Biomedical Sensor Foresight Workshop, 3 March, Cityconferensen, Stockholm

Basics and applications of QCM-D and nanoparticle plasmon sensing

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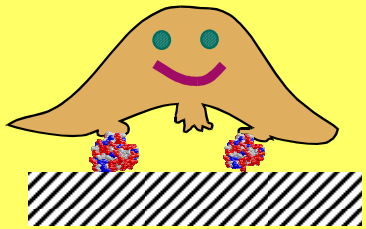
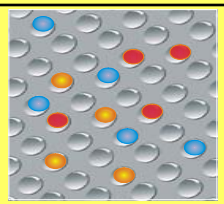
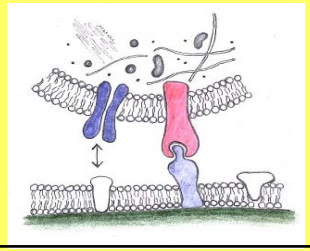
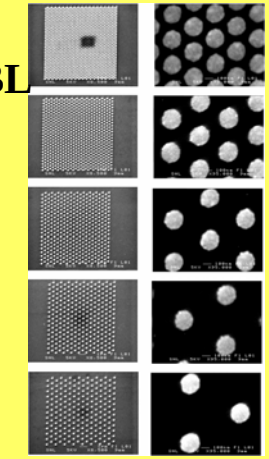
http://www.fy.chalmers.se/kemfys/

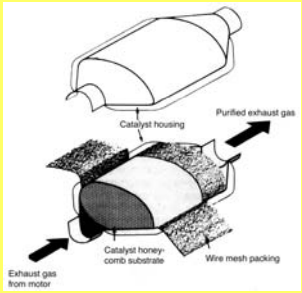


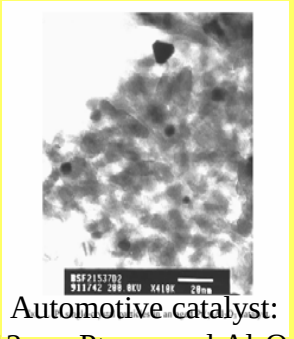




EBL



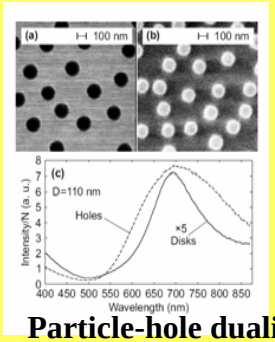




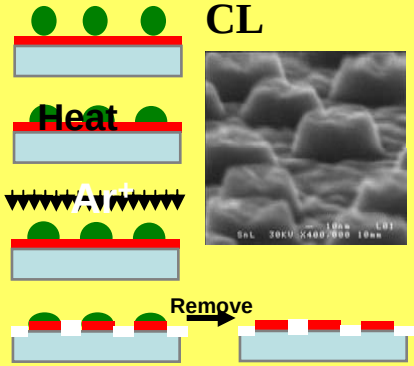
Automotive catalyst:
12 nm Pt on aged Al_2O_3

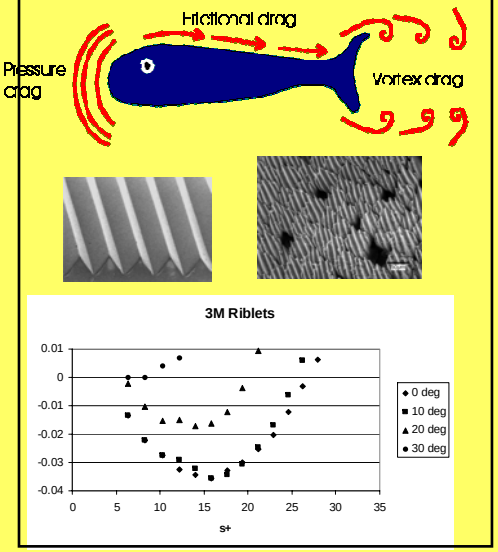
Chemical Physics Group Chalmers

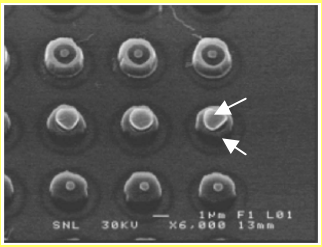
http://www.fy.chalmers.se/kemfys/

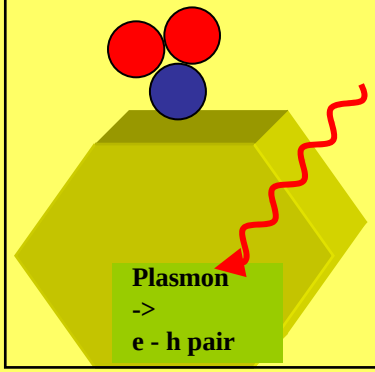


Particle-hole duality



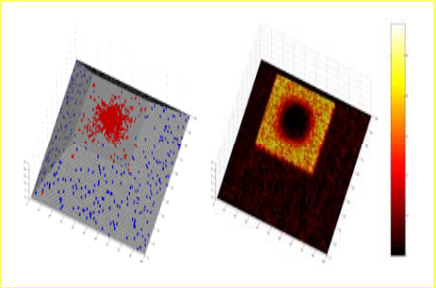






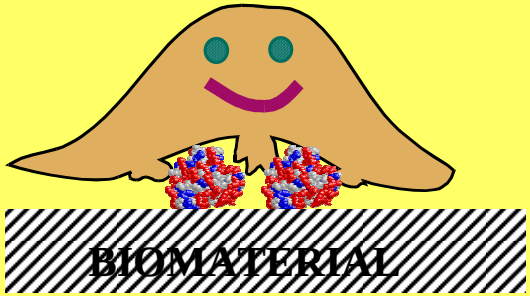
Applications:

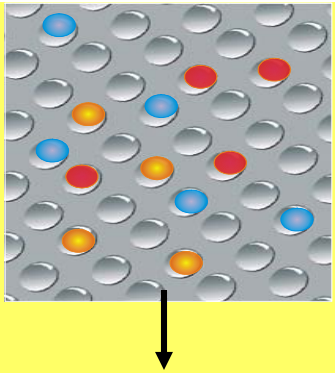
- ***Chemical and biosensing***
- ***Photocatalysis, e.g. water and air cleaning***
- ***Hydrogen production***
- ***Solar cells***
- ***Artificial photosynthesis***



B KASEMO

Biointerfaces

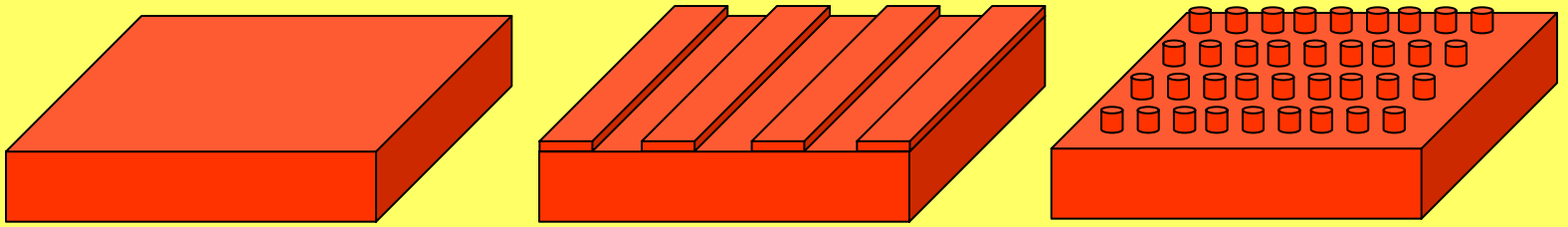


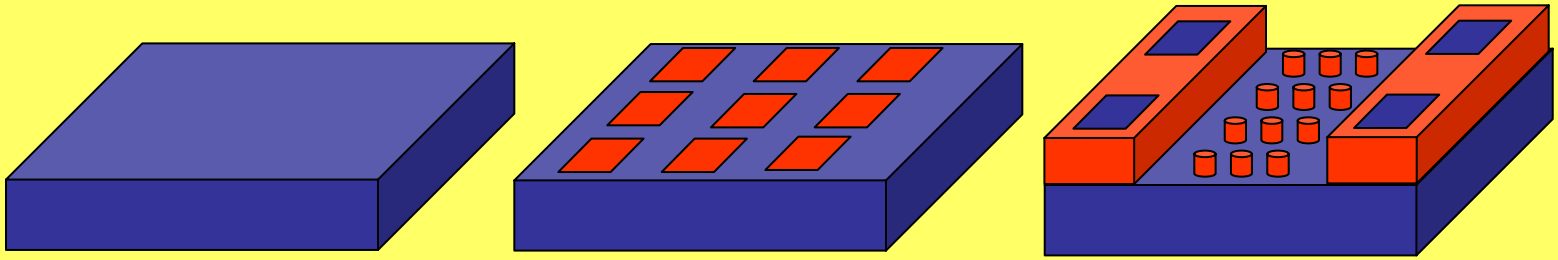


Flat homogeneous

Microtopography

Nanotopography





Uniform chemistry

Patterning

Hierarchical

Integration with microfluidics, readout etc

Applications

- Medical implants
- Tissue engineering
- Drug screening and design
- Biosensors
- Biochips and Labchips
- Bioelectronics
- Biomimetic materials science
- Biofouling prevention
- Artificial photosynthesis

Basic Research

- How are surfaces recognized by and affecting the properties and processes associated with biomolecules?
- Can we learn about basic life processes by using surfaces as controlled stimulii?

B. Kasemo, Surf. Sci. 500 (2001)

B. Ratner and D. Castner, Surf. Sci. 500 (2001)

MORE INFORMATION

- Vision Paper on NanoMedicine

- CORDIS Web-site (www.cordis.lu/technology-platforms)

- Reports (available on website)
- - Concept and Rationale: "Technology Platforms from definition to Implementation of a Common Research Agenda"

- - Information on individual platforms:

ETPs generally:	http://www.cordis.lu/technology-platforms/home_en.html
ETP Nanomedicine	http://cordis.europa.eu.int/nanotechnology/nanomedicine.htm

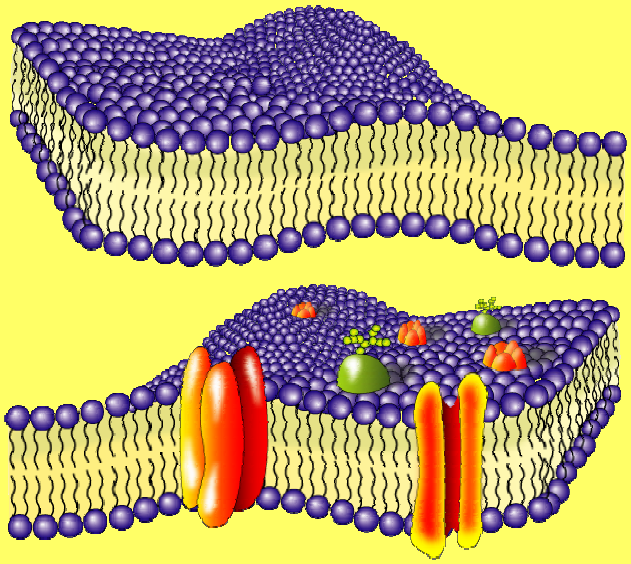
Surface-supported lipid membranes

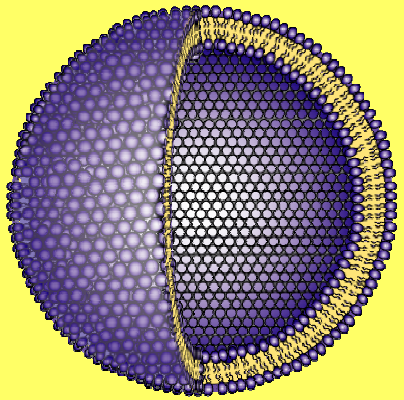
or

How to make the surface look and act like a real cell membrane

E. Sackmann, *Science* 271, 43 (1996).
C. Ziegler and W. Göpel, *Curr. Op. Chem. Biol.* 2, 585 (1998).
B. A. Cornell et al., *Nature* 387, 580 (1997).
C. Schmidt C et al., *Angew, Chem. Int. Ed.* 39, 3137 (2000).
R. Pantoja R et al., *Biophys. J.* 81, 2389 (2001).

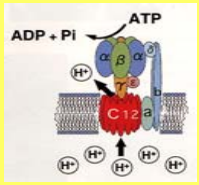
Artificial and real Cell Membranes and Liposomes

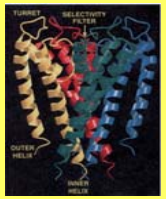


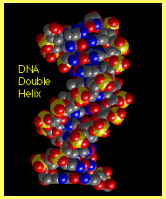


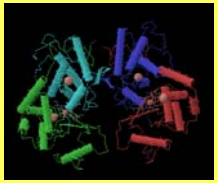
A spherical bag of a lipid bilayer membrane, enclosing a part of the solution in which they are formed.

