H2

ANDERSON SERANGOON JUNIOR COLLEGE
HIGHER 2
ANSWERS

2023 JC2 PRELIMINARY EXAMINATION

CANDIDATE NAME							
CLASS					INDEX NUMBER		

BIOLOGY

9744/03

PAPER 3
LONG STRUCTURED AND FREE RESPONSE QUESTIONS

15 SEPTEMBER 2023
FRIDAY

Candidates answer on the Question Paper.
No Additional Materials are required.

2 HOURS

READ THESE INSTRUCTIONS FIRST

Write your name and class on all the work you hand in.
Write in dark blue or black pen.
You may use an HB pencil for any diagrams or graph.
Do not use paper clips, highlighters, glue or correction fluid.

Section A
Answer **all** questions in the spaces provided on the Question Paper.

Section B
Answer **any one** question in the spaces provided on the Question Paper.

The use of an approved scientific calculator is expected, where appropriate.
You may lose marks if you do not show your working or if you do not use appropriate units.

For Examiner's Use	
1	/ 30
2	/ 10
3	/ 10
4 /5	/ 25
Total	/ **75**

At the end of the examination, fasten all your work securely together.
The number of marks is given in brackets [ ] at the end of each question or part question.

This document consists of **19** printed pages and **1** blank page

Section A

Answer **all** the questions in this section.

1 Proteins must fold into defined three-dimensional structures to gain functional activity. In the cellular environment, newly synthesised polypeptides are at great risk of misfolding and aggregation. Cells hence engage proteins called chaperones to assist in protein folding.

These chaperones have two roles:

1. They bind to proteins to promote folding.
2. They direct misfolded polypeptides for degradation in the cytosol.

However, polypeptides that are in the midst of folding may be mistaken by chaperones as misfolded proteins and then directed for degradation. Therefore, protein folding needs to be completed quickly to prevent premature degradation.

A recently discovered endoplasmic reticulum (ER) protein complex called S-E complex was found to delay premature degradation of polypeptides that are in the midst of folding. In its absence, approximately 30% of newly synthesised proteins that could otherwise fold correctly are degraded.

Fig. 1.1 illustrates these processes.

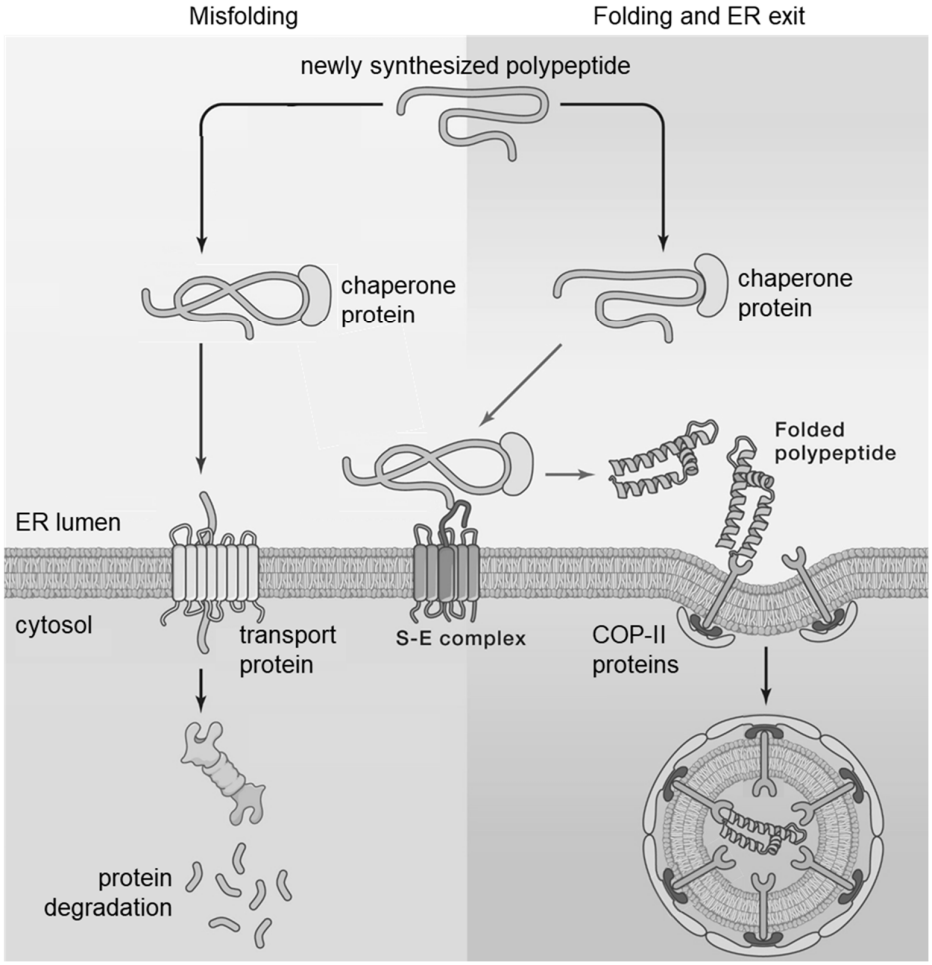


Fig. 1.1

With reference to Fig. 1.1,

(a) **(i)** suggest how the S-E complex allows polypeptides to complete their folding.

1. S-E complex (is a membrane-anchored protein that) **binds** to chaperone-polypeptide

2. Prevents polypeptide from being prematurely transported out of the ER for degradation
   OR
   Allows polypeptide to stay long**er** in the ER to complete folding

[2]

(ii) ER vesicle formation is not a random event but is carefully co-ordinated. Describe how ER vesicle formation is triggered.

