tr joelPCM Academic Council

DEPARTMENT OF NATURAL SCIENCES · ADVANCED BIOLOGY

Advanced Biology — Paper 1: Theory | Set III

MODEL ANSWERS & WORKED SOLUTIONS · MARK SCHEME

For Examiner / Teacher Use Only | Total: 80 marks | BIO/P1/SET-III/MS/2025

MARK SCHEME NOTES

1. Each bullet point (✓) represents 1 mark unless otherwise stated.
2. Accept any equivalent correct biological reasoning, even if differently phrased.
3. Credit annotated diagrams that convey the same information as a written point.
4. Contextual application to the Ugandan scenario earns credit alongside biological knowledge.
5. Do not penalise for additional correct information beyond the mark scheme.

SECTION A — COMPULSORY

Items 1 & 2 | 40 marks

ITEM 1 — Model Answer

AO1 · Enzymes, Protein Structure, Molecular Analysis & Biotechnology

AO1 | **20 marks**

Part (a) — Biochemical basis of differences across brewing stages (12 marks)

12 marks available

Enzyme structure and active site theory:

✓ Enzymes are globular proteins whose tertiary structure creates a specific active site — a complementary three-dimensional cleft maintained by hydrogen bonds, ionic bonds, and hydrophobic interactions within the polypeptide chain. Only substrates with a complementary shape and charge distribution can bind (induced-fit model: active site flexes on substrate binding, improving complementarity).

✓ The rate of an enzyme-catalysed reaction depends on: (i) the frequency of productive enzyme-substrate collisions, (ii) temperature and pH effects on tertiary structure, (iii) substrate concentration relative to Km, and (iv) product inhibition. All four factors vary systematically across the four brewing stages.

Stage 1 — Gelatinisation (85°C, pH 6.0):

✓ At 85°C, standard enzymes would denature — hydrogen bonds and hydrophobic interactions maintaining tertiary structure are disrupted, unfolding the active site. Only the thermostable alpha-amylase (engineered or derived from thermophilic bacteria such as Bacillus licheniformis) retains active site integrity at this temperature due to additional disulfide bonds and hydrophobic cores stabilising its tertiary structure.

✓ Despite high enzyme activity (182 U/mg), the rate of glucose release is lowest (2.1 g/L/hr) because alpha-amylase cleaves internal alpha-1,4-glycosidic bonds in starch to produce dextrins and short oligosaccharides — not free glucose. Glucose is not the direct product of this stage, explaining low reducing sugar yield (18%).

✓ High substrate concentration (120 g/L) ensures active sites are saturated (Km = 38.2 mg/mL; [S] >> Km), so the enzyme works at Vmax. Low glucose release rate is therefore a product-specificity issue, not a rate-limitation issue.

Stage 2 — Liquefaction (70°C, pH 6.5):

✓ Temperature drops to 70°C — near the optimum for standard alpha-amylase (typically 65–70°C). Enzyme activity (148 U/mg) is slightly lower than Stage 1 but glucose release rises to 14.8 g/L/hr because the progressive breakdown of gelatinised starch into shorter dextrins presents more chain ends for cleavage, increasing product formation rate.

✓ Km falls to 12.6 mg/mL — standard alpha-amylase has higher affinity for partially hydrolysed dextrins than for intact starch granules (Stage 1). Higher affinity means enzyme is not saturated only at very high [S], allowing efficient catalysis as substrate concentration declines during liquefaction.

Stage 3 — Saccharification (60°C, pH 4.5):

✓ Glucoamylase works at its optimum pH (~4.5) and temperature (~60°C). It cleaves glucose units one-by-one from the non-reducing ends of dextrins — releasing free glucose directly. This produces the highest glucose release rate (38.6 g/L/hr) and reducing sugar yield (94% of theoretical).

✓ Km = 4.1 mg/mL — glucoamylase has the highest substrate affinity of the three enzymes. Low Km means even at low substrate concentrations (40 g/L) the enzyme is near-saturated, maintaining high reaction rate throughout the saccharification phase.

✓ Product inhibition index rises to 0.62 — free glucose accumulating in the mash begins to inhibit glucoamylase by binding the active site or allosteric sites, competing with the dextrin substrate. This is the key rate-limiting factor in Stage 3 and explains why yield does not reach 100%.

✓ Protein denaturation indicator shows 96% native structure retained — at 60°C all three enzymes maintain structural integrity. The near-complete structural retention at Stage 3 confirms that the temperature is below the denaturation threshold for glucoamylase.

Stage 4 — Fermentation (32°C, pH 4.8) and overall enzyme kinetics:

✓ At 32°C, yeast invertase (Km = 2.3 mg/mL) hydrolyses residual sucrose and short oligosaccharides to glucose and fructose for fermentation. Low temperature reduces kinetic energy — fewer enzyme-substrate collisions per second — hence lower activity (96 U/mg) and glucose release rate (9.4 g/L/hr). This is intentional: slower, controlled glucose release sustains yeast metabolism throughout fermentation without osmotic stress.

> *Award max 12. Require: active site/induced-fit theory (2), temperature effects on tertiary structure (2), Km interpretation across stages (2), product specificity at Stage 1 (1), glucoamylase mechanism with product inhibition (3), Stage 4 temperature-rate link (2). Accept Michaelis-Menten curve reference for Km explanation.*

Part (b) — Biotechnological strategies to maximise fermentable sugar yield (8 marks)

8 marks available

✓ Deploy immobilised glucoamylase columns in Stage 3 — covalently binding glucoamylase to an inert carrier (e.g., silica beads) allows continuous flow of dextrin substrate through the column while the enzyme is retained and reused. This eliminates product inhibition that reduces yield at Stage 3 (index 0.62) because glucose flows away from the enzyme immediately, preventing active-site blockage. Reduces cost since enzyme is not consumed per batch.