Cell components

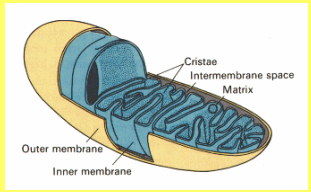


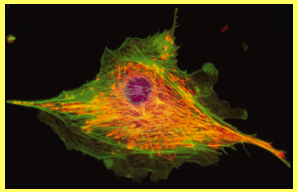






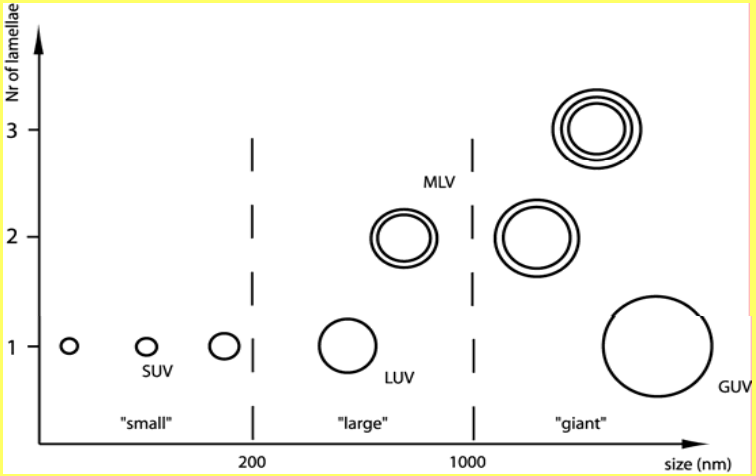
Motors Sensors DNA Enzymes



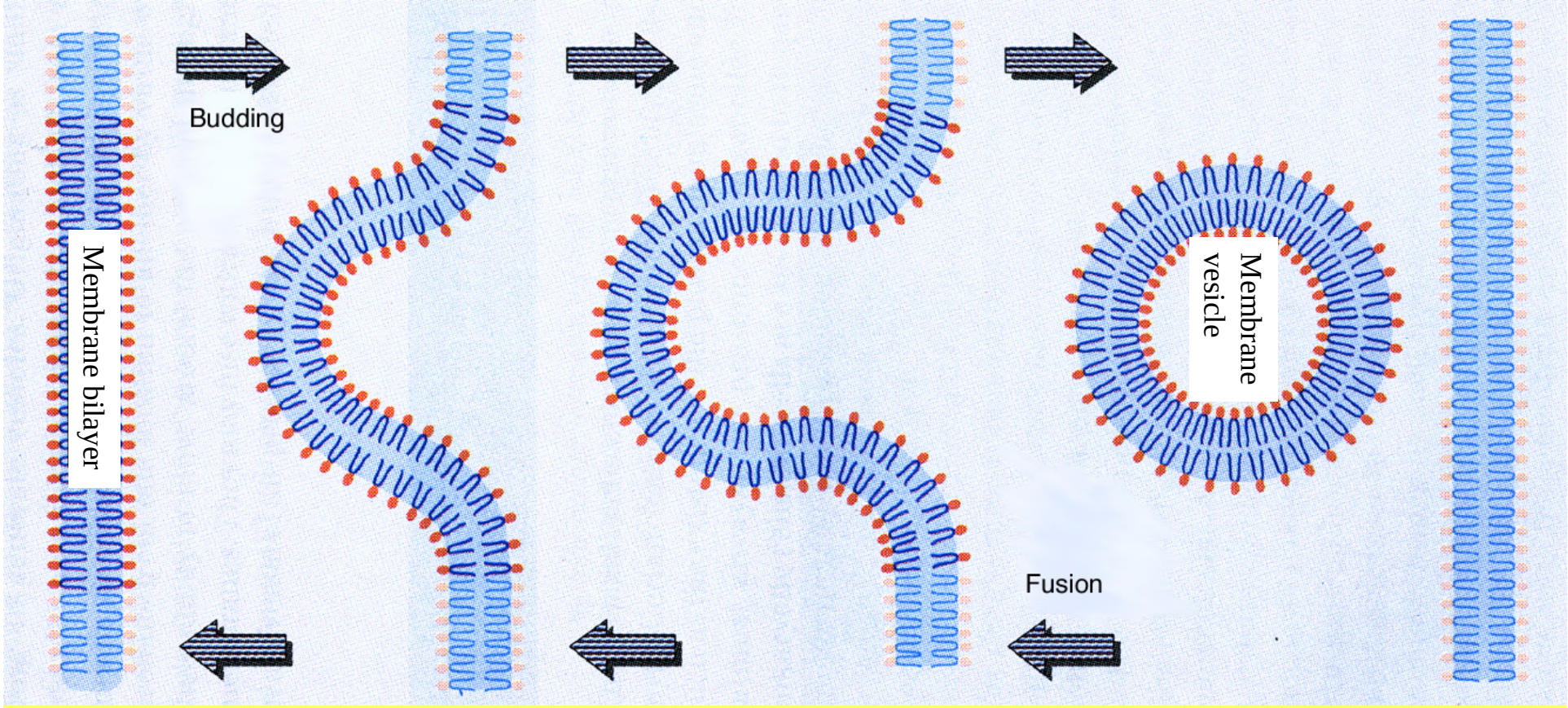


Nano- and Micro Scale Chemical Reactors

The size, type and content of liposomes can be controlled



Budding/fusion of vesicles

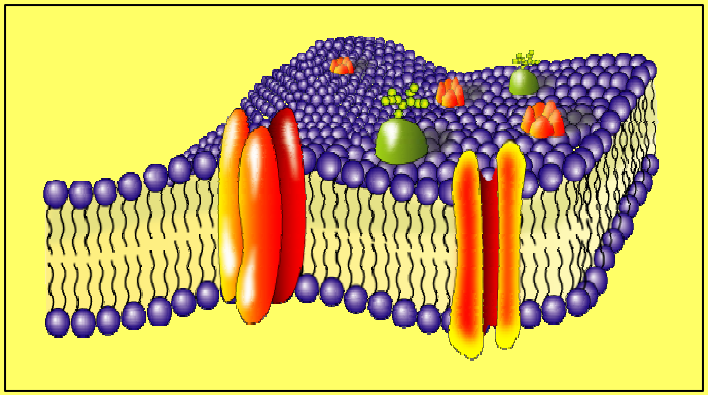


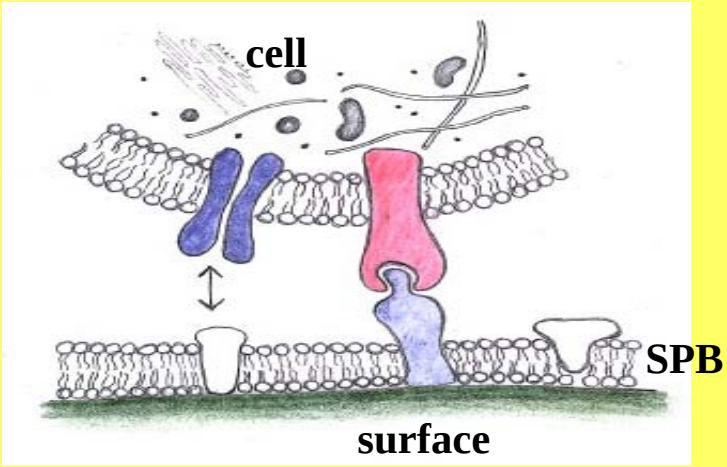
From Genes V, B. Lewin (1994), Oxford University Press

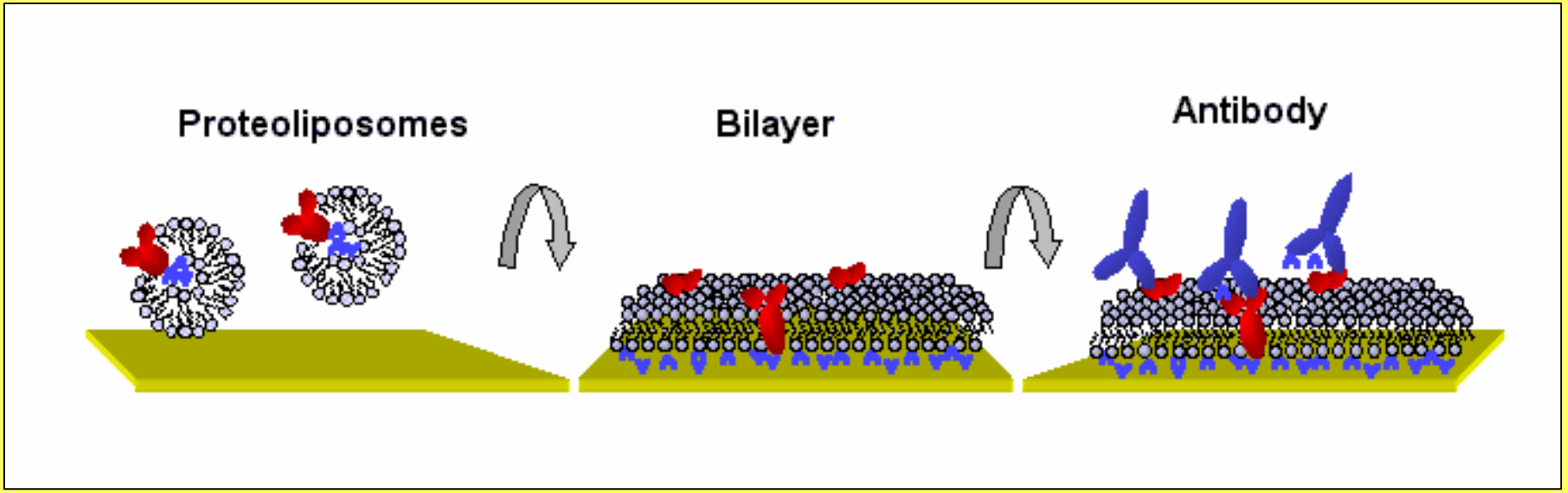
Applications of lipid vesicles and membranes

- Platforms for biosensing
- Ditto for cell engineering
- Drug targeting and screening
- Coatings on medical devices
- ……

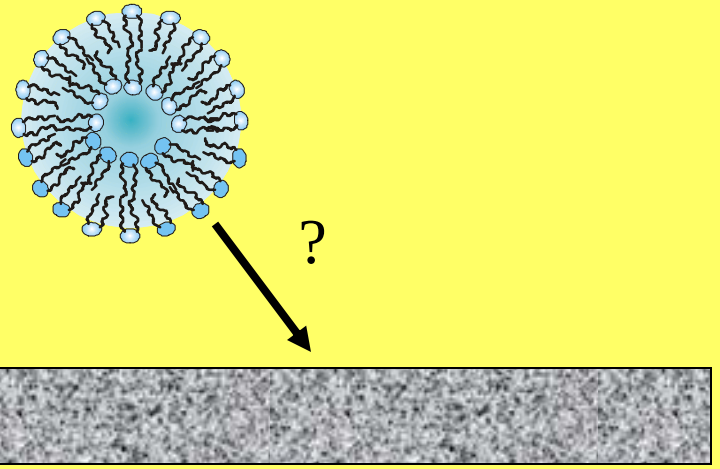
Functional bilayers and vesicles







Conversion of unilamellar (phospho)lipid vesicles to surface-supported bilayers* (biomimetic membranes)



SOME EARLY WORK

BRIAN & MC CONNEL, PNAS 81 (1984) 6195

NOLLERT, KIEFER, JÄHNIG, BIOPHYS. J. 69 (1995) 1447

STEINEM ET AL, BIOCHEM. BIOPHYS. ACTA 1279 (1996)169

SACKMAN AND TANAKA, TRENDS IN BIOTECHN. 18(2000) 58 + REFS

Jass, Tjärnhage, Puu, Biophys. J., 79 (2000) 3153

THEORY

SEIFERT ADV. PHYSICS 46 (1997) 13

BERNARD ET AL, LANGMUIR 16 (2000) 6809

ZHDANOV, KELLER, GLASMÄSTAR AND KASEMO JCP 112 (2000) 900

QCM-D, AFM, SPR AND ELLIPSOMETRY WORK

KELLER AND KASEMO, BIOPHYS. J. 75 (1998) 1397

REVIAKINE AND BRISSON, LANGMUIR 16 (2000) 1806

REIMHULT, HÖÖK, KASEMO, LANGMUIR 19 (2003) 1681

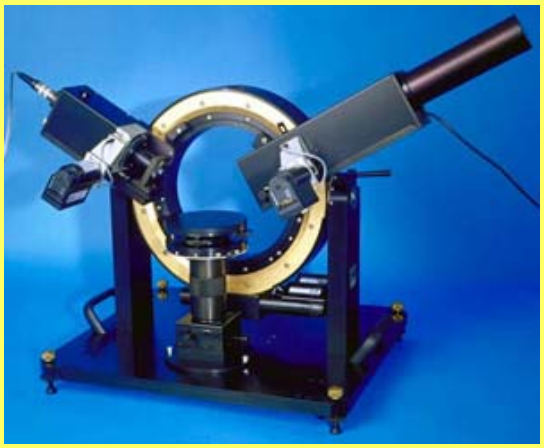
E. Reimhult, B. Kasemo and F. Höök , Anal. Chem 2005

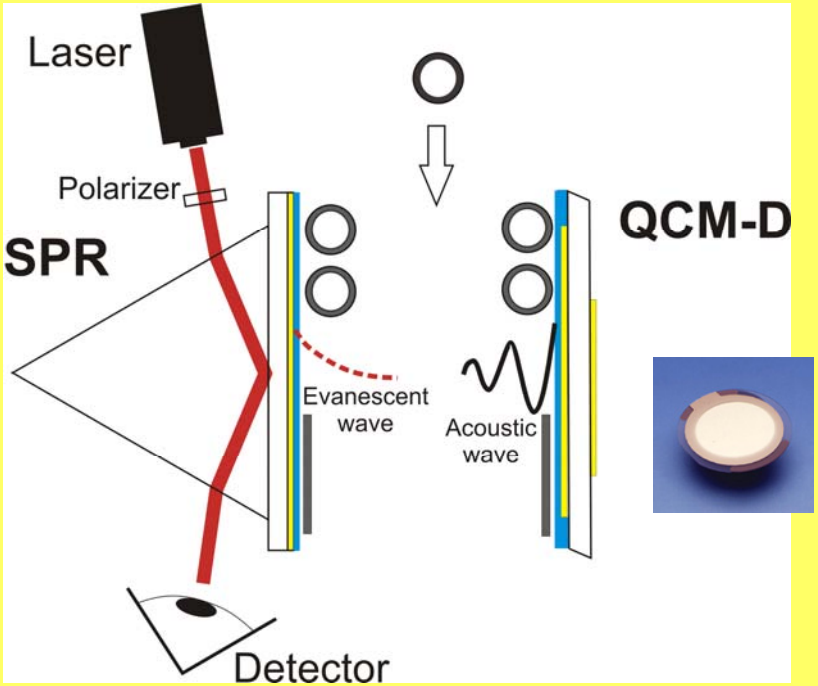
RICHTER AND BRISSON, LANGMUIR 20 (2004) 4609)

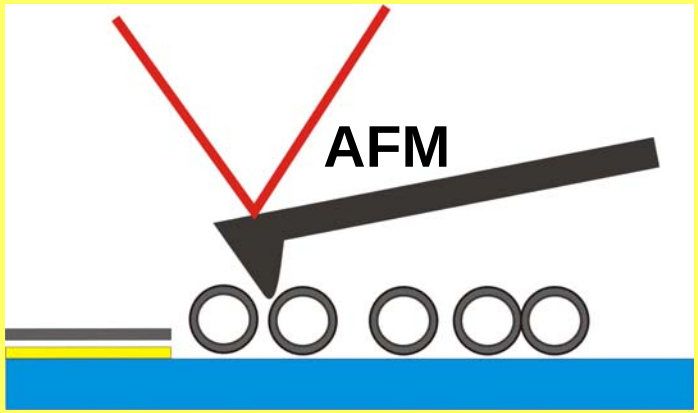
TEXTOR ET AL, UNPUBLISHED

Methods

Experimental tools



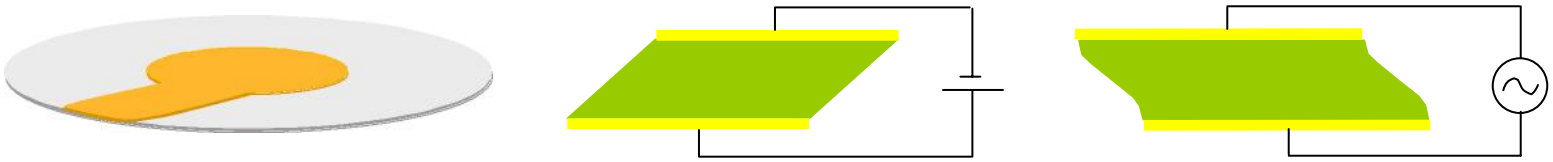




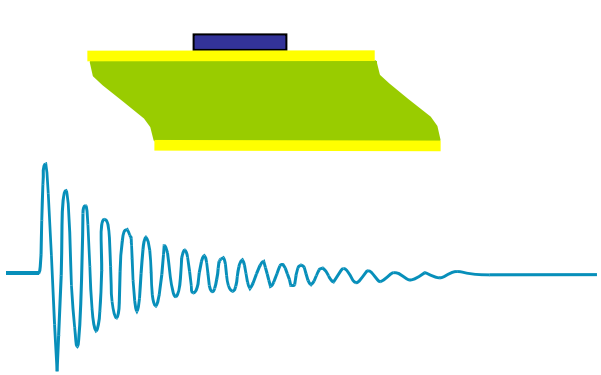
Monte Carlo Simulations (MCS)

Sensor surfaces prepared & checked by XPS, SEM, AFM, PVD, ozon cleaning, plasma etching and cleaning,

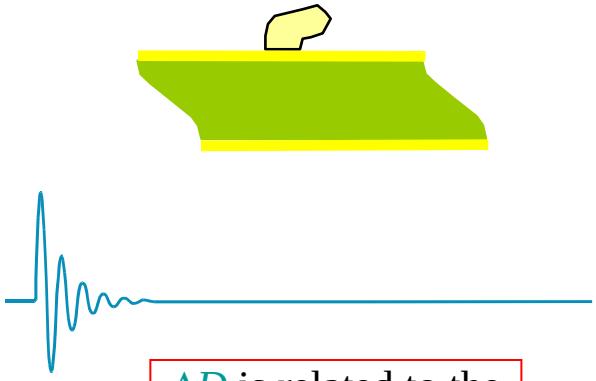
QCM-D sensing principle



AT-cut quartz with gold electrodes



Δf is proportional to the mass of the attached film (ng/cm^2 sensitivity)



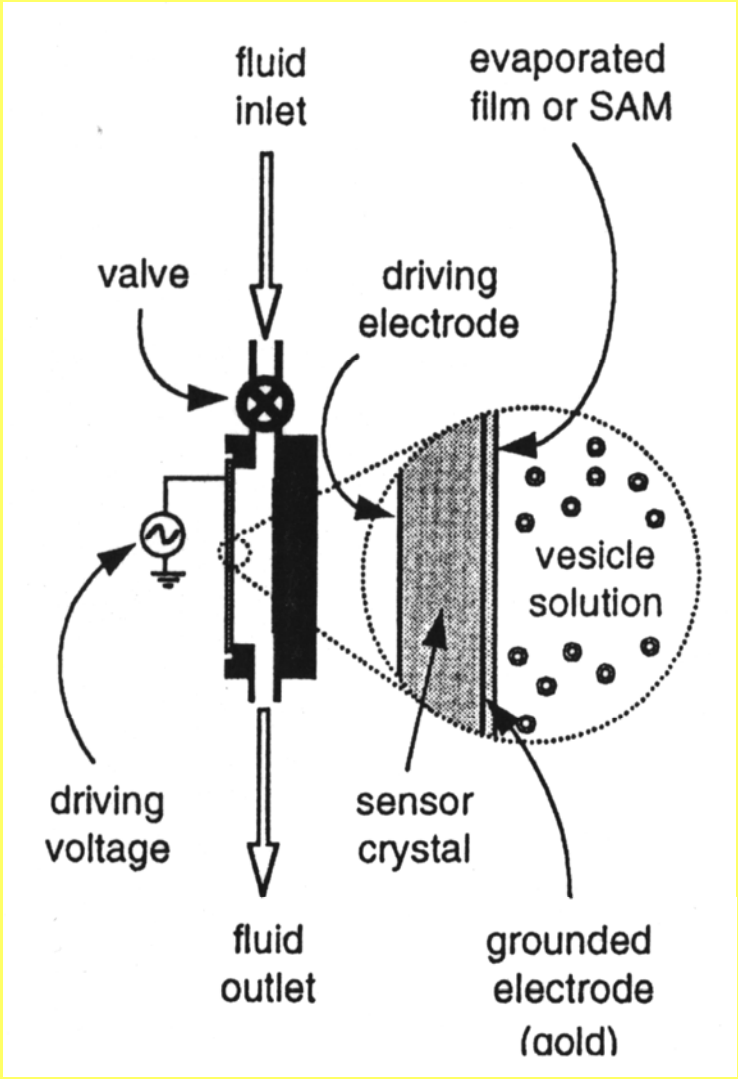
ΔD is related to the viscoelasticity

1) Rodahl, M., Höök, F., Krozer, A., Kasemo, B. and Breszinsky, P., *Quartz crystal microbalance setup for frequency and Q factor measurements in gaseous and liquid environments*, Review of Scientific Instruments 66 (1995) 3924-3930

