MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
370 HMMB

Final Exam: December 16, 2004 **Closed Book Exam**
Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Total
Max = 25	Max = 25	Max = 25	Max = 25	Max = 100

Extra Credit (2 pts.)

Cal was recently ranked 5th by the BCS. What does the acronym BCS mean (any creative answer will work)?

TABLE 5-6

Calculated Dispersion (γ_S^d) and Polar (γ_S^p) Contributions to Solid Surface Tension ($\gamma_S^d + \gamma_S^p$) (in units of dyne/cm for $|D| \geq 10.0$)

Number	Solid	$(\gamma_S^d)_m \pm \delta_m$		$(\gamma_S^p)_m \pm \delta_m$		$(\gamma_S)_m \pm \delta_m$		γ_c
1	Nylon 6,6	33.56	2.33	7.76	1.45	41.33	1.10	46
2	Polyethyleneterephthalate	36.59	3.02	2.88	1.12	39.48	1.96	43
3	Polystyrene	38.39	4.57	2.17	0.68	40.57	3.98	33
4	*n*-Hexatriacontane (s.c. $-CH_3$)	18.59	0.35	0.14	0.03	18.74	0.31	10–21
5	Paraffin	23.19	1.40	0.47	0.14	23.66	1.36	15–22
6	Polyethylene	31.29	2.21	1.10	0.42	32.39	1.80	31
7	Polyhexafluoropropylene	11.70	1.62	0.68	0.35	12.38	1.32	16.2
8	Polytetrafluoroethylene	14.54	0.88	1.02	0.22	15.56	0.71	18.5
9	Polytrifluoroethylene	21.88	1.15	2.92	0.46	24.81	0.73	22
10	Polyvinylidenefluoride	26.19	1.96	6.08	1.14	32.28	1.22	25
11	Polyvinylfluoride	31.15	0.91	5.49	0.51	36.64	0.65	28
12	Perchloropentadecaniecoic acid (m.l. $-C(Cl)=C(Cl)-$)	31.98	3.01	10.82	2.19	42.81	1.33	43
13	Polyvinylidene chloride	38.18	2.23	3.16	0.81	41.34	1.52	40
14	Polyvinylchloride	38.11	1.87	1.50	0.44	39.62	1.45	39
15	Perfluorolauric acid (m.l. $-CF_3$)	8.45	1.20	3.18	0.73	11.64	0.57	6
16	ω-monohydroperfluoroundecanoic acid (m.l. $-CF_2H$)	15.33	1.56	3.39	0.68	18.73	0.94	15
17	*n*-Octadecylamine (m.l. $-CH_3$)	22.03	1.25	0.97	0.31	23.01	0.98	24
18	Polymethylsiloxane	20.48	2.63	1.61	0.92	22.10	1.73	24
19	Poly[$C_7F_{15}CH_2OOC(CH_3)=CH_2$]	9.95	0.96	0.50	0.18	10.45	0.80	10.6
20	Poly[$C_8F_{17}SO2N(C_3H_7)CH_2OOCH=CH_2$]	10.26	0.89	0.39	0.16	10.66	0.74	11.1
21	80TFE:20 Kel—F cop.	16.33	1.69	1.88	0.67	18.52	1.12	20
22	60 TFE:40 Kel—F cop.	20.74	1.47	2.99	0.71	23.74	0.92	24
23	Polychlorotrifluoroethylene	23.83	2.85	3.10	1.20	26.93	1.74	31
24	50 TFE:50 Ethylene cop.	22.42	1.41	2.19	0.60	24.62	0.89	26–27

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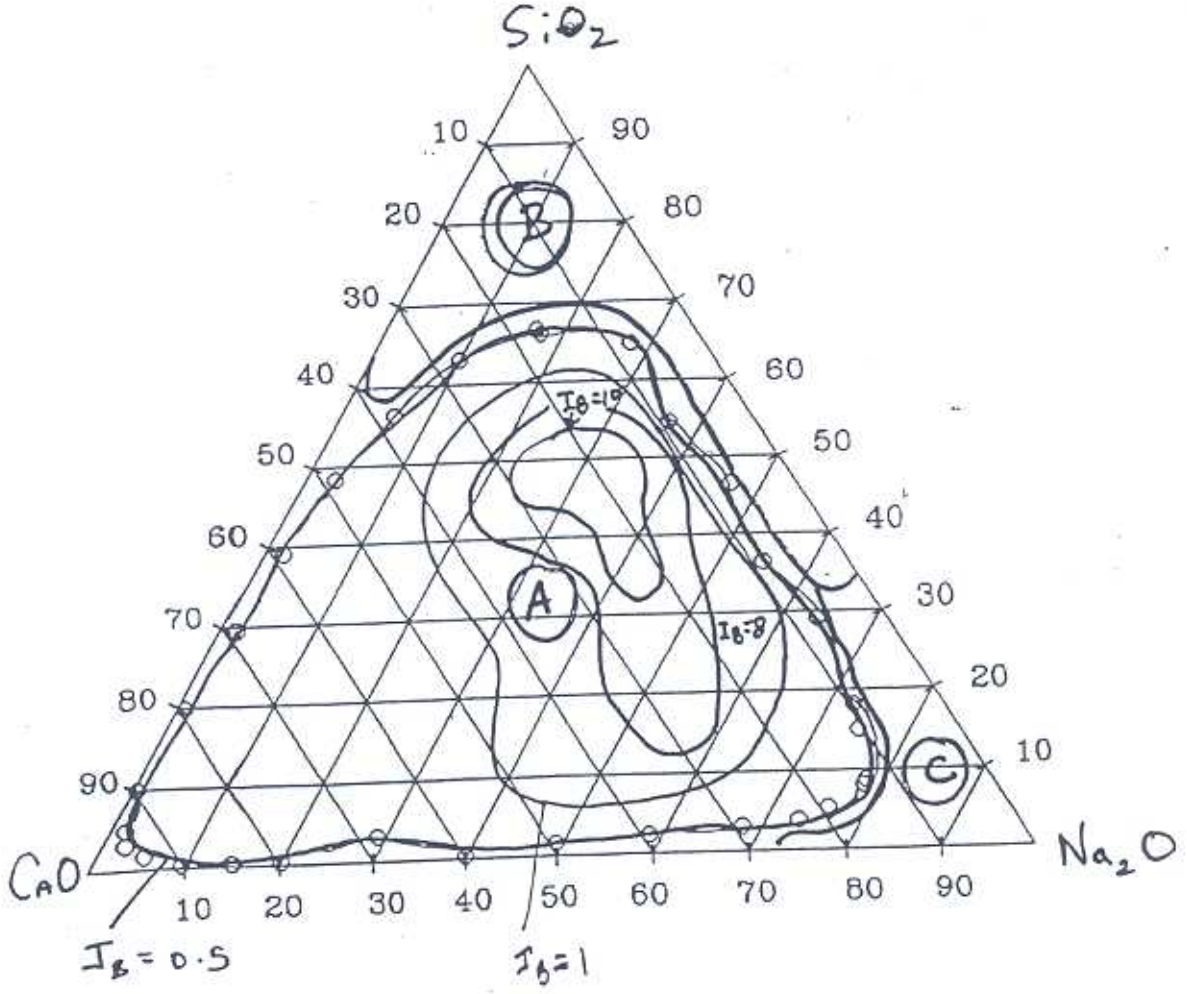
Name:_____

2. You are asked to design a modification to a polymer to be implanted in soft tissue (i.e., muscle, skin, etc.). Your modification should improve the attachment between soft tissue cells such as fibroblasts and the polymer. Before you modify your material, please explain the stages of wound healing and sequence of events related to the wound healing and inflammatory processes in soft tissues. What is your modification? How would you characterize your surface modification and evaluate the biological performance of the newly modified material? (20 pts.)



Ternary diagram of the "new" glass showing I_B as a function of composition.

Region (A): bonding to bone

Region (B): non-bonding

Region (C): non-bonding, hyperreactive

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 13, 2002 **Closed Book Exam**
Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Total
Max = 25	Max = 25	Max = 25	Max = 25	Max = 100

Extra Credit (2 pts.)

You have 10 candles for a cake and you want to place them in 5 rows of 4. How can the 10 candles be placed on the cake?

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2. You are trying to design a coating for a stainless steel stent and you decide to modify the stent with a long chain polymer such as either polyethylene glycol (pEG) or an oligosaccharide to improve the blood compatibility.

A. Explain how your polymer chain coating will intervene with the blood-clotting cascade?

B. Of the theories attributed to pEG's success in blood/protein-contacting environments, which are germane to most long-chain polymers? Conceptually explain these theories. Which properties make pEG unique?

C. For satisfactory blood-compatibility the repulsive energy per unit area between the pEG modified surface and molecules in solution separated by 5 nm should be greater than $1 Jm^{-2}$. Calculate the repulsive energy per unit area for pEG chains with a degree of polymerization of 50, l=0.4 nm per ethylene glycol group, and a maximum surface coverage (Γ) of 1 molecule/nm^2. Assume your coating can be modeled by the exponential approximation to the Alexander-de Gennes equation. Is the coating sufficient to prevent protein adsorption? If not, what could you change?

Name:_____

MSE/BioE C118

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MSE/BioE C118 Name:_____

3. You are designing an implantable reservoir based drug delivery system and are considering using either polyethylene or poly(trifluoroethylene) as the membrane controlling the delivery kinetics of a growth factor (i.e. protein). You conduct a protein adsorption study and find both polymers adsorb proteins to similar level, ~ 100 ng/cm^2.

A. You consider using either the critical surface tension (γ_c) or the minimum interfacial free energy hypothesis (i.e., γ_{SL} close to zero) to help you determine which material will adsorb less protein. Using poly(trifluoroethylene) as an example show that the theories contradict one another. Can you rely on these theories to predict protein adsorption behavior?

B. What equation would you use to explain the release of the drug (i.e., flux through the membrane)? Please explain the relevant terms.

C. How would the protein adsorption affect the drug delivery kinetics?

Name:_____

5. As a staff biomaterials scientist/engineer you are asked to evaluate a material being considered for blood contacting environments (e.g., grafts, catheters, etc.). The base polymer has excellent mechanical properties for a vascular graft, but poor blood-contacting performance. You decide to modify the material with polyethylene glycol (PEG) to improve the blood compatibility. You remember from your biomaterials class that PEG modifications demonstrate good performance under high flow rate conditions; however, the blood compatibility tests you perform show poor results, with protein and platelet deposition only after 6 hours of testing. You try to solve the dichotomy by analyzing the mechanisms of interaction between PEG and blood (i.e., blood components: proteins, platelets, etc.). (25 pts.)

A. What are the theories attributed to PEG's success in blood/protein-contacting environments? Conceptually explain these theories.

B. For satisfactory blood-compatibility the repulsive energy per unit area between the PEG modified surface and molecules in solution separated by 5 nm should be greater than 15 Jm^{-2}. Assuming your material can be modeled by the exponential approximation to the Alexander-de Gennes equation (see, end of exam), calculate the repulsive energy per unit area, W(D), at D=5nm. You know the number of ethylene glycol units (n) in the linear polymer is 10 and that l=0.4nm per ethylene glycol group. You measure the surface coverage (Γ) to be 2.41 molecules/nm^2.

C. What could you do to improve the blood-contacting performance of this material? [Hint: What can you do to change W(D)?]