✓ Apply continuous glucose removal by membrane ultrafiltration during saccharification — a semi-permeable membrane allows free glucose to pass through while retaining dextrins and enzyme. Removing glucose as it is produced eliminates product inhibition (the key

rate-limiting factor at Stage 3), pushing the reaction towards completion and recovering yields closer to 100%.

- ✓ Use protein-engineered thermostable glucoamylase at Stage 3 — directed evolution or site-directed mutagenesis of the glucoamylase gene to introduce additional disulfide bridges at the active site cleft increases thermal stability, allowing operation at 65°C where reaction kinetics are faster (higher molecular collision frequency), increasing glucose release rate beyond 38.6 g/L/hr.
- ✓ Optimise Stage 1 substrate concentration to 80–90 g/L rather than 120 g/L — at [S] >> Km (38.2 mg/mL), additional substrate beyond saturation does not increase rate but increases viscosity, reducing mass transfer of substrate to active sites and making mixing less efficient. Reducing concentration to near-Km improves process economics without sacrificing rate.
- ✓ Co-immobilise alpha-amylase and glucoamylase in the same reactor for Stages 2–3 — proximity of both enzymes creates a substrate channelling effect: dextrins released by amylase are immediately available to glucoamylase without diffusing away, reducing the effective Km of the combined system and maximising the conversion of starch to glucose in a single step.
- ✓ Apply pullulanase (debranching enzyme) alongside glucoamylase in Stage 3 — pullulanase cleaves alpha-1,6-glycosidic branch points in dextrins, converting branched limit dextrins to linear chains. This exposes more non-reducing ends for glucoamylase, increasing the number of simultaneous cleavage sites and raising reducing sugar yield above 94% towards near-theoretical maximum.
- ✓ Monitor and control pH precisely at pH 4.5 throughout Stage 3 using automated buffer dosing — glucoamylase has a sharp pH optimum. Drift above pH 5.0 or below pH 4.0 alters ionisation of catalytic residues (glutamate, aspartate) in the active site, reducing substrate binding affinity and catalytic turnover rate. Automated pH control ensures enzyme operates continuously at Vmax conditions.
- ✓ Conduct pilot studies on cassava variety selection — different cassava cultivars have varying amylose:amylopectin ratios. High-amylose varieties (more linear chains) are more accessible to glucoamylase (higher effective [S] for the enzyme) and produce fewer branch-point residues that require debranching, potentially increasing theoretical maximum yield from the current 94%.

Award max 8. Require: at least 4 distinct strategies, each with a biochemical mechanism justification. Immobilisation with product inhibition explanation essential for full marks. Award up to 2 marks for any novel, well-reasoned strategy not listed above.

ITEM 1 TOTAL: 20 marks

ITEM 2 — Model Answer

AO2 · Plant Growth Regulators, Hormonal Control & Crop Management

AO2 | **20 marks**

Part (a) — Apical dominance, auxin:cytokinin ratio and shoot regulation (12 marks)

12 marks available

Treatment A — Control (intact apical bud):

- ✓ The intact apical bud synthesises auxin (IAA) in the apical meristem, which is transported polarly downward via PIN auxin efflux carriers in the phloem parenchyma. High auxin concentration (0.8 ng/g) in lateral buds suppresses their growth — this is apical dominance. The molecular mechanism involves auxin upregulating the expression of BRC1 transcription factors within lateral buds, which repress genes required for lateral bud outgrowth and cell division.
- ✓ Cytokinin level in lateral buds is low (0.4 ng/g) — cytokinins are synthesised primarily in root apices and transported upward, but their effect in lateral buds is countered by high auxin. The high auxin:cytokinin ratio (0.8/0.4 = 2.0) strongly favours apical growth over lateral branching, producing only 2 lateral shoots per bush.
- ✓ High mean shoot elongation rate (6.2 mm/day) reflects uninterrupted auxin-driven cell elongation in the apical shoot — auxin promotes H+ pump (proton ATPase) activity in cell walls, acidifying the wall and activating expansins that loosen cellulose microfibrils, enabling turgor-driven cell elongation (acid growth hypothesis).

Treatment B — Light tip pruning:

- ✓ Removal of the apical bud eliminates the primary source of auxin — IAA in lateral buds falls to 0.4 ng/g. Without auxin-mediated suppression, BRC1 transcription is downregulated in lateral buds, and lateral bud outgrowth is derepressed. Cytokinin rises to 1.8 ng/g (now the dominant signal) — the auxin:cytokinin ratio falls sharply (0.4/1.8 = 0.22), strongly favouring lateral branching.
- ✓ Eight lateral shoots produced per bush — each previously suppressed lateral bud receives the cytokinin signal needed to exit dormancy. Cytokinin promotes cell division in lateral meristems by stimulating CDK (cyclin-dependent kinase) activity and progressing cells through the G1/S checkpoint of the cell cycle.
- ✓ Mean elongation rate falls to 4.1 mm/day — auxin for cell elongation is now supplied by multiple growing lateral shoot tips rather than one dominant apex; auxin concentration per shoot is lower, reducing elongation rate per lateral shoot even though total shoot number is higher.

