EEB313 Mid Project Report - Group F

Statement of author contributions:
Hannah: New project idea, natural history & references, expectations, previous code trial, statistical tests
Salwa: Description of question and project outline
Mia: Analysis plan (details of all analysis, some plans for remaining analysis)
LiYi (Hazel): Statement of redirection, modelling assumptions, biological interpretations in analysis plan

Statement of redirection (rationale)

The original hypothesis focused on genetic shift in susceptibility between Norway maples and sugar maples in the context of Powdery Mildew infection, proposing a critical threshold of allele frequencies that would lead to the transfer of the pathogen. However, as we delved deeper into the research, we realised that there is limited empirical evidence and studies that support the assumptions and the mechanisms proposed in our original plan. In particular, our initial assumption that the transfer of Powdery Mildew would result in tree mortality or increased susceptibility was not supported by available empirical data. Moreover, there is insufficient evidence to suggest that Powdery Mildew effectively jumps between sugar maple and Norway maple trees, unlike the well-documented cases of Brucellosis transmission amongst cattle.

New project idea

Our group has chosen to do a mathematical mechanistic SIR model (option 2) to examine the impact of culling and vaccination on the spread of Brucellosis in cattle.

Natural history

Brucellosis, primarily caused by Brucella abortus, is a significant concern in the cattle industry, both in North America and globally (OIE 2009). While Canada and the United States have implemented stringent brucellosis control measures, there are regions where culling is not as widely practiced, and the impact of these strategies can vary.

Canada's approach to brucellosis control involves rigorous testing, surveillance, and culling. Notably, between 2012 and 2017, Canada reported no cases of bovine brucellosis (CFIA 2018). The Canadian Food Inspection Agency (CFIA) has implemented stringent testing and surveillance programs, alongside the culling of infected cattle, contributing to the overall success of controlling brucellosis in the country (CFIA 2018).

In contrast, some regions in Sub-Saharan Africa, such as Chad, face challenges in adopting culling as a control strategy due to the essential role of cattle in livelihoods and food security. Economic and social factors in these areas make culling less feasible, resulting in persistent brucellosis issues, impacting cattle health, milk production, and human health due to ongoing zoonotic transmission (Schelling 2007).

The effectiveness of culling as a disease control strategy is contingent on several factors, including disease transmission dynamics, the completeness of eradication, economic and social consequences, timely reporting, and compensation availability for affected livestock owners (Corbel 2006). Incomplete culling may lead to disease persistence, while social and economic considerations, along with ethical concerns, can affect community willingness to participate in culling programs.

Additionally, the environmental dynamics of diseases like brucellosis, characterized by indirect transmission and environmental reservoirs, may not be fully addressed through culling and vaccination alone (Nicoletti 1991). A holistic approach that integrates ecological, economic, and social considerations, along with complementary control measures such as vaccination and biosecurity, often proves more effective in managing and preventing infectious disease spread (Musallam 2012).

It is crucial to recognize that wild animals, including elk, bison, and deer, can play a significant role in spreading brucellosis to domestic cattle. Wildlife may serve as reservoir hosts for Brucella species and shed the bacteria in their bodily fluids, creating a potential transmission risk when they interact with domestic cattle (Cross 2010). This aspect underscores the need for a comprehensive approach to brucellosis control that accounts for both domestic and wildlife reservoirs, emphasizing strategies like vaccination, surveillance, and habitat management in shared environments (Beja-Pereira 2009).

In conclusion, the multifaceted nature of brucellosis transmission underscores the importance of considering various factors and adopting a holistic approach to disease control that addresses ecological, economic, social, and wildlife-related aspects in tandem with traditional interventions like culling and vaccination. Understanding the role of wildlife in brucellosis transmission is pivotal for developing effective strategies to mitigate the impact of this disease.

