UNIVERSITY OF TORONTO

FACULTY OF APPLIED SCIENCE AND ENGINEERING

FINAL EXAMINATIONS, APRIL, 2001

Fourth Year - Program 5bme

MMS452S - BIOMATERIALS & BIOCOMPATIBILITY

Examiners - R.M. Pilliar, J.P. Santerre

Answer all 12 questions. Where appropriate, you may use point-form answers.
(N.B. Answer Part A questions in one set of examination booklets and Part B in another).

Part A:

Question 1 (5 marks)
Briefly define or describe each of the following terms:

- chondrocyte
- osteoinductivity
- osteoid
- integrin
- woven (fibrous) bone

Question 2 (15 marks)
Acrylic bone cement (pmma) is commonly used for fixation of knee joint implants.

a) Describe briefly the mechanism of fixation including a description of the polymerization reaction.
b) A limitation of pmma bone cement is its poor fracture resistance. Describe three different approaches that have been proposed for improving the fracture resistance while maintaining other desirable characteristics indicating the rationale for each approach.
c) A company proposes to mix 5 volume % bioactive particles into the conventional pmma cement formulation. The bioactive particles consist of mixed calcium phosphate (MCP) particles that are 5 to 10 μm in size. The MCP consists of approximately equal parts of hydroxyapatite [$Ca_{10}(PO_4)(OH)_2$] and tricalcium phosphate [$Ca_3(PO_4)_2$]. Do you think that this is a good idea? Explain including advantages and/or disadvantages of such an approach.

Question 3 (20 marks)

a) Describe the sequence of events that would be expected to occur in the 'interface zone' during osseointegration of a porous-surfaced Ti6Al4V endosseous dental implant. Include in your answer a brief description of the preferred geometry of the porous-surfaced region indicating reasons for this preference.
b) How would the healing events differ (if at all) assuming the use of a threaded cpTi implant prepared with an acid-etched surface? Indicate in your answer the reason(s) for the acid etching treatment.
c) How might either of these two designs be further modified in order to achieve faster osseointgration.
d) Outline a recommended patient treatment protocol for ensuring success of dental implants.

Question 4 (15 marks)

a) Describe the three phases of fracture healing indicating the normal time course for each phase and how the use of a 316L stainless steel compression plate and screws might affect this.
b) How would you expect the use of a self-reinforced polylactide plate and screws rather than 316L stainless steel to alter this response?
c) Which of the two implant systems referred to above (i.e. 316L stainless steel and self-reinforced polylactide) would you recommend for treatment of an adult with a complex tibial fracture? Why?

Question 5 (10 marks)

Wear debris generated from bearing surfaces of total joint replacements (hip, knee and others) is believed to be the cause of 'endosteal osteolysis'.

a) What is 'endosteal osteolysis' and why is it a concern?
b) As an expert consultant in the field of orthopaedic biomaterials, you are asked to recommend material(s) and a design to minimize the possibility of occurrence of endosteal osteolysis with a new total hip implant that is being planned. What are your recommendations and why? (Suggest both the material(s) and design for the system).

Question 6 (15 marks)

a) Draw a figure to show how threshold potential (or current) normally varies with post-implantation time for endocardial pacing. Explain the reason for this behaviour.
b) Would you expect similar behaviour with epicardial pacing? Explain.
c) Describe qualitatively how each of the following electrode designs would alter this behaviour; 1) a large diameter electrode (20 mm diameter) versus a small diameter electrode (6 mm), 2) a porous-tipped electrode (Pt-mesh) vs a smooth Pt electrode – same overall diameter), 3) a 316L stainless steel electrode vs a Ti electrode (all other factors being constant).
d) Polyurethane sheathing is currently favoured over silicone rubber (silastic) for protection of the conducting lead. Give two reasons for this.