1. **Folded protein binds** to the domain of **COP-II protein** facing the ER lumen

2. Such binding triggers ER membrane to undergo **budding** / **pinching off**

3. fusion of the two approaching ends of phospholipid bilayer forms a vesicle

[Any 2] [2]

(iii) explain how unfolded polypeptides in the ER are degraded.

1. Polypeptide transported through a **transport protein** embedded in the RER membrane
2. Attached to **ubiquitin** proteins (when in cytosol)
3. Targeted to the **proteasome**
4. For **hydrolysis** into **individual amino acids** / **shorter peptides**

[Any 3] [3]

Misfolded proteins in the ER tend to spontaneously associate with one another to form an aggregate, causing cellular toxicity. The misfolded proteins contained many amino acids in Fig. 1.2. Hence it is important that any misfolded protein is immediately degraded and does not remain in the ER for too long.

The presence of the amino acids in Fig. 1.2 in the primary sequence contributes to the misfolded proteins forming an aggregate with one another.

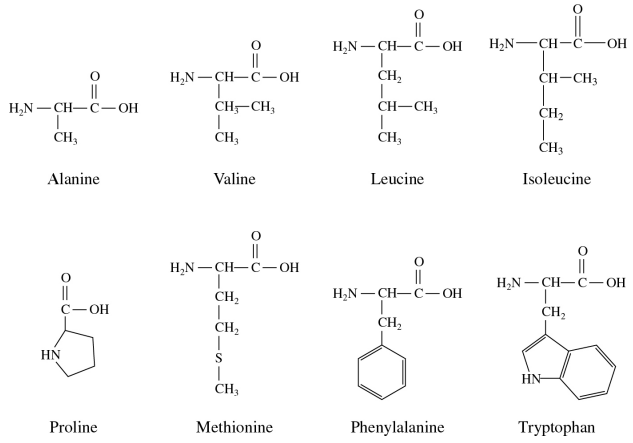


Fig. 1.2

(b) **(i)** Explain how the amino acids in Fig. 1.2 contribute to the misfolded proteins forming an aggregate with one another.

1. Misfolded proteins have their **hydrophobic** amino acid **R groups/side chains** exposed
2. The need to shield themselves away from the aqueous ER lumen
3. Hence, hydrophobic R groups from different misfolded protein associate with one another via **hydrophobic interaction**

[Any 2] [2]

(ii) Suggest how accumulation of protein aggregates in the ER can affect the function of the ER.

1. Such aggregate may interact with **enzymes / membrane proteins** to interfere with their function
2. constrains the ER lumen space available to metabolic enzymes / other proteins [1]

Accumulation of protein aggregates can also cause mitochondrial diseases (MD).

Mitochondria are found in all nucleated eukaryotic cells and are the principal generators of cellular ATP. The mitochondrial circular DNA genome comprises 37 genes, which code for 13 essential polypeptides for oxidative phosphorylation and the necessary RNA machinery for their translation within the mitochondria.

(c) **(i)** It was hypothesised that mitochondria arose when an early ancestor of the eukaryotic cell engulfed an oxygen-using, non-photosynthetic prokaryotic cell.

Explain two pieces of evidence for this hypothesis.

- Mitochondria is bound by a **double membrane** where the inner membrane is the original membrane of the prokaryotes while the outer one is the membrane of the phagocytic vesicle.
- Mitochondria contains **70S ribosomes** and **circular DNA** (not enclosed in nucleus).
- Mitochondria is **autonomous organelles** that grow and reproduce within the cell. [2]

One form of MD is caused by a mutation of a mitochondrial gene that codes for a tRNA.

- The mutation involves substitution of guanine for adenine in the DNA base sequence.
- This changes the anticodon on the aminoacyl-tRNA carrying leucine ($tRNA^{leu}$).
- This mutant $tRNA^{leu}$ also recognises the phenylalanine codon, resulting in the formation of a non-functional protein in the mitochondrion.

(ii) Suggest how the change in the anticodon of a tRNA leads to mitochondrial diseases.

- Change in the anticodon of the tRNA results in the incorporation of **leucine instead of phenylalanine into the polypeptide chain** during translation
- .. the different R-group of amino acid results in different folding of the polypeptide chain, hence, **change in the 3D conformation of the tertiary structure**
- Change in the protein/enzyme required for **oxidative phosphorylation**, hence, **less/ no ATP synthesised**. [3]

While some MDs are caused by mutations of mitochondrial genes inside the mitochondria, most MDs are caused by mutations of genes in the cell nucleus that are involved in the functioning of mitochondria. MDs caused by nuclear DNA mutations are autosomal recessive.

All of a person's mitochondria are inherited from their mother via the egg cell.

Two couples, couple **A** and couple **B**, had one or more children affected by a MD. The type of MD was different for each couple.

None of the parents showed signs or symptoms of MD.

- Couple **A** had four children who were all affected by a MD.
- Couple **B** had four children and only one was affected by a MD.

(iii) Using the information provided, suggest why all of couple **A**'s children had a MD and only one of couple **B**'s children had a MD.

couple **A**

- mutation occurs in the mitochondrial DNA during the formation of mother's eggs in the ovary
- all children have the affected mitochondria from the mother

couple **B**

- Mutation occurs in the nuclear DNA of the parents
- Parents are heterozygotes/ heterozygous at the gene locus

Accept: one parent carries the recessive allele and somatic mutation in child's nuclear DNA [4]

It has been shown that curcumin has considerable mitochondria-protective properties that could prevent MDs.

