SEVENTH FRAMEWORK PROGRAMME

nanoCI nanotechnology based cochlear implants

IEB 2014 Sheffield UK

Hes·so Haute Ecole Spécialisée de Suisse occidentale Fachhochschule Westschweiz University of Applied Sciences and Arts Western Switzerland

Nanotechnologies used in NANOCI

Nanotechnology-based implantable and interfaceable devices

Alexandra Kämpfer-Homsy, Edith Laux, Laure Jeandupeux, Julien Brossard, Loïc Piervittori, François Feuvrier, Harry Withlow, Oksana Banakh, *Herbert Keppner*

Partnership

MED EL

UPPSALA
UNIVERSITET

Hes·so
Haute Ecole Spécialisée
de Suisse occidentale
Fachhochschule Westschweiz
University of Applied Sciences and Arts
Western Switzerland

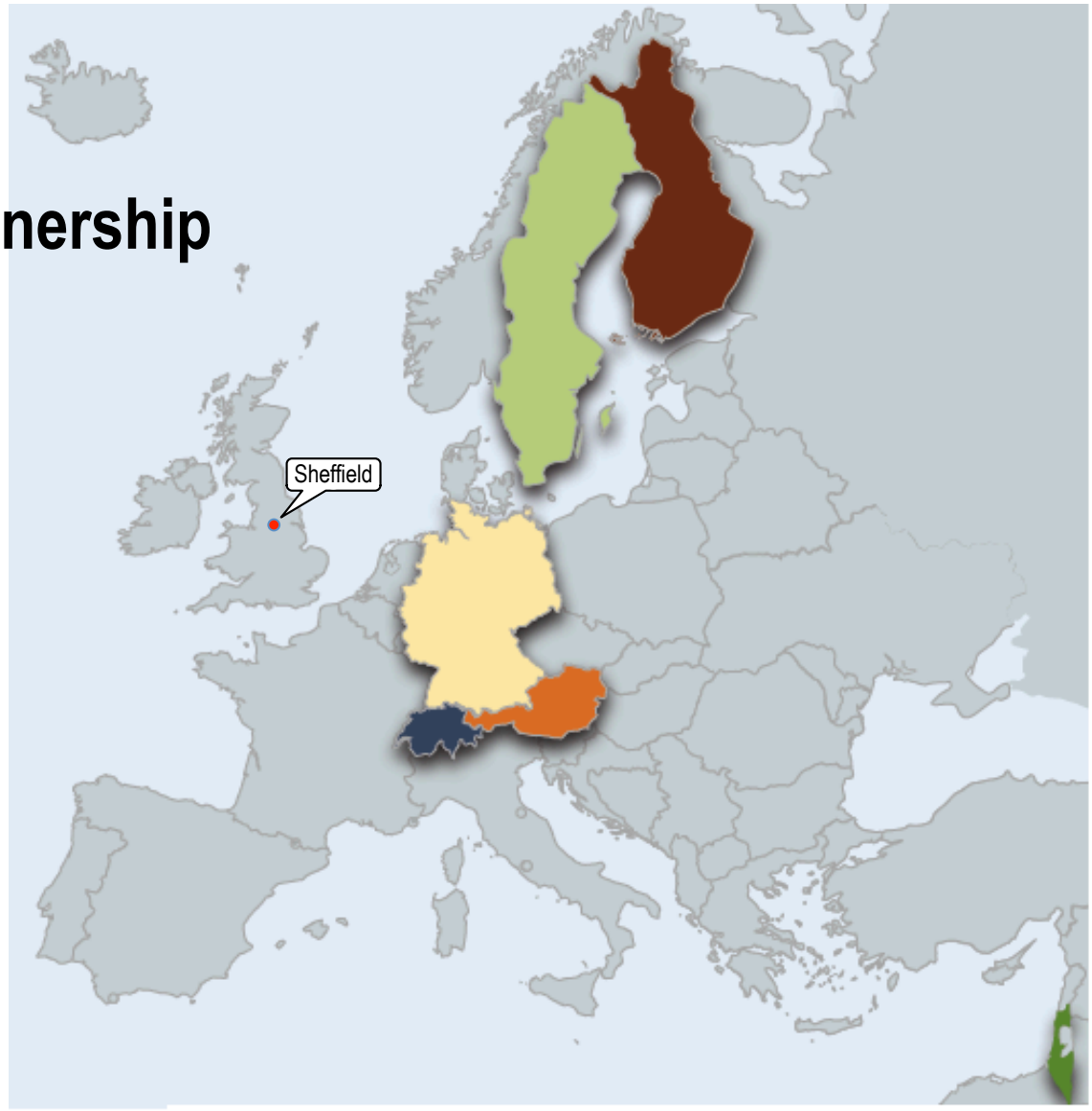
b
UNIVERSITÄT
BERN

Pascal Senn

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

UNIVERSITY
OF TAMPERE

Partnership



1 UNIBE
Bern, CH

2 UT
Tübingen, DE

3 UU
Upsala, SE

4 UTA
Tampere, FI

5 HES-SO
Délemont, CH

6 BIU
Tel Aviv, IL

7 EMC
Tübingen, DE

8 MED-EL
Innsbruck, AT

9 SCIPROM
Lausanne, CH

Outline

- Summary of the challenges
- Selected technologies

  drug dispensing: SOLID on Liquid deposition.

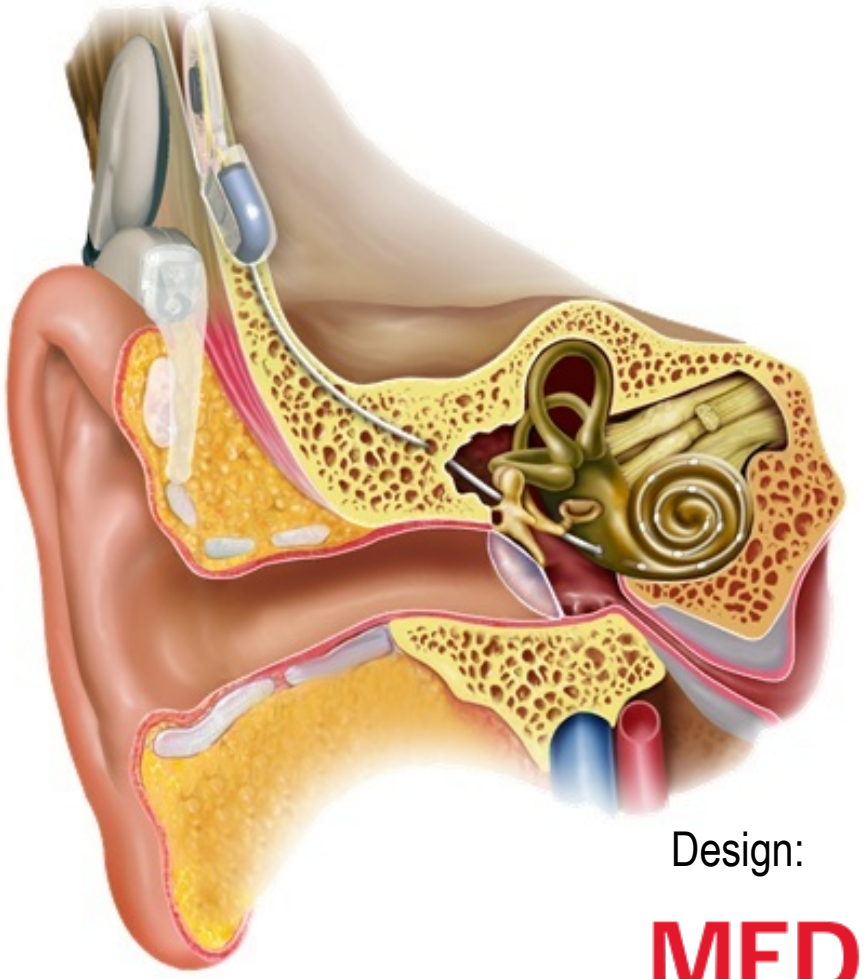
  surface conditioning: Deposition of nanoparticles by sonochemistry

  Conclusion and outlook.

Summary of the challenges

nanotechnology based cochlear implants

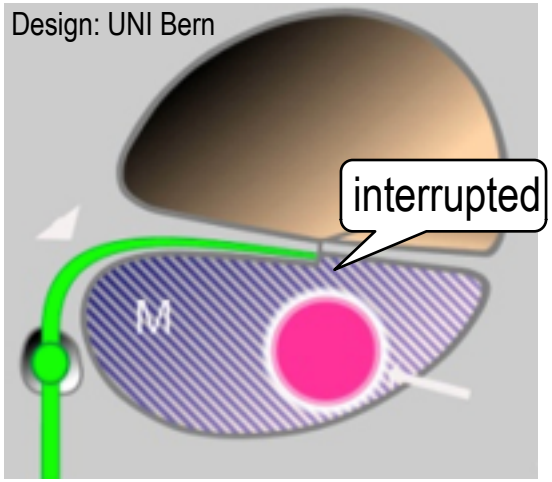
Development of a cochlear implant ….



