

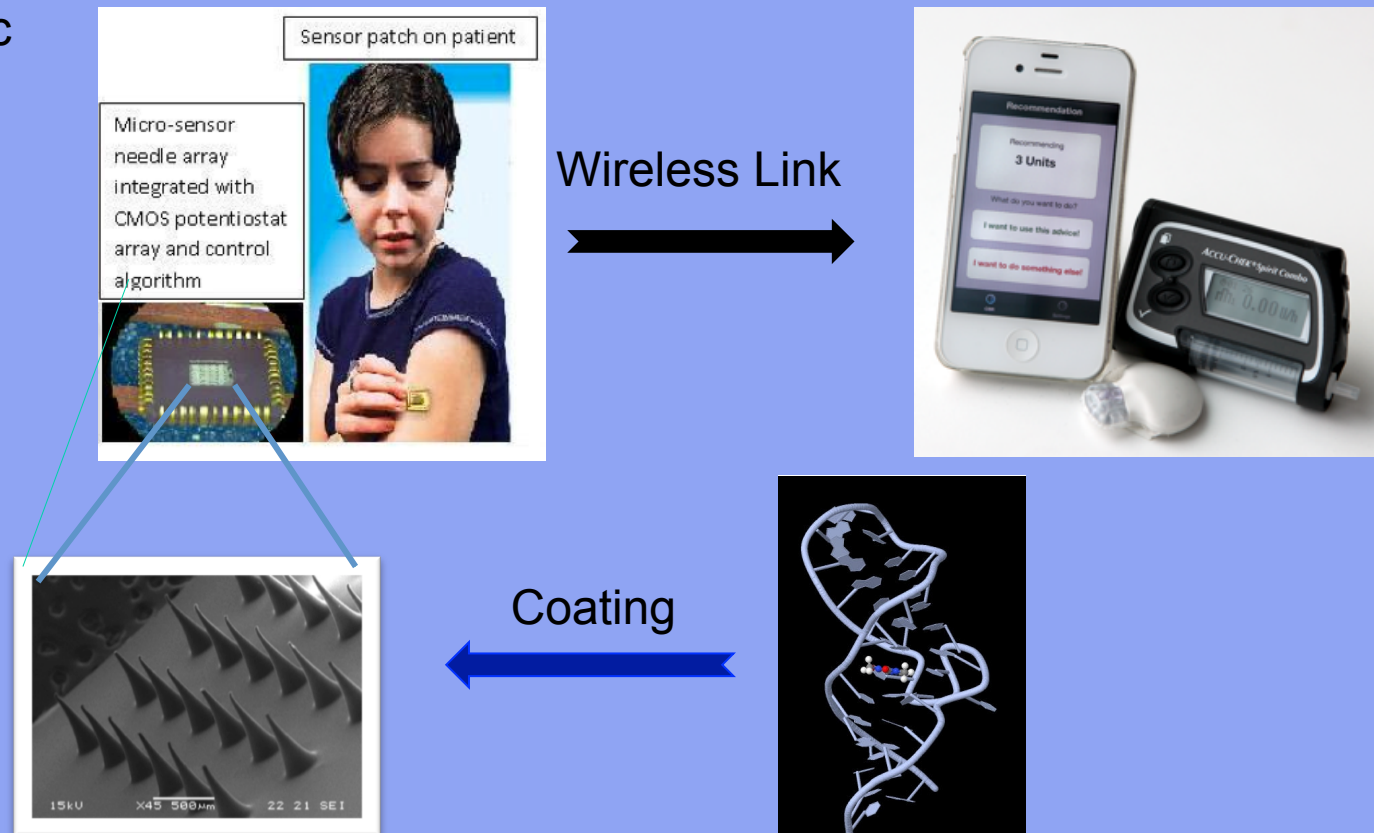
Minimally Invasive Sensors

Tony Cass

Dept of Chemistry & Institute for Biomedical Engineering

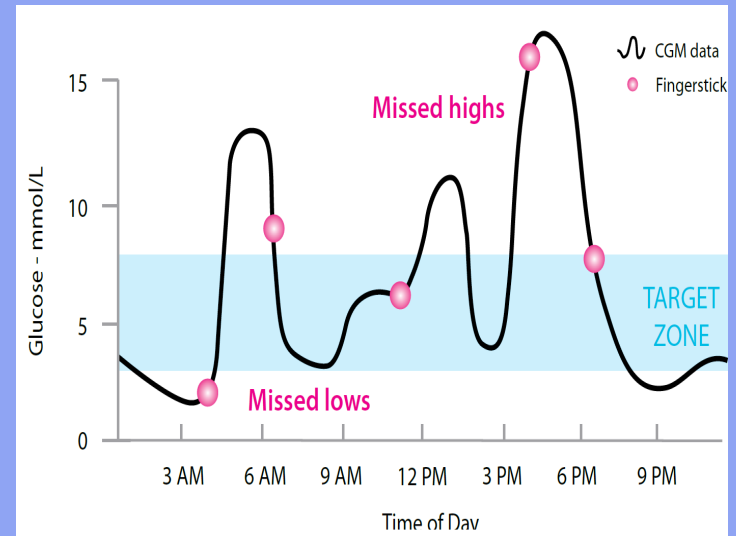
Wearable, Minimally Invasive Continuous Monitoring Devices

Daily Wear Devices Patient-Centric



Continuous Glucose Monitoring (CGM)

- Why?
 - Missed Excursions
 - Trending
 - Event prediction
 - Closed loop control



Despite these advantages only a few % of Type 1 Diabetics use CGM

Why?

Challenges in Continuous Glucose Monitoring

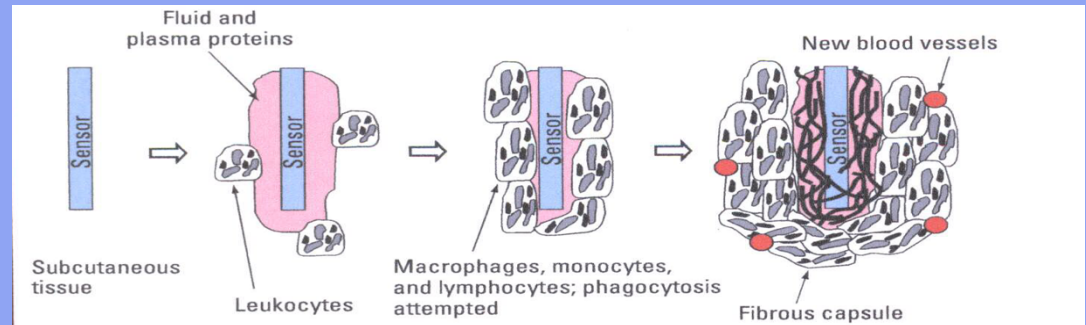
Implanted Sensors:

- Foreign body response

- Capsule formation

- Drift-Sensor and Environment

- Chemical Interferents



Non-Invasive Sensors

- Lack of specificity

- Complex instrumentation

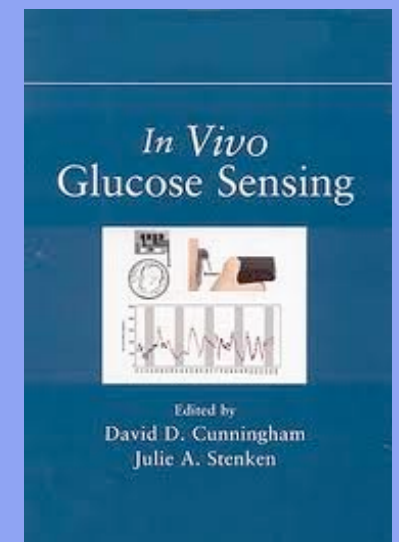
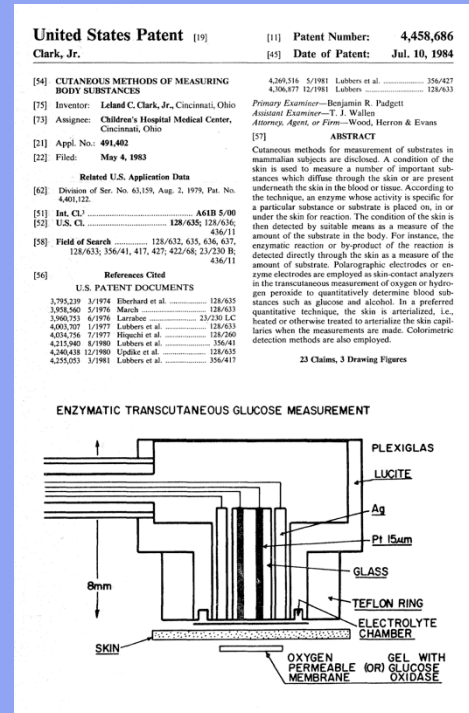
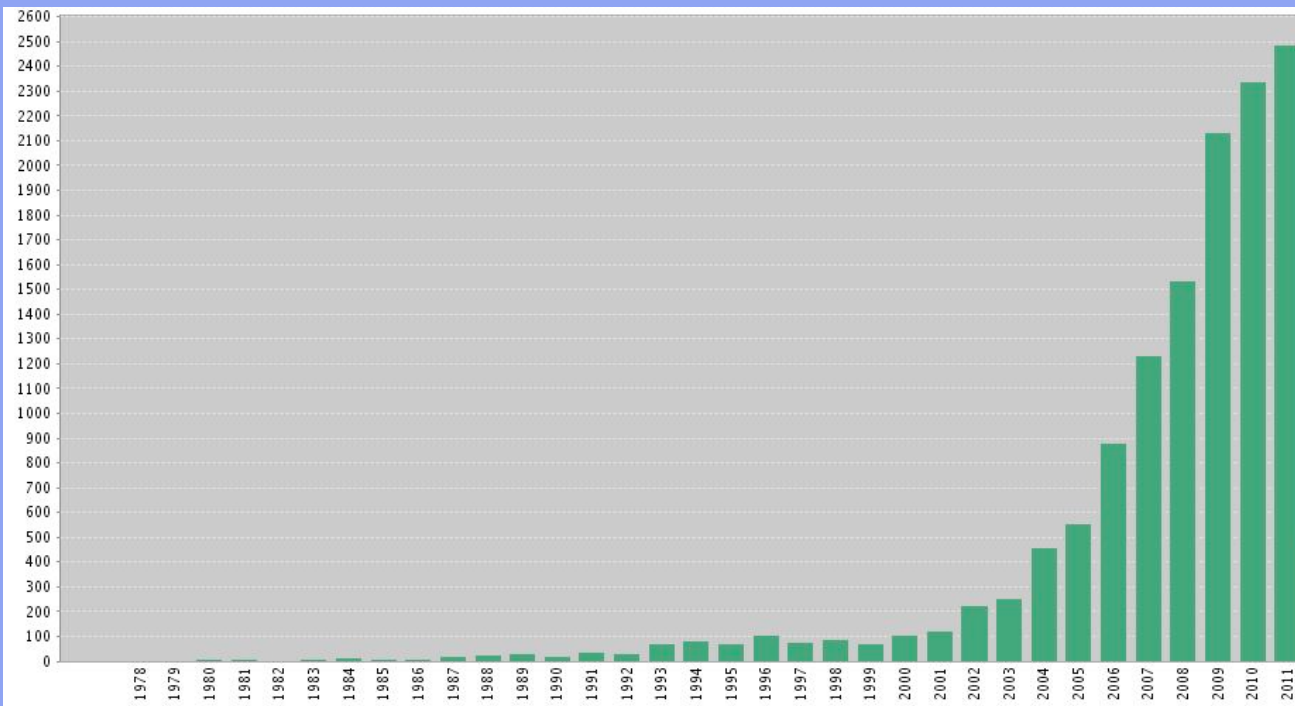
Sampling ('Inline') Sensors

- 'Local' concentrations

- Sampling rate

- Carry over

An Area of Great Academic & Commercial Activity

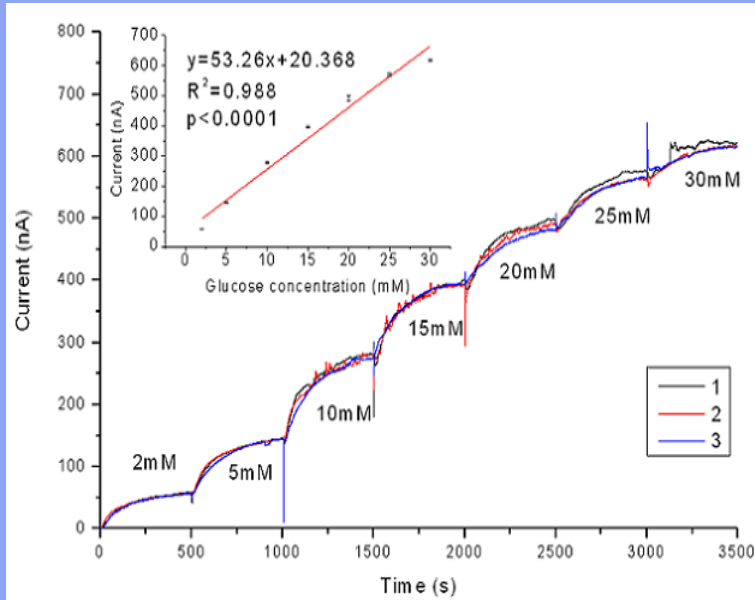
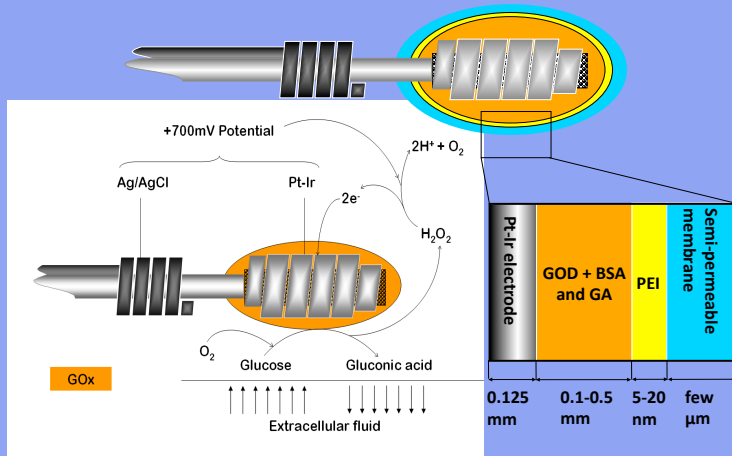


Measurement Compartments and Technologies

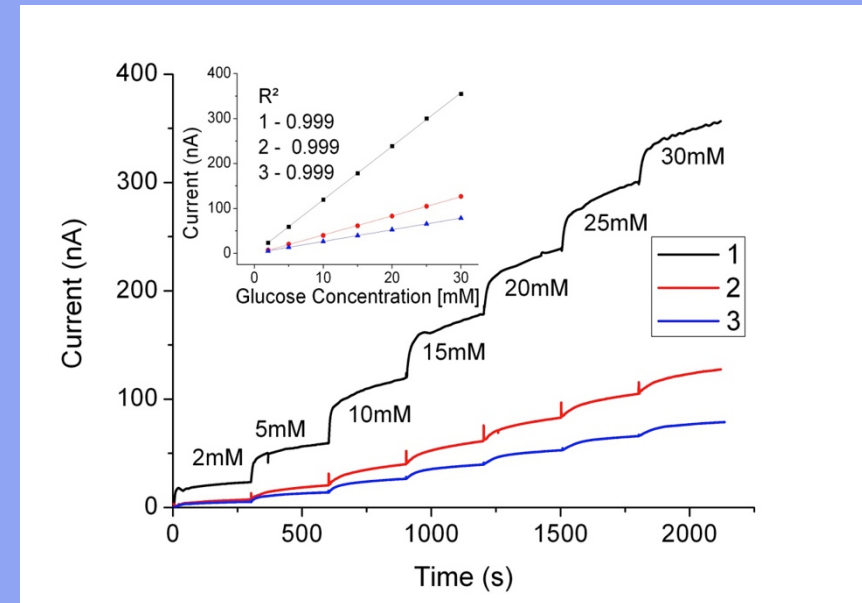
Principle	Modality	Compartment	Invasive
Kromoscopy	Optical	ISF	Non-invasive
Photoacoustic spectroscopy	Optical	ISF	Non-invasive
Optical coherence tomography	Optical	ISF	Non-invasive
Scattering/occlusion spectroscopy.	Optical	ISF	Non-invasive
Polarimetry	Optical	ISF/anterior chamber	Non-invasive
Thermal infrared	Optical	ISF	Non-invasive
Fluorescence	Optical	ISF	Non-invasive
Raman spectroscopy	Optical	ISF	Non-invasive
MIR spectroscopy	Optical	ISF	Non-invasive
NIR spectroscopy	Optical	ISF	Non-invasive
Impedance spectroscopy	Transdermal	Capillary blood	Non-invasive
Skin suction blister	Transdermal	ISF	Non-invasive
Sonophoresis	Transdermal	ISF	Non-invasive
Reverse iontophoresis	Transdermal	ISF	Non-invasive
Micropore/microneedle	Subcutaneous	Capillary blood/ISF	Minimally invasive
Intravenous implantable	Intravenous	Venous blood	Invasive
Microdialysis	Subcutaneous	ISF	Invasive
Subcutaneous sensor	Subcutaneous	ISF	Invasive