Description of the research question

Following our research into zoonotic diseases, we decided to develop a mathematical model to determine the effect of culling and immunisation on Brucellosis rates in cattle. This model would look to answer questions about the effect of disease control strategies such as culling and vaccination, on a number of different indicators of Brucellosis rates (ie, prevalence, transmission, incidence). The Susceptible-Infected-Recovered (SIR) model will be used to improve our understanding of the effects of culling and immunisation on brucellosis rates in a population of cattle. Specifically, this model will describe brucellosis transmission rates, recovery time and virulence. We will be introducing two vaccines named Vaccines A and B (A being a vaccine that impacts mortality rates and B being a vaccine that impacts transmission) to our SIR model. An equal fraction of the cattles in the population will be vaccinated with each vaccine over time. The SIR model will enable us to look at how the population differs over time in response. The interactions between these vaccines and culling (time and intensity of culling) will also be looked at. An SIR model will allow us to follow the long-run behaviour of brucellosis in cattle and the effects of immunisation and culling. To do this, we looked at previous SIR models that looked at the spread of Covid-19

in communities (Cooper 2020). By looking at models that explored the same parameters (e.g., transmission and recovery rates), we were able to decide on an appropriate model.

Expectations

- Interventions on farms that couple culling infected cattle with vaccination are anticipated to reduce transmission of Brucellosis more than interventions on farms that employ one solution or the other (culling or vaccination; not both)
- Interventions on farms that employ at least one of the two solutions (culling or vaccination) are anticipated to reduce Brucellosis transmission amongst cattle more than interventions that employ neither culling or vaccination
- Vaccine B will reduce Brucellosis transmission rates in cattle populations more than vaccine A

Modelling Assumptions

In the context of brucellosis in livestock populations, the SIR model assumptions can be contextualised as follows:

- Fixed Population: The model assumes that the herd size remains constant, not accounting for births, deaths unrelated to brucellosis, or the introduction of new cattle into the population. There is no introduction of new cattle into the population or movement out, which would affect the dynamics of the disease spread. The decision to maintain a fixed population allows the focus to be on disease progression without the variability of herd size changes.
- Homogeneous Mixing: Every cow has an equal probability of interacting with every other cow, which implies that your cattle population is well-mixed, and there is no structuring by age, sex, or other factors. Homogeneous mixing is chosen to simplify the calculation of transmission probabilities, facilitating a more straightforward analysis of intervention impacts.
- No Latency: As soon as cattle are exposed to the bacteria, they are capable of transmitting it to others without a latency period. No latency is assumed for the model to focus on the immediate capacity of the disease to spread.
- No Re-infection: Cows that have recovered from brucellosis, either through natural immunity or vaccination, are assumed to be completely immune and cannot become infected again.The assumption of no re-infection reflects a simplified version of immunity dynamics.
- Constant Contact Rate: The rate at which susceptible cows come into contact with infected cows is consistent, not varying over time or by changes in herd behaviour or management practices. A constant contact rate is chosen for its simplicity and to maintain the focus on the core dynamics of disease spread.
- Direct Transmission: The transmission of brucellosis is direct from one cow to another without intermediaries (eg. Environmental factors). Direct transmission is assumed for its relevance to the fundamental brucellosis spread among cattle.
- Uniform Susceptibility and Infectiousness: All cows are equally likely to catch brucellosis if exposed, and all infected cows are equally likely to transmit the infection

to others. Uniform susceptibility and infectiousness are chosen to avoid the complexities of individual variation within the herd.
- Constant Recovery Rate: The rate at which infected cows recover or are culled is constant and does not vary over time or between individual cows.
- No Effect of External Factors: The model does not consider external factors such as seasonal changes that might affect the transmission rates, or contact with wild animals/animal remains that may be infected. A constant recovery rate allows for a simplified understanding of the disease's progression through the herd over time.

