NATURAL SCIENCES TRIPOS **Part IA**

Monday 13th June 2022 9 am to 12 noon

MATHEMATICAL BIOLOGY

You have ***three hours*** *to answer this paper (plus any pre-agreed individual adjustments).*

You must answer eight questions, including at least one question from each of Sections A to E. Indicate your question selection on the form to the right.

All questions carry equal weight. Indicative proportions of marks are given for each question part.

You may use a calculator and the Mathematical Biology Formula Booklet.

Begin each answer on a ***separate*** *blank page.*

Answers should be ***hand-written,*** *either electronically on a tablet or on paper and then uploaded to Inspera. Make sure that your handwriting and any diagrams or equations are clear and legible in your submitted files.*

Where relevant, formulae, equations, diagrams, graphs and sketches should be drawn by hand, not prepared using a computer. Do not copy and paste any figures from other documents.

For full credit, calculation steps must be shown where necessary to explain your answers.

After you have completed the assessment:

Your answers should be submitted ***using either Inspera scan (see below) or by digital upload using the Inspera Upload Tool. Both options are available at the end of the paper.***

Note:

- The single Inspera Scan question code (at the end of the paper) **MUST** be noted during the exam.
- Please ensure that each Inspera Scan page is labelled appropriately, including your Blind Grade Number.

- Inspera Scan pages **MUST** be placed in the Inspera Scan folder at the completion of the exam, and left on your desk.
- Inspera Scan pages will be scanned by administrators after the completion of the exam.
- If you are using the Inspera Upload Tool, answers should be uploaded as a single document.

Stationery requirements:

- Rough work pad
- Inspera Scan pages
- Inspera Scan Folder

SECTION A

A1

(a) A smallholder visits a market to purchase stock. After examining all of the stock available, she creates a shortlist of 4 Jacob sheep, 8 Hebridean sheep and 12 Cotswold sheep.

(i) How many ways could she select 10 sheep (ignoring breed) from her shortlist?

[~10% marks]

After further consideration, the smallholder decides to purchase 2 Jacob, 4 Hebridean and 4 Cotswold sheep from the shortlist.

(ii) How many ways could she have selected this combination from the shortlist of sheep?

[~15% marks]

(iii) On returning to the farm, the sheep are randomly placed in a row of individual holding pens. What is the probability that the sheep are lined up in breed groups? [Answers must be shown in factorial form as well as in decimal form.]

[~20% marks]

(b) A continuous random variable, X, has a cumulative distribution function, F, given by:

$$F(x) = \begin{cases} 0 & \text{for } x < 0 \\ \dfrac{x^4}{4}(x+3) & \text{for } 0 \leq x \leq 1 \\ 1 & \text{for } x > 1 \end{cases}$$

(i) Find $p(X \leq 0.7 \mid X > 0.5)$.

[~15% marks]

(ii) Find an expression for the probability density function $f(x)$.

[~10% marks]

(iii) Given $Y = \dfrac{3}{X} + 4$, find $Var(Y)$.

[~30% marks]

A2

An ecologist is modelling an endangered population of lizards that reproduces seasonally. Her model includes adults and juveniles as distinct categories, and represents the following life-cycle events in each season:

- A proportion p of adults survives to the next season.
- A proportion q of juveniles survives to the next season and become adults.
- Each adult produces, on average, r offspring that hatch as juveniles in the next season.

(a) If j_n is the number of juveniles in the nth season and a_n is the number of adults, show that this model can be represented as a linear system:

$$z_{n+1} = \mathrm{M}\, z_n$$

where:

$$z_n = \begin{pmatrix} j_n \\ a_n \end{pmatrix} \text{ and } \mathrm{M} = \begin{pmatrix} 0 & r \\ q & p \end{pmatrix}$$

Note any additional assumptions you have made about the population in deriving this relationship.

