Math 19a, Midterm II readings reviews

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1 The case of the missing meat eaters

This article discusses the interesting fact that Australia lacks big mammalian predators. The author argues that the harsh climate imposed by the southern oscillation factor (El Niño), infertile soil due to the lack of geological processes this old continent and other environmental factors reduces the density of herbivores thereby making it very hard for large mammalian predators to survive because they require much more food and have big penalties for competition within species. However, Australia is very hospitable to a remarkable variety of big reptiles, who need much less food and can sustain longer without it as they don't need to maintain body temperature. This decreases their death rate (σ in the model below) and increases their benefit from the prey (efficiency, λ here).

In this case, the usual Lotka-Volterra predator-prey model applies:

$$\begin{aligned} \frac{dk}{dt} &= \alpha k - \beta k^2 - \gamma pk \\ \frac{dp}{dt} &= -\sigma p + \lambda pk, \end{aligned}$$

where k is the number of prey and p the number of predators. This model is extensively analyzed in Chapter 12. To summarize, in the case that $\alpha/\beta < \sigma/\gamma$ (either the death rate σ is large or the benefit from prey λ is small), the point $(k = \alpha/\beta, p = 0)$ is the only stable equilibrium in the first quadrant (biologically significant values), so in this case the predators will go extinct. In the other case $\sigma/\lambda < \alpha/\beta$, the stable equilibrium point is $(k = \beta/\lambda, p = \alpha/\gamma - \beta\sigma/(\lambda\gamma))$ and $p > 0$, which shows that predators with sufficiently low death rate (σ) and/or high prey benefit rate (λ), like reptiles, will survive.

2 Malaria: focus on Mosquito Genes

Malaria is one of the most common infectious diseases and an enormous public health problem. It is a vector-borne infectious disease caused by protozoan parasites. It is widespread in tropical and subtropical regions throughout the world. Each year, it causes disease in approximately 515 million people and kills between one and three million. The disease is caused by protozoan parasites of the genus Plasmodium, transmitted by female Anopheles mosquitoes. So far fighting the disease by exterminating these mosquitoes or by developing vaccines have been unsuccessful. This article proposes a new approach - creating transgenic mosquitoes resistant to malaria, whose resistance gene is attached to a highly movable part in the genome thereby increasing its chance to be passed among the population.

There are several different ways of creating resistant (inhospitable to malaria) mosquitoes, one of them is stopping the parasite from replicating on each of the three stages of reprodution or by simply making the mosquito hypersensitive to the parasite, dying instantly when infected and hence not allowing time for the parasite to develop. Both techiniques were unsucessful because genetically modified mosquitos were less fit than the wild ones, therefore, exponentially decreasing with time the number of resistance/hypersensitive genes in the population. A new approach suggested by researchers was to give the genetically modified mosquitos a little help enhancing the chances of passing the gene to the next generation by inserting the gene

inside mobile elements of the genome called transposable elements. These replicate themselves (most likely through an RNA intermediate) over the genome increasing their number of copies and enhancing the likelihood that the gene will be passed on. With that we could hope that the number of resistance/hypersensitivity genes would increase over time and start to spread over the population of wild mosquitos. There is a question on this article made by the books author: ‘Can the spread of the gene over time be modeled by an Advection Equation’. The answer is no. Advection equations model situations where there is one resultant force driving the spread of the subject (like the wind in the example given in class). In this example, there is no obvious direction for the spread of the resistance/hypersensitive gene throughout the continent. Therefore it could not be modeled by advection. If one considers the spread completely random (ignoring migration behaviour of the mosquitos) then it could be perhaps approximated by a diffusion model.

If everything was happening at one place, say in a closed room, then time would be the only variable and we can write a simple logistic equation for the proportion of resistant mosquitos in the entire population ($p(t)$) as

$$\frac{dp}{dt} = rp(1-p),$$

assuming that the resistant mosquitos will prevail (so 1 is the stable equilibrium here). If we consider the same situation over, say, Africa, then the resistant mosquitos will not only multiply at one place, but also diffuse over the whole continent. In this case their portion will be a function not only of time, but of location (x) also, denote it by $u(x,t)$ The rate of change in proportion will be equal to the proportion of resistant mosquitos which diffused across position x at time t + the proportion of resistant mosquitos that were created (birth - death) at this spot and moment, which is by the previous equation $ru(1-u)$. We suggest the following model (called Fisher's model):

$$\frac{\partial}{\partial t}u = \mu\frac{\partial^2}{\partial x^2}u + ru(1-u), \tag{1}$$

