Lecture 10:
Surface Modification of Biomaterials (Part II)

Surface Modification Methods

A. Plasma Treatments

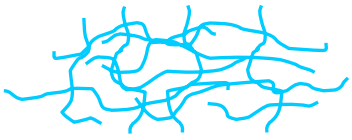
Plasmas: ionized gases (ions, electrons, free radicals, atoms, molecules) created by ion/electron impact under applied E-field: $A + e \rightarrow A^+ + 2e$

Uses

1. surface etching

- employs inert gases (e.g., Ar)
- purposes: remove impurities, increase roughness

2. surface reactions



- crosslink polymer surfaces
  modify transport properties, reduce surface mobility

- generate surface functional groups
  $\uparrow$ or $\downarrow \gamma_1$, create reactive surfaces

  O_2, CO_2, CO: -C-O-, -C=O, -O-C=O, -C-O-O

  N_2, NO_2, NO (nitric oxide): -C-N, -C=N, -C≡N (plus above)

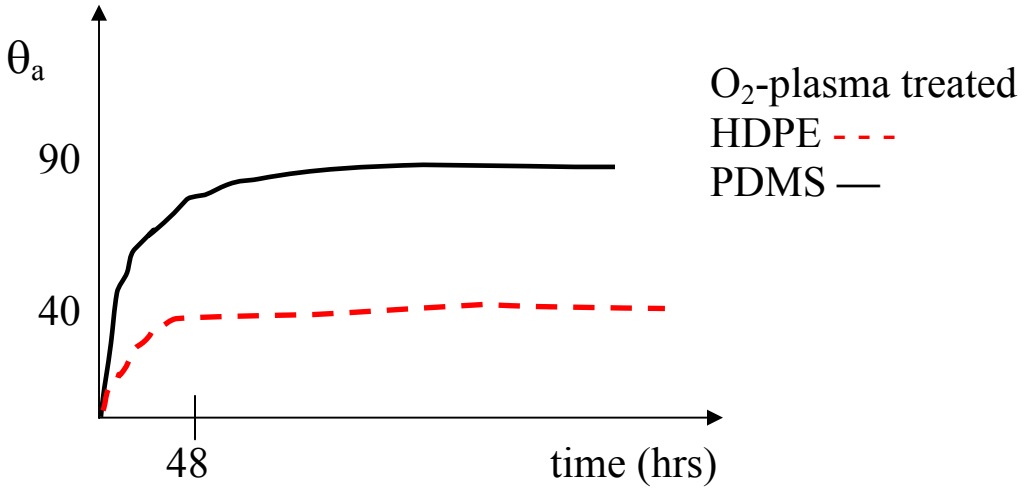
  NH_3 (ammonia): -NH, $-NH_2$ (plus above)

  CF_4, C_2F_6 (hexafluorethane): -CF, $-CF_2$, $-CF_3$

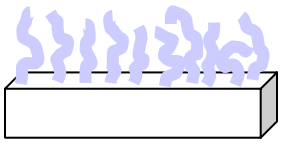
Drawbacks:

a. ill-defined surface chemistries

b. ***reconstruction*** nullifies treatment



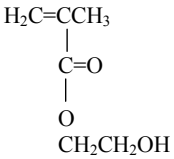
3. Coating Depositions

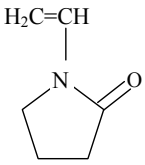


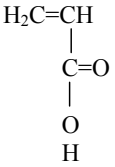
➢ graft polymerized layers

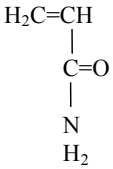
plasma + monomer ⇒ radically-polymerized surface layer

hydrophilic monomers: hydroxyethyl methacrylate (HEMA), N-vinyl-2-pyrollidone (NVP), methacrylic acid (MAA), acrylamide (AAm), etc.

