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Analyzing Avian Flu with a SIVA (Susceptible, Infected, Vaccinated, Asymptomatic) Compartment Model

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INTRODUCTION

Within the context of Epidemiology, compartmental models are quite popular as a logical framework for building systems of differential equations to understand the dynamics of disease spread, persistence, and (hopefully) the eventual exit from a biological system. One of the most basic compartmental models, the susceptible-infected-recovered (SIR) model, can help to understand both the probable number of infections and the time it takes the disease to propagate. This model was created in 1927, following the influenza pandemic in 1918. Because the compartment model is so simple and allows modelers to approximate behaviors of a disease using a small number of parameters, its use became more widespread [1]. In a compartment model, individuals in a closed population are separated into exclusive groups (compartments) based on their current disease status. These individuals are only allowed to be in a single compartment at a given time, but they can move from one compartment to another based on the parameters given in the model.

In this paper we try to simulate and understand a particular kind of compartmental model based upon a macro perspective of avian flu and how it can spread and present itself within a flock of birds. The avian flu is spread through secretions from an infected bird, whether that be saliva, nasal secretions, or feces. Many infected birds are asymptomatic, which can make it difficult to identify that a flock is being infected with a flu virus before it spreads greatly among the members of the flock. Farmers of poultry have different ways of addressing the flu problem, including but not limited to vaccination and culling. Culling consists of indiscriminately killing birds. The population of birds on the farm will be placed into four different compartments: Susceptible (S), Infected (I), Vaccinated (V), and Asymptomatic (A) birds. Susceptible birds are birds that could possibly contract the disease, and infected birds are those who currently have the disease. Vaccinated birds are those who were susceptible and received a vaccine before contracting the disease, thus giving them resistance to that disease. In particular, for this model we assume that vaccinated birds have complete and total immunity against the disease, meaning that they can host the disease after being vaccinated but do not suffer from the disease in any way. Furthermore, the asymptomatic compartment contains birds who were vaccinated and then caught the disease when they were exposed to it, but show no signs of having the disease or being affected by it. However, they can still spread the disease to other birds at a lower rate than infected birds.

More specifically, birds are introduced from the outside into the susceptible compartment at a constant rate of Λ. Also, each bird in classes S, V, and A dies at a natural rate of μ. Each infected bird (from I) dies at an enhanced rate $\nu > \mu$, which is included to simulate the

assumption that an infected bird would have a higher chance at dying compared to a healthy bird. To sufficiently spread the disease between birds, the contact rate for each bird is βN, where N is the total number of birds. So, whenever a susceptible bird encounters an infected bird, the disease spreads. However, when a vaccinated bird comes in contact with an infected bird in the same way, the vaccinated bird only contracts the disease with probability $\rho < 1$ and becomes asymptomatic when this occurs. Also, asymptomatic birds can spread the disease to other birds when contact is made, but with a probability $q < 1$. As a quick additional note, asymptomatic birds can infect vaccinated birds based on the interactions we just described, but by design the probability of the occurrence is now $q\rho$ which will be smaller than either probability. This is meant to reflect the argument that vaccinated birds are much less likely to share the disease amongst one another given that their immune systems can deal with the disease very quickly.

Including the already vaccinated birds, each bird is vaccinated at a random rate ψ. However, only the birds that are susceptible when they are vaccinated will enter the population V, as we assume that infected birds that are vaccinated after contracting the disease still have to fight the disease with the immune system they had before a vaccination could boost its strength. Similarly, vaccinated and asymptomatic birds are already vaccinated and since we do not consider a time dependent vaccination state, nothing changes for those birds. Also, birds are culled (or killed) at a random rate from all groups. This rate is cI for a parameter $c > 0$ where the number of infected birds is multiplied so that culling happens at a quicker rate when there is a large population of infected birds. This idea is meant to simulate the response a farmer (or flock owner more generally speaking) will have when there is more of a disease present in the flock. It is important to re-emphasize that in this model we do not consider the possibility for a vaccinated bird to lose immunity. If one wanted to consider this system with a specific vaccine or to compare vaccines based on the length of immunity one could add a rate of "de-vaccination" where vaccinated or asymptomatic birds lose their immunity over time. However, in this case we consider a shorter time frame where immunity is not lost (or one where the vaccine is extremely effective and long lasting). To accurately show how all of these components contribute to the avian flu outbreak, we drew a diagram of the compartment model, which is shown in Figure 1. The large boxes are the groups (susceptible, infected, vaccinated, and asymptomatic), and the arrows between show the rate at which birds enter or leave those groups as discussed previously. To make sure all arrows are understood, we will discuss a few here. Since a susceptible bird can be infected by either an infected bird or an ansymptomatic bird, we include two separate arrows indicating those situations. In the top arrow, we have a transmission rate of βN which is multiplied by S (those