where μ and r are just constants. We can try to find a solution for it in the form of a traveling wave: $u(x,t) = f(x+ct)$ (c- constant, to be determined). Substituting this u in the equation we find an equation for f

$$c\frac{df(s)}{ds} = \mu\frac{d^2f(s)}{ds^2} + rf(1-f).$$

3 Past Temperatures Directly from the Greenland Ice Sheet

This article is "predicting the past" from the present. The authors drilled holes in Greenland's thickest ice (3000 m deep!) and measured the temperatures down through the hole. The idea is that temperature propagates through the ice the same way particles diffuse through a substance (heat equation and diffusion equation are the same), so changes on the surface of the ice sheet propagate downwards with distance and time. Knowing the present temperatures along the hole is like knowing the boundary conditions (e.g. $T(0,z)$), which enables us to solve uniquely any diffusion-advection equation, and so find $T(x,t)$ for all x,t and in particular $T(0,t)$ for all t which would be the temperature at the surface for any time in the past. (Here T is the temperature, z is the depth, t time) If we assume this simple picture, we can write a diffusion (heat) equation for $T(t,z)$:

$$\rho c\frac{\partial}{\partial t}T = \frac{\partial}{\partial z}\left(K\frac{\partial}{\partial z}T\right) + f, \tag{2}$$

where ρ is the density of ice (and a function of depth), c is the ice heat capacity (and depends on the temperature T), K is the thermal conductivity (and depends on T and ρ) and $f(z)$ is the heat production term (from earth - geothermal heat).

This model, however, does not account for the fact that ice is not stationary - it flows, however slow it be. We need to add another variable - x, which is the horizontal distance, and an advection term. The ice is moving with horizontal velocity v_x and vertical velocityv_z and this movement contributes an advection term

to our equation. Having x, we should take into account that temperature diffuses horizontally also, so the diffusion term will have an additional $\frac{\partial}{\partial x}\left(K\frac{\partial}{\partial x}T\right)$ term in it, giving us the full model:

$$\rho c\frac{\partial}{\partial t}T = \frac{\partial}{\partial x}\left(K\frac{\partial}{\partial x}T\right) + \frac{\partial}{\partial z}\left(K\frac{\partial}{\partial z}T\right) - \rho c\left(v_x\frac{\partial}{\partial x}T + v_z\frac{\partial}{\partial z}T\right) + f. \tag{3}$$

Even though it is impossible to find an explicit solution to this equation, it is important to note that this equation is again fully predictive if we know the boundary condition $T(0,z)$ (i.e. what they measured down through the hole), so in theory we know $T(t,z)$ and in particular $T(t,0)$ - the air temperatures through the past times. The authors find a solution for $T(t,z)$ via statistical methods (they use an algorithm which generates random functions for $T(t,z)$, determines how far they are from being a solution, and averages out according to the output).

4 Fishing for answers: Deep Trawls Leave Destruction in Their Wake - But for How Long?

Deep trawls drag nets along the bottom of the sea in their quest for lobsters (or other bottom-dwelling delicacies). These nets however don't discriminate and destroy not only the lobster population but even species like tube worms, as they turn over the stones worms attach to. In general the trawls plough the sea bottom, homogenizing it and destroying habitat for species in the low ends of the food chain. That's why the fish and lobster populations decreases not only because of fishermen's catch but also because their food (e.g. the same tube worms) get destroyed. Janet Raloff (the author) discusses these issues and tries to raise an alarm of how big deep trawls' impact is.

We, however, are interested in modeling lobster population in the situation when deep trawls catch everything in certain areas. Chapter 16 discusses a model for the lobster population when there is a strip $(0 < x < R)$, where deep trawls are not allowed. The model is

$$\frac{\partial}{\partial t}u = \mu\frac{\partial^2}{\partial x^2}u + ru, \tag{4}$$

where $u(t,x)$ is the lobster population at time t and position x. Here r is the growth rate of the lobster population on its own, and μ is a lobster mobility rate (diffusion coefficient). This equation comes from the fact that the rate of change of lobsters = (lobsters which diffuse in - lobsters diffusing out) + (lobsters born - lobsters who died). This of course assumes that lobsters move randomly (like particles).