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 18, 2001 **Closed Book Exam (2 hours)**
Please answer all of the questions clearly and box your final answer. Make sure you clearly demonstrate how you came to your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Prob. 5	Total
Max = 20	Max = 20	Max = 20	Max = 20	Max = 20	Max = 100

MSE/BioE C118 Name:_____

1. You are designing a cell transplantation system based on encapsulating cells within a polymer shell and are considering using either poly(tetrafluoroethylene) or poly(dimethylsiloxane) for the shell material. You wish to encapsulate islet cells for the production of insulin to control diabetes. The material must allow for exchange of nutrients (i.e., oxygen), clearances of wastes, and delivery of insulin. (25 pts.)

   a. You consider using either the critical surface tension (γ_c) or the minimum γ_{SL} hypothesis to help you determine which material will adsorb less protein. Using poly(tetrafluoroethylene) as an example, demonstrate that the theories contradict one another. Can you rely on these theories to predict protein adsorption behavior?

   b. How would you characterize the material?

   c. You decide to use poly(dimethylsiloxane). How would you design the shell to control the delivery of insulin? Hint: what equation would you use to explain the release of the drug (i.e., flux through the membrane)?

   d. How would the protein adsorption affect the insulin delivery kinetics?

   e. What other potential problems could you face?

MSE/BioE C118 Name:_____

2. How would you create a new bioactive glass for improving the initial stability of orthopedic total joint replacements that exploit biological fixation? (25 pts.)

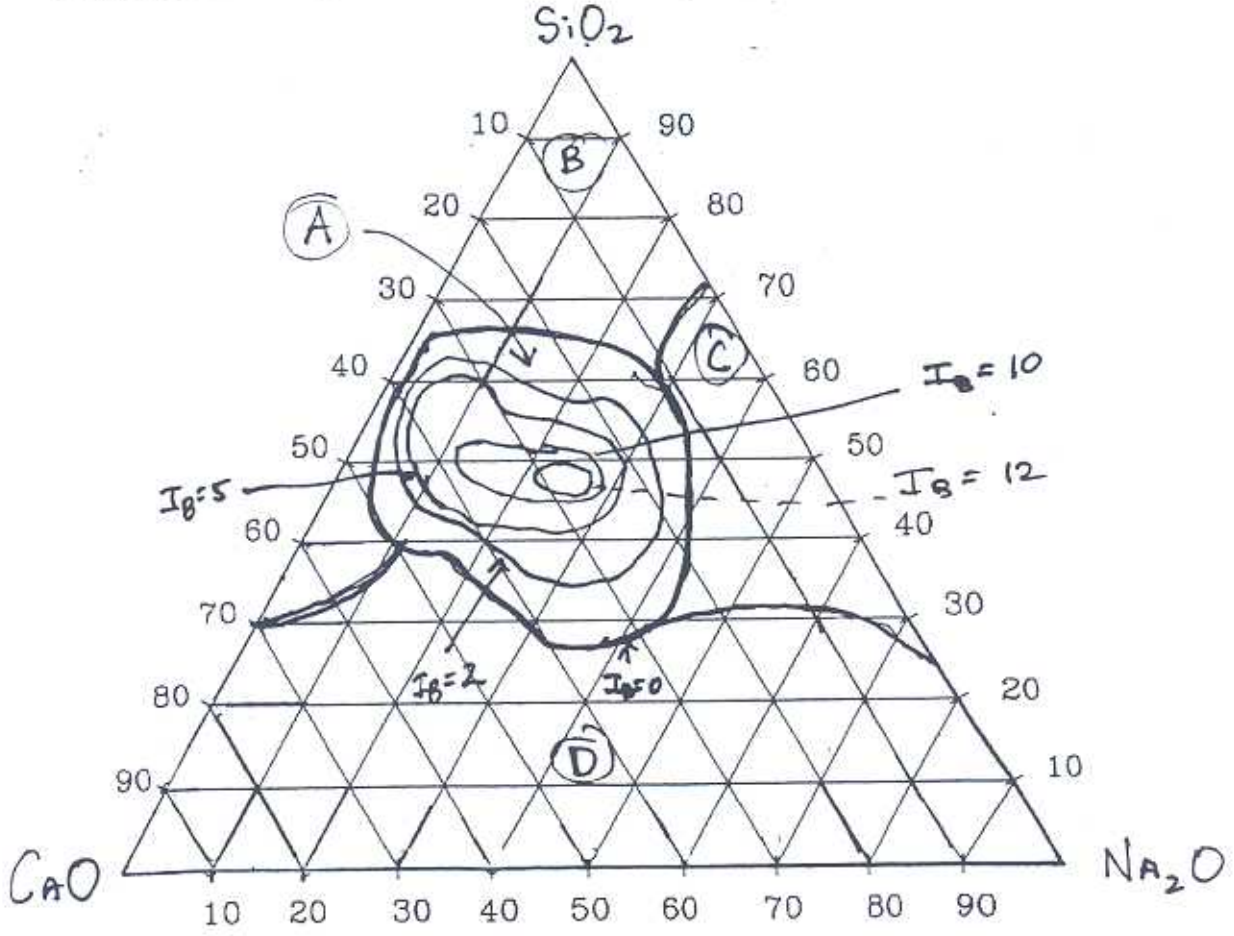
a) What experiments would you conduct to assess the biological performance of the bioglass and create the ternary phase diagram given below? First, define the index of bioactivity (I_B).

b) One of the glasses you develop seems promising, it has a composition of 45 wt.% SiO_2, 40 wt.% CaO, and 15 wt.% Na_2O? What is its I_B?

c) How does this glass compare to the binding activity of Bioglass® 45S5 (48 wt.% SiO_2, 26 wt.% CaO, and 26 wt.% Na_2O) and Ceravital® (55 wt.% SiO_2, 39 wt.% CaO, and 6 wt.% Na_2O)? What other materials are components of Ceravital®?

d) Assuming that the new glass develops an interface with bone similar to Ceravital®, describe the differences between the interface formed with these glasses and Bioglass 45S5? Which glass would have the highest interfacial bond strength with bone?

e) Which glass would you recommend for a bioactive glass coating? What are the limitations of using bioglasses and glass ceramics as coatings on total joint replacement to improve the interfacial bond strength between bone and the implant?



Ternary phase diagram of the "new" glass showing I_B as a function of composition. **Region A**: bone bonding; **Region B**: non-bonding, fibrous capsule formation; **Region C**: resorbable glasses: **Region D**: technically not practical.

MSE/BioE C118 Name:_____

Dupre equation: $W_{12} = \gamma_1 + \gamma_2 - \gamma_{12}$

$W_{12} = 2(\gamma_1 \gamma_2)^{1/2}$

Girifalco-Good-Fowkes: $\gamma_{12} = \gamma_1 + \gamma_2 - 2\sum_i(\gamma_1^i \gamma_2^i)^{1/2}$

i≡ dispersive, polar, ionic, metallic, acid–base, Lifshitz-van der Waals, etc.

γ_{H2O}^i $\gamma_{H2O} = 72.8$ ergs/cm^2, $\gamma_{H2O}^d = 21.8$ ergs/cm^2, $\gamma_{H2O}^p = 51$ ergs/cm^2

Young equation: $\gamma_{SV} = \gamma_{LV}\cos\theta + \gamma_{SL}$

Van der Waals' interaction free energy between a plate and a sphere

$$W_A(D) = \frac{-A_{123}R}{6D}$$

Van der Waals' interaction free energy between a plate and a plate

$$W_A(D) = \frac{-A_{123}}{12\pi D^2}$$

Electrostatic interaction free energy between a plate and a sphere

$$W_E(D) = \pi\varepsilon\varepsilon_o R_2\left(\phi_{13}^2 + \phi_{23}^2\right)\left[2\frac{\phi_{13}\phi_{23}}{\phi_{13}^2 + \phi_{23}^2}\ln\left(\frac{1+e^{-\kappa D}}{1-e^{-\kappa D}}\right) + \ln\left(1-e^{-2\kappa D}\right)\right]$$

Where 1= polymer surface
2= sphere (e.g., cell, protein)
3= medium

Electrostatic interaction free energy between a plate and a plate

$$W_E(D) = \left(64kT\rho_\infty u^2\right)e^{-\kappa D} \quad \text{Where} \quad u = \tanh\left(ze\phi_{13}/4kT\right)$$

Alexander-de Gennes equation: $W(D) \approx \frac{100L}{\pi s}\Gamma kT\exp\left(-\pi D/L\right)$ for D < 2L

Surface density $\Gamma = 1/s^2$

Alexander (1977) $L = nl^{5/3}/s^{2/3}$

Radius of gyration $R_g = ln^{1/2}/6^{1/2}$

Equations governing flux (g/cm^2-sec) through a membrane

$$J = \frac{EDK\Delta C}{\tau l} \qquad J = \frac{DK\Delta C}{l}$$

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 19, 2000 **Closed Book Exam (1.75 hours)**
Please answer all of the questions clearly and box your final answer. Make sure you clearly demonstrate how you came to your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Prob. 4	Total
Max = 15	Max = 20	Max = 20	Max = 20	Max = 25	Max = 100

4. You are given a new bioactive glass formulation purported to have superior bonding with bone. Your supervisor has asked you to determine its bioactivity and whether it is superior to existing bioactive glasses and glass/ceramics. You conduct tests that help you generate the "new" ternary bioactivity diagram shown below. Describe the general mechanism by which bioactive glasses and glass/ceramics bond to bone. What is the I_B for the new glass with a relative composition of 30 wt.% SiO_2, 50wt.% CaO, and 20 wt.% Na_2O? How does this glass compare to the binding activity of Bioglass® 45S5 (relative wt%'s: 48 wt.% SiO_2, 26 wt.% CaO, and 26 wt.% Na_2O). How would you change the composition of the glass to improve the index of bioactivity?. Give one application, including advantages and disadvantages, where you could use the glass with **your** new composition. (20 pts.)

BME-C44: Biological Performance of Materials **Prof. K.E. Healy, X3-4735**

Final Exam: 12/9/96 **Closed Book Exam**

Answer all of the questions. Useful equations, data, and physical constants appear at the end of the exam.

1. Structural ceramics (e.g., partially stabilized zirconia) are used for implants that experience high loads and extreme wear conditions, such as the femoral head of a total hip replacement. Explain the mechanism of the transformation toughening phenomena for ceramics containing tetragonal (t-) ZrO_2. The relationship between average grain size and yield strength has been given by the Hall-Petch equation,

$$\sigma_{yield} = \sigma_{96} + K/(d^{0.5})$$

What is the yield point for transformation-toughened ZrO_2 with the following physical properties: 96% dense ceramic, σ_{96} = 260 MPa; K= 0.8 MPa*$m^{0.5}$; and d= 4μm? How does this compare to the same material, ZrO_2, made with nanoparticles (grain size = 20 nm)? What might be some disadvantages of ceramics made from nanoparticles? (15 pts.)

