Biomathematics 301 Midterm 2014

Q1:	/15
Q2:	/15
Q3:	/30
Q4:	/30
TOT:	/90

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Student #____________________________________

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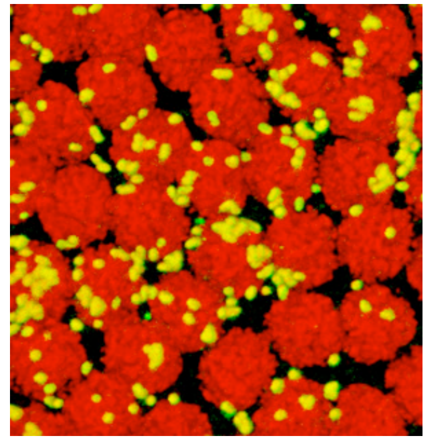


Fruit fly cells (red) infected by Wolbachia (yellow). - *University of Rochester*

Question 1 [15 points]: Wolbachia is a bacteria that frequently infects insects and is passed from mother to offspring (via the cytoplasm). Caspari and Watson (1959) modeled the frequency, p, of individuals infected with Wolbachia, assuming that infected individuals have a lower fitness, $1-s$, but uninfected females who mate with infected males suffer a cytoplasmic incompatibility reaction, reducing their fertility by a factor $1-\sigma$. The continuous-time version of this model is:

$$\frac{dp}{dt} = -s\, p\,(1-p) + \sigma\, p^2\,(1-p)$$

(a) What are the equilibria of this model? **[Show your work]**

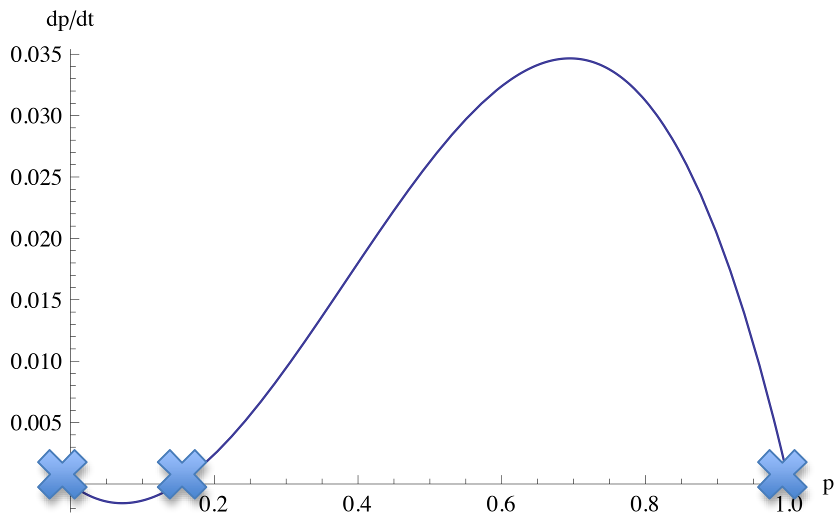
Setting dp/dt to zero:

$$\begin{aligned} 0 &= -s\,\hat{p}\,(1-\hat{p}) + \sigma\,\hat{p}^2\,(1-\hat{p}) \\ &= \hat{p}\,(1-\hat{p})(-s+\sigma\,\hat{p}\,) \end{aligned}$$

There are three solutions $\hat{p} = 0,\ 1,\ \dfrac{s}{\sigma}$

Points = 6

(b) The following graph shows the differential equation plotted against the current frequency of infected females for $s = 0.045$ and $\sigma = 0.3$. On this graph, mark all equilibria (X) and specify whether each one is locally stable (LS) or unstable (LU), based on the information contained in the graph.



