Bioactive Hydrogels for Implantable Biosensors

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Acknowledgments

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- DoD USAMRMC PRMRP

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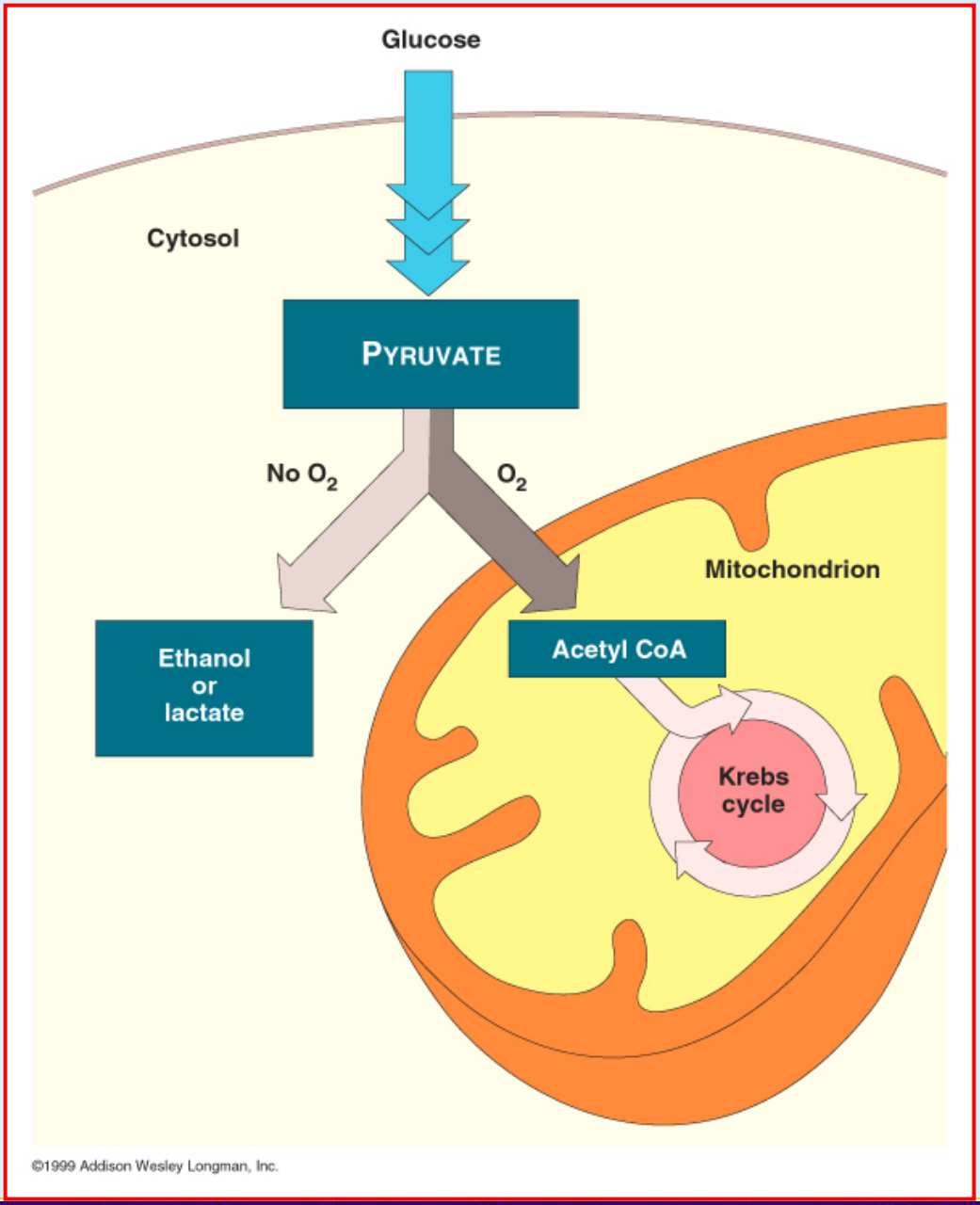
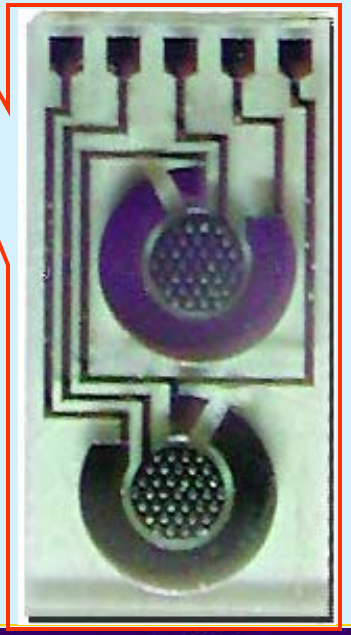
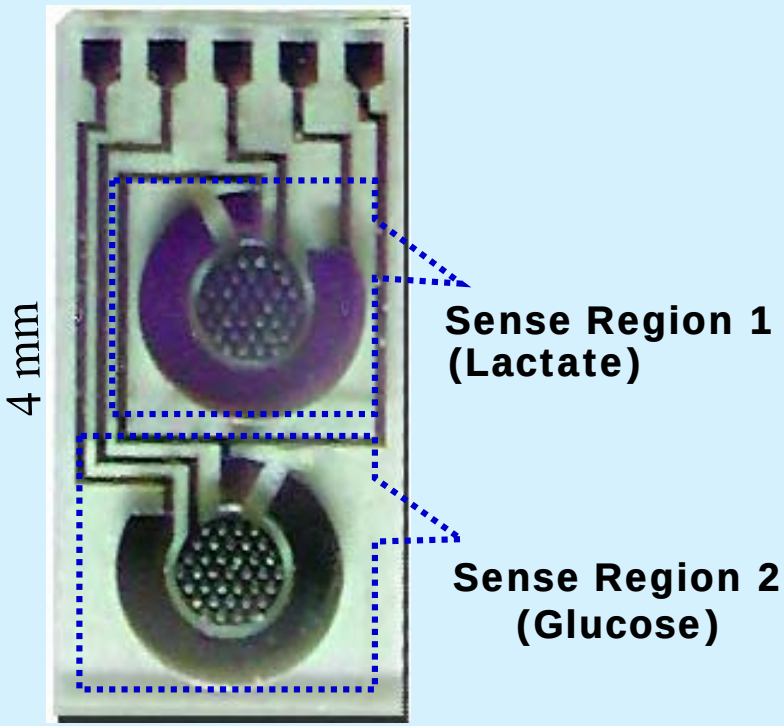
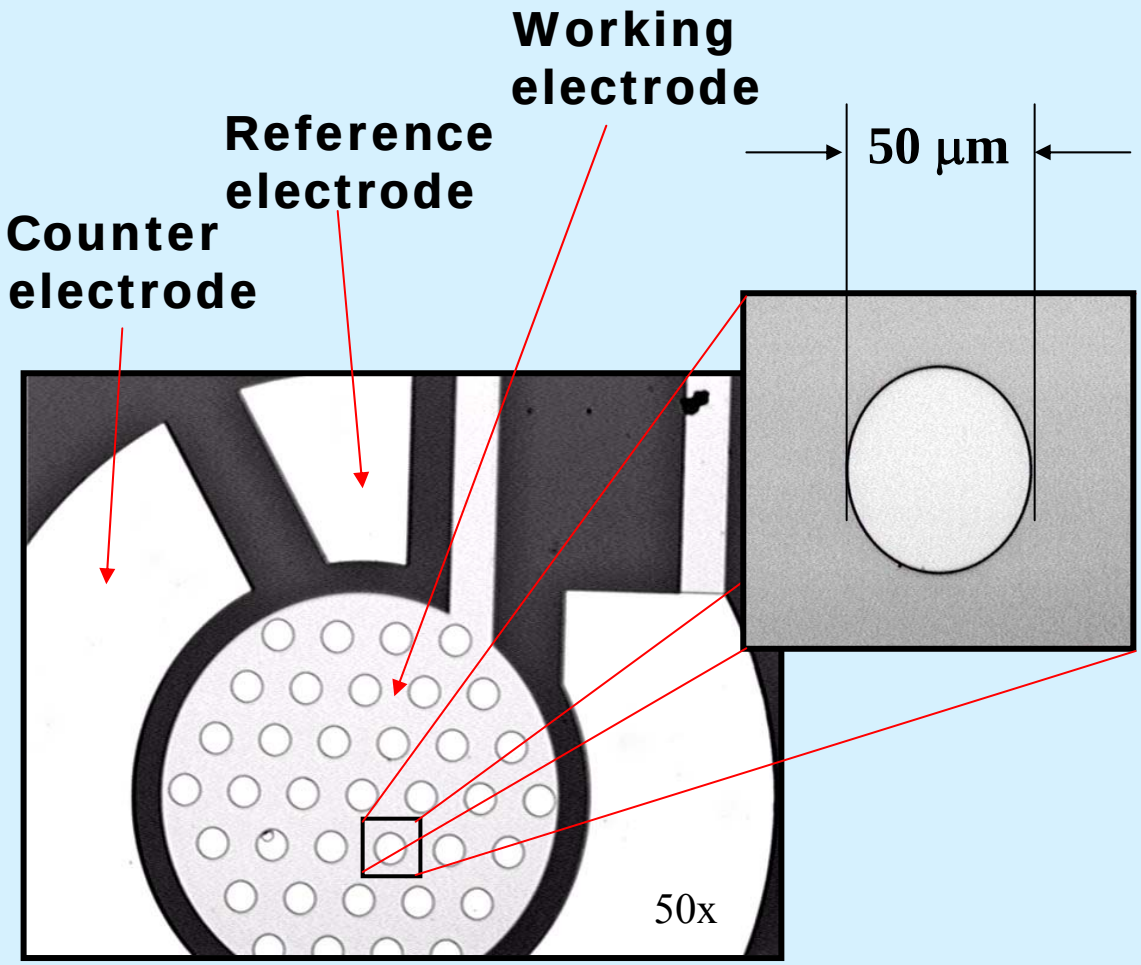
Implantable biosensors for glucose and lactate monitoring in trauma victims



