3G5 -2026

Crib

Q1

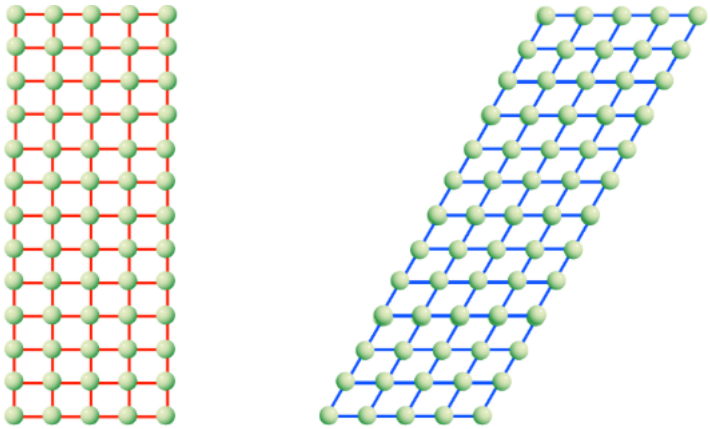
(a) A stent is an expandable tube used to open and widen blocked or occluded vessels. Narrowed regions in vessel are made of fatty plagues that restrict the movement of the blood to the tissue.

They can be classified into two main groups on the basis of the method of expansion: *balloon expandable* and *self-expanding stents*. Balloon expandable stent arrive premounted on a balloon anglioplasty catheter. While mounted, the stent is moved into place and the balloon is inflated to expand the stent to the desired diameter. Self-expanding stents come premounted or sheathed. Once deployed to the treatment area, the sheath is pulled back, allowing the stent to expand to its original (unconstrained) diameter.

Balloon expandable stents expand by *plastic deformation* by an angioplasty balloon while self-expanding ones use "*superelasticity*" or the "*shape memory*".

(b) Martensitic transformations occur by means of a phase change from a "parent phase" (frequently referred to as austenite) to a "martensitic" phase. The process involves co-operative shearing of the lattice, meaning that each atom moves a small distance relative to its neighbours in a well-defined way– see schematic below. This homogeneous shearing of the parent phase creates a new crystal structure, without any compositional change (no diffusion).

The key feature of this transformation is that it is diffusionless, allowing it to happen extremely rapidly. Additionally, each atom retains atomic correspondence with its neighbours, which enables the transformation to be reversible.



(c) One of the desirable mechanical characteristics for a stent is to have a low axial beam stiffness (high flexibility) before deployment, because this allows the stent to be pushed through vessels which may have high curvature. A low value of axial beam stiffness allows high curvature to be adopted without a large bending moment needing to be applied.

The figure shows that high orientation angles with respect to the horizontal (>50˚) lead to very low beam stiffnesses and hence to highly flexible tubes. While both tubes have low axial stiffnesses at high orientation angles, a ±q angle-ply would be more suitable because a single angle ply will tend to distort under bending.

Stents with high axial beam stiffness before expansion may apply excessive local pressures causing serious damage to the vessel wall. The subsequent repair process is complex with inflammatory and thrombotic pathways being activated. Platelets become adherent to the damaged vessel wall due to loss of the protective endothelium (inner layer of the blood vessels). These changes culminate in recurrence or restenosis also known as Neointimal Hyperplasia, and the need, because of luminal renarrowing, for further intervention.

(d) The reason for developing drug-eluting coatings is to treat in-stent restenosis, which is due to "Neointimal Hyperplasia". This is excessive tissue proliferation due to post-implant arterial injury (roughly analogous to a scar forming over an injury) and foreign body response. Drug-eluting coatings are used to overcome this problem. In drug-eluting stents, drugs are embedded in a polymer matrix that is coated onto the stent. The drug is released into the vessel by diffusion and/or polymer degradation over varying periods of time that can be engineered by the specifics of the polymer-drug system.

The main advantages of drug-eluting stents include: targeted drug delivery to precise area requiring treatment; ongoing delivery through phases of healing; no additional material or procedures required and ongoing delivery through phases of healing.

(e) There is interest in developing bioresorbable drug-eluting stents to replace permanent metallic stents in order to avoid long-term complications, such as those caused by a foreign body response. Bioresorbable stents must provide sufficient mechanical support to keep the vessel patent during healing and then gradually resorb, leaving a restored and functional vessel. From a mechanical perspective, the biggest challenge is designing a polymeric scaffold that can sustain the high strains involved in stent expansion, often a 100% or greater increase in diameter, without strut fracture. This must be achieved while maintaining controlled drug release and ensuring that stent degradation does not compromise mechanical integrity before the vessel has fully regenerated.