Design:

MED EL

Summary of the challenges

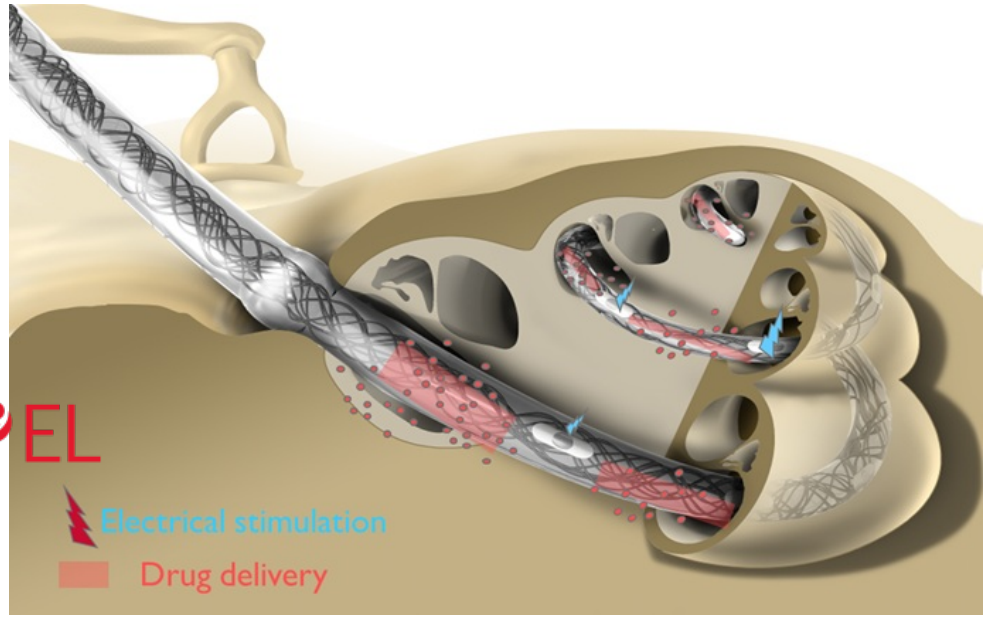


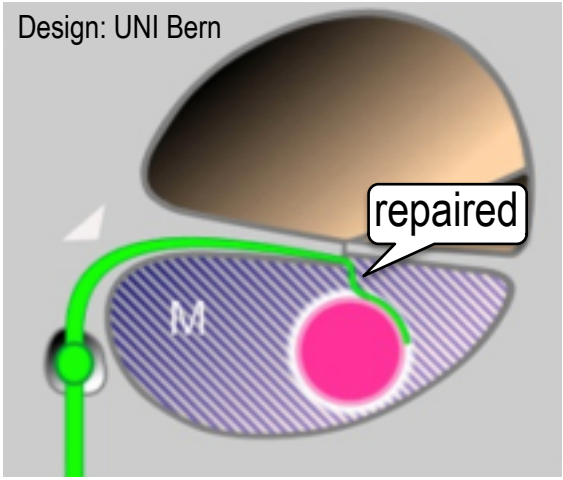
Essential elements for neuronal interfacing:

- Attraction of neuron-growth towards electrodes via selectively operating delivery of growth factors.
- Creation of a neuron-electrode junction allowing signal transmission.

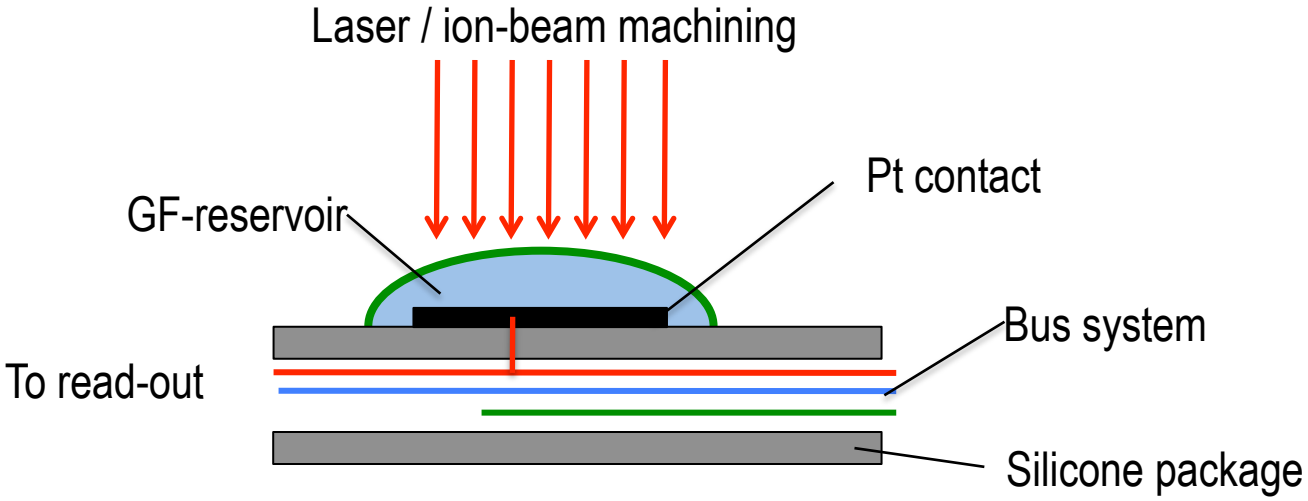
Design:

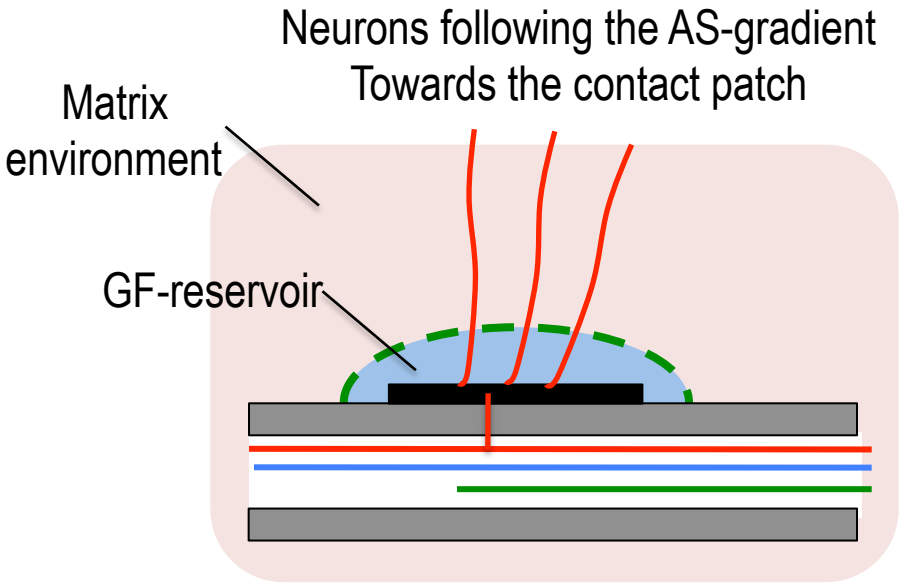
MED EL





Growth Factor (GF) emitting device (vision)





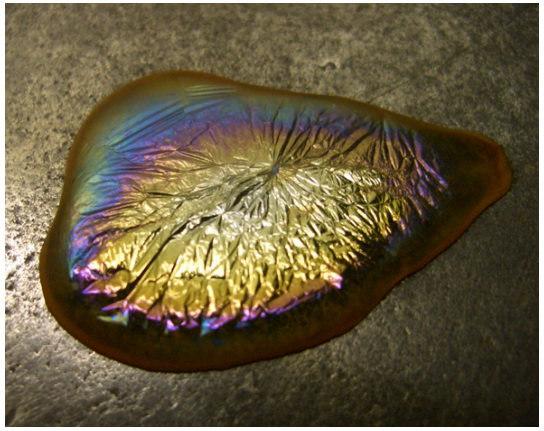
Technological Issue:
how to package the liquid?
Solid on liquid deposition wanted

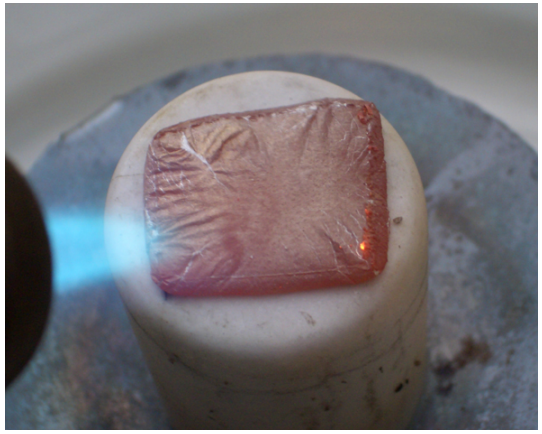
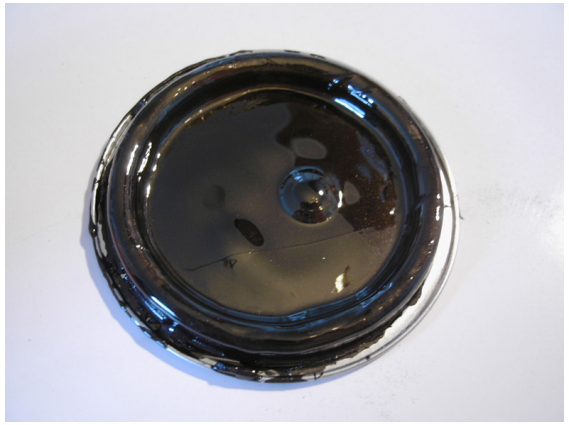
Solid on liquid deposition

Finding a solution: short walk in the garden:

Solid on liquid?