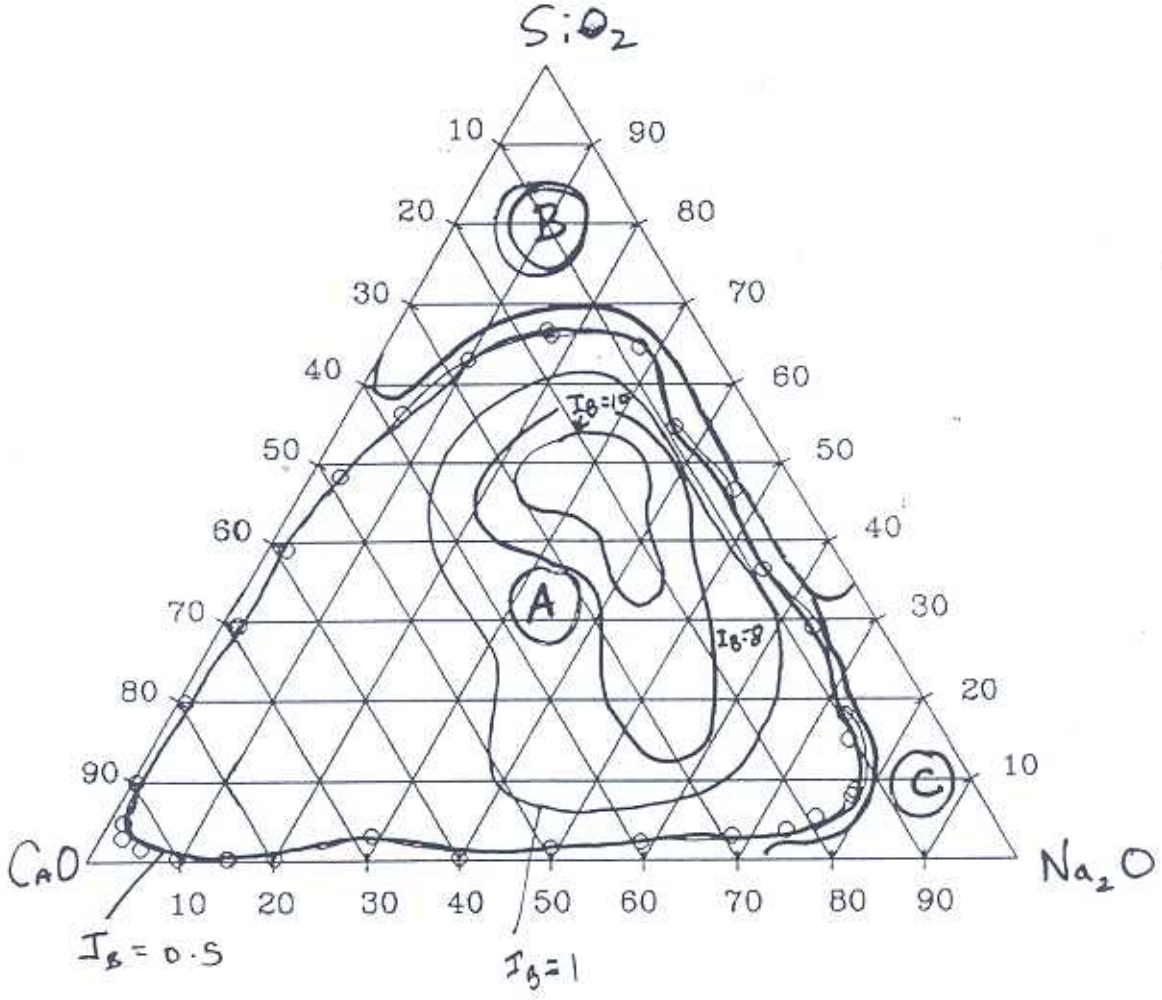
2. As a staff biomaterials scientist/engineer you are asked to evaluate a material being considered for blood contacting environments (e.g., grafts, catheters, etc.). The base polymer has excellent mechanical properties for a vascular graft, but poor blood-contacting performance. You decide to modify the material with polyethylene glycol (PEG) to improve the blood compatibility. You remember from your biomaterials class that PEG modifications demonstrate good performance under high flow rate conditions; however, the blood compatibility tests you perform show poor results, with protein and platelet deposition only after 12 hours of testing. You try to solve the dichotomy by analyzing the mechanisms of interaction between PEG and blood (i.e., blood components: proteins, platelets, etc.). (25 pts.)

A. What are the theories attributed to PEG's success in blood/protein-contacting environments? Conceptually explain these theories.

B. For satisfactory blood-compatibility the repulsive energy per unit area between the PEG modified surface and molecules in solution separated by 5 nm should be greater than 15 Jm^{-2}. Assuming your material can be modeled by the exponential approximation to the Alexander-de Gennes equation (see, end of exam), calculate the repulsive energy per unit area, W(D), at D=5nm. You know the number of ethylene glycol units (n) in the linear polymer is 10 and that l=0.4nm per ethylene glycol group. You measure the surface coverage (Γ) to be 2.41 molecules/nm^2.

C. What could you do to improve the blood-contacting performance of this material? [Hint: What can you do to change W(D)?]

3. You are asked **to design modifications** to a segmented polyurethane (SPU) transcutaneous (i.e., across the skin) catheter. You are aware that you need to maintain a tight seal around the catheter to prevent infection and provide good long term performance. Before you modify the SPU, please define the major stages of wound healing, and the sequence of events related to the wound healing and inflammatory processes in soft tissues. In suggesting your design, be aware that different activity is required along different portions of the catheter (e.g., outside or inside the body). How would you characterize your surface modification/s? Be sure to include expected outcomes of your tests! Finally, what kind of performance tests would you run on your modified device? (40 pts.)



Ternary diagram of the "new" glass showing I_B as a function of composition.

Region (A): bonding to bone

Region (B): non-bonding

Region (C): non-bonding, hyperreactive

BME-C44: Biological Performance of Materials
Dr. K.E. Healy, X3-4735
Final Exam: 6/7/95 3:00 - 5:00 p.m.

Answer all of the questions. Useful equations, data, diagrams, and physical constants appear at the end of the exam.

1. As a staff engineer for a biomedical device manufacturer you are given a new polymer to evaluate as a possible material for a small diameter vascular graft. This material is more compliant and has superior mechanical properties than PTFE and PET. You are asked to conduct a series of experiments to evaluate the blood-contacting performance of this material. *In vivo* blood-contacting experiments indicate that the material causes clotting when used in situations where the diameter of the graft is less than 4 mm. **Design a surface modification for this device.** Be sure to address the following: how you are intervening in the blood-clotting cascade, the type of modification, the physical, chemical, and biological principles underlying your choice of modification, potential longevity of coating, and any assumptions you make regarding the starting material's surface chemistry. (30 pts.)

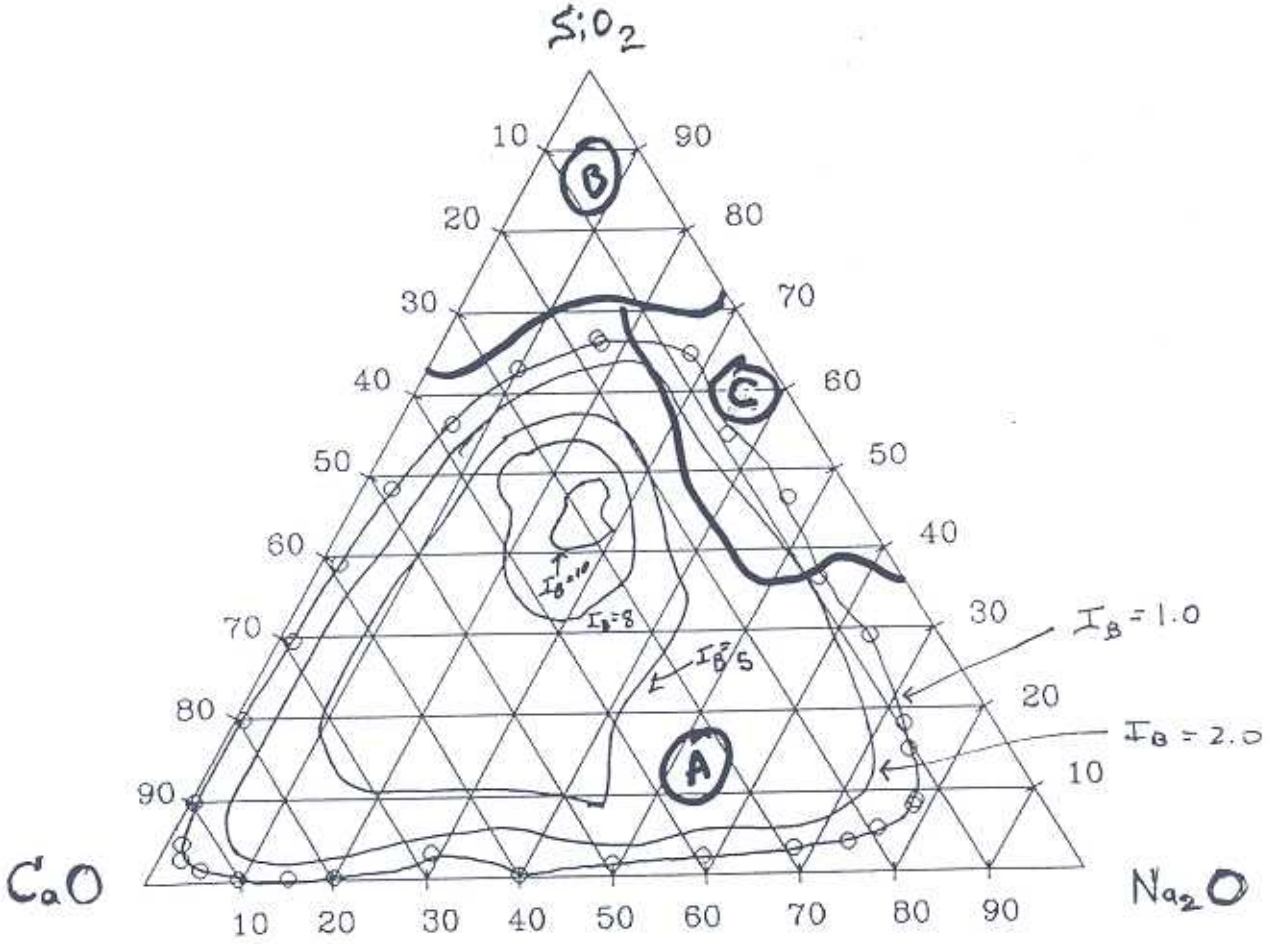
2. You are given a new glass formulation purported to have superior bonding with bone. Your supervisor has asked you to determine its bioactivity and if it is indeed better than existing bioactive glasses and glass/ceramics. You conduct tests that help you generate the "new" ternary bioactivity diagram on the next page. What is the index of bioactivity (I_B)? What is the I_B for the new glass with a composition of 50 wt.% SiO_2, 30 wt.% CaO, and 20 wt.% Na_2O? How does this glass compare to the binding activity of Bioglass® 45S5 (48 wt.% SiO_2, 26 wt.% CaO, and 26 wt.% Na_2O) and Ceravital® (55 wt.% SiO_2, 39 wt.% CaO, and 6 wt.% Na_2O)? Assuming that the new glass develops an interface with bone similar to Bioglass 45S5, describe the differences between the interface formed with these glasses and Ceravital®? Which glass would have the highest interfacial bond strength with bone? What are the limitations of using bioglasses and glass ceramics as coatings on total joint replacement to improve the interfacial bond strength between bone and the implant? (30 pts.)