that contract the disease) and $\frac{I}{N}$ (fraction of those that are infected) to achieve what we see in the diagram as βSI. Similarly, for the arrow below, we multiply the same βN by S. However, now we multiply by $\frac{A}{N}$ (the fraction of asymptomatic) since those are the ones transmitting, and since the transmitting group is the asymptomatic group we include the probability term $q < 1$ as we discussed previously. Together this yields $\frac{\beta SAq}{N} = q\beta SA$ as we see in the digram. Very similar logic can be used to derive the bottom two arrow between the vaccinated group and the asymptomatic group.

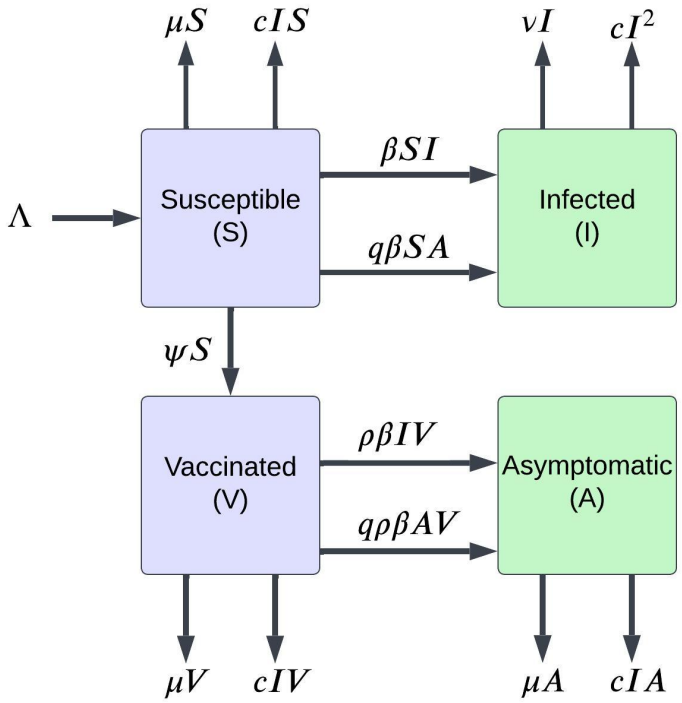

Figure 1: A compartment diagram of the SIVA model with all rates labeled

MATHEMATICAL DERIVATION AND FORMULATION

We now begin to create the system of differential equations that we will analyze with all of our assumptions, actions, and rates included. Each compartment is assigned a differential equation with respect to time t.

Beginning with the Susceptible compartment S, we include the incoming rate Λ, subtract those that are infected, vaccinated, naturally die, and culled. Note that infection can occur from either an infected bird or an asymptomatic bird which leads to two terms for that same

scenario. With that we write

$$\frac{dS}{dt} = \Lambda - \beta SI - q\beta AS - \psi S - cIS - \mu S$$

Each rate is multiplied by the compartment from which the action is derived, for example μ is multiplied to S since their natural death is determined by the group itself.