The limitations of our SIR model arise from its simplified assumptions: we consider a fixed cattle population, ignoring natural increases or decreases that could influence disease dynamics. We assume all cattle mix equally and have the same chance of getting and spreading brucellosis, which overlooks the complex social behaviors within a herd. Our model also presumes that once cattle recover, they're immune for life and that brucellosis is spread only through direct contact, not considering other possible transmission routes or different immune responses. Lastly, we assume the rate at which cattle recover or are culled is constant, which doesn't capture the real differences in individual animals' responses to the disease.

Analysis plan

To investigate the effect of culling and vaccines on the population of cattle during a disease endemic, we created a modified version of the Susceptibility, Infectious, Recover/Removed (SIR) model. The SIR model is used for epidemiological purposes and is useful for tracking the spread of disease in a population over time. 3 categories, individuals susceptible, infectious, recover/removed and their rate of change over time are all addressed using the SIR model which changes based on the number of individuals in each category at a given time and the rate of infection and recovery (Figure 1).

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

S - Number of susceptible individuals
I - Number of infected individuals
R - Number of recovered individuals
β - infection rate
γ - recovery rate

Figure 1: Basic SIR model obtained from the EEB313 website.

Our model aims to include these categories while addressing the effects of culling and vaccination rate by adding them as new parameters. After adjusting the SIR model to fit our new parameters we will use R to run the model and create a plot of each category over time.

Before even running the R code, we are able to make interpretations based on the equations at hand. The susceptibility rate of change will decline proportional to the rate of infection and vaccination as they are the only 2 parameters capable of changing individuals from being susceptible. We have also assumed that individuals cannot go back to being susceptible once they have already changed. In other words, the number of susceptible individuals will decline over time due to the rate of infection and vaccination. The rate of change of infected individuals is expected to increase due to the infection rate followed by a decrease due to the culling and recovery rate. How quickly the infection curve decreases depends on the strength of the vaccination rate and how quickly cattle are culled after showing symptoms. The recovery rate will only increase over time because we assume that once vaccinated the individual will never lose immunity meaning it can never go back to being susceptible and due to the recovery rate also contributing to this rate.

After working with this model, there are a few parameters we can add to make the model more realistic. For instance, vaccines are not effective 100% of the time after administration, so we could add a new parameter that addresses the fact that some vaccines are ineffective in individuals.

Statistical tests

In the context of our Brucellosis spread project, we can utilize linear regression to assess the specific impact of interventions, such as culling and vaccination, on disease dynamics over time. This allows us to quantify the relationships between intervention levels and disease outcomes and identify temporal trends in disease prevalence. Simultaneously, Maximum Likelihood Estimation (MLE) is invaluable for estimating crucial model parameters that are not directly observable, ensuring that our mechanistic model aligns closely with observed data and providing accurate parameter estimates. Additionally, ANOVA can be applied to investigate how variations in multiple intervention levels affect disease outcomes. It helps us determine the statistical significance of differences among various intervention groups and supports comparative analyses to identify which strategies lead to more effective disease control. Together, linear regression, MLE, and ANOVA play pivotal roles in providing statistical insights, optimizing the mechanistic model, and exploring the impact of interventions on Brucellosis dynamics.

Previous code trial

The provided R code sample (Figures 2 and 3) is a building block in our proposed mechanistic model using discrete time to simulate Brucellosis spread. It employs the Susceptible-Infectious-Recovered (SIR) model, which describes disease dynamics based on biological principles. This model divides time into daily intervals, where rates of change in the numbers of susceptible and infected individuals are calculated. Interventions like culling and vaccination are applied at each step, allowing for the study of control measures' impact on disease transmission dynamics. In essence, it's a mechanistic model that simplifies complex disease processes and uses discrete time for computational tractability. While this sample assumes that all effects of culling will reduce rate of transmission, we will adjust this in the final project to factor in the possibility of culling increasing the rate of transmission. Each time we run the new model in R (Figure 2), we will adjust the parameters to create