Curcumin is a yellow pigment found in the spice turmeric, which is used in curry powder.

Eight plant species are known to have roots that contain curcumin. All eight species are found in Asia and several of these belong to the genus *Gurcuma* in the ginger family (Zingiberaceae).

Fig. 1.3 shows the evolutionary relationships for five of the eight species with roots that contain curcumin. Lines that are not labelled represent other species that do not make curcumin.

Fig. 1.3

(d) **(i)** Name the term used to describe the organisation of species according to their evolutionary relationships, as shown in Fig. 1.3.

Phylogeny

[1]

(ii) The five species named in Fig. 1.3 occur in just two of the 400 or more families of flowering plants that exist.

Suggest why the ability to make curcumin is limited to these two families of plants.

- The **common ancestor** of these 2 families contained **genes** on curcumin production, which are only passed to members of these groups over generations.
- The 5 species from these 2 families of plants that can make curcumin, contain specific DNA sequences (e.g. **alleles**) that allow for its transcription and the corresponding translation process to synthesize curcumin.

☠ COMMON MISTAKE:

- Selection pressure arguments that only these two families live in environments where curcumin is selected for [Not supported by Fig. 1.1, which shows that most members of the two families do not produce curcumin].

[2]

One of curcumin's medicinal properties is also as a potent antivenom against snake bites. However, its efficacy varies across species of snake bites.

The venom of a snake contains many protein toxins which can damage the tissues of a victim who has been bitten. The snake bite can lead to significant disability or death within hours, and a specific antivenom would be necessary for treatment.

The following steps describe how a specific antivenom is traditionally produced.

- The venom of a snake is collected.
- An animal, often a horse, is injected with a controlled quantity of the venom.
- The horse's blood is withdrawn and the antibodies produced in response to the protein toxins are isolated.
- The isolated antibodies are purified and formulated as an injection.

The antivenom produced is effective only against the species of snake from which the venom is obtained.

(e) **(i)** State the type of immunity that is conferred by the antivenom when administered to the snake-bite victim.

Artificially-acquired, passive immunity; [1]

(ii) Describe how antibodies in the antivenom may reduce the harmful effects of toxins in the snake venom.

1. Through neutralisation where the binding of antibodies to the toxin prevents the toxin from binding to host cell receptors;
2. Through opsonisation, where the binding of the antibodies mark the toxin for phagocytosis by macrophages;
3. Through agglutination, where the binding of the antibodies clump together pathogens to cause many of the pathogens to undergo phagocytosis at the same time;
4. Through the activation of complement proteins, triggers the formation of pores in the cell surface membrane/ osmotic lysis of the targeted cell;

[2]

(iii) Explain why a particular antivenom is effective only against a specific species of snake.

1. Venom from different species of snake contain different protein toxins;
2. During the production of the antivenom, only B lymphocytes with receptors that have a binding site with a 3D conformation complementary to the protein toxins undergo clonal selection;
   OR
   The antibodies produced in response to the venom have antigen binding sites / variable domains that have a 3D conformation complementary to the protein toxins; [2]

(iv) Suggest why an injection containing inactivated protein toxins is not an effective treatment for a snake-bite victim.

Vaccines requires several days to take effect, as time is required for antigen presentation/ activation of T and B lymphocytes/ differentiation of B lymphocytes into plasma cells/ synthesis or secretion of antibodies; [1]

[Total: 28]

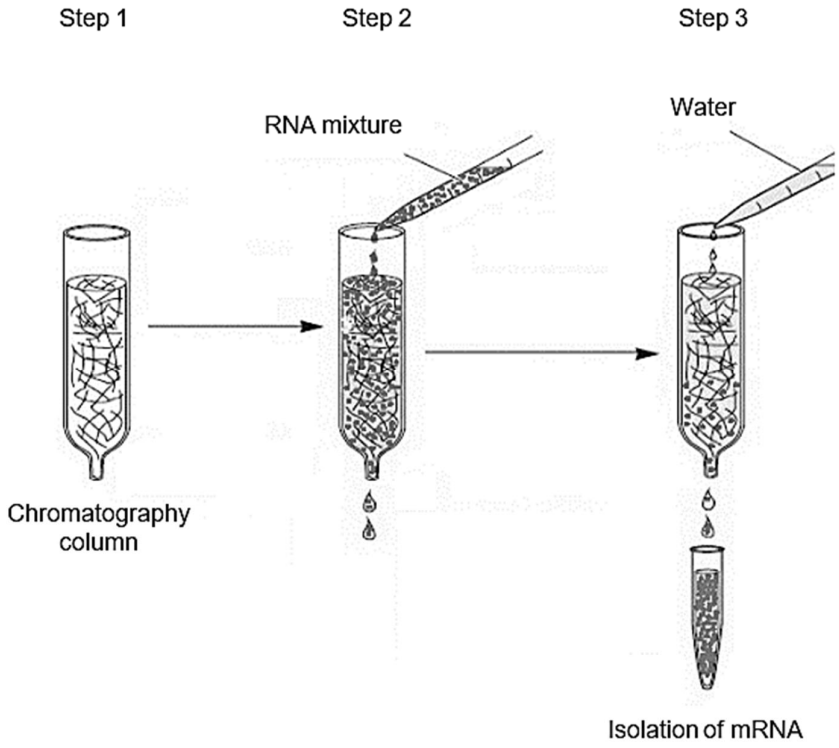
2 The sleep-wake pattern describes when, during a 24 hour day, a person is asleep and when they are awake. Sleep-wake patterns are in turn affected by a multitude of factors, including the levels of hormones such as melatonin.