(Oliver et al. Diabetic Med 2009)

Conventional Implanted Needle Electrodes

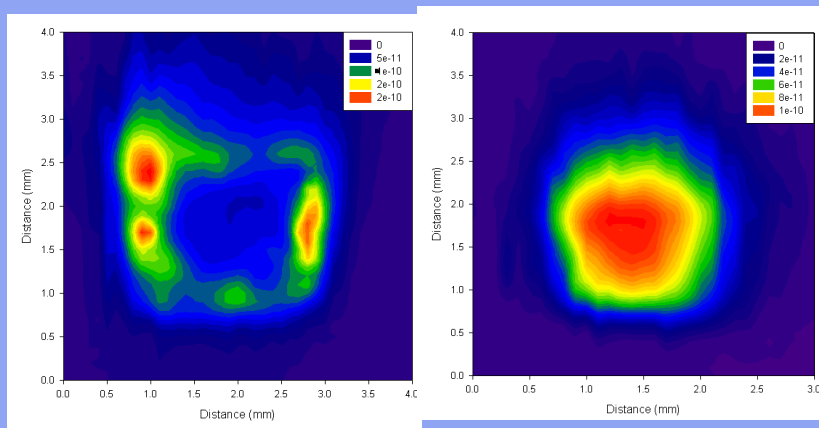


HEMA Hydrogel



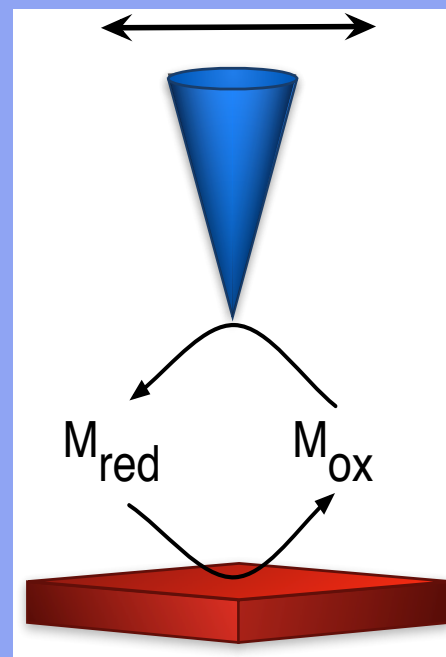
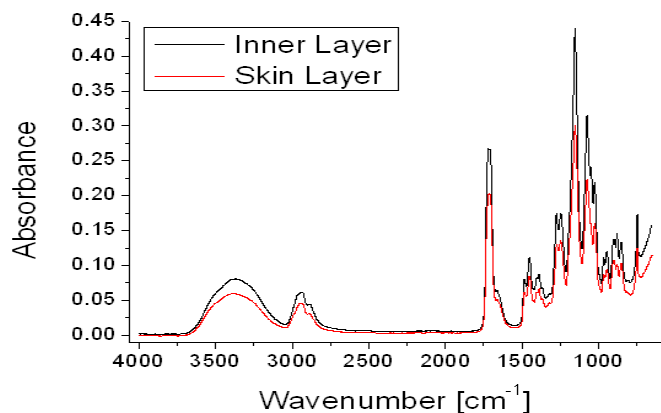
Epoxy-polyurethane