More and others

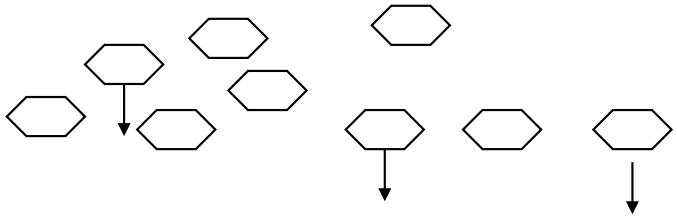
Natural SOLID systems seems to be either thermally, mechanically or chemically **unstable**

First “archaic” approach for obtaining better stability

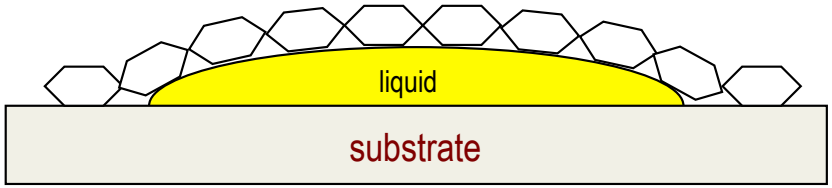
Mercury has a high density; paint spray come from the gas phase and polymerises on the surface of a Mercury droplet.

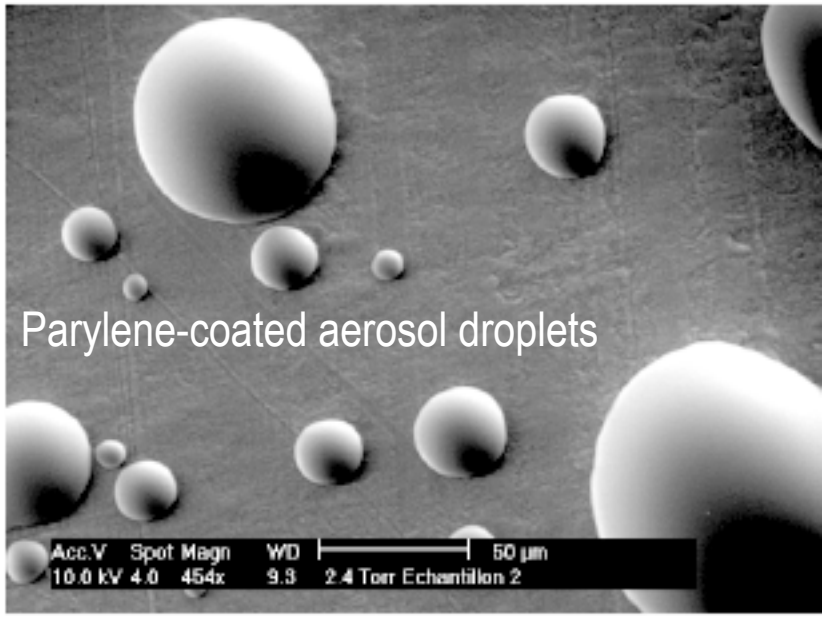
SOLID (Solid on liquid deposition): Coating of liquids and hermetical sealing using CVD Parylene.

H. Keppner, M. Benkhaira, Patent WO/2006/06395, Dec. 2004.
J. Charmet et al. Thin Solid Films 518 (2010) 5061–5065



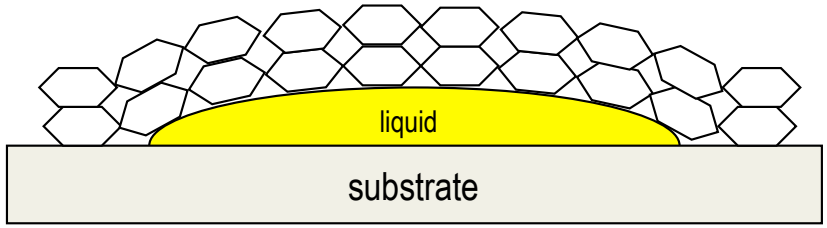
Monolayer of Parylène





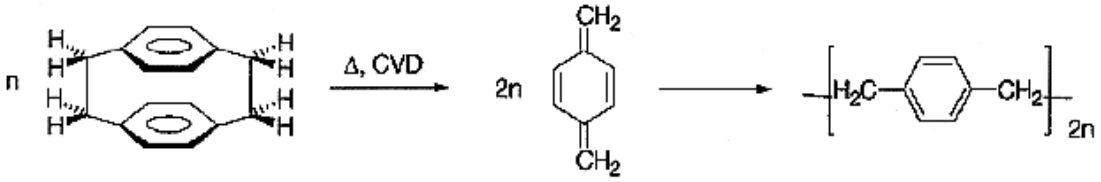
Parylene sealed silicon-oil drop attached at an optical fibre

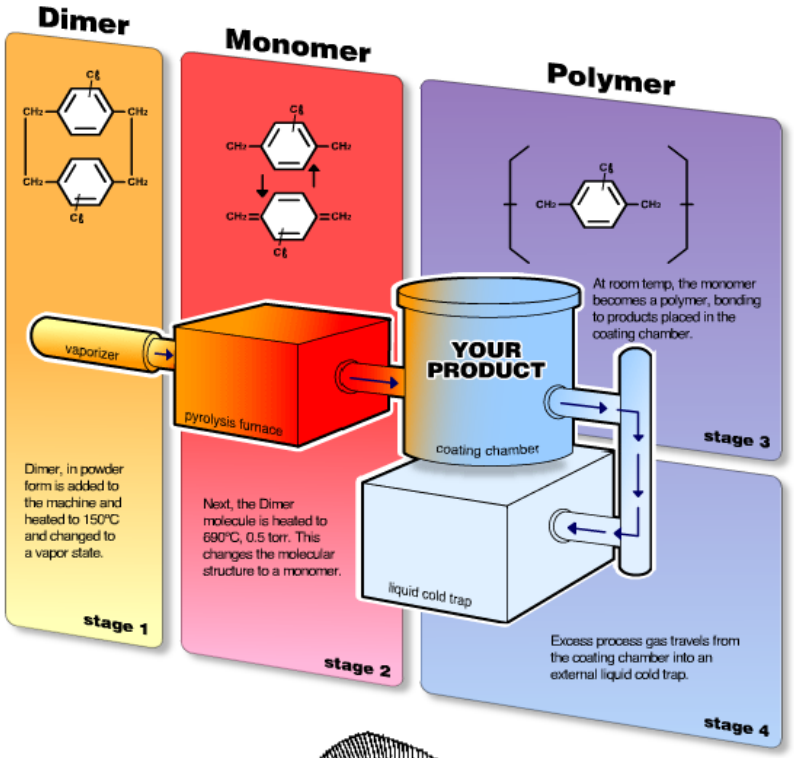
Later: mechanically stable coating

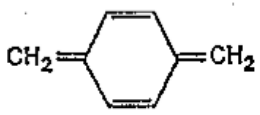


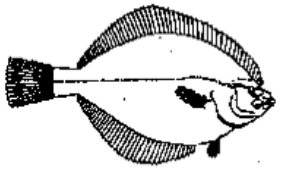
LPCVD deposition of Parylene (Poly-Chloro-Para Xylylene) :

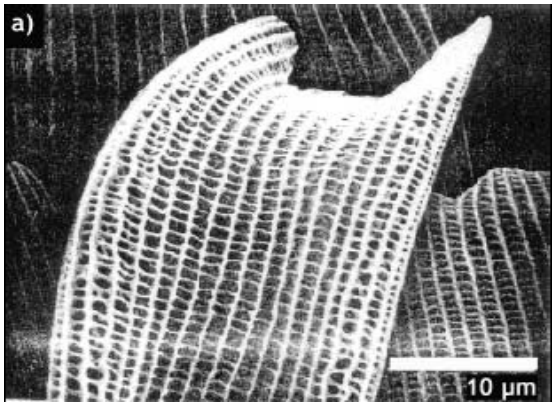
W.F. Gorham, J. Poly, Sci., Part A-1: Polym. Chem. 4 (1966) 3027