Q2

(a) (i) This answer is anticipated to be brief but accurate. Standards are referred to across multiple lectures, with the definition going from an initial version, to one more detailed later.

A basic answer would note aspects that communicate these are documented, internationally agreed approaches to complete a task or 'do something' from making a product to managing a process and many other things. The candidate may refer to them as 'A formulae that describes the best way of doing something'.

A good answer would build on this and note more precisely that it is a document established by consensus and approved by a recognised body that provides for

common rules and guidelines for activities to achieve the best degree of order.

A strong answer would communicate that these are all about ensuring produces meet technical and quality specifications, at the lowest cost, and adhere to regulations.

(a) (ii) The three examples do not need to be explained in detail but a good understanding needs to be shown about when standards are used when making medical devices and the answers should be appropriate to this particular wearable medical device also.

A basic example will list three examples (e.g. Biocompatibility, Sterilisation, Quality Management System, etc.)

A good answer would provide more detail about each (e.g. There are a range of biocompatibility tests that will be needed and standards linked to each, to ensure they are carried out in an approved and repeatable way by trained professionals, for example checking cytotoxicity. Each sterilisation technique will have its own standard for use that will guide on how to control and validate that sterilisation has occurred and to the sterility assurance level defined in the standard. The standard will give details about the quality management system that is needed to correctly document all of the process for medical device approval.)

A strong answer will link at least twice back to the wearable medical device (e.g. describing that biocompatibility tests will need to occur linked to the mode of use, and so in contact with skin for a certain duration, or that the Quality Management System will be tuned to a Class II medical device to ensure the correct level of safety but not being overly costly, etc.

(a) (iii) A basic answer will list four key concepts, for example, safe for staff to use, a suitable cycle time for the manufacturing speed, economical to use either in-house or at a third party, and for their to be methods to monitor. There are many other aspects that may be drawn upon, directly noted in the lectures (broad spectrum of efficacy, compliance with standards, not damaging materials, penetrates packaging and device, no toxic residue remaining, etc.)

A good answer will include points, such as those above, but also refer to the device, recognise that it is mostly polymer to ensure it is thin and flexible and also has delicate, small circuitry and note that there will need to be specific tests to ensure whichever sterilisation technique is selected, it does not change the mechanical properties, the device performance or other aspects, such as biocompatibility. A good answer will also make sure to note that there is an

anticipated re-use of these devices and so sterilisation will need to be selected that can be repeated again and again.

A strong answer will note the above, give a good amount of detail in all aspects and also a bit more about the potential issues of specific example sterilisation techniques. So for example, autoclave has a high temperature so may cause issues with the polymer, gamma radiation has been known to cause issues with polymers, ethylene oxide is excellent at compatibility but then will have issues with regard to the return of devices quickly due to the quarantine time, or because there are conductive lithographically-made sensors and electronics, they are going to be very small and easy to damage, and so a surface treatment may be better than one that penetrates through the

(b) (i) This is expected to be answered correctly by all candidates, noting that this is the study of ethics linked to health and care, or clinical care, covering legal, moral and social issues related to these topics. This does not have to be worded exactly as above, as long as an understanding is shown.

(ii) Consent was discussed in the lectures in terms of the voluntary consent of a human subject and so it is likely going to be answered with this in mind, consent to take part in trials with a medical device, indeed this is enough for a basic answer. For a good answer, the candidate will need to get across an understanding that consent is more complex in that the information has to be given to the patient, they have to have the ability to understand the information and what it may mean for them, and the patient can't have any other influences on their decision making. A strong answer may also bring in other aspects with regard to this concept emerging from the Nuremberg Code or they will discuss it with different working in relation to the Tuskagee Syphilis Study. A strong answer may note other aspects such as consent regarding use of data, but this is not expected to be normally brought up.

(c) (i) A basic answer will list 3 differences. A good answer will list 4 differences and give a clear explanation of at least 3. A strong answer will give all 4 differences and explain them clearly.

It is anticipated that candidates will describe differences such as

- The different standards employed (FDA vs ISO)

- The different approaches to classification, such as by precedent (US) or by self-selection through following guidelines (EU)

- Different quality management systems and so different criteria or approaches to be audited against

- Audits carried out in the EU by Notified Bodies, private companies, rather than the centralised FDA body that carries out the audits in US.