[~25% marks]

(b) The ecologist estimates that p = 0.1, q = 0.5 and r = 2.2 are suitable parameter values for the lizards she is studying. Find the eigenvalues and eigenvectors of M given these values.

[~30% marks]

(c) In a given year, if there are 19 juveniles and 20 adults, what do you calculate, using this model, for the expected numbers of juveniles and adults 25 years later?

[~25% marks]

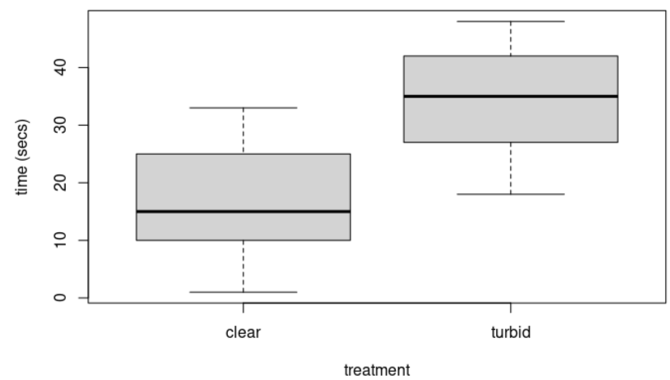
(d) What will be the ratio of juveniles to adults in the long term (as n goes to infinity), according to this model?

[~20% marks]

SECTION B

B3

(a) A behavioural ecologist wants to study the impact of turbidity on risk taking by minnows. Individual fish were tested in an assay where they were placed in a refuge and the time taken to emerge into an open arena was recorded. Thirteen fish were tested in a tank with clear water, and ten fish in one with turbid water.



For the clear treatment, he obtains a mean, $\bar{x}_1$, of 17.62 s, and for the turbid treatment, $\bar{x}_2$, of 33.50 s. The respective Sums of Squares are $SS_1 = 1331.08$ and $SS_2 = 964.50$.

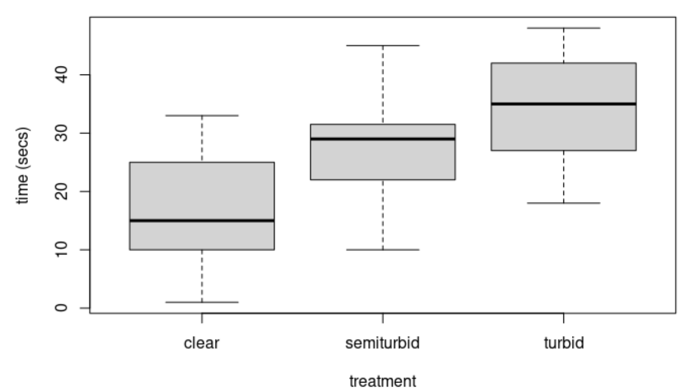
Test whether the turbidity affected the time to leave refuge (showing your work).

[~25% marks]

(b) Provide a sentence that you could use to report these results in a scientific paper.

[~10% marks]

(c) The behavioural ecologist now adds an additional treatment in which the water is semi-turbid, and tests 11 fish under such conditions. Combining the newly acquired data, he obtains:



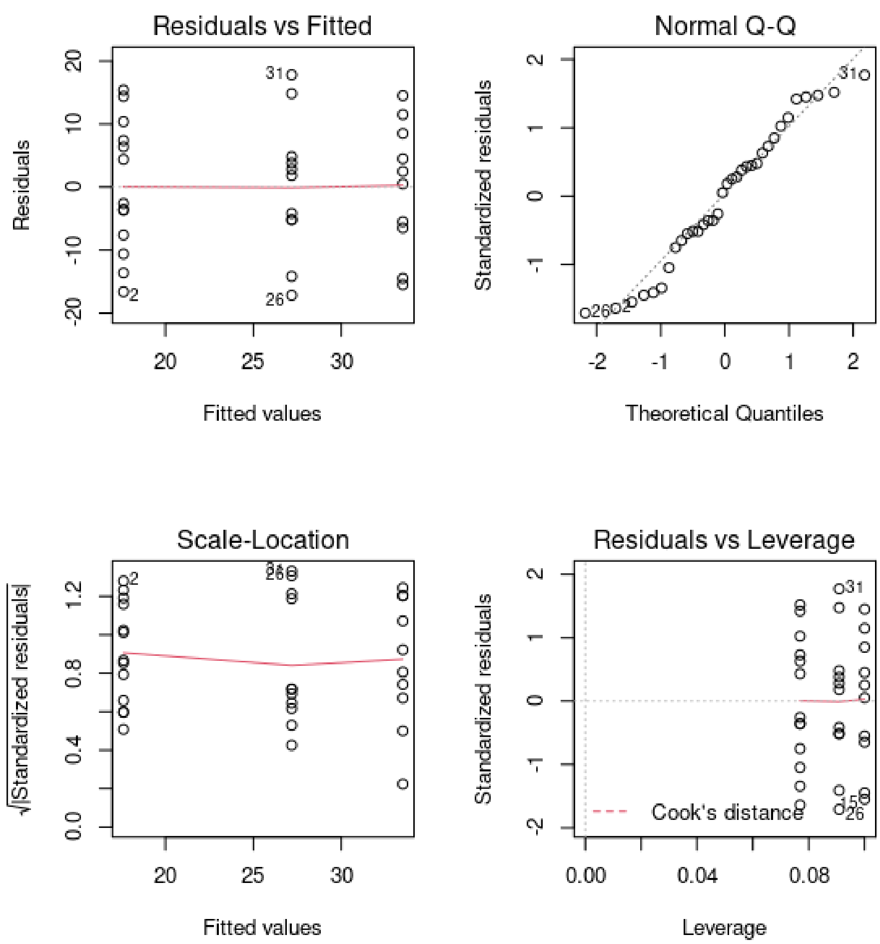
He uses a One-Way ANOVA to compare the different treatments:

	SS	Df	MS	F
Treatment	1478.8	**??**	**??**	**??**
Residuals	**??**	**??**	**??**	
Total	4928.0	33		

Complete the table (i.e. the cells with the symbol **??**). What conclusion would you draw about the effect of water turbidity on the time to leave refuge?

[~30% marks]

(d) What would you conclude from the diagnostic plots he obtained?



[~15% marks]

(e) Our behavioural ecologist also runs some Tukey's Honest Significant Differences tests:

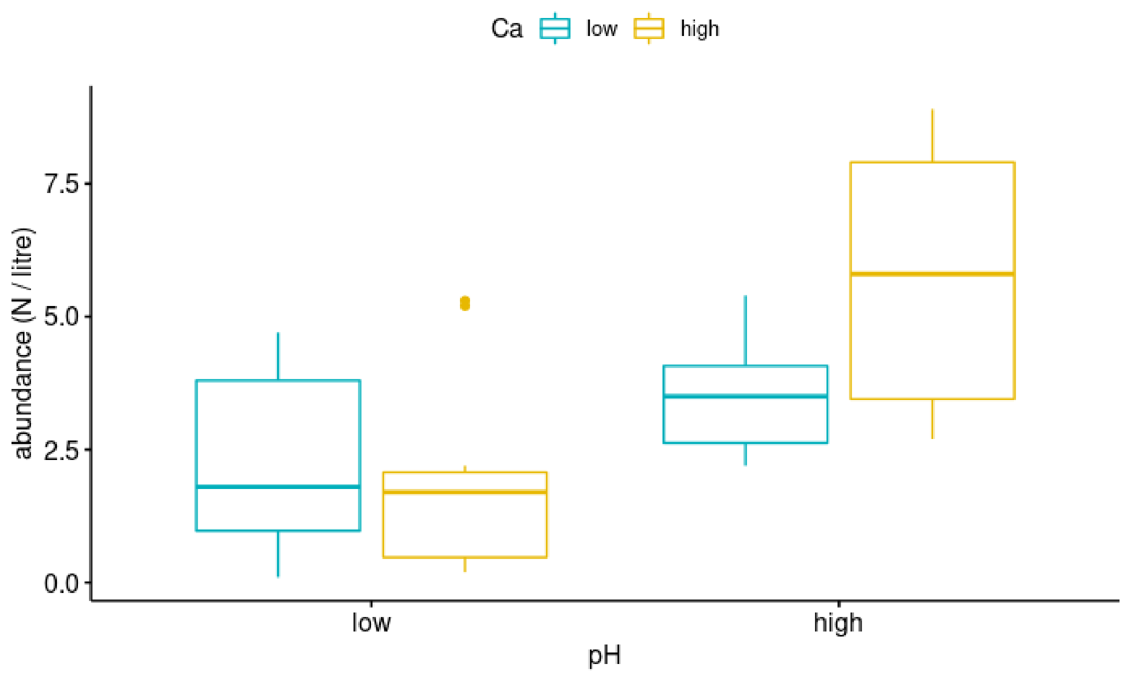
```
Tukey multiple comparisons of means
    95% family-wise confidence level

Fit: aov(formula = time ~ treatment, data = minnows)

$treatment
                       diff        lwr       upr
semiturbid-clear   9.566434  -1.069160  20.20203
turbid-clear      15.884615   4.964773  26.80446
turbid-semiturbid  6.318182  -5.025066  17.66143
```

Given the results above, write a sentence or two that you could use to summarise the omnibus test and the Tukey's tests in a scientific publication.

[~20% marks]

B4

(a) An ecologist wants to study the impact of lake acidification, resulting from industrial pollution, on the abundance of zooplankton. Lakes that have been polluted for long periods of time also suffer a loss of calcium (Ca), which by itself might affect zooplankton. To disentangle the effect of acidity (pH) and Ca concentration, the ecologist sets up a number of microcosms which have a combination of high (alkaline) or low pH (acid), and low or high Ca concentration (10 for each combination of treatment levels). After one week, he estimates the mean number of zooplankton per litre (N / litre) in each mesocosm:



He fits a linear model of the interaction between the two predictors, and compares it with an additive model:

	Res. Df	RSS	Df	SS	F
Additive	37	135.95			
Interaction	**??**	119.05	1	**??**	**??**

Complete the table (i.e. the cells with the symbol **??**). Is the interaction significant? (show your work)

[~20% marks]

(b) Based on the coefficients from the model with interaction:

```
Call: lm(formula = abundance ~ pH + Ca + pH:Ca, data = zooplankton)
Coefficients:
  (Intercept)         pHhigh         Cahigh  pHhigh:Cahigh
         2.28           1.18          -0.33           2.60
```

what would you predict as the mean number of zooplankton for a mesocosm with low pH and high Ca? And for one with high pH and high Ca?

[~10% marks]

(c) The ecologist also attempts to drop the individual factors from the additive model:

	Res. Df	**RSS**	**Df**	**SS**	**F**
- Ca	38	145.35			
Additive	37	**??**	**??**	9.40	**??**

	Res. Df	**RSS**	**Df**	**SS**	**F**
- pH	38	197.45			
Additive	37	135.95	**??**	**??**	**??**