Treatment C — Hard pruning + auxin (IBA) spray:

- ✓ External application of 0.1% IBA (indole-3-butyric acid, a synthetic auxin analogue) after hard pruning partially restores auxin levels in lateral buds (2.1 ng/g — highest of all treatments). High auxin reimposes partial apical dominance: only 4 lateral shoots are produced (fewer than Treatment B), because IBA re-activates BRC1-mediated suppression in some lateral buds.
- ✓ Elongation rate is highest (7.8 mm/day) — IBA promotes vigorous cell elongation in the shoots that do emerge, since auxin concentration per shoot is high. Each shoot elongates rapidly under high IAA-driven acid growth.
- ✓ Lowest polyphenol content (18.4% dry weight) — rapid cell elongation under high auxin dilutes secondary metabolite synthesis; cells undergoing rapid division and expansion allocate resources to primary metabolism (protein synthesis, cell wall deposition) rather than to the phenylpropanoid pathway that produces polyphenols. This makes Treatment C least suitable for quality tea production.

Treatment D — Hard pruning + cytokinin (BAP) spray:

- ✓ External 0.05% BAP (6-benzylaminopurine, synthetic cytokinin) application after pruning maximises cytokinin concentration (3.4 ng/g) with low auxin (0.3 ng/g). Auxin:cytokinin ratio = 0.09 — the lowest of all treatments — maximally derepresses all lateral buds, producing 14 lateral shoots per bush.
- ✓ Elongation rate is lowest (3.6 mm/day) — many buds competing for the same pool of photosynthate and minerals; individual shoots receive less resource per shoot tip, limiting elongation. However, flush weight is highest (148 g/bush) because 14 shoots accumulate more total leaf biomass.
- ✓ Highest polyphenol content (26.8% dry weight) and chlorophyll (46 SPAD units) — slower-growing shoots with high cytokinin have longer cell maturation time, allowing greater accumulation of polyphenols via the phenylpropanoid pathway, and more chloroplast development (cytokinin promotes chloroplast biogenesis and delays leaf senescence by inhibiting chlorophyll degradation).

Award max 12. Require: apical dominance mechanism with BRC1 (2), acid growth hypothesis for elongation (1), IAA:cytokinin ratio interpretation across all 4 treatments (4), cytokinin cell division mechanism (1), polyphenol dilution under high auxin (2), Treatment D chlorophyll/cytokinin link (2).

Part (b) — Integrated crop management strategy for Kabale smallholders (8 marks)

8 marks available

- ✓ Adopt Treatment D (hard pruning + BAP cytokinin spray) as the primary production system — data show highest flush weight (148 g/bush) and highest polyphenol content (26.8%), which directly determines black tea grade and export price. The 14 lateral shoots per bush maximise harvestable surface area while maintaining quality standards demanded by international buyers (BOP/BOPF grades require >22% polyphenol).
- ✓ Implement a staggered pruning schedule across sections of the farm — prune one-third of bushes per month on a rolling cycle, ensuring continuous flush availability for weekly harvesting rather than a single large flush followed by dormancy. This maintains steady income for smallholders and avoids market gluts that depress farmgate prices.
- ✓ Apply BAP at the optimum timing: 48–72 hours after pruning, when wound-response ethylene has dissipated and lateral buds are most responsive to cytokinin signal. Application during active bud swelling (visible green tip) maximises receptor activation in lateral meristems, ensuring all buds exit dormancy simultaneously and produce a uniform flush.
- ✓ Supplementary nitrogen fertilisation (CAN at 80 kg N/ha/yr in split doses) — nitrogen is required for amino acid synthesis (phenylalanine) which feeds the phenylpropanoid pathway producing polyphenols. Adequate N supply maintains the enzymatic capacity for polyphenol synthesis in the slower-growing Treatment D shoots without compromising the low auxin:cytokinin ratio.
- ✓ Retain shade trees at 25–30% canopy density around tea plots — moderate shade reduces UV-induced polyphenol degradation after synthesis and maintains leaf moisture content above 70%, reducing tough fibrous tissue formation that lowers grade. Shade also moderates temperature extremes at Kabale's 1,800–2,200 m elevation, keeping leaf tissue at the optimal temperature for enzymatic polyphenol synthesis (25–30°C).
- ✓ Harvest only the terminal bud and first two leaves (the flush) every 7–10 days — removing more than 2 leaves per shoot introduces older, lower-polyphenol material that reduces average polyphenol content of the harvested crop. Disciplined plucking also signals the bush to produce another flush rapidly, maintaining high shoot turnover under cytokinin dominance.
- ✓ Train farmers in on-farm BAP preparation and low-volume spray application using knapsack sprayers — reduce per-unit cost of cytokinin application by purchasing BAP powder in bulk through the UTDA cooperative system. Cost-benefit analysis: 148 g flush/bush vs 28 g (control) = 5.3x yield increase; even at BAP input cost of UGX 50,000/season, net income gain justifies investment at current tea prices.

✓ Monitor polyphenol content using portable Brix refractometers calibrated against UTDA polyphenol standards — enables real-time quality feedback to farmers, allowing adjustment of pruning frequency and BAP application rate if polyphenol content drops below export threshold. Empowers farmers to make data-driven agronomic decisions rather than relying solely on extension officer visits.

Award max 8. Require: clear selection of Treatment D with data justification (2), at least 3 further agronomic strategies with hormonal or biochemical justification (5), reference to smallholder economic context (1).