PSMBioChip Biotransducer Prototype





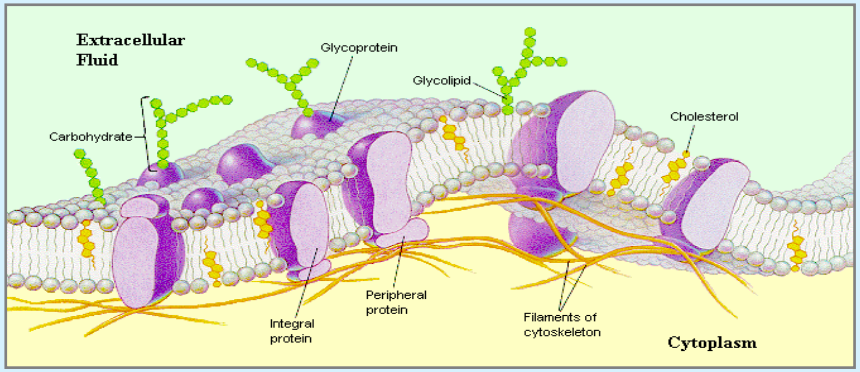


(a) **(b)**

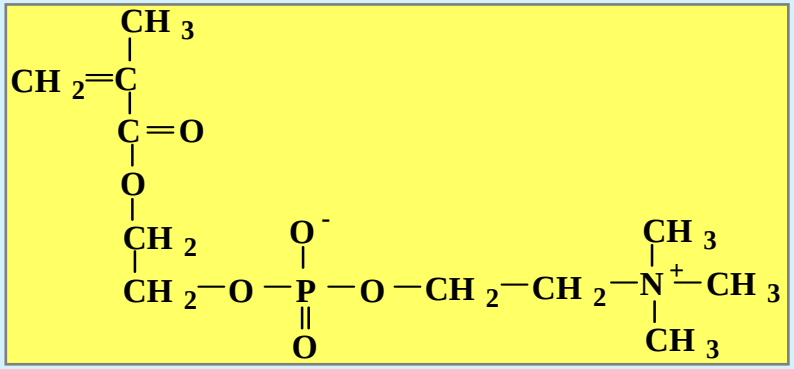
MDEA 5037 comprises 50 micron microdiscs, which number 37

Molecular Engineering Based on Biomimicry to Achieve Implant "Stealth"

- Proteins ***do not foul*** the surface of cells.
- Chapman, et al. (1984) suggested this was due the ***phosphorylcholine*** (PC) head group.
- Mimic the structural composition of a cell membrane by incorporating PC-containing moieties into polyHEMA-based hydrogels – "***Biomimicry***"