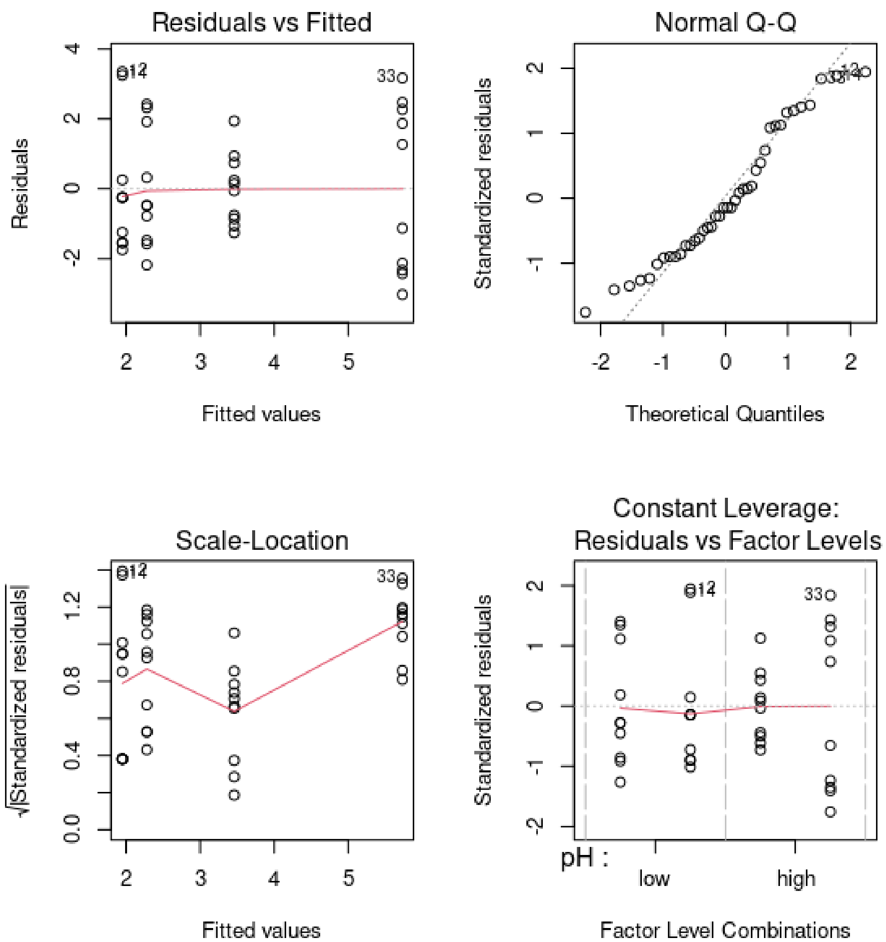
Complete the tables (i.e. the cells with the symbol **??**). Showing your work, what would you conclude from each of these drops? Was this step warranted?

[~30% marks]

(d) Provide a sentence that you could use to report the results in a scientific paper.

[~20% marks]

(e) What would you conclude from the diagnostic plots he obtained?



[~15% marks]

SECTION C

C5

The Richards' model can be used to represent plant disease epidemics. One way of writing that model assumes that $p(t)$, the proportion of infected plants at time t, is given by

$$\frac{dp}{dt} = \left(\frac{a}{b}\right) p(1 - p^b),$$

in which a and b are positive constants. The initial proportion of infected plants is p_0.

(a) Show that the substitution $q = 1/p^b$ can be used to transform the model into the linear differential equation

$$\frac{dq}{dt} = a(1 - q).$$

[~20% marks]

(b) Solve this differential equation for $q(t)$ and use your solution to find $p(t)$.

[~20% marks]

(c) Verify that your solution for $p(t)$ is correct.

[~25% marks]

(d) For which proportion of infected plants is the epidemic size increasing most rapidly?

[~15% marks]

(e) Find equilibrium value(s) of p in the Richards' model and investigate whether the equilibrium value(s) are stable or unstable.

[~20% marks]

C6

A population of the eastern spruce budworm, *Choristoneura fumiferana*, is modelled via

$$\frac{dB}{dt} = f(B) = rB,$$

in which $B(t)$ is the population size at time t and r is a positive constant.

(a) If the initial population size is B_0, solve the model to find $B(t)$

[~10% marks]

Budworms can be eaten by birds. The bird population is assumed to remain constant, meaning the net rate of predation can be modelled as

$$g(B) = \frac{pB^2}{a^2 + B^2},$$

in which a and p are constant parameters and where the numerical value of p would depend on the (fixed) size of the bird population.