- The need to register with a Competent Authority in each country (EU), as opposed to registering once with FDA (US)

- The different approaches to defining success of a clinical trial/investigation, in terms of effectiveness (US) or performance (EU).

(c) (ii) A basic answer will focus on one point briefly, and it is anticipated that this main one mentioned by all candidates is cost. A harmonised regulatory process would dramatically reduce the cost of having a medical device approved for use in both US and EU, avoiding the need for multiple processes.

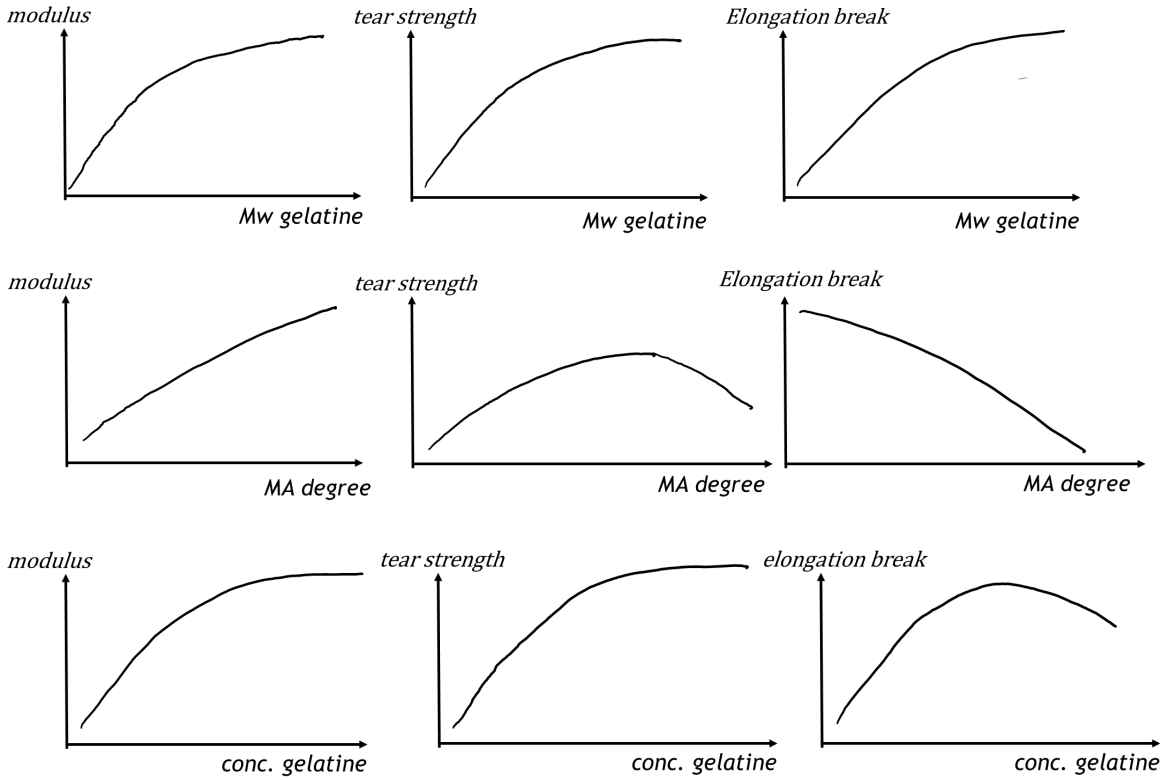
A good answer will note cost and at least one other aspect, such as for example that this would benefit the public and patients, by ensuring devices reached more people more quickly. There may be a comment that it could lead to a knock-on effect of reducing the cost of medical devices due to the reduced cost to the company. This is unclear, but is acceptable here as it is a possibility.

A strong answer will note three benefits, and for example, this could be in terms of safety or speed to market, by looking at the approaches of each existing process and taking the best elements of each.