Probing Membrane Diffusivity with SECM

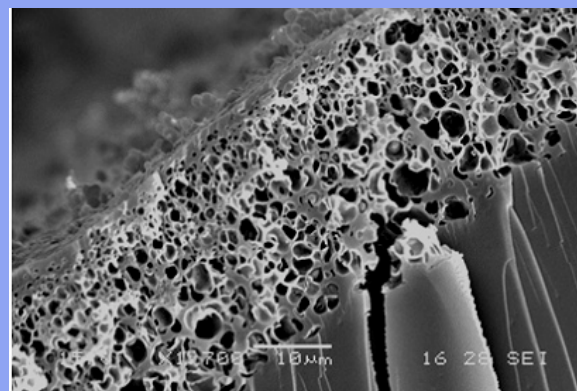


Membrane 1

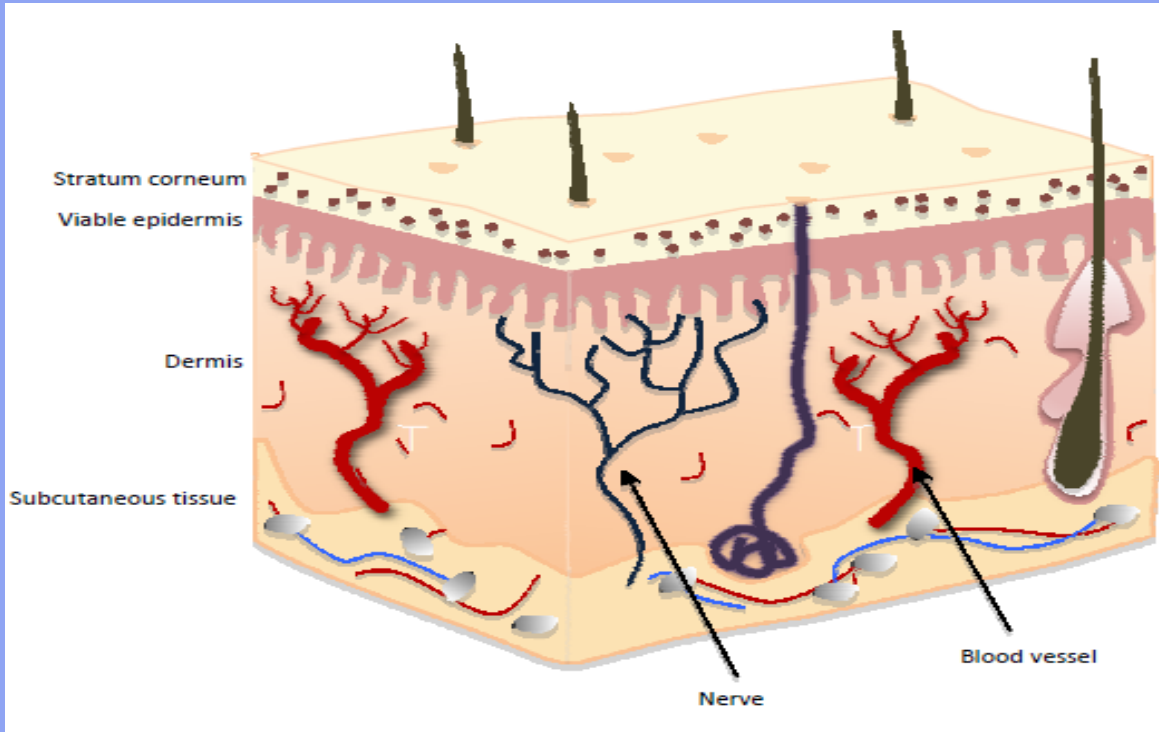
Membrane 2



SECM



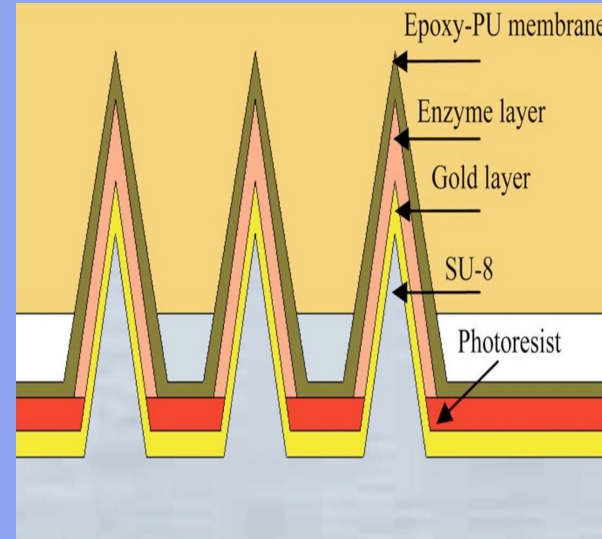
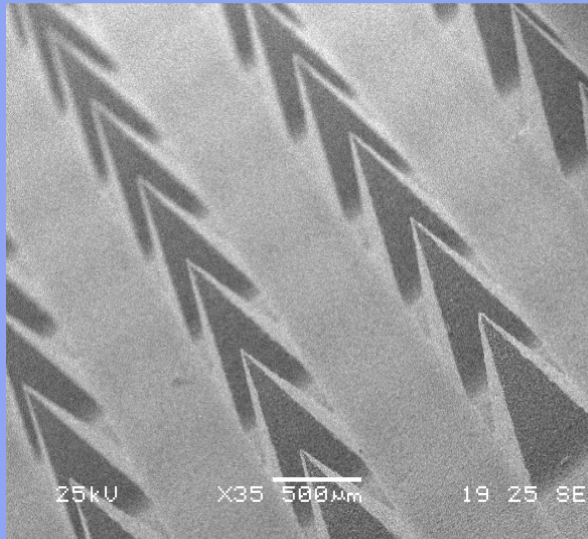
The Epidermal Interstitial Compartment