$$\frac{dI}{dt} = \beta SI + q\beta AS - \nu I - cI^2$$

For the Asymptomatic compartment we consider the incoming birds from those that have been vaccinated but contract the flu from an infected bird, or the less common case where another asymptomatic bird infects a vaccinated one. Again, we lose birds to natural death at rate μ and culling like other healthy compartments. This yields the equation

$$\frac{dA}{dt} = \rho\beta IV + q\rho\beta AV - \mu A - cIA$$

Finally, we consider the Vaccinated compartment. Here the only incoming birds are susceptible ones that happened to get vaccinated at rate ψ. Since a vaccinated bird can be sent to the Asymptomatic compartment we subtract those. Since they can get infected from infected or asymptomatic birds this provides us two new terms. Again as always, we then subtract the natural death and culling terms. This yields the equation

$$\frac{dV}{dt} = \psi S - \rho\beta IV - q\rho\beta AV - \mu V - cIV$$

Altogether we now achieve a system of ODEs that describe how each compartment changes in time:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta SI - q\beta AS - \psi S - cIS - \mu S \\
\frac{dI}{dt} &= \beta SI + q\beta AS - \nu I - cI^2 \\
\frac{dV}{dt} &= \psi S - \rho\beta IV - q\rho\beta AV - \mu V - cIV \\
\frac{dA}{dt} &= \rho\beta IV + q\rho\beta AV - \mu A - cIA
\end{aligned}$$

Given the complexity of our system with respect to how many parameters we introduced, we can narrow our exploration by focusing on the disease-free steady state system. In this scenario we take $I = A = 0$ as we assume that there is no longer any flu in our flock whether that be because they all succumbed to the illness or because they recovered and eradicated the disease from the flock. Additionally, since this is a steady state system we set all derivatives equal to 0 as well. Substituting this into our system, we achieve

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \psi S - \mu S = 0 \\
\frac{dI}{dt} &= 0 \\
\frac{dV}{dt} &= \psi S - \mu V = 0 \\
\frac{dA}{dt} &= 0
\end{aligned}$$

Now we are left with a much simpler system, of which we can determine a critical point where $S^* = \frac{\Lambda}{\mu+\psi}$ and $V^* = \frac{\Lambda\psi}{\mu(\mu+\psi)}$. Thus, we see that this critical amount of susceptible birds is related to the influx of birds into the system and inversely proportional to the rate at which they die and are vaccinated. The critical amount of vaccinated birds is similar but now the relationship with the vaccination rate is determined by μ. Additionally we now have an inverse-square relationship with respect to μ as opposed to linear before. To further understand the stability of this disease-free steady state system, we now consider the Jacobian of our system, of which we will analyze within the confines of the disease-free steady state. Computing this, we get

$$J = \begin{pmatrix}
\frac{\partial}{\partial S}(\frac{dS}{dt}) & \frac{\partial}{\partial I}(\frac{dS}{dt}) & \frac{\partial}{\partial V}(\frac{dS}{dt}) & \frac{\partial}{\partial A}(\frac{dS}{dt}) \\
\frac{\partial}{\partial S}(\frac{dI}{dt}) & \frac{\partial}{\partial I}(\frac{dI}{dt}) & \frac{\partial}{\partial V}(\frac{dI}{dt}) & \frac{\partial}{\partial A}(\frac{dI}{dt}) \\
\frac{\partial}{\partial S}(\frac{dV}{dt}) & \frac{\partial}{\partial I}(\frac{dV}{dt}) & \frac{\partial}{\partial V}(\frac{dV}{dt}) & \frac{\partial}{\partial A}(\frac{dV}{dt}) \\
\frac{\partial}{\partial S}(\frac{dA}{dt}) & \frac{\partial}{\partial I}(\frac{dA}{dt}) & \frac{\partial}{\partial V}(\frac{dA}{dt}) & \frac{\partial}{\partial A}(\frac{dA}{dt})
\end{pmatrix}$$

$$= \begin{pmatrix}
-\beta I - q\beta A - \psi - cI - \mu & 0 & -\beta S - cS & -q\beta S \\
\psi & -\rho\beta I - q\rho\beta A - cI - \mu & \rho\beta V - cV & -q\rho\beta V \\
\beta I + q\beta A & 0 & \beta S - \nu - 2cI & q\beta S \\
0 & \rho\beta I + q\rho\beta A & \rho\beta V - cA & q\rho\beta V - \mu - cI
\end{pmatrix}$$