Membrane bi-layer

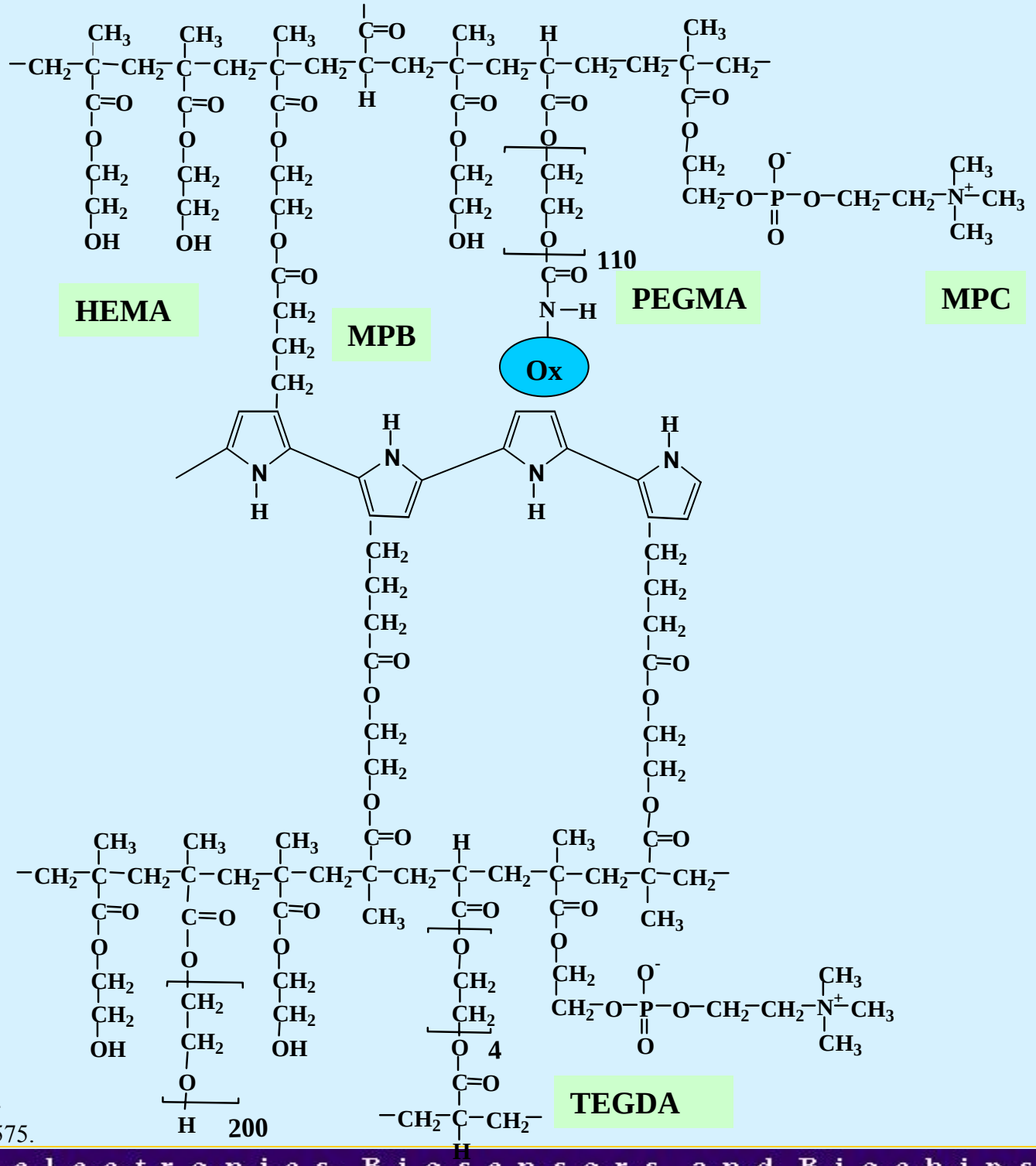


2-Methacryloyloxyethyl Phosphorylcholine (MPC)

Hayward J. A., Chapman D. "Biomembrane surfaces as models for polymer design: the potential for haemocompatibility" *Biomaterials* (**1984**) 4:135-142.

Durrani A. A., Hayward J. A., Chapman D. "Biomembranes as models for polymer surfaces" *Biomaterials* (**1986**) 7:121-125

Structure of the final bioactive composite membrane containing covalently attached enzyme



Guiseppi-Elie et al. *J. Macromol. Sci. - Pure and App.Chem.***(2001)** A38(12), 1575.

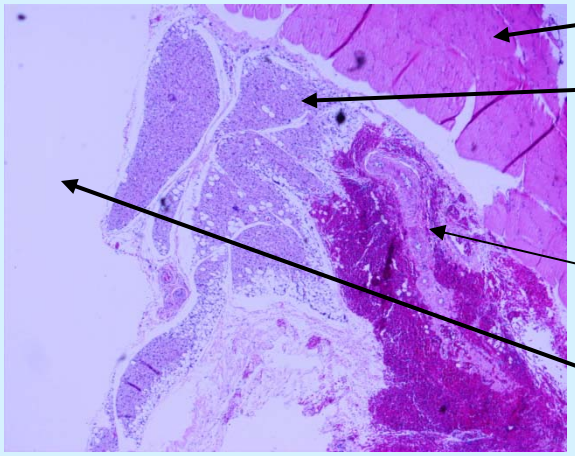
In-vivo Implantation in Sprague Dawley Hemorrhage Model

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

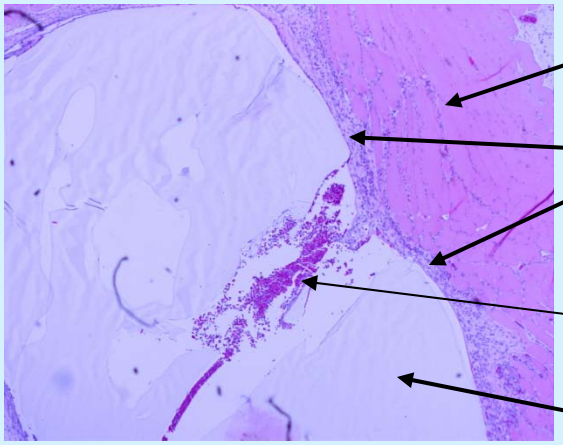
Residual area of Hemorrhage

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

HMF viability and infiltration as a function of PEG and PC content of 3% crosslinked p(HEMA) hydrogel

Human Muscle Fibroblasts (HMF)

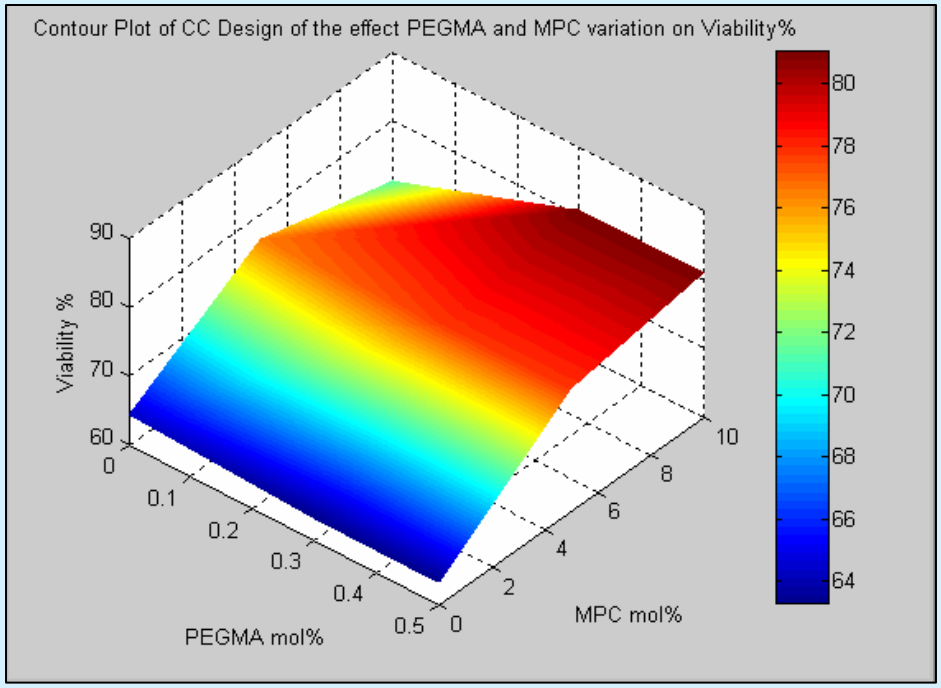
ATCC Designation: SJCRH30 [RC 13, RMS 13, SJRH30]; CRL-2061

Growth Properties: Adherent

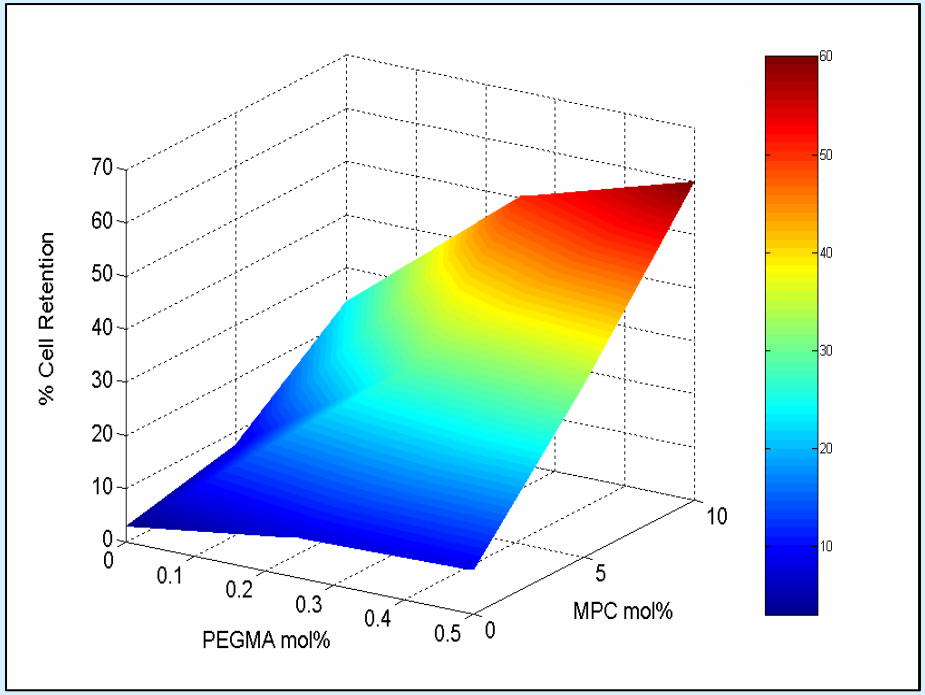
Morphology: fibroblast

Organism: Homo sapiens (human)