2) Rodahl, M. and Kasemo, B., *Frequency and dissipation-factor response to localized liquid deposits on a QCM electrode*, Sensors and Actuators B (1996) 111-116

3) Rodahl, M., Höök, F., Fredriksson, C., Keller, C., Krozer, A., Brzezinski, P., Voinova, M. and Kasemo, B., *Simultaneous frequency and dissipation factor QCM measurements of biomolecular adsorption and cell adhesion*, Faraday Discussions 107: Acoustic waves and Interfaces, Lester UK 107 (1998) 229

Measurement chamber and sensor crystal (Q-Sense AB)



Q-Sense New E4 system

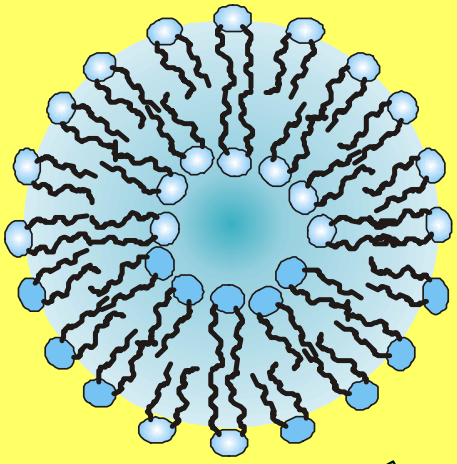
www.q-sense.com

4 sensor chambers that can be connected in series or in parallel

Take a look at the Q-Sense booth, and meet Patrik Bjöörn from Q-Sense

Q-Sense founded in 1996 by B Kasemo, M Rodahl, F Höök and A Krozer

A vesicle approaching a surface …

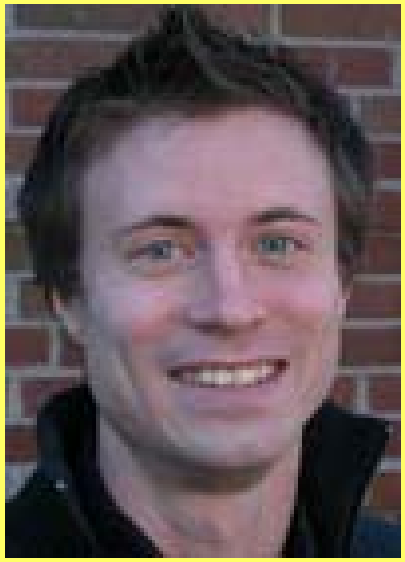


What will happen?

Adsorption of vesicles on SiO2 and TiO2 - dependence on vesicle size

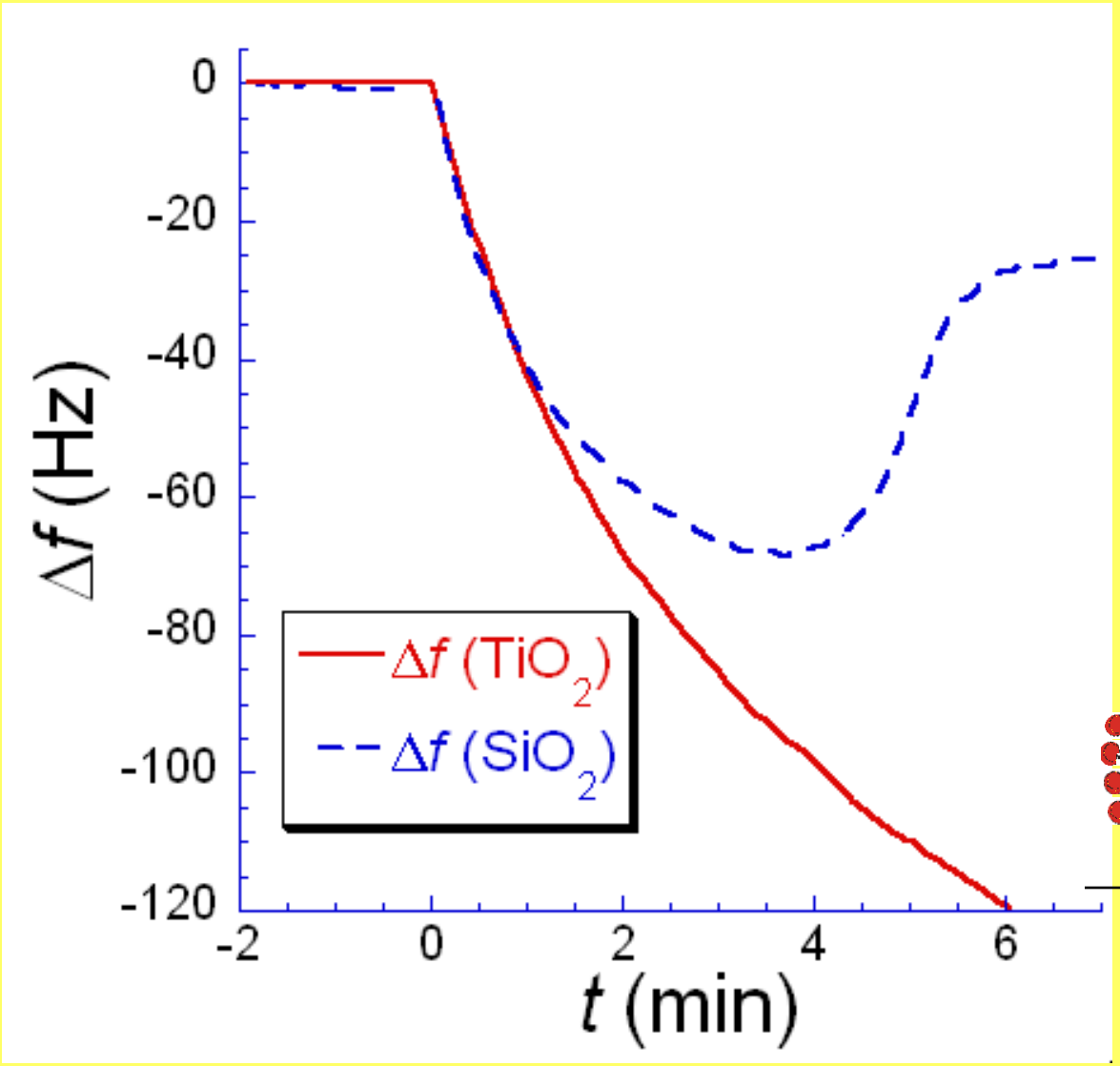
vesicles of diam. 25-200nm

Fredrik Höök, Lund Univ

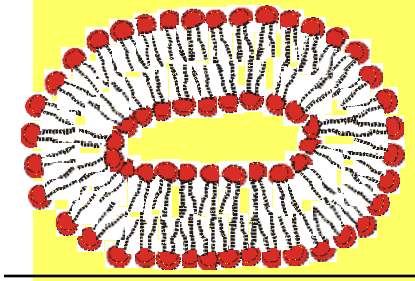


Erik Reimhult
- postdoc at IMRE, Singapore

Vesicle adsorption on SiO_2 and TiO_2

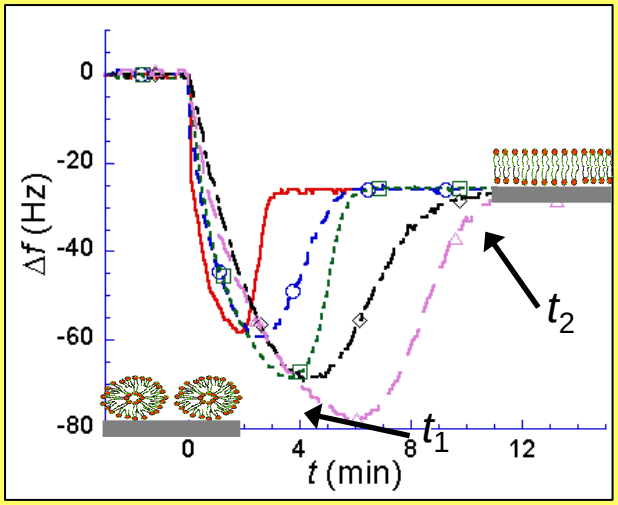


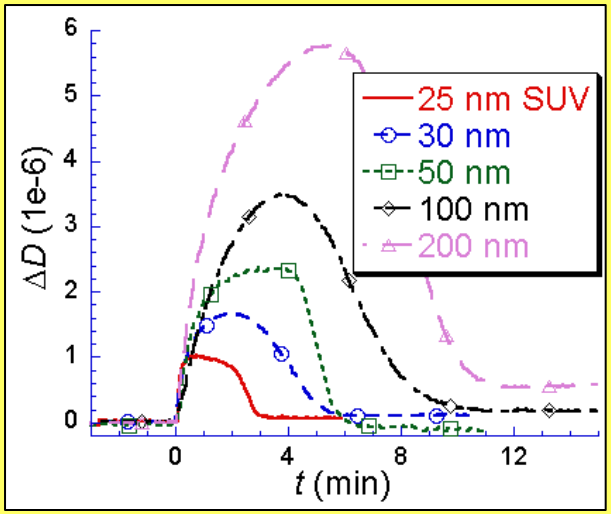
SiO_2



TiO_2

Typical QCM-D curves for adsorption of vesicles with different mean size

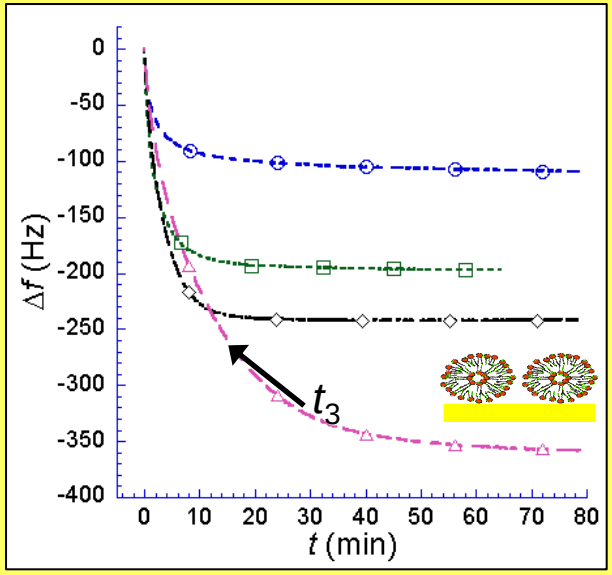


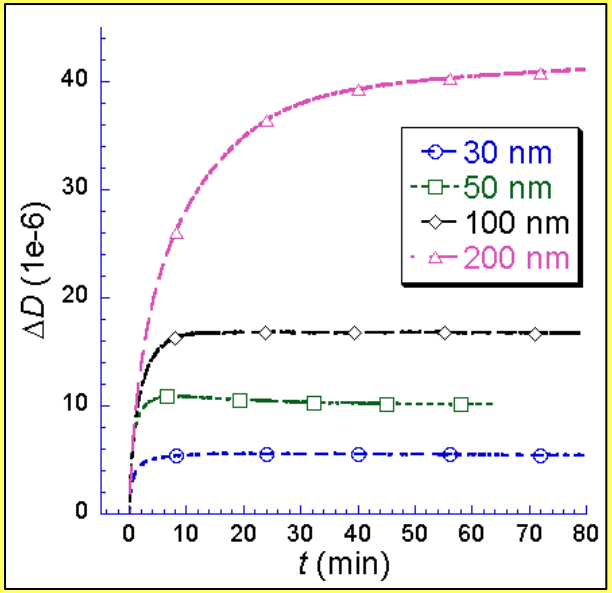


SiO_2

t_1 – rupture starts

t_2 – bilayer formation complete





TiO_2

t_3 – the surface is saturated with vesicles

E. Reimhult, F. Höök and B. Kasemo (2002), *JCP*, **117**(16):7401

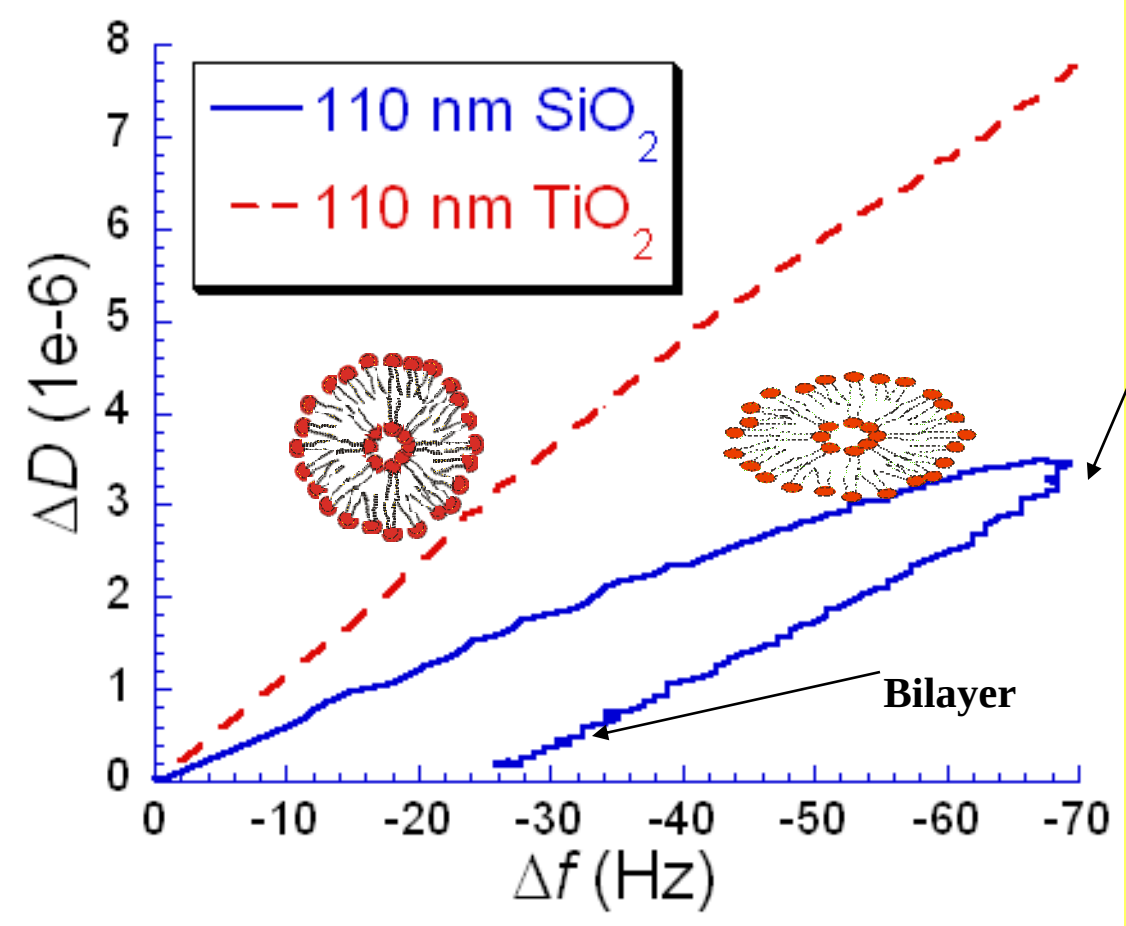
Reimhult, E., Höök, F. and Kasemo, B., Langmuir **19** (2003) 1681-1691

