An Implantable Biochip to Influence Patient Outcomes Following Trauma-induced Hemorrhage

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C3B®

url=http://www.biochips.org

ISMICT 2011 Montreux March 27-30, 2011

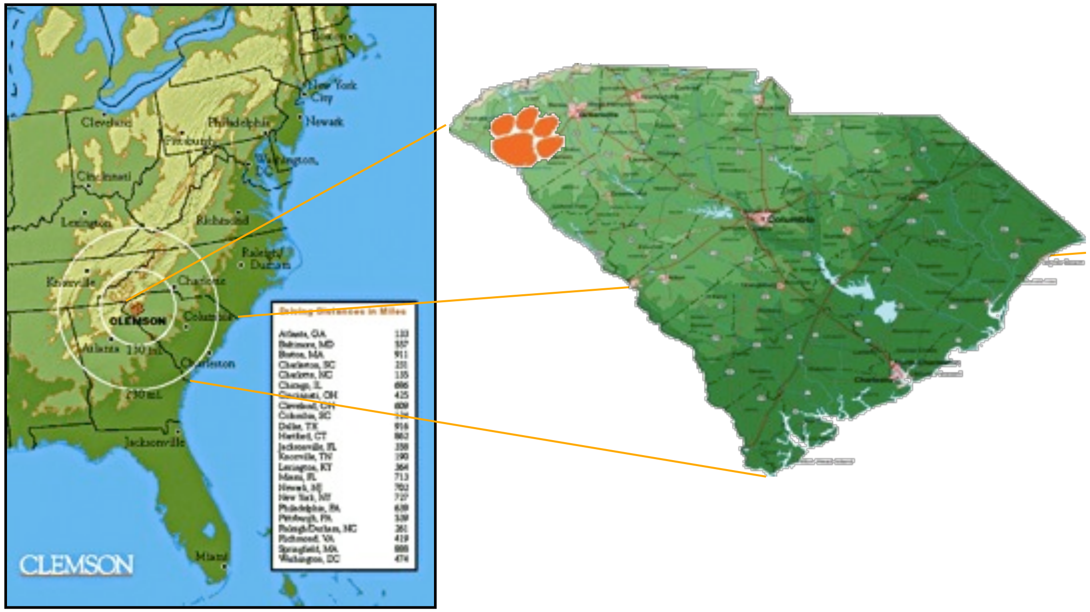
Security and Privacy in Implantable Medical Devices

SPIMD, EPFL, ELA2, Lausanne, Switzerland. April 1, 2011

Clemson ranks 22nd among the USA's 162 public doctoral-granting universities.

U.S. News and World Report, 2009

Clemson University
Clemson, South Carolina, USA



Founded in 1889, Clemson University is a South Carolina land-grant institution dedicated to teaching, research, and public service, and to improving the quality of life through education.

Clemson's 1,400-acre main campus, located in the Northwestern corner of South Carolina on the shores of Lake Hartwell, is surrounded by 17,000 acres of University farms and woodlands devoted to research.

Approximately 17,165 students, including 3,096 graduate students are enrolled in five colleges offering Baccalaureate and Graduate degrees in over 70 fields of study.

Disclosure

Anthony Guiseppi-Elie, Sc.D.
Founder, President and Scientific Director
Founded 1995

**ABTECH Scientific, Inc.*
Virginia Biotechnology Research Park
800 East Leigh Street, Suite 52
Richmond, Virginia 23219 USA

guiseppi@abtechsci.com **http://www.abtechsci.com**

http://www.abtechsci.com

ABTECH Scientific, Inc.

Founded in 1995 and located in the Biotechnology Research Park in Richmond, Virginia, ABTECH uses its platform electroactive polymer sensor technology (EPST™) to develop and deliver non-invasive, near-patient molecular diagnostic products of clinical significance.

ABTECH Scientific, Inc.

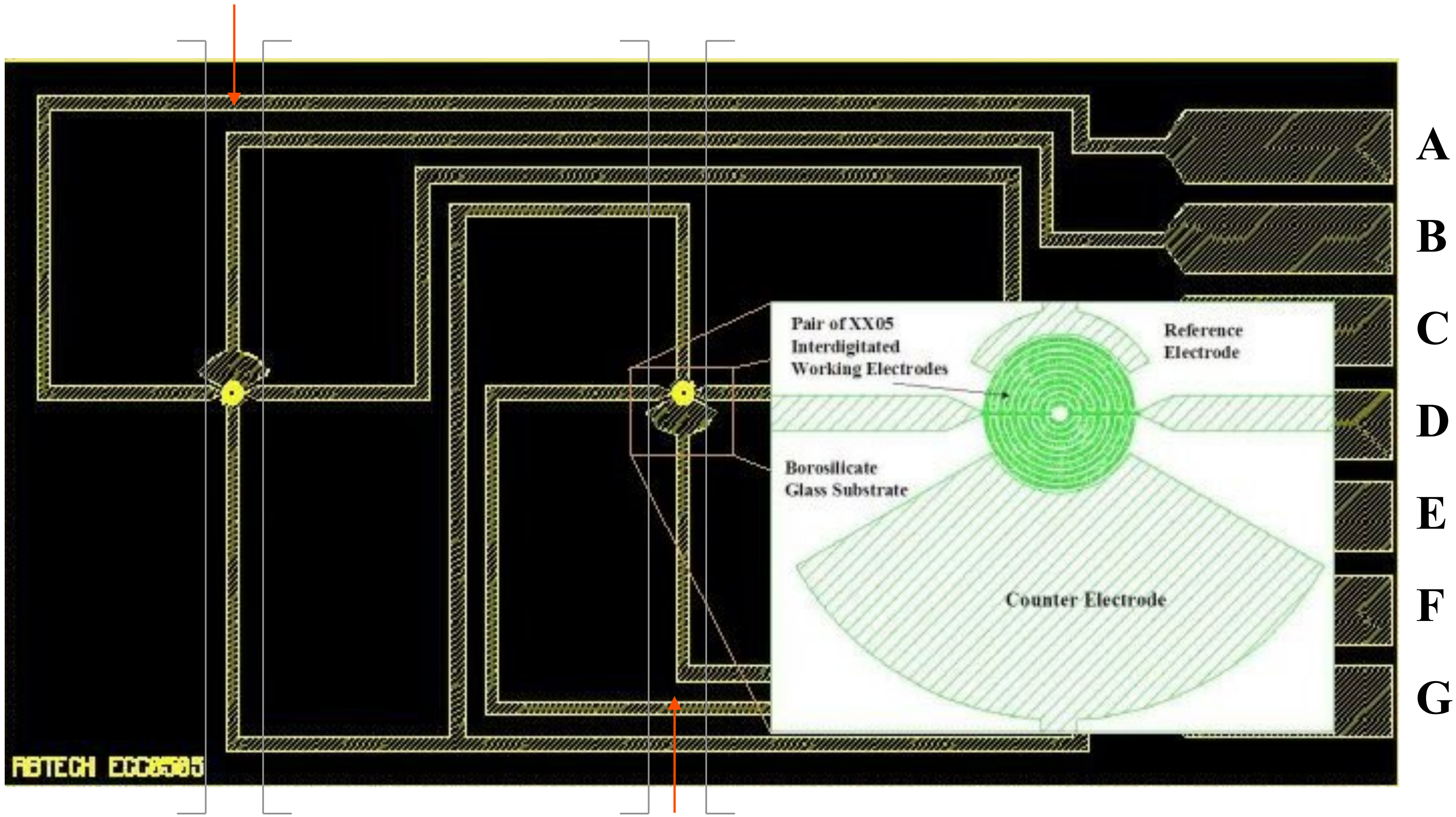
Laboratory Products Group

Microlithographically fabricated devices, related microelectrodes (pH and Ref), flow cell products (gas and liquid) and instruments that are used in research and development of electroconductive polymer sensor technology.

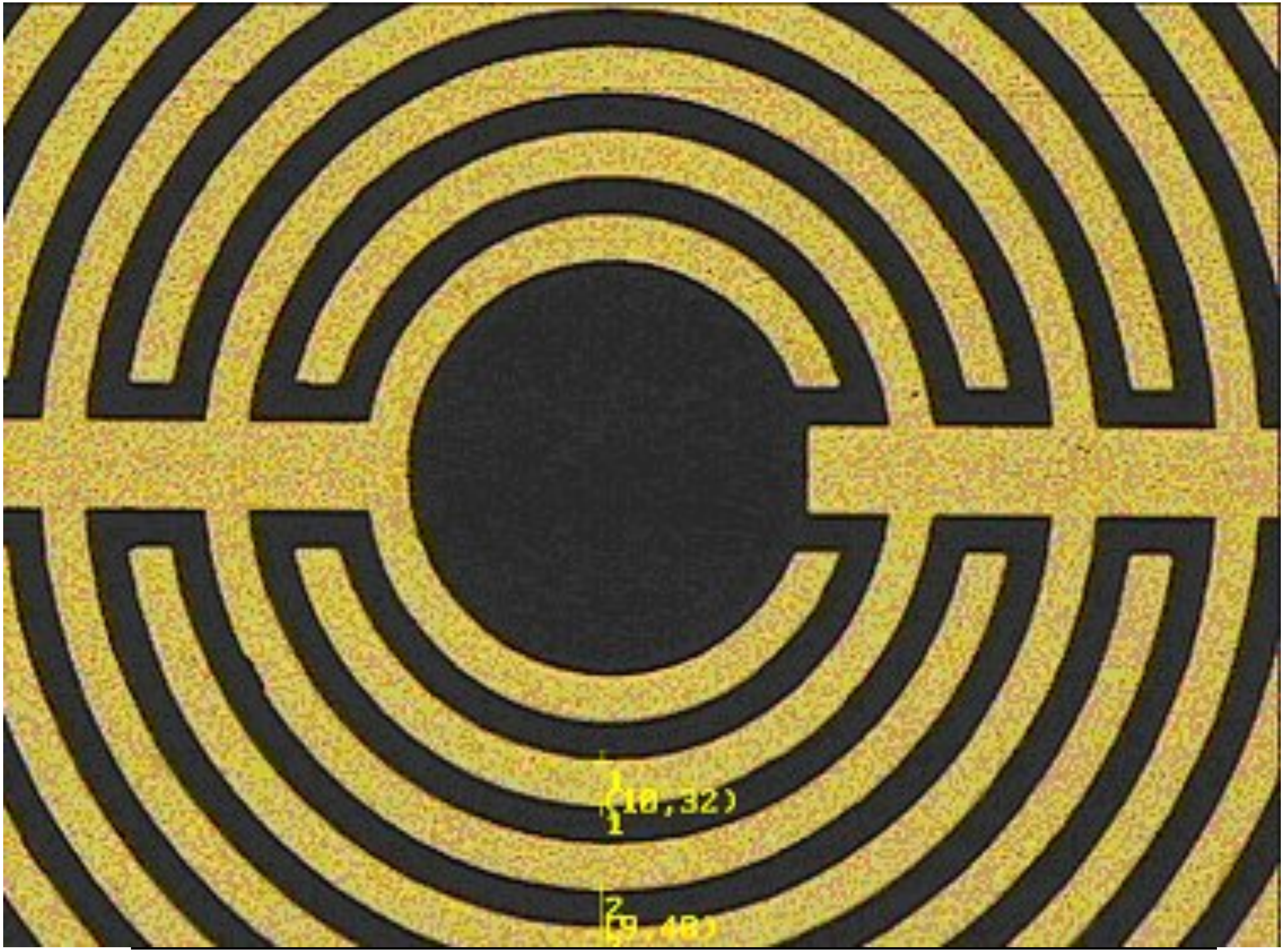
Advanced Products Group

Non-invasive, near-patient molecular diagnostic products of clinical significance and based on electroconductive polymer sensor technology.

Electrochemical Cell-on-a-Chip (ECC)



Electrochemical Cell-on-a-Chip (ECC)



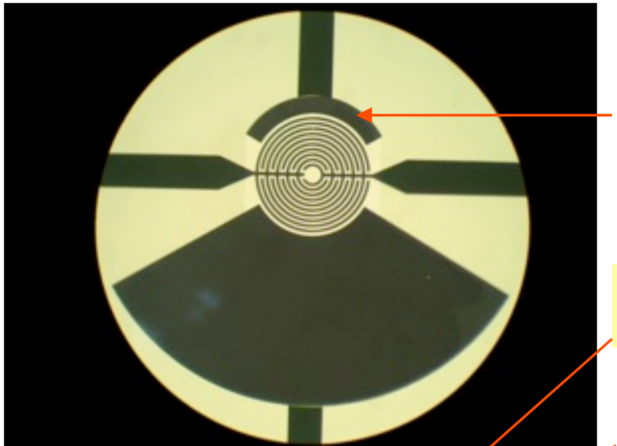
Electrochemical Cell-on-a-Chip (ECC)

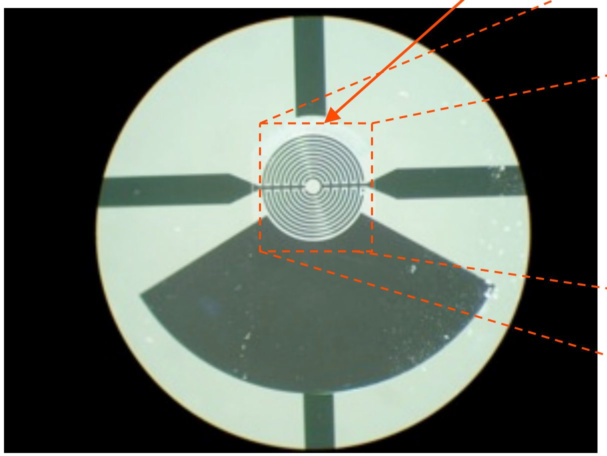
Counter Electrode

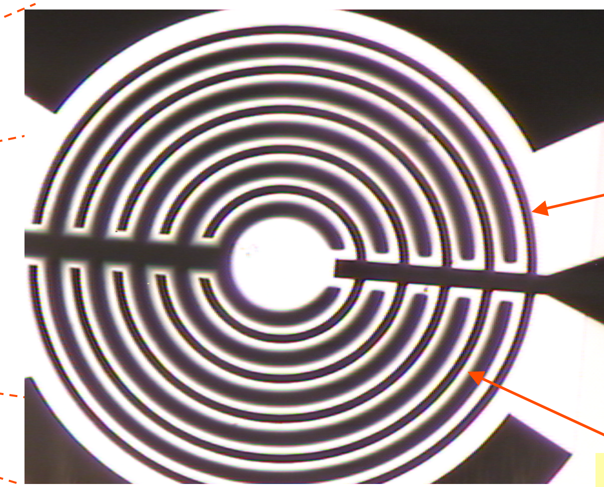
Interdigitated WE1 and WE2

Reference Electrode, Ag/AgCl

Si_3N_4 Passivation Layer







Electrochemical Flow Through Assay

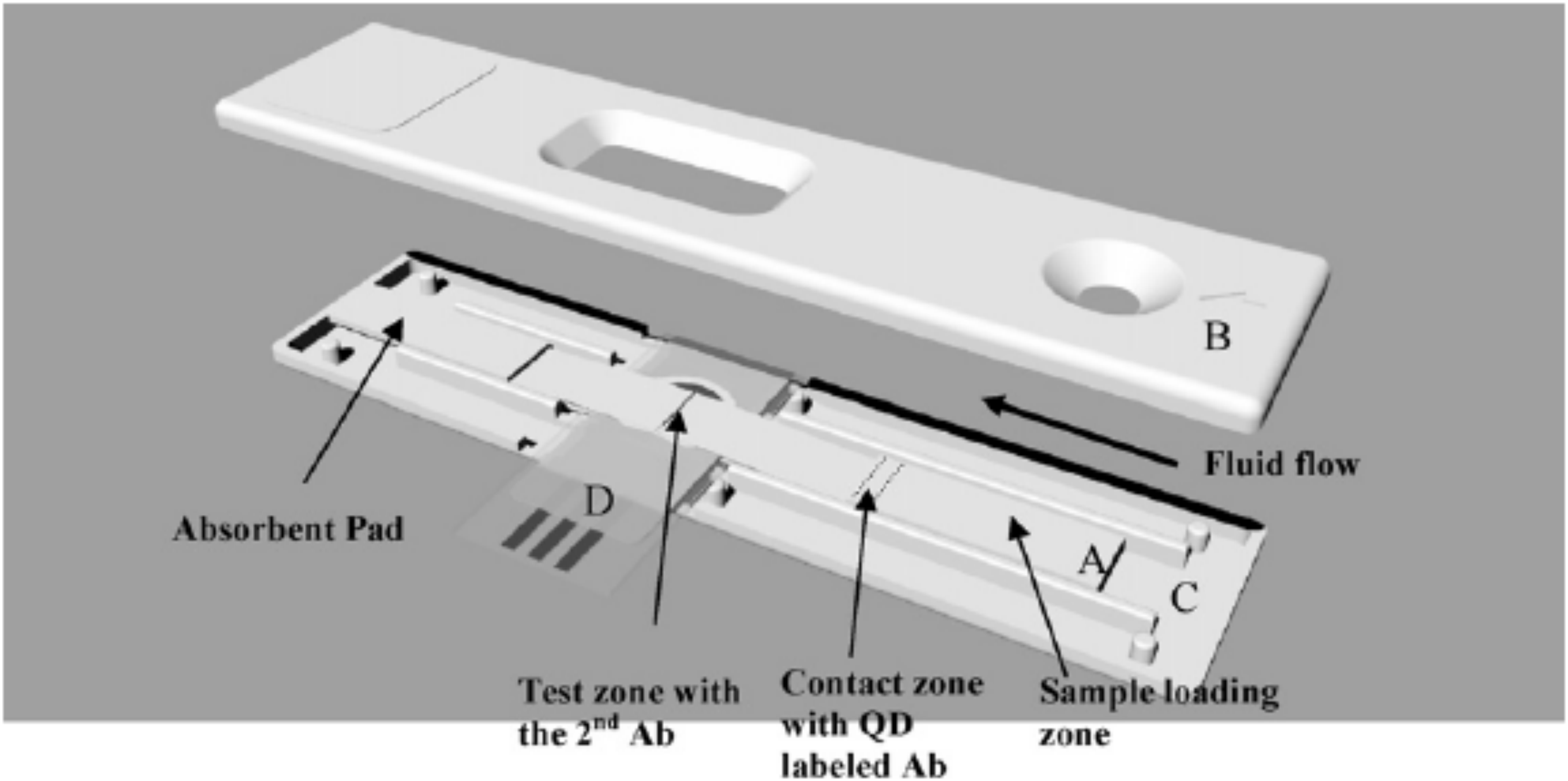
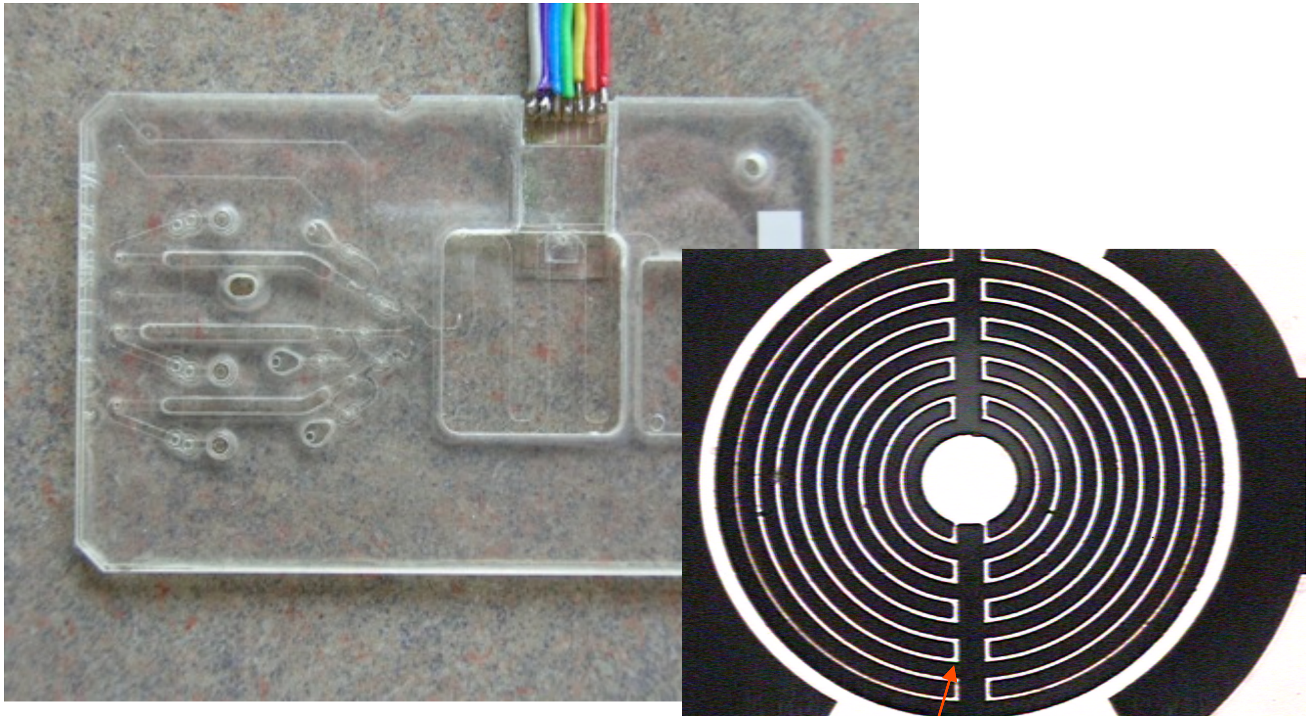


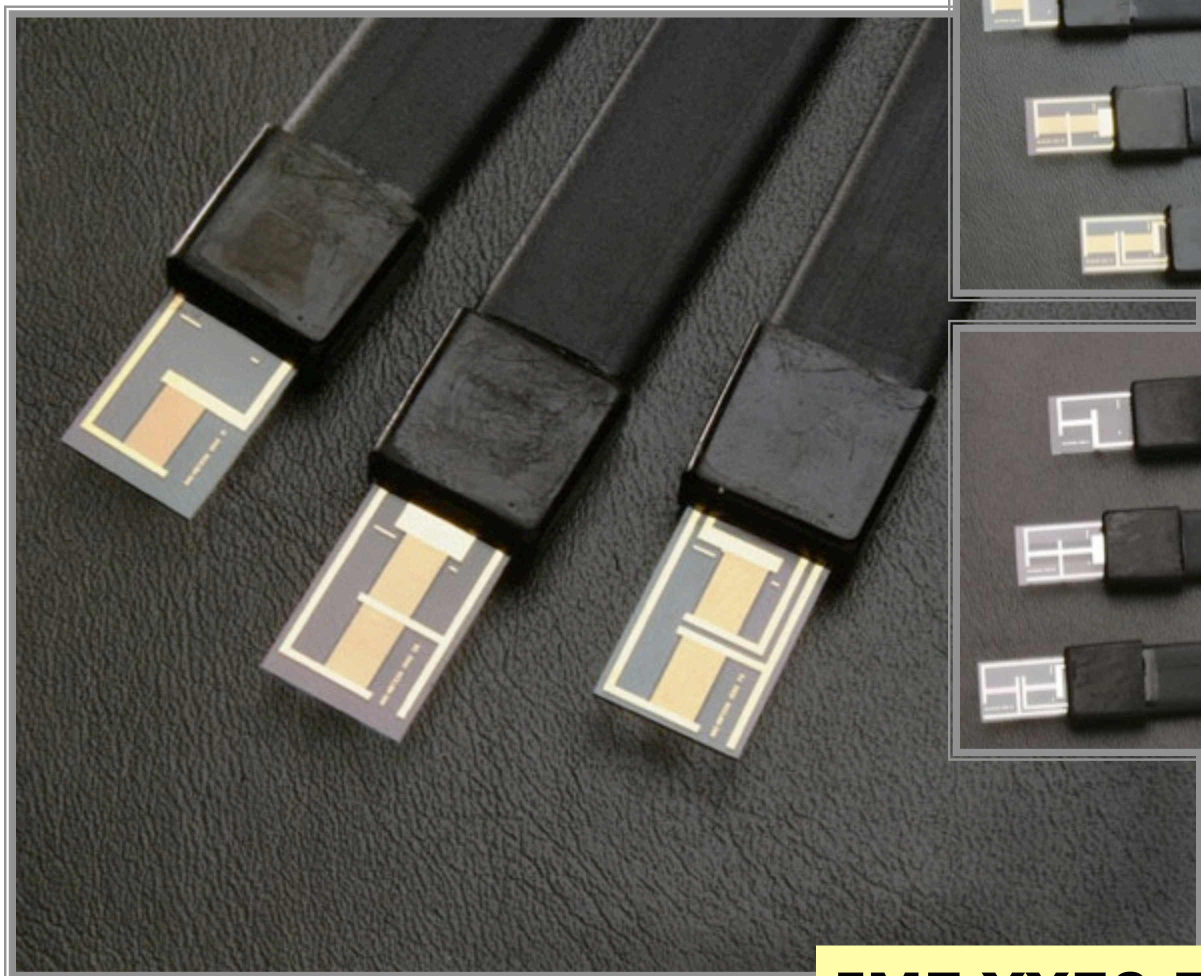
Fig. 1. Schematic diagram of the IEB. (A) A test strip; (B) a cover; (C) a bottom and (D) a SPE.

Electrochemical Cell-on-a-Chip (ECC) Integrated in a Microfluidic Cassette



An integrated biochip showing the microfabricated pattern of electrodes bonded and sealed into the Microncs' microfluidic T-cassette.