Tissue: Muscle, metastatic site



Viability of human muscle fibroblasts as a function of hydrogel composition

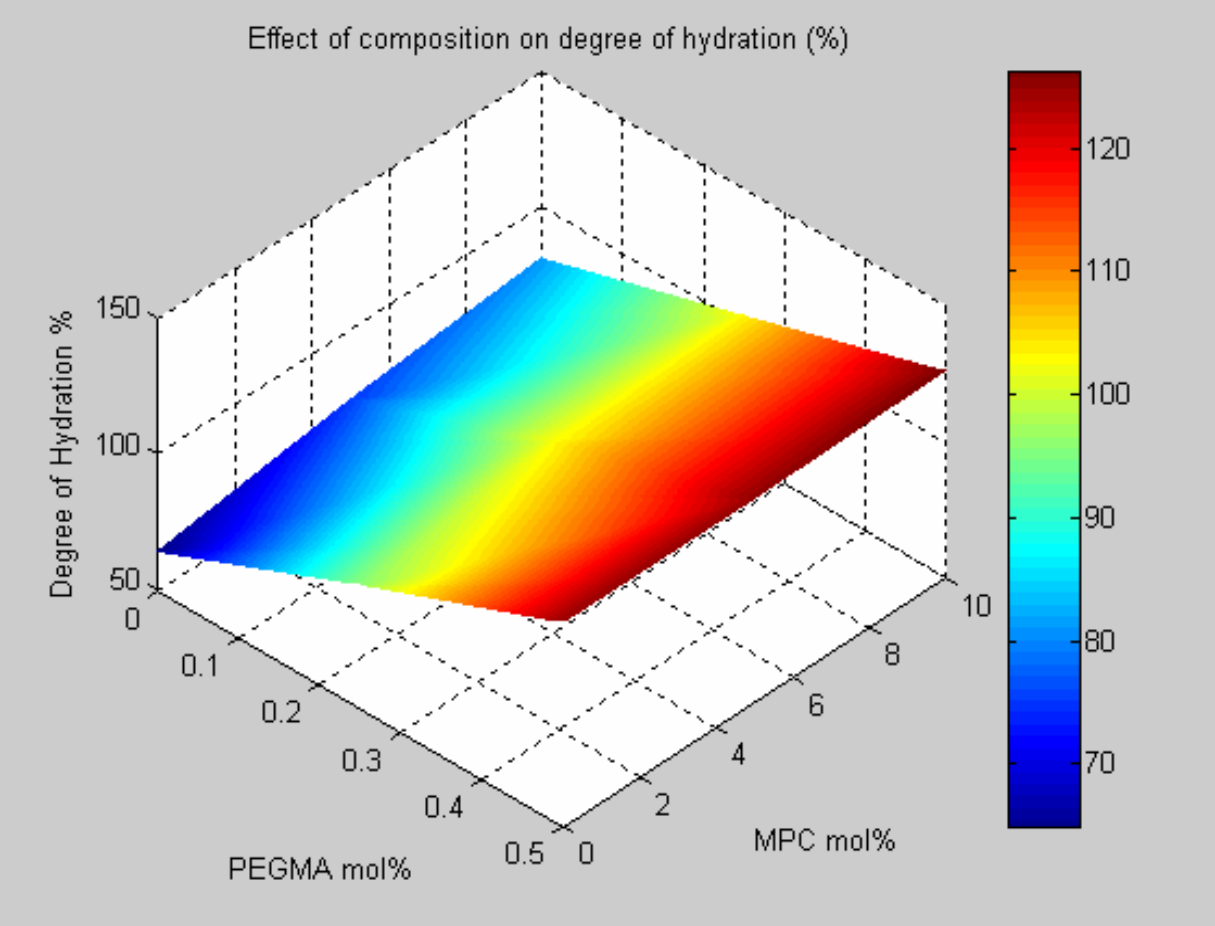


Retention of human muscle fibroblasts as a function of hydrogel composition

Central Composite Design

Hydration as a function of PEG and PC content of 3% crosslinked p(HEMA) hydrogel

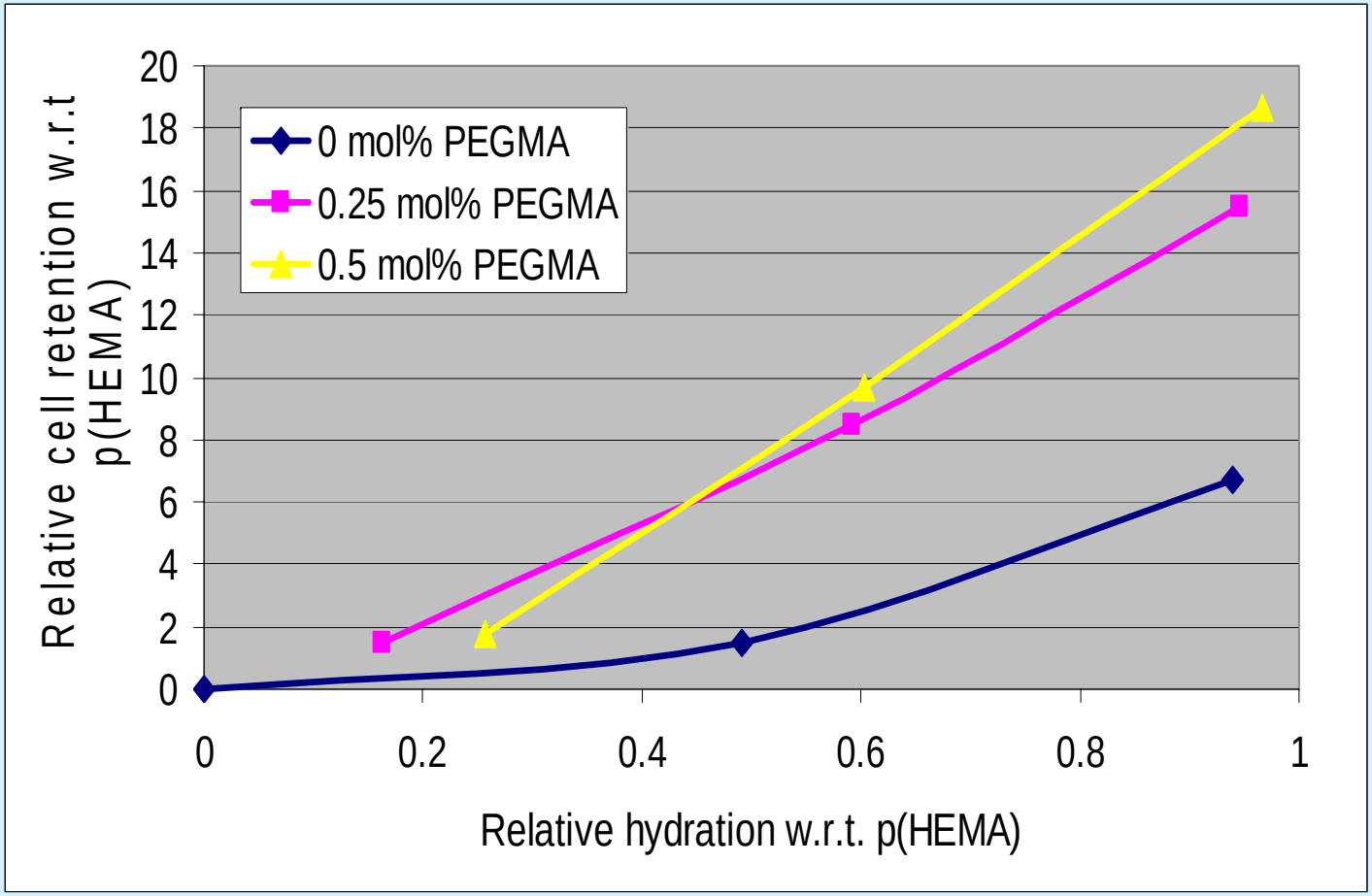
$$\text{Degree of hydration} = \frac{W_{wet} - W_{dry}}{W_{dry}} \times 100$$



Hydration percentage as a function of hydrogel composition

Correlation of cell retention and hydration -- relative to pure 3% crosslinked p(HEMA) polymer.