3. The relationship between grain size and yield strength has been given by the Hall-Petch equation,

$$\sigma_{yield} = \sigma_o + K/(d^{0.5})$$

What is the effect of grain size (d) on the yield point of polycrystalline ceramics, i.e. ZrO_2? What is transformation toughening? What are the yield points for transformation-toughened ZrO_2 with the following physical properties: nearly 100% dense ceramic (P=0); σ_o =300 MPa; K= 0.8 $MPa*m^{0.5}$; and d= 5μm? How does this compare to the same material with d= 15μm? How would an increase in porosity, i.e. P=10%, influence the mechanical properties of transformation-toughened ZrO_2? (20 pts.)

4. Select one presentation topic given by a fellow student in class [obviously you cannot select your own]. Identify the topic, address the materials used for the application from the standpoint of the general biological performance, and indicate the need for surface modification of the materials. Critically evaluate the design modifications presented in class, and suggest possible alternatives. (20 pts.)



Ternary diagram of the "new" glass showing I_B as a function of composition. Region (A): bonding; Region (B): NON-bonding; region (C): non-bonding, hypereactive.

5. As a staff biomaterials scientist/engineer you are asked to evaluate a material being considered for blood contacting environments (e.g., grafts, catheters, etc.). The base polymer has excellent mechanical properties for a vascular graft, but poor blood-contacting performance. You decide to modify the material with polyethylene glycol (PEG) to improve the blood compatibility. You remember from your biomaterials class that PEG modifications demonstrate good performance under high flow rate conditions; however, the blood compatibility tests you perform show poor results, with protein and platelet deposition only after 6 hours of testing. You try to solve the dichotomy by analyzing the mechanisms of interaction between PEG and blood (i.e., blood components: proteins, platelets, etc.). (25 pts.)

A. What are the theories attributed to PEG's success in blood/protein-contacting environments? Conceptually explain these theories.

B. For satisfactory blood-compatibility the repulsive energy per unit area between the PEG modified surface and molecules in solution separated by 5 nm should be greater than 15 Jm^{-2}. Assuming your material can be modeled by the exponential approximation to the Alexander-de Gennes equation (see, end of exam), calculate the repulsive energy per unit area, W(D), at D=5nm. You know the number of ethylene glycol units (n) in the linear polymer is 10 and that l=0.4nm per ethylene glycol group. You measure the surface coverage (Γ) to be 2.41 molecules/nm^2.

C. What could you do to improve the blood-contacting performance of this material? [Hint: What can you do to change W(D)?]

MSE/BioE C118 Name:_____

Dupre equation: $W_{12} = \gamma_1 + \gamma_2 - \gamma_{12}$

$W_{12} = 2(\gamma_1 \gamma_2)^{1/2}$

Gibbs equation: $d\gamma = -\Gamma kT\, dP/P$

Girifalco-Good-Fowkes: $\gamma_{12} = \gamma_1 + \gamma_2 - 2\sum_i(\gamma_1^i \gamma_2^i)^{1/2}$

i≡ dispersive, polar, ionic, metallic, acid-base, Lifshitz-van der Waals, etc.

γ_{H2O}^i $\gamma_{H2O} = 72.8$ ergs/cm^2, $\gamma_{H2O}^d = 21.8$ ergs/cm^2, $\gamma_{H2O}^p = 51$ ergs/cm^2

Young equation: $\gamma_{SV} = \gamma_{LV} \cos\theta + \gamma_{SL}$

Van der Waals' interaction free energy between a plate and a sphere

$$W_A(D) = \frac{-A_{123}R}{6D}$$

Alexander-de Gennes equation: $W(D) \approx 100L/\pi s\, \Gamma kT \exp(-\pi D/L)$ for $D < 2L$

$\Gamma = 1/s^2$

Alexander (1977) $L = nl^{5/3}/s^{2/3} = \Gamma^{1/2} R_F^{5/3}$

MSE/BioE C118 Name:_____

Dupre equation: $W_{12} = \gamma_1 + \gamma_2 - \gamma_{12}$

$W_{12} = 2(\gamma_1 \gamma_2)^{1/2}$

Girifalco-Good-Fowkes: $\gamma_{12} = \gamma_1 + \gamma_2 - 2\Sigma_i(\gamma_1^i \gamma_2^i)^{1/2}$

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$$W_A(D) = \frac{-A_{123}}{12\pi D^2}$$

Electrostatic interaction free energy between a plate and a sphere

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Where 1= polymer surface
2= sphere (e.g., cell, protein)
3= medium

Electrostatic interaction free energy between a plate and a plate

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Alexander (1977) $L = nl^{5/3}/s^{2/3}$

Radius of gyration $R_g = ln^{1/2}/6^{1/2}$

Equations governing flux (**g/cm^2-sec**) through a membrane

$$J = \frac{EDK\Delta C}{\tau l} \qquad J = \frac{DK\Delta C}{l}$$

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 13, 2002 . **Closed Book Exam**
Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Total
Max = 25	Max = 25	Max = 25	Max = 25	Max = 100

Extra Credit (2 pts.)

You have 10 candles for a cake and you want to place them in 5 rows of 4. How can the 10 candles be placed on the cake?

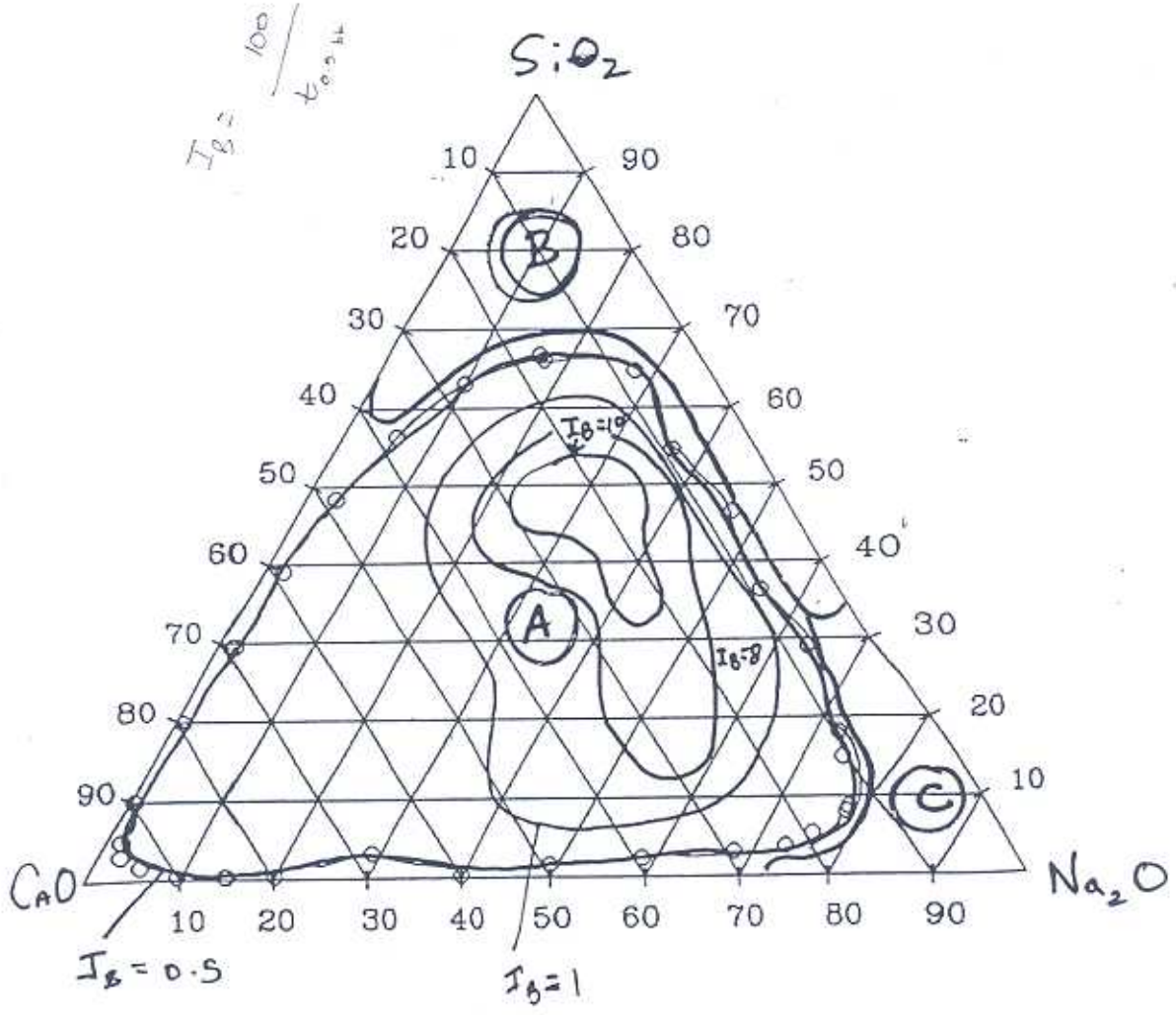
MSE/BioE C118 Name:_____

1. As a biomedical engineer in a cardiac device company you are trying to improve a segmented polyurethane (SPU) for a ventricular assist device. The device is primarily exposed to soft tissue and you wish to minimize the fibrous tissue surrounding the implant.

A. Explain the stages of wound healing and sequence of events related to the wound healing and inflammatory processes in soft tissues.

B. How would you modify and characterize the SPU?

C. How would you characterize your surface modification and evaluate the biological performance of the newly modified material?



Ternary diagram of the "new" glass showing I_B as a function of composition.

Region (A): bonding to bone

Region (B): non-bonding

Region (C): non-bonding, hyperreactive

4. Select one presentation topic given by a fellow student group in class [obviously you cannot select your own]. Identify the topic, address the materials used for the application from the standpoint of the general biological performance. Critically evaluate the design modifications presented in class, and suggest possible alternatives. (20 pts.)

2. You are asked to design a modification to a polymer to be implanted in soft tissue (i.e., muscle, skin, etc.). Your modification should improve the attachment between soft tissue cells such as fibroblasts and the polymer. Before you modify your material, please explain the stages of wound healing and sequence of events related to the wound healing and inflammatory processes in soft tissues. What is your modification? How would you characterize your surface modification and evaluate the biological performance of the newly modified material? (20 pts.)

3. You are given a new glass formulation purported to have superior bonding with bone. Your supervisor has asked you to determine its bioactivity and if it is indeed better than existing bioactive glasses and glass/ceramics. You conduct tests that help you generate the "new" ternary bioactivity diagram given on the next page. Define the index of bioactivity (I_B)? What is the I_B for the new glass with a composition of 30 wt.% SiO_2, 50 wt.% CaO, and 20 wt.% Na_2O? How does this glass compare to the binding activity of Bioglass® 45S5 (48 wt.% SiO_2, 26 wt.% CaO, and 26 wt.% Na_2O)? Assuming that the new glass develops an interface with bone similar to Bioglass 45S5, describe the differences between the interface formed with these glasses and Ceravital®? Which glass would have the highest interfacial bond strength with bone? What are the limitations of using bioglasses and glass ceramics as coatings on total joint replacement to improve the interfacial bond strength between bone and the implant? (20 pts.)