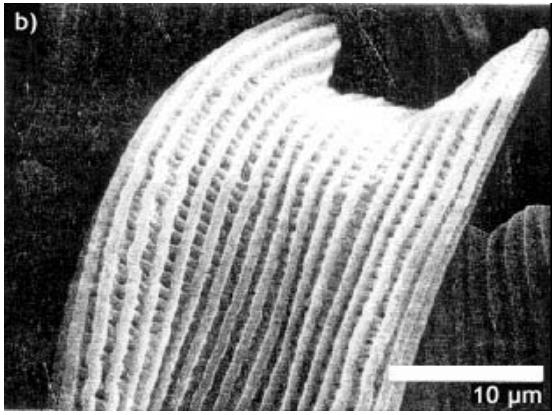










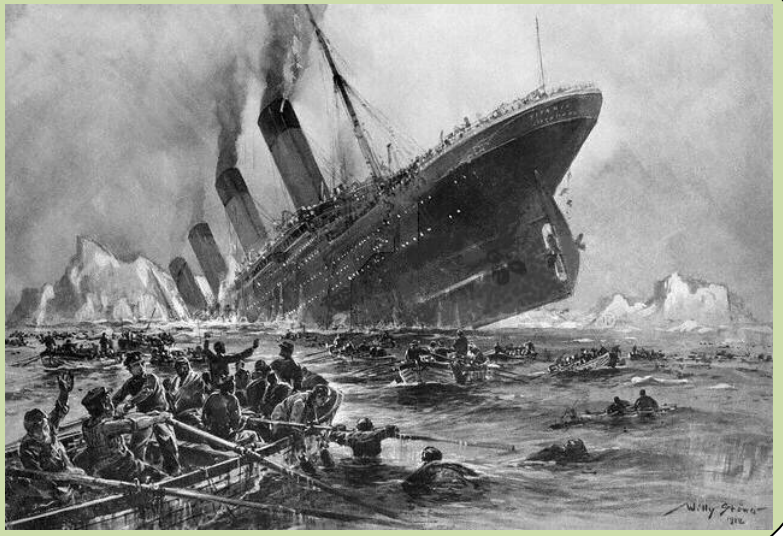


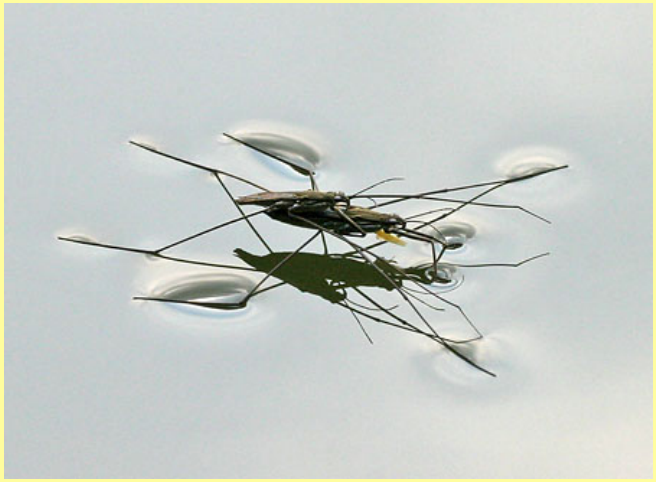
SEM micrograph from a Butterfly wing a) uncoated, b) Parylene coated
D.W. Grattan; *Can. Chem. News* **1989**, 25

Parylene layers are highly biocompatible

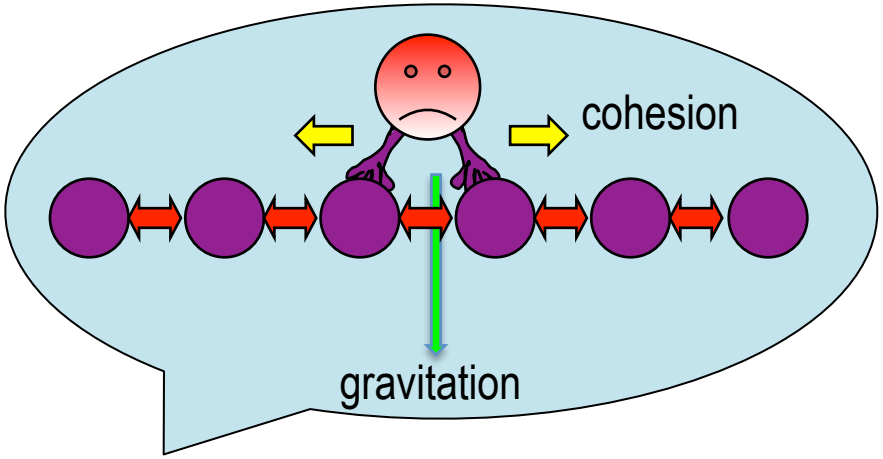
Why SOLID-technology may be considered as nanotechnology:

Large, high-density solid clusters tend to sink as soon as Archimedes' principle is not fulfilled

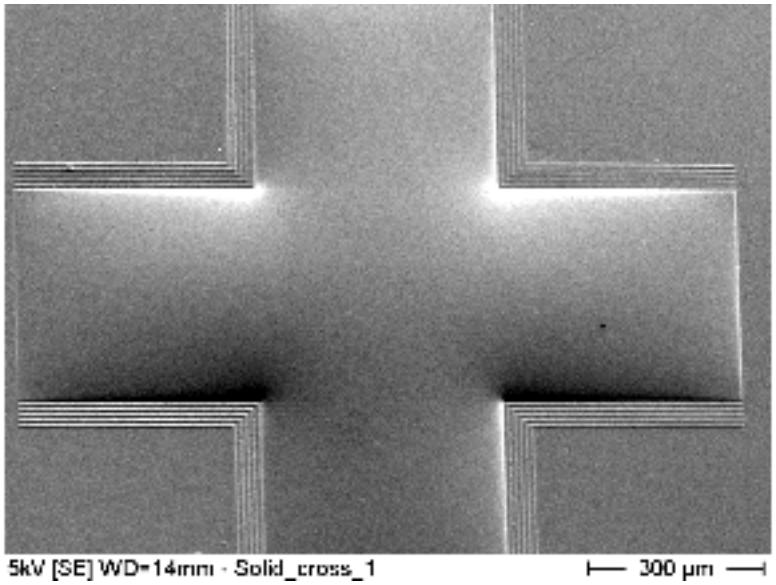


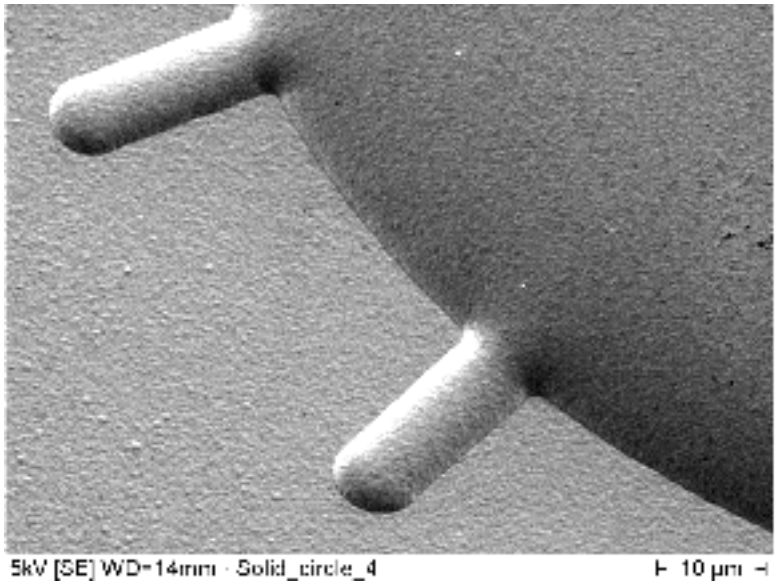


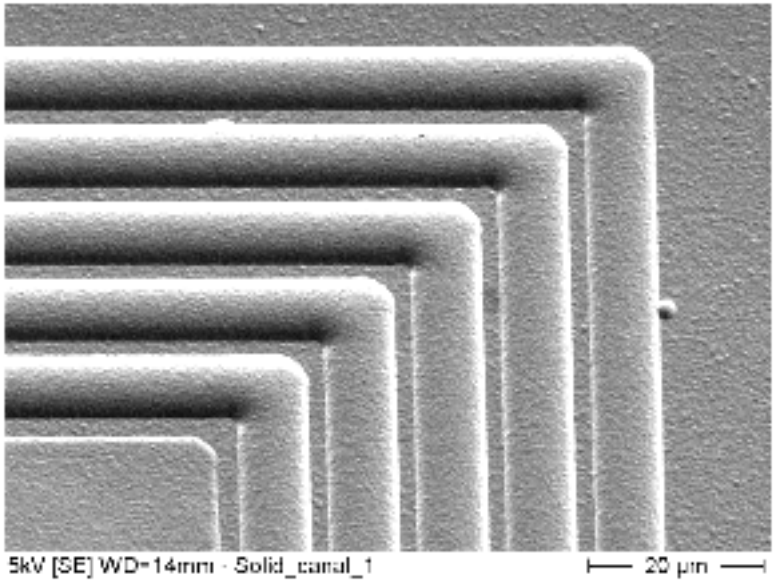
Smaller solid clusters have to overcome the surface energy and can swim.

