

23CGC824
Biochemical Engineering

Semester 1 2023/24

In-Person Exam paper

This examination is to take place in-person at a central University venue under exam conditions. The standard length of time for this paper is **2 hours**.

You will not be able to leave the exam hall for the first 30 or final 15 minutes of your exam. Your invigilator will collect your exam paper when you have finished.

Help during the exam

Invigilators are not able to answer queries about the content of your exam paper. Instead, please make a note of your query in your answer script to be considered during the marking process.

If you feel unwell, please raise your hand so that an invigilator can assist you.

You may use a calculator for this exam. It must comply with the University's Calculator Policy for In-Person exams, in particular that it must not be able to transmit or receive information (e.g. mobile devices and smart watches are **not** allowed).

Section A is **COMPULSORY** – attempt **ALL** parts of Question 1. Attempt **TWO** questions from Section B.

Part A carries 25 marks. Part B carries 50 marks.

Candidates should show full working for calculations and derivations.

Section A

This question is compulsory

1. The incidence of type 1 diabetes is increasing globally, but the reasons are incompletely understood. The condition can lead to serious long-term complications and can have significant quality of life implications. In the UK, which has one of the highest rates in the world, the incidence of type 1 diabetes is rising by 5% annually in children under five. In type 1 diabetes, the immune system attacks and destroys the β cells in the pancreas that make the hormone insulin. Insulin is normally produced in response to an increase in blood glucose levels, but type 1 diabetics do not produce enough insulin and must replace it with insulin injections, typically more than 65,000 times within their lifetime. Biochemical engineering techniques have advanced the production of artificial insulin, where previously insulin was extracted from animals such as pigs.

- (a) Discuss why genetically engineered artificial insulin production is preferable to animal-derived insulin. [4 marks]

You are tasked with making artificial human insulin from mRNA containing the insulin gene that was extracted from healthy β cells in the pancreas. You have been provided with a sample of extracted mRNA. The first step in developing the artificial insulin is generating a large quantity of pure nucleic acid insert for cloning.

- (b) Select a method for gene amplification and justify your choice. [7 marks]
- (c) Select a host cell for production and a type of vector for delivery of the gene to that host cell. Justify your selections. [4 marks]

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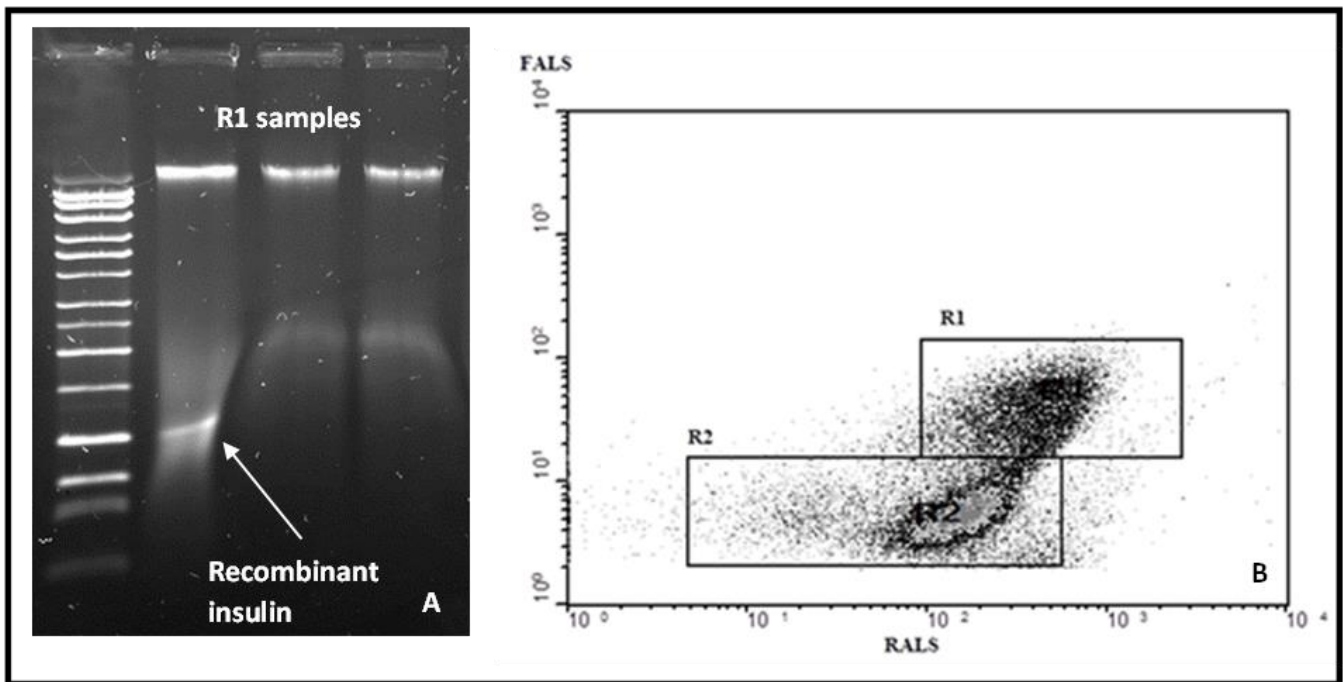