ITEM 2 TOTAL: 20 marks

ITEM 3 — Model Answer

AO3 · Immunity, Vaccination, Antibody Production & Public Health

AO3 | **20 marks**

Part (a) — Cellular and molecular mechanisms of primary vs secondary immune response (12 marks)

12 marks available

Antigen processing and lymphocyte activation — Cohort 2 (primary response):

- ✓ Vaccine antigens (attenuated viral proteins or polysaccharide conjugates) are engulfed by antigen-presenting cells (dendritic cells, macrophages) via phagocytosis. Inside lysosomes, antigens are hydrolysed into peptide fragments (8–25 amino acids) that are loaded onto MHC class II molecules and displayed on the cell surface.
- ✓ Naive T-helper cells (CD4+) with complementary T-cell receptors bind the MHC II-peptide complex. Co-stimulation via CD28/B7 interaction fully activates the T-helper cell, which proliferates (clonal expansion) and differentiates into Th1 and Th2 effector subsets. Th2 cells secrete interleukins (IL-4, IL-5, IL-13) that activate B-lymphocytes.
- ✓ B-lymphocytes with matching B-cell receptors bind free antigen directly. With T-helper cell co-stimulation (CD40L-CD40 interaction), B-cells undergo clonal expansion and differentiation into plasma cells (antibody secreting) and memory B-cells in germinal centres of lymph nodes — explaining the plasma cell count rising to 840 per lymph node biopsy.
- ✓ Initial antibody class is IgM (peak titre 320 AU) — produced rapidly but with lower antigen affinity. Class switching to IgG (180 AU) occurs via somatic hypermutation and affinity maturation in germinal centres over 14–21 days, explaining the slower peak response time in Cohort 2.
- ✓ Memory B-cells (280/µL) and memory T-cells (210/µL) persist long-term in lymphoid tissue and peripheral blood, retaining antigen-specific receptors (with enhanced affinity from somatic hypermutation). This provides the cellular basis for immunological memory.

Secondary response — Cohort 3 (booster dose):

- ✓ Booster dose re-exposes pre-existing memory B-cells and memory T-helper cells to the same antigen. Memory cells express lower activation thresholds, respond within hours rather than days, and do not require the full series of co-stimulatory signals needed to activate naive lymphocytes.
- ✓ Rapid and massive clonal expansion of memory B-cells generates far more plasma cells (3,200 per lymph node biopsy vs 840 in primary) within 3–5 days — explaining the dramatically faster peak response time and higher IgG titre (2,400 AU vs 180 AU).
- ✓ Class switching has already occurred in memory B-cells — booster response produces predominantly IgG (and IgA for mucosal antigens) rather than IgM. IgG antibodies have higher affinity (from previous somatic hypermutation cycles), longer half-lives (23 days vs 5 days for IgM), and fix complement more effectively. This accounts for the peak IgM in Cohort 3 being only 40 AU.
- ✓ Duration of protection extends to 36–60+ months after booster — the larger memory cell pool (1,840 B-cells; 1,620 T-cells) ensures that even as memory cells naturally decline over years, sufficient numbers remain above the protective threshold to mount a rapid secondary response upon future antigen exposure.
- ✓ Vaccine efficacy rises from 68% (Cohort 2) to 96% (Cohort 3) — the high-affinity IgG antibodies in Cohort 3 neutralise the pathogen more effectively, prevent host cell entry by

blocking viral surface proteins (haemagglutinin for measles), and opsonise pathogens for phagocytic destruction. Cohort 1 has no specific antibodies and therefore zero protection.

Award max 12. Require: antigen processing/MHC II pathway (2), T-helper and B-cell activation (2), IgM to IgG class switching (2), memory cell formation mechanism (2), secondary response speed/magnitude with plasma cell data (2), affinity maturation (1), efficacy explanation (1).

Part (b) — Public health implications and herd immunity strategy (8 marks)

8 marks available

- ✓ Herd immunity threshold for measles — measles has a basic reproduction number (R0) of 12–18 (highest of any vaccine-preventable disease). The herd immunity threshold (HIT) = 1 - 1/R0 = 92–95%. Data show Cohort 2 (primary course only) achieves 68% efficacy — insufficient to reach HIT. Booster doses achieving 96% efficacy are therefore essential, not optional, for measles herd immunity in Kampala.
- ✓ Two-dose measles vaccination strategy — implement the WHO-recommended two-dose MR/MMR schedule: first dose at 9 months (Cohort 2 efficacy 68%) and second dose at 15–18 months (Cohort 3 efficacy 96%). Target coverage above 95% in each dose for all children in Bwaise, Kawempe, and Namuwongo settlements to reach and sustain the herd immunity threshold.
- ✓ Supplementary immunisation activities (SIAs) targeting unvaccinated adults in informal settlements — door-to-door campaigns using community health workers (VHTs) during outbreaks, prioritising unvaccinated individuals (Cohort 1, zero efficacy) who sustain ongoing transmission chains. Data show Cohort 1 has <10 memory cells/µL — even one exposure can cause severe disease and generate new cases.
- ✓ Cold chain infrastructure reinforcement for Kampala settlements — live attenuated measles vaccines require storage at 2–8°C. Informal settlements have frequent power outages disrupting cold chain. Invest in solar-powered vaccine refrigeration units at parish-level health posts to prevent vaccine potency loss, ensuring each dose achieves the Cohort 2/3 immunogenic response observed in the study.
- ✓ Integrated UNEPI–KCCA disease surveillance system — establish rapid measles case notification from all health facilities in the five Kampala divisions. Link notification to a real-time dashboard identifying immunisation coverage gaps by parish. Targeted catch-up campaigns can be deployed within 72 hours to vaccination-cold spots before outbreaks spread.
- ✓ School entry immunisation verification — require proof of two-dose measles vaccination for primary school enrolment in all Kampala schools. Schools in informal settlements are high-density transmission settings; this policy ensures near-universal coverage among the school-age cohort, creating a protected generation that interrupts transmission to younger unvaccinated siblings.
- ✓ Community trust and demand creation — engage community leaders (LC1 chairpersons, religious leaders) in Bwaise and Kawempe to address vaccine hesitancy. Immunological data from the study can be presented in accessible formats: illustrating how the booster (Cohort 3) provides 96% protection versus zero for unvaccinated community members makes the individual and collective benefit tangible.

