

Question 1

Ebola haemorrhagic fever (EHF) is an infectious disease that affects both humans and non-human primates. In recent years, Ebola outbreaks have had a devastating effect on gorilla populations as reported, for example, in Leroy et al. (2004) and Barnejo et al. (2006). In order to understand the effects of Ebola on gorilla populations, a number of scientists, such as Rizkalla et al. (2007), Mamo and Koya (2015), Osemwinyen and Diakhaby (2015), and Kalu et al. (2016), have investigated epidemiological models. This exam question asks you to analyze two simple epidemiological models.

- (a) A simple model that sheds light on the initial effects of an Ebola outbreak is the Kermack–McKendrick model

$$\frac{dS}{dt} = -\beta S I, \quad (1a)$$

$$\frac{dI}{dt} = \beta S I - \alpha I, \quad (1b)$$

where S is the number of susceptible gorillas and I is the number of infectious gorillas. Briefly describe the meaning of each term and of each parameter (α and β , both positive) on the right-hand side of this system.

- (b) Find and draw the S and I zero-growth isoclines in the (nonnegative) S – I phase plane. What is the direction of the vector field in each portion of this phase plane. Find all nonnegative equilibria. Sketch typical orbits in the phase plane.
- (c) The above model has a threshold density of susceptible gorillas below which an epizootic outbreak will not occur. What is this threshold? Also, take the ratio of equations (1b) and (1a) and use the resulting first-order differential equation to obtain a first integral that can be used to predict the number of surviving gorillas in terms of the initial susceptible population.
- (d) The recovery of gorilla populations after an Ebola outbreak is also important (Genton et al., 2012). Consider an SIS epidemic model with demography,

$$\frac{dS}{dt} = \Lambda - \beta S I + \gamma I - \mu S, \quad (2a)$$

$$\frac{dI}{dt} = \beta S I - (\alpha + \gamma + \mu) I. \quad (2b)$$

Discuss the differences between model (2) and Kermack–McKendrick model (1). What is the meaning of each of the parameters (Λ , α , β , γ , and μ , all positive)?

- (e) Find and draw the S and I zero-growth isoclines in the (nonnegative) S – I phase plane. What is the direction of the vector field in each portion of your phase plane.
- (f) Find all nonnegative equilibria. Calculate the Jacobian (community matrix) for this system and use this Jacobian to characterize the nature and stability of each equilibrium. Keep your analyses lean and clean. (I don't want to see lots of ugly algebra.) Describe and classify any important bifurcations.
- (g) Can you rule out periodic solutions (closed orbits)? If so, describe how and do so.

References

- Barmejo, M., Rodriguez-Teijeiro, J. D., Illera, G., Barroso, A., Vila, C., and Walsh, P. D. 2006. Ebola outbreak killed 5000 gorillas. *Science*, **314**, 1564.
- Genton, C., Cristescu, R., Gatti, S., Levrero, F., Bigot, E., Caillaud, D., Pierre, J.-S., and Menard, N. 2012. Recovery potential of a western lowland gorilla population following a major Ebola outbreak: results from a ten year study. *PLoS ONE*, **7**, e37106.
- Kalu, A. U., Akuagwu, N. A., and Agwu, I. A. 2016. A mathematical model for the control of the spread of Ebola virus disease in West Africa – a disease-free equilibrium approach. *British Journal of Mathematics and Computer Science*, **12**, 1–9.
- Leroy, E. M., Rouquet, P., Fromenty, P., Souquiere, S., Kilbourne, A., Froment, J.-M., Bermejo, M., Sheilag, S., Karesh, W., Swanepoel, R., Zaki, S. R., and Rollin, P. E. 2004. Multiple Ebola virus transmission events and rapid decline of Central African wildlife. *Science*, **303**, 387–390.
- Mamo, D. J. and Koya, P. R. 2015. Mathematical modeling and simulation study of SEIR disease and data fitting of Ebola spreading in West Africa *Journal of Multidisciplinary Engineering and Technology*, **2**, 106–114.
- Osemwinyen, A. O. and Diakhaby, A. 2015. Mathematical modelling of the transmission dynamics of Ebola virus. *Applied and Computational Mathematics*, **4**, 312–320.
- Rizkalla, C., Blanco-Silva, F., Gruver, S. 2007. Modeling the impact of Ebola and bushmeat hunting on western lowland gorillas. *EcoHealth*, **4**, 151–155.

Question 2

Apes (gorillas and chimpanzees) face multiple threats from humans – habitat loss, hunting, and transmission of Ebola from humans to apes. In 2005, for instance, over 5,000 Gabonese gorillas died as a result of an Ebola outbreak. Hunting for bushmeat increased in the late 1990s as a result of economic development that concentrated salaried bushmeat customers into urban centers (transforming hunting from a subsistence to commercial enterprise).

