Problem Set 2 **BE.462J/3.962J**
Biodegradable Solid Polymers **Spring 2003**
Issued: Day 4
Due: Day 5
(20 pts total)

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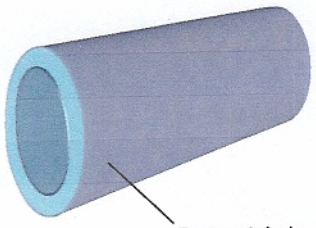
1. An early study in the development of peptide-presenting biomaterials showed that polymer surfaces bearing RGD peptides at a density equivalent to ~10^5 peptides per each cell was sufficient to promote cell attachment, spreading, and subsequent cell growth. In contrast, when whole fibronectin protein was adsorbed to polymer surfaces, it was found that many more copies of the intact protein were needed per unit area to obtain similar responses from cells. Explain this result. How should the binding of cell integrin receptors to a short RGD peptide compare with binding to native fibronectin?

2. In the article by Schense et al., Figures 1 and 2 show that different adhesion peptides incorporated into a natural biopolymer matrix (a fibrin fiber network) induce different degrees of neurite outgrowth from neuronal cells, even when conjugated to the matrix at the same total densities. Provide 2 physico-chemical reasons to explain how different peptides can provide different responses.

3. Compare and contrast the erosion characteristics expected for a device to be used *in vivo* that is fabricated from a polyesteramide vs. the characteristics of the same device fabricated using a polyanhydride.

4. ***Design* of *an artificial artery***. (10 pts) Shown below is a simplified schematic of the structure of an artery .The two primary features of an artery are the endothelial cell lining on the interior lumen of the vessel (contacting blood flow) and the smooth muscle cell layer surrounding the vessel, which can provide contractile force to support the mechanical integrity of vessels under blood pressure. Artificial blood vessels (vascular grafts) have been studied for many years and are in extensive clinical use, however, the simple synthetic grafts typically used (e.g. Dacron or poly(tetrafluoroethylene) (Teflon) polymer tubes) are not safe for small-diameter blood vessel replacement (vessel diameters < 6 mm) and show loss of patentcy, due to rapid occlusion of the grafts by depositing platelets. (Patentcy is the term used to describe an open, viable vessel.) Read the attached brief discussion of approaches to blood vessel engineering, and then answer the design questions below for an improved small-diameter artificial vessel based on the biomaterials design principles discussed in class so far and the prototype
design sketched below: The 'prototype' is to be sutured to the ends of natural blood vessels to replace diseased/blocked sections of vasculature.

'prototype' artificial vessel structure:



a. Describe the first events that will occur at the surface of a hydrophobic polymer like poly(tetrafluoroethylene) (structure shown below) when it is implanted as a vascular graft, and how these events could lead to graft occlusion.

$$-(CF_2\text{-}CF_2)_n-$$

$$-(CF_2\text{-}CF_2)_n-$$

b. Would you choose a degradable or non-degradable polymer for the artificial vessel scaffolding? Explain your choice. (5 pt.s extra credit: describe what polymer in particular you would choose and motivate why you'd make that choice.)

c. One strategy that could be applied to this artificial vessel would be to implant the polymer and seek to have native endothelial cells and smooth muscle cells from the adjacent native vessels migrate into the polymer scaffold to recreate the native inner and outer cellular lining of the graft. Describe a strategy to modify the 'prototype' scaffold in order to promote this process, and outline a preliminary experiment you could use to test the utility of your approach.

d. Inclusion of adhesion peptides in the inner surface of the artificial vessel could have both positive and negative effects on patentcy early after implantation- describe one positive and one negative outcome that could occur, depending on the choice of peptides utilized.