different scenarios where culling and vaccination effects/practices are different, emulating how farming practices and access to vaccines varies across cattle farms around the world. For each scenario in the model, a new graph will be generated (like Figure 3) and statistical analyses will be performed to examine the trends and patterns of the data and similarities/differences between scenarios.

```r
# Define parameters
beta <- 0.8  # Transmission rate
gamma <- 0.3  # Recovery rate
culling_effect <- 0.05  # Effectiveness of culling
vaccine_effect <- 0.2  # Effectiveness of vaccination

# Initial conditions
S0 <- 0.80  # Initial proportion of susceptible cattle
I0 <- 0.20  # Initial proportion of infected cattle
R0 <- 0     # Initial proportion of recovered cattle

# Simulation time
t <- seq(0, 20, by = 1)  # Simulate for 365 days

# Initialize storage for results
S <- numeric(length(t))
I <- numeric(length(t))
R <- numeric(length(t))

# Set initial conditions
S[1] <- S0
I[1] <- I0
R[1] <- R0

# Simulate disease spread over time
for (i in 2:length(t)) {
  # Calculate the rates of change using the SIR model
  dS <- -beta * S[i - 1] * I[i - 1]
  dI <- beta * S[i - 1] * I[i - 1] - gamma * I[i - 1]

  # Apply culling/isolation intervention
  culling_rate <- culling_effect * I[i - 1]
  dI <- dI - culling_rate
  R[i] <- R[i - 1] + culling_rate

  # Apply vaccination intervention
  vaccination_rate <- vaccine_effect * S[i - 1]
  dS <- dS - vaccination_rate
  R[i] <- R[i] + vaccination_rate

  # Update the compartments
  S[i] <- S[i - 1] + dS
  I[i] <- I[i - 1] + dI
}

# Calculate the proportion of recovered individuals
R <- 1 - S - I
```

Figure 2: First section of the sample code.