The interaction is surface specific

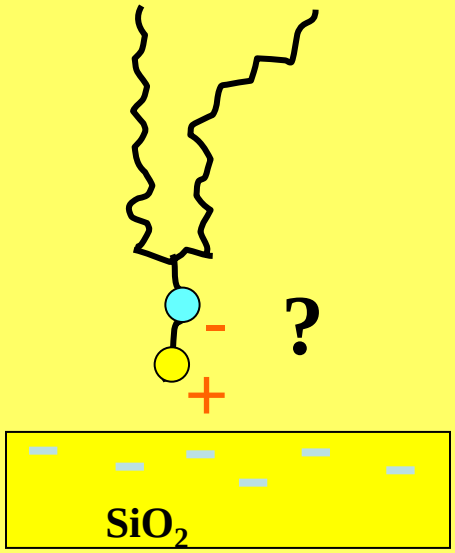
E. Reimhult

D vs. *f* plots

Lower $\Delta D/\Delta f$ on SiO_2 than on TiO_2



Rupture and fusion sets in



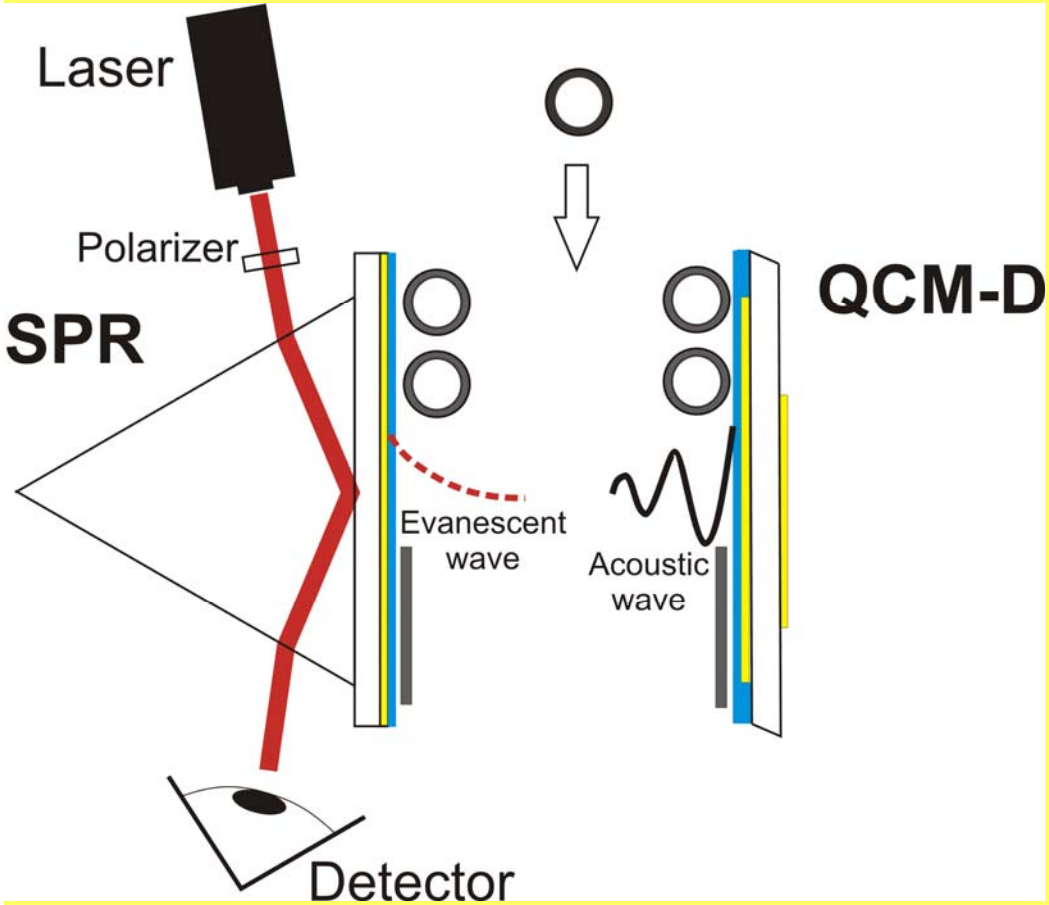
Greater deformation of vesicles on SiO_2. Bilayer does not form on TiO_2 from POPC

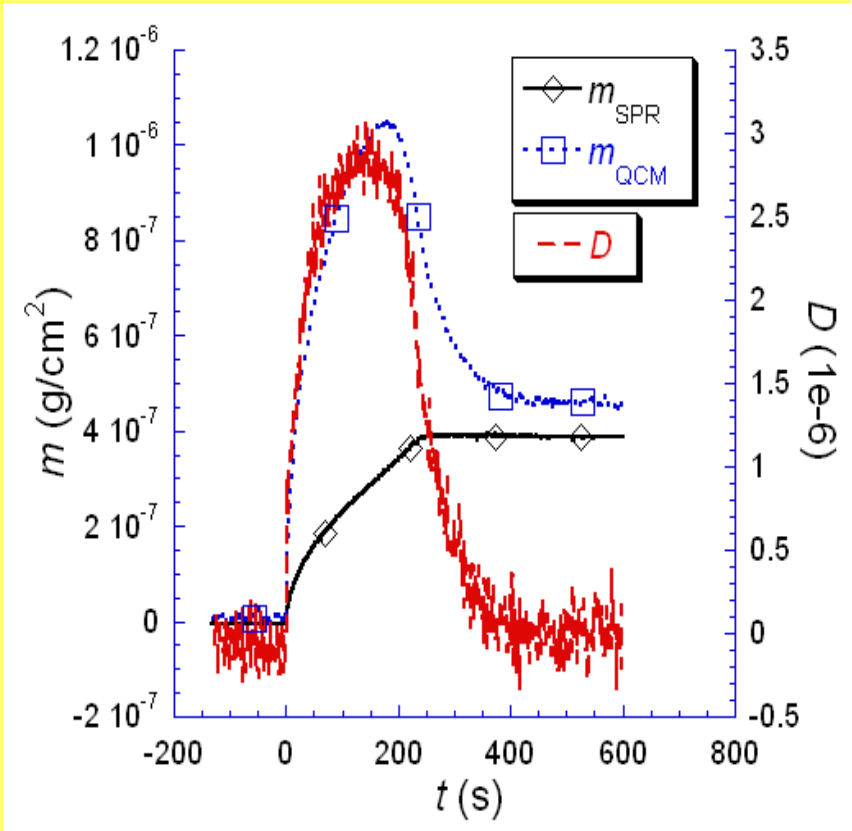
E. Reimhult, F. Höök and B. Kasemo, JCP, 117(16) (2000) 7401

Get additional information by combining QCM-D and SPR

E Reimhult, B Kasemo, F Höök, Anal. Chem., 76 (2004) 7211
E Reimhult, F Höök, B Kasemo Biophys. J submitted

Simultaneous SPR and QCM-D measurements on parallell surfaces in symmetric flow





Vesicle size: ~50 nm

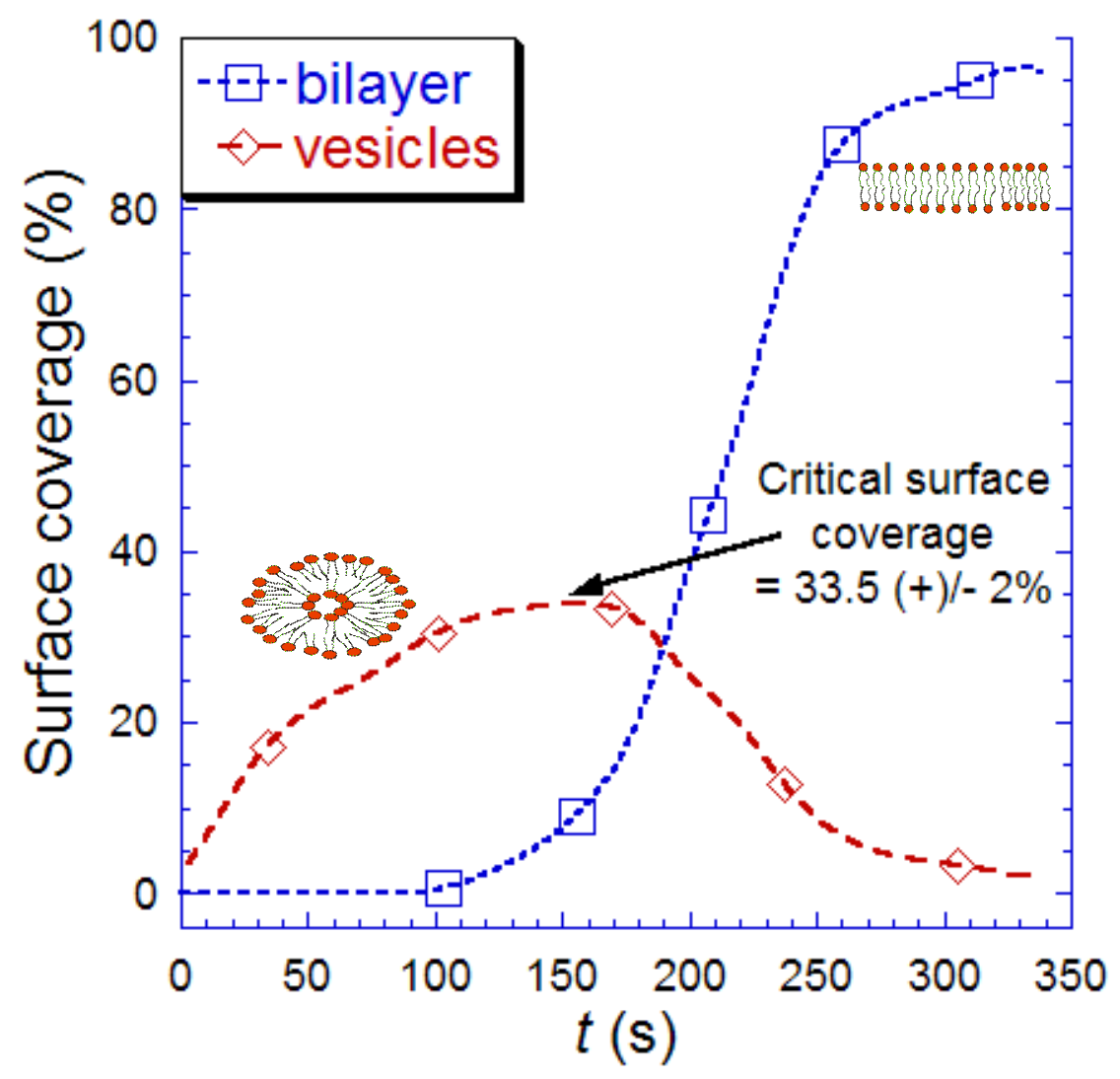
Lipid conc: 0.16 mg/ml

E Reimhult, B Kasemo, F Höök, Anal. Chem., 76 (2004) 7211
E Reimhult, F Höök, B Kasemo Biophys. J submitted

E. Reimhult

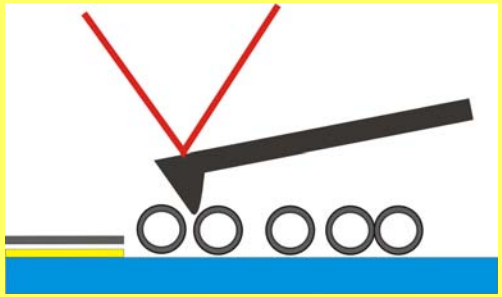
B KASEMO

Surface coverage of vesicles and SPB obtained by combined SPR and QCM



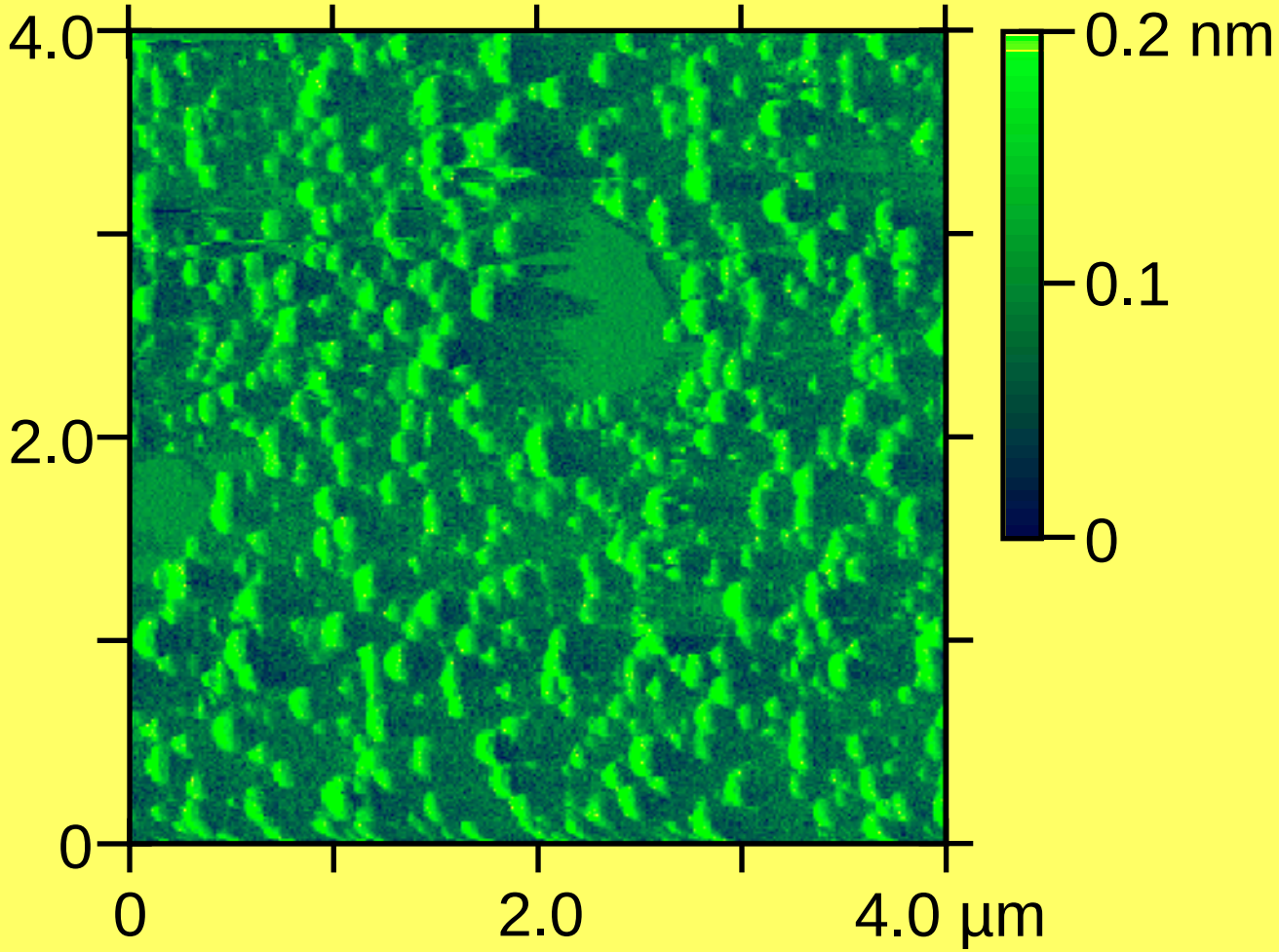
E. Reimhult, F. Höök and B. Kasemo *subm*. *Biophys J* and E. Reimhult, Kasemo and F. Höök. *Anal. Chem 76 (2004) 7211*

Microscopic information by AFM



Michael Zäch

AFM vs. QCM/SPR: 140 sec



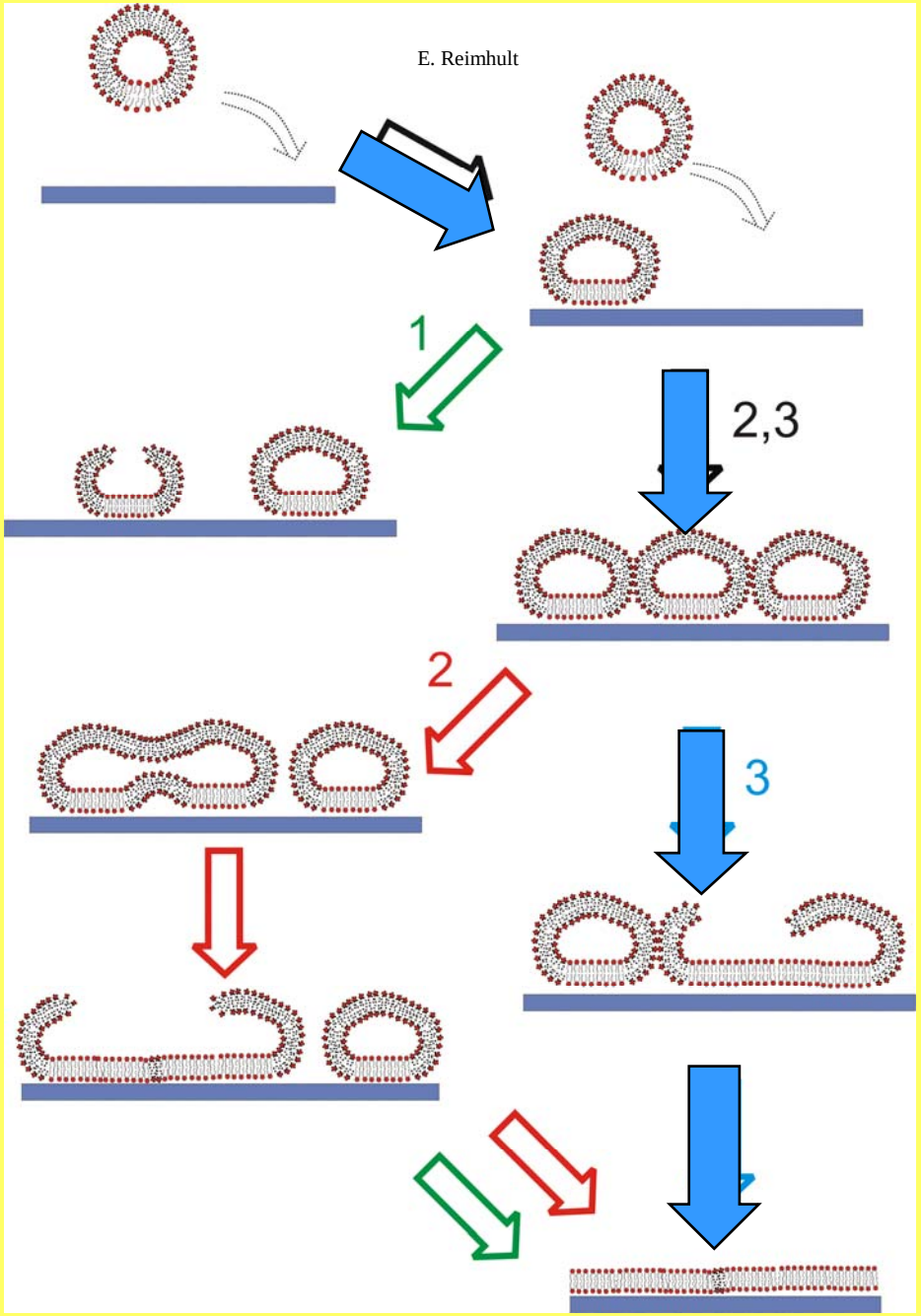
- No further significant growth of vesicles; only increase of vesicle density
- Larger bilayer patches visible.