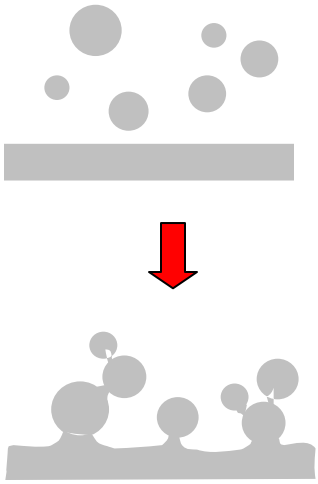








- plasma-sprayed coatings (inorganics)



fine powders injected in plasma ⇒
partial melting gives surface adhesion

HA (hydroxyapatite): bone bonding

Al_2O_3: ↑ hardness

CoCr, Ti: ↑ surface roughness/porosity
⇒ bone bonding

Four photos removed for copyright reasons.

Ti-Al-V implant with a) smooth surface; b) Ti plasma spray coating. Micrographs show bonding with bone after 4 weeks implantion in a canine. P = PMMA cement. B = new bone tissue. (B.H. Lee et al., *J. Biomed. Mater. Res.* **69A**, 279 (2004))

B. Other Orthopedic Biomaterial Treatments

- Ion implantation: high energy ion beam buries atoms into near-surface (up to 10^6 eV) (metals)

  - ↑ hardness & wear resistance
  - ↑ corrosion resistance

  ex. N implantation in Ti

- Electrolytic coatings

  - ↑ hardness & wear resistance
  - ↑ corrosion resistance
  - enhance bone bonding ability

  ex. Al_2O_3, ZrO_2, hydroxyapatite

Photo removed for copyright reasons.

Electrodeposited ZrO_2 coating on CoCrMo implant alloy. (Fig. 1a in S.K. Yen et al., *Biomaterials* **22**, 125 (2001))

C. Polymer/Organic Coatings

1. solvent coating/casting

polymer in VOC (volatile organic compound) dipped, sprayed, rolled or brushed on surface

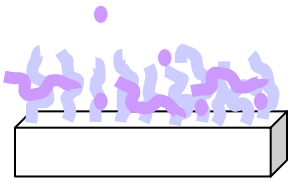
ex. TAXUS™ stents (Boston Scientific), Paclitaxel-eluting poly(styrene-isobutylene-styrene) block copolymer coating

Two photos removed for copyright reasons.

SEM images of TAXUS™ stent. (S.V. Ranade et al., *J. Biomed. Mater. Res.* **71A**, 625 (2004))

2. grafted polymer layers

- surface graft polymerization: plasma (incl. corona discharge) or radiation (γ or UV) generate surface free radicals that initiate chain polymerization



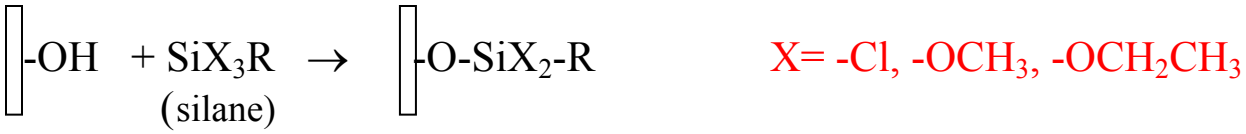
Drawbacks:

- poorly controlled thickness & molecular weight
- unreacted monomer
- unbound homopolymer

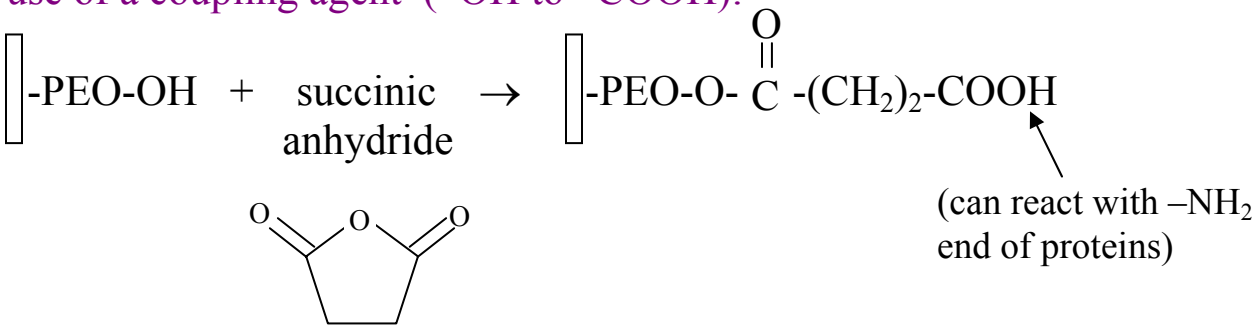
- condensation rxns: polymer or biomolecule bonded to functional groups on surface (-OH, -COOH, $-NH_2$)