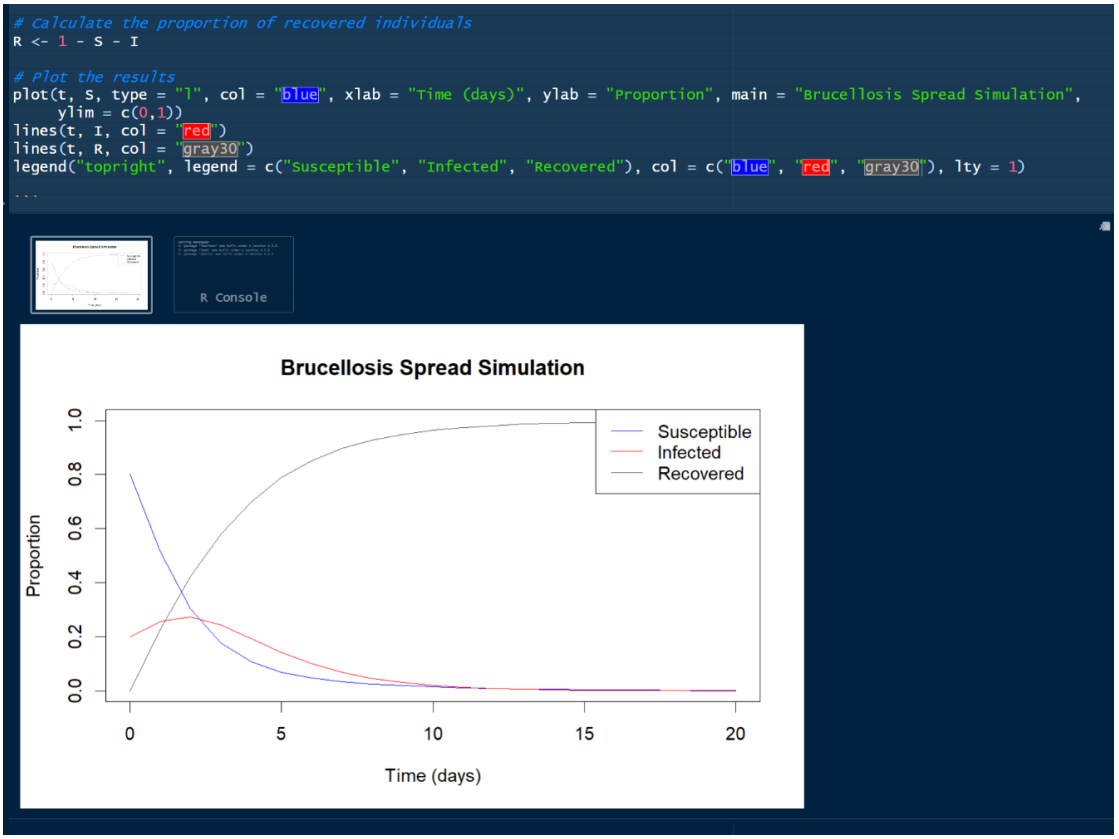

Figure 3: Second section of the sample code with a graph depicting the proportions of susceptible, infected, and recovered individuals within a population.

Biological interpretations

In our research, we've adapted an SIR model to better grasp how brucellosis spreads among cattle herds and to identify effective control measures. The model's insights suggest that a combination of selective removal of infected animals and widespread vaccination could significantly slow the spread of the disease. It also helps estimate the vaccination coverage necessary to avert widespread outbreaks.

However, the simplicity of our model might not encompass the complexity of cattle interactions and disease dynamics fully. It operates under the assumption that cattle, once recovered from brucellosis, cannot be reinfected, which might not hold against various strains or as immunity decreases over time. Furthermore, it does not account for natural changes in herd size, which could affect the trajectory of disease spread.

Our model is particularly suitable for stable herds with no new entries or exits. To enhance its utility across different farming contexts, we could refine the model by incorporating factors such as differential susceptibility among cows, the potential for vaccine failure, and alternative transmission pathways. Enriching our model in this way would allow for more accurate biological interpretations and provide a more robust foundation for developing brucellosis control strategies applicable to diverse agricultural settings.

References

Beja-Pereira, A., Oliveira, R., Alves, P. C., Schwartz, M. K., Luikart, G., & Godinho, R. (2009). Advancing ecological understandings through technological transformations in noninvasive genetics. Molecular Ecology Resources, 9(5), 1279-1301.

Cooper I, Mondal A, Antonopoulos CG. 2020. A SIR model assumption for the spread of COVID-19 in different communities. Chaos, Solitons & Fractals. 139:110057–110057.

Corbel, M. J. (2006). Brucellosis in Humans and Animals. World Health Organization.

Cross, P. C., Maichak, E. J., Brennan, A., Scurlock, B. M., Henningsen, J. C., Luikart, G., ... & Edwards, W. H. (2010). An ecological perspective on Brucella abortus in the western United States. Ecological Applications, 20(2), 398-410.

Musallam, I. I., Abo-Shehada, M. N., & Hegazy, Y. M. (2012). A review of the current status of Brucellosis in Egypt. Preventive Veterinary Medicine, 106(2), 215–223.

OIE (World Organisation for Animal Health). 2009. Brucella abortus RB51 vaccine. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

Schelling, E., Diguimbaye, C., Daoud, S., Nicolet, J., Boerlin, P., Tanner, M., & Zinsstag, J. 2007. Brucellosis and Q-fever seroprevalences of nomadic pastoralists and their livestock in Chad.

Nicoletti, P. 1991. Brucellosis: Past, Present, and Future. Prilozi, 12(1-2), 21–32.

USDA (United States Department of Agriculture) - Animal and Plant Health Inspection Service. 2019. Brucellosis in the United States, Annual Report.

CFIA (Canadian Food Inspection Agency). 2018. Bovine Brucellosis Surveillance Program.