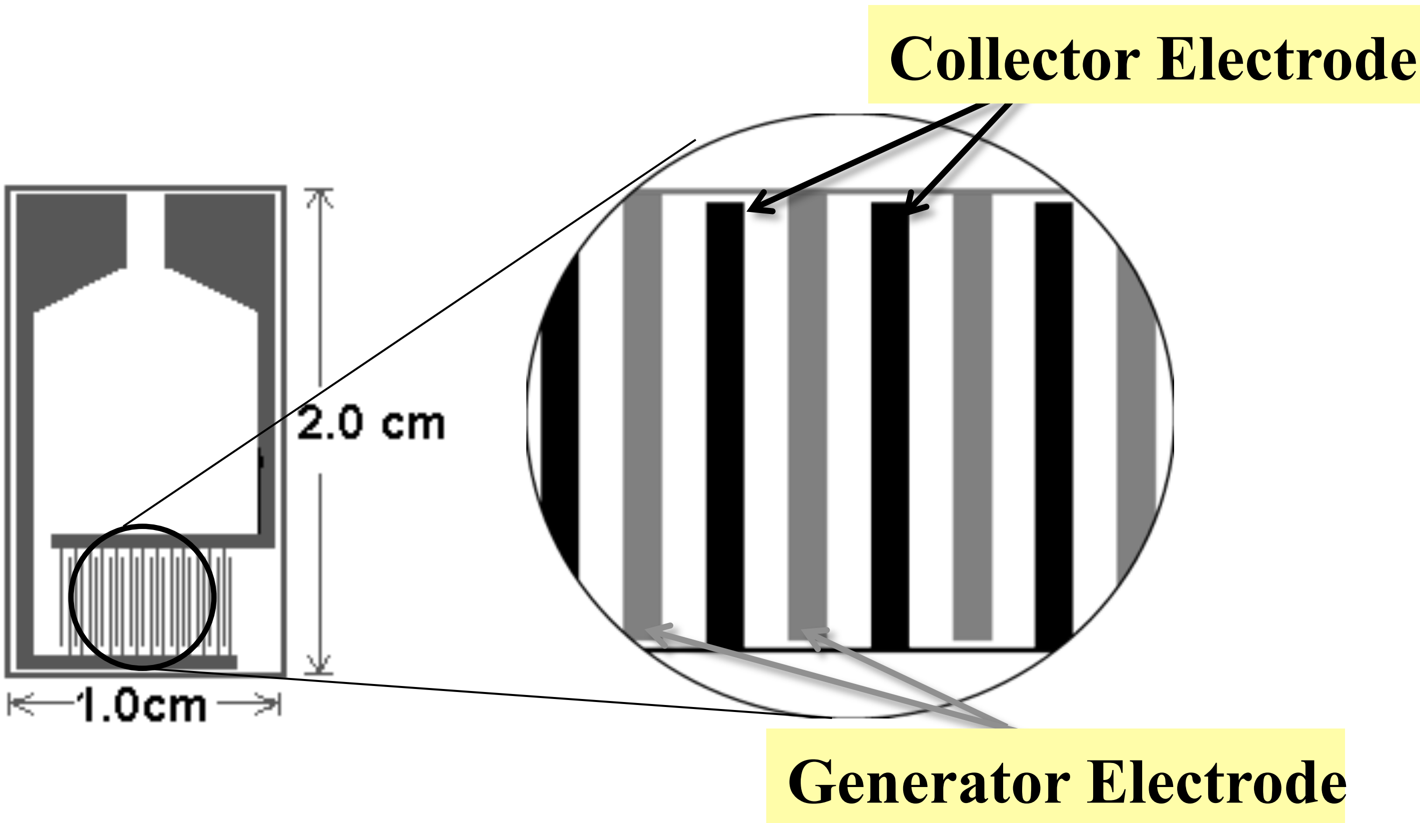
Microfabricated Interdigitated Microsensor Electrodes (IMEs)



XX = 05, 10, 15, 20 μm

IME XX50.5 M, CD, FD; Au, Pt, ITO

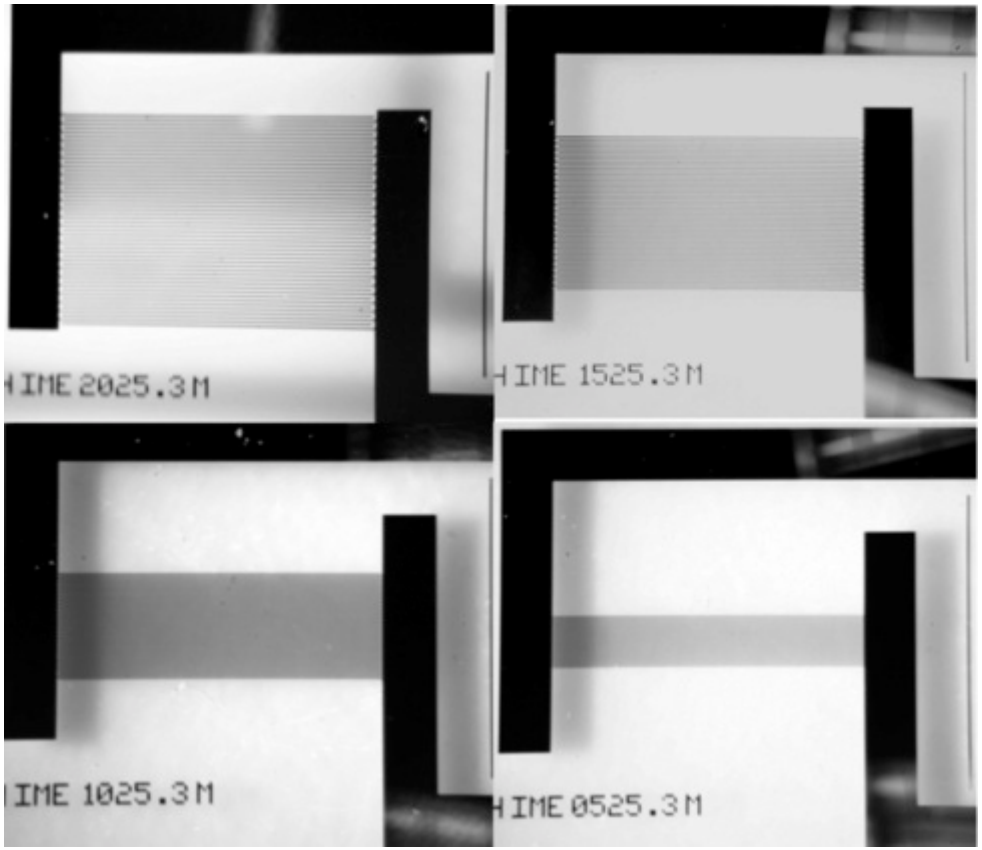
Schematic illustration of the IME XX25.3 chips IME XX50.5 chips

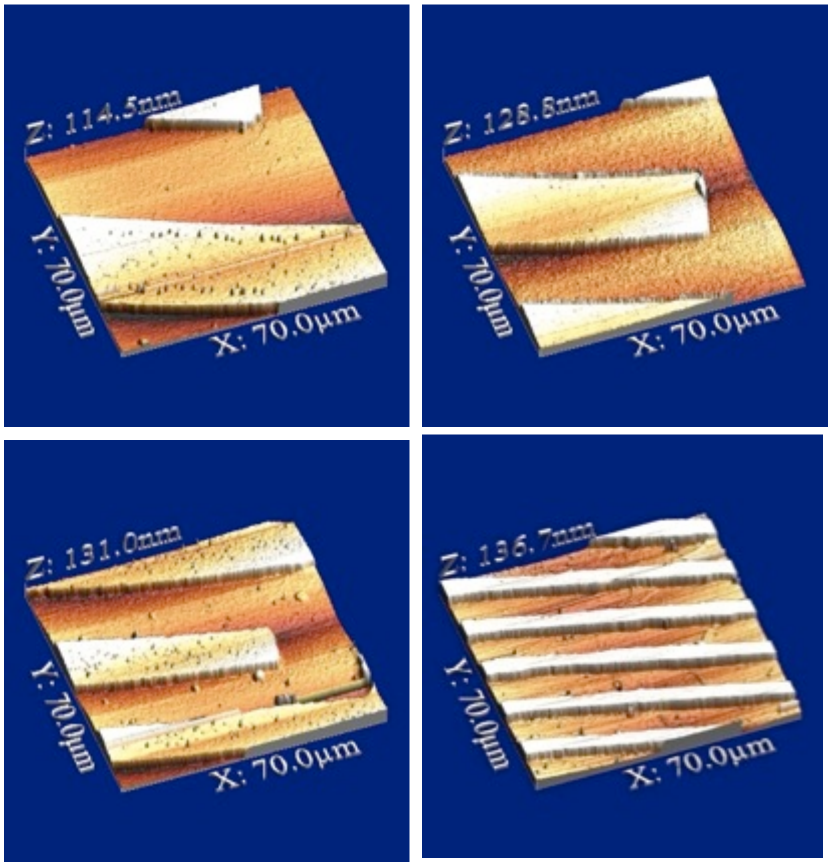


XX = Digit width = spacing = 05, 10, 15 & 20 microns

25 Bands on each bus	**50 Bands on each bus**
3 mm line length	**5 mm line length**

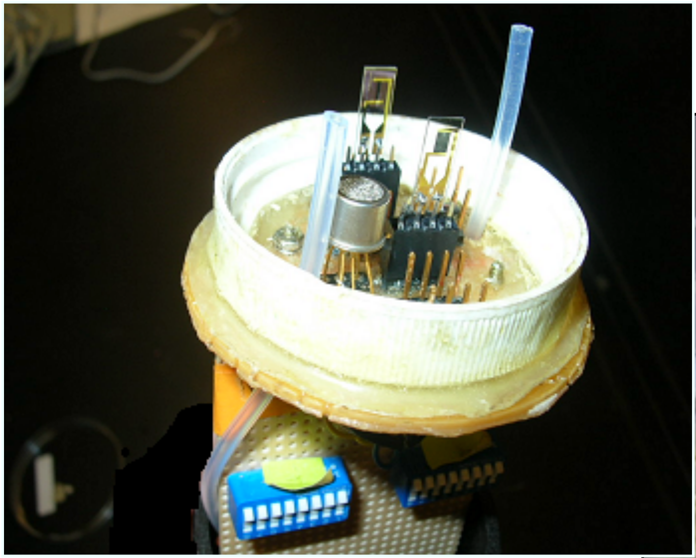
Photomicrograph and AFM Images IME XX25.3 chips

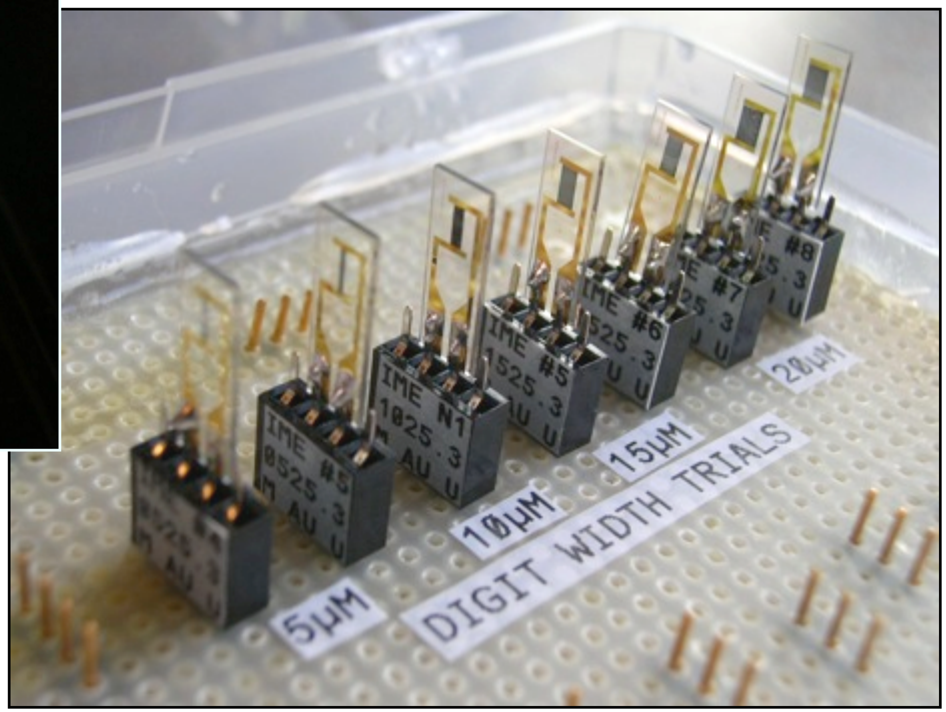




Sensor Arrays of VOC Responsive Polymers for the Electronic NOSE

- Chips of 05 μ m, 10 μ m, 15 μ m and 20 μ m with electropolymerized PPy, PTh or PAn



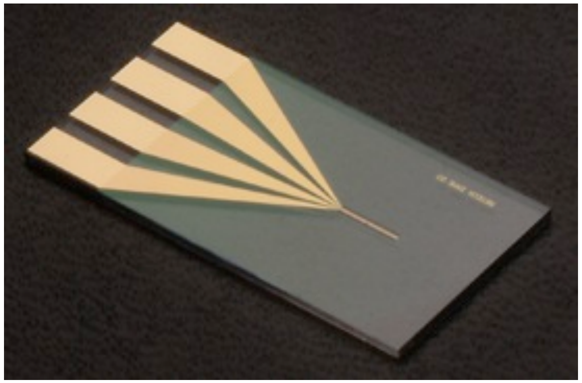


Microband Electrodes

Independently Addressable Microband Electrodes (IAMEs)

IAME XX04, Au, Pt or ITO

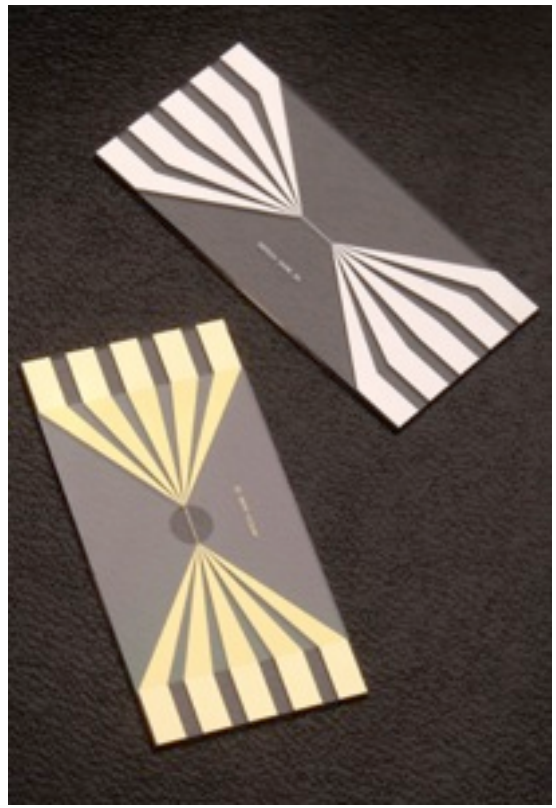
XX = 5, 10, 15, 20 mm



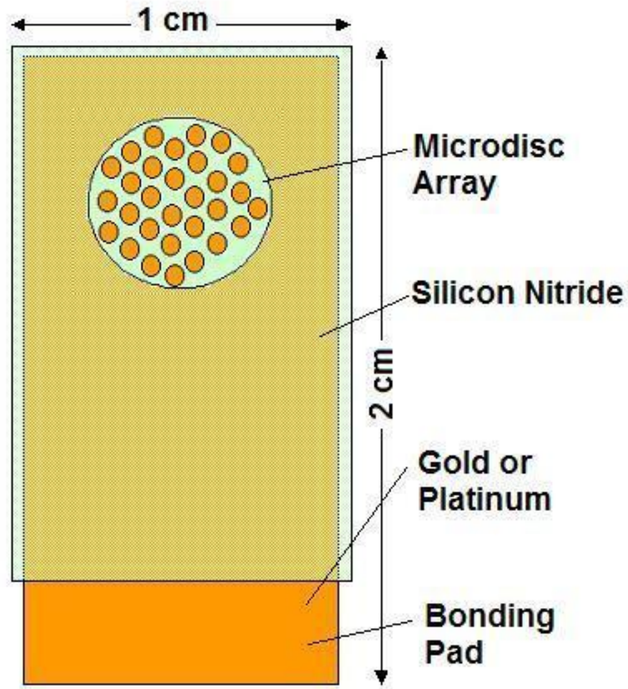
Independently Addressable Interdigitated Microsensor Electrodes (IAIMEs)

IAIME XX10, Au, Pt or ITO

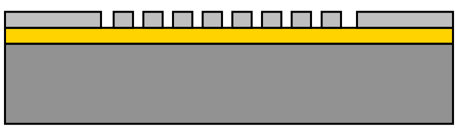
XX = 05, 10, 15, 20 mm

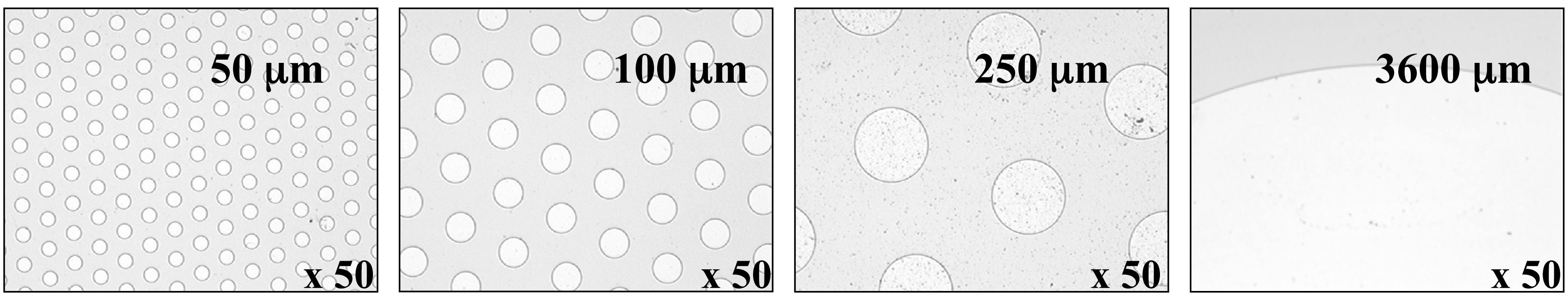


Microdisc Electrode Arrays 2

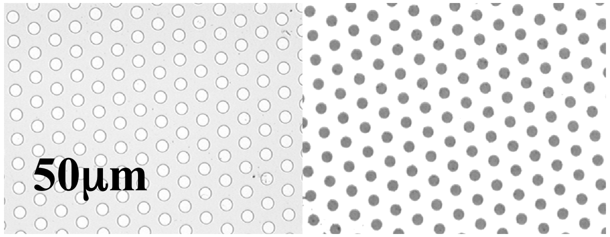


MDEA DEVICES	Disc dimensions / Number of Discs	Active Area	Conductor
MDEA 3600	D = 3,600 μm 1 disc	0.10 cm^2	Au, Pt, ITO
MDEA 250	D = 250 μm 207 microdiscs	0.10 cm^2	Au, Pt, ITO
MDEA 100	D = 100 μm 1,296 microdiscs	0.10 cm^2	Au, Pt, ITO
MDEA 050	D = 50 μm 5,184 microdiscs	0.10 cm^2	Au, Pt, ITO

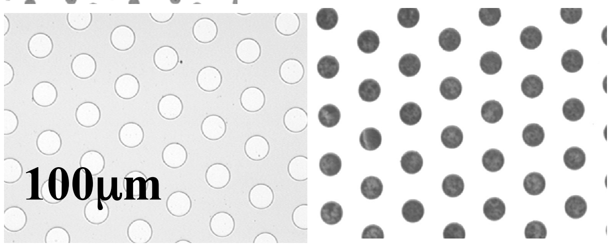




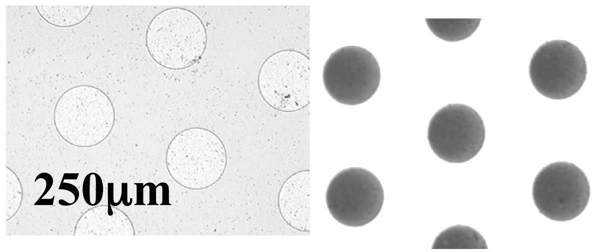
Microdisc Electrode Arrays 3



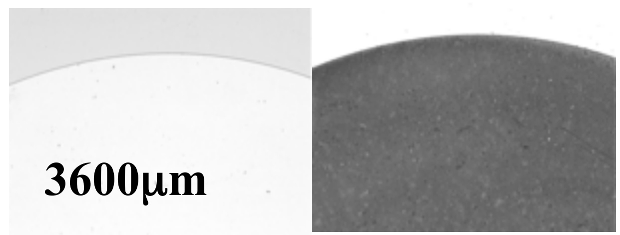
5,184 microdiscs



1,296 microdiscs



207 microdiscs



1 macro disc

ABTECH's Patents

A. Guiseppi-Elie; US Patent No. 5, 766, 934; Issued on June 16, 1998. "Chemical and Biological Sensor Devices Having Electroactive Polymer Thin Films Attached to Microfabricated Devices and Possessing Immobilized Indicator Moieties".

A. Guiseppi-Elie; US Patent No.: 5, 352, 574; Issued on: October 4th, 1994. "Electroactive Polymers with Immobilized Active Moieties".

A. Guiseppi-Elie; US Patent No.: 5, 312, 762; Issued on: May 17th, 1994. "Method of Measuring an Analyte by Measuring Electrical Resistance of a Polymer Film Reacting with the Analyte".

An Implantable Biochip to Influence Patient Outcomes Following Trauma-induced Hemorrhage

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Security and Privacy in Implantable Medical Devices

SPIMD, EPFL, ELA2, Lausanne, Switzerland. April 1, 2011

Improving Human Health Through Technology:

Research at the Center for Bioelectronics, Biosensors and Biochips (C3B™)

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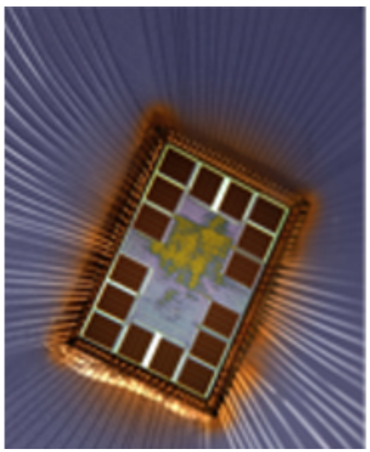
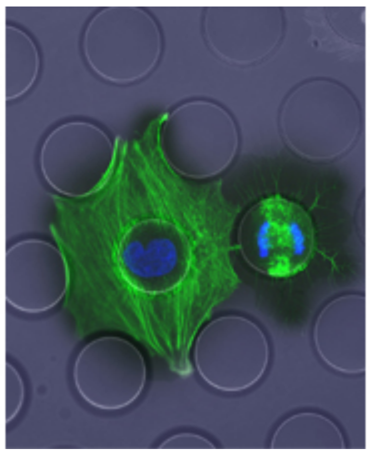
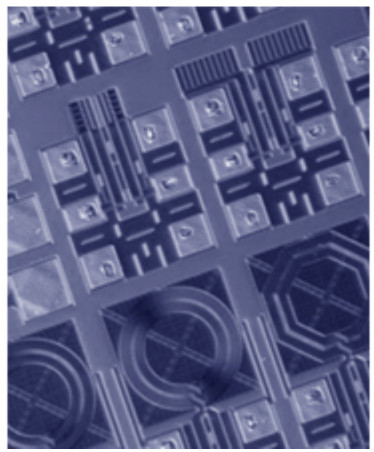
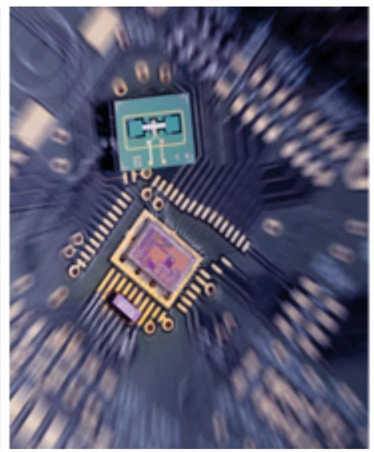
The CU-C3B is a national model for advanced nano-bio electronics



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Chenghong Lei, Ph.

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Gopakumar Sethuraman
Michael Zavatsky

School Students
e Myers
ren Koch
thew Sebastian

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C3B®

Grand Challenge Problems

The Bio-materials Interface: Enabling chronically implantable bioanalytical devices - **Bionics**

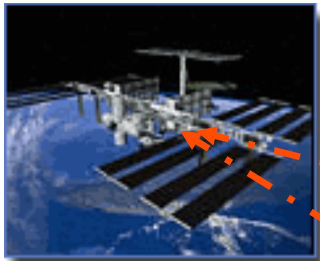
Bioelectronics: Enabling direct electronic communication between solid state devices and the biology -- **More than Moore**

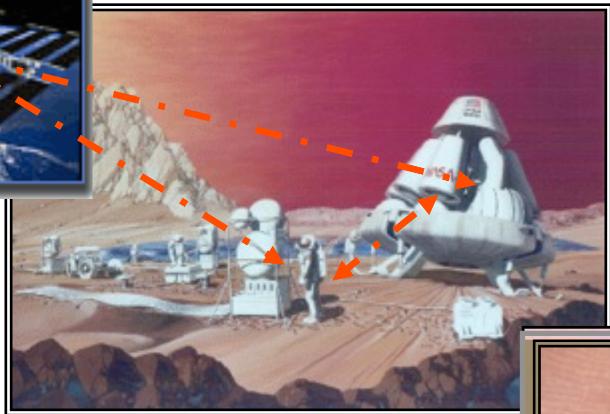
Goals of our Research

- **Design, synthesis and characterization of soft polymeric biomaterials** with *low interfacial impedance*, *fast ion transport*, *biomolecule hosting*, and *in-vivo biocompatibility*.
- **Implantable Biotransducers (sonde)** for continuous monitoring of interstitial glucose, lactate, pH and temperature.
- **Implantable integrated biochips** for interrogating and wireless reporting of physiologic parameters related to trauma induced hemorrhage and shock.