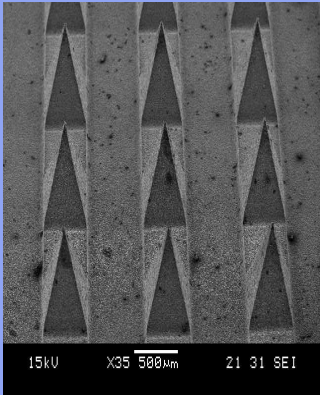
No vasculature
No nerve endings

Measurements in epidermal
Interstitial Fluid (ISF)
Metabolites, drugs, cytokines

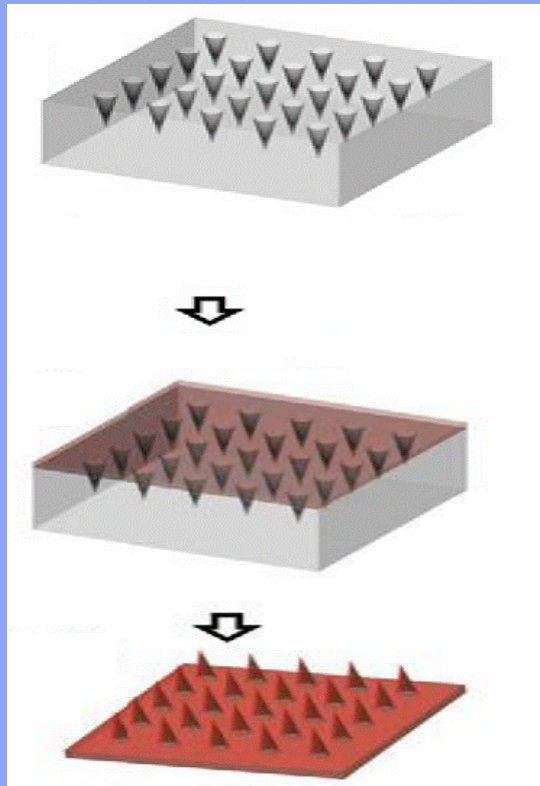
Design Concept



Fabrication of *in situ* μ spike Sensors



Master Machined
by Electric Discharge
Milling



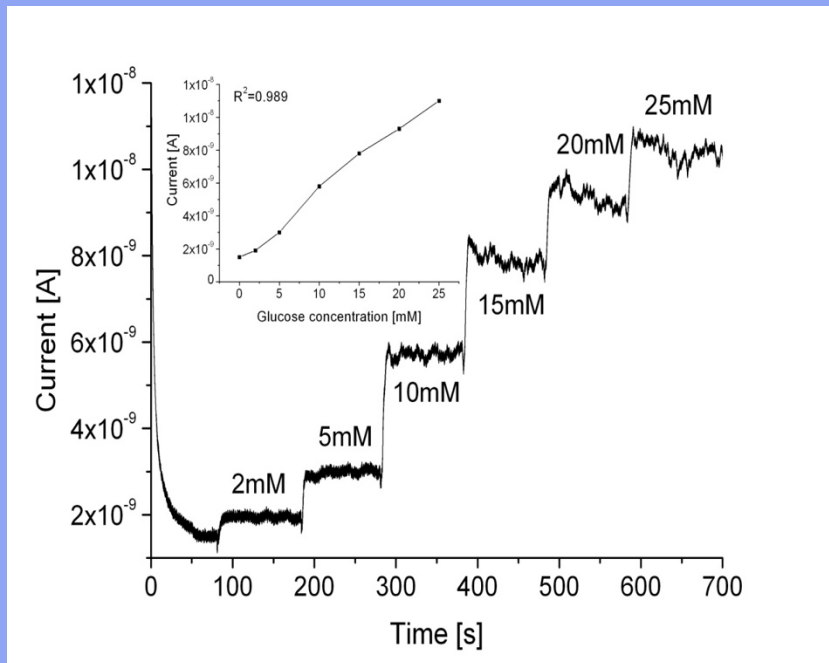
Silicone Mould

SU8-100 Microspikes

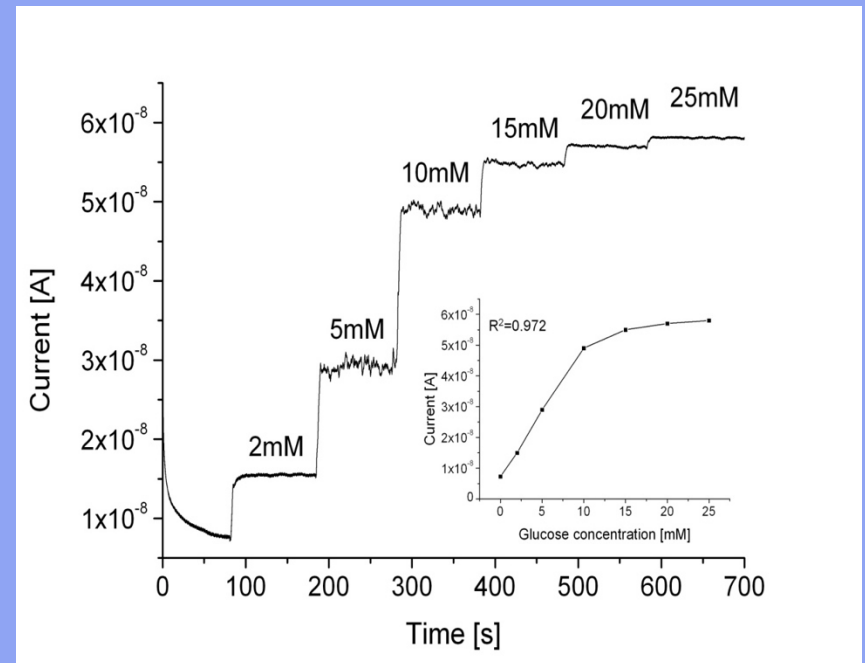
Gold Coated μ Spikes

Then functionalised

Minimally Invasive Glucose Sensors and Controlling Diffusion

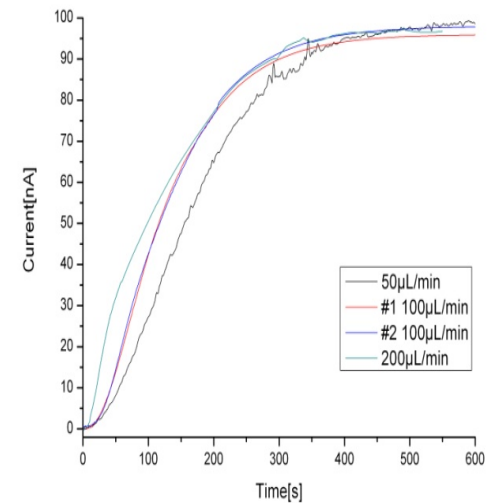
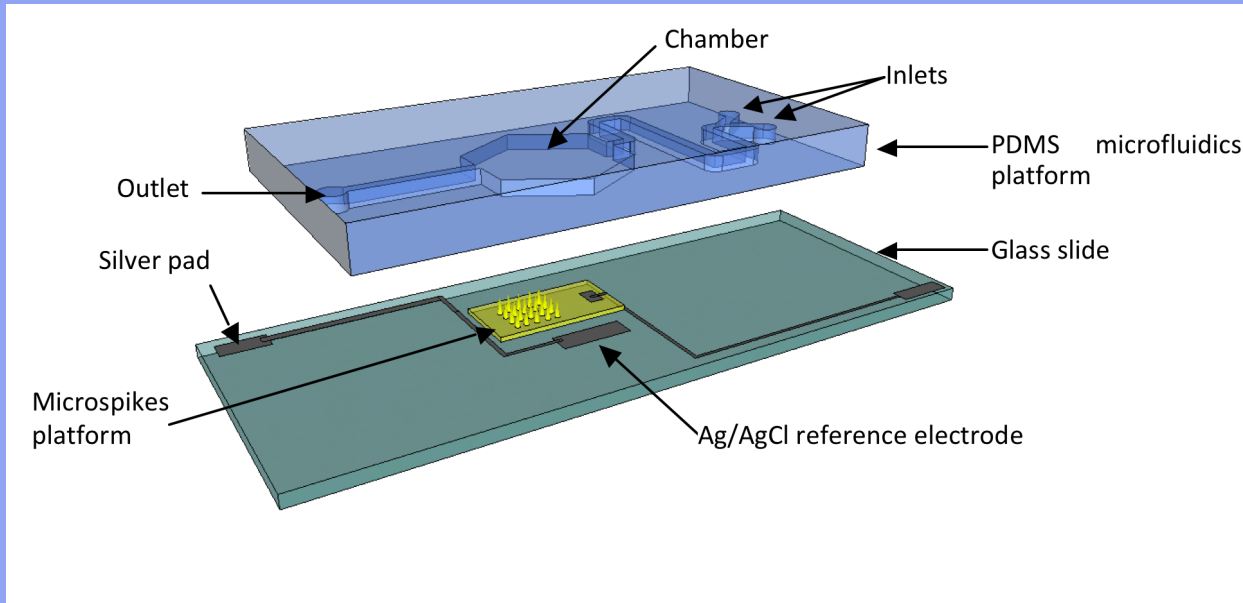


Epoxy-polyurethane

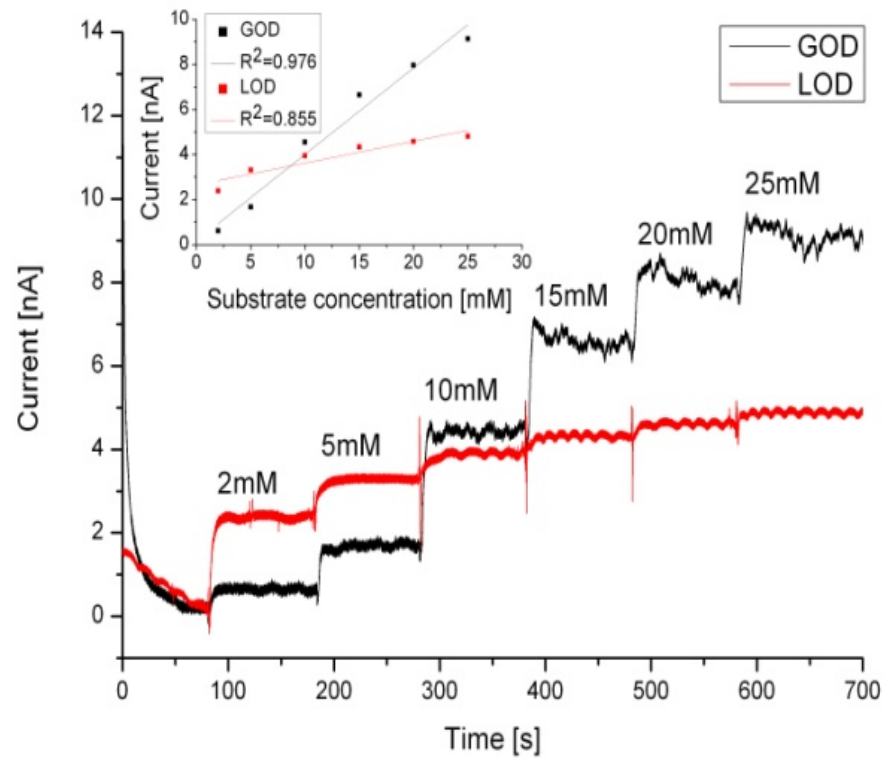


Nafion

System is Membrane Transport Limited



Lactate Too



Mechanical characterisation

- Transverse Fracture tests:
 - Method
 - Result : (n=11)
 - Mean : 24 N (range 19-29N)
 - = 3N/ μ Spike

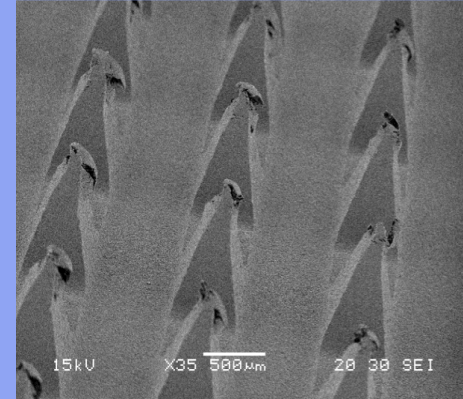
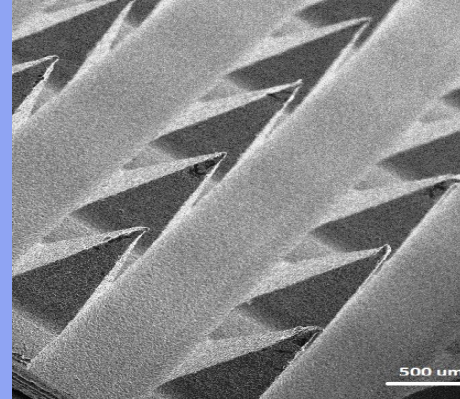
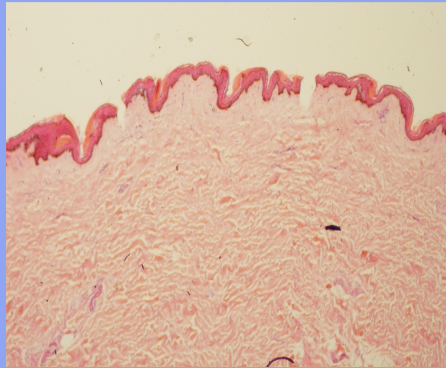
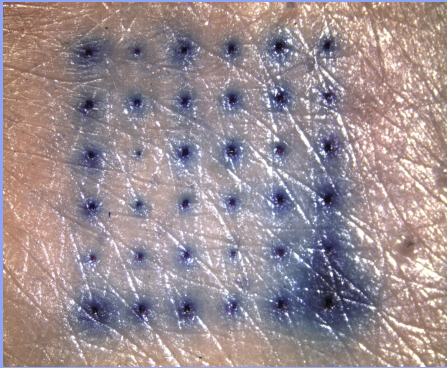
High Safety Margin

