Materials with Biological Recognition (continued)

TODAY:
Using materials to mimic cell-cell contacts
start new section: inorganic biomaterials

READING:
- Cell adhesion/ mech. props of substrates
- Enzymatic recognition of biomaterials
- Immobilized proteins

ANNOUNCEMENTS:
No class next Tues, 4/11
Ps posted this afternoon, due next Thurs.
Changes in signaling achieved by cytokine immobilization on surfaces

Image and figure text removed due to copyright reasons.
Please see: Figure 1 in Ito, Y. “Tissue Engineering by Immobilized Growth Factors.” Materials Science and Engineering C6 (1998): 267-274.
Surface immobilization can induce new function in cytokines: case of tethered EGF-triggered neuronal cell differentiation

PC12 cell line:
- induced to differentiate and extend axons under stimulation of **NGF** (nerve growth factor)
- induced to proliferate by **EGF**

Signal doesn’t trigger internalization of receptor; thus signal lasts longer and triggers differentiation

Signal triggers internalization of receptor; short signal triggers proliferation

Figure by MIT OCW.
NGF vs. EGF signaling in PC12 neuronal cells

(Traverse et al. 1994)
Changing the biological activity of cytokines by surface immobilization:

- EGF$_{s}$
- EGF$_{i}$

**Graphs:**
- Cell density vs. time
- MAP Kinase Activity vs. time
- pH Activity vs. time

**Images:**
- Cell morphology at 3h and 72hr

Ito 2001
Materials that mimic cell-cell contacts
Physiology of the immune response: cellular level

Immunological synapse (IS)

'Supramolecular activation clusters'

Replacing a partner cell with a surface:

Adhesion molecules

Signaling molecules

Adhesion molecules

TCR ligand

Adhesion receptors
PNMP photoresist

40 : 40 : 20 (wt:wt:wt)

\[
\begin{align*}
&\text{CH}_3 \quad \text{CH}_3 \\
&\text{CH} = \text{O} \\
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\begin{align*}
&\text{CH}_3 \quad \text{CH}_3 \\
&\text{CH} = \text{O} \\
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&\text{C} \\
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&\text{CH}_3 \\
&\text{CH}_3
\end{align*}
\]

Cationic substrate

Spincoat photoresist

UV

develop with PBS, pH 7.4
Methylene blue staining of patterned surface:

PNMP photoresist

40 : 40 : 20 (wt:wt:wt)

Cationic substrate
Spincoat photoresist

develop with PBS

(J. Doh and D.J. Irvine. JACS (2004))
Images removed due to copyright reasons.
In situ tracking of T Cell Receptor triggering

Image removed due to copyright reasons.
Please see: Molecular probes Web site - http://probes.invitrogen.com/

Image removed due to copyright reasons.
T cell migration on surfaces modulated by activation signals

Images removed due to copyright reasons.
T cells self-organize in response to synapse arrays

Graph and images removed due to copyright reasons.
Do surface-patterned ligands lead to full T cell activation?

T cells assemble immunological synapses on ‘synapse array’ surfaces

T cells centrally cluster TCRs and signaling molecules, with a peripheral ring of cytoskeletal components.

Images removed due to copyright reasons.
Using protein micropatterned surfaces to direct immune cells:

Images removed due to copyright reasons.
Images removed due to copyright reasons.

Imparting mobility: patterned supported lipid bilayers
Imparting mobility: patterned supported lipid bilayers

Image removed due to copyright restrictions.
Please see: Figure 1 in Mossman, et al. *Science* 310 (2005): 1191-1193.

Image removed due to copyright restrictions.
Please see: Figure 1 in Wu, et al. *PNAS* 101 (2004): 13798-13803.
Inorganic biomaterials

**Last time:** enzymatic recognition of biomaterials
    Cytokine signaling from biomaterials

**Today:** introduction to biomineralization and biomimetic inorganic/organic composites
    Interfacial biomineralization

**Reading:** Stephen Mann, ‘Biomineralization: Principles and Concepts in Bioinorganic Materials Chemistry,’ Ch. 3 pp. 24-37, Oxford Univ. Press (2001)

**Supplementary Reading:** -

**ANNOUNCEMENTS:**
Inorganic building blocks used by nature

Images removed due to copyright reasons.
Please see: http://ruby.colorado.edu/~smyth/min/minerals.html
Inorganic building blocks used by nature

Image removed due to copyright restrictions.
Inorganic building blocks used by nature

Table removed due to copyright restrictions.
Bioceramics: motivation for studying and mimicking biomineralization

Why seek to mimic biomineralization processes?

**Biology**
- Precise control of morphology, structures, (including those that defy classical 230 space groups of crystals)
- Occur at near-neutral pH, 370°C, and 1 atm

**Laboratory methods**
- Obtain only simple structures
- Typically require high temp. and pressures
- Relies on extreme pHs to form certain structures

Pieter Harting’s original hand drawings of calcareous microstructures (1872)
Bioceramics: motivation for studying and mimicking biomineralization

APPLICATIONS:

BIOMATERIALS:

- Replicate trabecular bone structure and its mechanical properties → this is still elusive

- Low-cost, reproducible, high-volume bone graft materials

STRUCTURAL MATERIALS:

Inorganic-organic composites have up to 3000x greater strengths than pure inorganic crystals
Complex macro- and microstructures of biological inorganic materials

Images of radiolarian, coccolith, and A. hexacona removed due to copyright restrictions.
Complex macro- and microstructures of biological inorganic materials

Organized at macro, micro, meso, nano length scales

**FIG. 1.** Hierarchical levels of structural organization in a human long femur. (Adapted with permission from J. B. Park, Biomaterials: An Introduction, Plenum Publ., 1979, p. 105.)
Paradigms in biomineralization
Further Reading

1. Voet & Voet. in *Biochemistry*.