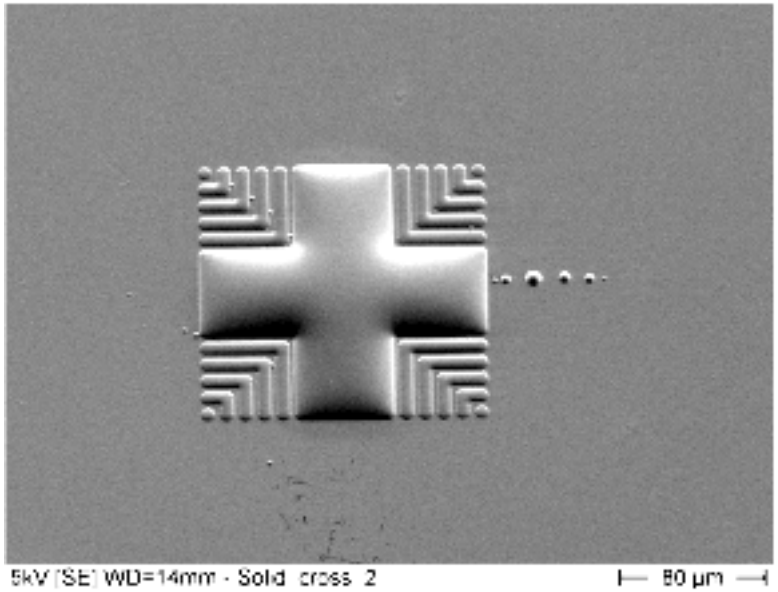


At molecule level, atoms or molecules are much more affected by cohesion forces rather than to gravitation.







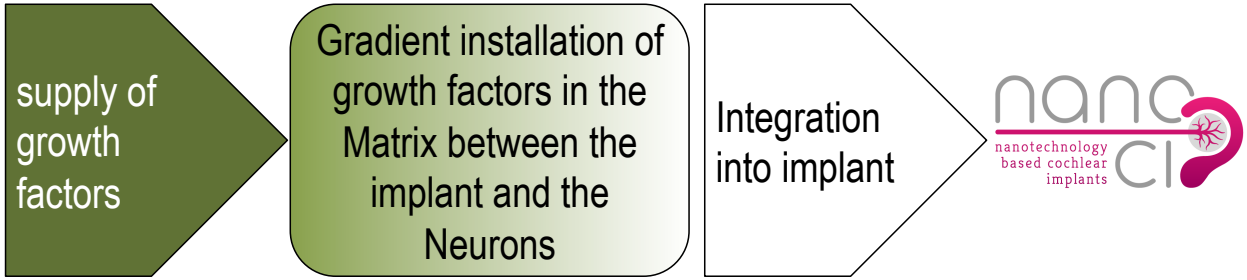


J. Charmet, H. Haquette, E. Laux, G. Gorodyska, M. Textor, G. Spinola Durante, E. Portuondo-Campa, H. Knapp, R. Bitterli, W. Noell, and H. Keppner. Liquid as template for next generation MEMS. J. Phys.: Conf. Ser., 182:012021, 2009.

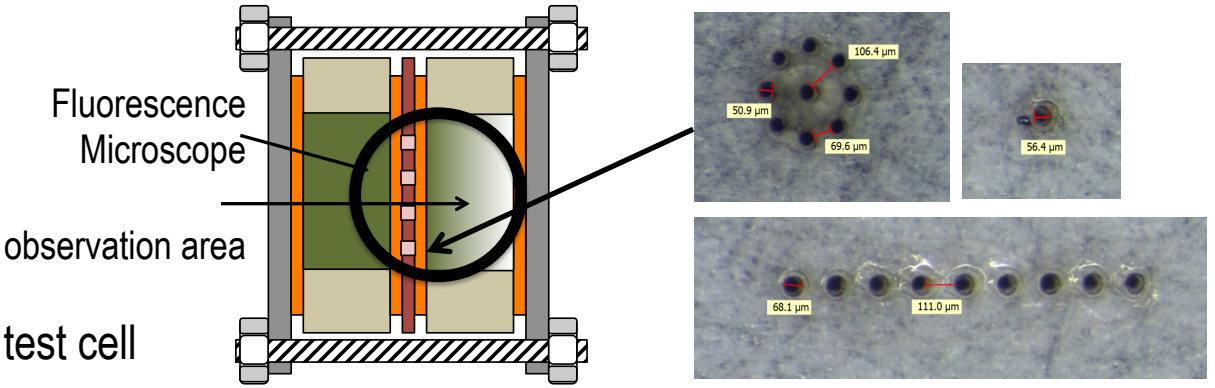
Controlled release of growth factors (GF)* from a localized well

*e.g. such as brain-derived neurotrophic factor (BDNF)

Objective:

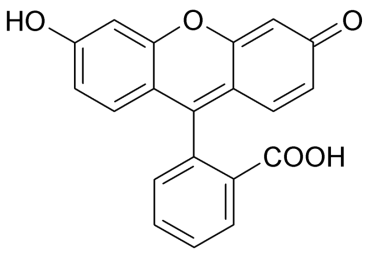


Experimental:

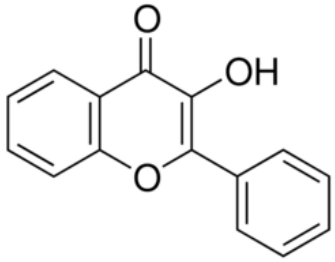


Membrane-plate with different pores

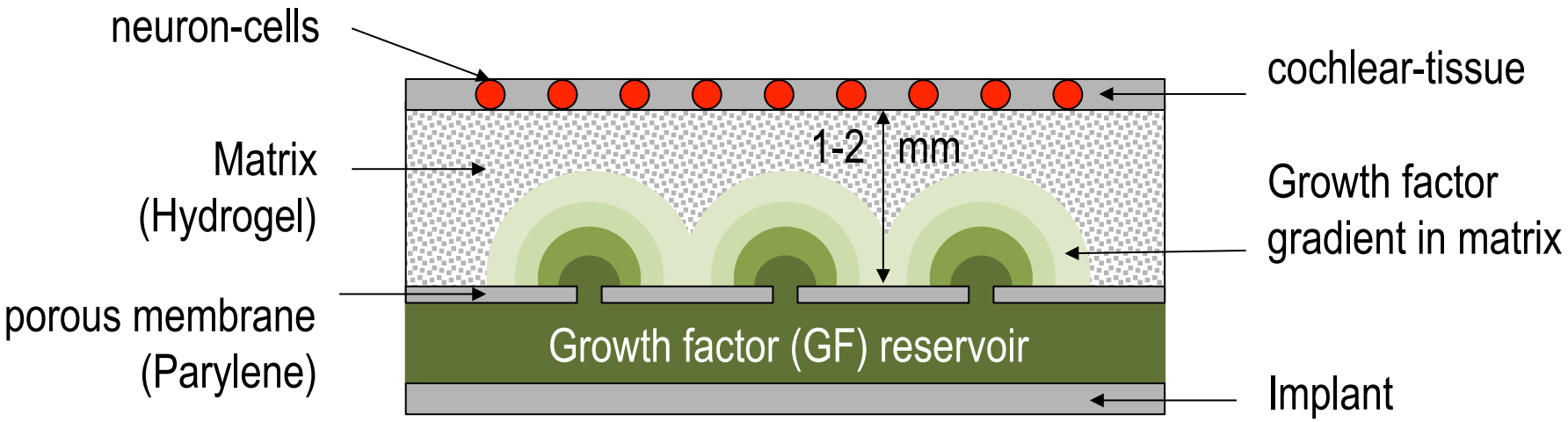
GF monitoring:



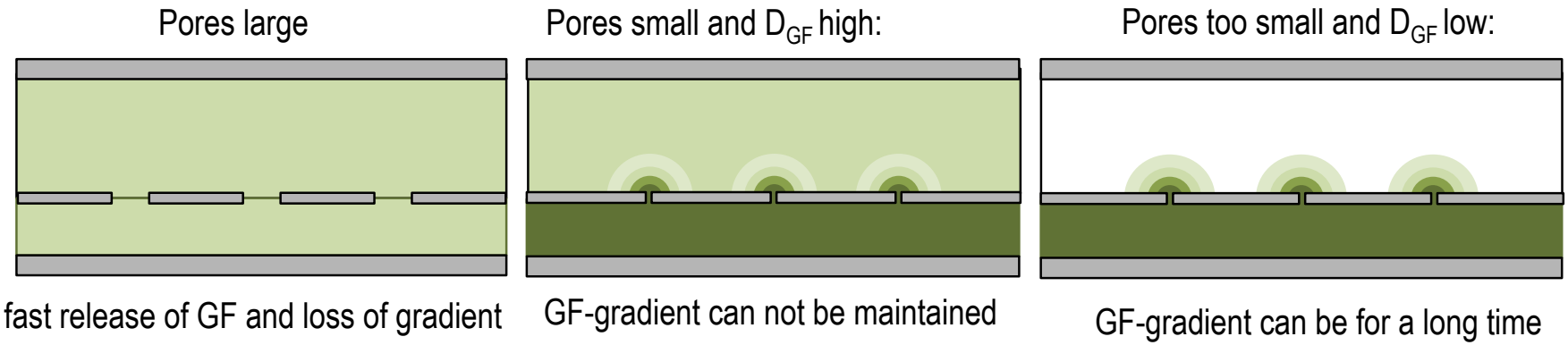
← Fluorescein:
marker + similarity
to Dihydroxyflavone
(possible GF) →