LS LU LS Points = 6

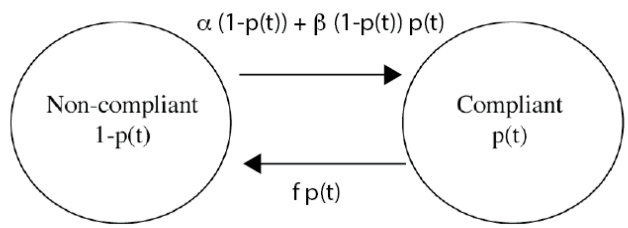
(c) A group is developing a strategy to fight Dengue fever by introducing Wolbachia-infected mosquitoes into the field. This particular strain of Wolbachia causes mosquitoes to die before the Dengue virus reaches their salivary glands, reducing the chance that a person bitten by a mosquito contracts the disease. If $s = 0.045$ and $\sigma = 0.3$ (as in the above figure), what advice would you give the researchers about the fraction of infected mosquitoes to introduce, given that they want the Wolbachia infection to spread in order to reduce the transmission of Dengue fever? [**Make a quantitative prediction using the information provided.**]

To expect the Wolbachia infection to spread, one would need to start the initial frequency above the unstable equilibrium at p = 0.15.

Points = 3

Question 2 [15 points]: Hand-washing is a key step in the prevention of hospital-acquired infections, yet the compliance levels are surprisingly low and variable, with baseline rates ranging from 5% to 89% and an overall average of 38.7% according to a 2009 WHO study[1]. Peer pressure and the norms of a hospital play an important role in the practices of a doctor. Let $p(t)$ represent the fraction of doctors at time t that follow appropriate hand-washing routines ("compliant"). Assume that, in the absence of peer pressure, a fraction α of the non-compliant doctors become compliant per time step. This fraction goes up by an additional $\beta\, p(t)$ in a particular hospital because compliant doctors are encouraged to ask non-compliant doctors to wash their hands. Also assume that a fraction, f, of doctors that are compliant stop following hand-washing procedures per time step.

(a) Complete the following flow diagram for this hospital. **Add arrows** and write in **total flow rates** associated with each arrow (i.e., if a flow rate is per capita, multiply it by the appropriate variable).



Points = 7

(b) Write down the recursion equation for the fraction of compliant doctors, $p(t)$, at time t. Assume that the time step is small (e.g., by day), so that doctors don't switch more than once within a time step.

$$p(t+1) = p(t) - f\ p(t) + \alpha\left(1 - p(t)\right) + \beta\ p(t)\left(1 - p(t)\right)$$

Points = 8

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[1] http://whqlibdoc.who.int/hq/2009/WHO_IER_PSP_2009.07_eng.pdf

Question 3 [30 points]: In class, we modeled diploid selection in discrete time. Here we consider the continuous time version. Let "recursion" stand for the equation for $p(t+1)$ in the discrete-time diploid selection model and measure the relative fitnesses using $W_{AA} = 1 + s$, $W_{Aa} = 1 + h\,s$, and $W_{aa} = 1$, where s is the selection coefficient favoring allele A and h is its dominance coefficient.

(a) I used one of the following *Mathematica* codes and the definition of a derivative to obtain a differential equation for the diploid model. For each case, say whether the method is correct or incorrect. If incorrect, diagnose the problem. Points = 7

Code	Correct? [Yes or No]	Diagnosis
D[recursion, p] **% /. s -> s*Δt** **%/Δt** **Limit[%, Δt -> 0]**	No	The definition of a derivative takes the difference in the dependent variable (here p) over a short change in the independent variable (here t): $\lim_{\Delta t \to 0} \frac{\Delta p}{\Delta t}$. There is no derivative taken in this definition. (Last sentence is sufficient.)
Factor[recursion - p] **% /. s -> s*Δt** **%/Δt** **Limit[%, Δt -> 0]**	Yes	
Factor[recursion - p] **% /. p -> p*Δt** **%/Δt** **Limit[%, Δt -> 0]**	No	As we shrink time, we don't want to shrink the allele frequency (we want to shrink the amount of change that occurs via selection).