B KASEMO

Scenario based on accumulated data

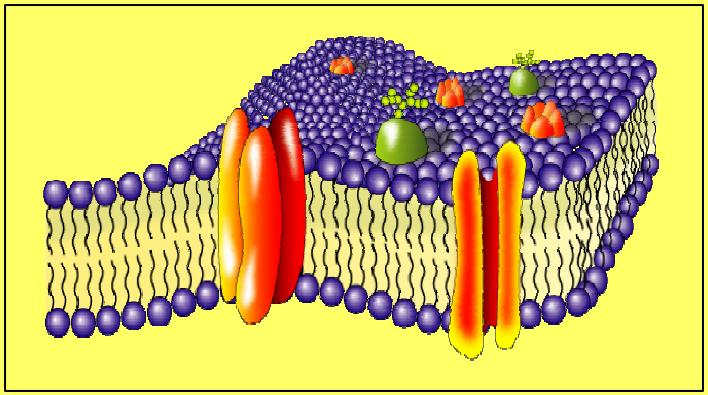
Three scenarios for vesicle rupture and bilayer formation on SiO_2

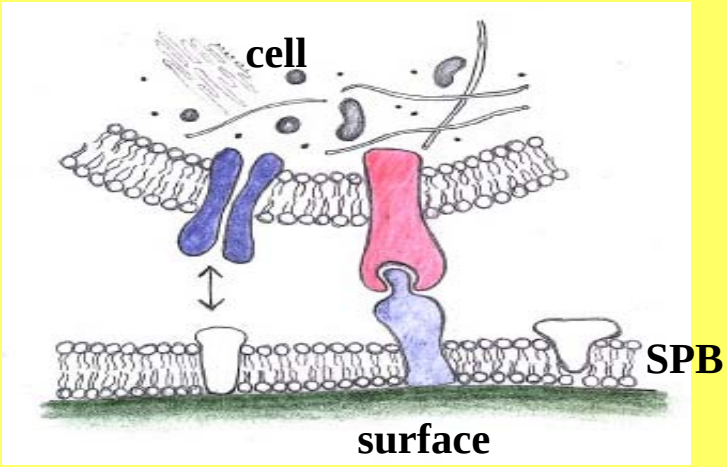
1. Spontaneous rupture
2. Liposome fusion
3. Critical surface coverage and auto-catalysis

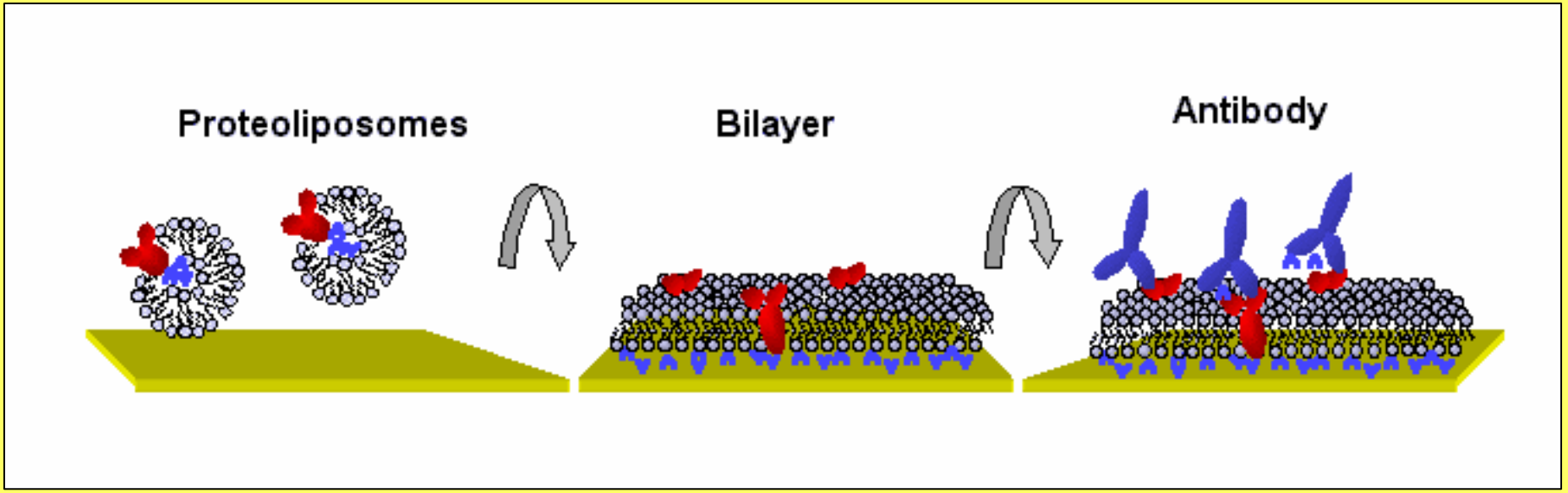


How can we go further and use the lipid bilayer membrane and/or supported vesicles

Functional bilayers and vesicles



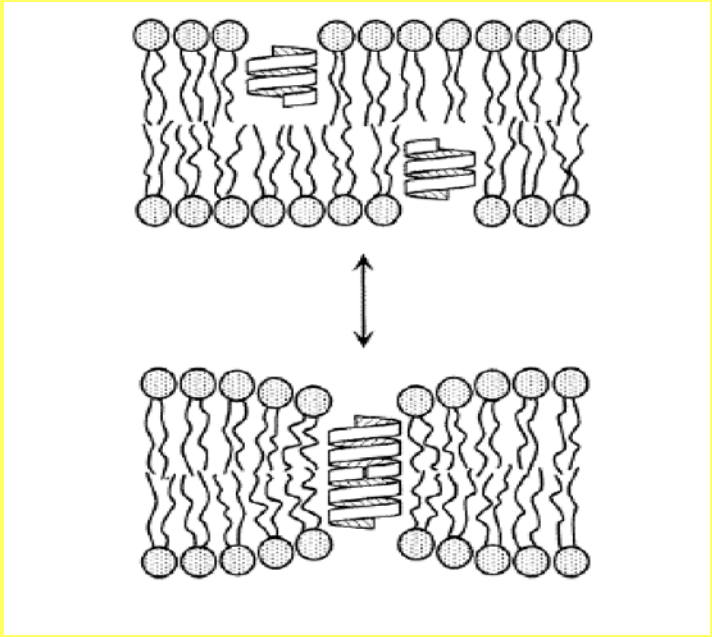




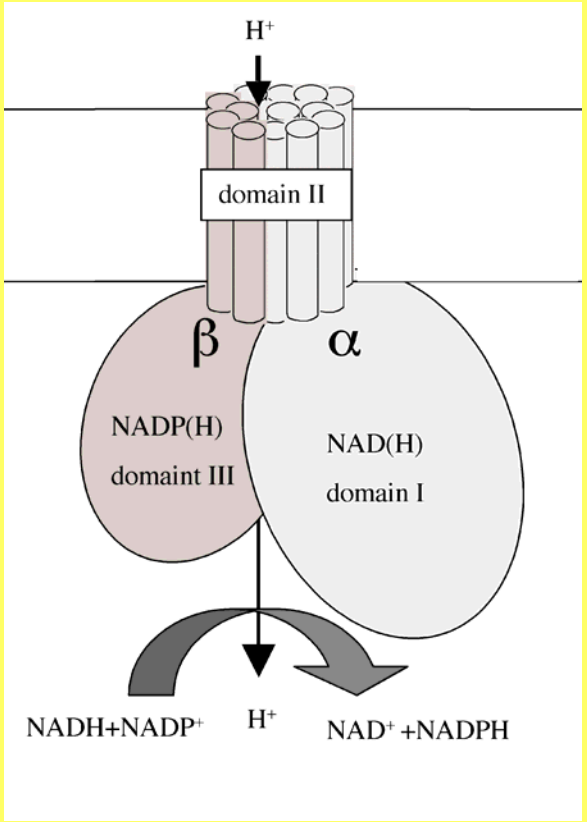
Can supported bilayers be formed in the same way as above, with incorporated membrane molecules?