Two examples of sleep wake-patterns are:

- pattern 1 – asleep during the night and awake during the day (normal)
- pattern 2 – asleep during the day and awake during the night.

To identify which genes have their expression changed by a person's sleep-wake pattern, researchers isolated mRNA from a group of volunteers with sleep-wake pattern 1, and the same group of volunteers whose sleep-wake pattern was changed to pattern 2.

mRNA from volunteer samples were isolated from total cytoplasmic RNA, using the following procedure in Fig. 2.1.



Step 1:	Set up a chromatography column which contains short lengths of uracil nucleotides attached to a solid support medium.
Step 2:	Add total RNA mixture to the chromatography column. RNA that do not hybridise with the uracil nucleotides will pass through and leave the column.
Step 3:	Add water to the chromatography column to remove and isolate the hybridised mRNA.

Fig. 2.1

(a) Explain why the procedure in Fig. 2.1 is effective in isolating mRNA from total cytoplasmic RNA.

1. mRNA is **mature** mRNA/ has undergone **post-transcriptional modification/ RNA processing/ polyadenylation** to possess a **3' poly-A tail**
2. **poly-A tail complementary base pairs with uracil nucleotides** in the chromatography column
3. while other RNA molecules (give one example: **rRNA/ tRNA/** etc) are **not adenine-rich/ do not have continuous sequence of adenine/ OWTTE** and are hence unable to complementary base pair with the uracil nucleotides/ move down and drip out of the column [3]

With the isolated mRNA, these researchers then used microarray analysis to determine changes in gene expression due to altered sleep-wake pattern.

Microarrays are used to detect the expression of thousands of genes at the same time. A microarray slide is printed with thousands of spots in defined positions. Each spot contains single-stranded DNA of known sequence, which acts as a probe to detect gene expression.

Fig. 2.2 shows a typical microarray slide.

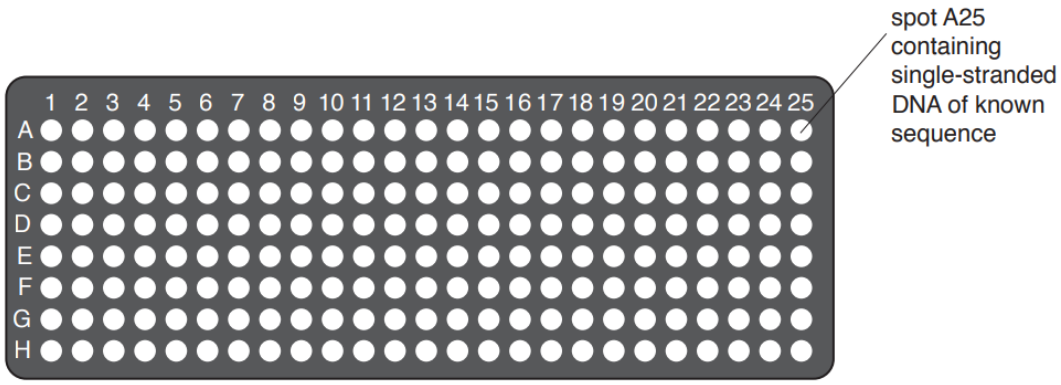


Fig. 2.2

The key steps in this microarray analysis are as follows:

- Each sample of mRNA is converted to complementary DNA (cDNA) and fluorescently labelled.
- Different colour fluorescent dyes are used for the samples taken from before and after the change in sleep-wake pattern.
- The samples are added to the slide and allowed to hybridise onto the DNA on a microarray slide.
- The microarray slide is then scanned to measure the expression of each gene.

(b) Name the enzyme used to convert each sample of mRNA to cDNA.

1. **reverse transcriptase** [1]

(c) Suggest how the level of each gene expression is determined.

1. *ref. to* **intensity/ brightness of fluorescent dye** [1]

(d) A summary of the results is shown in Table 2.1.

Table 2.1

sleep-wake pattern	number of genes with increased expression		
	during the day	during the night	all the time
pattern 1	661	733	108
pattern 2	134	95	8

(i) Suggest and explain how eukaryotic genes can be switched on and off at certain times of day, at the transcriptional level.

(suggest)

1. **light/darkness affects/changes** the level of **secretion of hormones/melatonin**
2. **melatonin/hormone** is a **ligand** that leads to **signal transduction/ cell signalling** that affects the level of gene expression

(explain how eukaryotic genes can be switched on/off at the transcriptional level)

3. **activator** binds to **enhancer** sequence, and **facilitates assembly of general transcription factors and RNA polymerase** to form the **transcription initiation complex**
4. **repressor** binds to **silencer** sequence, and **prevents assembly of the TIC/ recruits histone deacetylases/ prevent activator binding** [3]

(ii) Comment on whether the information in Table 2.1 is useful in concluding how an individual's health is affected by sleep-wake pattern.

1. Table 2.1 (merely) shows that **pattern 2 leads to fewer genes with increased expression** during the day, night and all the time.
2. **not useful** because **roles of genes in Table 2.1 in health is not stated/ specific genes directly involved in determining heath are not identified** [2]

[Total: 10]

3 Reef-building corals are marine invertebrates found in tropical seas and oceans. Each coral consists of a colony of animals called polyps which form by asexual budding.