(b) Find dg/dB and d^2g/dB^2, and verify that $d^2g/dB^2 = 0$ when $g(B) = p/4$.

[~20% marks]

(c) Sketch $g(B)$ as a function of B (for $B \geq 0$).

[~10% marks]

The model of the budworm population is updated to include predation by the bird population

$$\frac{dB}{dt} = f(B) - g(B) = rB - \frac{pB^2}{a^2 + B^2}.$$

(d) Show that the updated model has an equilibrium when $B = 0$, as well as up to two further equilibria given by solutions to the quadratic equation

$$B^2 - \left(\frac{p}{r}\right)B + a^2 = 0.$$

[~10% marks]

(e) Show that if $p > 2ar$ the quadratic has two positive solutions.

[~10% marks]

For the remainder of this question, you should assume that $p > 2ar$.

(f) Sketch a graph of dB/dt as a function of B.

[~15% marks]

(g) Sketch representative graphs of B as a function of t, showing behaviour for different initial sizes of the budworm population.

[~10% marks]

(h) Comment upon how the results of this model might be unrealistic for large times and suggest two distinct alterations to the model to mitigate this lack of realism.

[~15% marks]

SECTION D

D7

For the non-linear system of equations given by:

$$\frac{dx}{dt} = x^2 + y^2 - 4$$

$$\frac{dy}{dt} = x^2 + xy$$

(a) Find and classify all equilibria.

[~30% marks]

(b) Sketch the phase plane, marking on clearly the nullclines, equilibrium points, direction field and sufficient trajectories to illustrate the behaviour of the system.

[Note: all sketches should be drawn on a blank page by hand, not by using a computer to create a plot for you.]

[~30% marks]

(c) Consider the two pairs of initial conditions $(x_0, y_0) = (-1, -2)$ and $(x_0, y_0) = (-1, -2.5)$. Mark clearly the trajectories associated with these two initial conditions on the phase plane. Do these two trajectories correspond to solutions with the same long-term behaviour? Justify your answer using the direction field and location of nullclines.

[~20% marks]

(d) For the initial condition $(x_0, y_0) = (-1, -2.5)$, sketch the graphs for $x(t)$ and $y(t)$ on the same set of axes.

[~20% marks]

D8

This question models the joint dynamics of plants in a meadow, with density $V(t)$, and aphids, with density $A(t)$, that feed on the plants.

$$\frac{dV}{dt} = r\,V\left(\frac{1}{1+A} - \frac{V}{k}\right)$$

$$\frac{dA}{dt} = \alpha\,V\,A - \mu\,A$$

You can assume that all parameters are positive $(r > 0, k > 0, \alpha > 0, \mu > 0)$.

(a) In the absence of aphids, what type of growth do the plants follow and what do parameters r and k represent?

[~15% marks]

(b) Calculate the null-clines and stationary points of the system and show that aphids can only persist if $k > \mu/\alpha$.

[~40% marks]

(c) Prove the stability of a coexistence equilibrium when $k > \mu/\alpha$.

[~30% marks]

(d) Sketch the two possible configurations of the phase plot, including the direction fields.

[~15% marks]

SECTION E

E9

The following scheme describes a simplified mechanism for mixed inhibition of an enzyme catalysed reaction, in which the enzyme, E, facilitates the conversion of a single substrate, S, into a product, P, via the formation of an enzyme-substrate complex, ES. The inhibitor, I, can interact with both free enzyme E and the ES complex.

$$\begin{array}{ccccc} \mathrm{E + S + I} & \underset{k_2}{\overset{k_1}{\rightleftharpoons}} & \mathrm{ES + I} & \xrightarrow{k_3} & \mathrm{E + P + I} \\ k_5 \Big\uparrow\Big\downarrow k_4 & & k_7 \Big\uparrow\Big\downarrow k_6 & & \\ \mathrm{EI + S} & & \mathrm{EIS} & & \end{array}$$

(a) Construct a molar balance equation for the total concentration of enzyme that is present at time zero, $[\mathrm{E}]_0$.