Model systems; transmembrane proteins

Gramicidin A (GrA) 2.2 kD



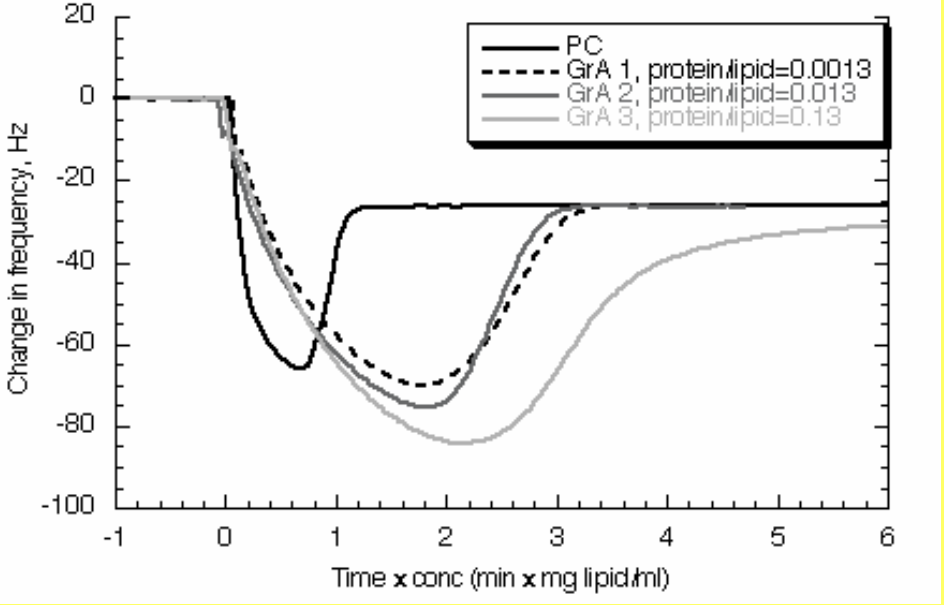
Transhydrogenase (TH) 103 kD

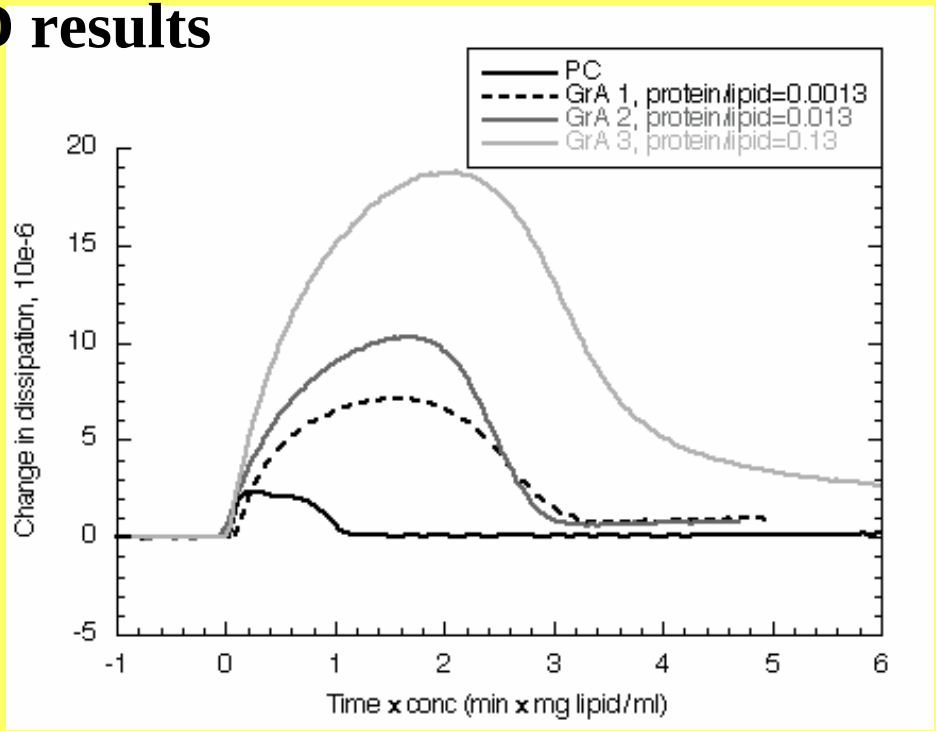


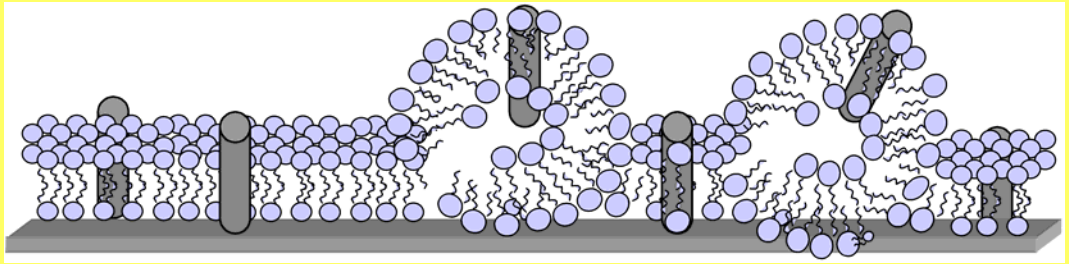
Ref: Granéli et al, Langmuir 2003

Bilayer formation from GrA-containing liposomes

QCM-D results



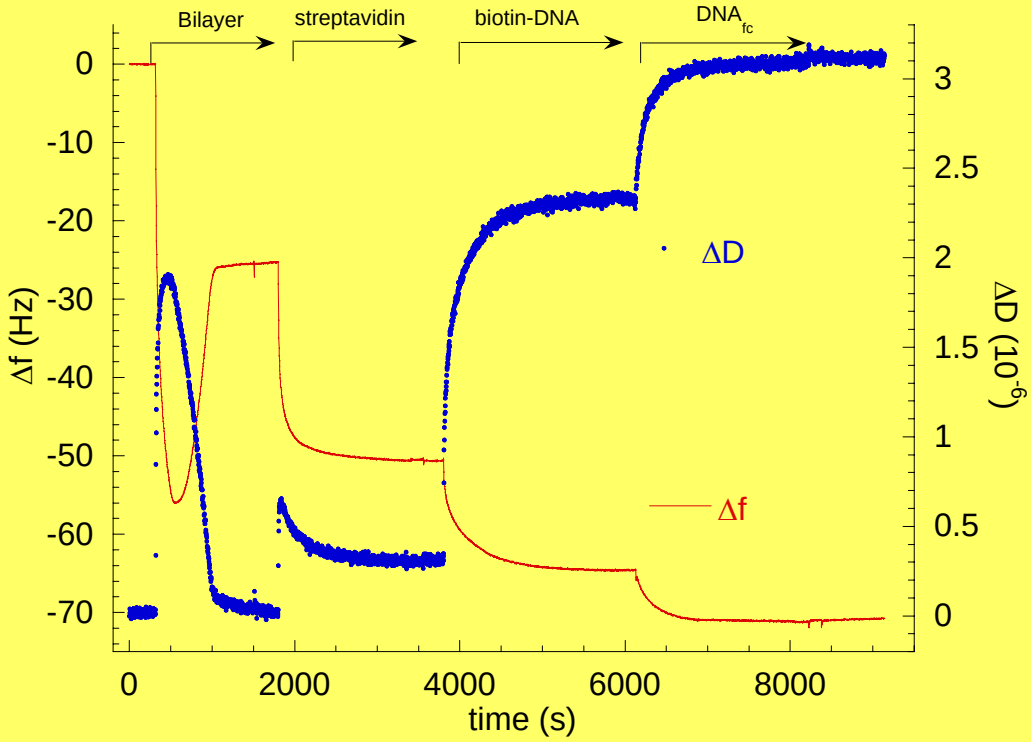


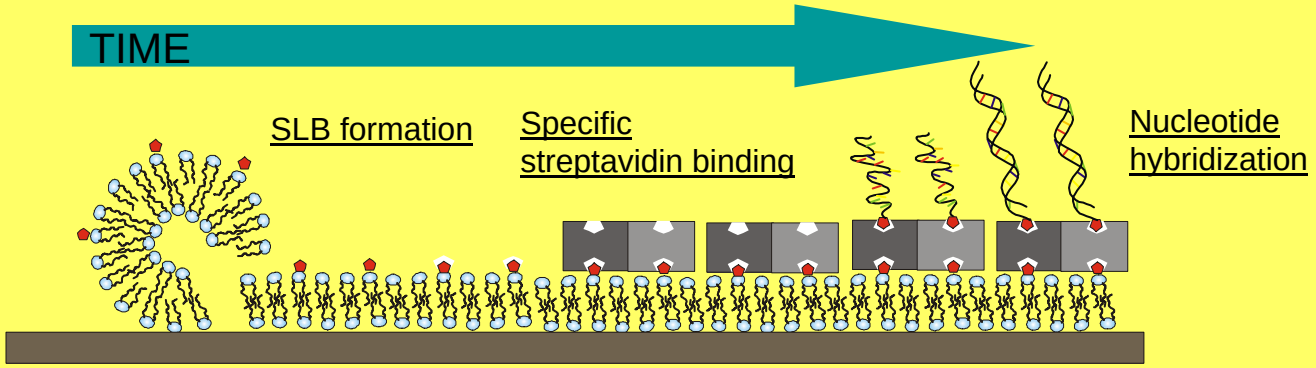


B KASEMO

Functional molecules can be coupled (tethered) to the bilayer

DNA-PNA Hybridization via Biotin-Streptavidin Coupling



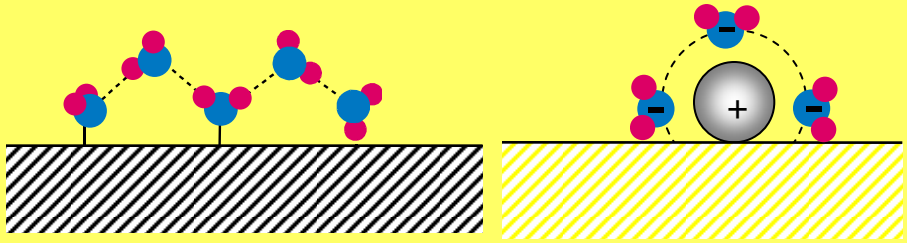


B KASEMO

QCM-D detection ranges from water to small molecules to lipds to cells

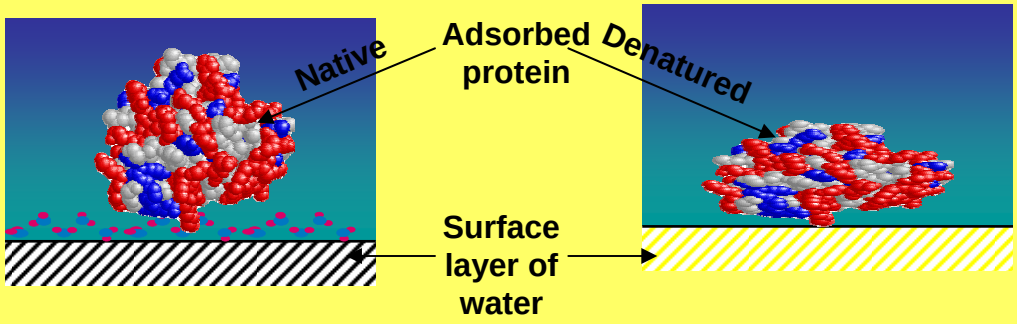
1.Surface + water

Different bonding orientations and bonding strengths

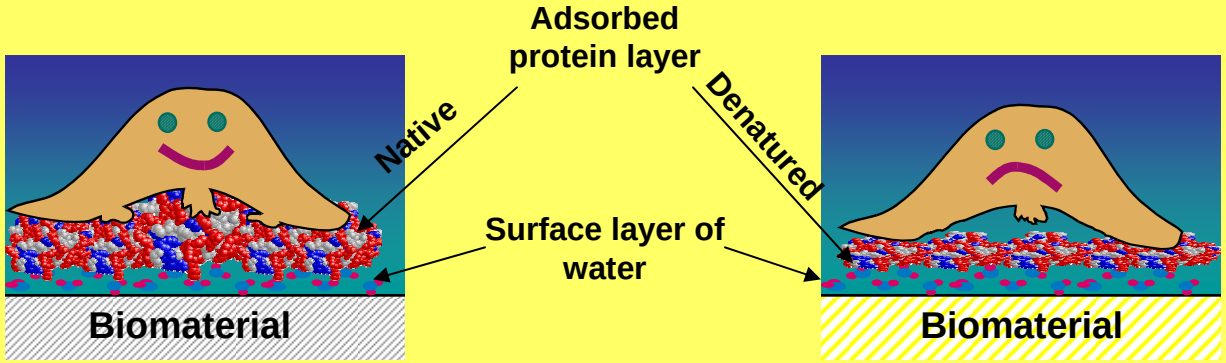


2. Surface + water + proteins

Native or denatured confirmation

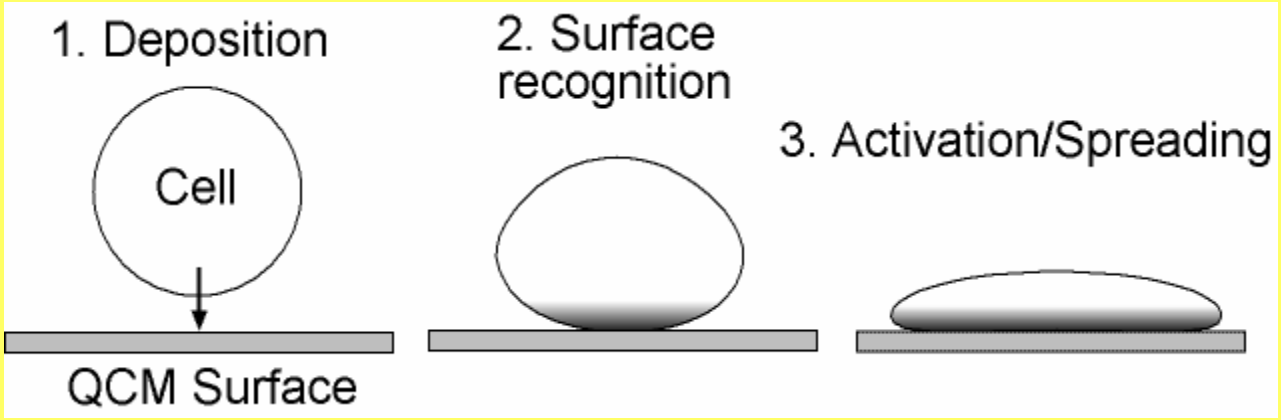


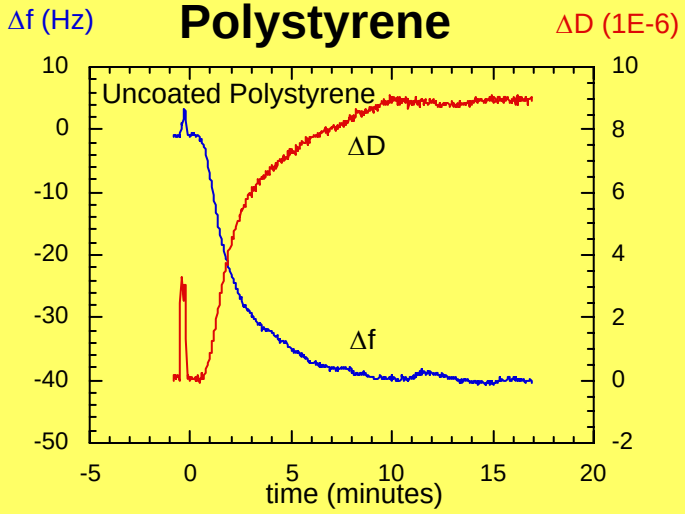
3. Surface + water + proteins + cells

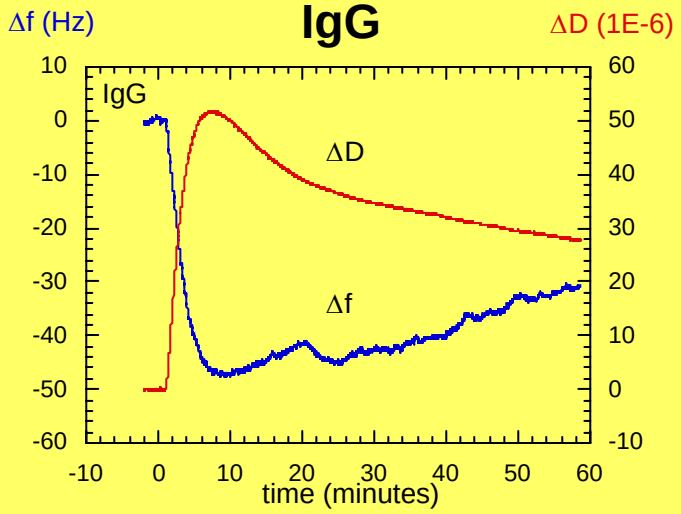


Cell interactions

Activation of human neutrophils



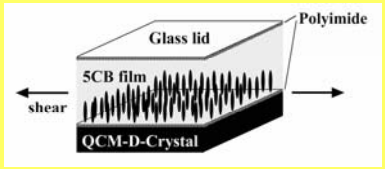




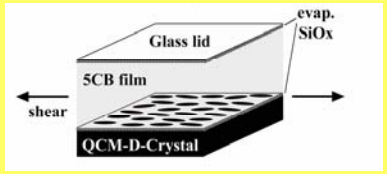
Fredriksson et al.: Langmuir (1998)14, 248J.
Mat Sci: Materials in Medicine 1998 9, 785

Phase transitions in soft matter - liquid crystals

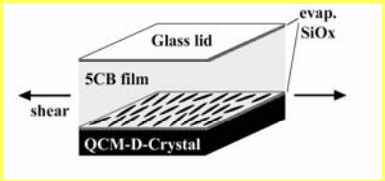
Results: near T_{NI}



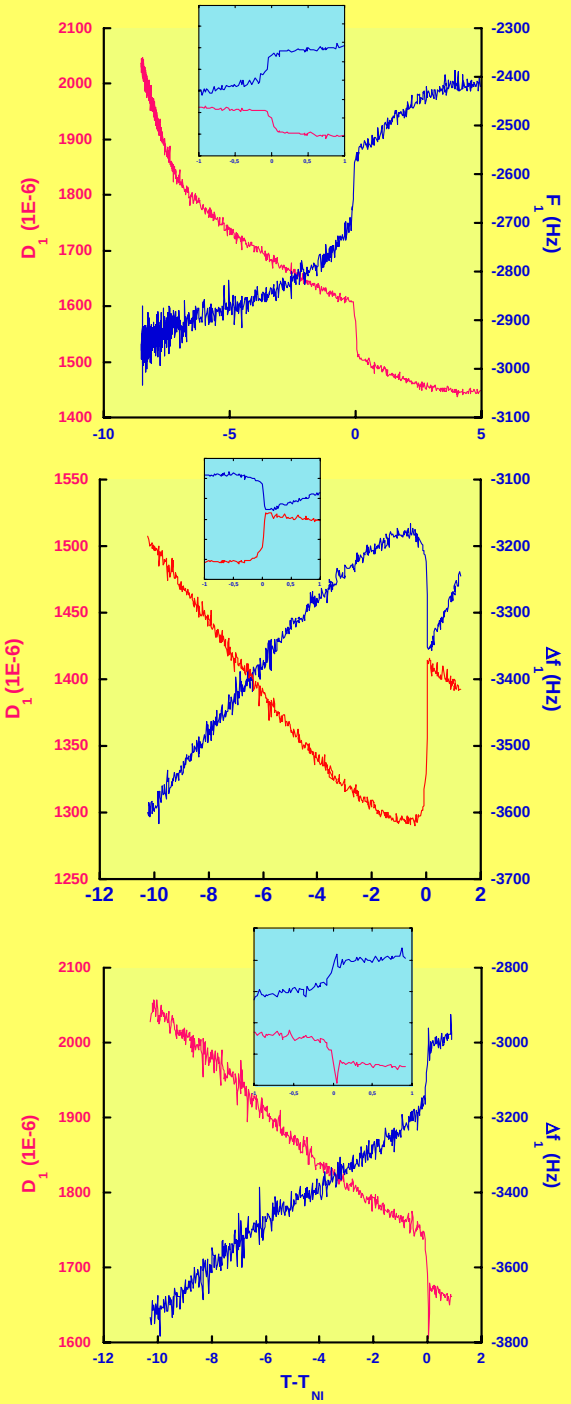
a



b

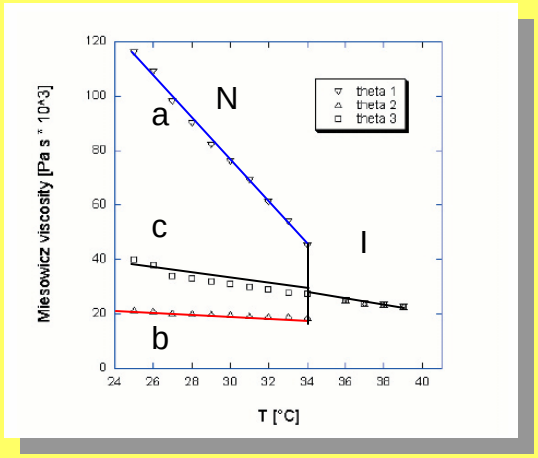


c



Features:

1) Observe the size of D_1!
2) By by Sauerbrey!
3) Compare D_1 to Miesewicz viscosities!



On a global level 5CB behaves as a viscous liquid: $\Delta D \propto \eta_{ij}$

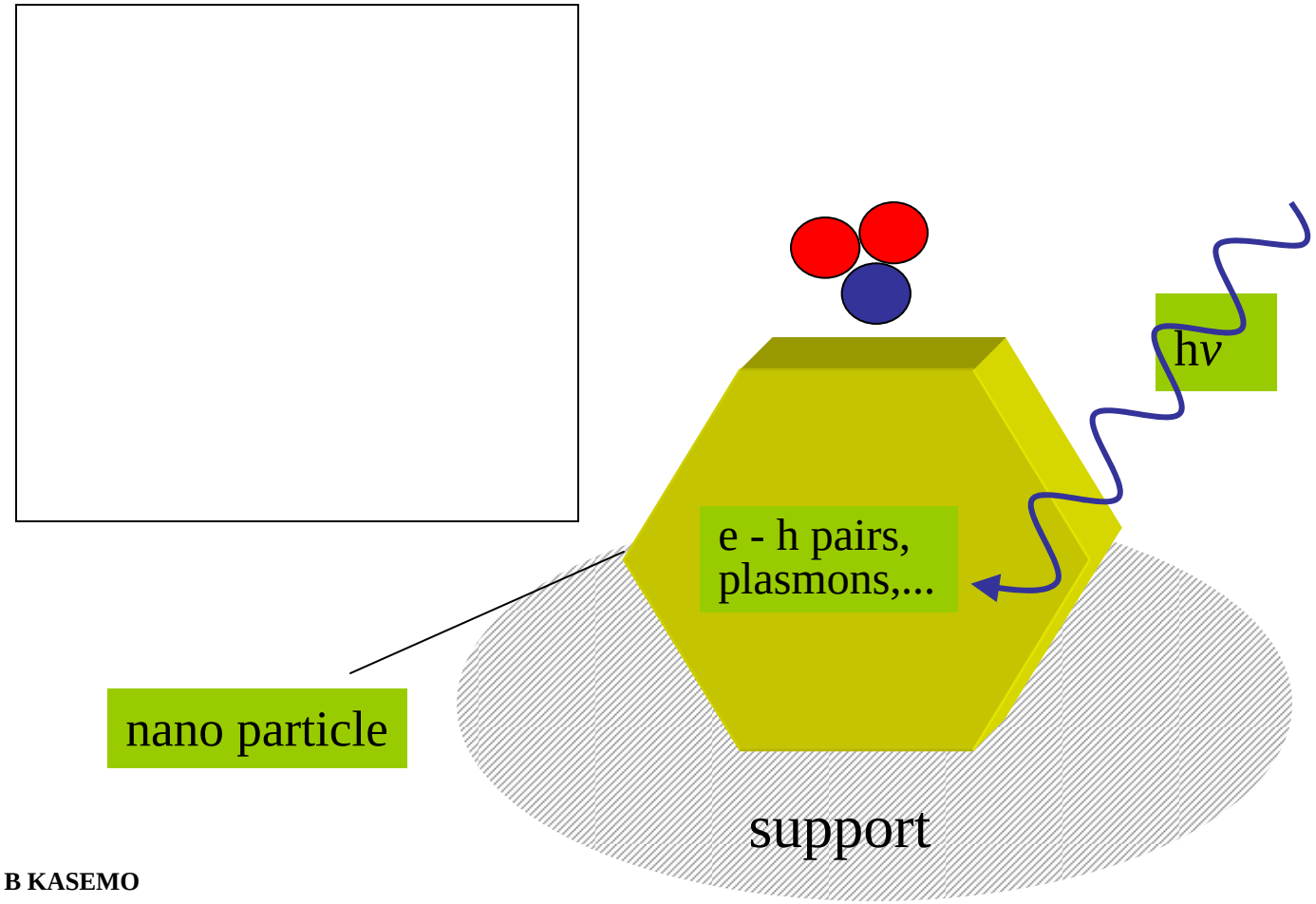
Forget elasticity.