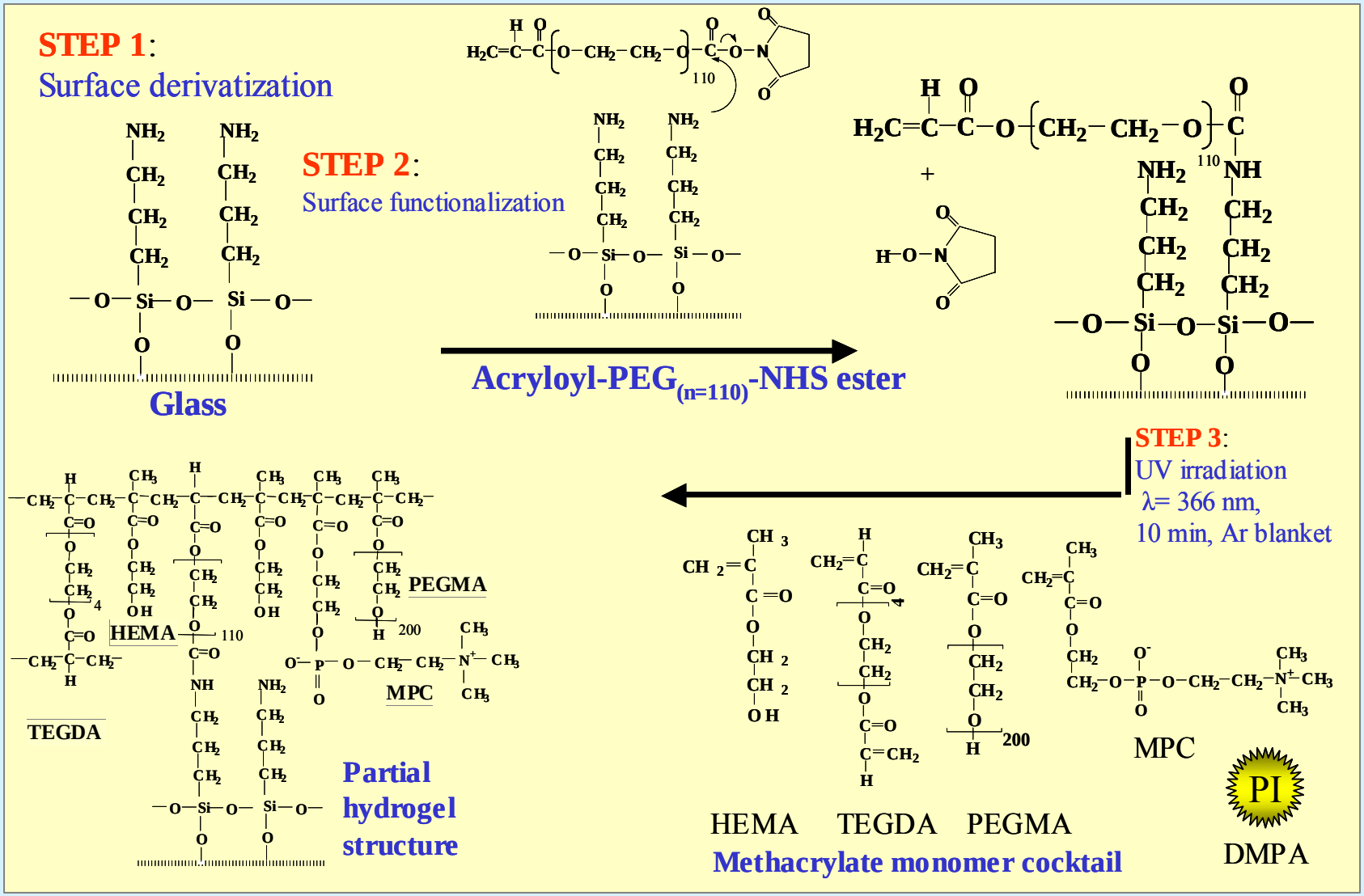
Cell (HMF) retention as a function of hydration



Slide 11

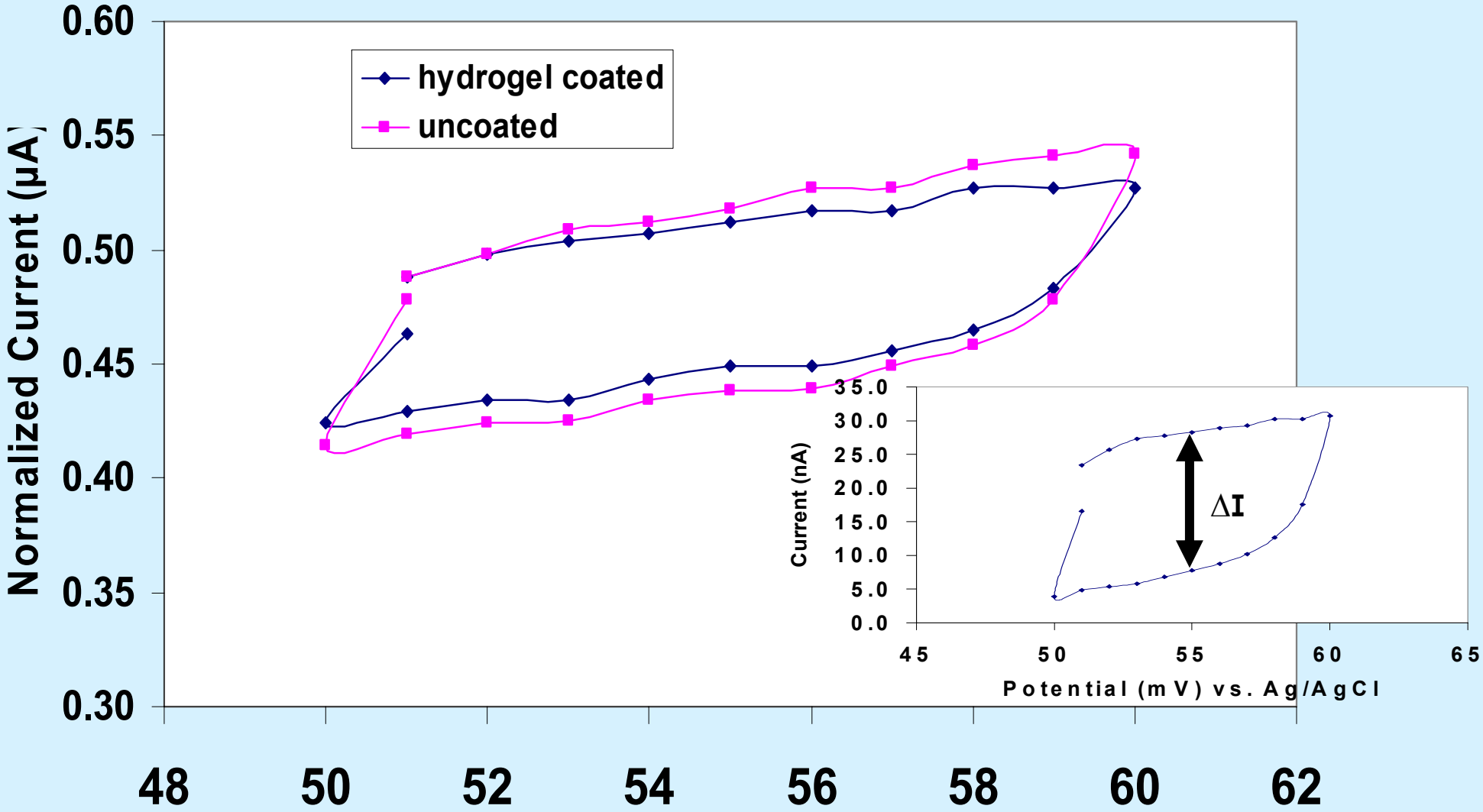
d1 The hysteresis is used to plot the correlation between hydration and dynamic contact angle because
1) there are only 6 points (6 formulations were used)
2) in the advancing and receding data there are is one point that does not follow the trend and hence throws the graph off the plot.
glad, 5/8/2005

