Comprehensive Exam 2019
Biomathematics 202: Structure, Function, and Evolution of Biological Systems

Consider the simplest Susceptible-Infected-Recovered (SIR) model.

$$\dot{S} = \frac{\mathrm{d}S}{dt} = -\beta IS$$

$$\dot{I} = \frac{\mathrm{d}I}{dt} = \beta IS - \gamma I$$

$$\dot{R} = \frac{\mathrm{d}R}{dt} = \gamma I$$

S is the number of susceptible individuals, I is the number of infected individuals, R is the number of recovered individuals, β is the infection rate, and γ is the recovery rate. These equations ignore births in the population as well as deaths from infection or anything else. These equations are used to model a variety of infectious diseases.

a. Explain the form of these equations in words. Is total population size (N=S+I+R) conserved for this system? Explain why or why not? What are the fixed/equilibrium points of this system? Interpret those fixed points as well as the point $S^* = \gamma/\beta$.
b. Guillain-Barre' Syndrome (GBS) is a rare syndrome in which a person's immune system attacks its peripheral nervous systems and can cause temporary paralysis or problems breathing. Most people recover after a few months but some die. This syndrome can be triggered by getting the flu, receiving the flu vaccine, or other causes. According to the Center for Disease Control (CDC), GBS is estimated to occur in about 1 in 100,000 people and death is about 1 in 1,000,000 people. Explain how to modify the SIR equations *only* to account for vaccinations and for this effect of GBS? Express your new equations in terms of two additional parameters—the vaccination rate, υ, and the fraction of people dying from GBS, δ. Do you need any extra compartments for people getting GBS or extra parameters? Is the total population size conserved for this new system? What will happen to this system in the limit of infinite time?
c. There is some evidence that there is a genetic component to the severity of the GBS symptoms and possibly the likelihood of getting GBS. For the purposes of the exam, assume that GBS is caused by a single mutation and that, on average, it reduces fitness by 10% compared with the average for the rest of the population. (You can think of this as a two-allele, single-locus model.) Based on the information in part b, what is the allele frequency, p, of people with the gene for GBS? Based on these numbers and the population genetics we covered in the course, what is the variance, V(p), in these allele frequencies across the entire population? What is the strength of selection as defined by $\partial \ln(\overline{w}) / \partial p$? Using Wright's equation write down the change in

allele frequency per generation. Comment on whether and why this rate of change is driven more by the variance or the selection strength.

d. Based on your answers to part c., approximately how many generations would it take for this mutation to be eliminated? You can assume that the world's population is 7 billion and that every single person gets vaccinated (corresponding to the fastest possible scenario).
e. To treat the problem more stochastically, what equation from class would you use to deal with stochastic predictions? How would V(p) and $\partial \ln(\overline{w}) / \partial p$ from part c. be included as part of that equation? Explicitly write out this equation and also its equilibrium solution. Considering these stochastic equations, would a mutation be eliminated by selection faster in very large populations or in small populations? What factors have we not considered that might help the GBS allele to persist for more generations?
f. Assume that in the future a genetic screen is found for people susceptible either to getting GBS or to dying from it. With this screen those people would be identified and not receive the vaccination. Write down the SIR equations you would use to model this system. Assume people infected with the flu develop GBS at the same percentage as those receiving the flu vaccine. Is the total population size conserved for this system? Will this lead to a higher rate of people getting GBS when the number of infected, I, starts with just one person? Will it depend on parameter values, and if so, which ones and how? (Note that we are assuming that the effects of GBS are worse and more deadly than the flu for people who have the GBS allele. Also note that GBS is likely caused by a suite of genes, not just one.)