4) An anomaly just before T_{NI}

B KASEMO

Nanoparticles, nanoholes and -arrays for amplified and taylored optical response, e.g. sensing.

http://www.fy.chalmers.se/projects/photonano



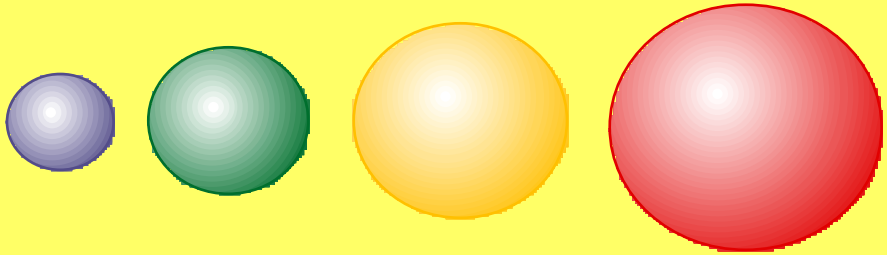
- **Basic mechnisms**
- **Solar - PV, H_2**
- **Photocatalysis for e.g. cleaning**
- **(Bio)sensors**
- **Materials processing**
- **(Optoelectronics)**

Photo Nano

Importance of shape and size for the localised surface plasmon resonance (LSPR) -theory

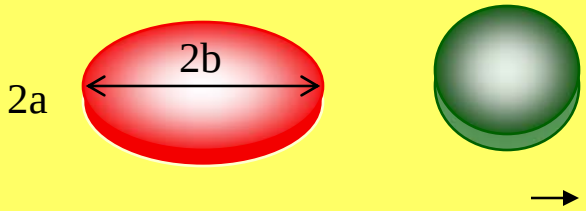
Spheres:

- LSPR redshifts for larger particles.
- Increased linewidth.
- Quadrupole resonance appears at shorter wavelength ∅ quasistatic approximation not valid



Oblate spheroids :

- Two LSPR associated with the minor, a, and major axis, b, of the spheroid respectively.
- Major axis LSPR redshifts as ratio r = b/a, increases
- Minor axis LSPR blueshifts as r increases

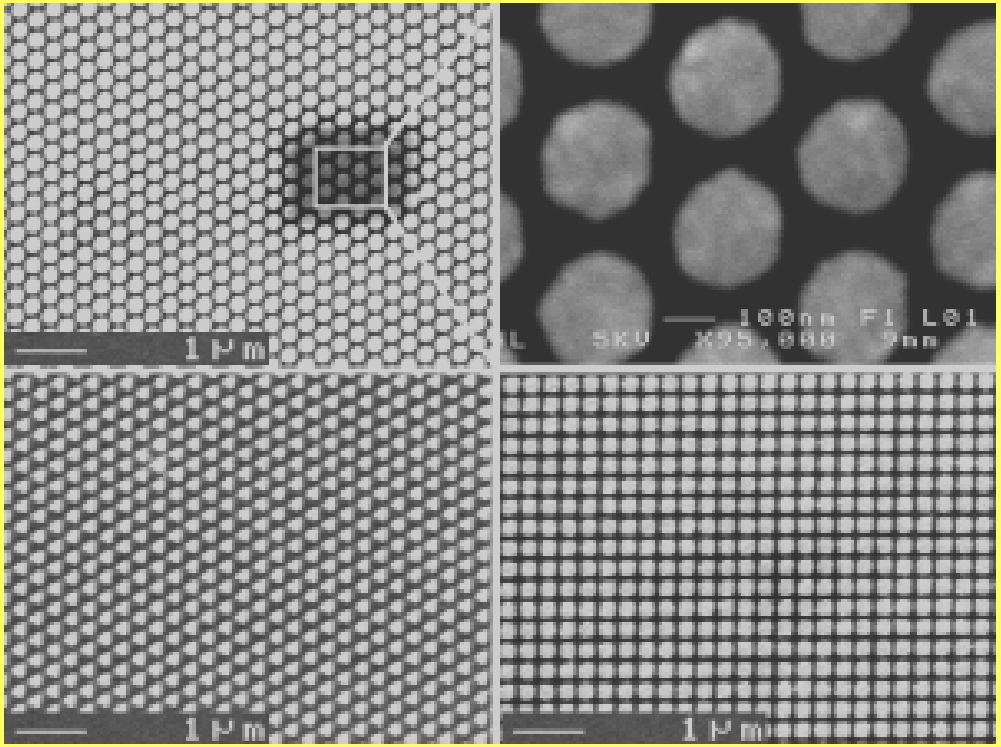


r = b/a

Linda Gunnarsson, Mikael Käll et al

Surface-enhanced Raman scattering (SERS) for probing biomolecules

SEM images of the nanopatterned silver particles (200 nm diameter)



Separation:

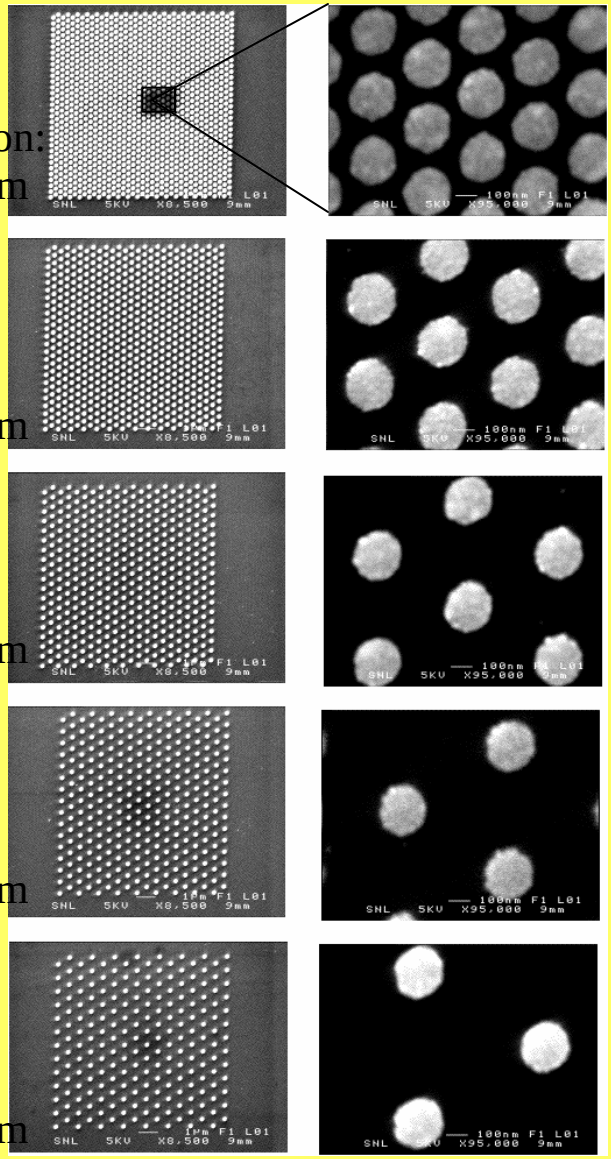
100 nm

200 nm

300 nm

400 nm

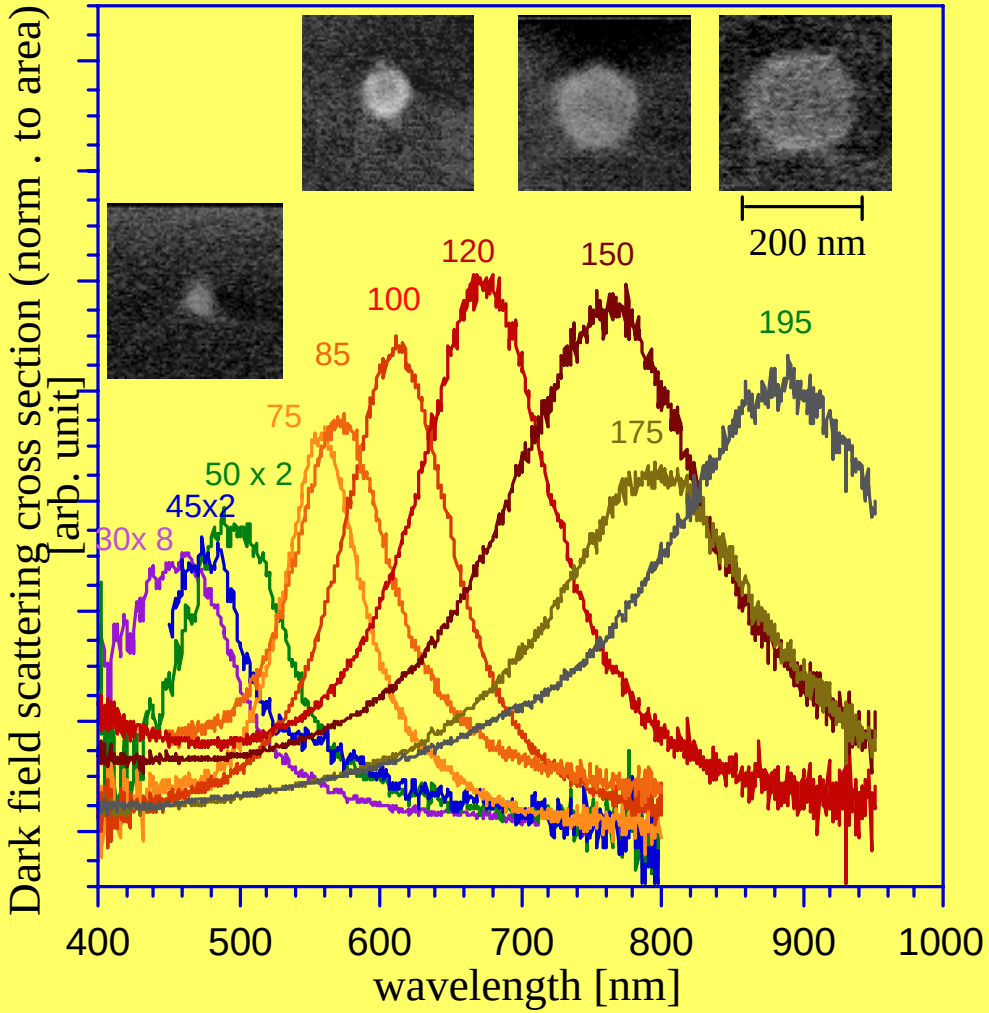
500 nm



B KASEMO

Darkfield scattering of single particles-

measured from arrays with 5 μm grating constant



Particle heights =20-25 nm

10 nm increase in diameter

↓

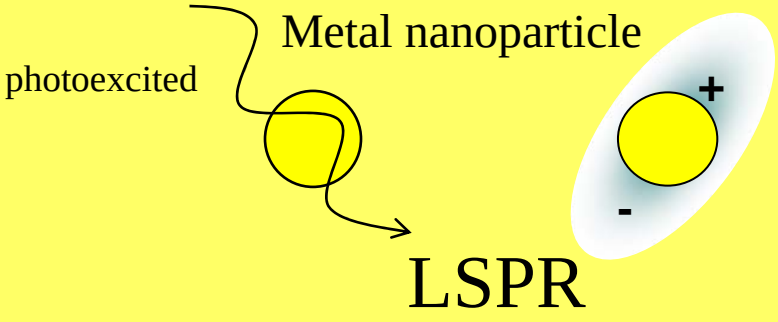
27 nm redshift in peak position

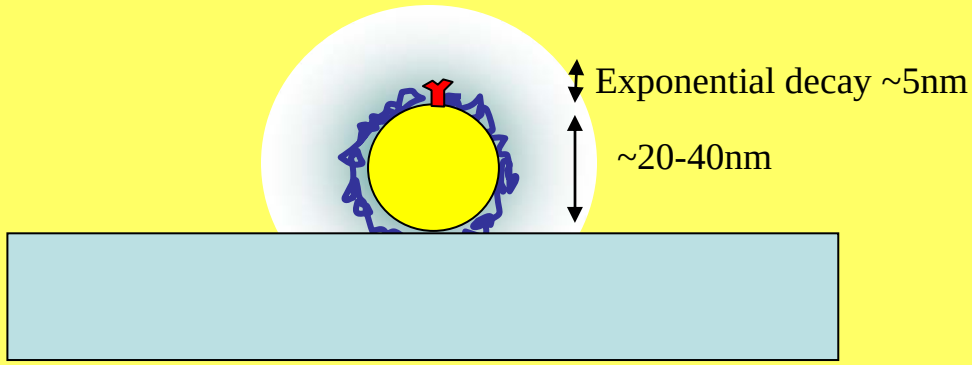
Linda Gunnarsson, Duncan Sutherland, Per Hanarp, + collaboration w. Mikael Käll's group,

L. Gunnarsson et al , manuscript in preparation

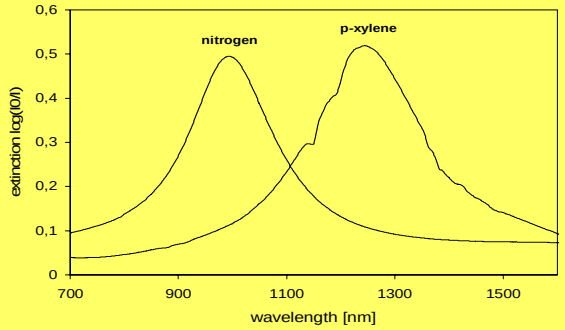
Integrated monitoring: Rational design of localised surface plasmon (LSPR) based nanoscale biosensors

Nanoparticle analogue of BIACORE SPR



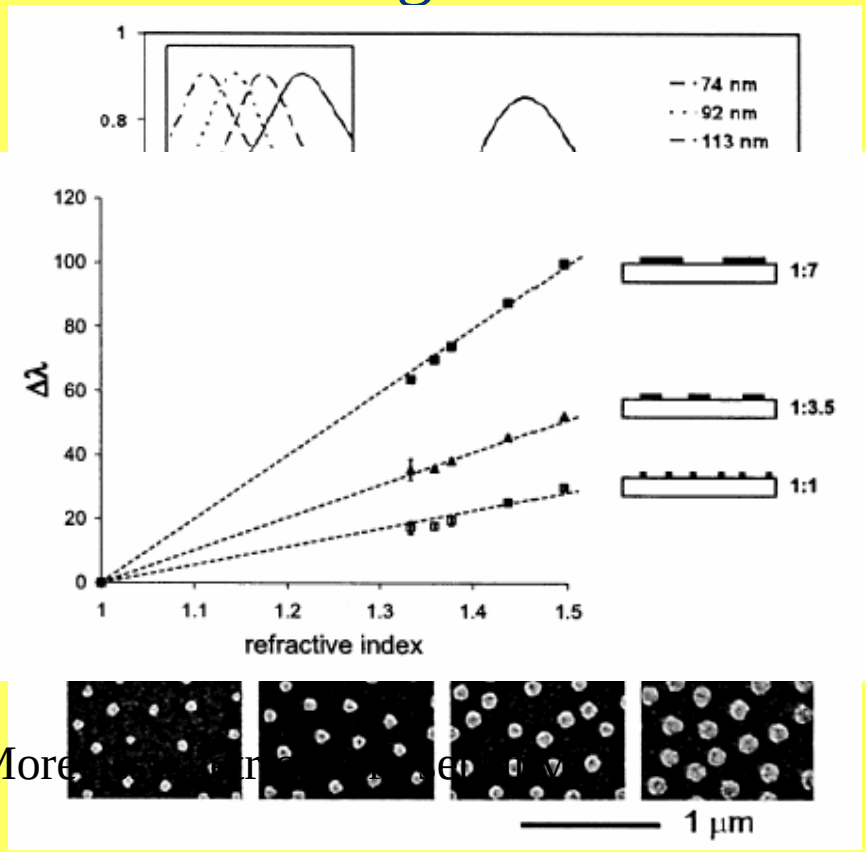


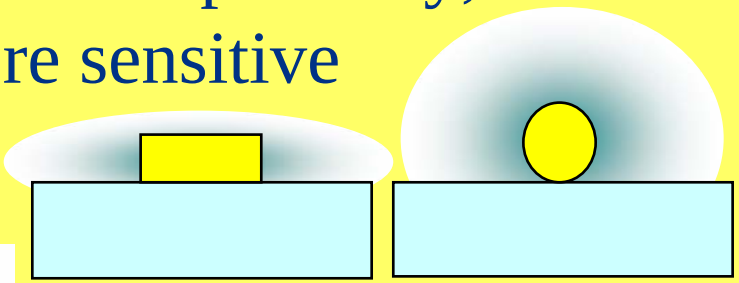
Sensitive to the local dielectric properties