Substrate surface modification, derivatization, monomer casting and hydrogel synthesis



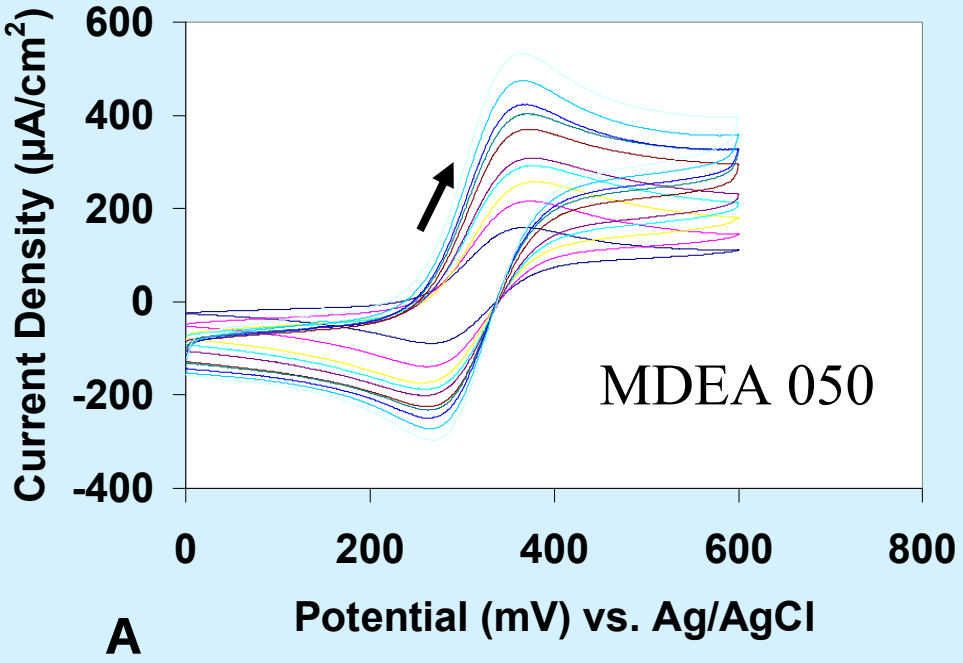
Sheena Abraham, Sean Brahim, Kazuhiko Ishihara and Anthony Guiseppi-Elie "Molecularly engineered hydrogels for implant biocompatibility" *Biomaterials* (2005), 26(23), 4767-4778.

Cyclic voltammetry in Tris/KCl (pH 7.2)

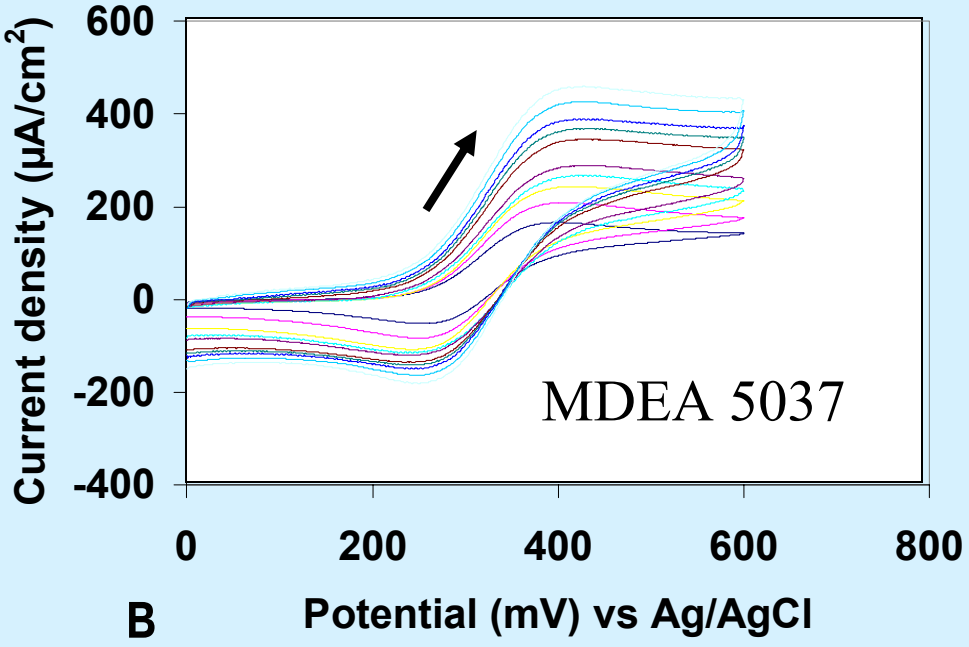


$$C_{DL} = \Delta I / 2\nu$$

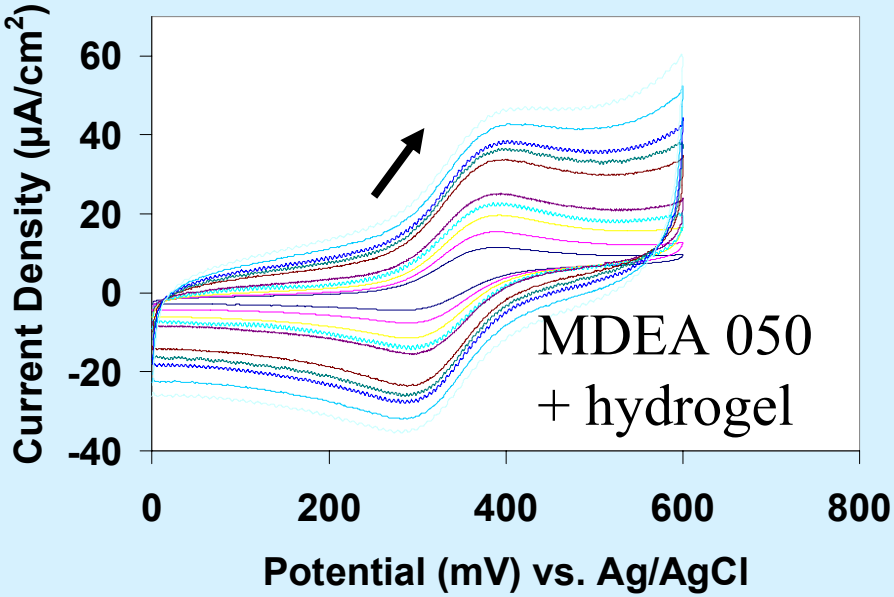
Ferrocene-ferrocenium oxidation-reduction at microdisc electrode arrays (MDEAs)