Scenarios for pore-size optimization



Cases study

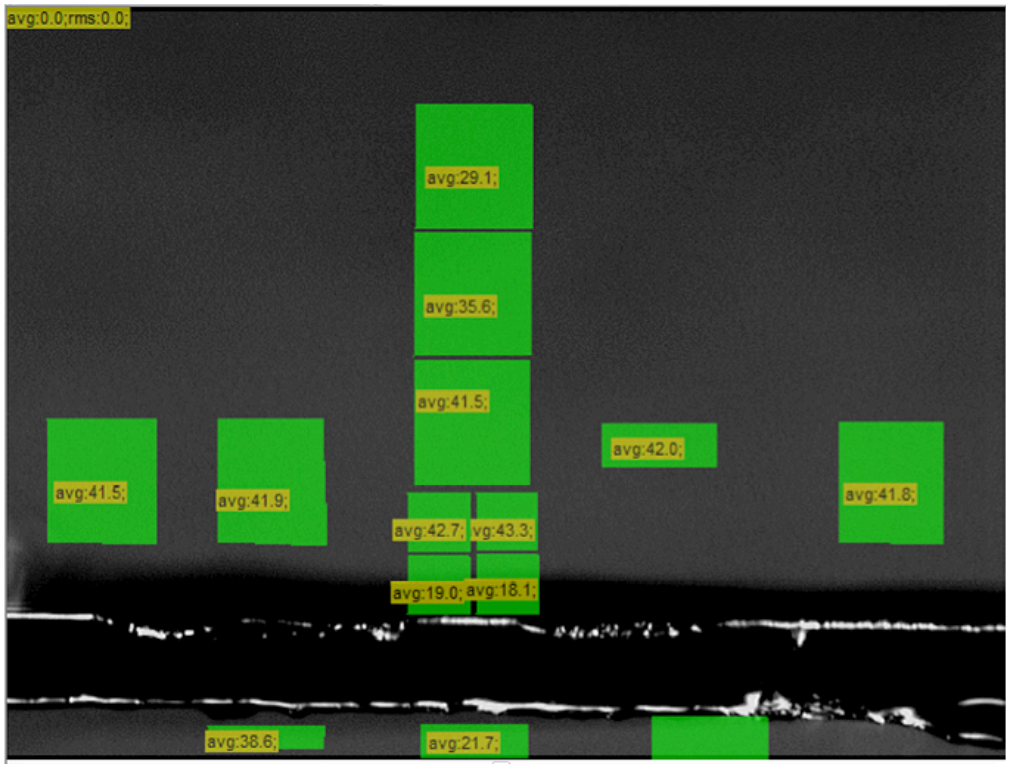


Design requirements:

The gradient of growth factors (GF) in the matrix (M) must be maintained during 4 days across 1-2 mm in order to allow oriented grow of the neuron cells toward the implant prior to be attached with the contact-pad.

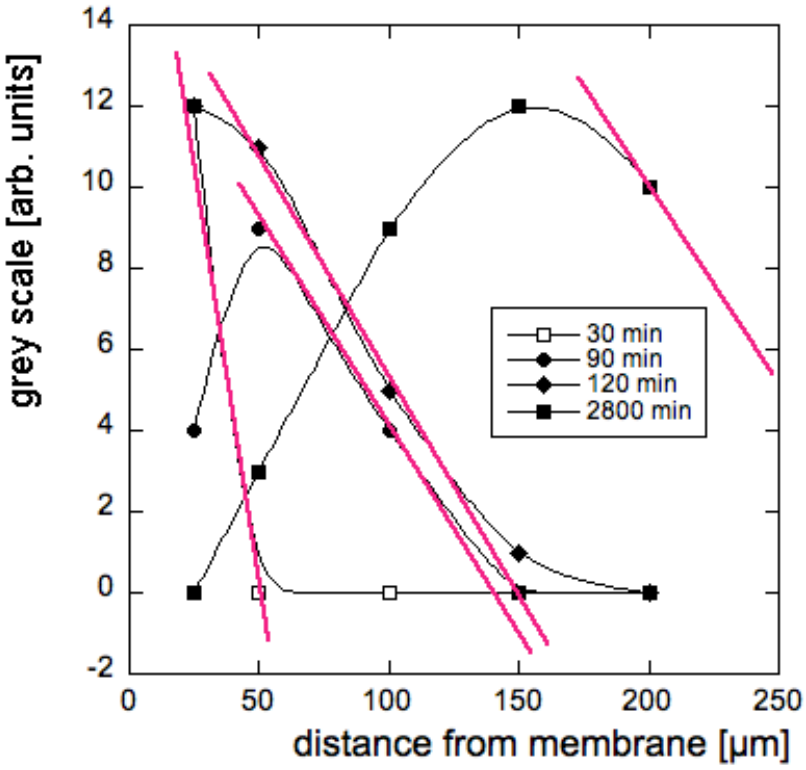
After the choice of M and GF the diffusion constant $D_{GF}(M)$ and the mobility $\mu_{AGF}(M)$ of GF in M will be determined (dependence on the molecular size of GF, the pore size, and diffusion coefficient of GF in M.

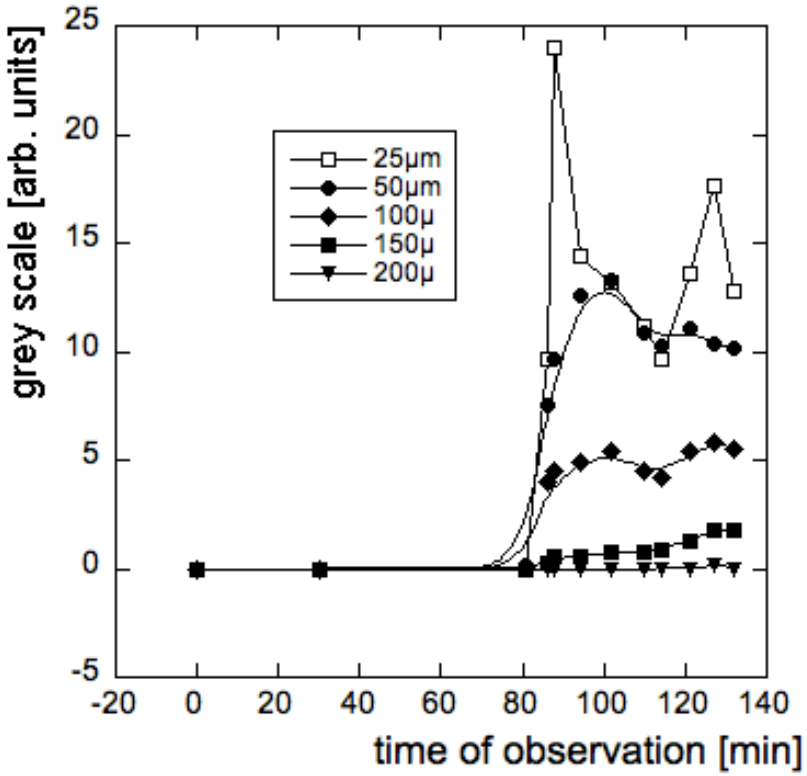
Fluorescence microscope Micrograph observing the spatially resolved intensity of light emitted by the Fluorescein molecules



Results

A 25 mmol/l fluorescein in glycerol solution diffuses through a single 50 µm opening



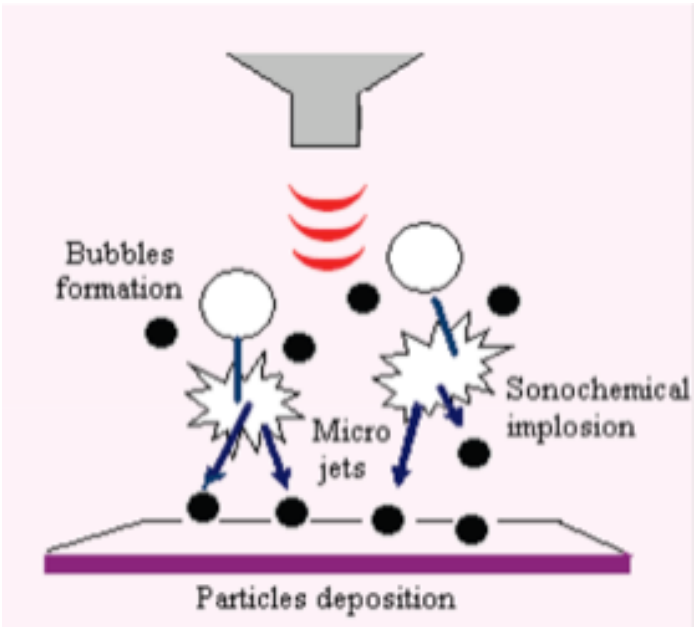


With a diffusion constant of $1.48 \cdot 10^{-5}$ mol /l·s·m and creates a gradient of concentration of 2.75 mol /l·m