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MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 19, 2000 **Closed Book Exam (1.75 hours)**
Please answer all of the questions clearly and box your final answer. Make sure you clearly demonstrate how you came to your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Prob. 4	Total
Max = 15	Max = 20	Max = 20	Max = 20	Max = 25	Max = 100

MSE/BioE C118 Name:_____

1. Structural ceramics (e.g., partially stabilized zirconia) are used for implants that experience high loads and extreme wear conditions, such as the femoral head of a total hip replacement. Explain the mechanism of the transformation toughening phenomena for ceramics containing tetragonal (t-) ZrO_2. The relationship between average grain size and yield strength has been given by the Hall-Petch equation,

$$\sigma_{yield} = \sigma_{96} + K/(d^{0.5})$$

What is the yield point for transformation-toughened ZrO_2 with the following physical properties: 96% dense ceramic, σ_{96} = 260 MPa; K= 0.8 MPa*$m^{0.5}$; and d= 4μm? How does this compare to the same material, ZrO_2, made with nanoparticles (grain size = 20 nm)? What might be some disadvantages of ceramics made from nanoparticles? (15 pts.)

Name:_____

2. The peptide sequence TVK has been identified as an epitope for promotion of hepatocyte attachment. As a bioengineer at a device company, you have been asked to investigate the efficacy of incorporating this peptide with a scaffold for tissue engineering to be implanted in the body. (20 pts.)

a. Describe the sequence of events that normally comprise the wound healing and inflammatory responses for soft tissue surrounding the scaffold.

b. How would you develop *in vitro* tests to quantitatively determine any increase in hepatocyte attachment compared with the unmodified scaffold? How would you characterize the modified scaffold surface?

MSE/BioE C118 Name:_____

3. You are trying to develop a strategy for a pharmaceutical company to prevent protein adsorption to their protein purification vessels and conduit. The vessels are made from 316L stainless steel. (20 pts.)

a. In deciding on a strategy you consider both the minimum interfacial free energy and the critical surface tension hypotheses as ways to minimize protein adsorption. Explain each theory and their inherent limitations in predicting protein adsorption to surfaces.

b. You decide to modify the material with polyethylene glycol (PEG) to improve the resistance to protein adsorption. You know the degree of polymerization is 100 for the linear polymer and that l=0.4nm per ethylene glycol group. How would you attach the PEG to the vessel? After grafting you measure the mean spacing between PEG molecules to be 1 nm. Compare the unperturbed radius of gyration (R_g) to the thickness (L) of the attached PEG brush layer.

c. To resist protein adsorption the interaction free energy between the PEG-modified surface and the proteins in solution must be at least 20 Jm^{-2} at a separation distance of 5 nm. Assuming the interaction between your PEG layer and protein can be modeled by the exponential approximation to the Alexander-de Gennes equation, calculate the repulsive energy per unit area, W(D)? Is this sufficient to prevent protein adsorption? If not, what would you change to increase the interaction free energy?

MSE/BioE C118 Name:_____

4. You are asked to evaluate a new polymer for cardiovascular applications. To evaluate the polymer you begin by making a contact angle measurement and find $\theta_{ADV}^{H_2O}$ is approximately 105°. Next you decide to conduct a static protein adsorption experiment where you perform both direct and successive addition of protein to the test solution. (20 pts.)

a. Draw protein adsorption isotherms for both the direct and successive adsorption experiments as a function of time.
b. Describe the mechanisms that led to the difference in the experimental curves.
c. What other characterization techniques would you use to evaluate the material?
d. How could you manipulate the protein adsorption behavior of this material to improve its biological performance?

Name:_____

5. You are trying to design a drug delivery system based on the biodegradable polymers poly(L-lactide), poly(D,L-Lactide), and poly(glycolide). Discuss the degradation mechanism for each in an aqueous environment. Explain the difference in the degradation rates of the isomers based on their microstructure. You make a copolymer of 85:15 poly(L-Lactide-*co*-glycolide), how is the degradation of this material different from the homopolymers. You then decide to use the double emulsion technique to create microspheres of 85:15 poly(L-Lactide-*co*-glycolide) containing vascular endothelial growth factor (VEGF) to be released over a 4-week period. What fabrication and material properties would you alter to achieve the desired release kinetics. Be sure to give an example curve of your release profile describing the mechanisms of VEGF release during the different stages. (20 pts.)

MSE/BioE C118 Name:_____

Dupre equation: $W_{12} = \gamma_1 + \gamma_2 - \gamma_{12}$

$W_{12} = 2(\gamma_1 \gamma_2)^{1/2}$

Gibbs equation: $d\gamma = -\Gamma kT\, dP/P$

Girifalco-Good-Fowkes: $\gamma_{12} = \gamma_1 + \gamma_2 - 2\sum_i(\gamma_1^i \gamma_2^i)^{1/2}$

i≡ dispersive, polar, ionic, metallic, acid-base, Lifshitz-van der Waals, etc.

γ_{H2O}^i $\gamma_{H2O} = 72.8$ ergs/cm^2 , $\gamma_{H2O}^d = 21.8$ ergs/cm^2 , $\gamma_{H2O}^p = 51$ ergs/cm^2

Young equation: $\gamma_{SV} = \gamma_{LV} \cos\theta + \gamma_{SL}$

Van der Waals' interaction free energy between a plate and a sphere

$$W_A(D) = \frac{-A_{123}R}{6D}$$

Electrostatic interaction free energy between a plate and a sphere

$$W_E(D) = \pi\varepsilon\varepsilon_o R_2\left(\phi_{13}^2 + \phi_{23}^2\right)\left[2\frac{\phi_{13}\phi_{23}}{\phi_{13}^2 + \phi_{23}^2}\ln\left(\frac{1+e^{-\kappa D}}{1-e^{-\kappa D}}\right) + \ln\left(1-e^{-2\kappa D}\right)\right]$$

Where 1= polymer surface
2= sphere (e.g., cell, protein)
3= medium

Alexander-de Gennes equation: $W(D) \approx \frac{100L}{\pi s}\Gamma kT \exp\left(-\pi D/L\right)$ for D < 2L

Surface density $\Gamma = 1/s^2$

Alexander (1977) $L = nl^{5/3}/s^{2/3} = \Gamma^{1/3}R_F^{5/3}$

Radius of gyration $R_g = ln^{1/2}/6^{1/2}$

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 18, 2001 **Closed Book Exam (2 hours)**
Please answer all of the questions clearly and box your final answer. Make sure you clearly demonstrate how you came to your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

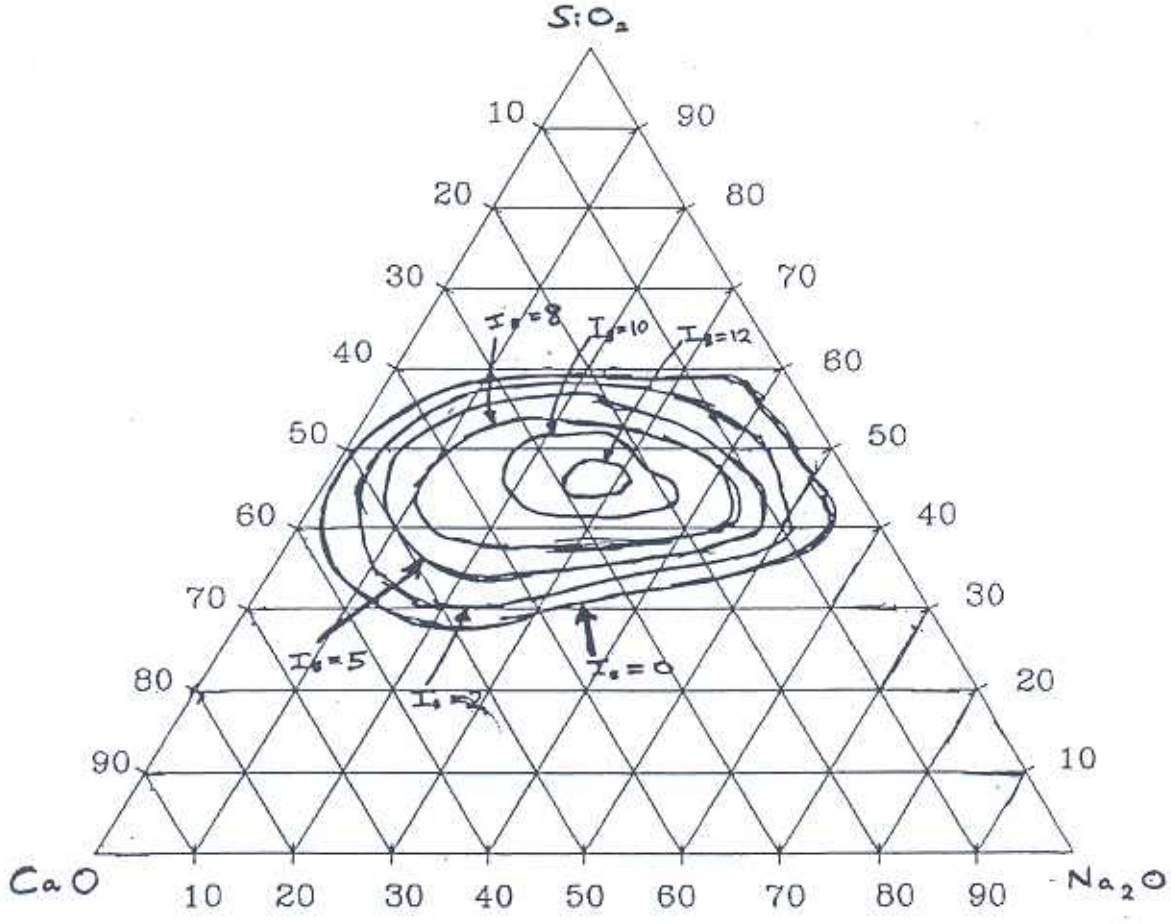
ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Prob. 5	Total
Max = 20	Max = 20	Max = 20	Max = 20	Max = 20	Max = 100

MSE/BioE C118 Name:_____

1. You are given the ternary phase diagram below for the index of bioactivity of bone bonding as a function of bioactive glass composition. (20 pts.)

a. Define the index of bioactivity (I_B)?
b. What experiments would you perform to construct the ternary phase diagram?
c. What is the I_B of Bioglass® 45S5 (48 wt.% SiO_2, 26 wt.% CaO, and 26 wt.% Na_2O)?
d. Give the composition and I_B of a bioactive glass that would have greater interfacial bonding with bone compared to Bioglass® 45S5. Explain the mechanism by which both glasses bond with bone and the reason why your glass would have a greater interfacial bond strength.



MSE/BioE C118 Name:_____

1. You are designing a cell transplantation system based on encapsulating cells within a polymer shell and are considering using either poly(tetrafluoroethylene) or poly(dimethylsiloxane) for the shell material. You wish to encapsulate islet cells for the production of insulin to control diabetes. The material must allow for exchange of nutrients (i.e., oxygen), clearances of wastes, and delivery of insulin. (25 pts.)

   a. You consider using either the critical surface tension (γ_c) or the minimum γ_{SL} hypothesis to help you determine which material will adsorb less protein. Using poly(tetrafluoroethylene) as an example, demonstrate that the theories contradict one another. Can you rely on these theories to predict protein adsorption behavior?

   b. How would you characterize the material?

   c. You decide to use poly(dimethylsiloxane). How would you design the shell to control the delivery of insulin? Hint: what equation would you use to explain the release of the drug (i.e., flux through the membrane)?

   d. How would the protein adsorption affect the insulin delivery kinetics?

   e. What other potential problems could you face?