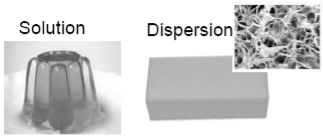
Q3

(a)

(i)

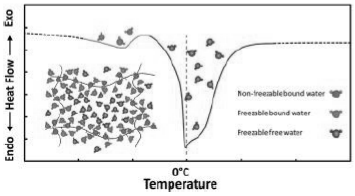


(ii)



Hydrogel *vs.* Sponge

Three types of water present in hydrogel: free water, freezing bound water, non-freezing bound water



States of water in hydrogel:

- Free water – water that is not intimately bound to the polymer chain and behaves like bulk/pure water, i.e. undergoes thermal transition at temperature analogous to bulk water (at 0°C)
- Freezing bound water – water that is weakly bound to the polymer chain and undergoes a thermal phase transition at a temperature lower than 0°C
- Bound water (non-freezing water) – water tightly bound to the polymer, which does not exhibit a first order transition over the temperature range from -70 to 0°C

Physical:

Structural: sponge has visible porosity, structurally more robust

Biochemical: cell adhesive motif exposure, and enzymatic degradability is reduced in the sponge case compared to hydrogel case.

Application: hydrogel: cell encapsulation for cell delivery, biocompatible encapsulation process; sponge: skin graft, structurally more robust than hydrogel.

(b)

Minutes to hours — protein adsorption and provisional matrix

Immediately after implantation, plasma proteins rapidly adsorb to the sensor surface. Platelet activation and a thin fibrin matrix can form within hours. This conditioning layer introduces an additional diffusion barrier and alters local partitioning, slowing glucose transport to the sensor, this results in baseline drift, reduced sensitivity, and increased response time as the layer thickens.

Day 1–7 — inflammation

Neutrophils and monocytes/macrophages are recruited to the site, releasing reactive oxygen species and proteases. Edema could increase the diffusion path for glucose. The microenvironment becomes acidic (pH change) and warmer (temperature change), affecting enzyme activity and thus sensor reading.

As neutrophils wane, macrophages dominate, adhering to the sensor and secreting cytokines and reactive oxygen species. These can degrade polymer membranes or alter permeability, making mass-transfer properties unstable. Local vascular changes are insufficient to restore normal glucose flux. Sensor output shows progressive sensitivity loss and longer lag times, as biological layers act as diffusion barriers and dampen dynamic glucose changes.

Week 2 — early foreign-body response and fibrous encapsulation

By the second week, macrophages may fuse into foreign-body giant cells, and fibroblasts begin depositing collagen, forming a fibrous capsule. This capsule significantly reduces effective glucose diffusivity and limits local perfusion, creating a stagnant layer around the sensor. Glucose readings become increasingly inaccurate, with reduced sensitivity and delayed response to systemic changes. Calibration curves flatten, and offsets grow, making algorithmic compensation essential but insufficient for full recovery.

Practical implications within two weeks

Within 14 days, the sensor environment evolves from well-perfused tissue to a stratified barrier with active glucose consumption and diffusion resistance. Combined with chemical degradation of sensing elements, these changes drive performance drift.

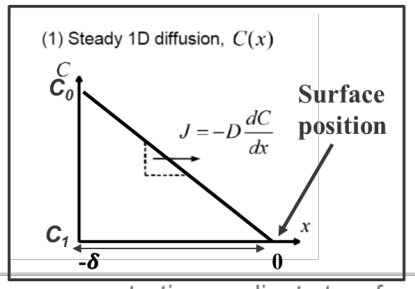
(c)

(1) enzymatic degradation, e.g. through collagenases; (2) hydrolysis, collagen contains peptide bonds that can undergo hydrolysis in aqueous environments; (3) mechanical erosion due to the shear flow of the blood.

4.

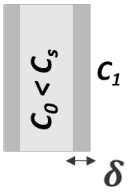
(a)

$$\frac{1}{A}\frac{\partial m_d}{\partial t} = \left|J_{surface}\right| = \left|-D\frac{\partial C}{\partial x}\Big|_{surface}\right|$$



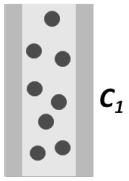
NB. Drug concentration gradient at surface is the same as bulk drug concentration gradient within the membrane