Each coral polyp has the following structure:

- two layers (inner and outer) of epithelial cells that enclose a central gut cavity
- a non-cellular gelatinous layer
- a thin layer of symbiotic bacteria over the polyp's outer epithelial cells

Zooxanthellae are a group of unicellular photosynthetic eukaryotes that live within the coral polyp's inner epithelial cells. They have chloroplasts and photosynthetic pigments with structures similar to those in plant cells. Without zooxanthellae, coral polyps are white in colour.

Fig. 3.1 shows a transverse section through a polyp and a close-up view of a zooxanthellae producing H_2O_2 and reactive oxygen species due to damages in its chloroplast when sea temperatures are high.

It was observed that proteins in the chloroplast were not denatured due to the higher temperature, but membranes became more leaky. Although water was taken in at a much faster rate, rate of oxygen production decreased drastically.

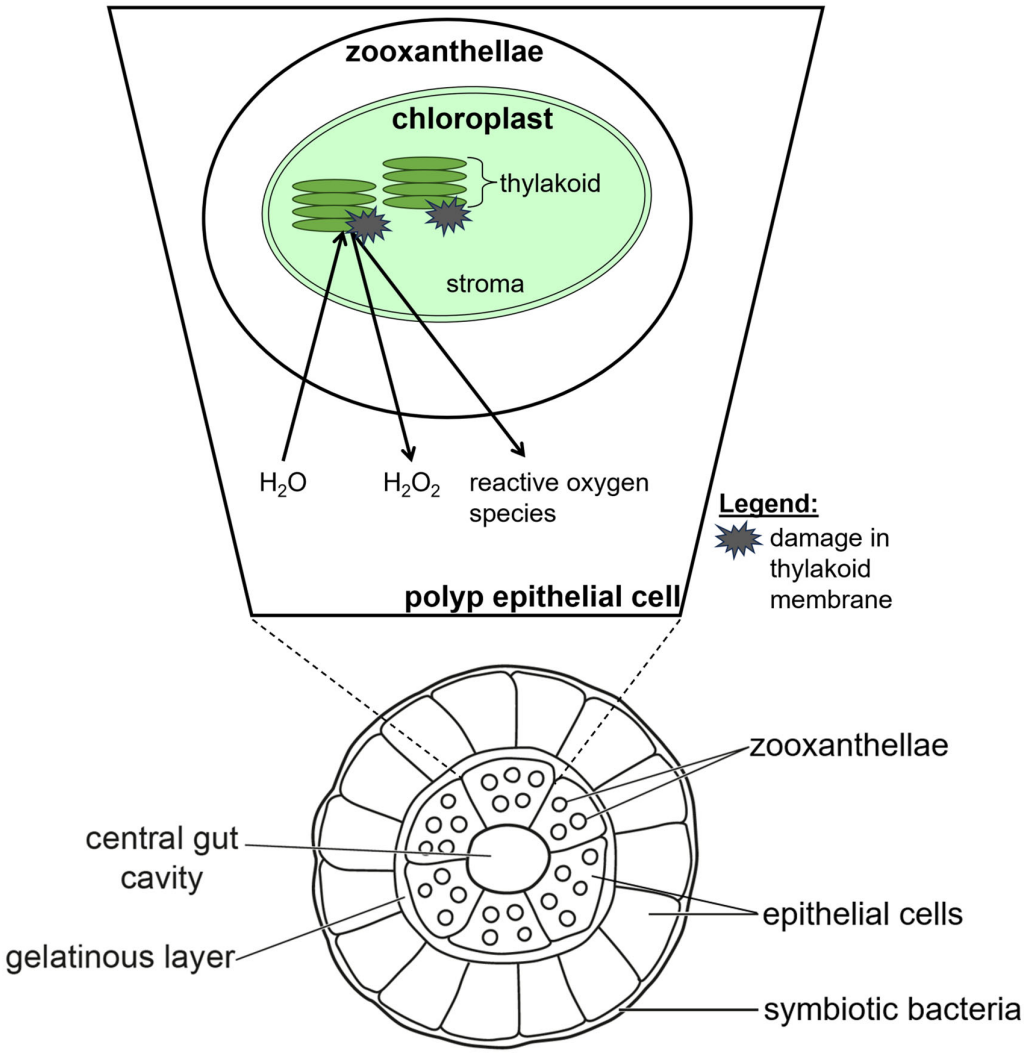


Fig. 3.1

In 2016, higher than usual sea temperatures due to the El Nino effect caused about 65% of Singapore's coral reefs along the fringes of the Southern Islands and in the north-east to be moderately or severely bleached.

(a) Using the information given,

(i) explain how rising sea temperatures affect photosynthesis in zooxanthellae. [4]

1. increase in sea temperature **cause damage to thylakoid membranes** → increased membrane **fluidity**, cannot maintain **proton gradient** across thylakoid membrane;
2. ~~2.~~ **Lesser ATP produced, ~~rate of Calvin cycle decreases/stops~~** ~~as~~
3. **PGA cannot be reduced to G3P**,
4. **RuBP cannot be regenerated** in the absence of ATP and NADPH
5. **Electron flow in ETC** is faster **to release more energy for proton pumps** to pump H+ into thylakoid space to restore proton gradient;

(ii) suggest why zooxanthellae are expelled by coral polyp epithelial cells when sea temperatures are high. [2]

1. Zooxanthellae **no longer photosynthesising and producing food**, therefore expelled.
2. **H_2O_2 and reactive oxygen species** produced by the zooxanthellae during photosynthesis **diffuses into the cytoplasm of the coral (inner) epithelial cell → cause damage / death** of zooxanthellae / polyp epithelial cell;

Extensive land reclamation in Singapore over the last few decades has severely impacted the water turbidity (extent of water murkiness due to suspended particles) and hence the amount of light available to coral reefs in shallow waters.