Opportunities for *in-vivo* Biosensors

Lactate and Glucose Monitoring

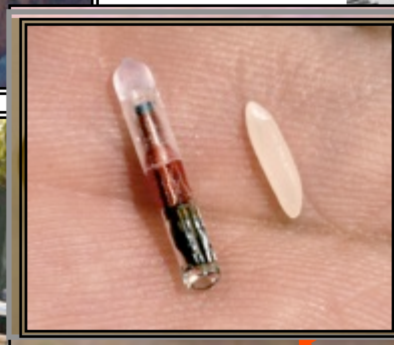


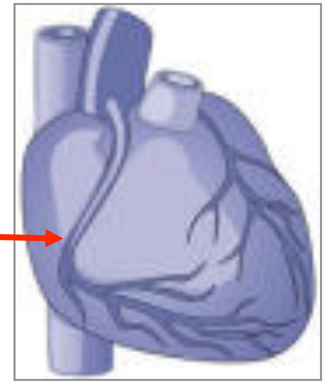


Manned Space *Flights*

Diagnostics

Trauma Management





Congestive Heart Failure and Transplanted Organ Health

Battlefield

Trauma outcomes

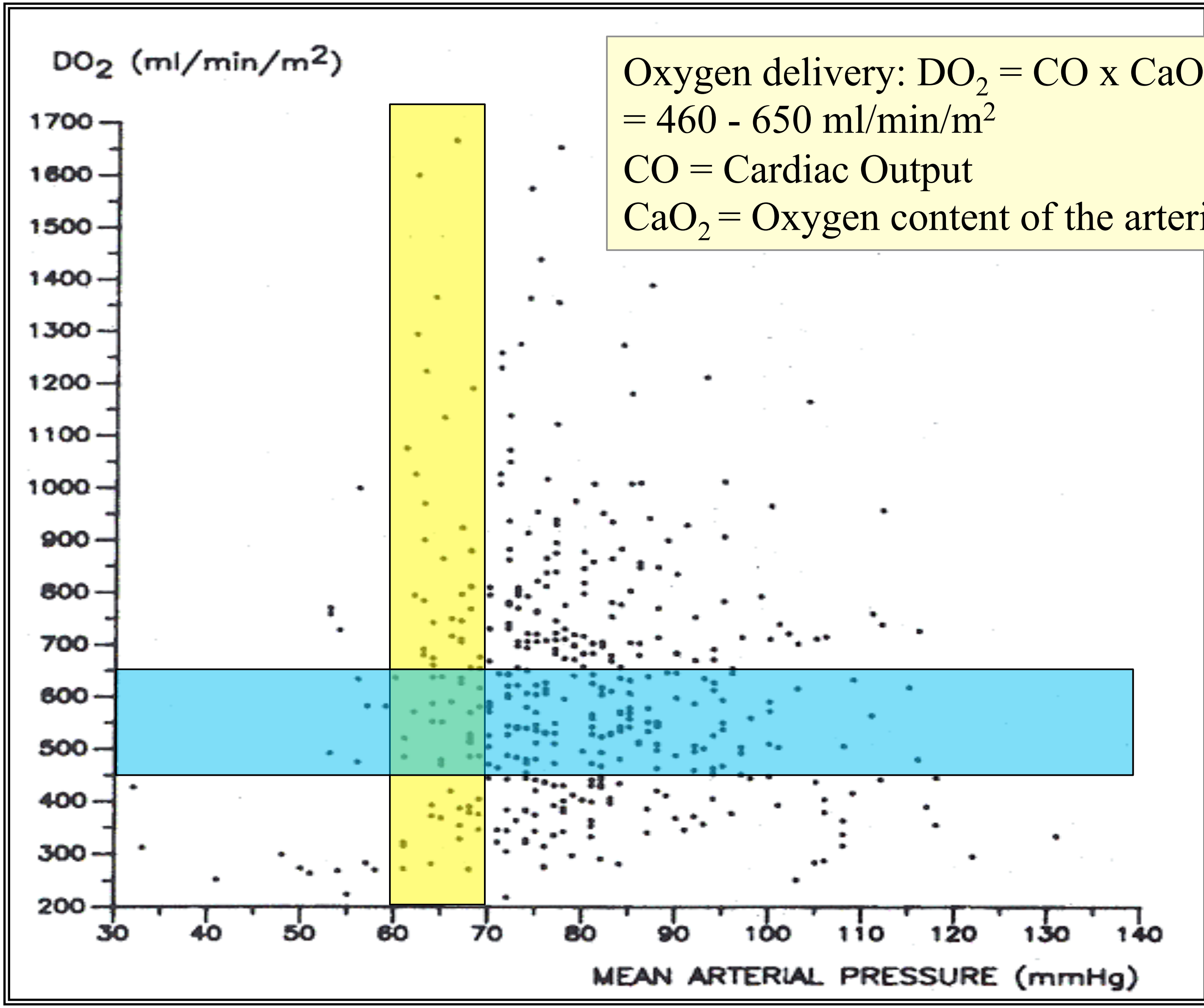
Chronic Diabetes Care

The Case for Monitoring

- ✦ Trauma - the No.1 killer of persons < 50 yrs old.
- ✦ Death from hemorrhage is implicated in 50-68% of battlefield trauma cases (Col. Erin Edgar)
- ✦ During hemorrhage induced trauma and following surgery, hemodynamics and physiology are delicate and can change rapidly
- ✦ Need to initiate *immediate* and *continuous* monitoring of **molecular indicators** of global physiologic stress.

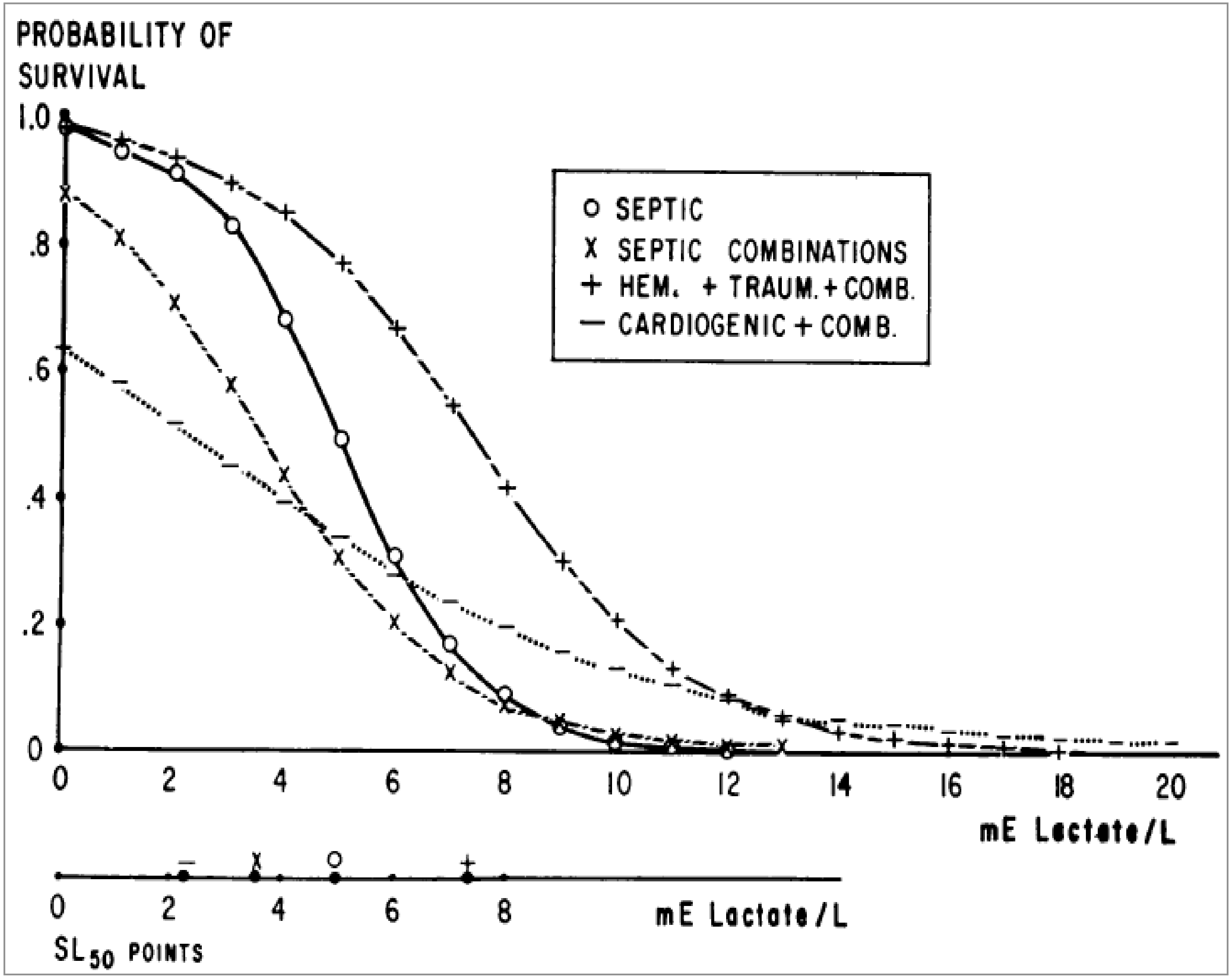
Being Fooled by Vital Signs (e.g. Blood Pressure)

Oxygen Delivery: $DO_2 = CO \times C_aO_2$
460 - 650 ml/min/m^2



Oxygen delivery: $DO_2 = CO \times CaO_2$
= 460 - 650 ml/min/m^2
CO = Cardiac Output
CaO_2 = Oxygen content of the arterial blood

Lactic Acidosis: A Prognosticator in Trauma



Huckabee, W. E. (1963) "LACTIC ACIDOSIS." The American Journal Of Cardiology 12: 663-666

Vitek, V. and R. A. Cowley (1971) "Blood lactate in the prognosis of various forms of shock." Annals Of Surgery 173(2): 308-313

Broder, G. and M. H. Weil (1964) "EXCESS LACTATE: AN INDEX OF REVERSIBILITY OF SHOCK IN HUMAN PATIENTS" Science 143: 1457-1459

What motivates our focus on lactate?

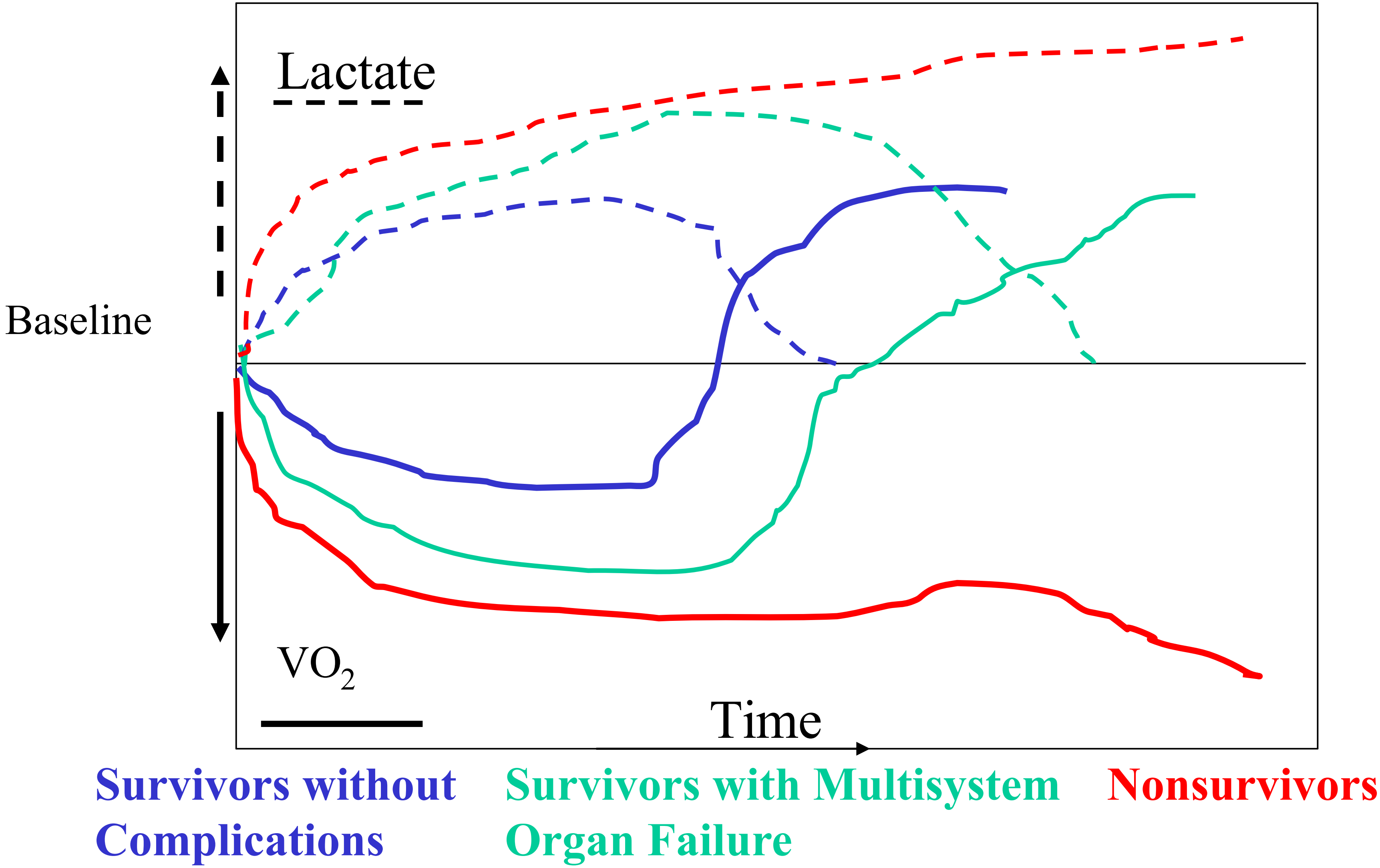
- **Mortality/Morbidity**
  - Patients who have an arterial lactate level of more than 5 mmol/L and a pH of less than 7.35 are critically ill and have a very poor prognosis. The multicenter trials have shown a mortality rate of 75% in these patients.
- **However, if lactate levels normalize in:**
  - 24 hrs = 90-100% survival
  - 24-48 hrs normalization = 75% survival
  - >48 hrs = 13%

Kyle J. Gunnerson, MD and Sat Sharma, MD, FRCPC, e-Medicine WebMD, April 14, 2010 http://emedicine.medscape.com/article/167027-overview

Gunnerson KJ, Saul M, He S, Kellum JA. Lactate versus non-lactate metabolic acidosis: a retrospective outcome evaluation of critically ill patients. *Crit Care*. Feb 10 2006;10(1):R22

HYPOTHESIS: Clinical Outcomes Related to Peripheral Perfusion Following Trauma:

The case for continuous lactate monitoring

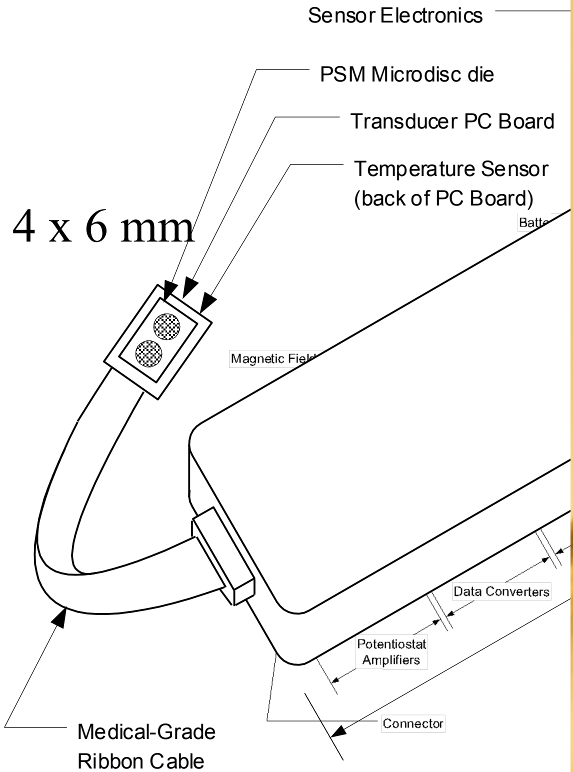


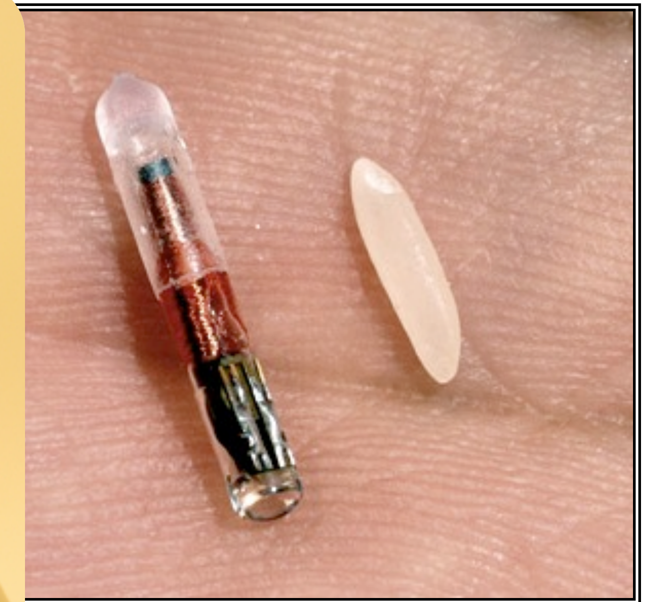
PSMBioChip System
(Physiologic Status Monitoring)

Discrete Prototype Device

ASIC Device

4 x 6 mm





igital Angel
CORPORATION
VERICHIP

An Implantable Biochip for Physiologic Status Monitoring

Glucose, Lactate, pH and Temperature

Implantable Biochips

IEEE SENSORS JOURNAL, VOL. 5, NO. 3, JUNE 2005 345

Design of a Subcutaneous Implantable Biochip for Monitoring of Glucose and Lactate

Anthony Guiseppi-Elie, Sean Brahim, Gymama Slaughter, and Kevin R. Ward

1856 IEEE SENSORS JOURNAL, VOL. 9, NO. 12, DECEMBER 2009

Fabrication and Packaging of a Dual Sensing Electrochemical Biotransducer for Glucose and Lactate Useful in Intramuscular Physiologic Status Monitoring

Abdur Rub Abdur Rahman, Gusphyl Justin, Adilah Guiseppi-Wilson, and Anthony Guiseppi-Elie, *Member, IEEE*

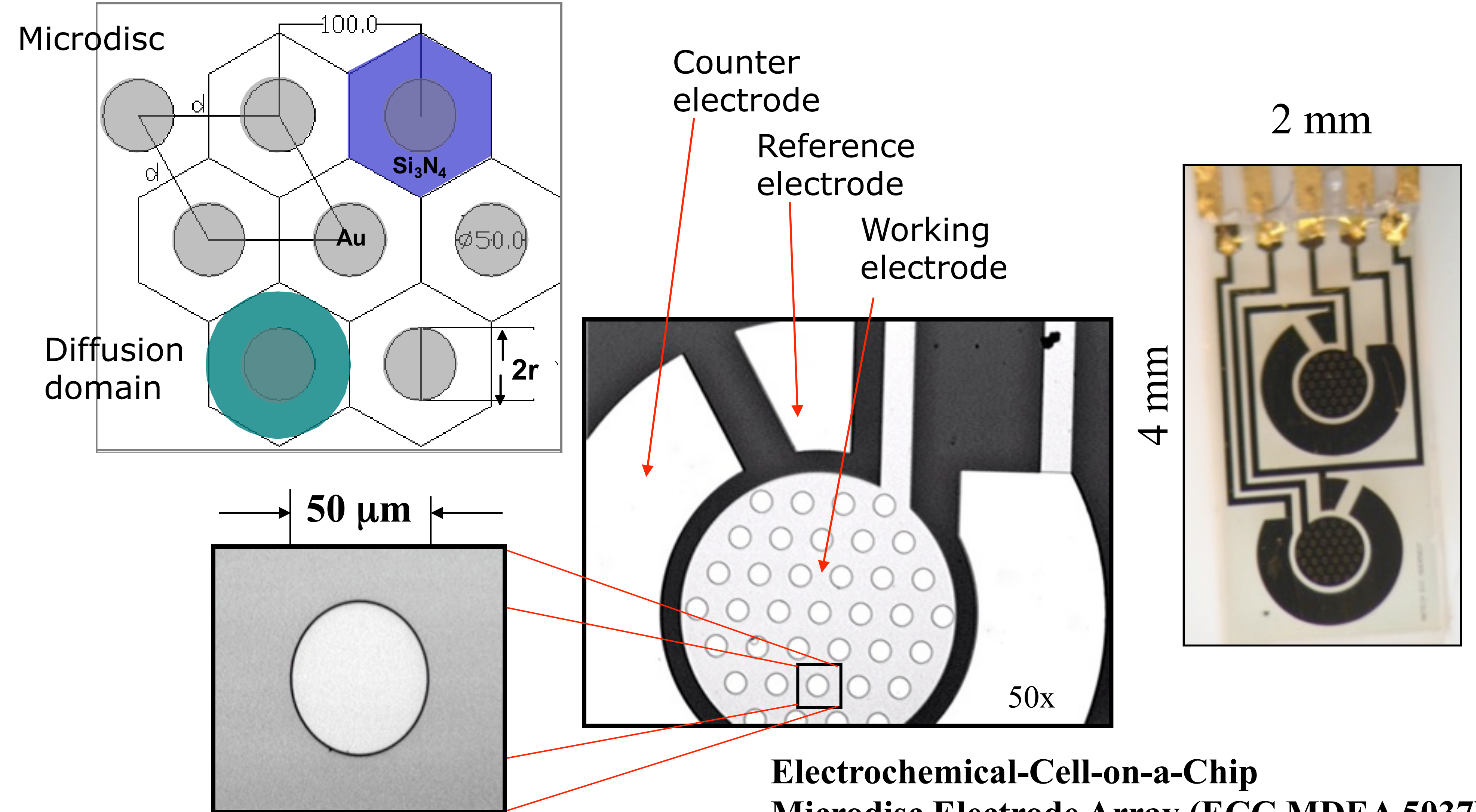
Anal Bioanal Chem
DOI 10.1007/s00216-010-4271-x

ORIGINAL PAPER

An implantable biochip to influence patient outcomes following trauma-induced hemorrhage

Anthony Guiseppi-Elie

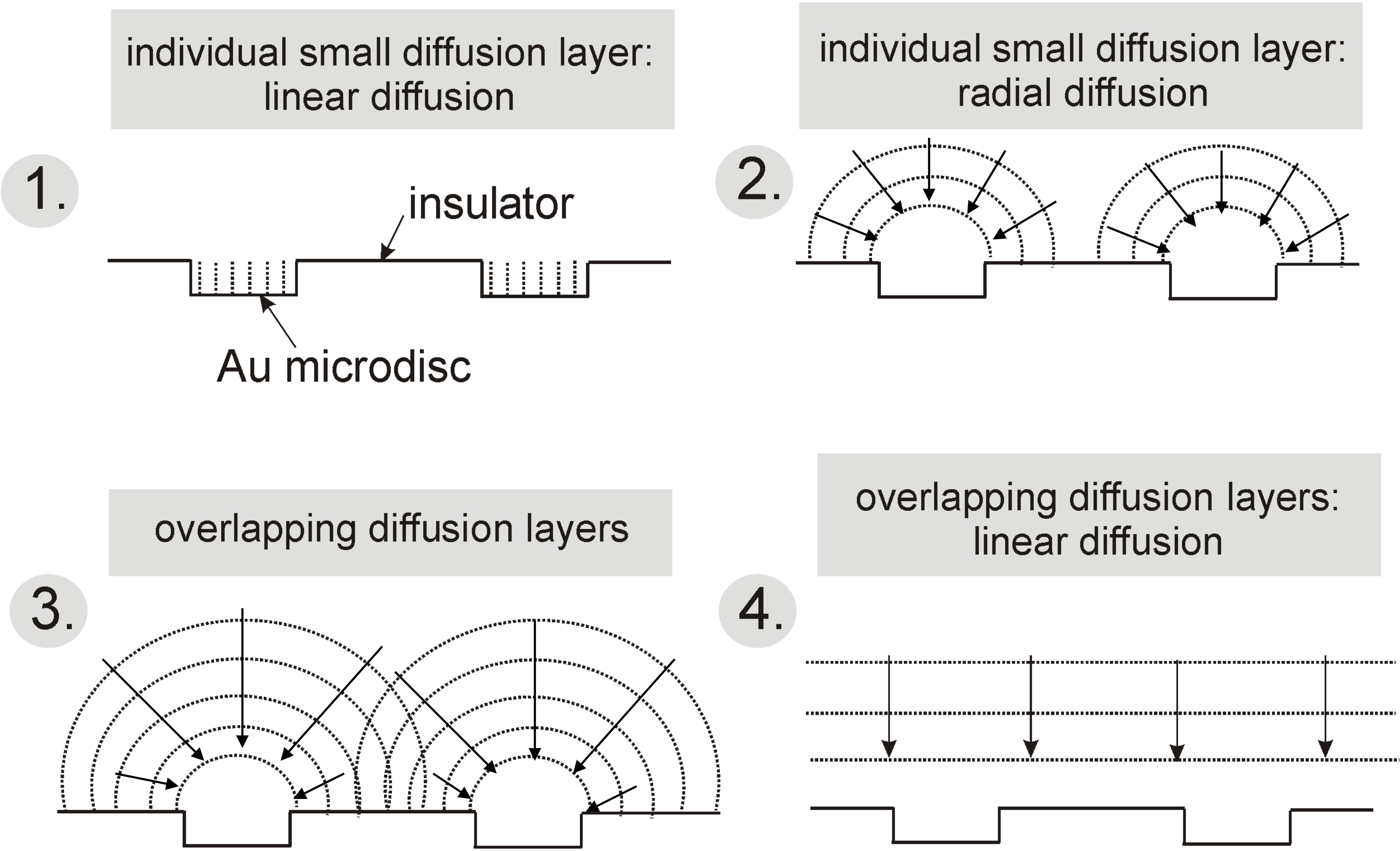
Front-end biotransducer for discrete component prototyping of the PSMBioChip



Electrochemical-Cell-on-a-Chip Microdisc Electrode Array (ECC MDEA 5037)

A. Guiseppi-Elie, S. Brahim, G. Slaughter and K. R. Ward, "Design of a Subcutaneous Implantable Biochip for Monitoring of Glucose and Lactate", (**2005**) *IEEE Sensor Journal*, 5(3), pp. 345-355.