You wish to know how ape densities have changed in Gabon from the mid 1980's, prior to this economic expansion and Ebola outbreaks, to the mid 2000's following this expansion and initial Ebola outbreaks. Data have been collected consisting of line transect surveys of ape nests in several distinct region, or "zones", in Gabon. These "zones" consist of unique regions distinguished by topographical or other barriers to movement. For each line transect, the nearest distance to an urban center "UrbanD", and the nearest distance to an Ebola outbreak ("EbolaD", human Ebola outbreaks were first detected in 1994) are measured using GIS. All linear distance measurements are in kilometers.

The data:

Use the csv file "apedata.csv".

The columns are

UrbanD: distance (km) from sampling site to nearest urban center

EbolaD: distance (km) from sampling site to nearest Ebola outbreak from 1994-2002

Zone: A-H, distinct regions in Gabon

Period: Time period of survey, either "Early 1980s" (1983-1985), prior to first human Ebola outbreak and the commercialization of bushmeat hunting, and "Early 2000's (2001-2003).

TransectLength: length of line transect survey (km)

ApeCount: count of ape nests (chimpanzee and gorilla nests combined)

Your Task: Use these data to ask whether hunting, human ebola outbreaks, or both, have likely reduced ape densities in Gabon. You are free to use your favorite method of testing alternative hypotheses (e.g. information theory, null-hypothesis testing), but be sure to explain your choice.

Your response should include the following:

2A) Explain the modeling approach you use, and give rational for the choice

2B) Include the usual model diagnostics, and also the necessary summary tables, figures, etc. that describe the results

2C) Provide a biological interpretation of coefficients that describe the differences in ape density across time and space

2D) Summarize your results with a "Discussion" section that provides clear and concise synthesis of the analysis and the conclusions you draw from the analysis. This should also indicate any limitations based on the data, and suggest what additional lines of research are warranted (based on your analysis).

Scoring Rubric

Developed an appropriate model that allowed for testing the main hypothesis, where the model adequately captured elements of the data structure. Provide good rationale for the choice of model and framework for testing alternative hypotheses.

20

Generated results that are consistent with the data (no bugs)

10

Diagnostics were used appropriately to check the model and make adjustments as needed

20

Appropriate biological interpretation of the model coefficients

15

Model adequately addressed hypothesis, and reached conclusions that were supported by the data.

15

Results were clearly presented and discussion provided a clear and concise summary of the analysis and noted limitations / strengths

20

Question 3

Consider the Kermack-McKendrick model from Question 1. A stochastic formulation of this model keeps track of the number of susceptible gorillas, S_t , and the number of infectious gorillas, I_t . These counts, (S_t, I_t) , evolve according to a continuous-time Markov chain on the state space $\{0, 1, 2, \dots\} \times \{0, 1, 2, \dots\}$, with the infinitesimal rates

$$\lambda_{(m,n),(k,l)} = \begin{cases} \beta mn & \text{if } k = m - 1, l = n + 1, \\ \alpha n & \text{if } k = m, l = n - 1, \\ 0 & \text{otherwise.} \end{cases}$$

- (a) Write a computer program to simulate epidemic trajectories during the first 4 months of Ebola spread through a small gorilla population. Set $\alpha = 0.8$, $\beta = 0.02$, $(S_0, I_0) = (999, 1)$ and plot 10 random paths of both variables on the interval $[0, 4.0]$.
- (b) Using the same parameter values, estimate the probability of the epidemic dying off by the end of the fourth month, meaning that $I_{4.0} = 0$.
- (c) Suppose we observe the dynamics of an Ebola outbreak in the gorilla population continuously, so that we know that numbers of susceptible and infectious gorillas at each time point. Use one of the simulated paths from part (a) as your data and compute maximum likelihood estimates of α and β . Provide asymptotic 95% confidence intervals for these parameters.
- (d) Initial stages of an epidemic can be modeled by a continuous-time linear birth-death process. The main assumption of this approximation is that the number of susceptible individuals stays (approximately) constant during some time interval, so only the number of infected individuals is changing stochastically. Formulate this approximation mathematically by defining the appropriate linear birth-death process and its per particle birth and death rates.
- (e) Repeat the simulation from part (a), but now with the birth-death process. Cap the number of infectious gorillas at 1000.
- (f) Shorten the observation period from $[0, 4.0]$ to $[0, 0.25]$ and repeat the estimation of α and β from part (c), but now under both (correct) SIR model and (incorrect) birth-death model. Provide confidence intervals for both sets of estimates. Comment on the accuracy of the birth-death model approximation of the SIR model when the goal is to estimate parameters of the model of Ebola spread through the gorilla population.

Question 4: Optimization:

The Western lowland gorilla (*Gorilla gorilla gorilla*) is a critically endangered primate threatened by poaching, and more recently, by Ebola hemorrhagic fever. A conservation organization based in the Democratic Republic of Congo has launched a new effort to protect the species by identifying and securing as many contiguous habitat patches suitable for and currently occupied by gorillas as possible. Wildlife biologists within the organization determined, via use of census data, that the populations each need at least 50 ha of contiguous habitat to survive. Using geographical and satellite data, they delineated a set of habitat patches within a focus area that were deemed suitable for the gorillas. Then, they intersected these patches with ownership boundaries to identify the landowners whose lands they would target for purchase or conservation easements. The resulting 100 polygons are depicted on Figure 1 below. The conservation organization wishes to identify as many spatially independent (non-adjacent and non-overlapping) clusters of these 100 patches as possible. Each cluster must be contiguous and have an area of at least 50 ha. The clusters must also be disconnected from each other to minimize Ebola transmissions across populations. Two clusters of habitat patches are assumed to be disconnected if they don't share a common boundary or a habitat patch.