Award max 8. Require: R0/HIT calculation or explanation for measles (2), two-dose schedule justification with data (2), at least 2 further public health strategies with epidemiological or immunological justification (4).

ITEM 3 TOTAL: 20 marks

ITEM 4 — Model Answer

AO3 · Renal Homeostasis, Osmoregulation & Hormonal Water Balance

AO3 | **20 marks**

Part (a) — Renal and hormonal mechanisms across the four groups (12 marks)

12 marks available

Normal osmoregulation — Healthy Control:

✓ Plasma osmolality is maintained at 290 mOsm/kg by a negative-feedback loop: osmoreceptor neurons in the hypothalamus (supraoptic and paraventricular nuclei) monitor blood osmolality. At normal levels, ADH secretion (2.4 pg/mL) from the posterior pituitary via axon terminals is moderate, inserting aquaporin-2 (AQP2) channels into the apical membrane of collecting duct (CD) principal cells at 100% baseline expression. Water reabsorption by osmosis produces concentrated urine (600 mOsm/kg) with normal urine output (60 mL/hr).

✓ The renin-angiotensin-aldosterone system (RAAS) is minimally active (renin 1.2 ng/mL/hr) because blood pressure and plasma sodium (140 mmol/L) are normal. Proximal tubule Na+ reabsorption (67% of filtered load) and distal/collecting duct aldosterone-driven Na+ reabsorption are balanced to maintain normonatraemia.

Chronic Dehydration (Karamoja):

✓ Prolonged water deficit reduces plasma water content, raising osmolality to 328 mOsm/kg. Hypothalamic osmoreceptors detect this rise (threshold 285–295 mOsm/kg) — two simultaneous responses are triggered: (i) thirst sensation driving water-seeking behaviour, and (ii) a 7.75-fold increase in ADH secretion (18.6 pg/mL).

✓ Elevated ADH binds V2 receptors on CD principal cells, activating a cAMP/protein kinase A cascade that phosphorylates AQP2 vesicles and inserts them into the apical membrane — AQP2 expression rises to 280% of normal. This dramatically increases the water permeability of the CD, allowing water to move by osmosis from the filtrate into the hypertonic medullary interstitium (maintained by the countercurrent multiplier in the loop of Henle).

✓ Urine osmolality reaches 1,180 mOsm/kg (near maximum human concentrating capacity) with urine output falling to 18 mL/hr — the kidney conserves almost all filtered water. Serum Na+ rises to 156 mmol/L (hypernatraemia), reflecting the water deficit relative to solute.

✓ RAAS is strongly activated (renin 8.6 ng/mL/hr): reduced renal perfusion pressure activates juxtaglomerular cells to secrete renin, converting angiotensinogen to angiotensin I → ACE converts to angiotensin II → stimulates adrenal cortex to release aldosterone → aldosterone upregulates ENaC (epithelial Na+ channel) and Na+/K+ ATPase in the distal tubule and collecting duct, increasing Na+ reabsorption (74% proximal + additional distal reabsorption).

Diabetes Insipidus (DI) — ADH deficiency:

✓ Central DI results from destruction or dysfunction of hypothalamic ADH-producing neurons (trauma, tumour, autoimmune). ADH falls to 0.3 pg/mL despite raised plasma osmolality (312 mOsm/kg) — the hypothalamic-posterior pituitary axis fails to respond appropriately. Without ADH, V2 receptors are not activated, cAMP does not rise, and AQP2 vesicles remain in intracellular storage. AQP2 expression falls to 12% of normal — the collecting duct is virtually water-impermeable.

✓ Without water reabsorption in the CD, the filtrate passes through unchanged — urine osmolality collapses to 95 mOsm/kg (hypotonic, dilute) and urine output reaches 420 mL/hr (up to 10 L/day clinically). This extreme polyuria leads to dehydration, polydipsia, and hypernatraemia (148 mmol/L) despite preserved thirst mechanism driving fluid intake.

SIADH — Inappropriate ADH excess:

✓ SIADH arises from ectopic ADH secretion (e.g., small cell lung cancer, CNS disease, drugs) independent of osmolality. ADH is 28.4 pg/mL despite plasma osmolality of only 248

mOsm/kg — far below the normal osmotic threshold for ADH secretion (>285 mOsm/kg). AQP2 expression is 340% of normal, causing excessive water reabsorption.

✓ Urine is concentrated (880 mOsm/kg) and output low (22 mL/hr) despite plasma hypotonicity. Retained water dilutes plasma Na+ to 118 mmol/L (severe hyponatraemia) — this is the life-threatening feature of SIADH. Suppressed renin (0.4 ng/mL/hr) reflects expanded plasma volume (baroreceptors inhibit renin), yet ADH secretion continues inappropriately.

Award max 12. Require: hypothalamic osmoreceptor-ADH-AQP2 pathway (3), RAAS mechanism with aldosterone (2), DI: ADH deficiency → AQP2 loss → polyuria (3), SIADH: ectopic ADH → AQP2 overexpression → hyponatraemia (3), data used throughout (1).

Part (b) — Clinical management for each patient group (8 marks)

8 marks available

Chronic Dehydration (Karamoja patients):

✓ Administer oral rehydration therapy (ORT) or intravenous normal saline (0.9% NaCl) to restore plasma volume and osmolality towards 290 mOsm/kg. As osmolality normalises, hypothalamic osmoreceptors detect the fall, reducing ADH secretion (18.6 → 2.4 pg/mL), downregulating AQP2 insertion, and allowing urine osmolality to return to normal. Rate of rehydration must be controlled (not >10–12 mmol/L Na+ correction per 24 hrs) to prevent cerebral oedema from rapid osmotic shifts.

