1. (12 pts) Bone tissue engineering generally involves the implantation of a synthetic or biologically derived material that upon implantation allows for bone in-growth and eventual replacement. In a recent publication, De Groot and coworkers (*Tissue Eng.* **2003**, *9*, 535) compared the structures of 3 commercially produced biphasic calcium phosphate (BCP) porous scaffolds for bone tissue engineering. BCP is a two phase material of hydroxyapatite and tricalcium phosphate. SEM images below illustrate cross-sections of the scaffolds manufactured by Zimmer (left image), Dytech (middle image) and IsoTis (right image). Scale bar is 1 mm.

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See Fig. 3, top images, in Li, Shihong, Joost de Wijn, Jiaping Li, Pierre Layrolle, and

Klaas de Groot. "Macroporous Biphasic Calcium Phosphate Scaffold with High

Permeability/Porosity Ratio." *Tissue Eng* 9 (2003): 535-548.

a) (4 pts) What aspects of the primary chemical structure, higher order (meso) structure and/or microstructure make these scaffolds useful for bone tissue engineering?

Calcium phosphate is chosen for this application because it can be resorbed in vivo through action by osteoclasts (bone remodeling cells) and is biocompatible (hydroxyapatite is the mineral component of bone.) The porous microstructure enables bone cells to penetrate the structure and allows transport of vital nutrients.

b) (6 pts) Download the article by De Groot and coworkers through the MIT library. What processing approaches resulted in the dramatically different pore morphologies observed in the SEM images for the 3 BCP scaffolds?

The BCP scaffold by Zimmer was prepared by compressing hydroxyapatite (HA) and tricalcium phosphate (TCP) powders with naphthalene particles, followed by pyrolisis of the naphthalene and sintering to produce the porous structure shown. The Dytech scaffold was produced by foaming a slurry of HA and TCP powders, water and surfactant with nitrogen, followed by calcination and sintering. The IsoTis scaffold was prepared by molding a mixture containing a BCP slurry, polymethyl methacrylate (PMMA), MMA monomer, and naphthalene, followed by pyrolysis of the organic components and sintering.

c) (2pts) A table of the scaffold porosities and specific permeabilities measured by De Groot and coworkers is provided below. Explain why the IsoTis scaffold, with the lowest porosity, exhibits the highest permeability.

Manufacturer	Specific permeability (m^2)	Porosity (%)
Zimmer	0.02×10^{-9}	75
Dytech	0.12×10^{-9}	80
IsoTis	0.34×10^{-9}	60

The permeability of the IsoTis scaffold is highest because of the interconnectivity of its pores. The methods of manufacture for the Zimmer and Dytech scaffolds led to more isolated pores that are not as useful for tissue engineering.

2) (16 pts) Recently, Yokoyama and coworkers described the preparation of protein-resistant surfaces on polystyrene (PS) through the addition of 10% of a block copolymer additive (PS-*b*-PME3MA) whose structure is shown below (A. Oyane et al., *Adv. Mater.* **2005**, *17*, 2329; H. Yokoyama et al., *Macromol.* **2005**, *38*, 5180). Contact angle measurements performed on annealed blends with different block copolymer contents are also shown.

a) (3 pts) Explain why the advancing contact angle first decreases then plateaus as the block copolymer content in the blend is increased.

As block copolymer is added to the blend, it segregates to the blend surface with the PME3MA block located preferentially at the surface. As the block copolymer content reaches ~20%, the surface is saturated with block copolymer, so that further addition does not result in a further decrease in contact angle.

b) (6 pts) What possible energetic driving forces might lead to the phenomenon in (a)?

The surface segregation of the block copolymer may be driven by entropic and enthalpic forces, including i) a positive enthalpy of mixing for PS and PME3MA, which favors exclusion of PME3MA from the bulk film; ii) lower surface energy of the methyl groups on the side chains of PME3MA; and iii) chain end localization at the surface to reduce entropic penalties associated with surface restrictions on polymer chain conformations.

c) (3 pts) Based on the contact angle data, approximate the composition of the surface for 10 wt% bulk concentration of PS-*b*-PME3MA.