3. Polysaccharides are attractive materials for creating non-fouling surfaces and provide an alternative to polyethylene glycol (pEG). Assume classic polymer brush equations explain the behavior of polysaccharides tethered to surfaces.

a. Calculate the radius of gyration (R_g) for a polysaccharide with a degree of polymerization (40,000) and bond length (l=0.3 nm). How is the R_g related to the Flory radius in both a good and poor solvent? Is water a good or poor solvent for most polysaccharides?

b. What criterion would you use to design the surface density (i.e., surface excess, Γ) of the polysaccharide molecules? Define your assumptions and calculate that Γ.

c. Is the interaction free energy of the surface, using the Γ you defined, sufficient to prevent protein adsorption and act as a non-fouling surface?

d. What advantages do polysaccharides have over polymers like pEG as non-fouling coatings?

4. You are making a vascular equivalent and have identified the peptide sequence KEH that promotes vascular smooth muscle cell attachment. As a bioengineer at a medical device company, you have been asked to investigate the efficacy of incorporating this peptide within a scaffold for engineering a vascular tissue equivalent. (25 pts.)

a. How would you immobilize the peptide to a 50:50 poly(glycolide-co-lactide) copolymer?

b. How would you develop *in vitro* tests to quantitatively determine any increase in smooth muscle cell attachment compared with the unmodified scaffold? How would you characterize the modified scaffold surface?

c. Describe the sequence of events that normally comprise the wound healing and inflammatory responses for soft tissue surrounding an implant material.

d. Do you foresee a similar wound healing response with your vascular tissue equivalent.

MSE/BioE C118 Name:_____

4. You would like to design a scaffold (i.e., porous body) for engineering the regeneration of tissue in the body. What are the three key components of tissue engineering? After considering the materials available commercially, you decide to use biodegradable polymers for the scaffold. What are the advantages of using a biodegradable polymer for this application? For your biodegradable polymers you are considering using poly(L-lactide), poly(D,L-lactide-co-glycolide), or poly(sebacic acid-hexadecandioic acid anhydride) [poly(SA-HAD anhydride)]. Discuss the degradation mechanisms and rates for each in an aqueous environment. You decide to make the scaffold out of 25:75 poly(D,L-lactide-co-glycolide), how would you make a scaffold out of this material? How fast would you expect it to degrade and why? What kind of processing could you perform to extend the lifetime of the scaffold? How would you enhance the growth of cells within the scaffold?

MSE/BioE C118 Name:_____

Dupre equation: $W_{12} = \gamma_1 + \gamma_2 - \gamma_{12}$

$W_{12} = 2(\gamma_1 \gamma_2)^{1/2}$

Girifalco-Good-Fowkes: $\gamma_{12} = \gamma_1 + \gamma_2 - 2\sum_i(\gamma_1^i \gamma_2^i)^{1/2}$

i≡ dispersive, polar, ionic, metallic, acid-base, Lifshitz-van der Waals, etc.

γ_{H2O}^i $\gamma_{H2O} = 72.8$ ergs/cm^2 , $\gamma_{H2O}^d = 21.8$ ergs/cm^2 , $\gamma_{H2O}^p = 51$ ergs/cm^2

Young equation: $\gamma_{SV} = \gamma_{LV} \cos\theta + \gamma_{SL}$

Van der Waals' interaction free energy between a plate and a sphere

$$W_A(D) = \frac{-A_{123}R}{6D}$$

Van der Waals' interaction free energy between a plate and a plate

$$W_A(D) = \frac{-A_{123}}{12\pi D^2}$$

Electrostatic interaction free energy between a plate and a sphere

$$W_E(D) = \pi\varepsilon\varepsilon_o R_2\left(\phi_{13}^2 + \phi_{23}^2\right)\left[2\frac{\phi_{13}\phi_{23}}{\phi_{13}^2 + \phi_{23}^2}\ln\left(\frac{1+e^{-\kappa D}}{1-e^{-\kappa D}}\right) + \ln\left(1-e^{-2\kappa D}\right)\right]$$

Where 1= polymer surface
2= sphere (e.g., cell, protein)
3= medium

Electrostatic interaction free energy between a plate and a plate

$$W_E(D) = \left(64kT\rho_\infty u^2\right)e^{-\kappa D} \qquad \text{Where} \qquad u = \tanh\left(ze\phi_{13}/4kT\right)$$

Alexander-de Gennes equation: $W(D) \approx \frac{100L}{\pi s}\Gamma kT\exp\left(-\pi D/L\right)$ for D < 2L

Surface density $\Gamma = 1/s^2$

Alexander (1977) $L = nl^{5/3}/s^{2/3}$

Radius of gyration $R_g = ln^{1/2}/6^{1/2}$

Equations governing flux (**g/cm^2-sec**) through a membrane

$$J = \frac{EDK\Delta C}{\tau l} \qquad J = \frac{DK\Delta C}{l}$$

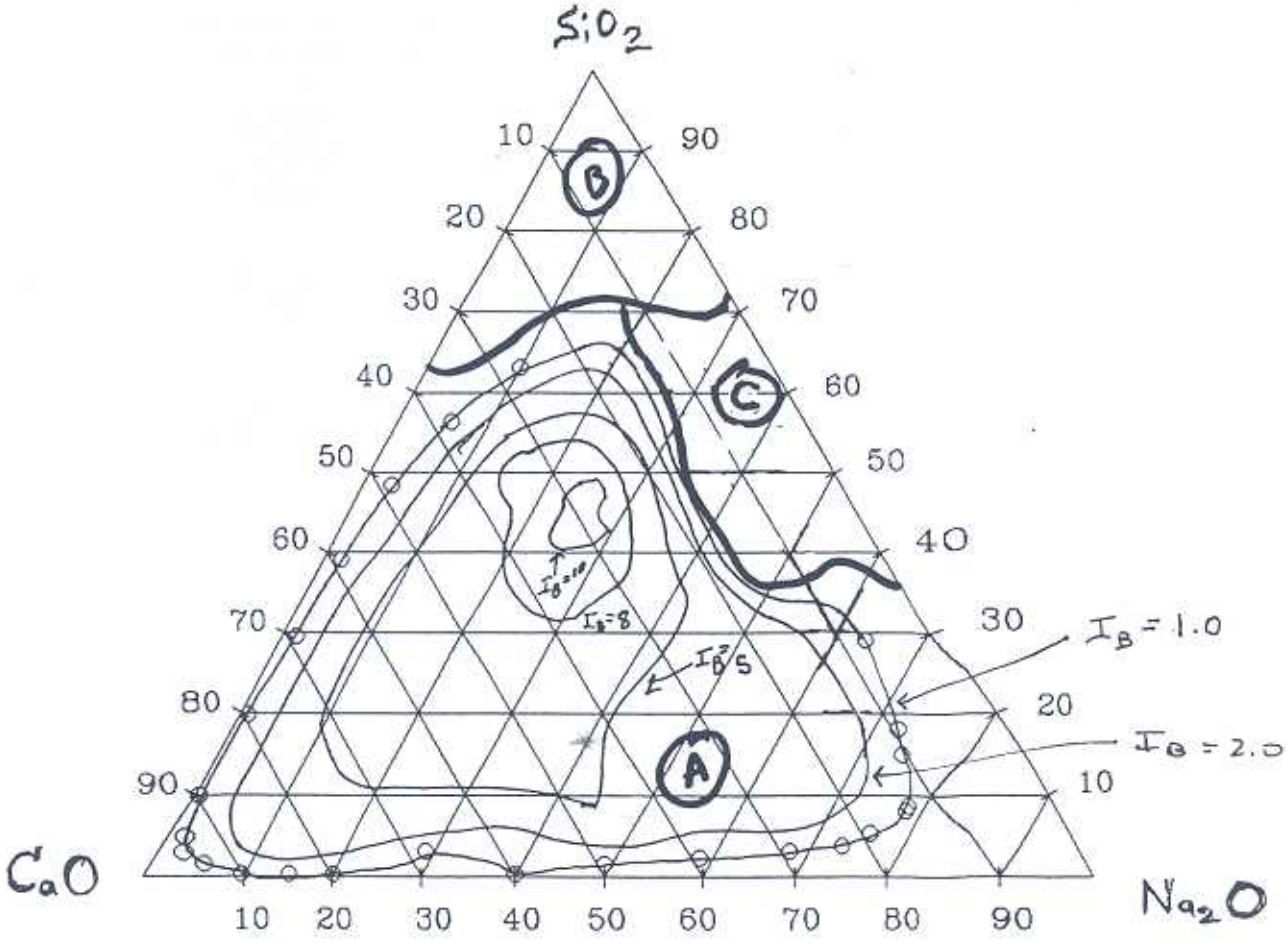
4. You are making a vascular equivalent and have identified the peptide sequence KEH that promotes vascular smooth muscle cell attachment. As a bioengineer at a medical device company, you have been asked to investigate the efficacy of incorporating this peptide within a scaffold for engineering a vascular tissue equivalent. (25 pts.)

a. How would you immobilize the peptide to a 50:50 poly(glycolide-co-lactide) copolymer?

b. How would you develop *in vitro* tests to quantitatively determine any increase in smooth muscle cell attachment compared with the unmodified scaffold? How would you characterize the modified scaffold surface?

c. Describe the sequence of events that normally comprise the wound healing and inflammatory responses for soft tissue surrounding an implant material.

d. Do you foresee a similar wound healing response with your vascular tissue equivalent.



Ternary diagram of the "new" glass showing I_B as a function of composition. Region (A): bonding; Region (B): NON-bonding; region (C): non-bonding, hyperreactive.

MSE/BioE C118 Name:_____

3. As a staff biomaterials scientist/engineer you are asked to evaluate a material being considered for blood-contacting environments (e.g., grafts, ventricular assist devices, catheters, etc.). The base polymer has excellent mechanical properties, but poor blood-contacting performance. To improve the blood compatibility you decide to modify the material with a new polymer (pX) that behaves in a similar manner to polyethylene glycol (pEG); however, it is easier to graft to the base material. For optimum blood-compatibility assume the relationship between the chain spacing (s) and radius of gyration (R_g) for pX scales with that observed for protein adsorption for pEG. (25 pts.)

a. Of the theories attributed to pEG's success in blood/protein-contacting environments, which are germane to most long-chain polymers like pX? Conceptually explain these theories.

b. Derive an expression for pX surface density (molec./area) in terms of the degree of polymerization (10,000) and bond length (l=0.147 nm) that would optimize blood-compatibility. Assume an ideal solvent, i.e. the intramolecular expansion factor is unity. What is this optimal surface density?

c. Assuming your material can be modeled by the exponential approximation to the Alexander-de Gennes equation, calculate the interaction free energy per unit area, W(D), at R_g. Is this energy sufficient to repel protein adsorption and platelet adhesion?

d. Explain how solvent and temperature affect the pX protrusion from the surface (i.e., L). How would solvent and temperature affect W(D) and therefore blood-compatibility.

MSE/BioE C118 Name:_____

1. Deployment of an intravascular stent using an angioplasty balloon initiates a classic wound healing response. (25 pts.)

a. Explain each stage of the wound healing and inflammatory response starting with the initial events.

b. Discuss a modification presented in class from a group other than your own that you could use to improve the native wound healing response. Make sure you explain the mechanism/s by which this modification would alter the wound healing response.

c. What techniques would you use to characterize the modification?