A

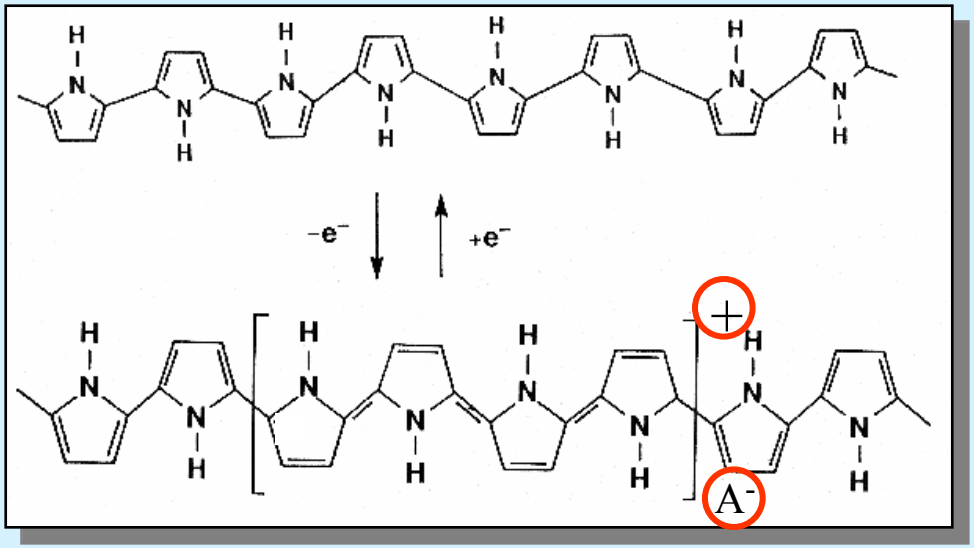


B



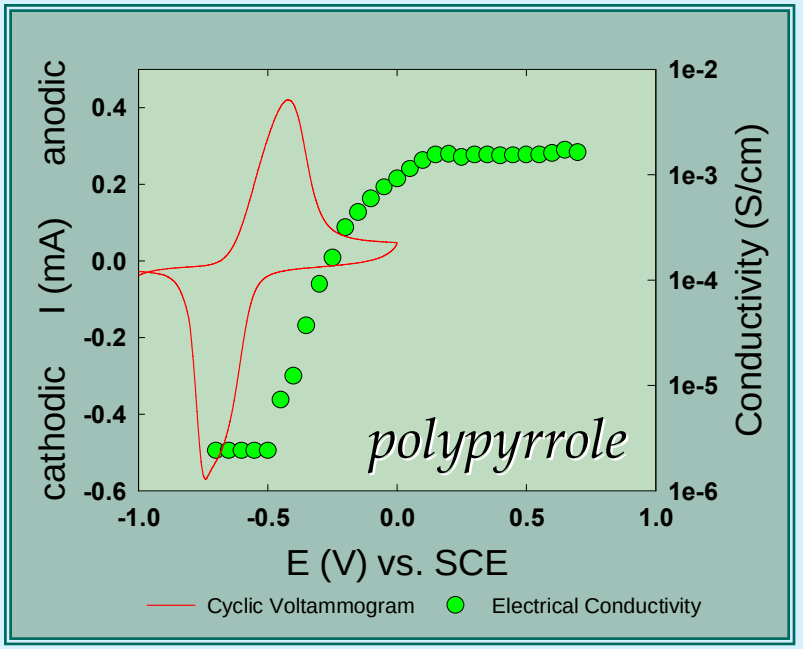
C

Chemical structure, electrochemical and electrical properties of conducting electroactive *polypyrrole* films



Developed in late 1970s as materials for polymer batteries…

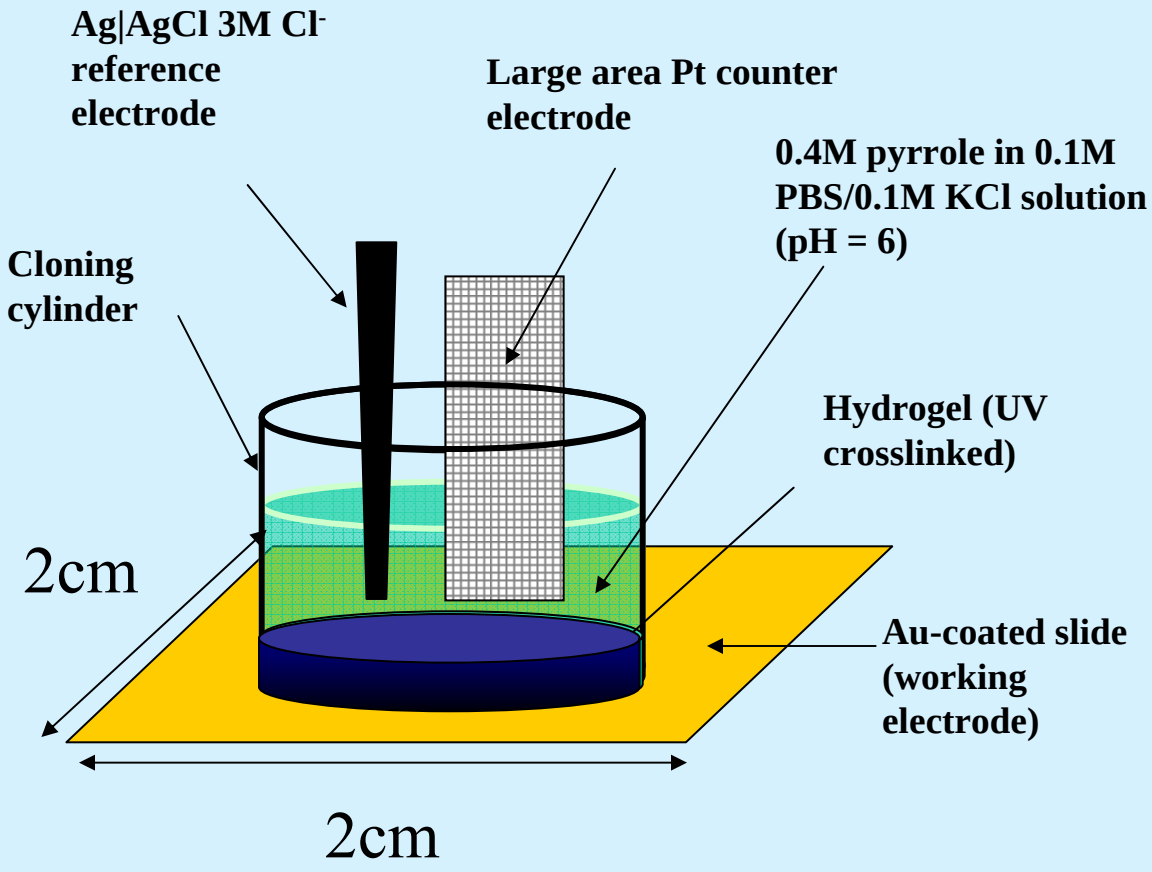
- Polyelectrolyte
- Redox switchable (ms)
- High chemical stability
- High hydrolytic stability
- Demonstrated biocompatibility