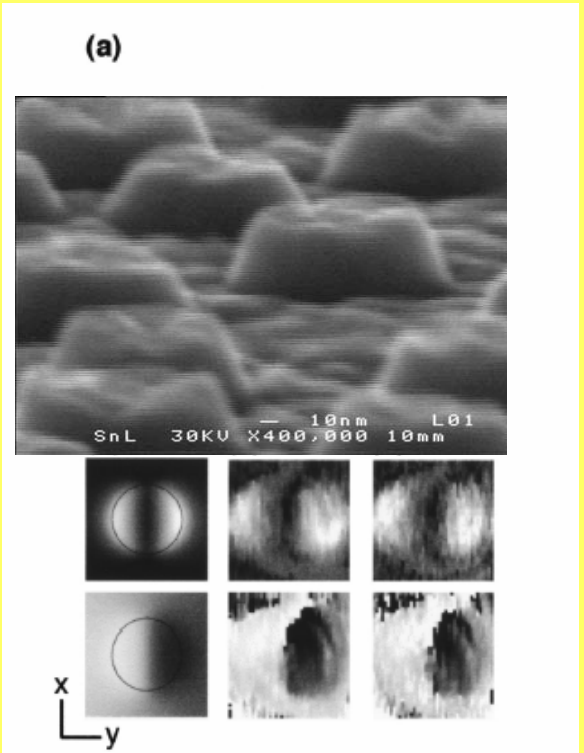


Basis for a sensor

Assymetric particles: Tunable spectrally, higher field and more sensitive







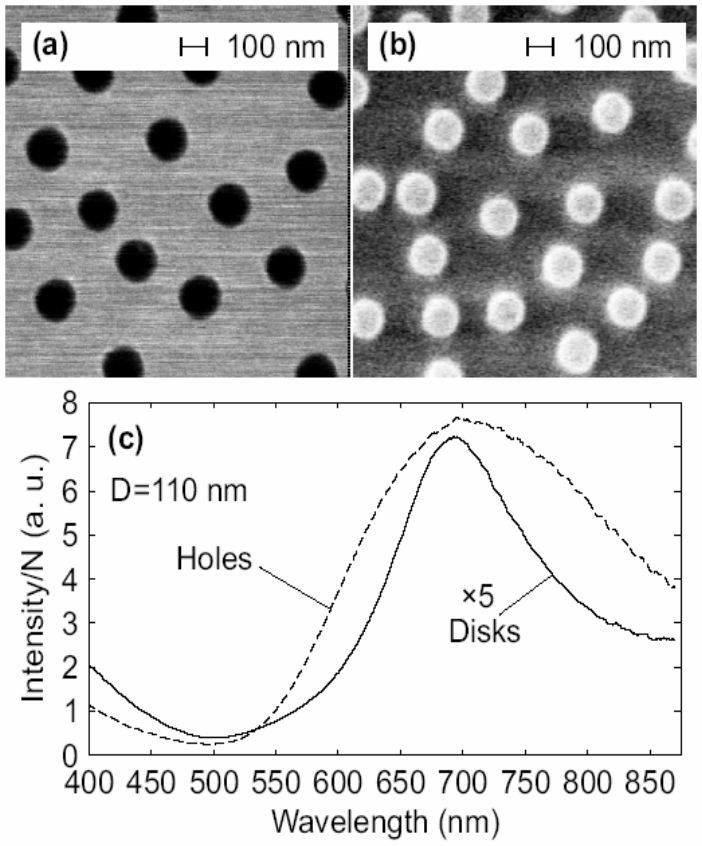
More [illegible]

P. Hanarp et al. *J. Phys. Chem. B, 2003* 107, 5768

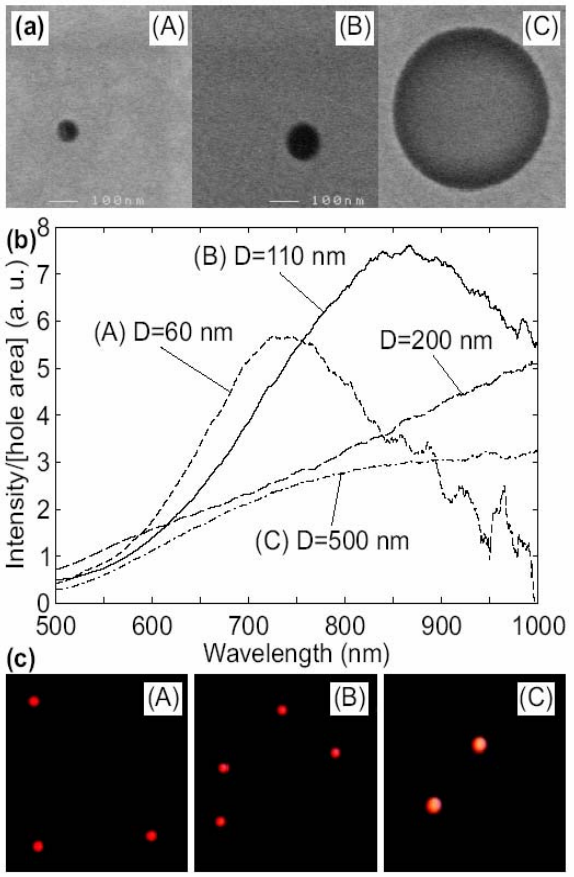
R. Hillenbrand et al *Applied Physics Letters* 83 (2): 368-370 2003. Collab. MPI Germany

Hanarp/Sutherland

Hole – particle symmetry



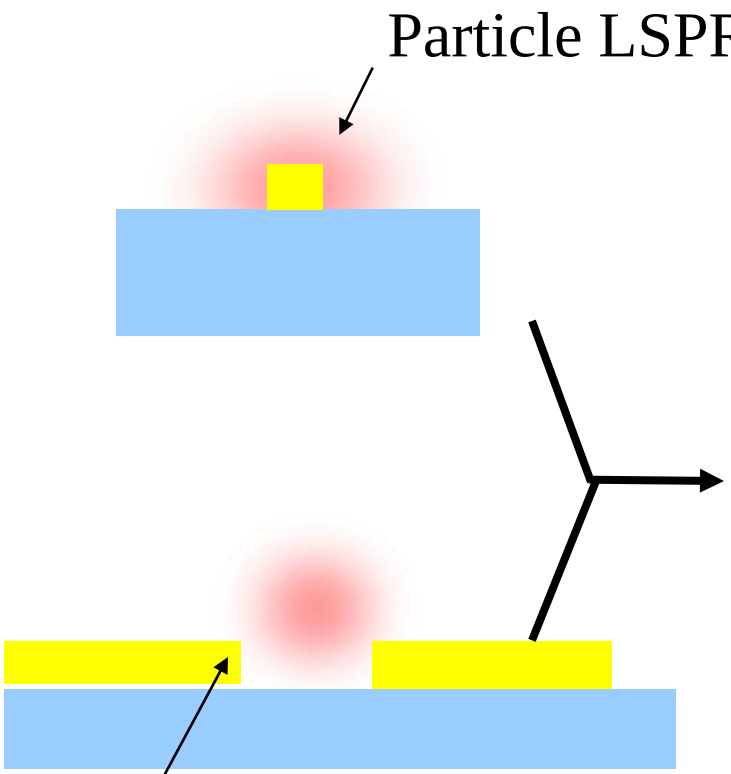
J. Prikulis et al *Nano Letters* 2004



Sutherland and Käll

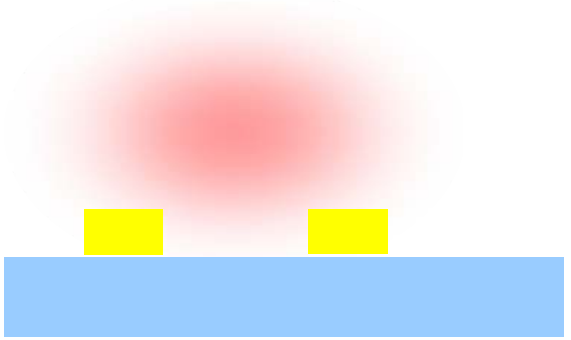
Superimposed structures for better sensors?

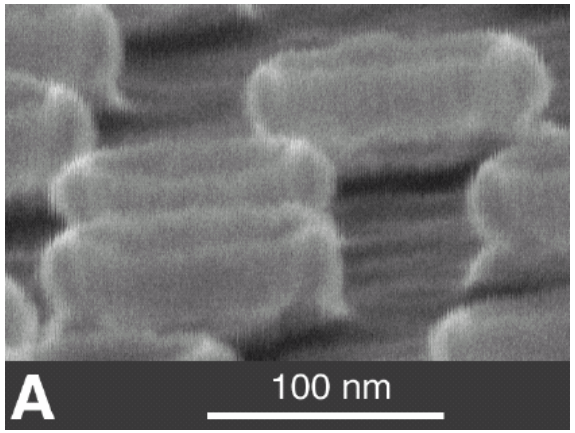
Surface plasmon modes



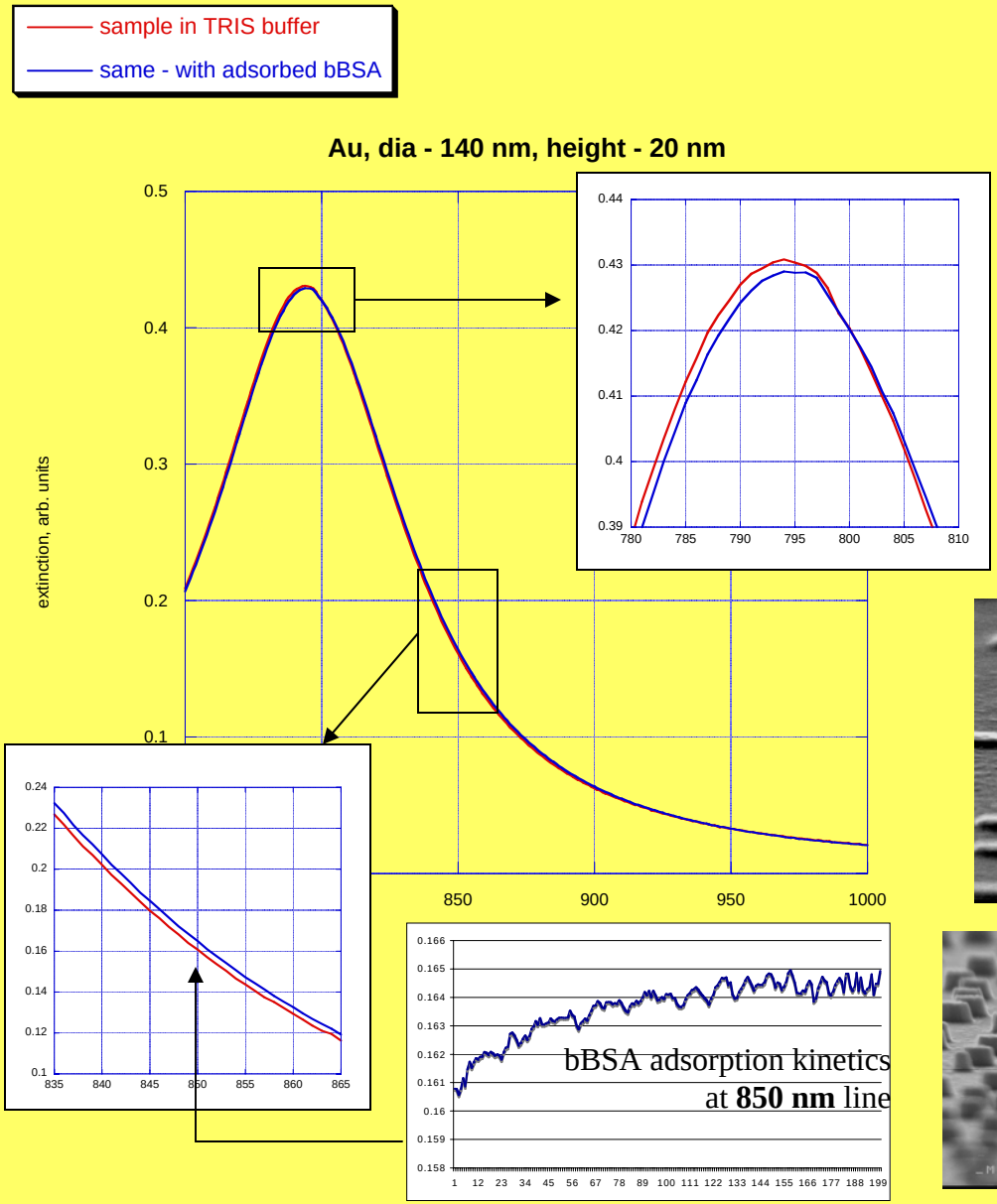
Superimpose a particle and a slightly smaller hole

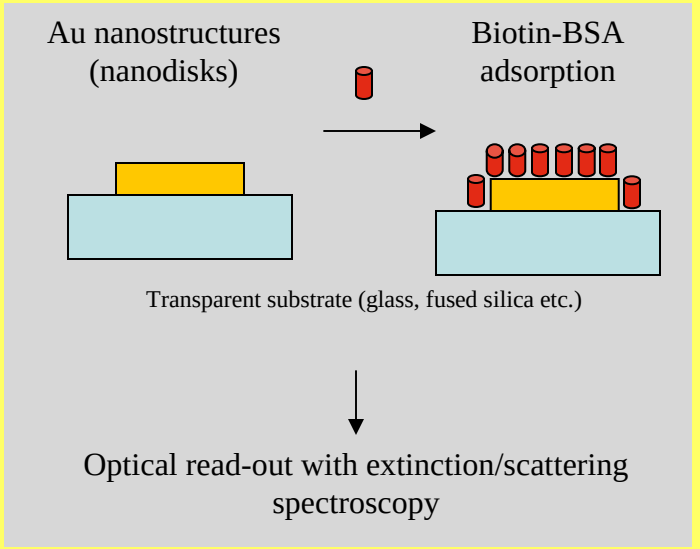
Ring LSPR

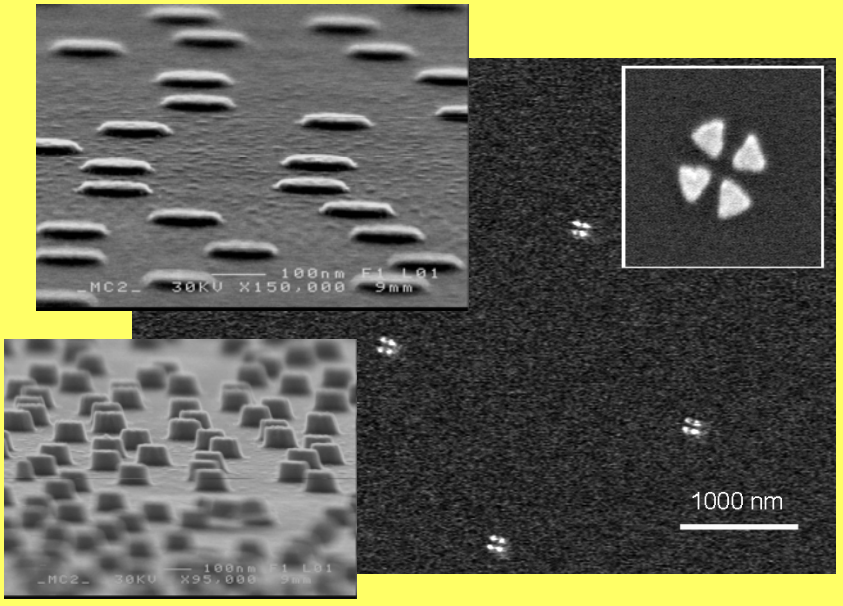




Biosensing with Localized Plasmons







B KASEMO

Some comments and reflections

- At the generic (platform) level there are large synergies between different biointerface applications (drugs, sensors, stem ccell engineering,..)
- To focus and make a real product and commercialize it is a totally different story; mind set, money, way of working,..
- Combination of different physical principles in sensing
- Nanotechnology eneterss almost all aspects of biointerface R&D

Simulations

Vladimir P. Zhdanov
Kristian Dimitrevski

Vesicle and SPB adsorption; QCM-D, SPR, AFM expts.

Erik Reimhult, Singapore
Michael Zäch
Fredrik Höök, Lund U.
Craig Keller
Karin Glasmästar, Aminotech, Norway

Functional SPBs

Fredrik Höök Lund U
Annette Granéli, Columbia U., N.Y.
Charlotte Larsson, Astratech
Indriati Pfeiffer
Jason Benkoski, NIST

QCM-D development

Michael Rodahl, now at Q-Sense AB
Fredrik Höök, now prof at Lund U.
Anatol Krozer IMEGO
Malin Edvardsson
Marina Voinova

Colloidal lithography and optical properties of nanoparticles (NSPR)

Duncan Sutherland
Per Hanarp

Electron beam lithography and (G)SERS

Linda Gunnarsson

Cell force sensor and cell experiments

Julie Gold (Group leader)
Sarunas Petronis, MIC Denmark
Ann-Sofie Andersson
Karin Glasmästar
Nina Tymchenko
Johan Gustafsson
Dorota Dahlborg

Shark skin mimic

Igor Zoric,
Håkan Rapp

Lotus leave mimic

Dinko Chakarov
Per Holgersson

Optical sensing

F Höök
D Sutherland
Andreas Dahlin, Lund U.
Elin Larsson
Alexandre (Sasja) Dmitriev

Liquid crystals

Christoph Langhammer
Igor Zoric

Collaborations

- **M. Textor, J. Vörös, et al, - ETH**
- **B. Liedberg, P. Konradsson, I. Lundström - Linköping U.**
- **Mikael Käll, Chalmers**
- **VP Zhdanov, Inst Catalysis, Novosibirsk**
- **Peter Eriksson, Gothenburg Univ. Hospital**
- **R. Richter, A. Brisson -Bordeaux U.**
- **F Besenbacher, Aarhus U.**
- **I. Reviakine - Bordeau->ETH->Houston**
- **W. Knoll et al - MPI Mainz, U.Singapore**
- **A Richter - Karolinska Inst.**
- **E Arenas - - " -**
- **R van Duyne, Northwestern U**
- **Q-Sense AB**

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Heterogeneous catalysis for emission cleaning and nanofabricated model catalysts

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Nanofabricated model catalysts and fuel cell electrodes

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Photo active nanostructures for solar cells (H2, electricity), photocatalysis and sensing

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