MSE/BioE C118 Name:_____

2. You would like to create a new bioactive glass to bond to bone and decide to examine glasses made from SiO_2, CaO, Na_2O, and P_2O_5. (25 pts.)

a. What is the index of bioactivity (I_B)?
b. What experiments would you perform to generate the ternary phase diagram given below?
c. What is the I_B of a bioactive glass with 80 wt.% SiO_2, 10 wt.% CaO, and 10 wt.% Na_2O? Does this glass bond to bone?
d. How would you change the glass composition to maximize the I_B?
e. Does the glass with maximum I_B have greatest interfacial bonding with bone compared to glass compositions. Explain your answer in terms of the mechanism by which bioactive glasses bond with bone.

Ternary phase diagram of the "new" glass showing I_B as a function of composition. Region A: bonding; Region B: non-bonding; Region C: non-bonding, hyper-reactive

MSE/BioE C118 Name:_____

4. You would like to design a scaffold (i.e., porous body) for engineering the regeneration of tissue in the body. What are the three key components of tissue engineering? After considering the materials available commercially, you decide to use biodegradable polymers for the scaffold. What are the advantages of using a biodegradable polymer for this application? For your biodegradable polymers you are considering using poly(L-lactide), poly(D,L-lactide-co-glycolide), or poly(sebacic acid-hexadecandioic acid anhydride) [poly(SA-HAD anhydride)]. Discuss the degradation mechanisms and rates for each in an aqueous environment. You decide to make the scaffold out of 25:75 poly(D,L-lactide-co-glycolide), how would you make a scaffold out of this material? How fast would you expect it to degrade and why? What kind of processing could you perform to extend the lifetime of the scaffold? How would you enhance the growth of cells within the scaffold?

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
465 Evans Hall

Final Exam: December 12, 2003 **Closed Book Exam**
Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Total
Max = 25	Max = 25	Max = 25	Max = 25	Max = 100

Extra Credit (2 pts.)

What product did John Scharffenberger make prior to chocolate?

2. The peptide sequence TVK has been identified as an epitope for promotion of hepatocyte attachment. As a bioengineer at a device company, you have been asked to investigate the efficacy of incorporating this peptide with a scaffold for tissue engineering to be implanted in the body. (20 pts.)

a. Describe the sequence of events that normally comprise the wound healing and inflammatory responses for soft tissue surrounding the scaffold.

b. How would you develop *in vitro* tests to quantitatively determine any increase in hepatocyte attachment compared with the unmodified scaffold? How would you characterize the modified scaffold surface?

MSE/BioE C118 Name:_____

3. You are trying to develop a strategy for a pharmaceutical company to prevent protein adsorption to their protein purification vessels and conduit. The vessels are made from 316L stainless steel. (20 pts.)

a. In deciding on a strategy you consider both the minimum interfacial free energy and the critical surface tension hypotheses as ways to minimize protein adsorption. Explain each theory and their inherent limitations in predicting protein adsorption to surfaces.

b. You decide to modify the material with polyethylene glycol (PEG) to improve the resistance to protein adsorption. You know the degree of polymerization is 100 for the linear polymer and that l=0.4nm per ethylene glycol group. How would you attach the PEG to the vessel? After grafting you measure the mean spacing between PEG molecules to be 1 nm. Compare the unperturbed radius of gyration (R_g) to the thickness (L) of the attached PEG brush layer.

c. To resist protein adsorption the interaction free energy between the PEG-modified surface and the proteins in solution must be at least 20 Jm^{-2} at a separation distance of 5 nm. Assuming the interaction between your PEG layer and protein can be modeled by the exponential approximation to the Alexander-de Gennes equation, calculate the repulsive energy per unit area, W(D)? Is this sufficient to prevent protein adsorption? If not, what would you change to increase the interaction free energy?

MSE/BioE C118 Name:_____

3. Polysaccharides are attractive materials for creating non-fouling surfaces and provide an alternative to polyethylene glycol (pEG). Assume classic polymer brush equations explain the behavior of polysaccharides tethered to surfaces.

a. Calculate the radius of gyration (R_g) for a polysaccharide with a degree of polymerization (40,000) and bond length (l=0.3 nm). How is the R_g related to the Flory radius in both a good and poor solvent? Is water a good or poor solvent for most polysaccharides?

b. What criterion would you use to design the surface density (i.e., surface excess, Γ) of the polysaccharide molecules? Define your assumptions and calculate that Γ.

c. Is the interaction free energy of the surface, using the Γ you defined, sufficient to prevent protein adsorption and act as a non-fouling surface?

d. What advantages do polysaccharides have over polymers like pEG as non-fouling coatings?

4. You would like to design a microsphere to deliver zero-order release kinetics of a relatively hyrophobic drug to promote new blood vessel growth in an ischemic limb. (25 pts.)

a. Of the following polymers poly(glycolide), 50:50 poly(D,L-lactide-co-glycolide), and poly(sebacic acid-hexadecandioic acid anhydride) [poly(SA-HAD anhydride)], discuss the degradation mechanisms of each in an aqueous environment.

b. After making microspheres from each material using the double emulsion technique you measure the drug delivery kinetics. Sketch representative delivery profiles for each material under identical solution conditions. Describe the mechanisms associated with changes in your plots.

c. How could you modify the microsphere or its fabrication to obtain near zero-order release kinetics?

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
370 HMMB

Final Exam: December 16, 2004 **Closed Book Exam**
Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Total
Max = 25	Max = 25	Max = 25	Max = 25	Max = 100

Extra Credit (2 pts.)

Cal was recently ranked 5th by the BCS. What does the acronym BCS mean (any creative answer will work)?

MSE/BioE C118 Name:_____

2. Select one presentation topic given by a *different* group in class [you cannot select your own]. Identify the topic, address the materials used for the application from the standpoint of the general biological performance. Critically evaluate the design modification presented in class, and suggest possible alternatives. (20 pts.)

MSE/BioE C118 Name:_____

4. You are asked to evaluate a new polymer for cardiovascular applications. To evaluate the polymer you begin by making a contact angle measurement and find $\theta_{ADV}^{H_2O}$ is approximately 105°. Next you decide to conduct a static protein adsorption experiment where you perform both direct and successive addition of protein to the test solution. (20 pts.)

a. Draw protein adsorption isotherms for both the direct and successive adsorption experiments as a function of time.
b. Describe the mechanisms that led to the difference in the experimental curves.
c. What other characterization techniques would you use to evaluate the material?
d. How could you manipulate the protein adsorption behavior of this material to improve its biological performance?

Name:_____

5. You are trying to design a drug delivery system based on the biodegradable polymers poly(L-lactide), poly(DL-Lactide), and poly(glycolide). Discuss the degradation mechanism for each in an aqueous environment. Explain the difference in the degradation rates of the isomers based on their microstructure. You make a copolymer of 85:15 poly(L-Lactide-*co*-glycolide), how is the degradation of this material different from the homopolymers. You then decide to use the double emulsion technique to create microspheres of 85:15 poly(L-Lactide-*co*-glycolide) containing vascular endothelial growth factor (VEGF) to be released over a 4-week period. What fabrication and material properties would you alter to achieve the desired release kinetics. Be sure to give an example curve of your release profile describing the mechanisms of VEGF release during the different stages. (20 pts.)

MSE/BioE C118 Name:_____

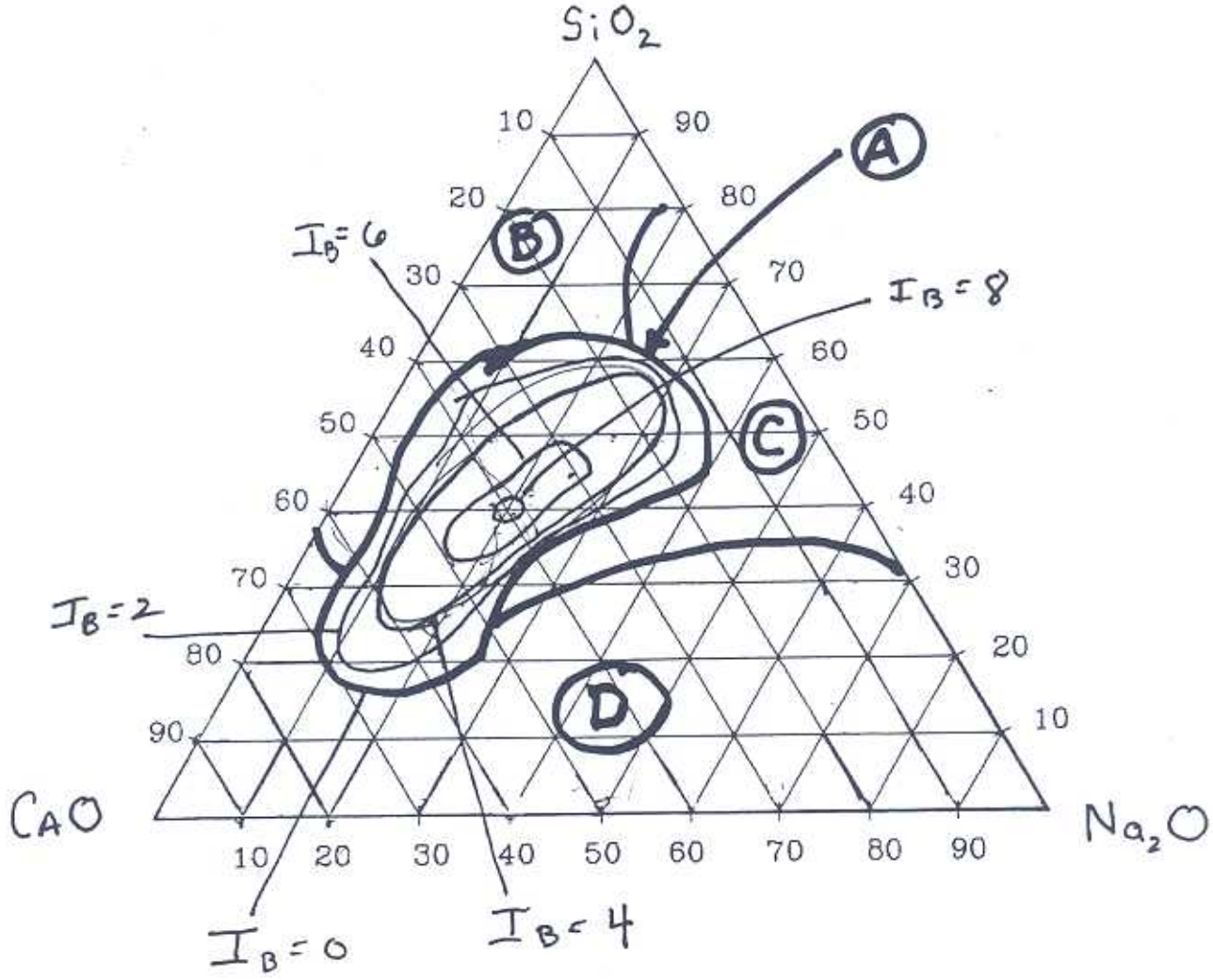
1. You would like to create a new bioactive glass to bond to bone and decide to examine glasses made from SiO_2, CaO, Na_2O, and P_2O_5. (20 pts.)

a. Examine the ternary phase diagram below and define a series of experiments that you would need to perform to create the diagram.

b. What is the composition (wt%) of glass with maximum I_B?

c. Which glass composition would give the greatest interfacial bonding with bone? Justify your answer in terms of the mechanism by which bioactive glasses bond with bone.

d. Which glasses have compositions that would also bond to soft tissue?