-OH groups: on metals, glasses, ceramics

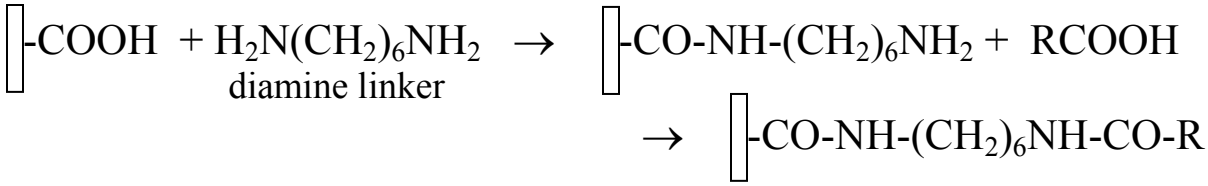
direct covalent attachment to –OH:



use of a coupling agent (–OH to –COOH):



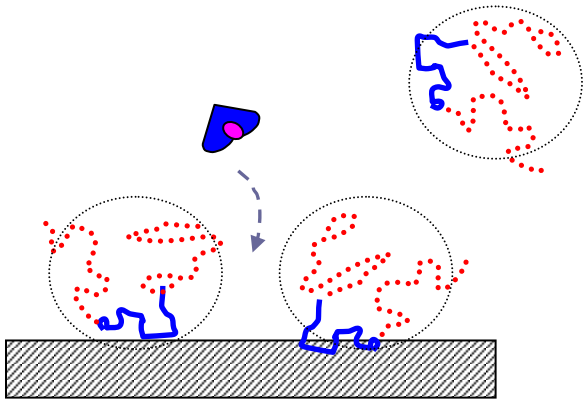
use of a coupling agent (–COOH to $–NH_2$):



3. Adsorption from solution

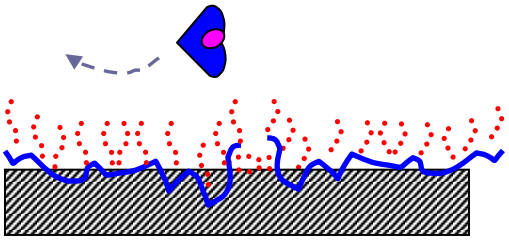
- amphiphilic macromolecules: block copolymers

ex. Pluronics PEO-PPO-PEO triblocks
used in pharmaceutical formulations as a dispersing agent

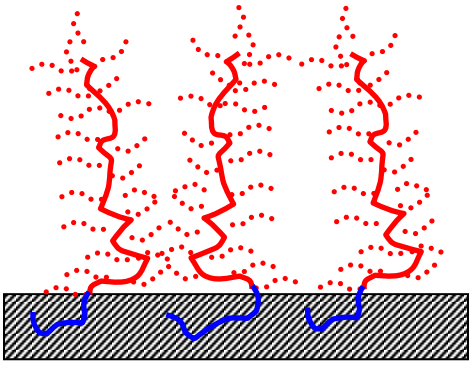


Drawbacks:
- low coverage (steric limitations)
- not covalently bound—cells can rearrange!