We can now consider when $I = A = 0$ and compute the Jacobian for our disease-free steady state.

$$J_{at\ steady\ state} = \begin{pmatrix} -\psi-\mu & 0 & -\beta S^* - cS^* & -q\beta S^* \\ \psi & -\mu & -\rho\beta V^* - cV^* & -q\rho\beta V^* \\ 0 & 0 & \beta S^* - \nu & q\beta S^* \\ 0 & 0 & \rho\beta V^* & q\rho\beta V^* - \mu \end{pmatrix}$$

As one might expect, our next instinct is to compute the eigenvalues of our Jacobian matrix and consider their sign to determine under what conditions we might have stability or instability in our system. We can abuse the fact that the second column only contains one nonzero element, and when we then compute the determinant of the resulting 3x3 matrix, we see yet again that we have just $-\psi-\mu$ as the only nonzero term. Thus we can write the determinant of $J-\lambda I$ as

$$\det(J-\lambda I) = (-\mu-\lambda)(-\psi-\mu-\lambda)\det\begin{pmatrix} \beta S^* - \nu - \lambda & q\beta S^* \\ \rho\beta V^* & q\rho\beta V^* - \mu - \lambda \end{pmatrix} = 0$$

Immediately we can discard the first two eigenvalues which present them selves quite clearly, being $\lambda_1 = -\mu$ and $\lambda_2 = -\psi-\mu$ as they are both going to remain negative since we only consider positive parameter values. This would result in a stable system which is not very interesting. Instead we focus now on the quadratic result we obtain when we evaluate the determinant of the remaining 2x2 system.

$$\det\begin{pmatrix} \beta S^* - \nu - \lambda & q\beta S^* \\ \rho\beta V^* & q\rho\beta V^* - \mu - \lambda \end{pmatrix} = \lambda^2 + (\mu + \nu - \beta S^* - q\rho\beta V^*)\lambda + \mu\nu - \mu\beta S^* - q\rho\nu\beta V^* \tag{1}$$

Setting this equal to zero and applying the quadratic formula we obtain:

$$\lambda = \frac{(\beta S^* + q\rho\beta V^* - \mu - \nu)}{2} \pm \sqrt{(\frac{(\beta S^* + q\rho\beta V^* - \mu - \nu)}{2})^2 + \mu\beta S^* + q\rho\nu\beta V^* - \mu\nu}$$

For ease of discussion and visualization, let us denote

$$a = \frac{(\beta S^* + q\rho\beta V^* - \mu - \nu)}{2}$$
$$b = \mu\beta S^* + q\rho\nu\beta V^* - \mu\nu$$

This creates the opportunity for a variety of results depending on the sign and magnitude of a and b. If we have both of them positive then clearly we have a positive eigenvalue and we achieve an unstable system. However, if a is positive and b is negative, this would require further analysis as their relative magnitudes would determine the resulting sign of λ. We can reduce the number of possibilities however by making a keen observation about $b < 0$ and what it implies.

$$\mu\beta S^* + q\rho\mu\beta V^* - \mu\nu < \mu\beta S^* + q\rho\nu\beta V^* - \mu\nu = b < 0$$

We made one small change above that retains the inequality we desire by noting the important fact we discussed in the introduction regarding ν and μ. Since ν is the death rate assigned to infected birds, we required it to be greater than μ as realistically infected birds should have a higher rate of mortality given their illness. Thus, making this one substitution in the middle term allows us now to factor out a common μ. This yields:

$$\mu(\beta S^* + q\rho\beta V^* - \nu) < 0$$
$$\beta S^* + q\rho\beta V^* - \nu < 0$$

If we look closely, we see that this is almost identical to a, except for the fact that a subtracts one more μ term. However, since this is guaranteed to be positive, we have just shown that when $b < 0$, we automatically have that $a < 0$ as well. Therefore, the cases where $b < 0$ can be disregarded as they will certainly lead to a stable system. Now, we can focus on two cases where $b > 0$ and $a > 0$ or $a < 0$. If $a, b > 0$ then clearly we can achieve instability as $a + \sqrt{a^2 + b}$ will most certainly be positive. Additionally, if $a < 0$ and $b > 0$, then $a + \sqrt{a^2 + b}$ will also be positive as the square root term is guaranteed to have a greater magnitude than a. Thus, we are able to achieve instability so long as $b > 0$ and we consider the eigenvalues of the form $a + \sqrt{a^2 + b}$.