Axial Force/Insertion Force

100N/5N =20:1

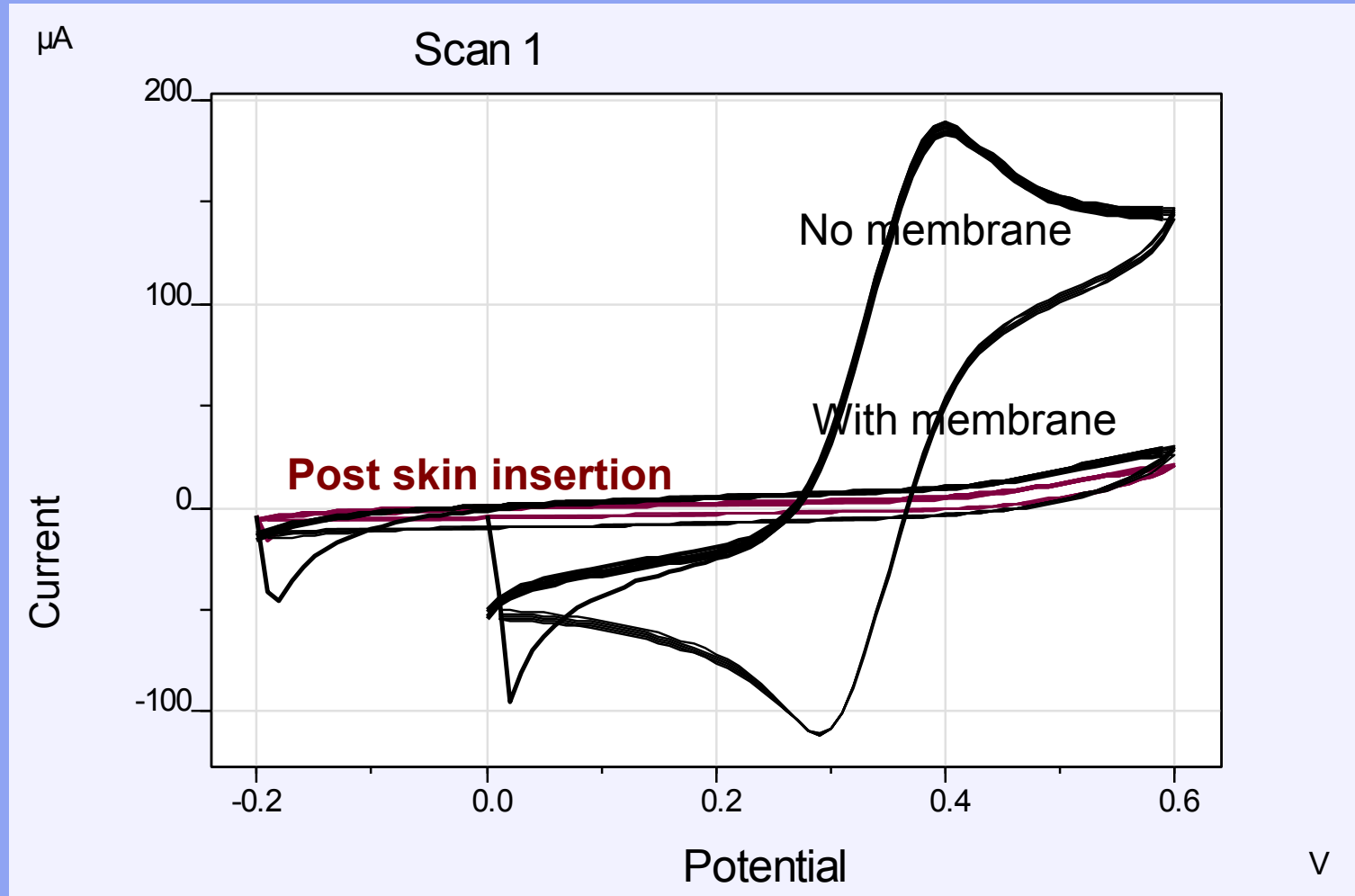


Skin Penetration



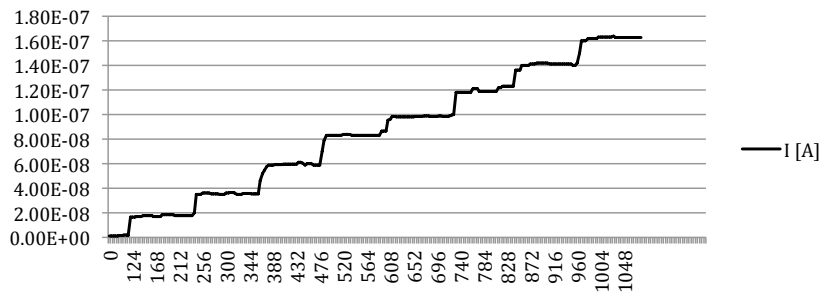
Membrane Survives Skin Penetration & Removal

Comparison of CV before membrane, post membrane & post insertion at 10N for 30 sec.



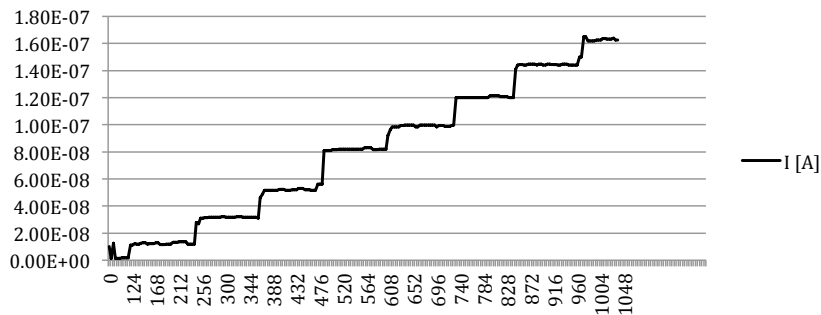
Devices can be Sterilised by γ -Irradiation