Alternate amphiphile architectures:



amphiphilic combs
(shag carpet)



bottle brush
(glycocalyx mimic)

➢ polyelectrolyte multilayers (PEMs)

electrostatic assembly: alternate adsorption of polycation and polyanion monolayers

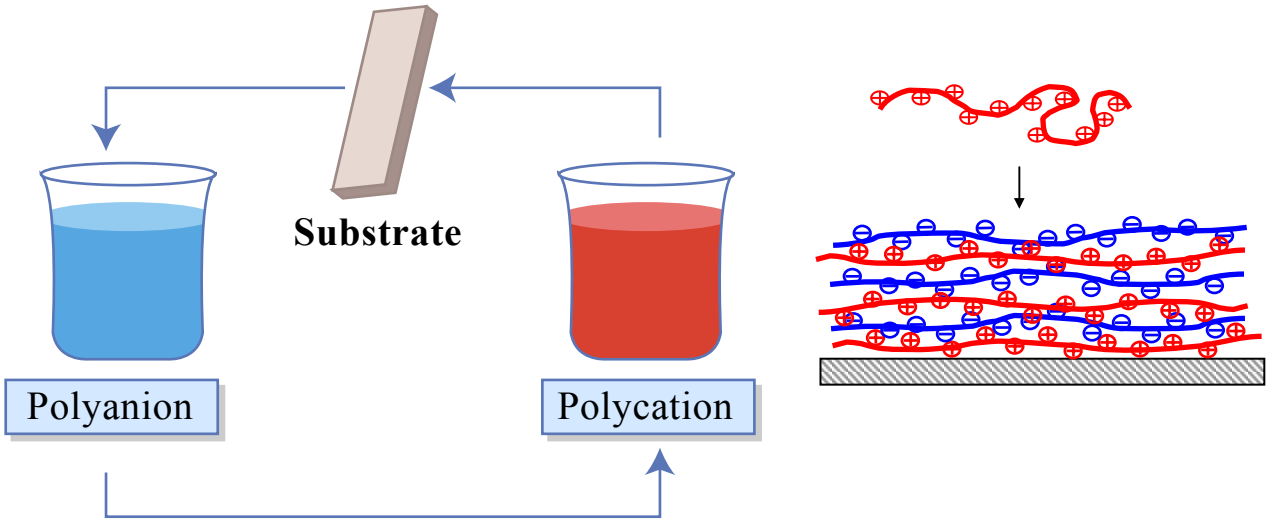


Figure by MIT OCW.

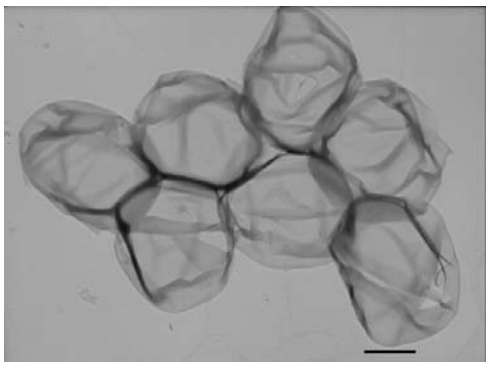
Advantages:

- fabricate surface coatings incorporating diverse components (proteins, DNA, drugs…)

- can deposit onto numerous surfaces, any topography

ex. PEM encapsulation of cells
alginate (a polysaccharide, –)/polylysine (+)

- water-based
no organic residuals, compatible with biological components

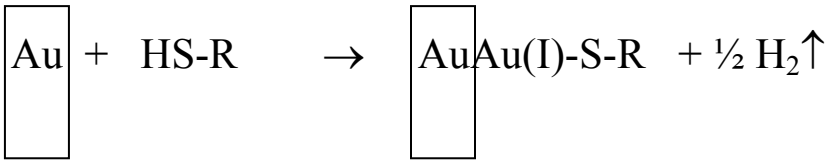


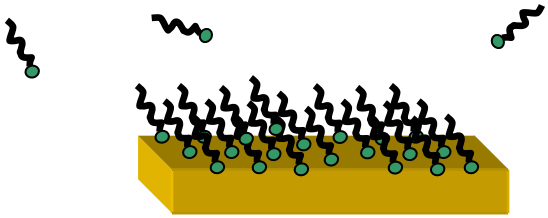
PEM hollow microcapsules built on PS microsphere templates subsequently dissolved. (Rubner & coworkers, MIT)

Courtesy of Prof. Michael Rubner. Used with permission.