Now that we have determined when we can achieve instability in the disease-free steady state system, we can define a reproduction number for our model based on the value of b given that $b > 0$ guarantees a positive eigenvalue for our Jacobian. Thus, we simply denote $\mathscr{R}_0 = b + 1$ such that when $\mathscr{R}_0 > 1$, we guarantee instability in our system, and when $\mathscr{R}_0 < 1$ we guarantee stability in our system. We can try to understand the reproduction number by

looking at its composition:

$$\begin{aligned}\mathscr{R}_0 &= \mu\beta S^* + q\rho\nu\beta V^* - \mu\nu + 1 \\ &= \frac{\mu\beta\Lambda}{\mu+\psi} + \frac{q\rho\nu\beta\Lambda\psi}{\mu(\mu+\psi)} - \mu\nu + 1 \\ &= \frac{\beta\Lambda(\mu^2 + q\rho\nu\psi)}{\mu(\mu+\psi)} - \mu\nu + 1\end{aligned}$$

If we compare the $\mu^2 + q\rho\nu\psi$ term to the denominator $\mu^2 + \mu\psi$ we see that they are quite similar. In fact, depending on how $q\rho\nu$ relates to μ we can achieve equality or possibly grow and reduce the term by changing the magnitude of $q\rho\nu$ compared to μ. If the birds are not severely affected by the infection, and so $q\rho\nu$ is not large compared to μ, we would be increasing the stability of the system. This contrasts with the possibility for the disease to be very effective at spreading and killing, in which case the numerator would grow compared to the denominator and so a lot more birds would die and therefore destabilize the system. Similarly, since the numerator is multiplied by $\beta\Lambda$, we see that transmission rates and the influx rate of birds will play a role in increasing the possibility for chaos in our system when they are increased, which would lead to instability as we might expect. We further explore the vaccination rate as it pertains to the reproduction number further along.

Since we are able to achieve a reproduction number above 1 based on the positive eigenvalue we derived previously, we know that there is a selection of parameters that will yield an endemic level of the disease in the flock. In Layman's terms this means that we can select parameters to allow the disease to persist at a stable but nonzero level throughout our flock of birds indefinitely. If this level were to spike suddenly then we would achieve an epidemic.

One might now want to better understand how the vaccination rate of the flock affects the ability for there to be an endemic level in the flock for this particular disease. If we consider just the setup of this scenario with the given mechanics and assumptions, it is not far fetched to think of a possibility where the parameters are such that the Asymptotic compartment grows so large, and the natural death rate μ is so low (comparatively speaking), that the vaccinated birds infect susceptible birds effectively (implying a high ρ value) and cause a lot more birds to be infected and then die directly because of the higher rate of vaccinations. With this idea in mind, we take the derivative of $\mathscr{R}_0 = b + 1$ with respect to ψ (the vaccination rate) to try and better understand how the reproduction number can be affected by ψ if other variables are held fixed and possibly create the particular event we just discussed. The

derivative is

$$\frac{\partial(b+1)}{\partial\psi} = \frac{\partial b}{\partial\psi} = \frac{\beta\Lambda(q\rho\nu-\mu)}{(\mu+\psi)^2}$$

Analyzing this derivative, we see that there is in fact a possibility for it to be positive where $q\rho\nu > \mu$. If not, b would decrease as we increase ψ meaning that increasing our rate of vaccination would reduce instability. Plotting this function with $\beta\Lambda(q\rho\nu-\mu) = 50$ and $\mu = 2$ (note that these values were chosen semi-arbitrarily as they are just meant to provide a visualization of how the derivative looks when $q\rho\nu > \mu$ is satisfied), we obtain:

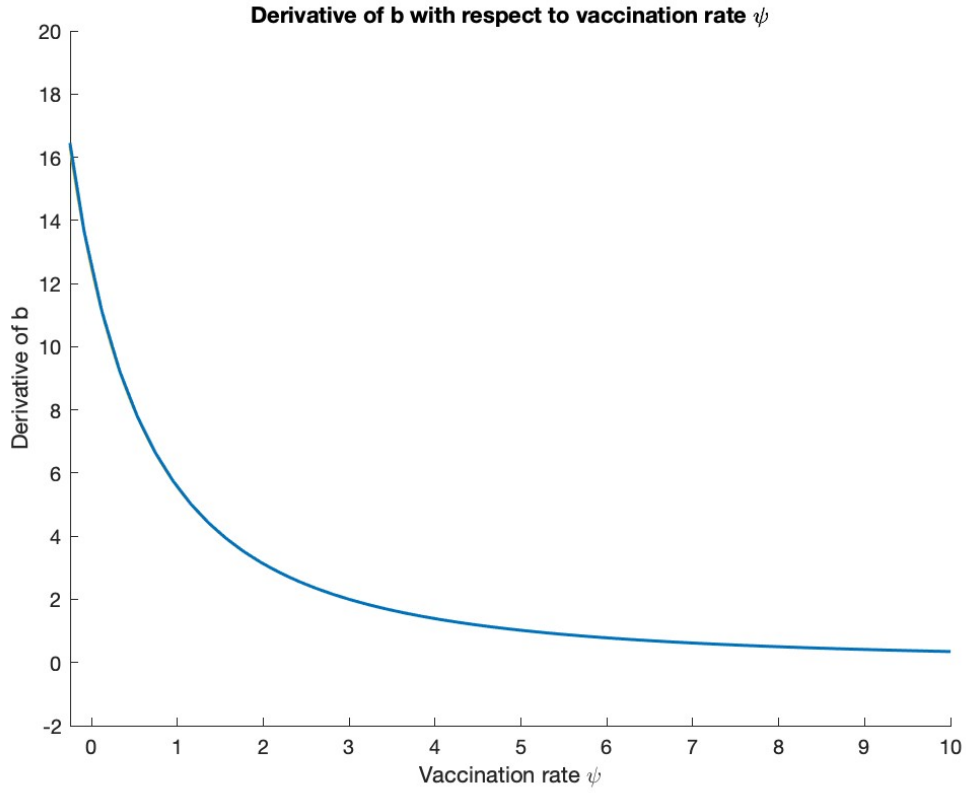

Figure 2: The derivative of b with respect to ψ on the interval $\psi \in [-0.25, 10]$

From the plot it is clear that with well chosen values of q, ρ, ν, μ the change in b (and therefore $\mathscr{R}_0$ with respect to ψ will be positive for all values of $\psi > 0$. It is important to note however that the acceleration is clearly negative and thus the effect of increasing ψ past a certain threshold (again dictated by the combination of parameters) will become quite minimal. Nevertheless, we are able to display a scenario that can occur within the confines of our system's assumptions where increasing the vaccination rate has a negative impact

on the stability of the disease-free steady state and therefore (under the right combination of parameters) could cause the stability to tip from stable to unstable by simply increasing ψ independently of the other parameters. Obviously this is counter-intuitive and counter-productive to the purpose of vaccinations, but analyzing these possibilities presents an important point when it comes to considering different methods of curbing disease spread, especially for diseases that can still remain on a host that is immune to the disease. Stated very clearly, if we create a scenario with a lot of birds where they live happy long lives when they are disease free or vaccinated, but have the ability to carry and transmit the disease quite quickly once vaccinated, we can see how vaccinating a lot of birds would create a relatively large asymptomatic population that could initially make it look like the disease has been eradicated, but when the farmer (or however birds enter the system) introduces more susceptible birds into the system, they contract the disease very quickly and die from it before the next round of vaccination can make a difference. In short, increasing vaccination itself is not necessarily a guaranteed positive for a flock of birds unless they are all vaccinated at once, die naturally quite quickly, or the disease does not live on vaccinated birds/doesn't transmit from vaccinated birds to non-vaccinated birds well ($q\rho$ much less than 1).

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