Design of the microdisc electrode array (MDEA)

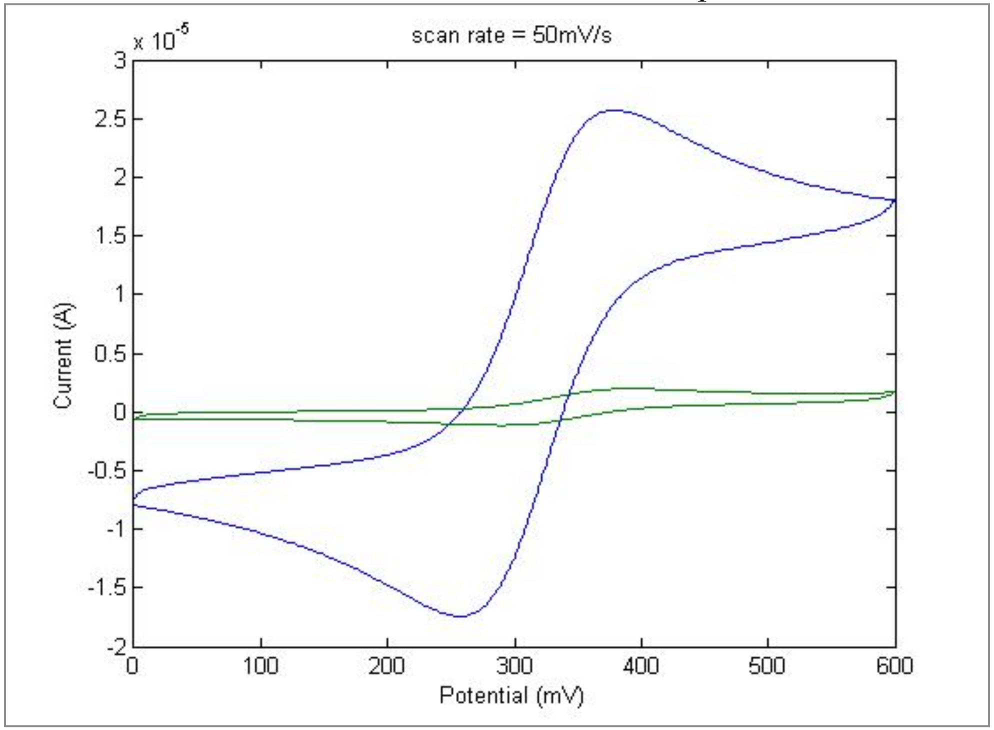


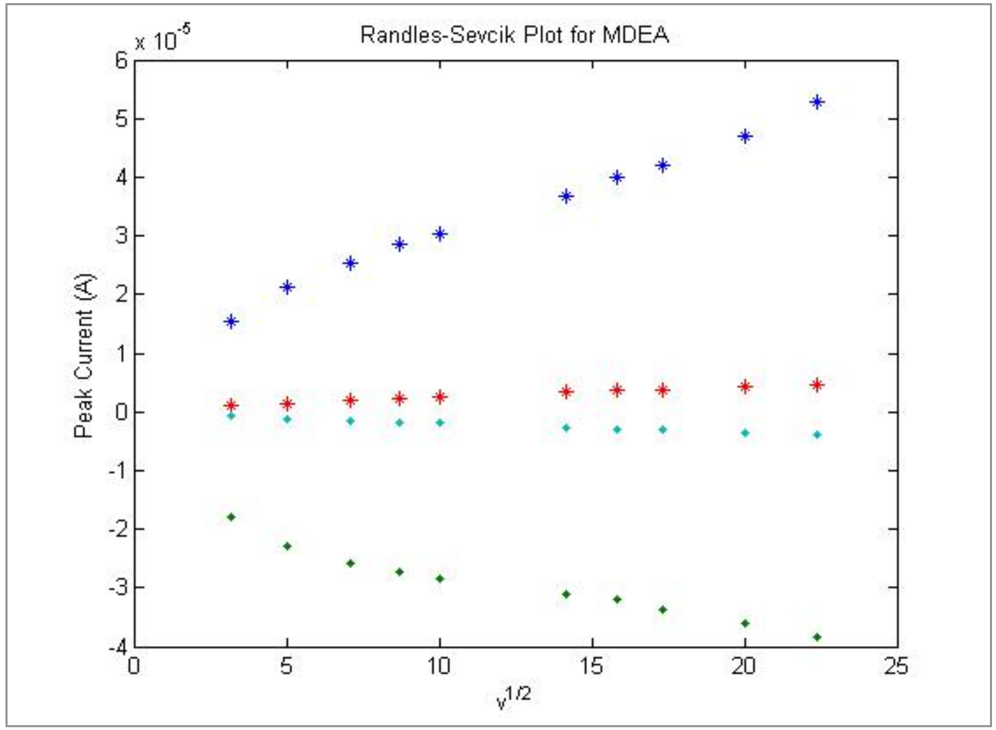
Abdur Rub Abdur Rahman and Anthony Guiseppi-Elie "Design Considerations in the Development and Application of Microdisc Electrode Arrays (MDEAs) for Implantable Biosensors" *Biomedical Microdevices* (**2009)** 11:701-710.

MDEA50 and MDEA50*|hydrogel

qualified by CV in 1.0 mM FcCOOH in TRIS Buffer

$$I_p = 2.687 \times 10^5 n^{3/2} v^{1/2} D^{1/2} A C_{ox}$$





Reduced voltametric peak currents

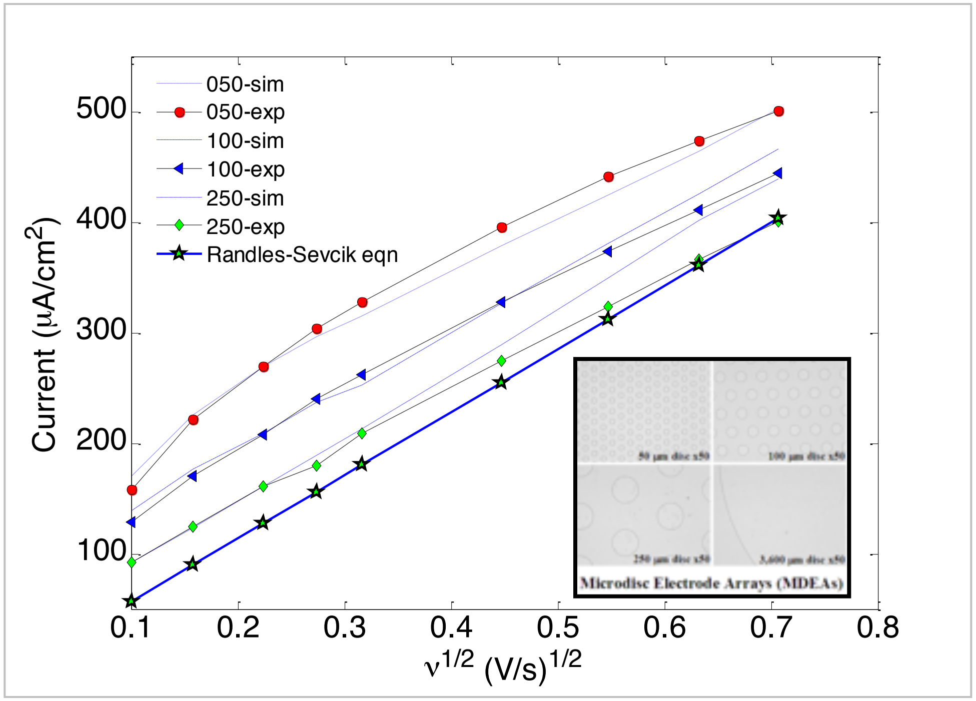
Reduced apparent area of the electrode

G. Justin, S. Finley, A. R. Abdur Rahman, and A. Guiseppi-Elie (**2008**). "Biomimetic Hydrogels for Biosensor Implant Biocompatibility: Electrochemical Characterization using Micro-Disc Electrode Arrays (MDEAs)." *Biomedical Microdevices:* **(2009)** 11:1, 103..

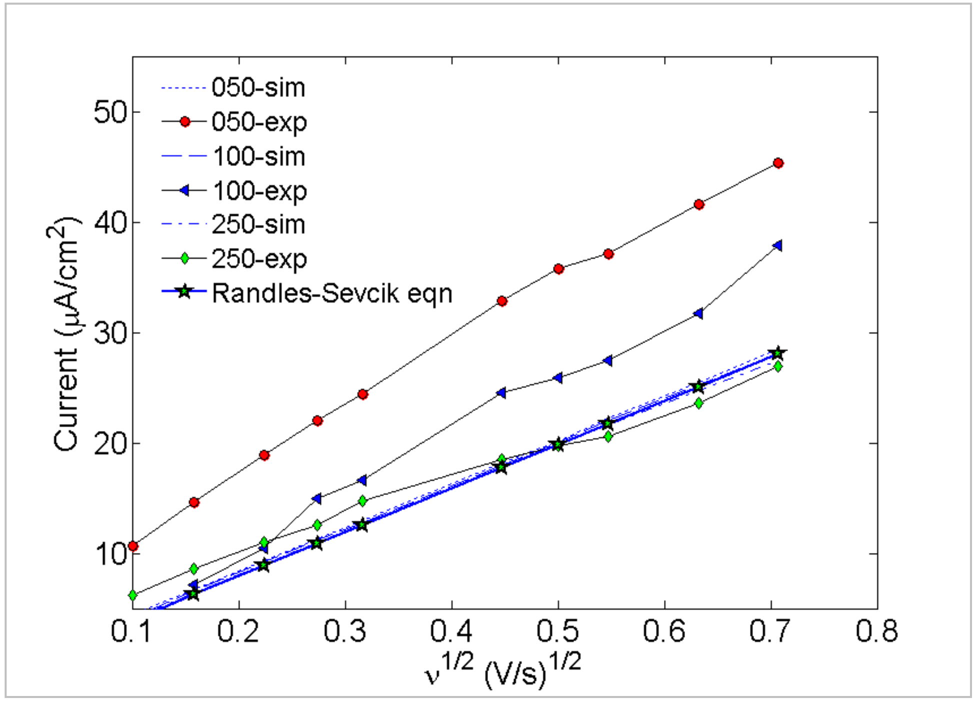
Performance enhancement of the microdisc electrode array format of the PSMBioChip

$$I_p = 2.687 \times 10^5 n^{3/2} v^{1/2} D^{1/2} A C_{ox}$$

Un-Coated



Hydrogel Coated

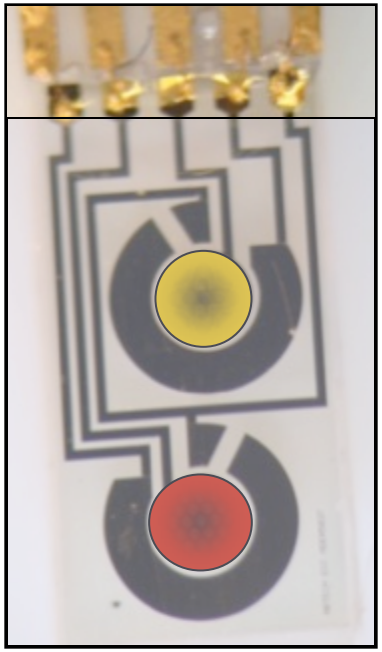


Enhanced effective area with reduction of disc diameter

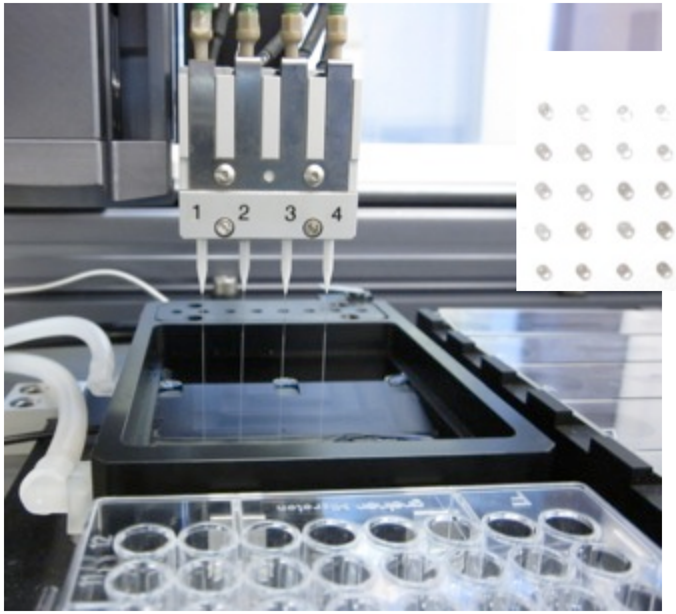
Enhancement maintained for 50 μm device beneath hydrogel

G. Justin, A. R. Abdur Rahman, and A. Guiseppi-Elie, "Bioactive Hydrogel Layers on Microdisc Electrode Arrays: Cyclic Voltammetry Experiments and Simulations," *Electroanalysis* (**2009**) (accepted)

Conferring biological specificity to a multi-analyte bioanalytical biochip – How?



MDEA 5037

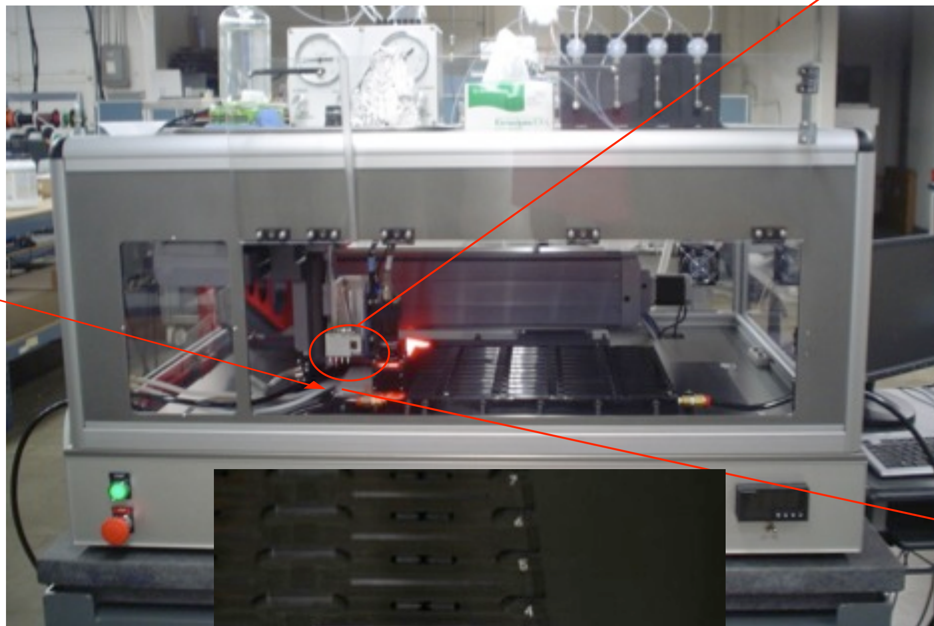


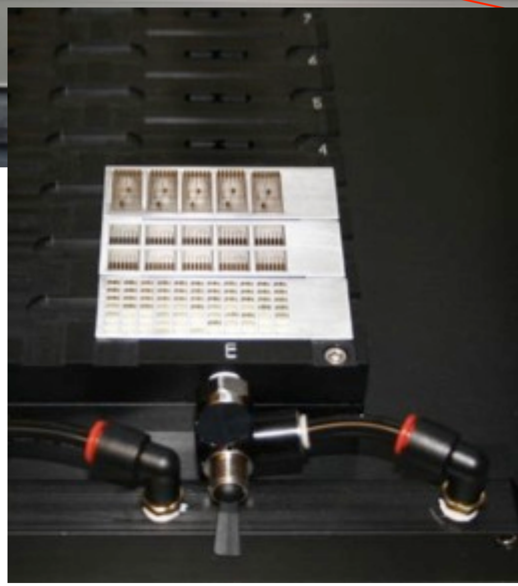
- **Micro-solenoid, non-contact printing**
- **Micro-contact quill or pin printing**
- **Ink-jet printing**
- **Spin-coating and electropolymerization**

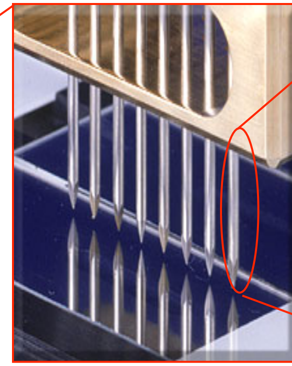
Custom Spot Production

Microarray Array Fabrication
BioDot AD 3400

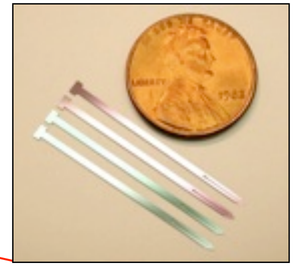
Hydrogel
Enzyme
Cocktails

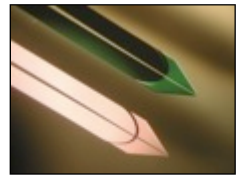






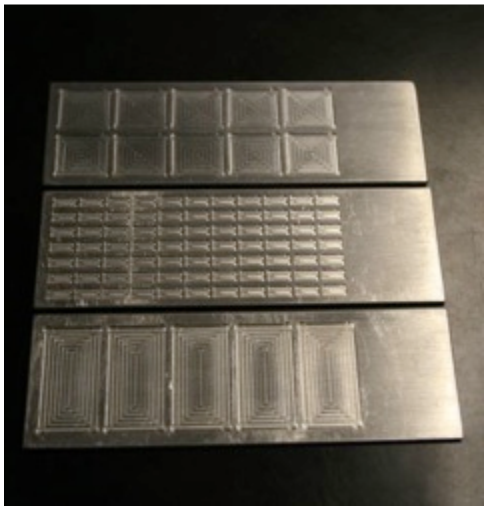
Silicon Pins

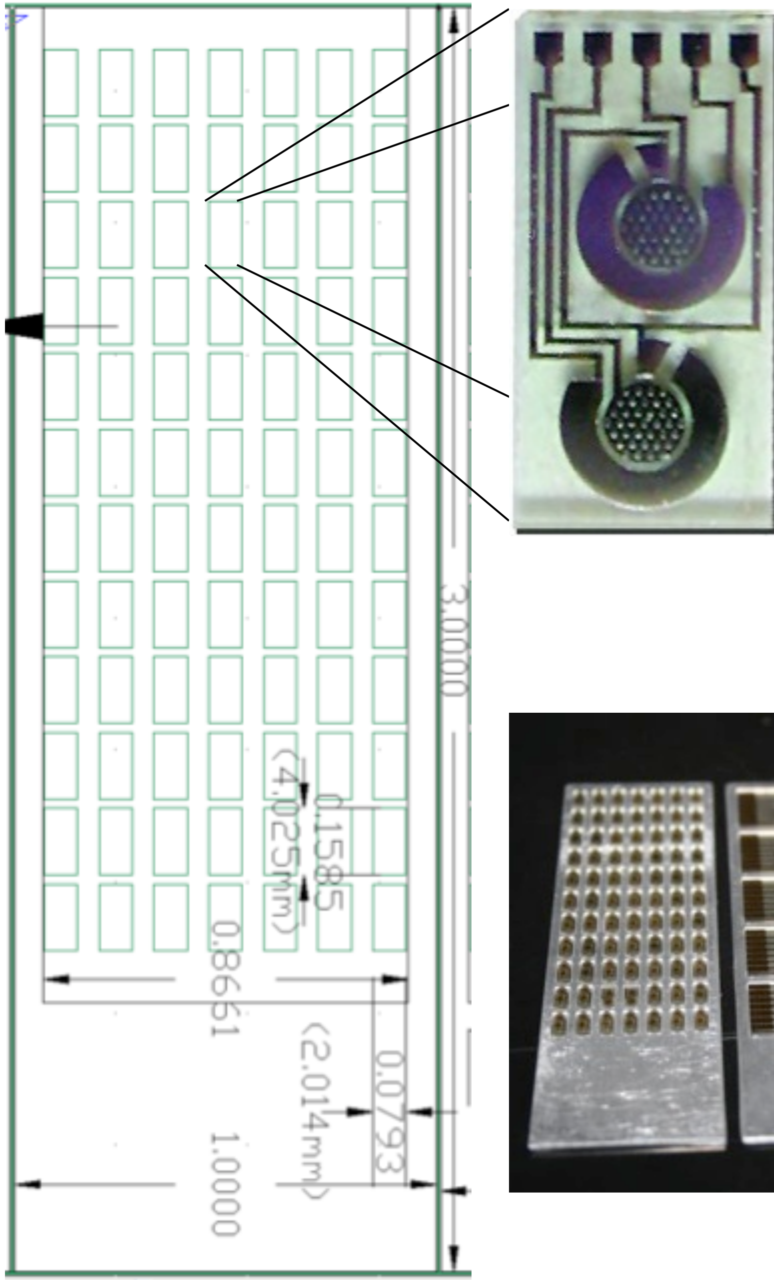


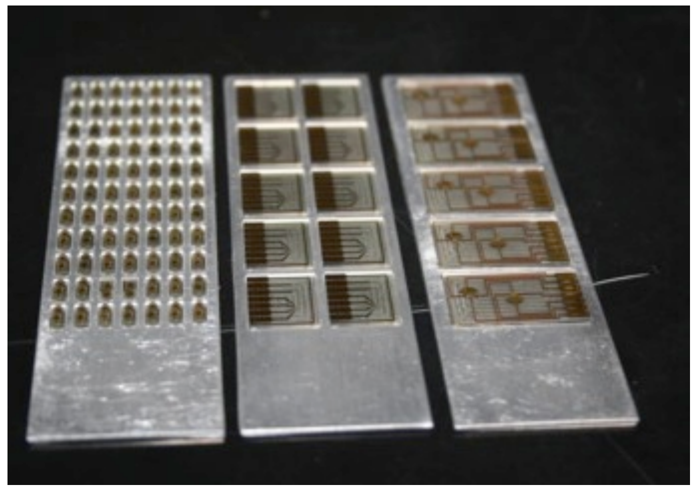


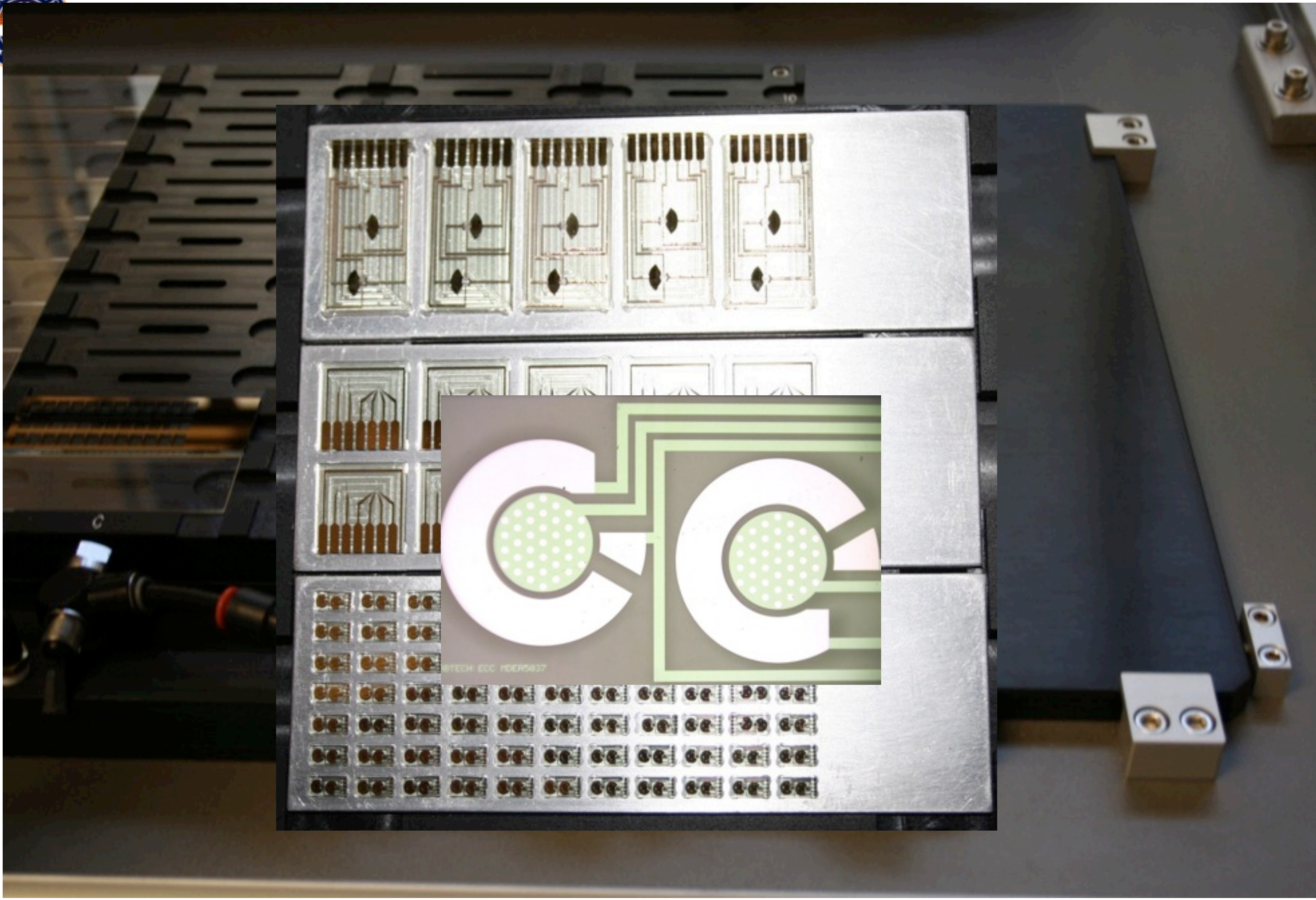
Custom Spot Production on Die

1” x 3”
Die Carrier
Fits Plattern








TECH ECC MDER5037

Electroconductive Hydrogels

556

Full Paper

Electroconductive Hydrogels:
Properties of Polypyrrole-Poly

Sean Brahim,[a] *Anthony Guiseppi-Elie*[a,b]*

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Box 843038, 601 West Main Street, Richmond, Virginia 23
[b] Departments of Chemical Engineering and Emergency Me
Box 843038, 601 West Main Street, Richmond, Virginia 23
*e-mail: guiseppi@vcu.edu

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Biomaterials 26 (2005) 4767–4778

Biomaterials

www.elsevier.com/locate/biomaterials

Molecularly engineered p(HEMA)-based hydrogels for implant biochip biocompatibility