[~5% marks]

(b) Write down two differential equations that describe how the rates of change of [ES] and [P] vary as a function of time, *t*.

[~10% marks]

(c) If

$$K_8 = \frac{[\mathrm{E}][\mathrm{S}]}{[\mathrm{ES}]} = \frac{k_2 + k_3}{k_1}, \quad K_9 = \frac{[\mathrm{E}][\mathrm{I}]}{[\mathrm{EI}]} = \frac{k_5}{k_4} \quad \text{and} \quad K_{10} = \frac{[\mathrm{ES}][\mathrm{I}]}{[\mathrm{ESI}]} = \frac{k_7}{k_6},$$

apply the steady state approximation to the enzyme-substrate complex and construct an expression for [ES] in terms of constants and the current concentrations of free enzyme, [E], and free substrate, [S].

[~10% marks]

(d) Next, construct expressions for [EI] and [ESI] in terms of constants and the current concentrations of free enzyme, [E], free substrate, [S], and free inhibitor, [I].

[~10% marks]

(e) Construct an expression for the current concentration of free enzyme [E] in terms of constants and the current concentrations of free substrate, [S], and free inhibitor, [I].

[~10% marks]

(f) Construct an expression for the rate of change of product concentration, [P], in terms of constants and the current concentrations of free substrate, [S], and free inhibitor, [I].

[~10% marks]

(g) Use your results from part ***(f)*** to show that v_0, the initial rate of formation of product, obeys a rate law equation of the form:

$$v_0 = \frac{V_{MAX}'[S]_0}{K_M' + [S]_0}$$

where $[S]_0$ is the initial concentration of substrate. State any approximations you have made and explain how V_{MAX}' and K_M' depend on the values of other constants and the concentrations of specific species.

[~30% marks]

(h) Would you expect the value of V_{MAX}' to be larger or smaller than the value of V_{MAX} that would have been determined if no inhibitor had been present? Explain your answer.

[~5% marks]

(i) If enzyme E acts in the middle of a metabolic pathway and the purpose of inhibiting it is to reduce the rate of production of product P, explain what advantage there might be in using an inhibitor with mixed characteristics over one that possesses purely competitive characteristics.

[~10% marks]

E10

A pair of birds can each visit either of two alternative foraging locations. Each bird prefers a different location, but both prefer to forage together (as they are more vulnerable to predation when alone). Thus each bird must decide whether to visit its own preferred site (referred to as 'Selfish' behaviour), or whether to visit the other's preferred site (referred to as 'Accommodating' behaviour). The matrix below shows the payoff to a bird, depending on its own choice of behaviour (listed down the left-hand side of the matrix) and that of the other (listed along the top of the matrix):

		Other's Behaviour:	
		Selfish	Accommodating
Own Behaviour:	Selfish	$2 - k$	2
	Accommodating	$2 - c$	$2 - c - k$

This matrix is based on the assumption that each bird receives a baseline payoff of 2, but pays a cost of c if it visits its non-preferred site, and a cost of k if it ends up foraging alone (where $0 < c,\ k \leq 1$).

(a) Under what circumstances is each strategy evolutionarily stable?

[~15% marks]

(b) Determine the circumstances under which the game yields a mixed evolutionarily stable strategy (ESS). What is the frequency of Selfish behaviour at such an ESS?

[~35% marks]

(c) Use your results from part ***(b)*** to derive an expression for the probability that the two birds forage together at the mixed ESS.

[~25% marks]

(d) Use your results from part ***(b)*** to derive an expression for the mean payoff to a bird at the mixed ESS.

[~25% marks]