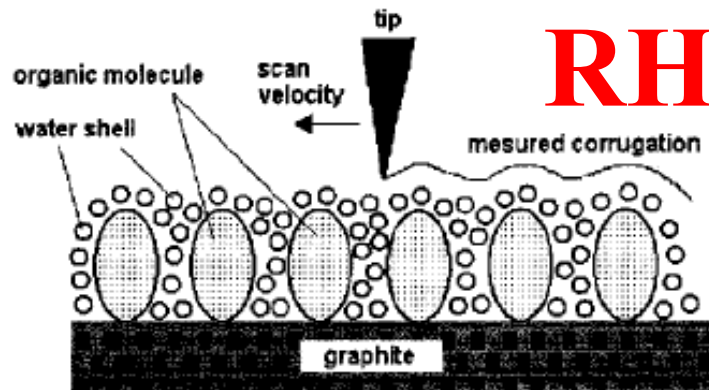


(A)

$RH < 50\%$

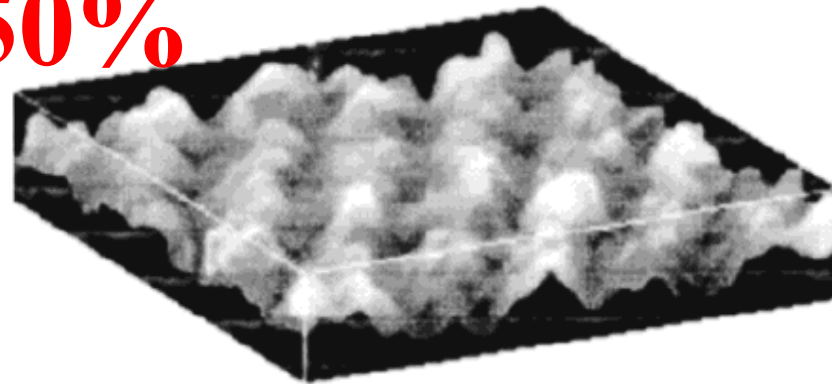


(A)



(B)

$RH > 50\%$



(B)

STM imaging showed water molecule stored in the intra-molecular space in the thin film

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 found 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