Sheena Abraham[a], Sean Brahim[a], Kazuhiko Ishihara[d], Anthony Guiseppi-Elie[a,b,c,*]

[a] *Center for Bioelectronics, Biosensors and Biochips (C3B), Virginia Commonwealth University, P.O. Box 843038, 601 West Main Street, Richmond, Virginia 23284-3038, USA*
[b] *Department of Emergency Medicine, Virginia Commonwealth University, Richmond, Virginia 23284-3038, USA*

Biomaterials 31 (2010) 2701–2716

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Contents lists available at ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Review

Electroconductive hydrogels: Synthesis, characterization and biomedical applications

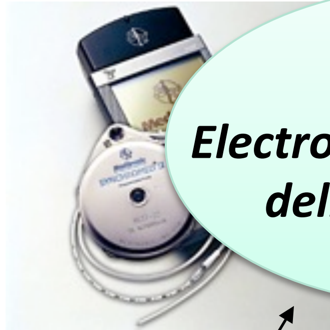
Anthony Guiseppi-Elie[a,b,c,*]

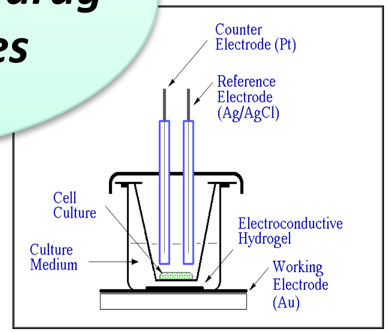
[a] *ABTECH Scientific, Inc., Biotechnology Research Park, 800 East Leigh Street, Richmond, VA 23219, USA*
[b] *Center for Bioelectronics, Biosensors and Biochips (C3B), Clemson University Advanced Materials Center, 100 Technology Drive, Anderson, SC 29625, USA*
[c] *Department of Chemical and Biomolecular Engineering, Department of Bioengineering, Department of Electrical and Computer Engineering, Clemson University, Clemson, SC 29634, USA*

Clinical Applications for Electroconductive Hydrogels

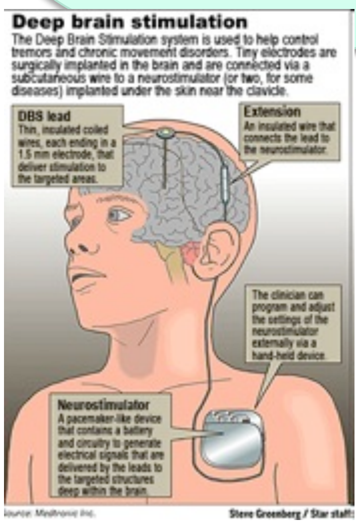
In vivo Physiological Status Monitoring biosensors

Electrostimulated drug delivery devices



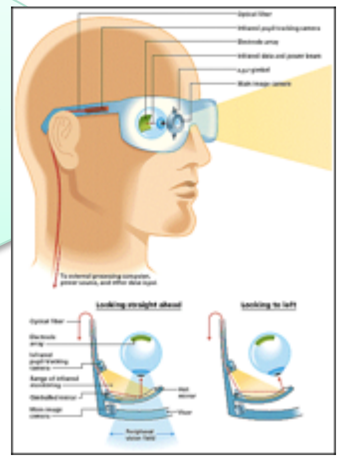


Deep Brain Stimulation Devices

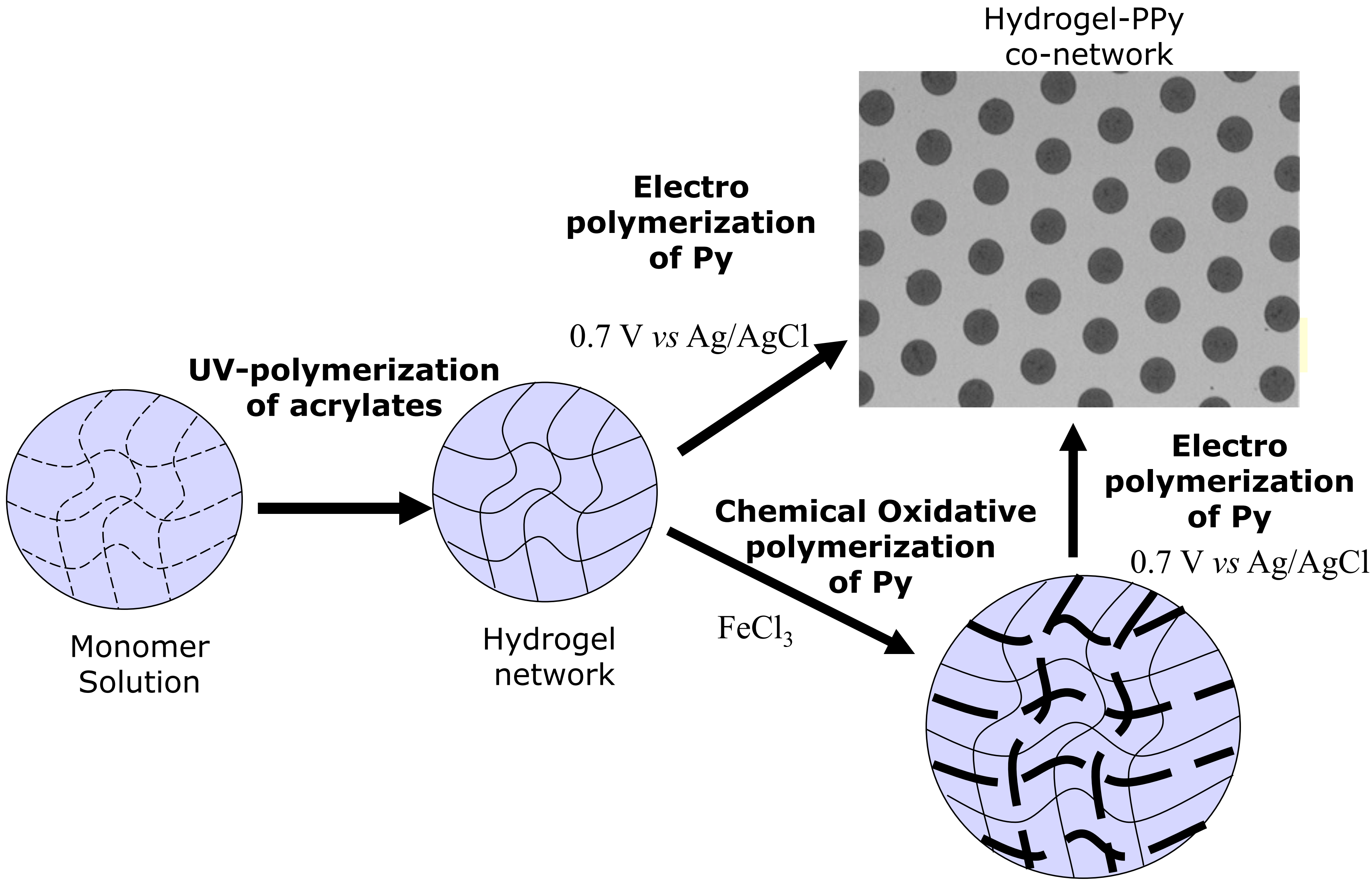


Implantable Biofuel Cells

Neural prostheses



Generalized Synthesis of Electroconductive Hydrogels



Anthony Guiseppi-Elie "Electroconductive Hydrogels: Synthesis, Characterization and Biomedical Applications" *Biomaterials*, (**2010**) 31(10) 2701-2716.

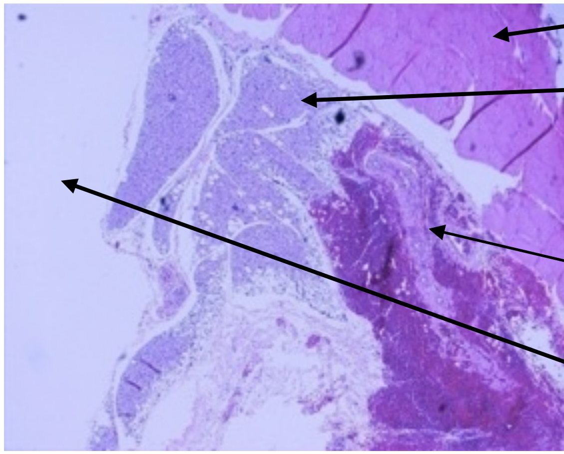
In-vivo Implantation in Sprague Dawley Hemorrhage Model

After implantation for 2 weeks in the trapezius muscle

A

un-modified p(HEMA)

Significant encapsulation and accumulation of foreign body material



Muscle

Area of Moderate Fibrosis and inflammation with foamy histocytes around the site where hydrogel was placed

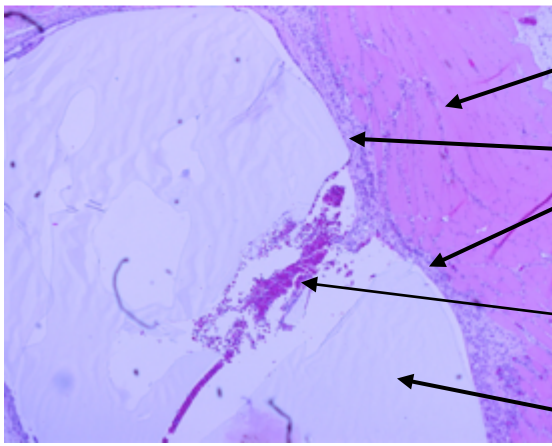
Residual area of Hemorrhage

Area where hydrogel existed

B

1 mol % MPC

Thin band of encapsulation and much reduced residual inflammation



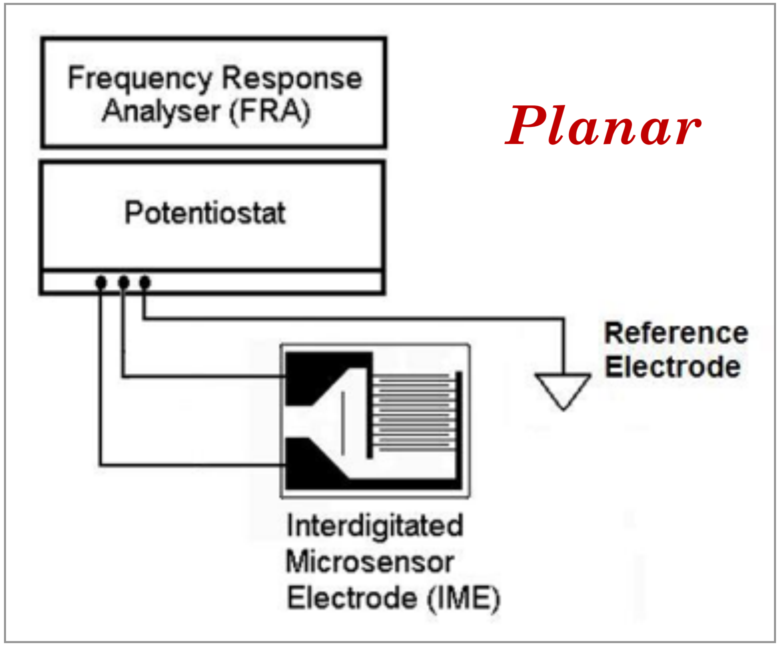
Muscle

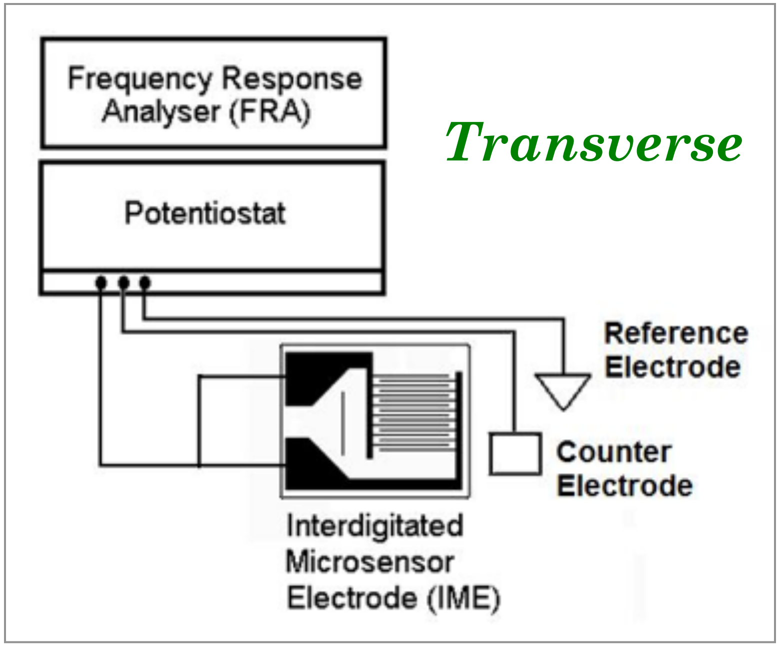
Rim of new connective tissue forming a capsule and some residual inflammation around hydrogel

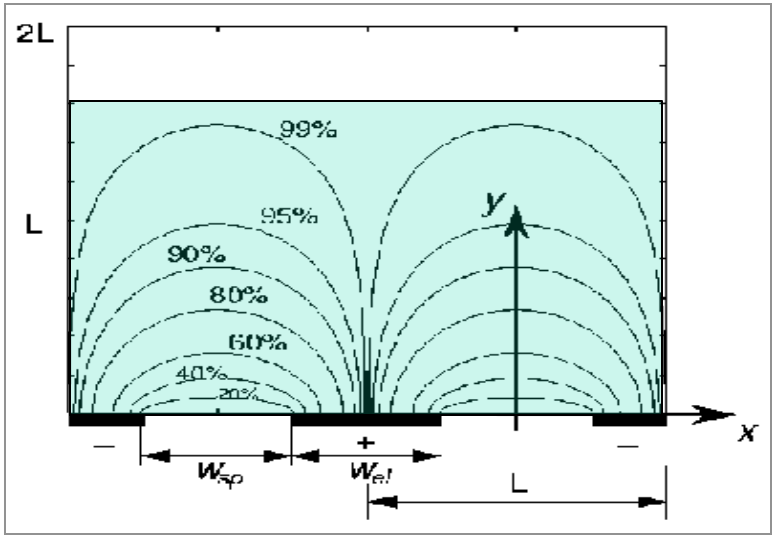
Residual area of Hemorrhage

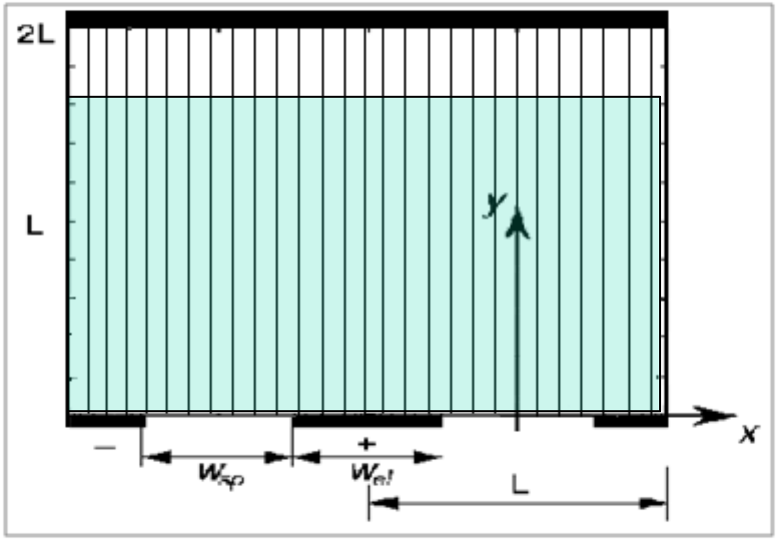
Hydrogel

Electrochemical Impedance of Electroconductive Hydrogels – Planar and Transverse Interrogation

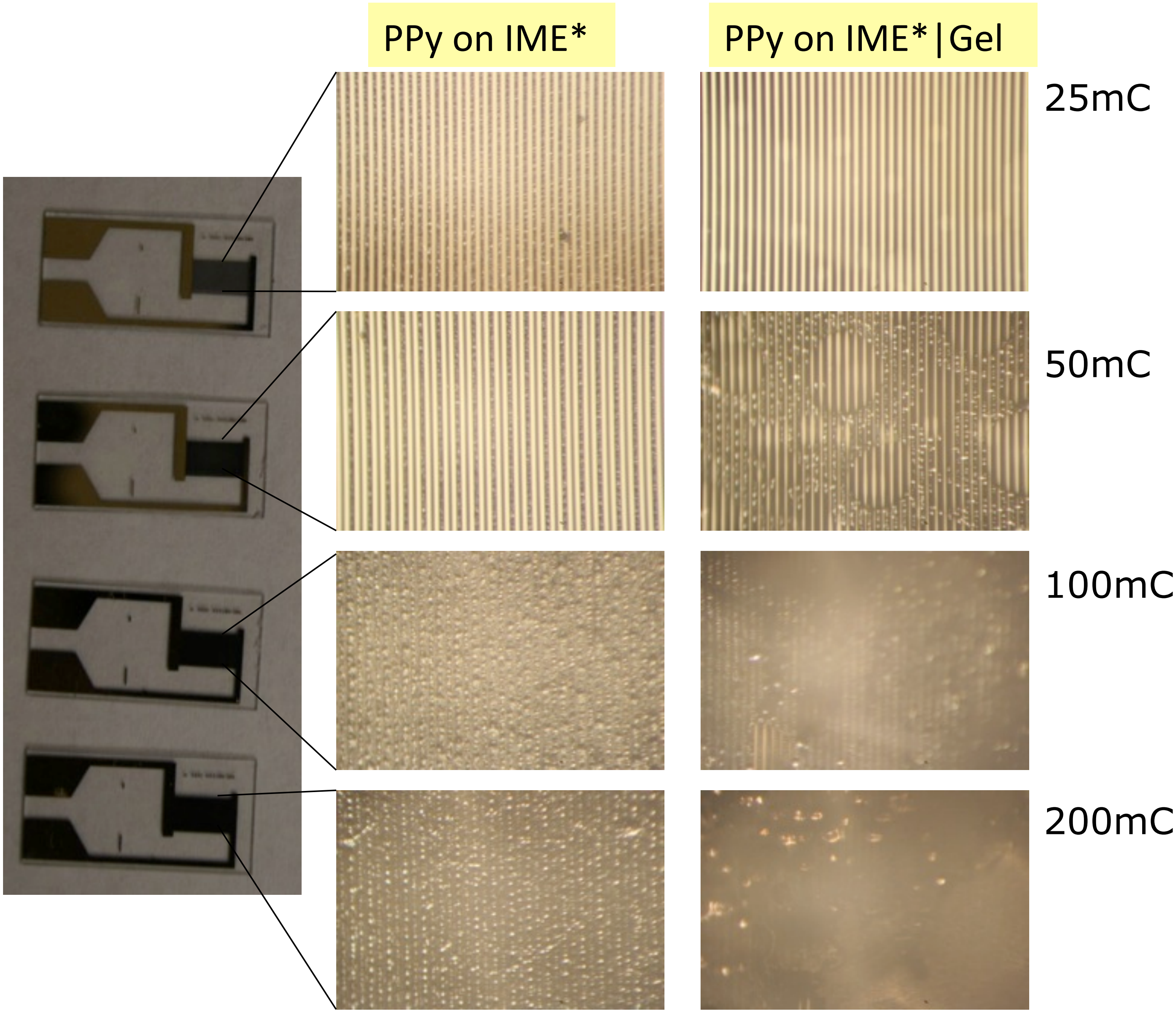






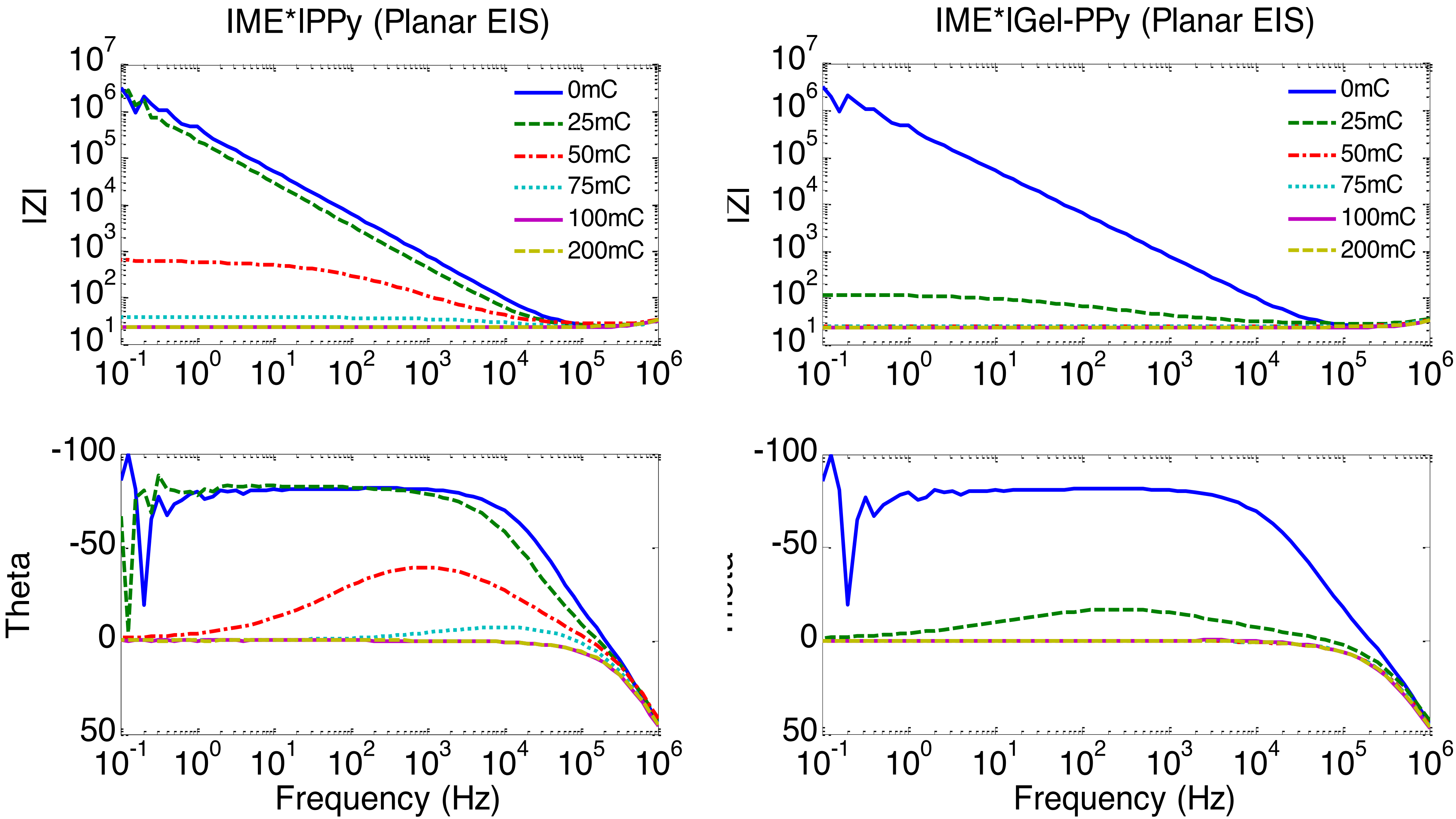


Liju Yang, Adilah Guiseppi-Wilson, Anthony Guiseppi-Elie "Design Considerations in the Use of Interdigitated Microsensor Electrode Arrays (IMEs) for Impedimetric Characterization of Biomimetic Hydrogels" *Biomedical Microdevices* (**2011**) 13(2):279-89.



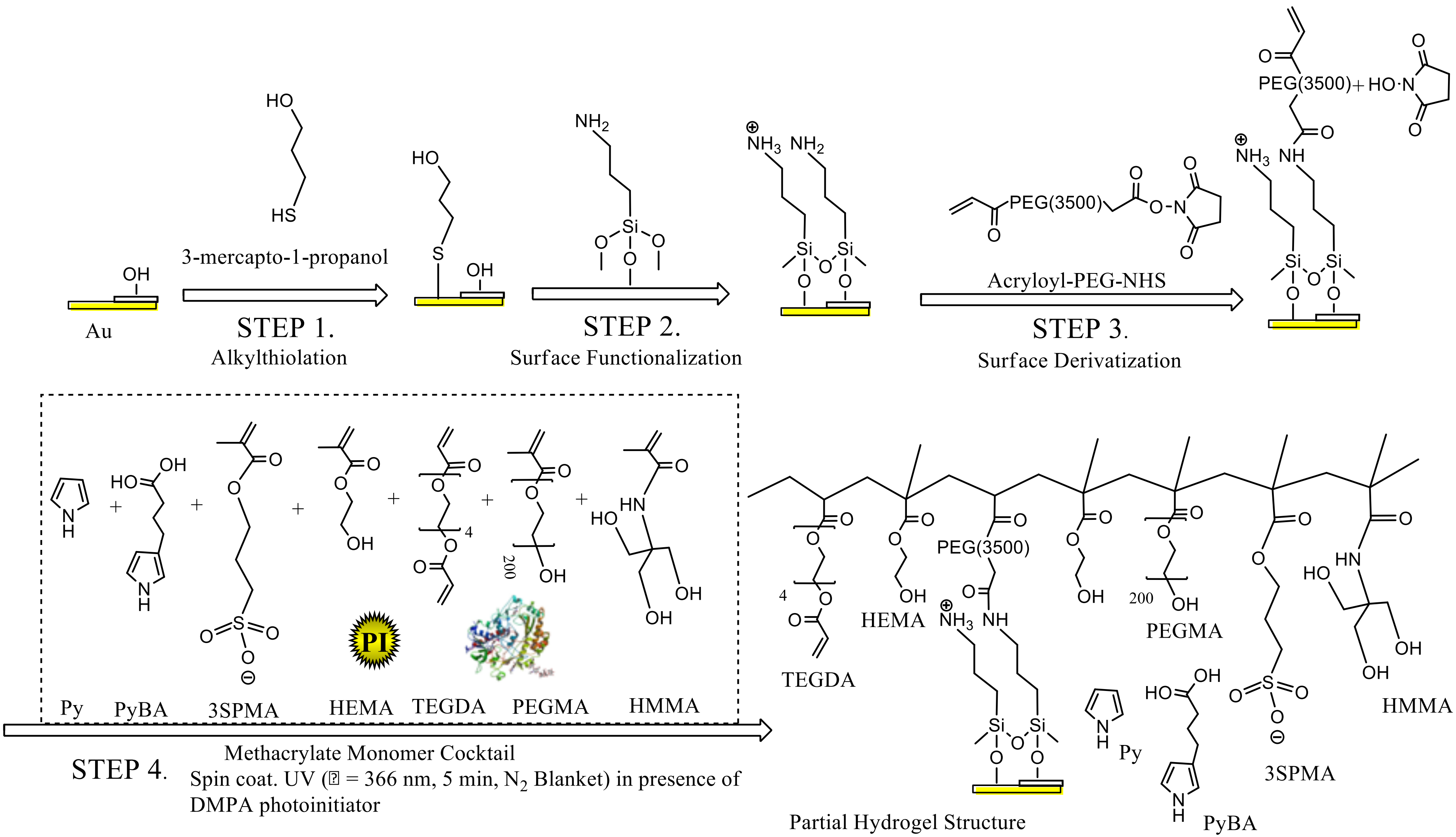
Electropolymerized PPy films grown on IME* (left) and on IME*|Gel devices (right).