- self-assembled monolayers (chemisorption): ordered (close-packed) monolayers of organics (head group with short hydrocarbon tail)

alkane thiols on Au (model surfaces or biosensors/arrays)





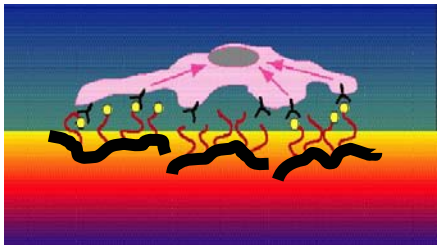
- useful for "model" surfaces
- biosensor applications
- SPR studies

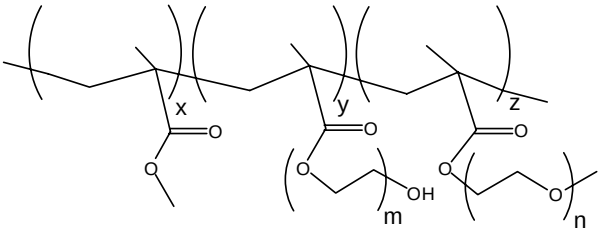
4. Surface Segregation

- small amount of surface agent is added to bulk biomaterial

- additive selectively segregates during annealing
(water-based annealing for hydrophilic additives)

ex., amphiphilic acrylic comb polymer/PLA tissue engineering scaffolds





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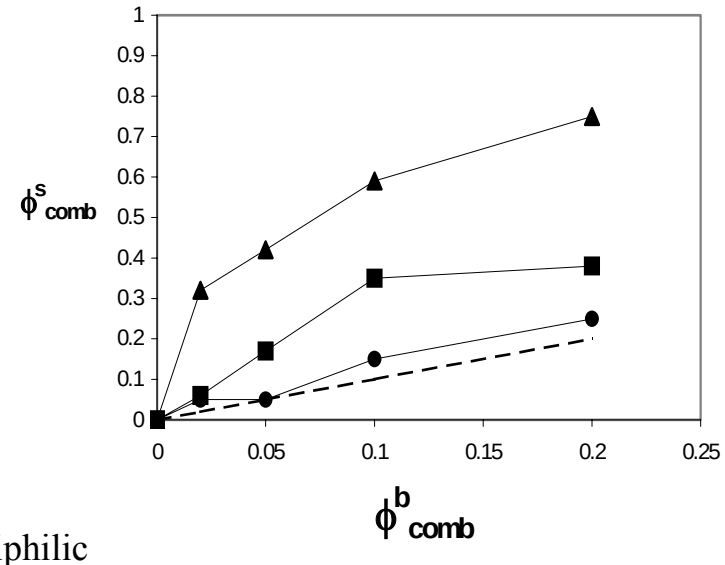


PLA scaffold with surface segregated amphiphilic comb copolymer. SEM image (left) and XPS data of comb surface vs. bulk concentration. (D.J. Irvine et al., *Biomacromol.* **2**, 545 (2001))

▲ annealed in water 70°C
■ unannealed
● annealed in vacuum 120°C
- - - no surface excess

D. Patterned Surface Modification

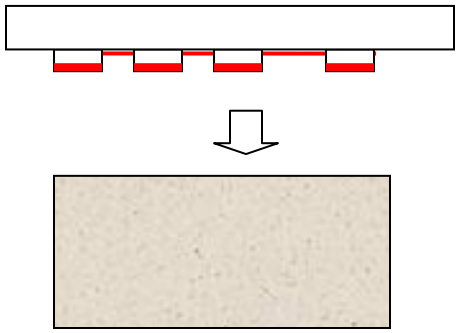
desired for:

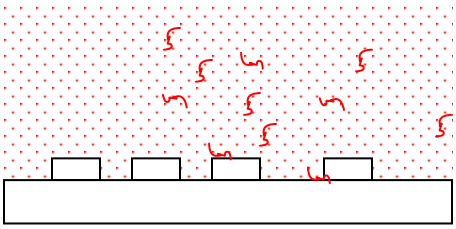
- gene, protein or cell microarrays
- biosensors
- combinatorial studies
- directed cell migration, cell sorting
- structuring engineered tissue