Ternary phase diagram of the "new" glass showing I_B as a function of composition. **Region A**: bone bonding; **Region B**: non-bonding, fibrous capsule formation; **Region C**: resorbable glasses: **Region D**: technically not practical. Note: All glasses have a constant 6% P_2O_5.

MSE/BioE C118 Name:_____

3. As a staff biomaterials scientist/engineer you have synthesized a new material for blood-contacting environments (e.g., grafts, stents, ventricular assist devices, catheters, etc.). Your new polymer (pBC) behaves in a similar manner to polyethylene glycol (pEG); however, it is easier to graft to existing base materials (e.g., PTFE) for the aforementioned devices. For optimum blood-compatibility assume the relationship between the chain spacing and radius of gyration for pBC scales with that observed for protein adsorption for pEG. (25 pts.)

a. Of the theories attributed to pEG's success in blood/protein-contacting environments, which are germane to most long-chain polymers like pBC? Conceptually explain these theories.

b. Derive an expression for pBC surface density (molec./area) in terms of the degree of polymerization (10,000) and bond length (l=0.15 nm) that would optimize blood-compatibility. Assume an ideal solvent. What is this optimal surface density?

c. Assuming your material can be modeled by the exponential approximation to the Alexander-de Gennes equation, calculate the interaction free energy per unit area, W(D), at R_g. Is this energy sufficient to repel protein adsorption and platelet adhesion?

d. Explain how solvent and temperature affect the pBC protrusion from the surface (i.e., L). How would solvent and temperature affect W(D) and therefore blood-compatibility.

MSE/BioE C118 Name:_____

4. Ventricular assist devices (VADs) act to supplement the cardiac output of the heart for patients who have weakened ventricular walls due to a myocardial infarction. You have been asked to evaluate a VAD that will be implanted into the upper abdomen. The device consists of a pump surrounded by a hard shell of a segmented polyurethane (SPU) and flexible tubes of the same material connecting the pump to the heart's chambers. (15 pts.)

a. How can you control the modulus of the material?

b. Another possible strategy to treat the patient is to strengthen the wall of the heart itself through injection of growth factor containing microspheres. How would the inflammatory/wound healing response differ between the implanted VAD and the injection of microspheres? (HINT: first describe the general inflammatory/wound healing pathway)

c. What effect does an aqueous environment have on a segmented polyurethane, and how will this effect the biological performance of the VAD? What added effect does the inflammatory response have?

MSE/BioE C118 Name:_____

5. Controlled drug delivery is important for numerous applications spanning cancer therapy to tissue engineering.

a. Materials for controlled drug delivery typically degrade by either homogeneous or heterogeneous mechanisms. Explain the difference between these two mechanisms and define at least one material for each mode of degradation.

b. Sketch a typical protein delivery profile for a microsphere that degrades homogeneously. Explain the features of your curve.

c. Sketch a typical protein delivery profile for a microsphere that degrades heterogeneously. Explain the features of your curve.

d. For materials that degrade homogeneously, how could you process the microsphere to better control constant dosage?

MSE/BioE C118 - Biological Performance of Materials

Prof. K. E. Healy
370 HMMB

Final Exam: December 15, 2005 5-7PM **Closed Book Exam/One sheet of notes**

Please answer all of the questions clearly and box your final answer. Useful equations, data, and physical constants appear at the end of the exam.

NAME:_____

ID NUMBER:_____

Prob. 1	Prob. 2	Prob. 3	Prob. 4	Prob. 5	Total
Max = 20	Max = 20	Max = 25	Max = 15	Max=20	Max = 100

Extra Credit (2 pts.)

What is Hawaii's highest point?

UNITS AND SYMBOLS

Much of the published literature and equations on intermolecular and surface forces are based on the CGS system of units. In this book the *Système International* (SI) is used. In this system the basic units are the **kilogramme** (kg) for mass, the **metre** (m) for length, the **second** (s) for time, the **kelvin** (K) for temperature, the **ampère** (A) for electrical quantities, and the **mole** (mol) for quantity of mass. Some old units such as gramme (1 gm = 10^{-3} kg), centimetre (1 cm = 10^{-2} m), ångstrom (1 Å = 10^{-10} m) and degree centigrade (°C) are still commonly used although they are not part of the SI system. The SI system has many advantages over the CGS, not least when it comes to forces. For example, force is expressed in newtons (N) without reference to the acceleration due to the earth's gravitation, which is implicit in some formulae based on the CGS system.

Derived SI units

Quantity	SI unit	Symbol	Definition of unit
Energy	Joule	J	$kg\ m^2\ s^{-2}$
Force	Newton	N	$kg\ m\ s^{-2} = J\ m^{-1}$
Power	Watt	W	$kg\ m\ s^{-2} = J\ s^{-1}$
Pressure	Pascal	Pa	$N\ m^{-2}$
Electric charge	Coulomb	C	A s
Electric potential	Volt	V	$J\ A^{-1}\ s^{-1} = J\ C^{-1}$
Electric field	Volt/metre		$V\ m^{-1}$
Frequency	Hertz	Hz	s^{-1}

Fraction	10^9	10^6	10^3	10^{-1}	10^{-2}	10^{-3}	10^{-6}	10^{-9}	10^{-12}
Prefix symbol	G	M	k	d	c	m	μ	n	p

FUNDAMENTAL CONSTANTS

Constant	Symbol	SI	CGS
Avogadro's constant	N_0	6.022×10^{23} mol^{-1}	6.022×10^{23} mol^{-1}
Boltzmann's constant	k	1.381×10^{-23} J K^{-1}	1.381×10^{-16} erg deg^{-1}
Molar gas constant	$R = N_0 k$	8.314 J K^{-1} mol^{-1}	8.314×10^{7} erg mol^{-1} deg^{-1}
Electronic charge	$-e$	1.602×10^{-19} C	4.803×10^{-10} esu
Faraday constant	$F = N_0 e$	9.649×10^{4} C mol^{-1}	9.649×10^{4} C mol^{-1}
Planck's constant	$h(\hbar = 2\pi h)$	6.626×10^{-34} J s	6.626×10^{-27} erg s
Permittivity of free space	ε_0	8.854×10^{-12} C^2 J^{-1} m^{-1}	1
Mass of $\frac{1}{12}$ of ^{12}C atom*	u	1.661×10^{-27} kg	1.661×10^{-24} g
Mass of hydrogen atom	m_H	1.673×10^{-27} kg	1.673×10^{-24} g
Mass of electron	m_e	9.109×10^{-31} kg	9.109×10^{-28} g
Gravitational constant	G	6.670×10^{-11} N m^2 kg^{-2}	6.670×10^{-8} g^{-1} cm^3 s^{-2}
Speed of light in vacuum	c	2.998×10^{8} m s^{-1}	2.998×10^{10} cm s^{-1}

* Atomic mass unit (also denoted by a.m.u. and a.u.)

CONVERSION FROM CGS TO SI

1 Å (Ångstrom) = 10^{-10} m = 10^{-8} cm = 10^{-4} μm = 10^{-1} nm
1 litre = 10^{-3} m^3 = 1 dm^3
1 erg = 10^{-7} J
1 cal = 4.184 J
1 kcal mol^{-1} = 4.184 kJ mol^{-1}
1 kT = 4.114×10^{-14} erg = 4.114×10^{-21} J at 298 K (~25°C)
= 4.045×10^{-14} erg = 4.045×10^{-21} J at 293 K (~20°C)
1 kT per molecule = 0.592 kcal mol^{-1} = 2.478 kJ mol^{-1} at 298 K
1 eV = 1.602×10^{-12} erg = 1.602×10^{-19} J
1 eV per molecule = 23.06 kcal mol^{-1} = 96.48 kJ mol^{-1}
1 cm^{-1} (wavenumber unit of energy) = 1.986×10^{-23} J
1 dyne = 10^{-5} N
1 dyne cm^{-1} = 1 erg cm^{-2} = 1 mN m^{-1} = 1 mJ m^{-2} (unit of surface tension)
1 dyne cm^{-2} = 10^{-1} Pa (N m^{-2})
1 atm = 1.013×10^{6} dyne cm^{-2} = 1.013 bar = 1.013×10^{5} Pa (N m^{-2})
1 torr = 1 mm Hg = 1.316×10^{-3} atm = 133.3 Pa (N m^{-2})
0°C = 273.15 K (triple point of water)
1 esu = 3.336×10^{-10} C
1 poise (P) = 10 gm cm^{-1} s^{-1} = 10^{-1} kg m^{-1} s^{-1} = 10^{-1} N s m^{-1} (unit of viscosity)
1 stokes (St) = 10^{-4} m^2 s^{-1} (unit of kinematic viscosity: viscos density)
Debye (D) = 10^{-18} esu = 3.336×10^{-30} C m (unit of electric dipole moment)

CONVERSION FROM SI TO CGS

1 nm = 10^{-9} m = 10 Å = 10^{-7} cm
1 J = 10^{7} erg = 0.239 cal = 6.242×10^{18} eV
= 5.034×10^{22} cm^{-1} = 7.243×10^{22} K
1 kJ mol^{-1} = 0.239 kcal mol^{-1}
1 N = 10^{5} dyne
1 Pa = 1 N m^{-2} = 9.872×10^{-6} atm = 7.50×10^{-3} torr = 10 dyne cm^{-2}
1 bar = 10^{5} N m^{-2} = 10^{-5} Pa = 0.9868 atm = 750.06 mm Hg

USEFUL QUANTITIES AND RELATIONS

Energy equivalent, mc^2, of one atomic mass unit (u) = 1.492×10^{-10} J
Mean volume occupied per molecule = (MW)/(N_0 × density)
Mass of any atom or molecule = (MW) × (1.661×10^{-27}) kg
Standard volume of ideal gas = 22.414 m^3 mol^{-1} (1 mol^{-1})
$kT/e = RT/F = -25.69$ mV at 298 K
1 C m^{-2} = 1 unit charge per 0.16 nm^2 (16Å^2)
κ^{-1} (Debye length) = $0.304/\sqrt{M}$ nm for 1:1 electrolyte at 298 K, where
1 M = 1 mol dm^{-3} ≡ 6.022×10^{26} molecules per m^3
Mass of the earth = 5.976×10^{24} kg
Density of earth (mean) = 5.518×10^{3} kg m^{-3}
Values of gravitational acceleration, g:
Equator (9.780 m s^{-2}), north and south poles (9.832 m s^{-2}),
New York (9.801 m s^{-2}), London (9.812 m s^{-2}).

COMMON SYMBOLS

A	Hamaker constant (J), area (m^2), Helmholtz free energy
a	Atomic or molecular radius (m), headgroup area (m^2)
a, b	Constants in equations of state
a_0	Bohr radius (0.053 nm)
C	Interaction constant (J m^6), aqueous solute concentration in mole fraction units (mol dm^{-3}/55.5)