Part B:

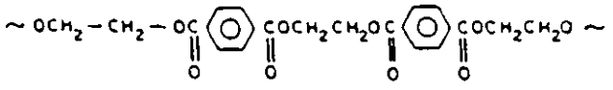
Question 7 (5 marks)
Briefly define or describe each of the following terms:

- stent
- Factor XII
- Heparin
- homograft
- intimal hyperplasia

Question 8 (10 marks)
You are working for the ACME Modern Age Technology firm. The company's motto is "We are plastics". Your first assignment is to design a biodegradable vascular graft out of their inventory of synthetic/organic monomers.

a) Draw or name two chemical groups that your monomers will contain in order to permit the formation of your hydrolysable bonds and the formation of the polymer when they are reacted.
b) List 3 design criteria that your degradable polymer chains will have. State the intended functions that each of these design criteria will provide to your material.
c) Which of the following three sterilization methods would be preferred for your material? A. ethylene oxide gas sterilization, B. Steam sterilization or C. Radiation sterilization. Provide a **brief rationale** for your choice.

Question 9 (20 marks)
Polyethylene terephthalate (PET) is a polyester that has found extensive use as an implant vascular graft material as well as use in other medical applications. The structure of this material is given below.



a) Under what class of polymers is this material classified, i.e. a fibre, an elastomer, a flexible plastic or a rigid plastic? Rationalize your selection based on the polymer chain's molecular structure and the associated material's physical state.
b) Is this polymer considered to be biodegradable? Explain your answer.
c) The material is processed into vascular grafts using both weaving and knitting operations. Describe the difference in products that would be generated from these two processes. Identify where in the vasculature it would be appropriate to apply each of them.
d) The material is considered to be relatively thrombogenic. Describe an approach, which could be used to reduce the thrombogenic nature of a knitted PET graft.

Question 10 (10 marks)
Most mechanical valve leaflets are fabricated from pyrolytic carbon which have the characteristics of a baked ceramic, while tissue valves are composed of naturally and chemically crosslinked biopolymers. You are asked to describe two prominent failure modes that are distinct to each of these valves leaflet types. Your description should be discussed in terms of the inherent features of the materials themselves.

Question 11 (15 marks)

The application of biomaterials in drug therapy is rapidly becoming an important mode of delivery for pharmaceutical agents in vivo since it allows for targeting the diseased site and eliminates a significant number of issues associated with the more classical systemic delivery of drugs. This has been specifically recognized in the cardiovascular area.

a) You have been asked to develop a drug delivery system that could limit the degradation of the endothelium wall lining in a patient beginning to show signs of a stenosed lesion in a coronary artery. What would be a minimally invasive procedure that could be used to deliver a drug loaded device to such a location.

b) Two polymer systems that have been used for the delivery of drugs at the above sites have included co-polymer systems of hydroxy ethyl methacrylate/methyl methacrylate ($CH_2=C(CH_3)CO_2CH_2CH_2OH$ / $CH_2=C(CH_3)CO_2CH_3$), and L-lactide/glycolide ($HOCH(CH_3)CO_2H$ / $HOCH_2CO_2H$). For each copolymer system, briefly describe the rationale for the use of the individual monomers in a drug delivery system.

c) After examination of the monomer systems in b), describe whether they would be polymerized by step growth or chain growth reactions.

d) If each system were loaded with similar amounts of an anti-proliferative agent to control smooth muscle cell growth in the stenosed lesion, would you anticipate that their drug release kinetics would be similar? Provide a rationale for your answer.

Question 12 (20 marks)

Polyurethanes consist of a very versatile group of co-polymers that have been used extensively throughout the medical device field in applications ranging from blood bags and dialysis membranes to sutures and catheter lines.

a) Polyether-urethane elastomers have an ability to form very strong materials because of their molecular structures while at the same time exhibit good flexibility. What molecular features are responsible for the strength and flexibility of this type of material?

b) If you were to use a polyether-urethane material to design and fabricate a heart valve name 10 design features that would be important for the development of such a device, given your knowledge of mechanical and bioprosthetic valves.

c) Name two distinct degradation modes that could occur in a heart valve made from a polyether-urethane and highlight what features of the material render them particularly susceptible to those two failure modes. Clearly outline separately, the specific differences for each failure mode.