Current [A] VS Time [s]
Sample 7 - Pre-Sterilization Pre-Insertion

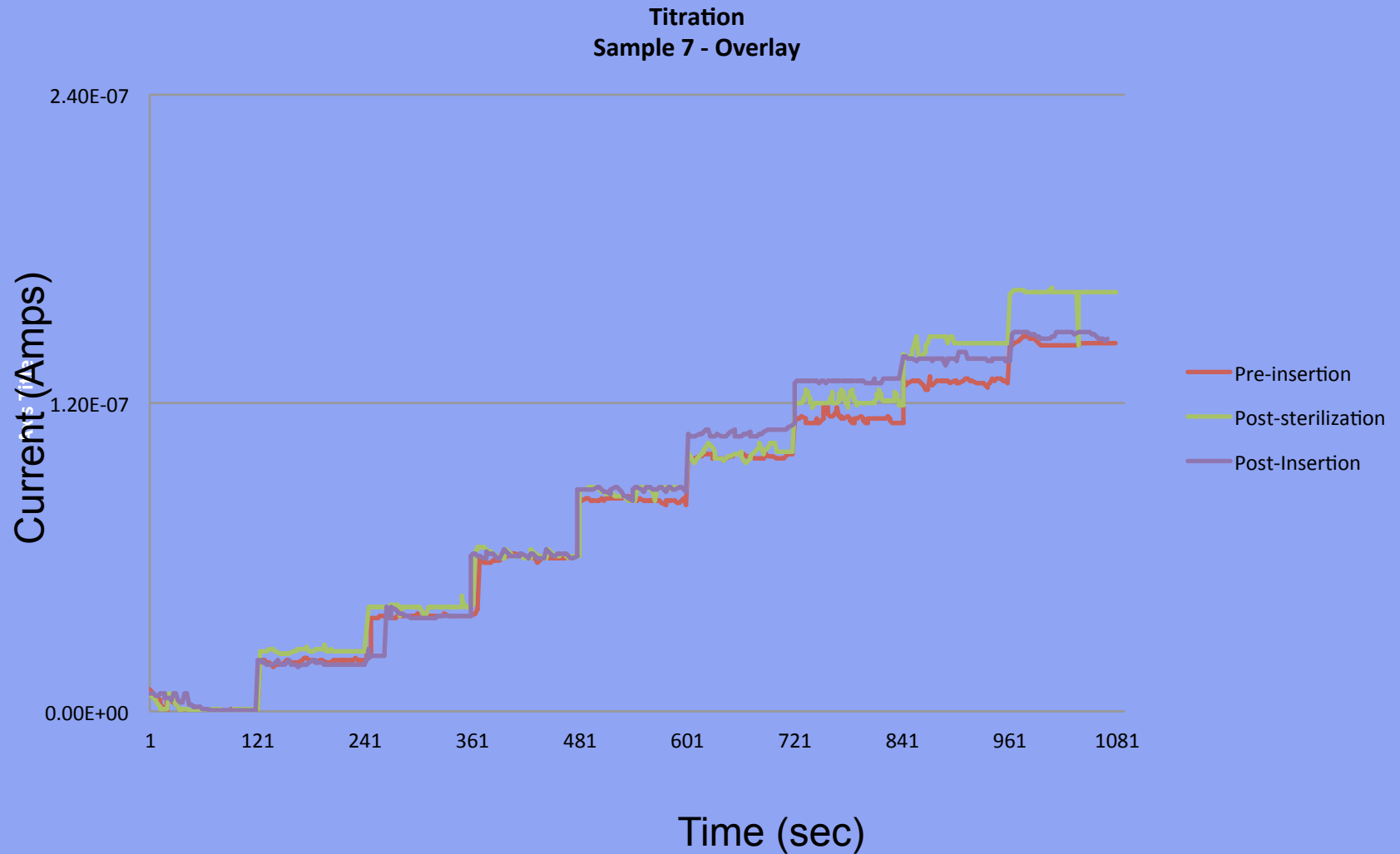


Post-sterilization

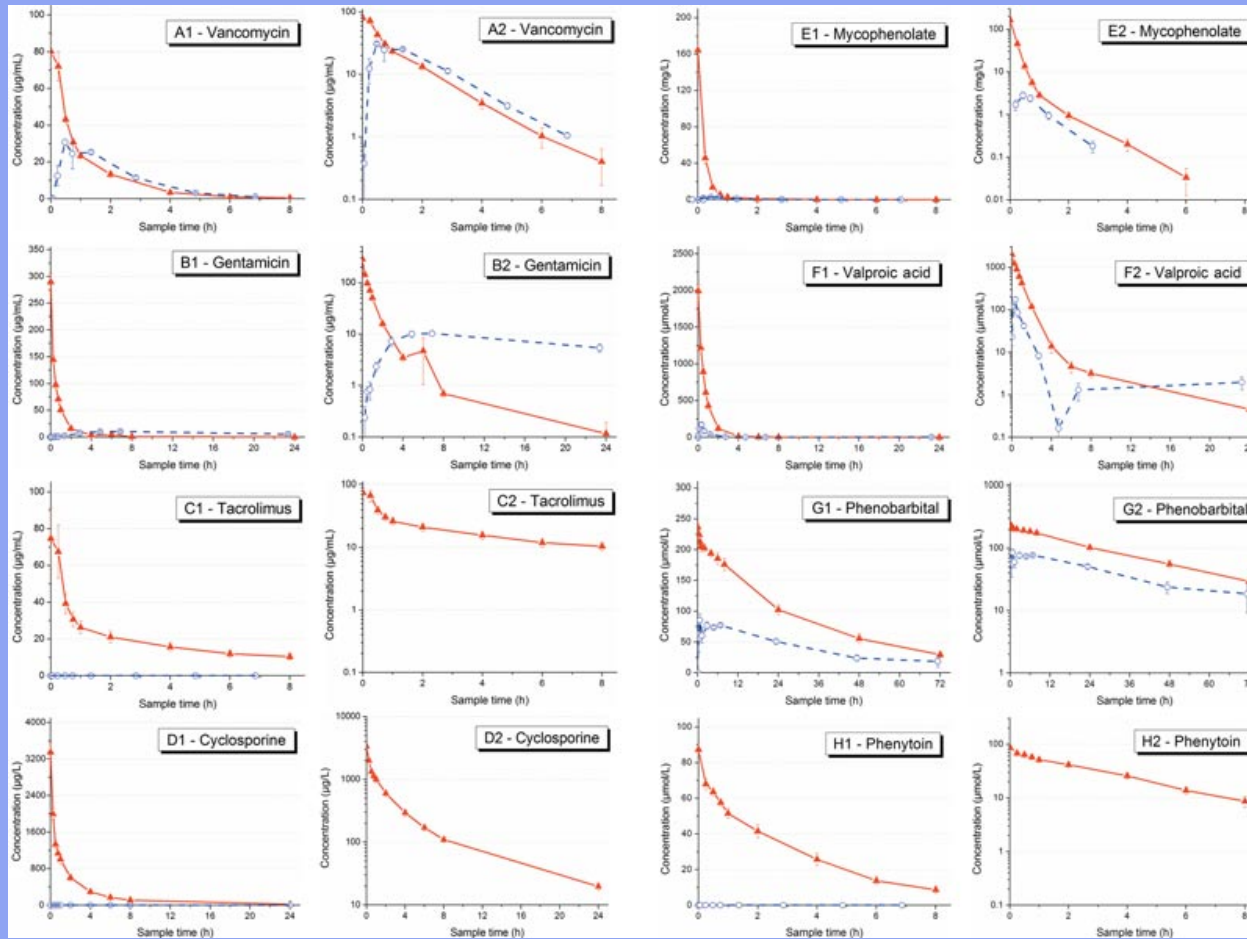
Current [A] VS Time [s]
Sample 7 - Post Sterilization Pre-Insertion



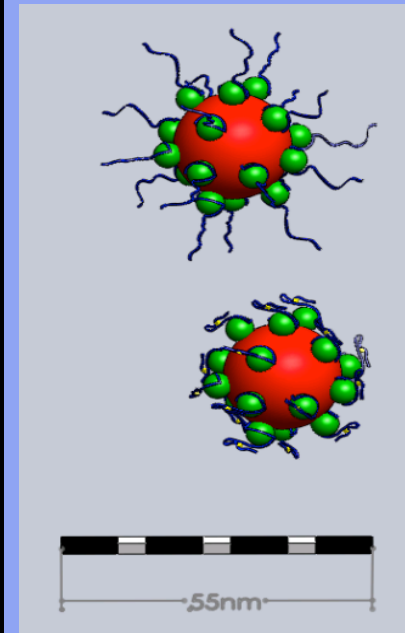
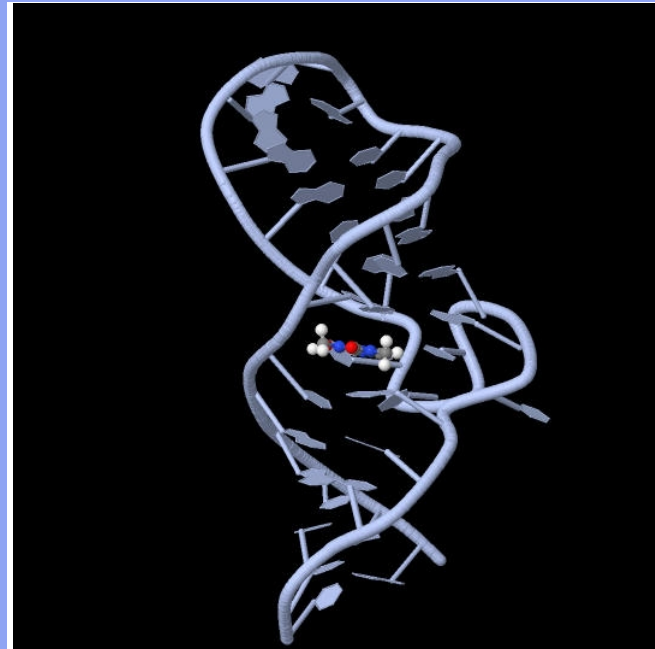
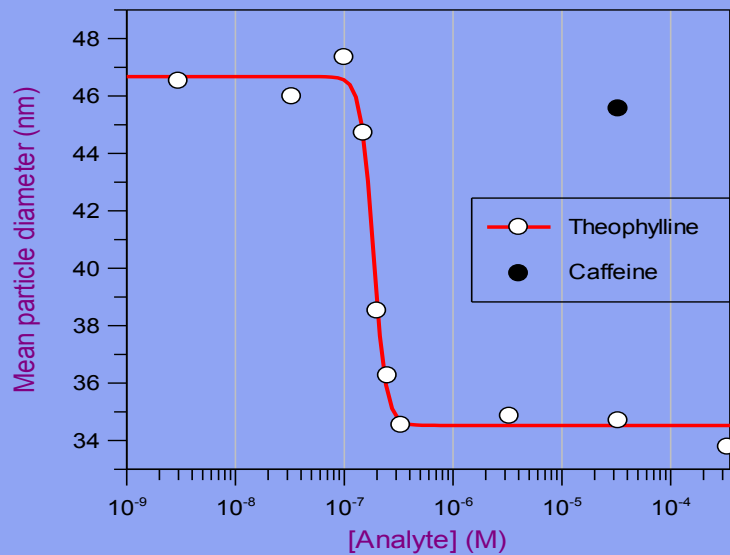
Post insertion too looks good!