Figure 1. A. Agarose gel electrophoresis of cloning products from cloned cells. **B.** Flow cytometry analysis of production of recombinant insulin, showing forward scatter on the x-axis (RALS) and side scatter on the y-axis (FALS) of cloned cells (R1) and control cells (R2).

Figure 1 shows the results from analysis of cloned production cells by flow cytometry and agarose gel electrophoresis after observation of lower-than-expected levels of recombinant insulin from production cultures.

- (d) Analyse the results shown in Figure 1 and comment on the success of recombinant insulin cloning. [4 marks]
- (e) Suggest strategies to further investigate problems within the cloning process and provide examples of critical points for controlling accuracy within the process to improve the levels and quality of recombinant insulin production. [6 marks]

Section B

Attempt **TWO** out of the **THREE** questions in this section

2. Therapeutic monoclonal antibodies (mAbs) can be used to treat many diseases including some types of cancer. For example, Bevacizumab is one type of therapeutic mAb that is used to prevent or treat tumours in blood vessels, as it targets a protein called VEGF that affects tumour growths in blood vessels.
- (a) You are responsible for the design of a bioprocess for the production of Bevacizumab using an adherent mammalian cell line. Please use a schematic diagram to briefly explain the key components or the main unit operations in this bioprocess. [9 marks]
- (b) In order to design an economically feasible mAb manufacturing process, list and evaluate 8 relevant factors or elements that should be considered during this bioprocess design. [8 marks]
- (c) Freeze-drying has been proposed by the design team for the preparation of the final mAb product. As the team leader in this design project, you have some concerns about freeze-drying the target mAb product. Please use this opportunity to specify and justify your concerns. [8 marks]

3. (a) Gene therapy is a technique that uses gene(s) to treat, prevent or cure a disease or medical disorder. Often, gene therapy works by adding new copies of a gene that is broken, or by replacing a defective or missing gene in a patient's cells with a healthy version of that gene.
- (i) Compare and contrast the two commonly used types of gene therapy products. [2 marks]
- (ii) Further explain the action mechanisms of these gene therapy products. [3 marks]
- (b) Recent studies have shown that stem cell therapy may be a viable new treatment option for Crohn's Disease, as it is able to greatly improve patient symptoms without the exorbitant recurring costs of traditional medications. Based on the donor and recipient of the cells, please propose and evaluate 3 possible available cell sources for the manufacture of cell therapy products. [8 marks]
- (c) Define and compare swarm intelligence and agent-based model (ABM). Explain why ABM can be used for the simulation of cells during cell and or tissue cultures. [5 marks]
- (d) Microalgae have been considered as a promising alternative for the production of 3rd generation biofuels due to their high photosynthetic conversion efficiency. Please identify and explain at least 7 drawbacks associated with the open systems that are usually used for the large-scale culture of microalgae. [7 marks]

4. Cellulases are the important enzymes both industrially and in the natural world because they play a major role in the global carbon cycle by degrading insoluble cellulose to soluble sugars. *Aspergillus* and *Trichoderma* spp. are well known fungi for efficient production of cellulases via submerged fermentation (SmF) or solid-state fermentation (SSF).

(a) Contrast and compare submerged fermentation (SmF) and solid-state fermentation (SSF). [9 marks]

(b) As the leader of the process design team, you have decided to select SSF for the production of cellulase. Please justify this decision mainly based on the further explanations of the benefits associated with SSF. [8 marks]

(c) A horizontal drum reactor has been selected for the production of cellulase in SSF. With the aid of a schematic diagram, briefly illustrate the main components of this SSF reactor. [5 marks]

(d) In extracted cellulase solutions from the SSF, the cellulases might be digested by the potential proteases. Please recommend 3 methods to prevent the digestion of cellulase in the downstream process design. [3 marks]

END OF PAPER

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