Please formulate and code the above problem as a spatial optimization model to answer the question of many spatially independent habitat clusters can be identified within the land-base in Figure 1. Once done, please reformulate the model and see how many clusters can be protected with a \$20 million budget. The size and purchase price of the parcels are listed in the enclosed Parcels Table. The adjacency relations among the parcels are included in the Adjacency Table, which is also attached. Please clearly define your decision variables and the parameters and sets that you are going to use in your mathematical formulation. Please explain each constraint and function in detail.

Please submit:

- (1) the mathematical formulation of your proposed model along with the variable definitions and explanations;
- (2) a text file in CPLEX format that shows the model populated with the real data;
- (3) a CPLEX solution file;
- (4) a map of solutions (see map on next page); and
- (5) a brief solution analysis, discussion and conclusions.

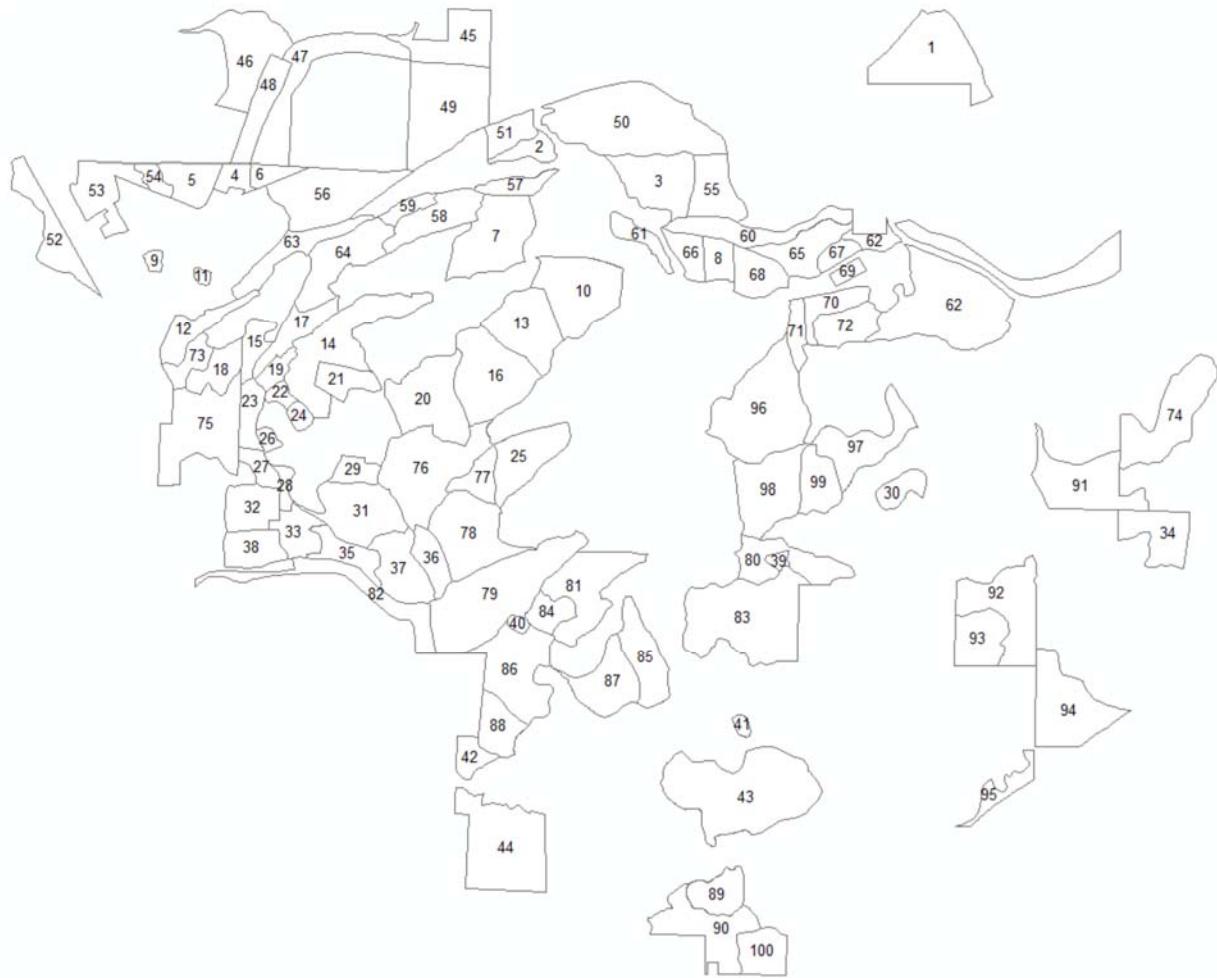


Figure 1. Habitat patches for Western lowland gorillas