A Platform for Other Analytes Therapeutic Drug levels



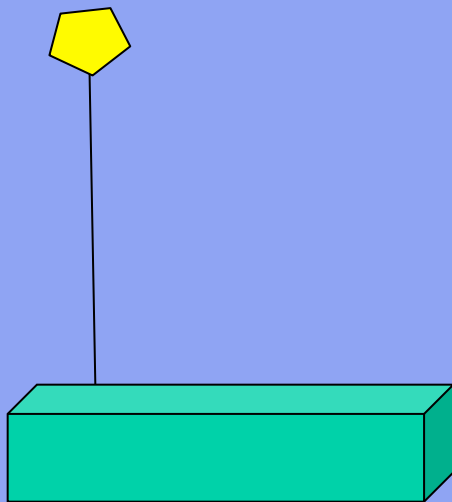
Measuring Conformational Change on a Nanoparticle Surface



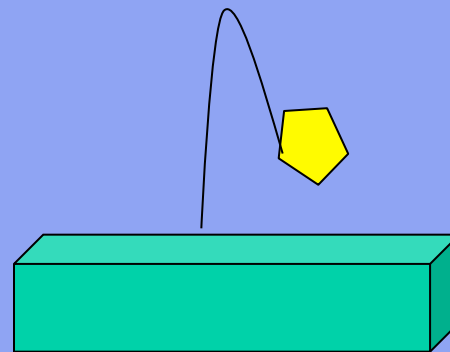
$K_D = 200 \text{ nM}$ cf 300 nM in solution

Electrochemical Sensing: Exploiting Distance Dependence of Electron Transfer

$$k_{et} \propto e^{-\beta(d-d_0)} \cdot e^{\frac{-(\Delta G^0 + \lambda)^2}{4RT\lambda}}$$

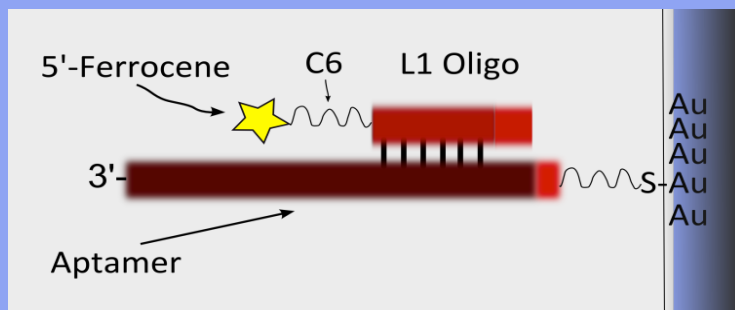
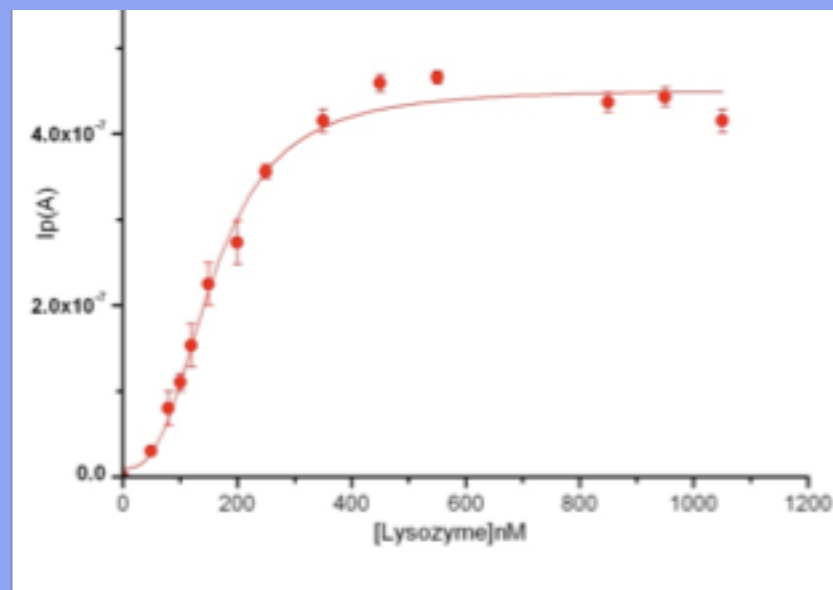
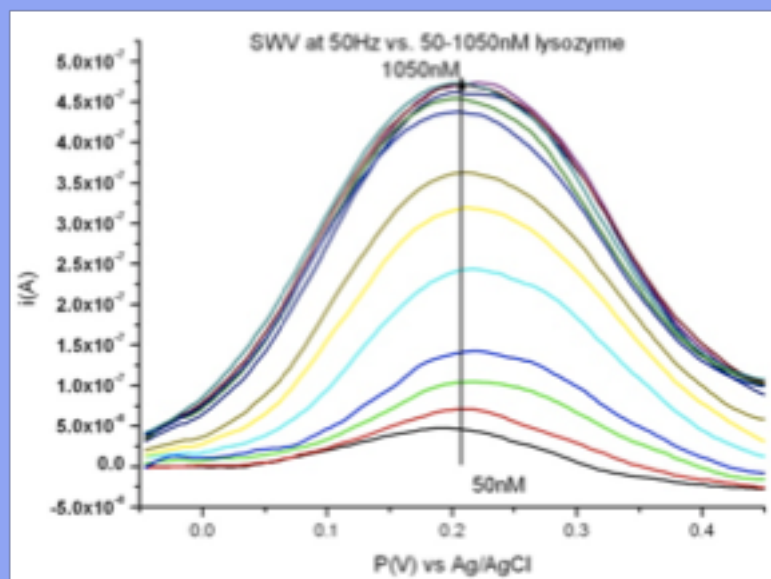


Far=Low Current

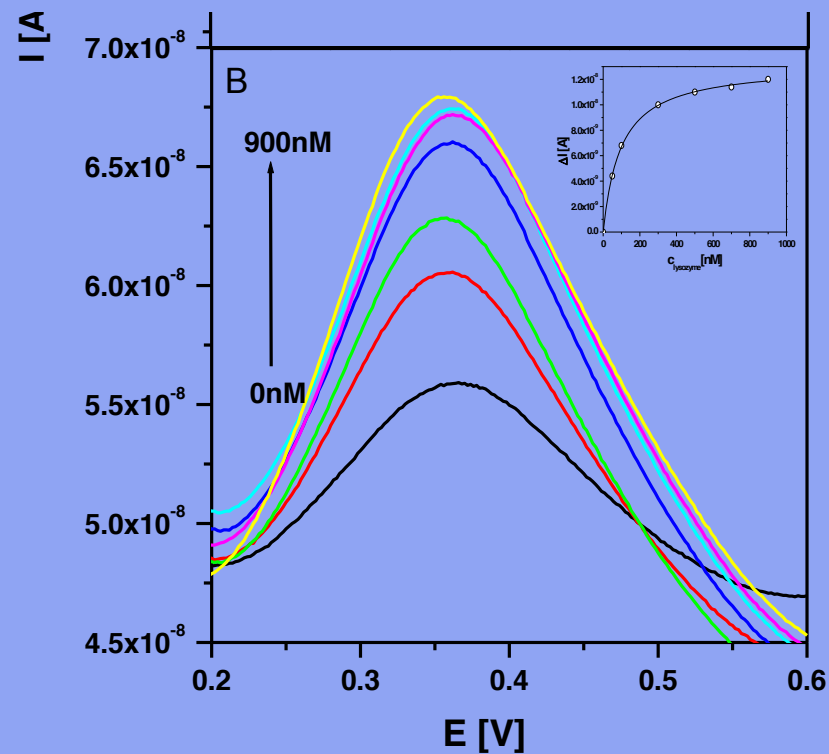
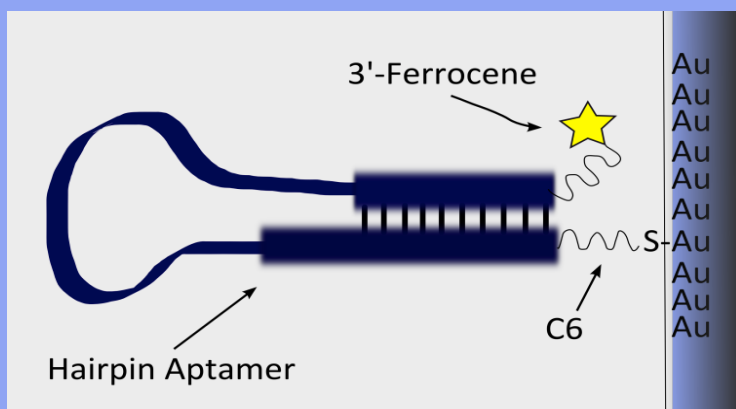


Near= High Current

A DNA Aptamer Against Lysozyme



Aptamer Beacon Assembly



Acknowledgements

Microfluidics and Glucose Microspikes

Science & Engineering Team

Sanjiv Sharma
Harish Santhanam
Jakub Trezbinski
Anna Radomska
Alex Cook

Clinical Team

Des Johnson
Nick Oliver
Ahmed El-Laboudi

Aptamers team

Thao Le
Steve Scott
Yangyang Zhang
Anna Radomska