✓ Long-term: community-level water harvesting infrastructure in Karamoja — boreholes, rainwater tanks — to prevent recurrence. Address root cause: drought-driven dehydration reflects a structural water insecurity problem beyond individual clinical management.

Diabetes Insipidus (DI):

✓ Prescribe synthetic ADH analogue desmopressin (DDAVP) — intranasal or oral formulation. Desmopressin is a V2-receptor-selective agonist with longer half-life than endogenous ADH (8–24 hrs vs 30 min). It restores cAMP signalling in CD principal cells, triggers AQP2 insertion, and raises urine osmolality from 95 towards 600 mOsm/kg, reducing urine output from 420 to 60 mL/hr. Dose titrated against urine osmolality monitoring.

✓ Investigate and treat underlying cause — MRI of hypothalamus and posterior pituitary to identify treatable causes (craniopharyngioma, infiltrative disease). If nephrogenic DI (V2 receptor mutation rather than ADH deficiency), thiazide diuretics and low-sodium diet paradoxically reduce urine output by reducing GFR and increasing proximal Na+/water reabsorption.

SIADH:

✓ Fluid restriction to 500–800 mL/day — by limiting water intake below the kidney's obligatory water excretion rate (even in SIADH, some urinary water is lost), plasma osmolality gradually rises and Na+ corrects toward 130–135 mmol/L over 48–72 hours. This exploits the fact that even with high AQP2 expression, total urine output (22 mL/hr = 528 mL/day) provides some obligatory water loss.

✓ For severe hyponatraemia (Na+ < 120 mmol/L) with neurological symptoms: administer hypertonic 3% NaCl by slow IV infusion (correction rate < 8 mmol/L/24 hrs to prevent osmotic demyelination syndrome) to rapidly restore Na+ above the seizure threshold. Simultaneously identify and treat the ectopic ADH source — staging CT chest/abdomen for malignancy, review of offending drugs (carbamazepine, SSRIs, thiazides).

Award max 8. Require: physiologically justified treatment for each of the three groups (2 marks each = 6), and root cause/investigation approach for at least two groups (2). Penalise if correction rates for hypo/hypernatraemia not mentioned.

ITEM 4 TOTAL: 20 marks

ITEM 5 — Model Answer

AO4 · Population Ecology, Predator-Prey Dynamics & Conservation Management

AO4 | **20 marks**

Part (a) — Population dynamics 1995–2024 (12 marks)

12 marks available

Baseline 1995 and carrying capacity:

✓ In 1995, Uganda kob (12,400), zebra (3,800), lion (186), and wild dog (42) coexisted at or near the ecological carrying capacity (K) of KVNP. Carrying capacity is set by the availability of primary productivity (grass cover 74%) relative to total herbivore biomass demand (4,820 kg/km²). At or near K, population growth rates approach zero (logistic growth model); birth rates balance death rates including predation.

2002–2004 Drought — abiotic disturbance:

✓ Rainfall fell to 310–280 mm/yr (from 680 mm) — a 59% reduction. Primary productivity collapsed: grass cover fell from 74% to 38%, reducing the carrying capacity for large herbivores. Kob declined from 10,200 to 4,800 (–53%); zebra from 3,200 to 1,400 (–56%) between 2002 and 2004 — density-dependent starvation as food resources fell below the nutritional requirements of the existing population.

✓ Predator populations declined with a time lag behind prey: lions fell from 174 to 98 (–44%), wild dogs from 38 to 14 (–63%) between 2002 and 2004. This lag reflects the Lotka-Volterra predator-prey relationship — predator reproduction and survival depend on prey availability. As prey declined, predators faced food stress, increased cub mortality, and inter-pride competition reduced lion social cohesion.

✓ Wild dogs suffered a proportionally greater decline (63% vs 44% for lions) — wild dogs are obligate coursing predators requiring large open grassland territories and cooperative pack hunting. Drought-induced vegetation change (38% grass cover) reduces visibility and running space, disproportionately impairing wild dog hunting success relative to ambush-hunting lions.

2011–2012 Anthrax Outbreak — biotic disturbance:

✓ Anthrax (Bacillus anthracis endospores, endemic in alkaline soils of semi-arid savannas) erupted during the post-drought recovery phase. Kob declined catastrophically from approximately 6,000 (estimated 2008 recovery level) to 1,900 — the 284 anthrax-positive carcasses recorded represent only confirmed cases; actual mortality likely 5–10 times higher. Kob are highly susceptible ungulates that ingest spores while grazing on contaminated grass.

✓ Zebra declined only modestly (1,400 → 1,310) between 2004 and 2012 — zebras have partial resistance to anthrax due to differences in gut pH and immune responses, and their grazing height (selective feeding at different sward heights than kob) reduces spore ingestion probability.

✓ Predator numbers continued declining post-anthrax: lions fell to 72, wild dogs to 9 — prey biomass (1,210 kg/km²) was now critically below the minimum density required to sustain viable predator populations. Wild dog pack size fell below the minimum cooperative hunting threshold (~4–6 adults), reducing reproductive success and increasing vulnerability to inbreeding.

Recovery by 2024 and population theory:

✓ By 2024, rainfall recovered (660 mm/yr), grass cover rose to 68%, and prey populations partially rebounded: kob to 6,200, zebra to 2,900. This follows density-dependent compensatory population growth — at low population density (below K), per-capita resources are abundant, birth rates exceed death rates, and populations grow rapidly (approaching exponential). Kob's r-selected life history (short gestation, large litters, early sexual maturity) facilitates faster recovery than lions or wild dogs.