Scientists measured the percentage of coral cover and water turbidity to the south of mainland Singapore over a period from 1988 to 2010. Some of the results are shown in Fig. 3.2.

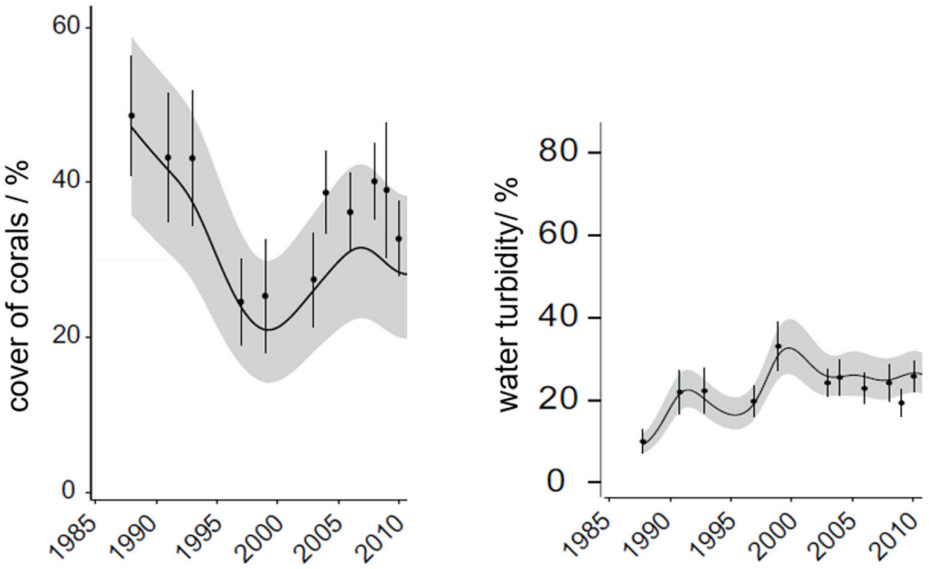


Fig. 3.2

(b) **(i)** Describe the relationship between percentage coral cover and water turbidity. [2]

1. [**quote trend**] When water turbidity increased, percentage coral cover decreased
2. [**quote data from same period** *(to specify)*] e.g. cover of corals decreased from about 45% in 1986 to about 21% in 1999, while water turbidity increased from 10% in 1986 to 30% in 1999, cover of corals increased from about 21% in 1999 to about 32% in 2007, while water turbidity decreased slightly from about 30% in 1999 to about 25% in 2003 and remained constant thereafter.

(ii) Suggest why high percentage water turbidity may be protective against coral bleaching. [1]

3. High percentage water turbidity leads to **lower light intensity** → **reduced rate of light dependent reactions/ photolysis of water**, hence lesser hydrogen peroxide and reactive oxygen species produced, lesser zooxanthellae expelled/dying;

(e) While coral reefs in Singapore have been showing signs of recovery since 2010, recovery rate has been slow.

Explain why individual coral species have low genetic diversity **and** how this affects their chances of survival in response to environmental change from global warming. [3]

1. Coral polyps reproduce mainly by asexual budding → (most) cells are **genetically identical → hence low genetic diversity**

2. Coral populations have low genetic variation, hence **low phenotypic variation**

3. Environmental changes from global warming (e.g. increased sea temperatures and ocean acidification) leads to **changes in selection pressure** → if all have same phenotype that are at **selective disadvantage / are selected against**, may be **wiped out**;

[Total: 12]

Section B

Answer **one** question in this section.

Write your answers on the lined paper provided at the end of this Question Paper.

Your answers should be illustrated by large, clearly labelled diagrams, where appropriate.

Your answers must be in continuous prose, where appropriate

Your answers must be set out in sections **(a)**, **(b)**, as indicated in the question.

4 **(a)** Explain why cancer cells and bacteria cells are able to divide rapidly. [15]

CANCER CELLS (MAX 9):

Genetic mutations causing dysregulation of cell cycle:
Comment: Should also give details of loss of cell cycle checkpoints?

1. **Protooncogene** can undergo a **gain of function mutation** to become an **oncogene**.
2. **Mutation** of **only one** protooncogene / **allele** (to oncogene) leads to **excessive production** of **normal protein** / **hyperactive** protein
3. E.g., ***ras*** gene / ras G protein (accept other relevant examples of mutated genes) leads to **continuous signal transduction** / cell signalling despite the absence of growth factor binding to receptor
4. leads to **uncontrolled** (and rapid) **cell division**
5. **Tumour suppressor genes** can undergo a **loss of function mutation**.
6. Mutation of **both alleles** lead to **uncontrolled cell division**
7. E.g., mutation in ***p53*** tumour suppressor gene leads to **non-functional p53 transcription factor**
8. which cannot trigger the **expression of** genes coding for **DNA repair enzymes** /
9. genes coding for **proteins that trigger apoptosis** of mutated cells **not expressed**
10. **DNA damage** **cannot be repaired**
11. **Cells with mutations** pass through the **cell cycle checkpoints** and **continue dividing**, giving rise to **daughter cells with mutations**.
12. Over the long term, the accumulation of mutation in cells lacking p53 leads to an **increased frequency of oncogenes and mutated tumour suppressor genes**.