Electrochemical Impedance of Electroconductive Hydrogel of P(Py-co-PyBA) vs. PPy - Planar



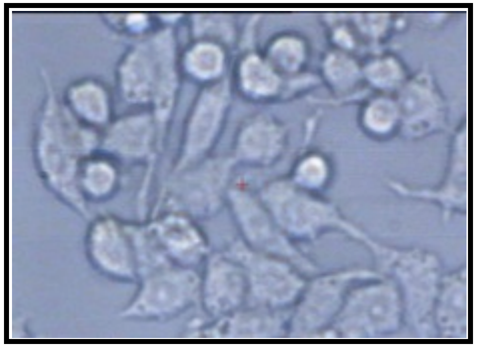
IME*|PPy and IME*|Gel-P(Py-*co*-PyBA) : Planar EIS (co-planar counter and working electrodes). Bode impedance magnitude and phase plots for the IME*|PPy (left) and IME*|Gel-P(Py-*co*-PyBA) (right) measured using the co-planar arrangement of counter and working electrodes.

Substrate surface modification, derivatization, monomer casting and electroconductive hydrogel synthesis

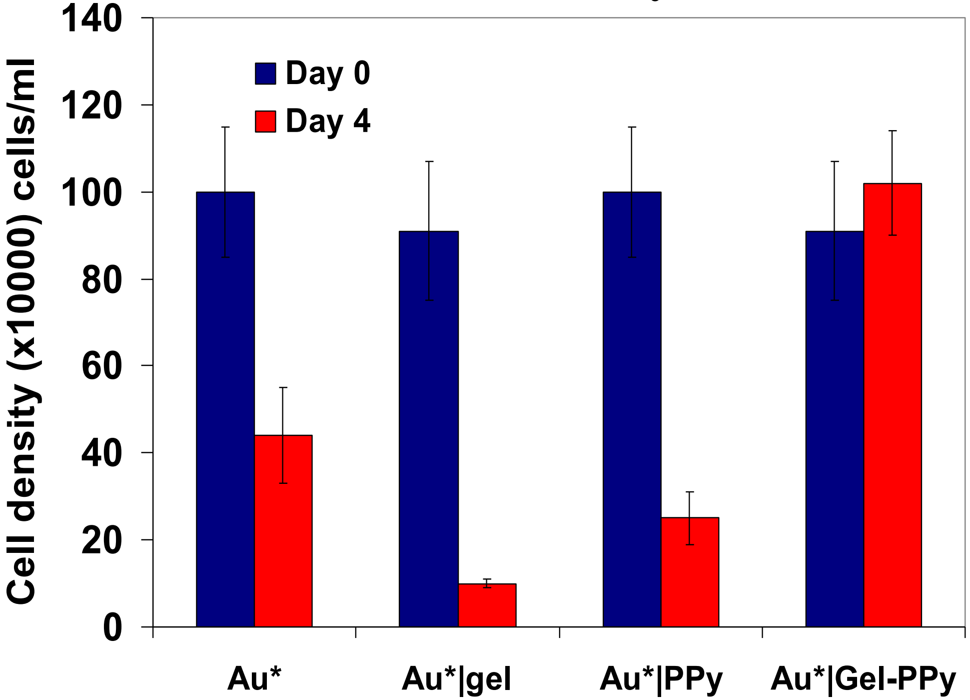


Anthony Guiseppi-Elie, Lauren Koch, Stephen H. Finley and Gary E. Wnek "The Effect of Temperature on the Impedimetric Response of Bioreceptor Hosting Hydrogels" *Biosensors and Bioelectronics* (**2011**) 26(5) 2275–2280.

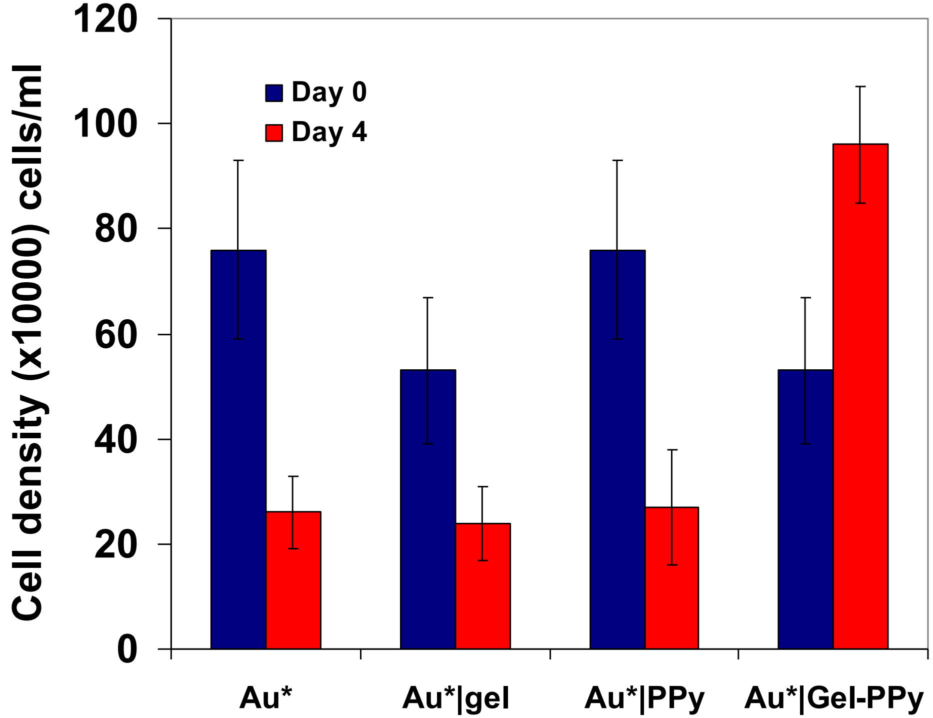
Cell viability as a function of Au electrode surface composition (after 4 days)



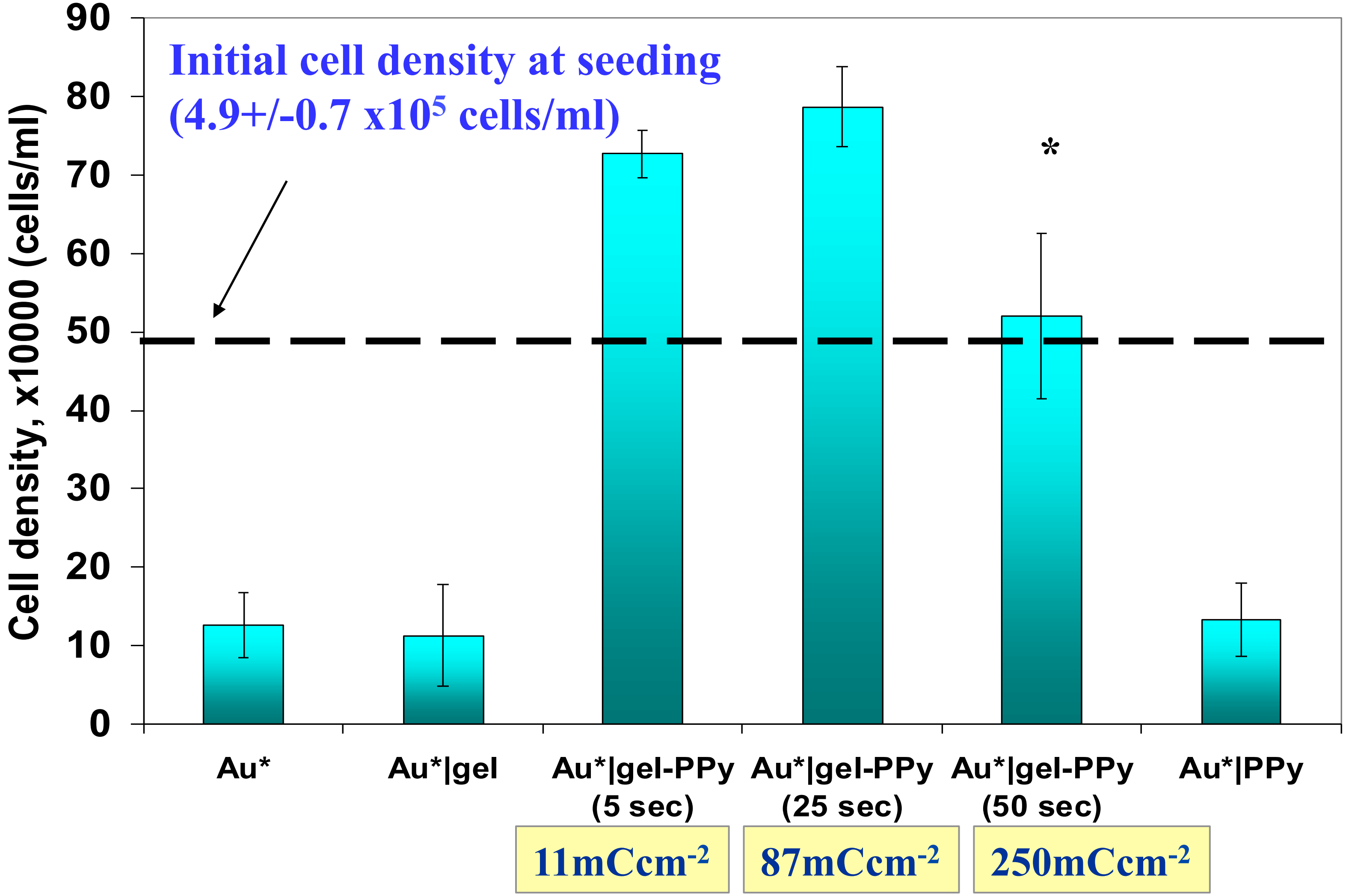
PC12 - Pheochromocytoma



RMS 13 – Human Muscle fibroblasts



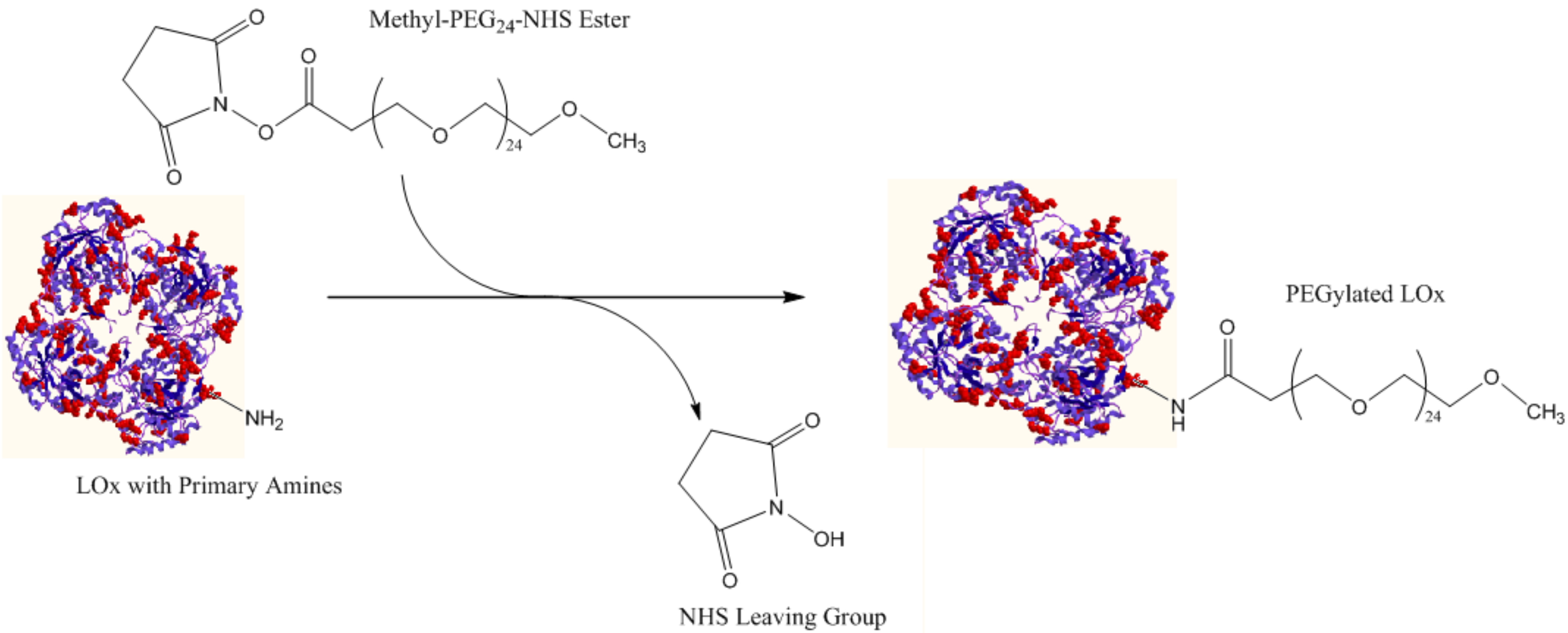
Cell densities following trypsinization (5 min) and enumeration of RMS13 and PC12 pre- (blue bars) and post- (red bars) incubation for 4 days on Au*, Au*|hydrogel, Au*|PPy, Au*|hydrogel-PPy surfaces



Comparison of PC12 cell densities post-incubation (for 4 days) on Au*, Au*|hydrogel, Au*|PPy, Au*|hydrogel-PPy (5, 25 and 50 second electropolymerization times). Initial seeding cell density was 4.9+/-0.7 x10^5 cells/ml (broken line). * Indicates a p-value greater than 0.05.

Gusphyl Justin and Anthony Guiseppi-Elie*, "An Electroconductive Blend of p(HEMA-*co*-PEGMA-*co*-HMMA-*co*-SPMA) Hydrogels and p(Py-*co*-PyBA): In Vitro Biocompatibility" *Journal of Bioactive and Compatible Polymers* (**2010**), 25 (2) 121-140.

PEGylation of LOx at Lysine Residues

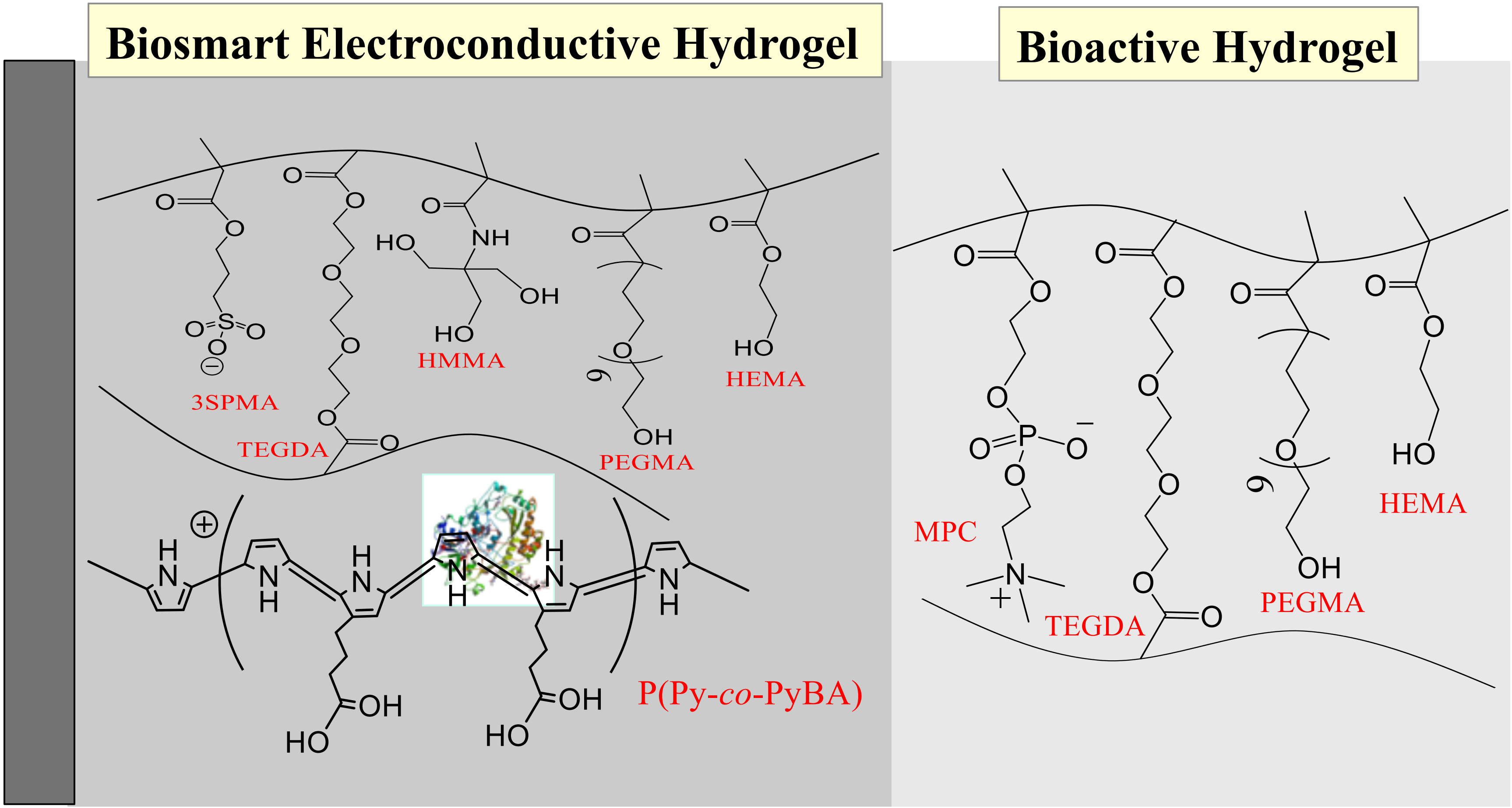


$$\text{L-Lactate} + O_2 \longrightarrow \text{Pyruvate} + H_2O_2$$

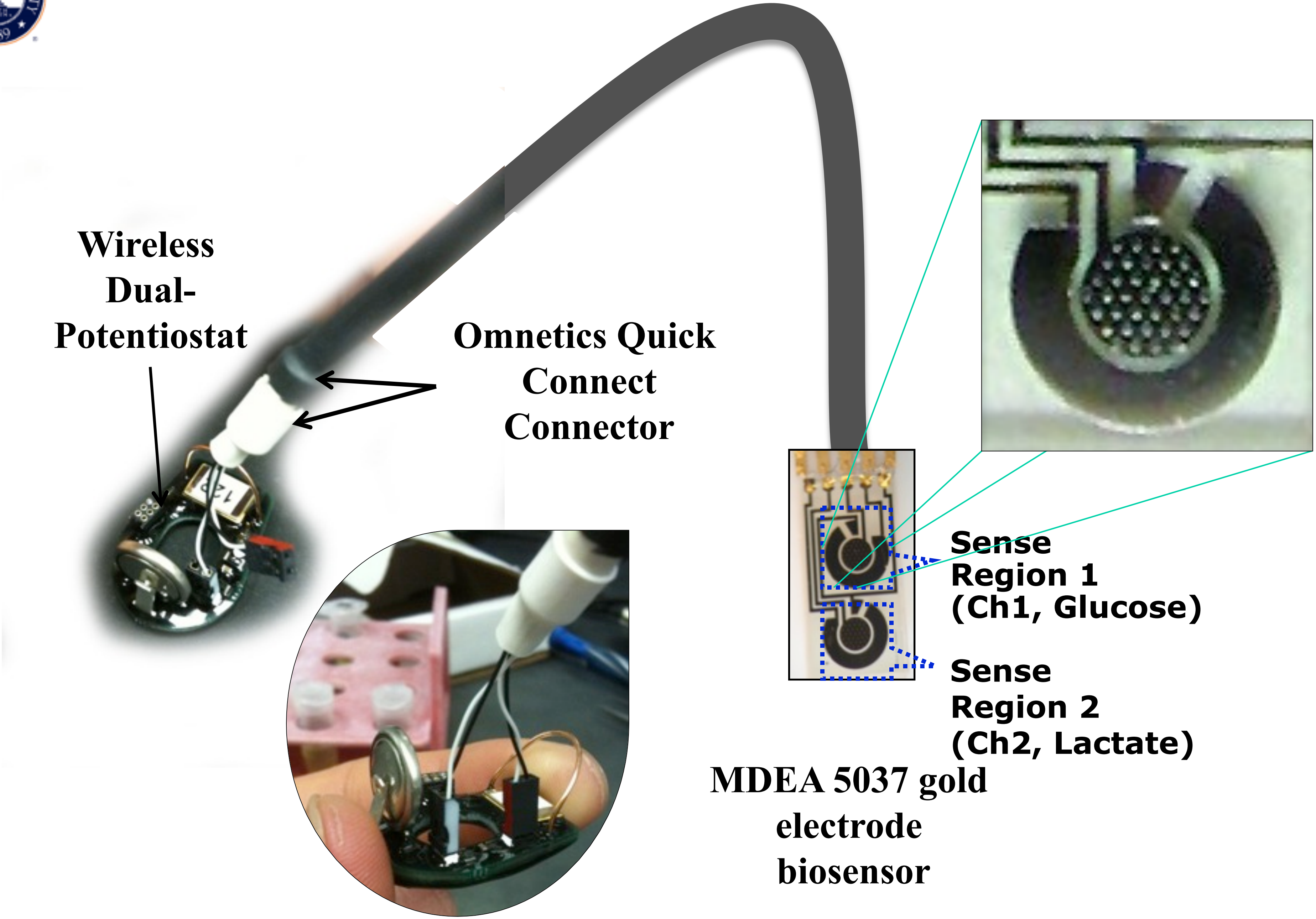
$$\beta\text{-D-glucose} + O_2 \longrightarrow \text{glucono-}\delta\text{-lactone} + H_2O_2$$

- Enzyme activity via kinetic assay: v_{max}, K_M, k_{cat}, k_{cat}/K_M
- MW and MW distribution via capillary gel electrophoresis:

Schematic illustration of the molecular constituents of a poly(HEMA-*co*-PEGMA-*co*-HMMA-*co*-SPMA)/P(Py-*co*-PyBA) electroconductive hydrogel containing an oxidoreductase enzyme and bioactive hydrogel topcoat containing phosphoryl choline (MPC).

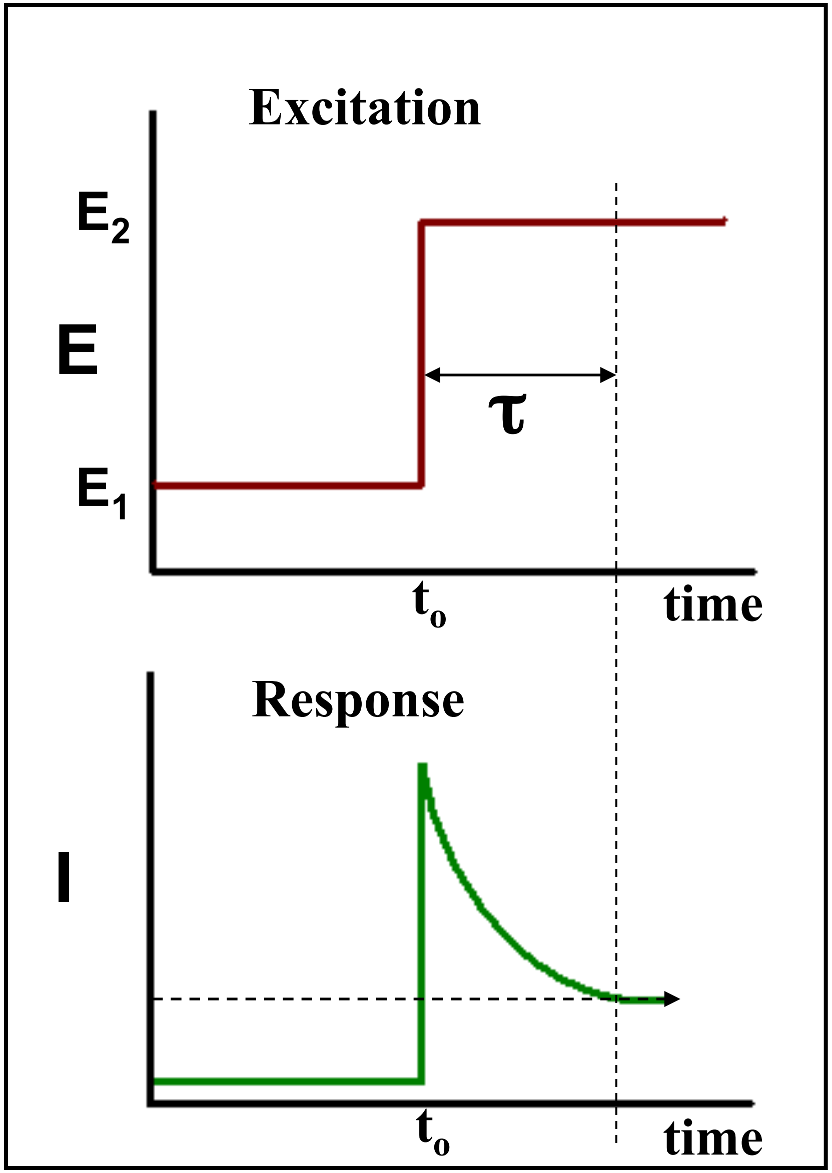


Anthony Guiseppi-Elie "Electroconductive Hydrogels: Synthesis, Characterization and Biomedical Applications" *Biomaterials*, (**2010**) 31(10) 2701-2716.