(b) The resulting differential equation is $\frac{dp}{dt} = s\,p\,(1-p)(h+p-2\,h\,p)$. Begin a separation of variables by rewriting the differential equation with the variables separated: Points = 4

$$\int \frac{1}{p(1-p)(h+p-2hp)}\,dp = \int s\,dt$$ [Or s may be put on the left]

[Do not carry out the integration!]

(c) The equilibria of this model occur at $\hat{p}=0$, $\hat{p}=1$ and $\hat{p}=h/(2h-1)$. Determine the values of h for which this last equilibrium is biologically valid (i.e., $\hat{p}$ is a frequency). Make no assumption about the sign of h. [**Hint:** It may help to handle cases where $(2h-1)$ is positive and negative separately.]

For $\hat{p}$ to be a valid frequency, which requires it to lie between 0 and 1.

- First, assume that $(2h-1)$ is positive (i.e., $h > ½$): then $\hat{p}=h/(2h-1)$ will be positive if $h > 0$. In addition, $\hat{p}$ will be less than one if $h/(2h-1)<1$, which requires $h<2h-1$, that is $h>1$. This gives three conditions ($h > ½$, $h > 0$, $h > 1$), which are only all met if $h > 1$.

- Second, assume that $(2h-1)$ is negative (i.e., $h < ½$): then $\hat{p}=h/(2h-1)$ will be positive if $h < 0$. In addition, $\hat{p}$ will be less than one if $h/(2h-1)<1$, which requires $h>2h-1$ (note that you have to switch the inequality when multiplying both sides by a negative number), that is $h<1$. This gives three conditions ($h < ½$, $h < 0$, $h < 1$), which are only all met if $h < 0$.

Thus, the polymorphism is valid only if $h > 1$ (corresponds to heterozygote advantage assuming $s > 0$) or $h < 0$ (corresponds to heterozygote disadvantage).

Points = 6

(d) Perform a stability analysis for the model of diploid selection, $\frac{dp}{dt}=s\,p\,(1-p)(h+p-2\,h\,p)$, at the equilibrium $\hat{p}=0$. What is the condition required for this equilibrium to be stable?

Calling dp/dt = f, we have to take the derivative of the differential equation (f) with respect to p. Using the product rule: $\frac{df}{dp}=s\,(1-p)(h+p-2\,h\,p)+s\,p\,(-1)(h+p-2\,h\,p)+s\,p\,(1-p)(1-2\,h)$ and plugging in $\hat{p}=0$ gives $\left.\frac{df}{dp}\right|_{p=0}=s\,h$. Given this is a continuous time model, this must be negative ($s\,h < 0$) for $\hat{p}=0$ to be stable.

Points = 8

(e) Fill in the blanks below to complete the Mathematica code that you would use to perform the stability analysis for the equilibrium $\hat{p} = h/(2h-1)$:

D[s p (1 - p) (h + p - 2 h p) , _p_________]

Factor[%_/. p -> h/(2 h – 1)____________] Points = 3

(f) *Mathematica* answers $(1-h)h\,s/(2h-1)$, which can be simplified to $(1-h)\hat{p}\,s$. Based on this information, are the following statements true or false? Points = 2

True or False [Circle one]: The approach to $\hat{p} = h/(2h-1)$ will be oscillatory when $h > 1$.

True or False [Circle one]: $\hat{p} = h/(2h-1)$ is locally stable when $h > 1$.

Question 4 [30 points]: The extinction of a species can cause a cascade of extinction events for species that depend on it. Consider a plant that is exponentially declining at rate *r* (e.g., due to habitat loss), with the number of plants at time *t* given by the general solution for the exponential model, $p(t) = p_0\, e^{-rt}$. Here we model the rate of decline of an herbivore, *h*(*t*), that depends fully on this plant for food according to the differential equation:

$$\begin{aligned}\frac{dh}{dt} &= f\,p\,h - d\,h \\ &= f\left(p_0\, e^{-rt}\right)h - d\,h\end{aligned}$$

where *f* is the rate of consumption of the plant by the herbivore and *d* is the death rate of the plant.