Rearranging Cassie's equation, $f_{PS} = \dfrac{\cos\theta - \cos\theta_{BC}}{\cos\theta_{PS} - \cos\theta_{BC}}$

From advancing angle data at f_{PS} = 1, 0.9 and 0,

$$f_{PS} = \frac{\cos 90 - \cos 72}{\cos 98 - \cos 72} = 0.69$$

The surface fraction of block copolymer is therefore 0.31 for 0.1 bulk concentration.

d) (2 pts) For blend systems with >20% block copolymer, what is the molecular origin of the large hysteresis in the contact angle (i.e., the much lower receding contact angle value compared with the advancing angle)?

The PME3MA blocks located at the surface initially arrange so that the low energy –CH₃ groups are oriented upwards, giving rise to a relatively high advancing angle. Once underneath the water droplet, the chains rearrange to place the hydrophilic ethylene oxide groups in contact with water. This is the surface sampled when the liquid is withdrawn in a receding angle measurement.

e) (2 pts) How might the contact angle results change if the terminal group of the methacrylate side chain were changed to a hydroxyl (-OH)?

Exchanging the methyl groups with –OH groups would create a more hydrophilic surface and lead to a lower advancing angle, assuming the methacrylate block localizes at the surface. From an energetic standpoint, -OH groups might reduce the miscibility of the methacrylate block with PS, increasing the driving force for PME3MA surface segregation. However, replacing the nonpolar methyl groups with the more polar hydroxyl groups lowers the driving force for chain end segregation at the surface.

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Please see: Scheme 1 and Fig. 9 in Yokoyama, H., T. Miyamae, S. Han, T. Ishizone, K. Tanaka, A. Takahara, and N. Torikai. "Spontaneously Formed Hydrophilic Surfaces by Segregation of Block Copolymers with Water-Soluble Blocks." *Macromolecules* 38 (2005): 180-5189.

3) (12 pts) Chen et al. investigated adhesion of endothelial cells on titanium oxide coatings as a possible surface treatment to reduce thrombogenesis on arterial stents. (*Surface & Coatings Tech.* **2004**, *186*, 270). X-ray diffraction measurements revealed the as-prepared coatings to be amorphous, while coatings heat-treated for 0.5 hours at 700 °C were crystalline. Contact angle measurements were made utilizing different liquids to determine values for the polar and disperse components of the surface energy, as listed in the table below.

a) (3 pts) Can the work of cohesion for titanium oxide be estimated from the measurements of Chen et al.? Explain.

The titanium oxide surfaces are not pure oxide interfaces, since the measured surface energies are an order of magnitude lower than one might expect for a metal oxide. Thus the work of cohesion cannot be accurately calculated from these measured values.

b) (3 pts) What chemical groups might you expect to observe on the titanium oxide surface?

It is likely that water and carbon dioxide from the atmosphere have chemisorbed on the surface. One could expect to find –OH groups from water adsorption, and CO_3^{2-} groups. Hydrocarbons might also be physisorbed on the surface.

c) (2 pts) Why is the measured surface energy of the titanium oxide coating lower after heat treatment?

During crystallization, the atoms rearrange to allow lower energy planes to facet the surface, reducing the oxide surface energy relative to the amorphous oxide surface.

d) (4 pts) Based on the surface energies provided, calculate the work of adhesion between the surface and water for the amorphous and crystalline coatings. How might this influence protein adsorption?

material	γ^p (dyn/cm)	γ^d (dyn/cm)	γ (dyn/cm)
amorphous titanium oxide	30	29	59
crystalline titanium oxide	14	26	40
water	51	22	73

The work of adhesion between water and the crystalline oxide is given by:

$$W_{CW} = 2(\gamma_C^p \gamma_W^p)^{1/2} + 2(\gamma_C^d \gamma_W^d)^{1/2} = \textbf{101 dyn/cm}$$

The work of adhesion between the amorphous oxide and water can be similarly calculated as:

$W_{AW} = \textbf{131 dyn/cm}$

The higher work of adhesion of water to the amorphous phase might suggest that water molecules will be more difficult to displace by proteins on the amorphous surface than the crystalline surface.