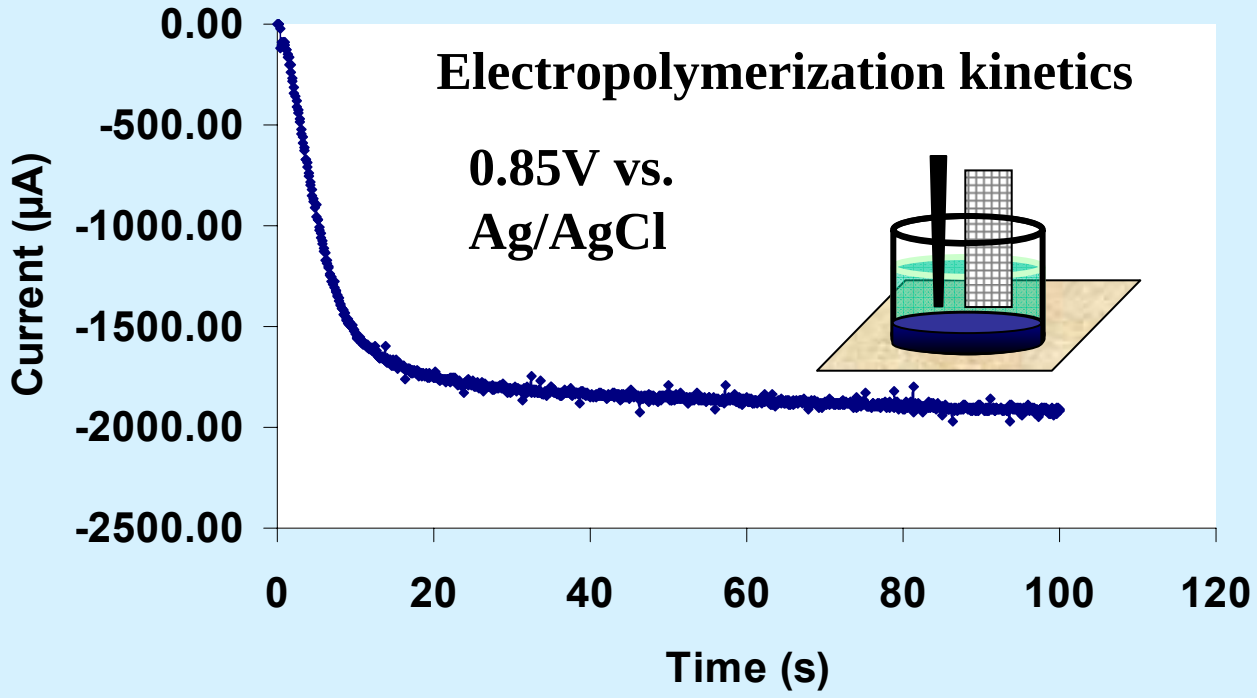


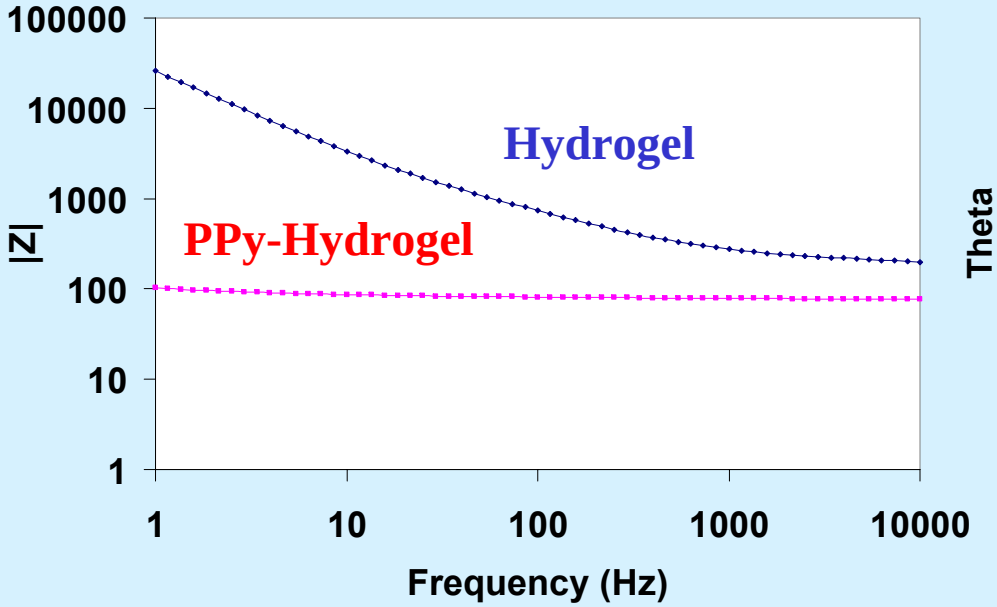
Guiseppi-Elie et al. In Handbook of Conductive Polymers 2nd Edition (1997), Chapter 34, p 963.
Guiseppi-Elie et al. In, Electrical, Optical, and Magnetic Properties of Organic Solid State Materials, Mat. Res. Soc. Symp. Proc. Vol. 413; 1996, p 439.

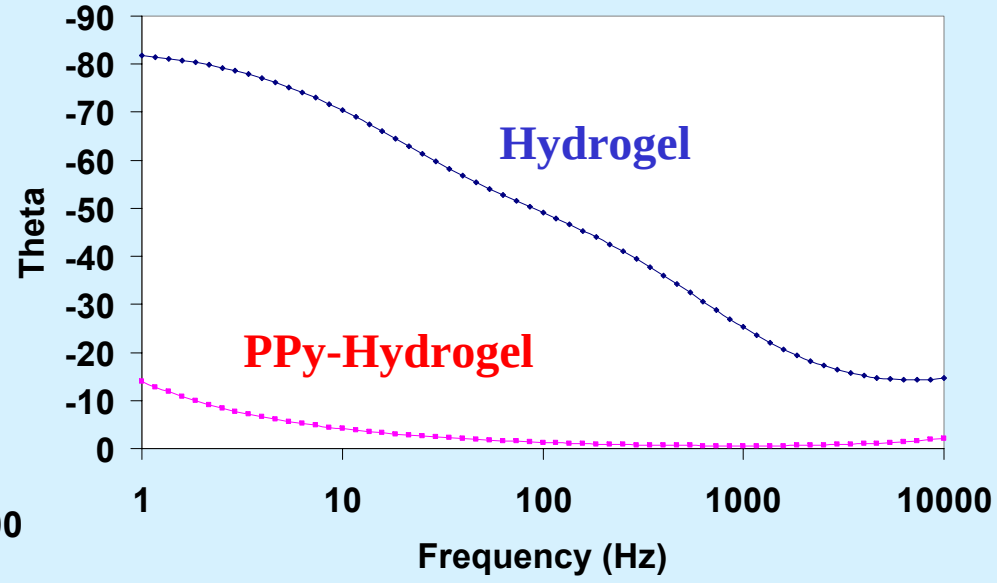
Electropolymerization of Polypyrrole (PPy) Within p(HEMA)-based bioactive hydrogels

Apparatus connected to a Princeton Applied Research (PAR) Potentiostat/Galvano-stat in conjunction with a Solartron frequency response analyzer (FRA) for electropolymeriza-tion (+0.85V for 100 sec) and impedance measurements (1Hz to 10kHz).




Electropolymerization kinetics
0.85V vs.
Ag/AgCl
Current (μA)
0.00
-500.00
-1000.00
-1500.00
-2000.00
-2500.00
0
20
40
60
80
100
120
Time (s)


Hydrogel
PPy-Hydrogel
|Z|
100000
10000
1000
100
10
1
1
10
100
1000
10000
Frequency (Hz)


Hydrogel
PPy-Hydrogel
Theta
-90
-80
-70
-60
-50
-40
-30
-20
-10
0
1
10
100
1000
10000
Frequency (Hz)

Viability Study: Human muscle fibroblasts (RMS 13) and Rat pheochromocytoma cells (PC12)

- Neuronal progenitor cell line (PC12) and human muscle fibroblasts (RMS13) grown in F-12K and RPMI 1640, respectively.
- Cells seeded onto hydrogel-polypyrrole coated gold surfaces.
- Cell viability determined.

Summary

- Cell viability is enhanced by the incorporation of phosphorylcholine moieties into the pHEMA-based hydrogel..
- Polypyrrole reduces the electrical impedance of hydrogel coated gold electrodes.
- Hydrogel coated onto MDEAs increases impedance (decreased diffusion coefficient compared to aqueous solution).

Acknowledgments

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