For this paper we can discuss a different situation - suppose that trawls have been only allowed to plough in a given strip of length R $(0 < x < R)$ before $t = 0$, then how are the lobsters going to repopulate the devastated stripe. The equation is the same, what changes are the initial conditions. The deep trawls wiped out all lobsters in that strip at time 0, while everywhere else the population remained the same as before and is also homogenous (i.e. the same at every location, here it's 1), so

$$u(0,x) = \begin{cases} 0 & ,0 \le x \le R \\ 1 & ,x < 0 \text{ or } x > R \end{cases} \tag{5}$$

According to chapter 15.2 (page 227) the general solution to the diffusion equation (4) is

$$u(t,x) \quad = \quad \frac{1}{(4\pi\mu t)^{1/2}}e^{rt}\int_{-\infty}^{\infty} u(0,s)e^{-(x-s)^2/4\mu t}ds, \tag{6}$$

where we can substitute (5) for $u(0,s)$ and then $a = s - x$ to obtain the solution given on page 254 (note the typo there, a factor of e^{rt} is missing!)

$$u(t,x) = \frac{e^{rt}}{(4\pi\mu t)^{1/2}}\int_x^{\infty} e^{-a^2/4\mu t}da + \frac{e^{rt}}{(4\pi\mu t)^{1/2}}\int_{R-x}^{\infty} e^{-a^2/4\mu t}da. \tag{7}$$

5 Dynamics of Stripe Formation; A Reaction-Diffusion Wave on the Skin of the Marine Angelfish P; Letters to Nature

These articles consider the formation of stripe patterns on the skin of angelfish. On cellular level the cell pigment (color) is determined by the level of the expression of certain gene. In this paper the authors assume that there are two enzymes governing the expression of the gene, which also control each other's synthesis. These enzymes are available in the extracellular space and their concentration levels are proportional to the pigment expression. These articles assume that the enzymes (I and A) move randomly through the extracellular space, i.e. diffuse.

The reaction-diffusion model proposed by Kondo and Asai is the one in Fig.1 on page 283

$$\begin{aligned} \frac{\partial A}{\partial t} &= c_1 A + c_2 I + c_3 - D_A \frac{\partial^2 A}{\partial x^2} - g_A A \\ \frac{\partial I}{dt} &= c_4 A + c_5 - D_I \frac{\partial^2 I}{\partial x^2} - g_I I. \end{aligned}$$

Here I and A are the concentrations of inhibitor and activator enzymes, D_I and D_A are their diffusion constants (it's very likely there is a typo and the signs in front of D_A and D_I are +). The reaction terms are respectively $c_1 A + c_2 I + c_3 - g_A A$ and $c_4 A + c_5 - g_I I$, with g_A and g_I decay rates (perhaps due to absorption in cells) and $c_1 A + c_2 I + c_3$ and $c_4 A + c_5$ the production rates of the activator and inhibitor.

In order to figure out if such a model gives us stripe we need to check whether the stable equilibrium solution is periodic (or "patterned") in some way, e.g. it is a function with sines and cosines. For example, if we had only one gene and activator (without the I term), our model would look like

$$\frac{\partial A}{\partial t} = D \frac{\partial^2 A}{\partial x^2} + aA + c, \tag{8}$$

where $cA + c$ is the reaction term, production - degradation of A. We would get stripes if at the end A was alternating between low and high concentrations (low and high pigment), or in other words if there was a stable equilibrium $D\frac{\partial^2 A_e}{\partial x^2} + aA_e + c = 0$, such that it's solution A_e would exhibit the pattern we like.

In this article they solve the equations numerically and show that the solutions show the same stripe pattern as in angelfish (here with time the fish and the domain of x grows). However they receive objections from two other authors that there is no justification why the proposed model is the method stripes are formed. Moreover, when considering the presumably more realistic 2D model, the solutions turn out to be unstable. The original authors respond that reaction-diffusion is one possible and simple explanation of the phenomenon and the one-dimensional case is in fact closer to nature in this case. As it turns out in a later paper (1999) of Maini et al, a better model for stripe formation is a reaction-diffusion plus incorporation of cell movement (two types of cells giving different colors).

6 Readings 18.4

6.1 Direct and Continuous Assessment by Cells of Their Position in a Morphogen Gradient

This article is a powerful example of the nature and importance of diffusion. Embryonic undifferentiated cells differentiate under the influence of certain activators (morphogens). The activators are assumed to diffuse through the intracellular matrix and the expectations are that the levels of exposure to the activators would determine which genes get expressed.

In this article the authors find a ratchet-like behavior for cell activation. Cells differentiate by expressing a certain gene (in this case Xbra) when they receive a minimun concentration of activation signals, and if they receive a concentration greater than a certain threshold, the cells undergo a different process that blocks the activation of Xbra and generates a different response (expression of Xgsc). Hence the ratchet-like behavior

is related to the defined thresholds for differentiation - cells can switch their gene response to changes in the morphogen levels at the cells' positions (gradient). Moreover, during the exposure cells can only increase but not decrease the level of their response.