Abdur Rub Abdur Rahman, Gusphyl Justin, Adilah Guiseppi-Wilson and Anthony Guiseppi-Elie* "Fabrication and Packaging of a Dual Sensing Electrochemical Biotransducer for Glucose and Lactate Useful in Intramuscular Physiologic Status Monitoring" *IEEE Sensors Journal* (**2009**) 9(12): 1856-1863

Principle of operation of the amperometric biotransducer



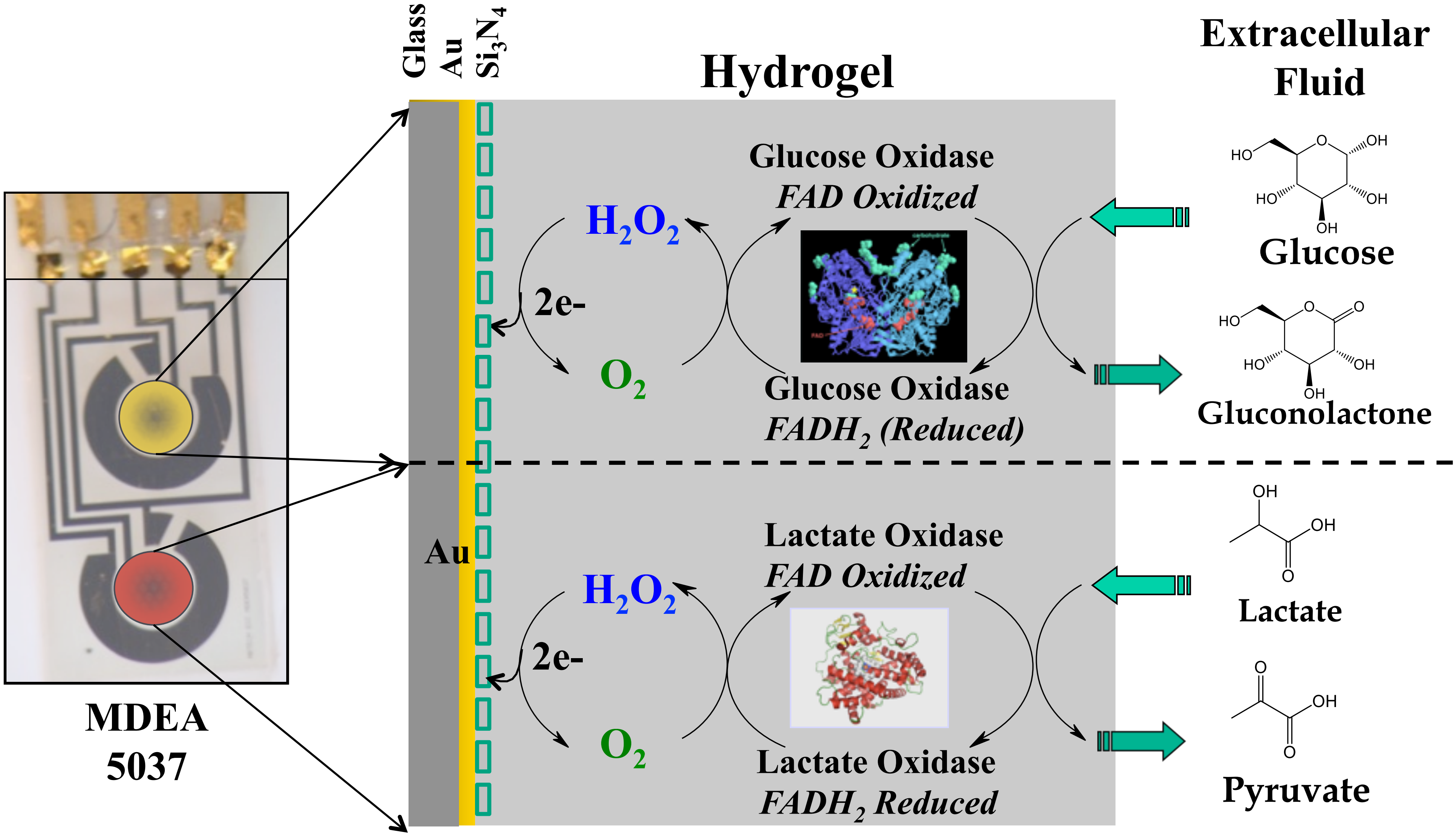
Chronoamperometry (CA)

- ✦ Cottrell's Equation

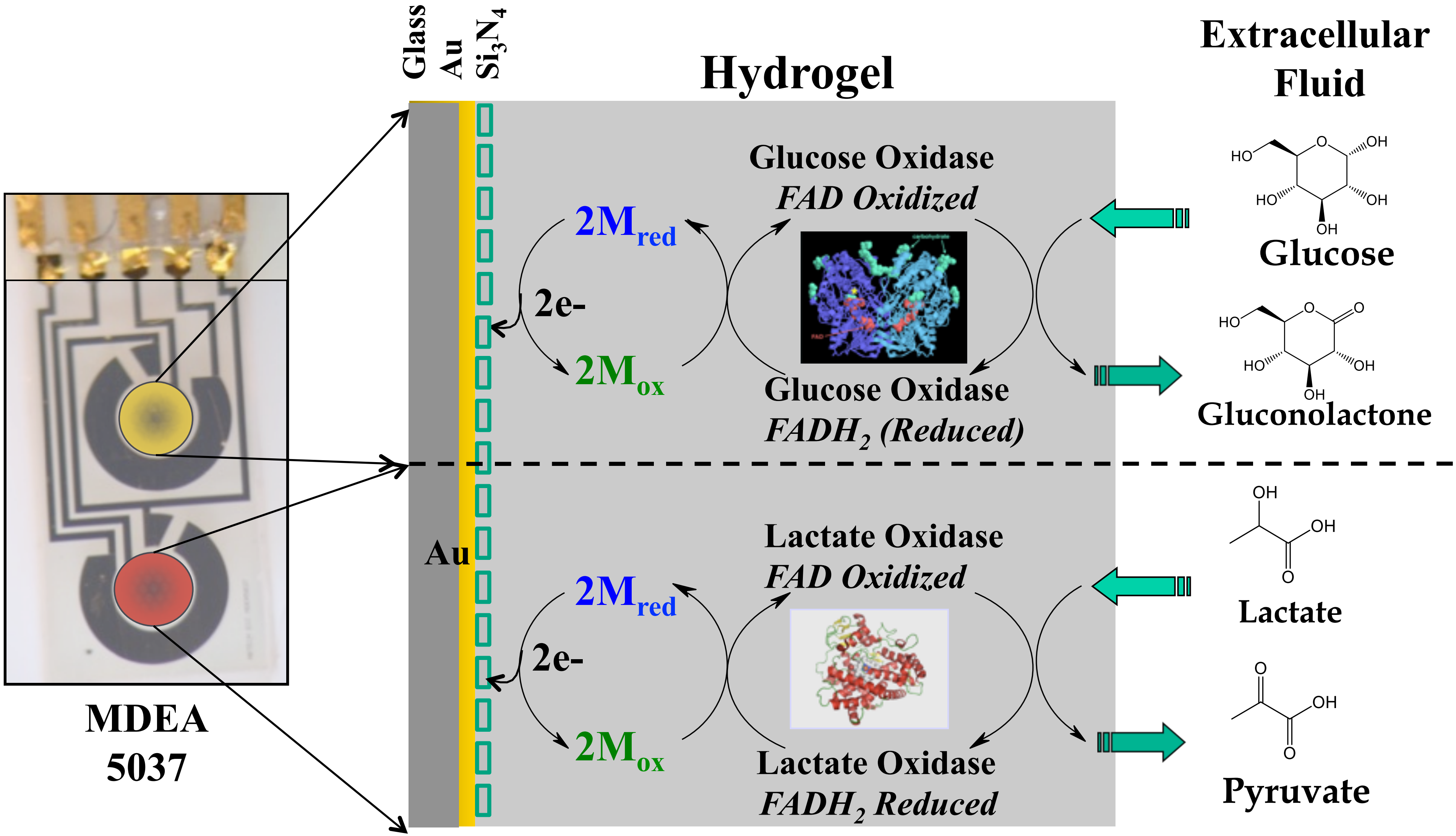
$$i(t) = \frac{nFA\,D_o^{1/2} C_o^{*}}{\pi^{1/2} t^{1/2}}$$

- ✦ E_1- No redox activity
- ✦ E_2- $|E| > E°'$
- ✦ τ - step size (determined experimentally)
- ✦ Quiescent solution

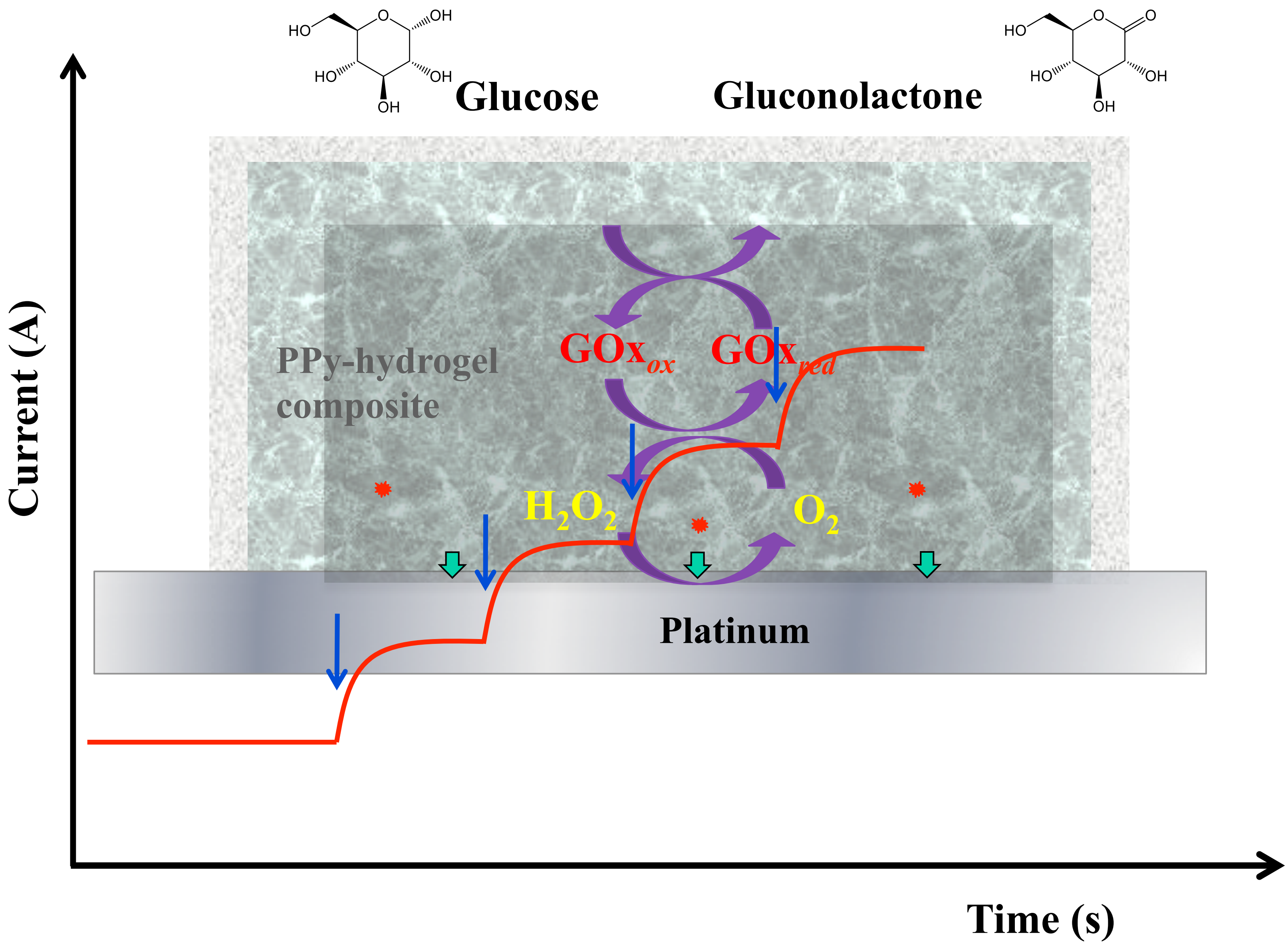
Fabrication of the electrochemical p(HEMA)/Glucose and Lactate TYPE I biotransducers



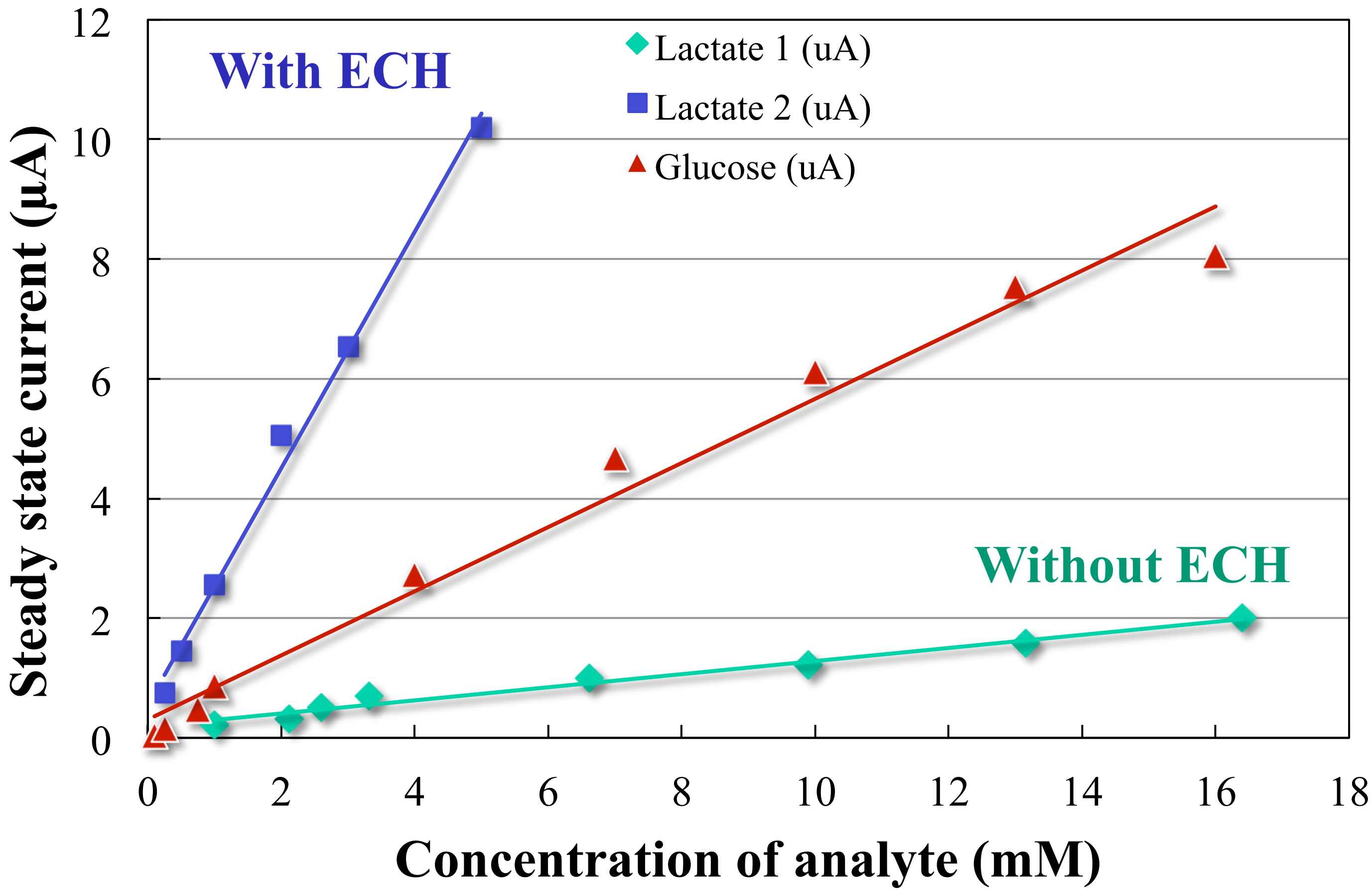
Fabrication of the electrochemical p(HEMA)/Glucose and Lactate TYPE II biotransducers



Evaluation of the electrochemical p(HEMA)/Glucose and Lactate Dose-Response of TYPE I biotransducers

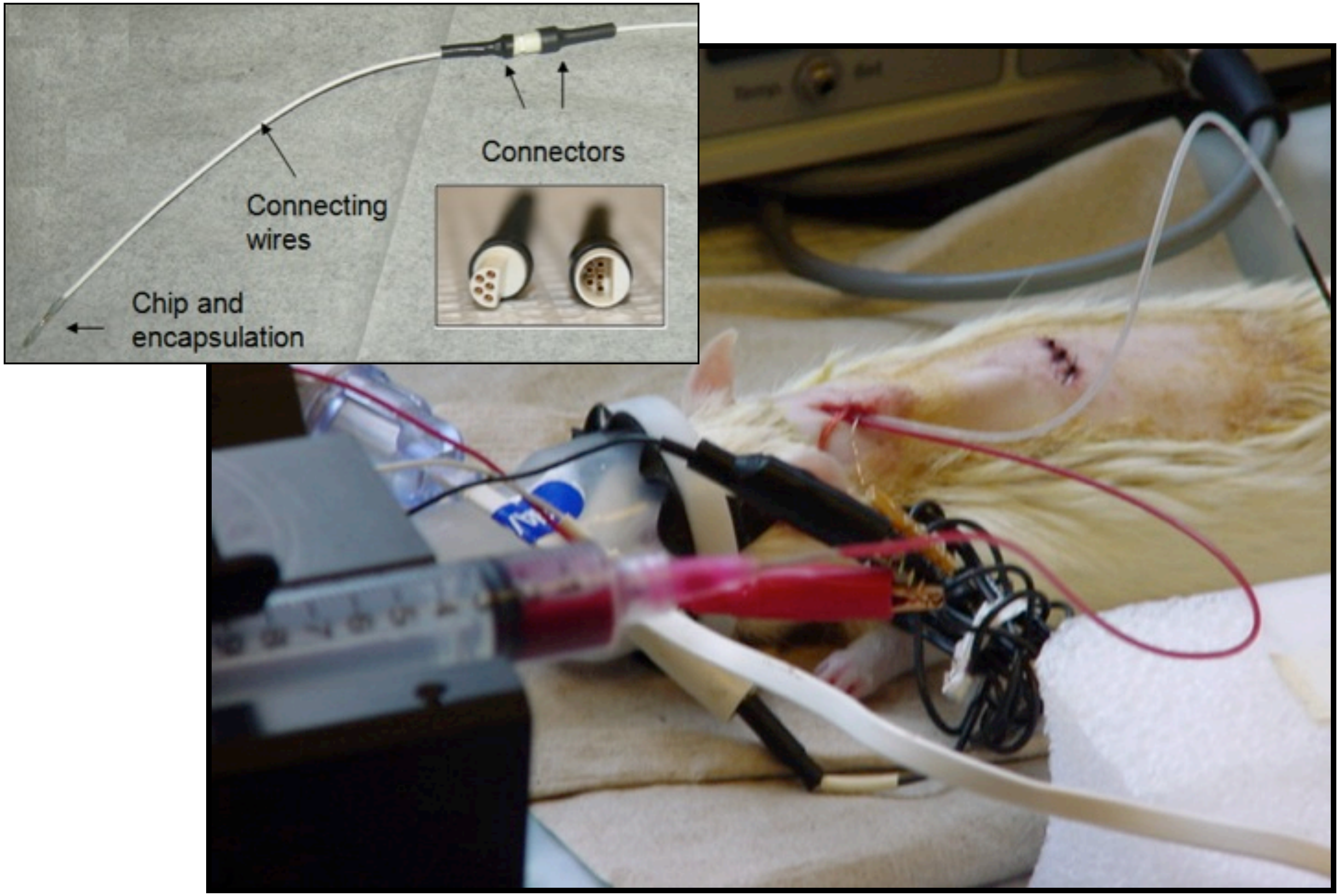


In vitro calibration of the dual responsive glucose and lactate biotransducer – different lactate sensitivities



MDEA 5037 lactate and glucose biosensor incorporating electroconductive polymer bio-smart hydrogel membrane of composition 80:10:2.5:2.5:5.0 mol% (HEMA:TEGDA:PEGMA:MPC:Py) in 0.1 M PBKCl, pH 7.0 at RT.

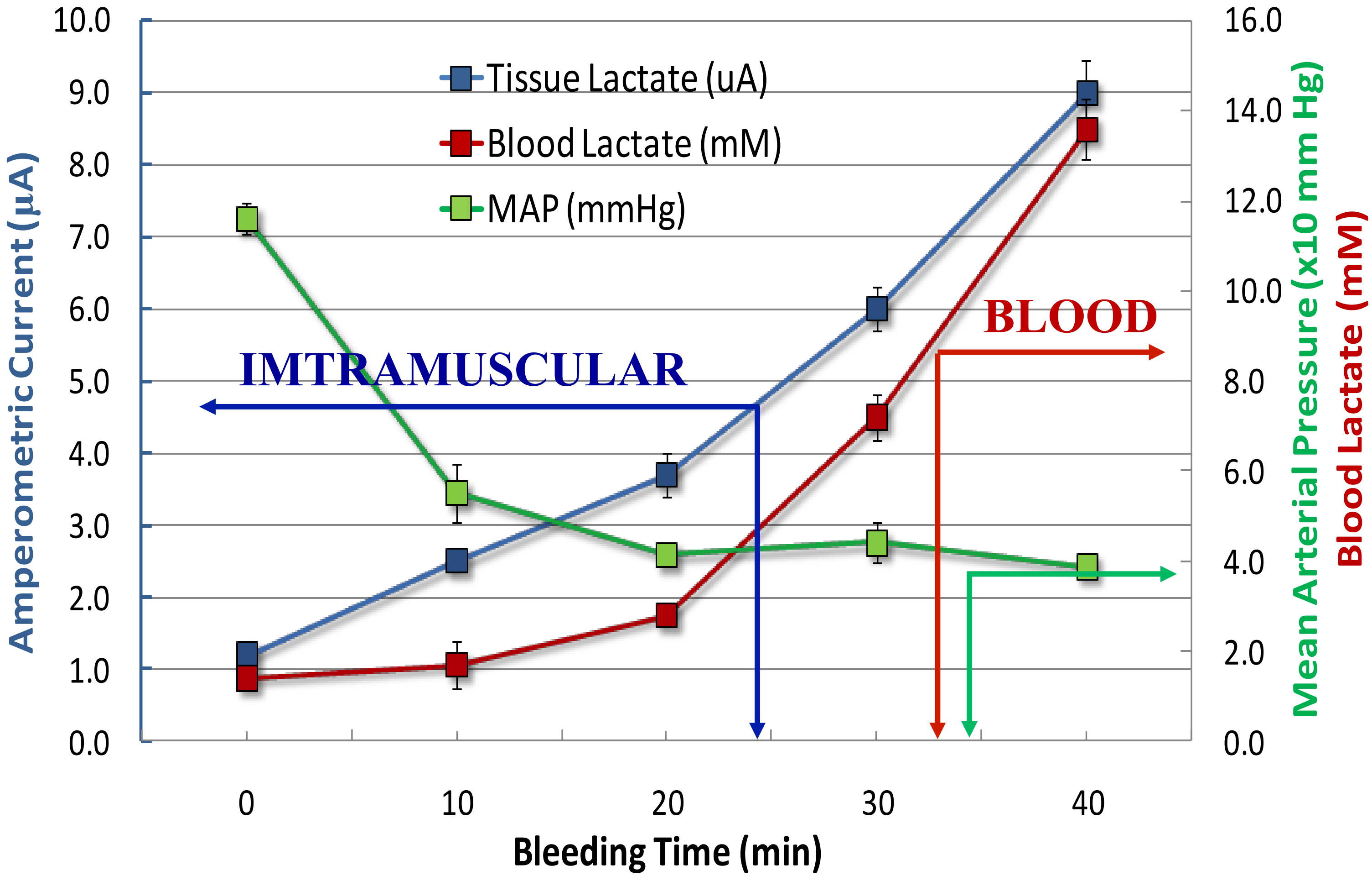
A catheterized and instrumented Sprague Dawley rat under controlled hemorrhage conditions with intramuscularly (trapezius) implanted PSM Biochip.



Christian Kotanen and Anthony Guiseppi-Elie "Development of an implantable biosensor system for physiological status monitoring during long duration space flights" *Gravitational and Space Biology* (**2010**), *23(2) 55-63*

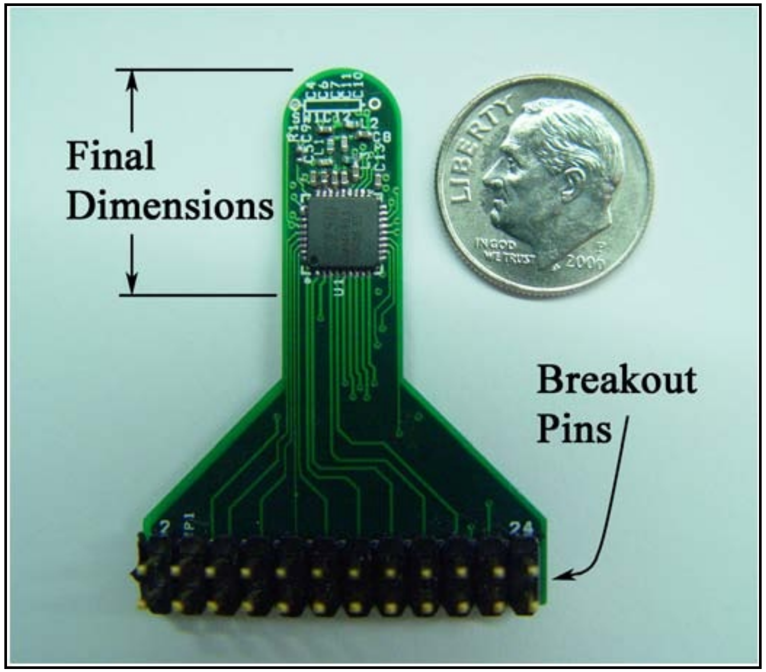
In vivo amperometric performance of the implanted PSMBioChip during hemorrhage – Sprauge Dawley rat model.

