UNIVERSITY OF TORONTO

FACULTY OF APPLIED SCIENCE AND ENGINEERING

FINAL EXAMINATIONS, APRIL, 1997

Fourth Year - Program 5bme

MMS452S - BIOMATERIALS & BIOCOMPATIBILITY

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Note - Answer 4 of 5 questions only for each of the three parts (A,B,C). All questions are of equal value. Point form answers are acceptable. Answer Parts A, B, and C in separate examination booklets.

PART A: Answer 4 of the 5 questions only.

1. Hydroxyapatite plasma-sprayed coatings have been reported as being 'bioactive'. What does this imply? Describe briefly the necessary conditions for achieving 'osseointegration' of a hydroxyapatite plasma-sprayed endosseous dental implant. List two major concerns for long term use of such surface coatings for stabilization of femoral hip implant components.

2. Porous-coated implants can be formed by sintering powder particles or fine wires made of 316L stainless steel, Co-based alloys, or Ti or one of its alloys. Which of these materials would you recommend for coating tibial and femoral components of total knee replacements and why? Which form would you recommend (wire or powder) and why? Finally, describe briefly the sintering process to be used for forming the recommended coating and the desired characteristics of the final porous coat.

3. Draw a plot of the expected 'threshold voltage' versus 'time in function' curve for a cardiac pacing system incorporating a smooth-surfaced Pt-Ir electrode lead positioned within the right ventricle. Explain why the curve is shaped as indicated. How would this plot differ if a porous-coated ring electrode made of the same material was used?

4. Polymethylmethacrylate (pmma) is used for fixing some prosthetic implant components in surgical sites. Explain how it works. List three approaches currently used to improve the performance of 'bone cement' and explain why these are effective.

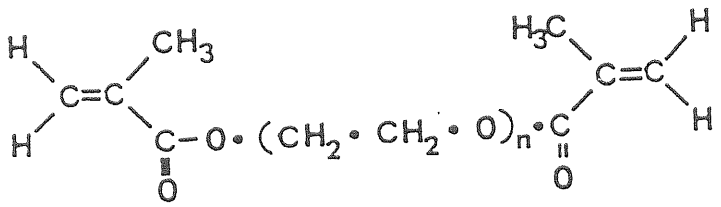
5. Describe the three phases of bone fracture healing and how the use of a metallic intramedullary rod might affect these phases. Recommend a preferred design for the implant including the preferred material for its fabrication.

PART B: Answer 4 of the 5 questions only.

1. Polymer chain interactions:
a) What inter-atomic interactions characterize the difference between a polymer single chain and a polymeric material. Qualify your answer with a very short description of these interactions as they pertain to a polymer chain and a polymeric material.

b) Why does a material containing short chain molecules such as hexamethylene ($CH_3(CH_2)_4CH_3$) possess significantly weaker physical properties than a material comprised of polyethylene chains $-(-CH_2CH_2)_n-$?

2. The chemical structure of a common dental composite resin monomer is triethylene glycol dimethacrylate (see structure below).
a) Would the polymerization of this monomer proceed via a step growth or chain growth polymerization?
b) Would you expect the polymer generated from such a monomer to be a linear or cross-linked polymer?
c) Would this polymer be expected to generate a significant number of crystallizable domains? A complete answer will contain a brief explanation to support your claim.



n=3 : TEGDMA.

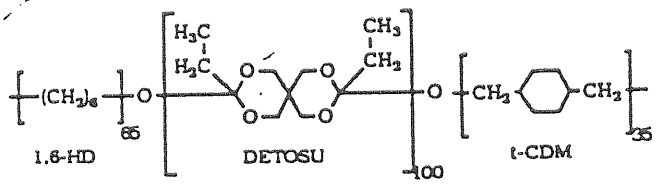
3. A new polymeric elastomer has been developed which contains pendent molecules of heparin (an anticoagulant agent which accelerates the natural process for the deactivation of clotting factors). In in-vitro studies, in which the materials were exposed to a solution of purified thrombin, it was found that the deactivation of the latter pro-coagulant agent occurred very rapidly upon the addition of physiological concentrations of an anti-thrombin agent. Following the preparation of the material into the form of a large diameter vascular graft and subsequent implantation it was found that the material no longer expressed its heparin-like character and hence clotting was not inhibited. Briefly, provide one rational explanation as to why the material did not perform as expected from the in-vitro studies?

4. Polyurethanes are used in many medical components because of their wide range of mechanical properties and moderate biocompatibility. A polyurethane elastomer called "B-10" has been selected for the blood pump housing and electrical lead wire insulation material in an implantable artificial heart system. During animal trials it was noted that after six months implantation the blood pump housings looked as good as the original implants, however the electrical insulation material showed severe surface cracking. Briefly, explain why there was a difference in biostability performance of the same material for the two components?

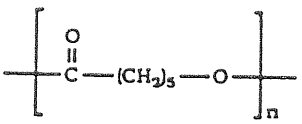
5. Biodegradable polymers have found extended use in the field of biomaterials as sutures, drug delivery devices and more recently as scaffolds for tissue engineering. The chemical structures for the repeat units of three such polymers are given below along with their glass transition temperatures.

Poly (ortho-ester) (Tg = 55 °C)
Poly (lactic acid) (Tg = 58 °C)
Poly (ε-caprolactone) (Tg = -62 °C)

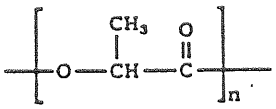
a) Based on the information provided (i.e. structure and T_g), describe the anticipated physical properties (i.e. initial modulus, tensile strength and elongation at break) of the three materials relative to each other.
b) Which of these three materials do you anticipate will show a significant presence of crystalline domains in addition to their amorphous phases, while the material is used in-vivo?
c) What mode of sterilization would be recommended for each of these materials. Provide a brief rationale for your answer.



Poly(DETOSU- 1,6 HD-t-CDM ortho ester)



Poly(ε-caprolactone)



Poly(lactic acid)

PART C: Answer 4 of the 5 questions only.

1. You are presented with the results of experiments to design a new vascular graft. In species A the experiments demonstrated that the internal surface of the graft was completely endothelialized. In species B only 1% of the internal surface of the graft endothelialized, contiguous with the host tissue. What parameters would you seek to evaluate in elucidating the difference in pattern of endothelialization in species A and species B?

2. Experimental data demonstrate that a material which you are developing shows particularly high affinity to fibrinogen. You wish to use the material in a wound healing site where the polymerization of fibrin to create a temporary scaffold along which cells will migrate is of key importance to the successful use of your material. By what methods would you ensure that the fibrin which forms at the material surface when implanted is sufficiently well bound to withstand the changing biological environment during the wound healing sequence? How would you test the efficacy of this aspect of your experimental material?

3. Antigen shedding is a problem which has been specifically identified in conjunction with the implantation of a new drug delivery device. What would you anticipate to be the general design structure of this device? What would you anticipate to be the biological sequelea of antigen shedding? How would you modify the device in an attempt to eliminate the problem?

4. In a block co-polymer you wish to render one polymer angiogenic and the other resistant to cell adhesion. How would you design such a material? How would you test the efficacy of the material in a biological assay?

5. You wish to design a tissue-engineered bone-graft. Which material properties and which biological properties would you focus your attention on in designing a scaffold?