** Only need to consider the diffusion profile within the membrane thickness, δ



$$\frac{\partial m_d}{\partial t} = \frac{DKA}{\delta}(C_0 - C_1)$$

$$m_d = \frac{DKA}{\delta}(C_0 - C_1)t$$



$C_0 > C_s$

$C_1 << C_s$

$$\frac{\partial m_d}{\partial t} = \frac{DKA}{\delta}C_s$$

$$m_d = \frac{DKA}{\delta}C_s t$$

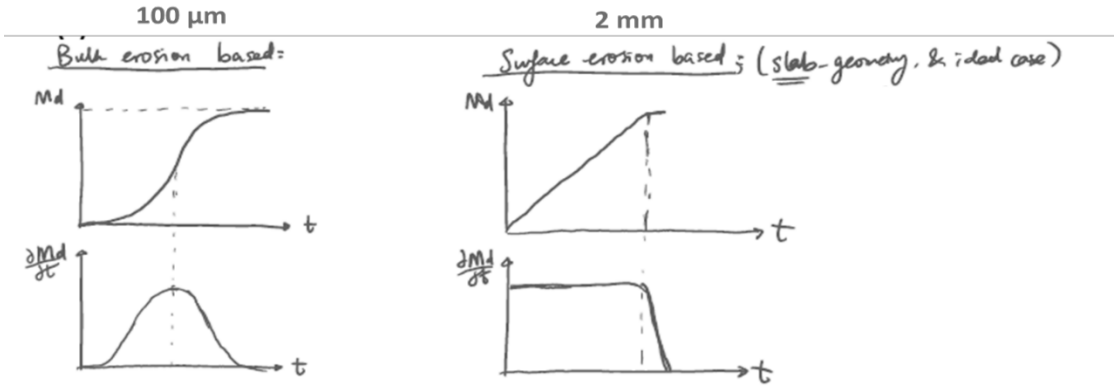
K= membrane 'partition' coefficient (unit-less metric of drug solubility in the membrane)

Approximately constant release rate (* for a slab geometry).

Assumptions: Fick's diffusion; uniform drug distribution in the matrix; a single diffusion constant in the membrane.

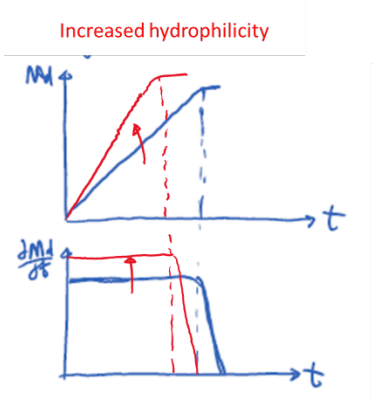
(b)

(i)

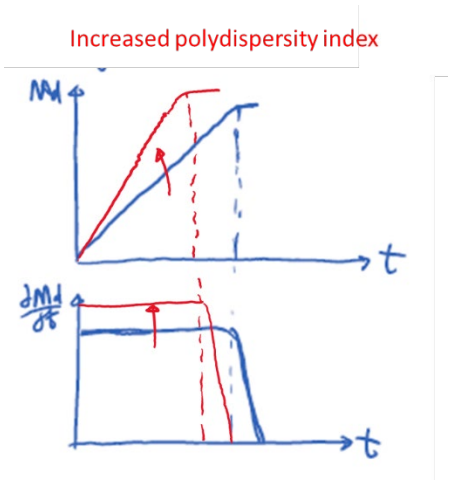


(ii)

Increased hydrophilicity of the side-chains increase the rate of hydrolysis (thus decreased hydrolysis time scale), and therefore critical thickness reduces.

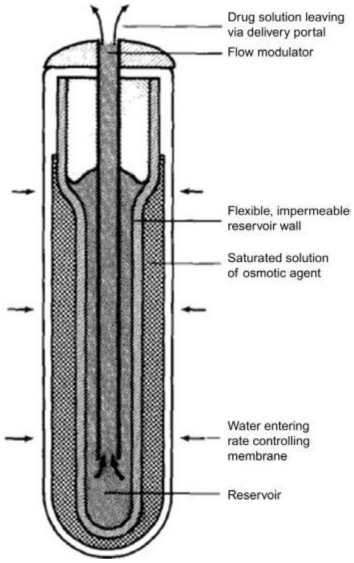


Increased polydispersity index decrease the packing density of the polymer chains, thus increase the rate of hydrolysis (thus decreased hydrolysis time scale), and therefore critical thickness reduces.



(c)

Osmotic pumps consist of an inner core containing drug and osmogens, coated with a semipermeable membrane. As the core absorbs water, it expands in volume, which pushes the drug solution out through the delivery ports. Osmotic pumps release drug at a rate that is independent of the pH and hydrodynamics of the dissolution medium.


Drug solution leaving via delivery portal
Flow modulator
Flexible, impermeable reservoir wall
Saturated solution of osmotic agent
Water entering rate controlling membrane
Reservoir