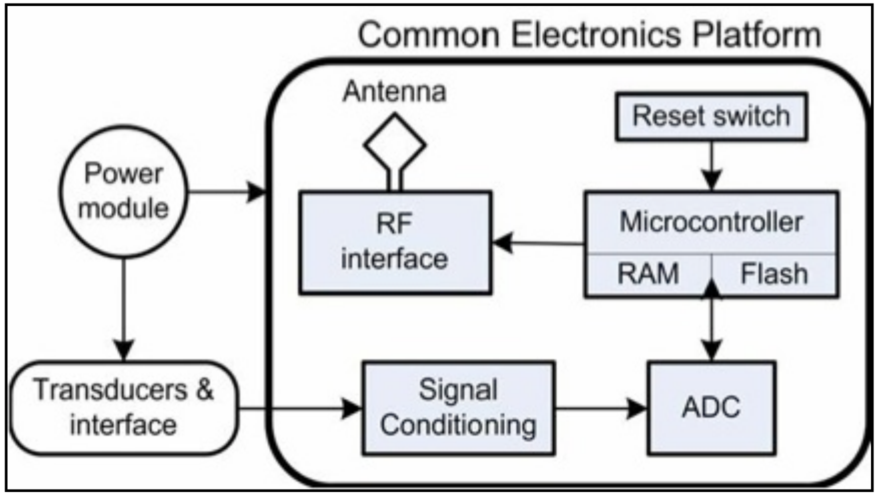
Amperometric response of an intramuscularly implanted lactate biosensor during hemorrhage, the mean arterial pressure (MAP) and the systemic blood lactate obtained using a YSI Biostat Bioanalyzer.

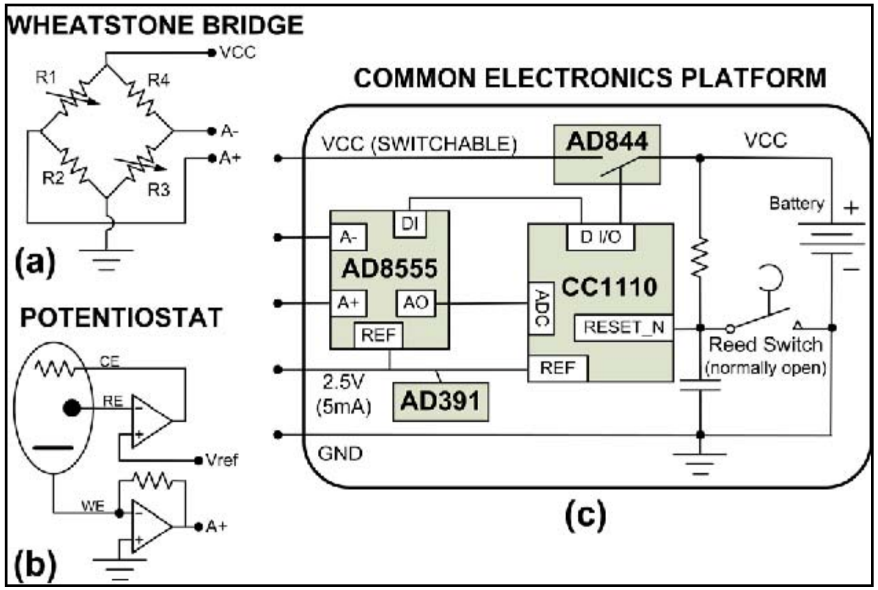


Anthony Guiseppi-Elie "An Implantable Biochip to Influence Patient Outcomes Following Trauma-induced Hemorrhage" *Journal Analytical and Bioanalytical Chemistry* (**2011**) 399(1), 403-419.

Discrete component prototyping of the PSMBioChip





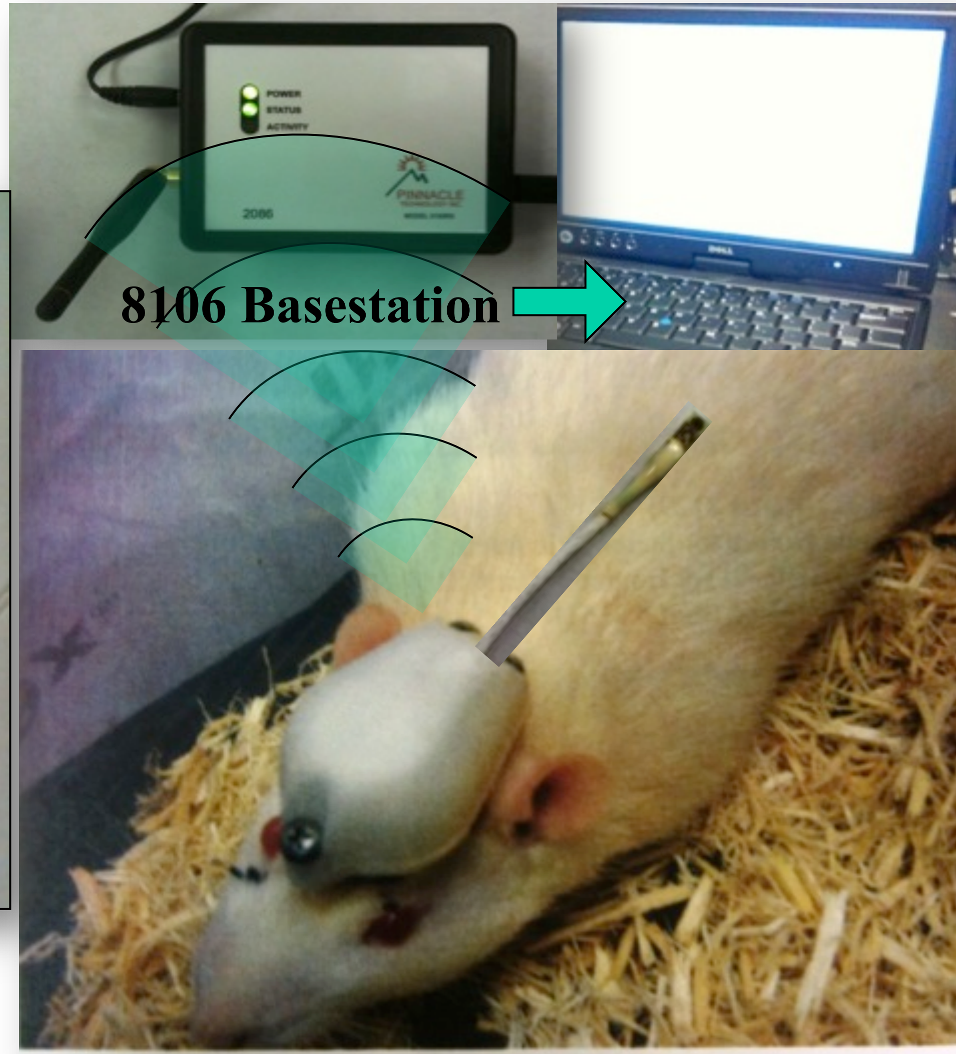


TI /ChipCon CC1110

- 8051 Microprocessor
- 9-14 bit ADC
- RF Transcever
  - MICS: 402-405 MHz

R. H. Farahi, T. L. Ferrell, A. Guiseppi-Elie and P. Hansen, "Integrated Electronics Platforms for Wireless Implantable Biosensors" *IEEE Transactions Life Science Systems and Applications Workshop* (**2007)** IEEE/NIH, p 27–30.

A Sprague Dawley rat equipped with a head mounted wireless transmitting dual potentiostat to support intramuscular bioanalytical measurements of lactate and glucose in the trapezious muscle.

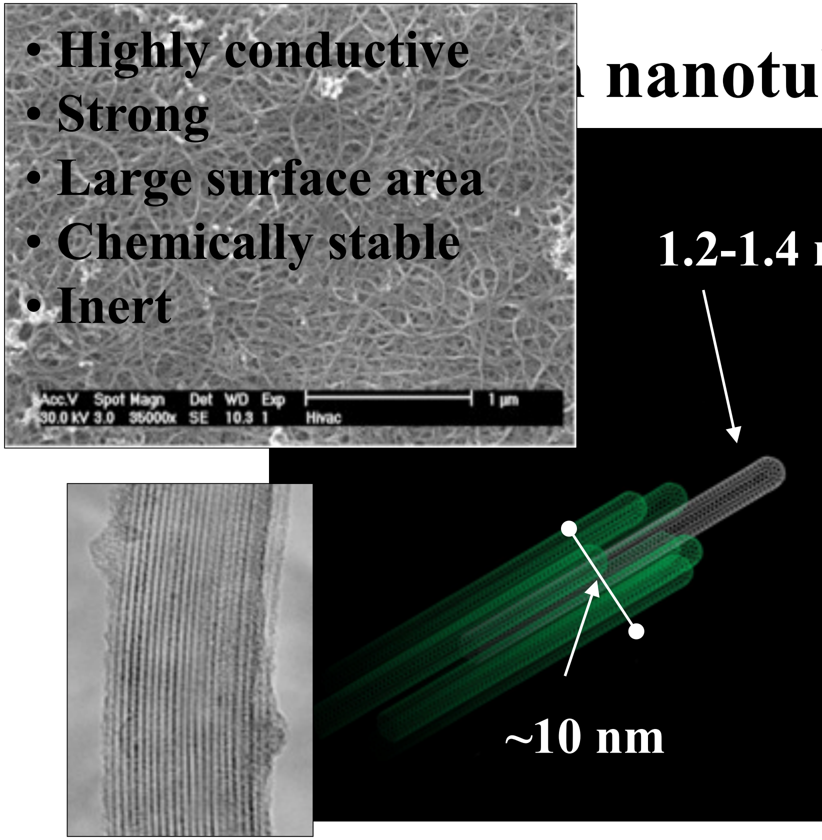


Status

- CDMRP funded small vertebrate animal studies ongoing at Clemson University
- IP ownership released by Clemson University to Guiseppi-Elie, successfully transferred to ABTECH Scientific, Inc.
- Collaborative program established with Tripler Army Medical Center – Dr. Catherine Uyehara, Chief, Dept. Clinical

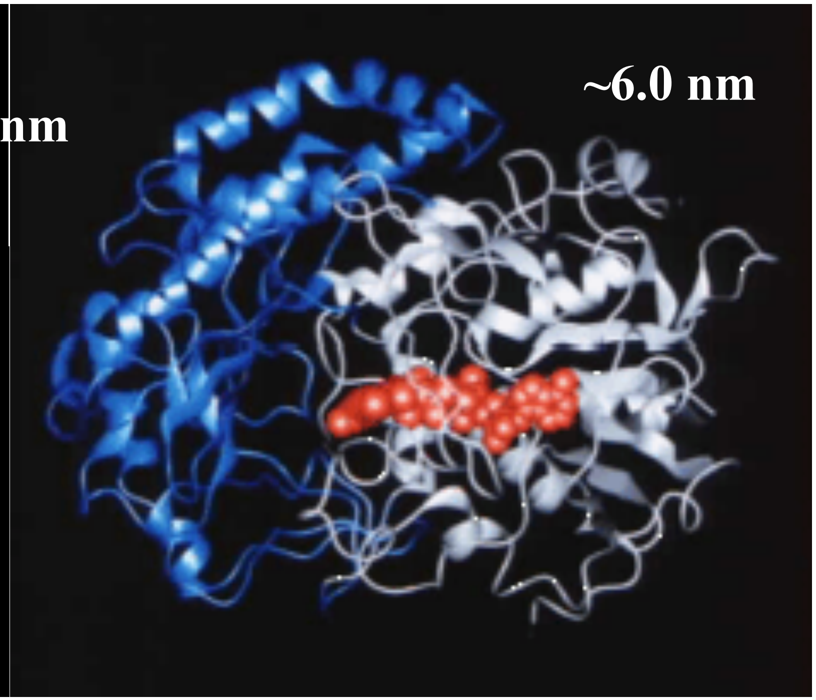
Molecular Bioelectronics: Direct Electronic Control of Enzyme Kinetics Enabled by Compatibility of Scales – TYPE III Biotransducers

Nanotube filaments penetrate the glycoprotein shell and attain tunneling proximity to the cofactor. Impact on bioactivity via denaturation is minimum.



Carbon nanotubes
Courtesy: CNST

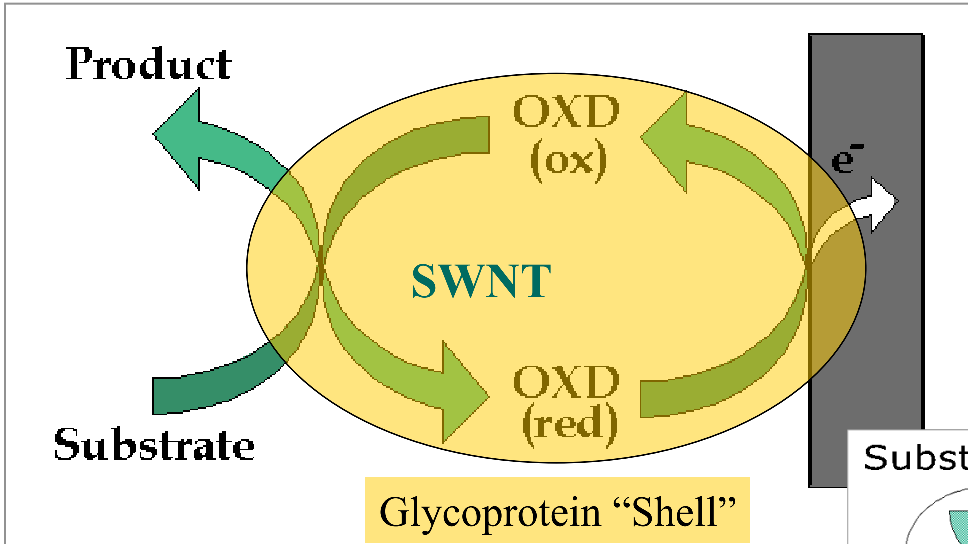
Enzyme subunit



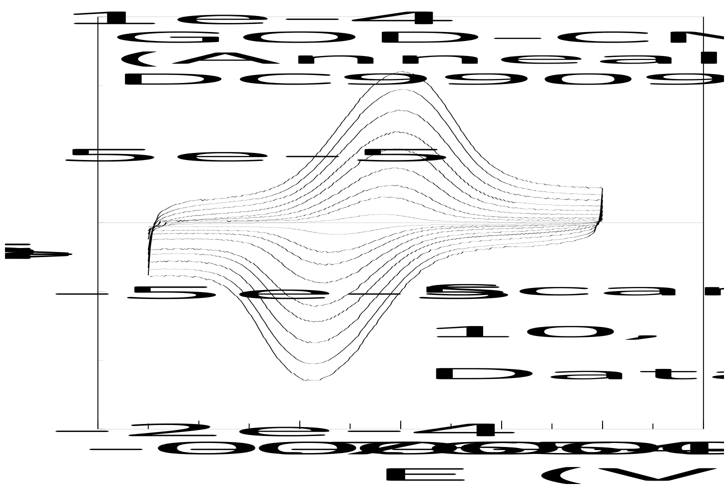
Glucose oxidase
Courtesy: NCBI

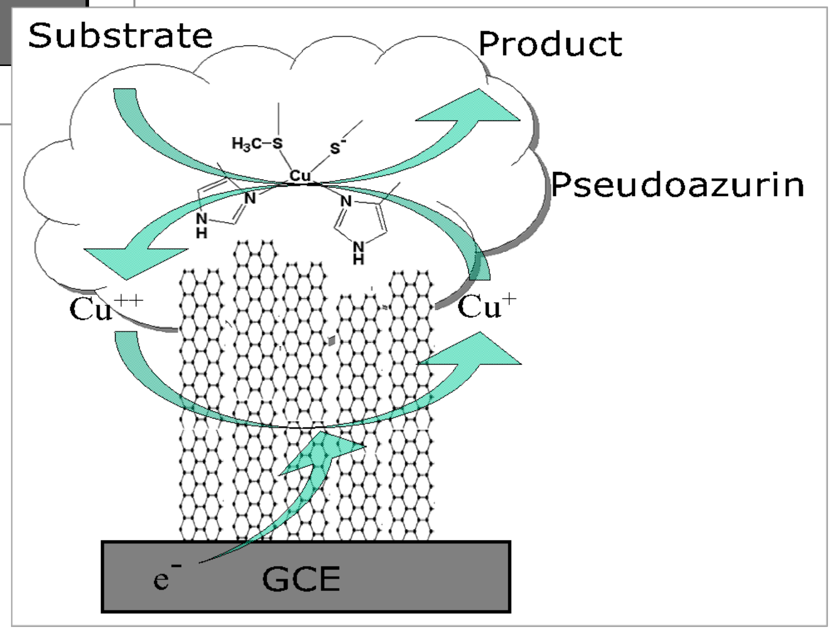
A sphereoidal shape:
6.0 nm x 5.2 nm x 3.7 nm

Amperometric enzyme biosensor - *Direct*



Direct Biosensor
No mediator molecule needed
Oxidation possible
Reduction possible

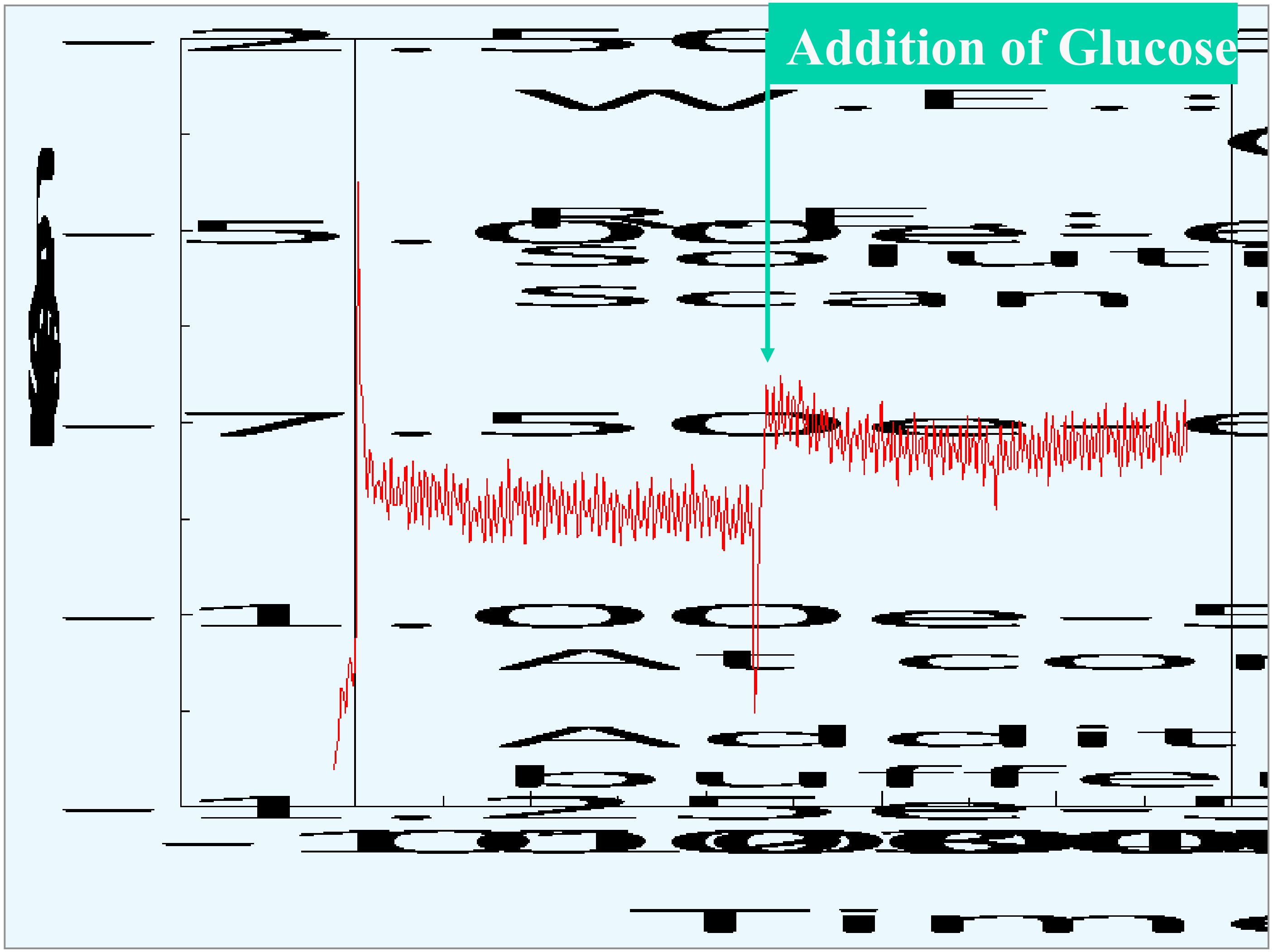




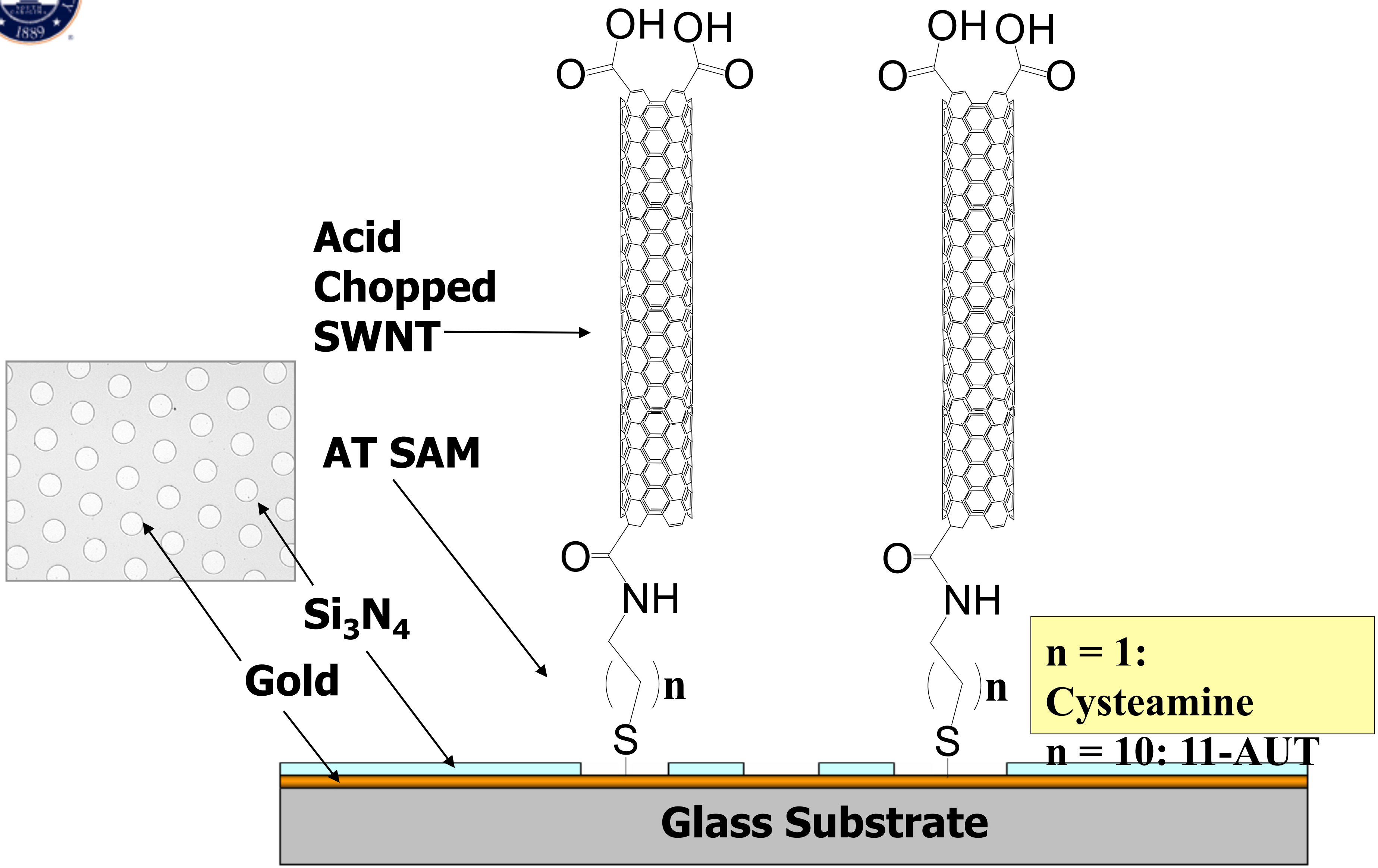
Sean Brahim, Nikhil K. Shukla and Anthony Guiseppi-Elie "Nanobiosensors: Carbon Nanotubes in Bioelectrochemisty" In *Nanotechnology in Biology and Medicine* (**2006**), Tuan Vo-Dinh, Ed.; CRC Press, New York

Anthony Guiseppi-Elie, Sean Brahim, Gary Wnek, Ray Baughman, "Carbon Nanotube Modified Electrodes for the Direct Bioelectrochemistry of Pseudoazurin" *NanoBiotechnology* (**2005**), 1(1) 83.

Molecular Bioelectronics
Direct Electronic Control of Enzyme Function



Anthony Guiseppi-Elie, Chenghong Lei and Ray H. Baughman "Direct electron transfer to glucose oxidase using carbon nanotubes" *Nanotechnology* (**2002**) 13 (5) 559-564.



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Summary

- “Bio-smart” materials by design; combining molecular biorecognition (enzymes), biocompatibility (PEG and MPC), interference shielding (PPy) and redox mediation (M) within p(HEMA)-based hydrogel
- Polymers are non-cytotoxic and support excellent viability and restricted proliferation
- *In vitro* measures of biocompatibility are highly correlated with extent of hydration.
- Biotransducer design using E’Cell-on-a-Chip (ECC) microlithographically fabricated microdisc arrays
- Systems integration and form-factor
- Demonstrated physiologic status monitoring


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