Conclusion: the observed system could be potentially be used if fluorescein would be replaced by DHF

2) Deposition of nanoparticles by sonochemistry

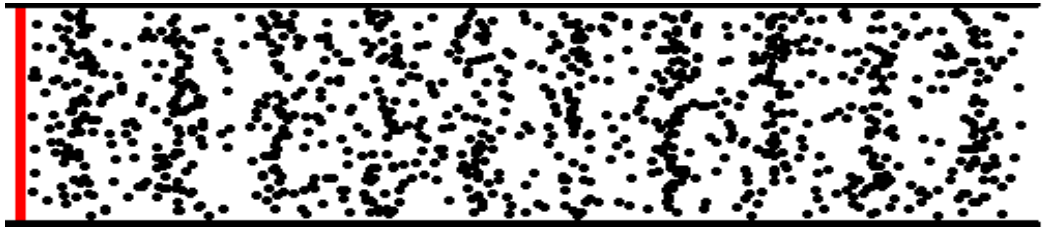
Pioneer input from A. Gedanken / Bar ilan University



Nanoparticles in liquids are interacting with a high frequency acoustic field (20 kHz 3 kW)

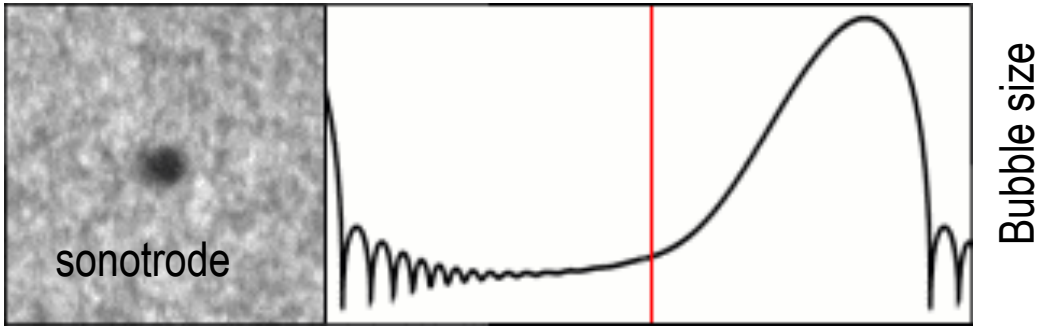
principle of sonochemistry

Sound = pressure waves = periodic compression / expansion- cycles
traveling through a medium possessing elastic properties (gas, liquid, solid)



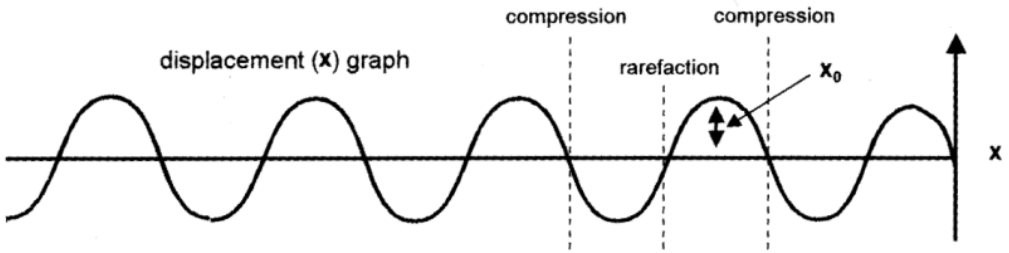
20 kHz

Acoustic Cavitation = creation, growth, and implosive collapse of bubbles in a liquid

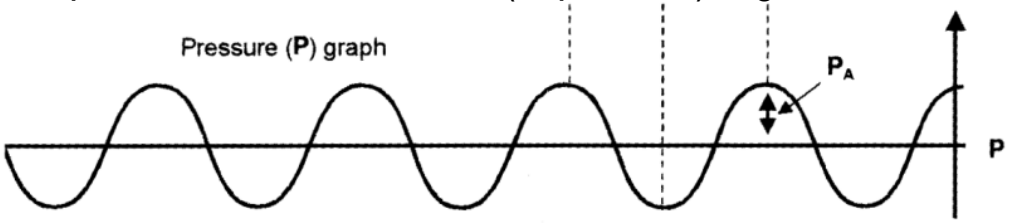


Ref. Jiri Pinkas Department of Chemistry Masaryk University Brno Czech Republic

Further considerations: Acoustic pressure



Compression and rarefaction (expansion) regions

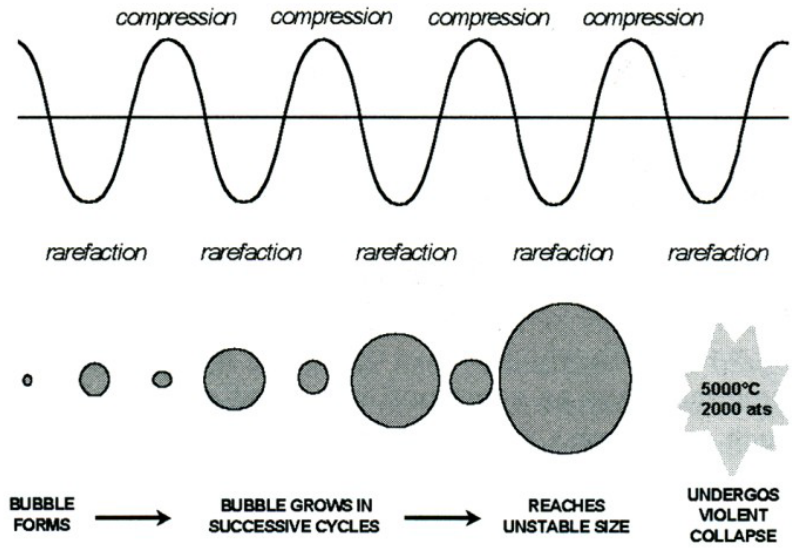


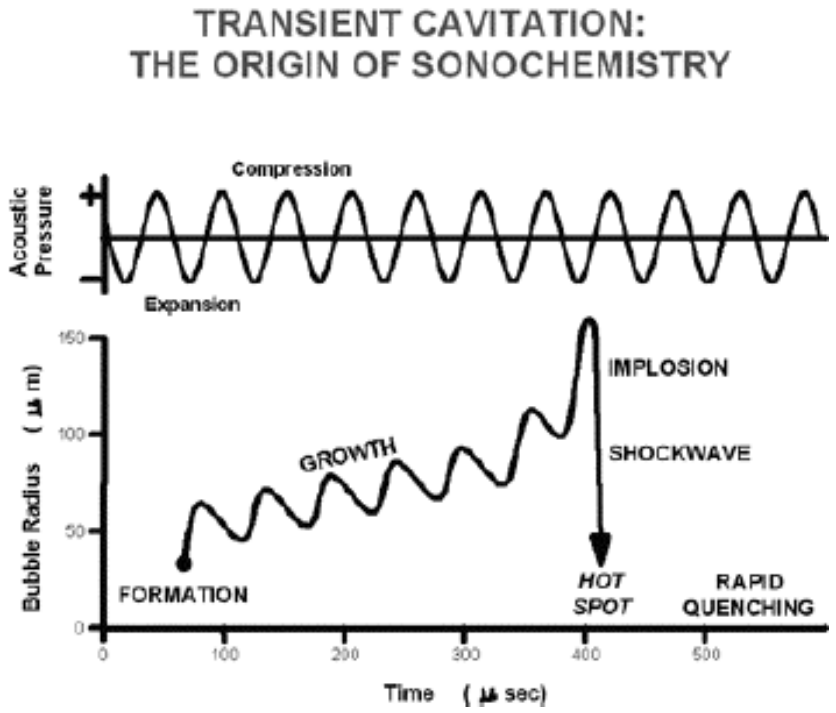
$$P_A = \sqrt{2I\rho c}$$

P_A = driving pressure amplitude [Pa]; I = irradiation intensity [W m^{-2}]
(500 W system - 1.3 105 W m^{-2}); ρ = liquid density [kg m^{-3}]
c = sound velocity in liquid [m s^{-1}] (Water 1482 m s^{-1})
P_A = 620 700 Pa = 6.2 bar

Acoustic Cavitation

Bubbles collapse = spherically symmetrical implosion,
shear forces, adiabatic compression, life time 1-2 µs
Hot spot = end of the collapse temperature of the gas inside bubble 5000–20 000°C (for 1 ns)
surrounding liquid layer 2000 °C pressure 500 –1500 bar Extreme cooling rates $10^{10}Ks^{-1}$