(a) What is the general solution for *h*(*t*) in this model, assuming an initial number h_0 of herbivores?

$$\begin{aligned}\frac{dh}{dt} &= f\,p\,h - d\,h \\ \frac{dh}{h} &= \left(f\left(p_0\, e^{-rt}\right) - d\right)dt\end{aligned}.$$

Integrating both sides: $\ln(h) = f\left(p_0 \frac{e^{-rt}}{-r}\right) - t\,d + c$. Anchoring the equation at t = 0,

$\ln(h_0) = f\left(p_0 \frac{1}{-r}\right) + c$, which allows us to replace *c* in the general solution:

$\ln(h) = f\left(p_0 \frac{e^{-rt}}{-r}\right) - t\,d + \ln(h_0) - f\left(p_0 \frac{1}{-r}\right)$. Finally, exponentiating both sides:

$h = \exp\left(f\left(p_0 \frac{e^{-rt}}{-r}\right) - t\,d + \ln(h_0) - f\left(p_0 \frac{1}{-r}\right)\right)$, which is fine or can be simplified as:

$h = h_0 \exp\left(f\left(p_0 \frac{e^{-rt}-1}{-r}\right) - t\,d\right)$.

Points = 18

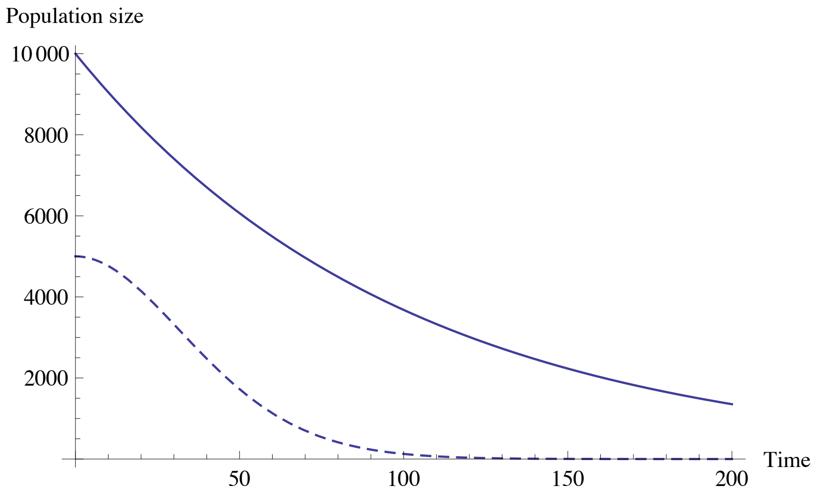
(b) Write down one check that you could perform to make sure that your general solution is reasonable and say whether or not your solution passes or fails the check:

Check:________Setting t = 0, we should regain $h = h_0$ ________________________________**Passes or Fails**

(Or you could take the derivative of the solution with respect to t to regain the original differential equation)____[Circle one]

Points = 6

(d) The following plot shows this model for a particular community:



Circle one: The plant population is shown as a curve that is **Solid or Dashed**.

Circle one: The herbivore population is shown as a curve that is **Solid or Dashed**.

Justify your choice in one or two sentences.

We were told that the plant is declining exponentially, and only the solid curve has the shape of exponential decline.

Points = 4

(e) The plant grows in two communities. In the first community, the plant's herbivore is a small beetle that eats a small amount of leaves. In the second community, the plant's herbivore is a mammal that eats whole plants.

Circle one: The model analyzed here is more appropriate for the **First or Second** community.

Justify your choice in one or two sentences.

Notice that the herbivore has no impact on the numbers of plants (these decline exponentially at a rate that doesn't depend on the number of herbivores). This model is thus harder to justify for an herbivore that eats and kills whole plants and may be more appropriate for a small beetle that eats only a small amount of leaves. Points = 2