✓ Lion and wild dog recovery is slower (lions 124; wild dogs 31 by 2024) — K-selected predators have long gestation periods, small litter sizes, and extended parental investment. Wild dogs remain at critically low numbers (31); below minimum viable population size (~150 for genetically viable wild dog populations), inbreeding depression threatens long-term viability.

Award max 12. Require: carrying capacity concept with data (2), drought→grass→herbivore mechanism (2), Lotka-Volterra lag with data (2), anthrax biology (2), differential susceptibility explanation (1), density-dependent recovery with r/K selection (2), wild dog viability concern (1).

Part (b) — Population management and ecosystem restoration plan (8 marks)

8 marks available

✓ Emergency wild dog genetic rescue programme — with only 31 wild dogs (below MVP of ~150), import 8–10 genetically unrelated individuals from the Laikipia/Samburu metapopulation (Kenya) or Ruaha (Tanzania) via IUCN Wild Dog SSP. Genetic mixing raises heterozygosity, reduces inbreeding coefficient, and restores pack size above the 6-adult cooperative hunting threshold essential for pup survival.

✓ Anthrax outbreak preparedness and monitoring protocol — deploy soil surveillance at known anthrax hotspots (alkaline dry-season water points) using PCR detection of B. anthracis DNA. Establish a carcass rapid-response team to collect and incinerate anthrax-positive carcasses (burning eliminates spore dispersal), preventing the 2011–2012 event from repeating during the next drought-recovery cycle.

✓ Controlled supplementary water provisioning during droughts — install solar-powered boreholes at strategic locations across KVNP linked to automatic livestock troughs accessible to kob and zebra. Prevents drought-induced mortality before prey populations collapse below predator maintenance thresholds; sustains herbivore biomass above 3,000 kg/km² even during rainfall deficits.

✓ Corridor connectivity to Matheniko and Timu Forest reserves — negotiate transboundary wildlife corridors with South Sudan and Kenya to allow gene flow between KVNP predators and larger metapopulations. Lions at 124 and wild dogs at 31 are both below effective population sizes for long-term genetic viability within KVNP alone; corridor access to larger populations prevents genetic erosion.

✓ Ecosystem-based fire management regime — reintroduce controlled rotational burning across KVNP to maintain a mosaic of short and tall grassland. Short grass supports kob (grazing preference) while tall grassland provides ambush cover for lions and coursing ground for wild dogs. Post-drought recovery of grass cover to 68% can be accelerated to above 80% within 5 years with active burning management, restoring K for herbivores.

✓ Community wildlife conservancy buffer zones around KVNP boundaries — work with Ik, Didinga, and Acholi communities on the park boundary to establish community conservancies where wildlife can seasonally move without conflict. Human-wildlife conflict (retaliatory lion killing, bushmeat poaching) is a key source of adult mortality not captured in the census data; reducing it accelerates predator population recovery.

✓ Long-term population viability analysis (PVA) modelling — use VORTEX software to model extinction probability for wild dogs and lions under different management scenarios (drought frequency, anthrax recurrence, poaching rates). PVA outputs guide evidence-based minimum viable population targets and trigger points for emergency interventions, replacing reactive management with proactive adaptive conservation.

Award max 8. Require: wild dog genetic rescue with scientific justification (2), anthrax preparedness protocol (1), at least 3 further strategies with ecological or population-level justification (5).

ITEM 5 TOTAL: 20 marks

ITEM 6 — Model Answer

AO4 · Mendelian and Non-Mendelian Genetics, Inheritance Patterns & Genetic Counselling

AO4 | **20 marks**

Part (a) — Molecular and chromosomal basis of inheritance patterns (12 marks)

12 marks available

G6PD Deficiency — X-linked recessive:

- ✓ The G6PD gene is located at Xq28 on the X chromosome. Males are hemizygous (XY) — they carry only one copy of the X chromosome and therefore only one allele of the G6PD gene. A single copy of the recessive G6PD-deficiency allele (G6PD*) is sufficient to cause the condition in males, as there is no second X chromosome to provide a dominant wild-type allele. This explains the high male prevalence of 18.4%.
- ✓ Females are diploid for X-linked genes (XX). To be affected, a female must be homozygous for the recessive allele (X*X*). Using Hardy-Weinberg: if q (frequency of G6PD* allele) = sqrt(0.184) = 0.429, then frequency of affected females = $q^2 = 0.429^2 = 0.184$... However, data show only 2.1% of females are affected, consistent with q approximately 0.145 (sqrt of 0.021) — the discrepancy reflects the actual allele frequency in the Busoga population, not a Hardy-Weinberg violation, as the population is not in strict equilibrium.
- ✓ Carrier females (X*X+) constitute 34.6% of the female population — they carry one defective allele but produce sufficient G6PD enzyme from the functional allele on the other X chromosome. G6PD activity in carrier females is 52% of normal — consistent with lyonisation (X-inactivation): approximately 50% of cells randomly inactivate the maternal X and 50% the paternal X. Cells expressing X* produce no functional enzyme; cells expressing X+ produce normal enzyme; the average of ~50% activity explains the carrier data.
- ✓ The 8.8:1 male-to-female affected ratio — mathematically, for X-linked recessive traits, if allele frequency is q, then affected males = q and affected females = q^2. Since $q < 1$, $q >> q^2$ always. At $q \approx 0.184$, ratio = $q/q^2 = 1/q \approx 5.4$. The observed 8.8:1 reflects the actual population allele frequency and confirms X-linkage beyond any autosomal explanation (which would give ~1:1).
- ✓ Molecular mechanism of haemolytic crisis: G6PD enzyme catalyses the first step of the pentose phosphate pathway (glucose-6-phosphate → 6-phosphogluconate), generating NADPH. NADPH maintains glutathione in its reduced form (GSH), which neutralises reactive oxygen species (ROS) in erythrocytes. G6PD-deficient males (8% enzyme activity) cannot regenerate GSH — oxidative stress from fava bean vicine/convicine metabolites or antimalarial drugs overwhelms the RBC, causing Heinz body formation and haemolysis.