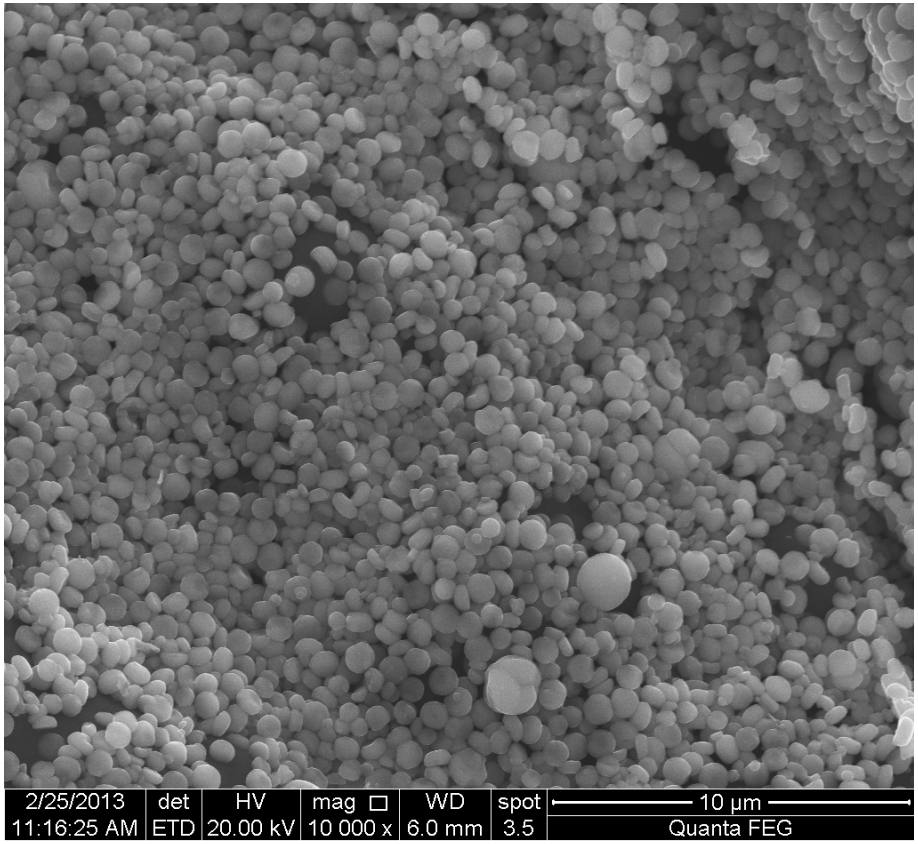


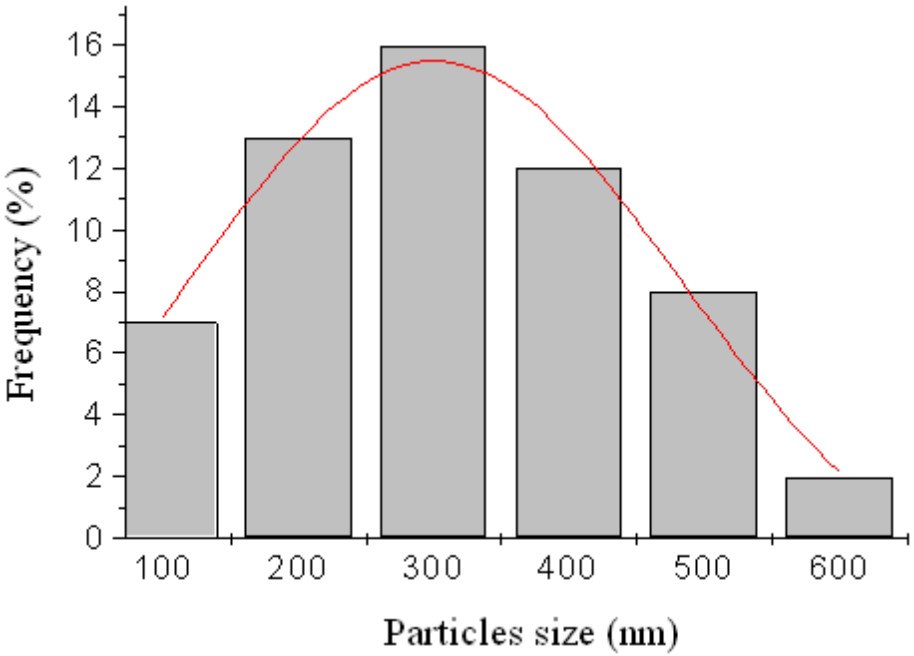
Ref. Jiri Pinkas Department of Chemistry Masaryk University Brno Czech Republic

Summary: Sonochemical reactions

- Chemical changes / reactions induced by ultrasound
- No direct interaction of ultrasound fields with molecules
  (in contrast to photons, heat, electro-magnetic fields)
- Liquid phase reactions driven by cavitation effects, radical generation, bond- breaking
- Solid state reactions - introduction of defects
- **Extreme acceleration of nanoparticles in the imploding bubble (shockwave-induced nano-particle implantation)**
- **Isotropic implantation in complex objects form all sides; hence cylindrical objects and tissues can be homogeneously be treated.**

Implantation of ZnO, MgF_2 nanoparticles using sonochemistry

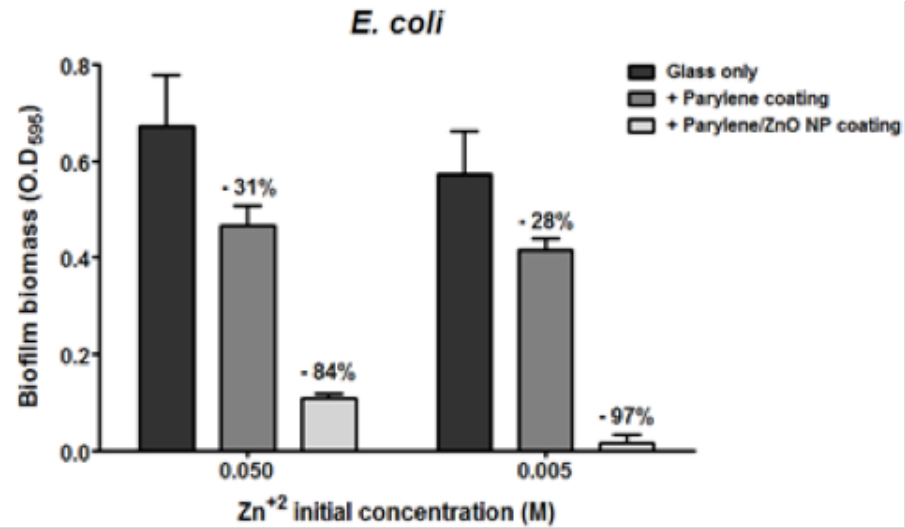


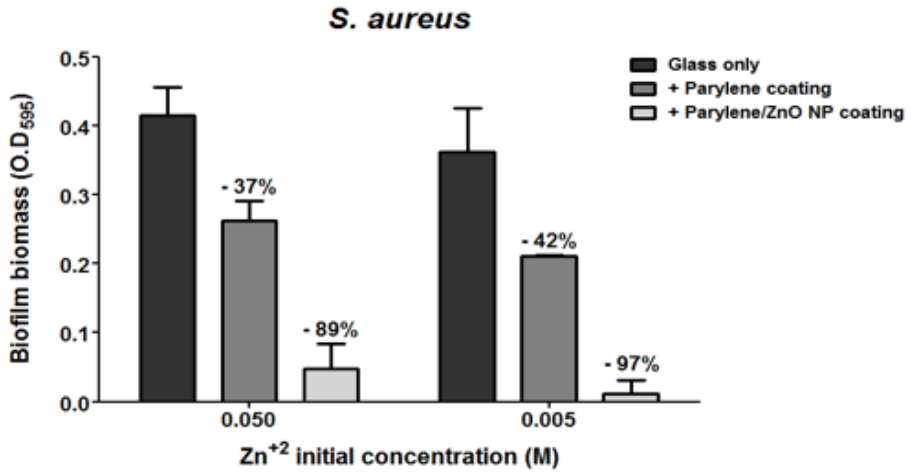


Bar-Ilan University

nanotechnology based cochlear implants

Results





Biofilm biomass formation resulted after 24 hours of treatment with pure glass slides, glass slides coated solely with Parylene and glass slides coated with Parylene and ZnO nanoparticles. No leaching of nanoparticles was observed at long term.

Gedanken, A. Using Sonochemistry for the Fabrication of Nanomaterials. *Ultrason. Sonochem.* 2004, 11, 47-55.

Summary and Conclusion

Solid on liquid deposition is a platform technology allowing integrating liquids as functional “layer” in microsystems

Sonochemistry is a method allowing isotropic implantation of nanoparticles into all kind of surfaces such as metals, ceramics and even textiles.

Acknowledgement

The project NANOCI is funded within the 7th EC framework programme in NMP.2011.1.4-4, Grant agreement no: 281056