Angiogenesis:

13. Activation of genes that signal/promote **angiogenesis** (e.g., VEGF ligands [FYI only]), the **formation of blood vessels**
14. ensuring that cancer cells receive a **continual supply of oxygen and other nutrients** (e.g., glucose for respiration to produce more ATP for cell division → synthesis of proteins, for mitosis, etc.

AVP (Max 1):

15. (Due to mutations in genes coding for proteins involved in cell-cell adhesion and e.g. growth factor receptors,) cancer cells ignore growth factor signalling to stop dividing and continue to grow freely over one another and over normal cells.

16. Activation of **telomerase gene** → Presence of telomerase to lengthen telomeres, telomeres do not reach critical length. These cells avoid cell senescence and apoptosis, resulting in limitless replicative potential
17. (In early stages of tumour development), tumours will usually present **tumour antigens** (may be proteins encoded by oncogene) on its cell surface membrane.
18. (Cells of) the immune system may not recognise these tumour antigens (due to various means) and will not launch an immune response → increase the chances of rapid, uncontrolled cell growth.

BACTERIA CELLS (MAX 7):

1. Bacterial division occurs through **binary fission**,
2. a straightforward process of (cell elongation), **DNA replication**, and **separation into two daughter cells**.
3. Hence, bacteria exhibit short generation times (OWTTE) due to faster replication of chromosome because **genome is smaller in size** (than eukaryotic chromosomes) / has lesser number of base pairs / bacteria only has 1 chromosome vs eukaryotes like human have 46 chromosomes.
4. Because **lesser non-coding DNA / genes**
5. **Lack of a nucleus** eliminates the need and time required for disintegration of the nuclear envelope like in eukaryotes (excluding higher plants)
6. **No formation of spindle fibres required** for separation of bacteria chromosome (and plasmids) into daughter cells → shortens time required for binary fission;
7. **Lack of membrane bound organelles** removes time required for organelle replication → e.g., synthesis of internal membranes and proteins (accept relevant examples);

QWC 1 m : at least one correct point addressing cancer cells and one correct point addressing bacteria cells.

(b) Discuss the factors which may reduce the probability that cancer will occur. [10]

1. minimised exposure to **ionising radiation/X-rays/ gamma-rays**
2. which causes structural **damage to DNA/ physical breakage in DNA**
3. minimised exposure to **chemical carcinogens** / **ethidium bromide** / **tar** in **cigarette smoke**
4. which cause **gene mutations/ interfere with DNA replication**
5. (genetic predisposition) inheritance of **normal/ unmutated tumour suppressor genes** or a normal/unmutated **proto-oncogene**;
6. *ref. to* such an individual needing to accumulate mutations of these genes in his lifetime to develop cancer, compared to an individual who has already inherited these mutated genes
7. **healthy immune system**
8. *ref. to* healthy population of specialised immune cells/ natural killer cells present to kill any developing tumour cells
9. **age**/ *ref. to* a younger individual being less likely to be affected by cancer than an older individual
10. *ref. to* cancer involving the accumulation of somatic mutations **over time**/ **many years**
11. minimised exposure to **cancer-causing viruses**/ or give example, e.g. h**uman papillomavirus (HPV)**
12. via **vaccination**
13. which could **introduce viral oncogene**
14. minimised exposure to **ultra-violet radiation**
15. *ref. to* formation of **pyrimidine dimers** caused by ultra-violet radiation which will interfere with DNA replication
16. **early detection** of primary tumours before **malignant** cancer
17. AVP, e.g. hormone levels (e.g. lower levels of oestrogen lead to reduced risk of breast cancer)

QWC: at least three factors that reduce the probability of cancer developing well-discussed; question is directly answered.

[Total:25]

5 **(a)** Explain how antibiotics and vaccines work in managing diseases. [15]

ANTIBIOTICS (MAX 7)

1. Antibiotics usually work by targeting specific **cellular structures or pathways unique to bacteria** (so that mammalian cells are unaffected).

Inhibition of peptidoglycan cell wall synthesis:

2. **Inhibition** of **peptidoglycan cell wall synthesis** → **loss of mechanical strength** of the cell wall.
3. Bacteria **cannot survive changes in osmotic pressures,** (resulting in changes to cell shape and size), which may ultimately lead to **cell lysis.**
4. Accept example: **Penicillin** acts as a **competitive inhibitor** to **transpeptidases** and **blocks the cross-linking of peptidoglycan** units by **inhibiting peptide bond formation**.

Inhibition of protein synthesis

5. **Initiation and elongation** phases of (mRNA) translation may be inhibited by antibiotics.
6. Antibiotics may also result in protein mistranslation by promoting **tRNA anticodon mismatch with mRNA codon** (e.g., aminoglycosides can induce an alteration in the conformation of the complex formed between an mRNA codon and its activated aminoacyl-tRNA at the ribosome, promoting tRNA mismatching)
7. **50S inhibitiors** (such as linocosamide e.g., clindamycin) **block** the access of **peptidyl-tRNAs** to the ribosome, subsequently **blocking elongation**, and eventually triggering dissociation of peptidyl-tRNA.
8. **30S inhibitors** (such as tetracyclines) may work by **blocking access of aminoacyl-tRNAs** to the **A site** of the (large ribosomal subunit of the) ribosome.