Familial Hypercholesterolaemia — Autosomal dominant:

- ✓ The LDLR gene on chromosome 19p13 encodes the LDL receptor (LDLR) expressed on hepatocytes and peripheral cells. FH is autosomal — the gene is not on a sex chromosome — so males and females are equally affected (0.8% vs 0.9%), producing an approximately 1:1 sex ratio consistent with autosomal inheritance.
- ✓ FH is dominant — one mutant allele is sufficient to cause the condition. Heterozygotes (LDLR+/-) produce approximately 50% of normal receptor number on hepatocyte surfaces. Reduced LDLR causes impaired endocytosis of LDL particles: LDL binds LDLR, the complex is internalised via clathrin-coated pits, and LDL is degraded in lysosomes to release cholesterol for cellular use. With half the normal receptor number, hepatic LDL clearance is halved, raising plasma LDL to 6.8 mmol/L (vs normal <3.0 mmol/L).
- ✓ FH homozygotes (LDLR-/-) have virtually no functional LDL receptors — plasma LDL reaches 18.4 mmol/L. From childhood, LDL deposits in arterial walls, macrophages engulf LDL forming foam cells, and atherosclerotic plaques develop in coronary and cerebral arteries

by age 12–20 years, explaining the early first cardiovascular event (12–20 years) in untreated homozygotes.

✓ Pedigree pattern distinguishes FH from G6PD: FH appears in every generation (vertical transmission), affects both sexes equally, and approximately 50% of offspring of an affected parent are affected (monohybrid cross: Aa × AA → 50% Aa affected, 50% AA unaffected). G6PD skips generations in carrier females, predominantly affects males, and daughters of affected fathers are obligate carriers.

Award max 12. Require: hemizygosity explanation with prevalence data (2), carrier lyonisation mechanism with 52% activity data (2), male:female ratio mathematical basis (2), G6PD NADPH/glutathione haemolysis mechanism (2), LDLR endocytosis pathway (2), homozygote FH cardiovascular data (1), pedigree pattern distinction (1).

Part (b) — Integrated screening and counselling programme for Busoga (8 marks)

8 marks available

✓ Universal newborn screening for G6PD deficiency using fluorescent spot test (FST) — a drop of blood on filter paper is tested for G6PD enzyme activity using a fluorescence assay (cost ~UGX 8,000/test). All male neonates identified as G6PD-deficient are enrolled in a registry. Parents receive immediate counselling: avoid fava beans, naphthalene mothballs, and first-line antimalarials (primaquine, dapsone) — replace with artemether-lumefantrine which is safe in G6PD deficiency.

✓ Cascade testing for FH — upon identifying one FH-affected individual (proband), systematically test all first-degree relatives (parents, siblings, children). Since FH is autosomal dominant with 50% transmission probability, each proband is expected to identify 1–2 affected relatives not yet diagnosed. Early identification before age 10 allows statin therapy initiation that reduces LDL by 40–50%, preventing premature cardiovascular events.

✓ Integrate genetic testing into the existing antenatal care (ANC) platform at all Iganga district health centres — all pregnant women and their partners are offered G6PD carrier testing and FH LDL screening as part of the ANC package. Couples where both partners carry G6PD* (female X*X+; male X*Y) are counselled that 50% of sons will be affected; couples with FH heterozygosity are counselled on 50% transmission risk per child.

✓ Subsidised statin access for FH patients — rosuvastatin (generic, ~UGX 15,000/month) reduces hepatic cholesterol synthesis by inhibiting HMG-CoA reductase, upregulating LDLR expression in residual functional alleles (for heterozygotes), and reducing plasma LDL from 6.8 toward <3.0 mmol/L. Negotiate procurement through NMS (National Medical Stores) to ensure consistent supply at district level.

✓ Community education campaign in the Lusoga language addressing both conditions — many Busoga families attribute haemolytic anaemia (G6PD crises) to witchcraft or food poisoning, delaying appropriate treatment. Radio programmes through Busoga's community radio stations explaining the genetic basis, dietary triggers, and safe drug choices reduce preventable haemolytic episodes and hospital admissions.

✓ Train Iganga District Hospital nurses and clinical officers as genetic counsellors — task-shifting genetic counselling from specialist physicians (scarce in rural Uganda) to trained nurses allows the programme to scale from Iganga to all Busoga sub-districts without requiring additional specialist posts. Training should cover pedigree drawing, risk communication, informed consent, and psychosocial support for affected families.

✓ Establish a Busoga Genetic Diseases Registry linked to the national HMIS — longitudinal tracking of G6PD and FH patients allows monitoring of treatment adherence, complication rates (haemolytic crises, cardiovascular events), and programme effectiveness. Data fed into the Ministry of Health's annual disease surveillance report strengthens the evidence base for national genetic screening policy expansion.

Award max 8. Require: specific screening test for G6PD with mechanism (2), FH cascade testing with statin justification (2), at least 2 further community/health system strategies (3), acknowledgement of resource constraints or community context (1).

ITEM 6 TOTAL: 20 marks