➢ Microcontact printing (μCP): (G. Whitesides, Harvard)

- conventional lithography methods used to fabricate a template from which PDMS (silicone) "stamp" is formed

- "ink" is a SAM (or other molecule) for selective deposition





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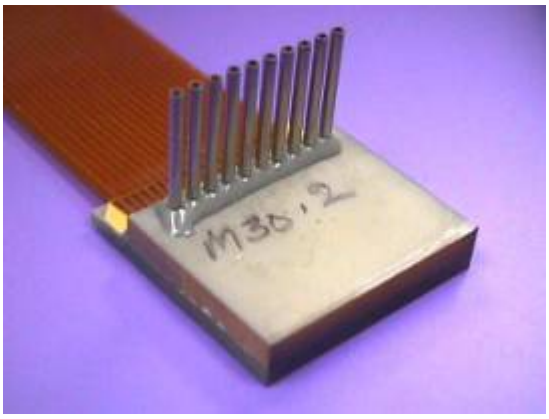
Bovine endothelial cells cultured on Au surface printed with SAMs having alkane and EG-terminated alkane tails and exposed to fibronectin. (Figure 5(B) in R.S. Kane et al., *Biomaterials* **20**, 2363 (1999))

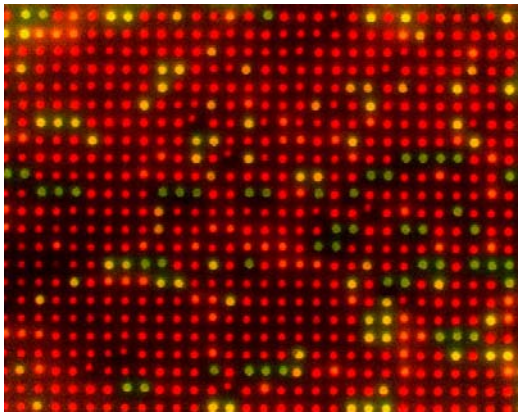
- polymer and protein stamping also possible
- employed for feature sizes ~2-50 μm

- Inkjet printing

- modification of conventional printing technology
- faster, lower resolution patterning vs. μCP
- deposited molecule surface density determined by drop concen.
- bioinks of biomolecules, cells possible

MicroFab Technologies, Inc.
http://www.microfab.com/





MicroFab Technologies, Inc. prototype 10-nozzle printer head and printed array of multiple dye molecules. (images from http://www.microfab.com/)

Fluorescently-labeled fibroblast growth factor (FGF) ink-jet printed onto fibrin matrix. Printed spots ~75 μm. (Figure 2 in E.D. Miller et al., *Biomaterials* **27**, 2213 (2006))

- Photo-patterning methods

  - UV photomasking to selectively cleave a polymer film

Figures removed for copyright reasons.

Nitrobenzyl methacrylate units of copolymer cleaved under UV to create negatively charged regions. Using a photolithography mask allows creation of patterned polyanion regions (shown stained with cationic dye). (J. Doh and D.J. Irvine, *JACS* **126**, 9170 (2004))

  - UV photomasking to selectively crosslink a polymer film

Figures removed for copyright reasons.

Vinyl benzyl acrylate units of PAA-based copolymer crosslink under UV to create PEMs with lower swelling/higher modulus. (S.C. Olugebefola et al., *Langmuir*, submitted)

- Molecular imprinting

- biological components used as a template to create surface binding sites with specific chemistry & topology

- process: polymerize around template, extract template molecule
  $\Rightarrow$ imprint of template with complementary chemistry

- imprint exhibits selective adsorption of template molecule

Figure removed due to copyright reasons.

B.D. Ratner & coworkers,
Nature **398**, 1999, p. 593.

Graph removed for copyright reasons.

BSA is selectively adsorbed to BSA-imprinted surface in competitive adsorption with IgG. (B.D. Ratner & coworkers, *Nature* **398**, 593 (1999))