Inhibition of nucleic acid synthesis

9. **Affecting topoisomerase function** (modulation/regulation of **chromosome supercoiling** by strand breakage and rejoining) would **inhibit DNA replication** (and transcription), leading to bacteria cell death and preventing disease progression.
10. Accept example: **Quinolone** (class of antimicrobials e.g., Ciprofloxacin) targets **DNA gyrase** and **topoisomerase** (IV), leading to **double-stranded DNA breaks**.
11. (Rifamycin) drugs **inhibit transcription** by **binding to RNA polymerase**

Inhibition of cell membrane function

12. A **disruption in the cell membrane** could result in **leakage of important solutes** essential for the cell's survival. (However, as both eukaryotic and prokaryotic cells have cell membrane, this class of antibiotics are poorly selective and can often be toxic for systemic use in the mammalian host. Most clinical usage is therefore limited to topical applications e.g., creams for skin infections).

Inhibition of other metabolic processes

13. Antibiotics act on **folic acid pathway** which results in bacteria unable to produce precursors important for **DNA synthesis.**

VACCINATION (MAX 7)

14. Vaccination is the process where a **harmless** form of a **whole pathogen** (can be either inactivated or live attenuated) **or antigens** from a pathogen (e.g., antigen subunits, toxoid)
15. Vaccination/immunisation is a **form of artificial/acquired active immunity** to stimulate a person's immune system
16. Vaccination uses the property of **immunological memory** → long-lasting protection against **infectious disease**.
17. Idea of vaccines **elicit a primary immune response** / **FIRST innate and adaptive** immune **response** against an antigen, so that a **secondary response** is initiated upon an infection.
18. Activated B cells **differentiate** to form antibody-secreting **plasma cells** (short-lived) and **memory B cells** (long-lived)
19. Activated T cells **differentiate** to form **effector T cells / helper and cytotoxic T cells** (short-lived) and **memory T cells** (long-lived).
20. **Subsequent exposures** to the **pathogen/antigen** during an infection after vaccination **stimulates the memory B and T cells** as they **recognise/binds** to the **specific** antigen present on the pathogen.
21. Triggering a **much stronger and rapid/faster secondary immune response**
22. **antibodies** specific for that antigen are **produced at a much higher level** by **plasma cells** and have **higher affinity** to the antigen.
23. (the immune system can) **recognise** and **remove** the **pathogens** during an infection **before they can cause disease** in the host.
24. Individuals infected will have less severe symptoms / no symptoms
25. Herd immunity → protection of individuals who cannot be vaccinated (e.g., children, elderly, immunocompromised)

QWC 1 m : at least one correct point addressing antibiotics and one correct point addressing vaccines.

(b) Discuss, with examples, why antibiotics and vaccines may have limited effect in managing diseases. [10]

Discuss why **antibiotics** may have limited effect in managing diseases.

[Max 6]

1. gene **mutation** in bacterial genome creates **new alleles** that confer antibiotic resistance
2. *ref. to* example of possible outcomes of gene mutation, e.g. changing the 3D conformation of proteins or enzymes which are targets of pre-existing antibiotics/ resulting in new enzymes or transport proteins that can either break down or transport the antibiotics out of the cell respectively, rendering them ineffective
3. overuse of antibiotics exerts a **selection pressure**
4. where **susceptible bacteria** are at a **selective disadvantage** and killed/ **resistant bacteria** are at a **selective advantage** and able to reproduce
5. **increase in frequency of alleles** that confer antibiotic resistance
6. alleles for antibiotic resistance passed to daughter bacteria via **binary fission** (vertical gene transfer)
7. horizontal gene transfer through **conjugation/ transformation**/ **transduction** will also allow alleles for antibiotic resistance to be transferred among different species of bacteria
8. these resistant bacteria may then be transferred to humans through **meat products**/ **human-human infections**
9. *ref. to* use of antibiotics being reactive (to minimise disease becoming severe and to reduce spread to others)/ not preventive
10. AVP, e.g. antibiotics only treat bacterial and not viral infections

Discuss why **vaccines** may have limited effect in managing diseases. [Max 6]

[Max 6]

11. **choice of epitopes/antigens** in vaccine design to create immunological memory against might be **wrongly predicted**/ **not effective** in stimulating optimal memory
12. **antigenic drift**/ **mutations** in pathogen leading to vaccines losing effectiveness
13. *ref. to* **lack of proof-reading** during viral replication
14. *ref. to* **short generation time** of viruses
15. **antigenic shift** in **influenza** viruses leads to new antigens on surface against which current vaccines are not deigned against
16. **low rate of vaccine uptake** by population leads to **ineffective herd immunity**
17. **live, attenuated vaccines** may **regain virulence** and cause disease
18. *ref. to* **HIV** evading host immune system by integrating as a **provirus** within host cell
19. *ref. to* ***Mycobacterium tuberculosis*** evading host immune system by forming **tubercules**
20. *ref. to* an vaccinated individual developing **more severe dengue disease/ DHF/ DSS** if infected with a **different dengue virus serotype**
21. *ref to* **adverse reactions/ anaphylaxis** developing in some individuals after vaccination
22. cost/ stringent transport conditions of vaccines hinder distribution hence use
23. AVP

QWC: at least three possible reasons for the limited effectiveness of antibiotics AND vaccines discussed.

[Total:25]