6.2 Activin signaling and Response to a Morphogen Gradient

This paper addresses the important question of how activation signals are passed to cells. It is generally accepted that signaling molecules are diffused through the extracellular matrix, but it could also be possible that cell to cell contact made connections for transfer of activation molecules. Given that cell to cell contacts are extremely common and abundant and that many cells differentiate in regional bulks, that would be an easy to accept idea.

The experiments show evidence that cells do differentiate through diffusing activation signals. The main experiment placed one provider cell that served as a source of activin (the activation signal molecule), surrounded by cells that are able to activate and pass on the activin and others that are incapable of passing activin. They observed that cells behind the activin passing incapable cells were able to differentiate, therefore not relying on cell to cell transfer of activin.

Moreover, the authors determine similarly to the previous paper that the level and nature of cell differentiation depends on the distance from the activin source, or in other words - the amount and duration of exposure to morphogens.

This makes room for mathematical modeling on cell differentiation through diffusion equations.

7 Hantavirus Outbreak Leads to PCR

This article is about the sudden appearance of an absent so far type of virus in the US, the hantavirus. The virus causes the so called hantavirus pulmonary syndrome (HPS), which can lead to tachycardia, then to cardiovascular shock and eventually death. The virus is carried by rodents(they are vectors for the disease) and is passed to humans through air (aerosol from rodents' urine and feces). In 1993 26 cases in the South West have been reported and even though the virus has been expected to spread, it actually didn't and so the case of its appearance remains in the history so far.

The hantavirus outbreak case is important as the first case when scientists were able to identify and study the viral properties without having the virus itself. After they figured out that the virus in the American Southwest is similar to the Hantaan viruses in East Asia, they used DNA primers from the known Hantaan virus to start a Polymerase Chain Reaction (PCR) in tissues of infected patients and thus amplify and isolate the viral DNA present in the tissues. Even without the virus, having its genes is already a significant advantage to studying the virus and creating antiviral medications.

For our purposes this article is interesting in the sense that it motivates the study of the traveling wave solutions to the diffusion equations, which we did in chapter 21. In the case of a viral epidemic one of the first questions we'd ask is how fast does the virus spread and how soon will it reach us.

The model for this article is the one in chapter 21:

$$\frac{\partial}{\partial t} = \frac{\partial^2}{\partial x^2} u + ru(1-u). \tag{9}$$

Here $u(x,t)$ is the percentage of virus carrying mice at time t and position x (assuming they are moving along a line). The term $ru(1-u)$ is the reaction term - without the presence of diffusion, e.g. mice confined in a room, it shows the rate at which the virus spreads. This rate we chose as $ru(1-u)$, because it's our logistic model (we expect that eventually all mice get infected, so 1 is a stable equilibrium and 0 - unstable). The diffusion term $\frac{\partial^2}{\partial x^2} u$ indicates that mice are roaming around randomly, i.e. diffusing.

We are interested in a traveling wave solution, so $u(x,t) = f(x-ct)$. In this case the speed of the wave is c. In chapter 21 we established that in the case $c^2 > 2r$ there is always a solution f, such that

$$f(s) \to 1 \text{ as } s \to -\infty,$$

$$f(s) \to 0 \text{ as } s \to \infty,$$

$$0 < f(s) < 1 \text{ for all } s \text{ and } f \text{ is decreasing.}$$

This is a biologically relevant solution to our situation and its existence as long as $c > \sqrt{2r}$ shows that the speed of the wave can be very large, in other words our infection can be spreading really fast.

8 Snowshoe Hare Populations: Squeezed from Below and Above; Impact of Food and Predation on the Snowshoe Hare cycle

This is an especially interesting article that tries to identify how many variables are defining the oscillatory variation in the hare population. A logical assumption is that hare population, predator population and hare food (e.g. grass) amount are related, but which relation(s) is(are) responsible for the oscillation (periodicity) in the hare population is to be determined. For this purpose the authors performed an ecological experiment - they enclosed areas in the hare's natural habitat (southern Yukon) where they were able to control food supply and/or predator access. They observed that changing only one factor (either doubling food or decreasing predation about 2 times) leads to doubling or tripling of the hare population, however changing both factors simultaneously increased population by 11. This is not an additive effect, so there must be a three-fold interaction here (this conclusion is based on research the authors cite, which is not included in our book).

The principle used in this reasoning is that if you had a one parameter system (e.g. $\frac{dh}{dt} = f(h)$, where $h(t)$ is the hare population t time t), then $h(t+1)$ is a function of $h(t)$ (i.e. if you plot $h(t+1)$ versus $h(t)$, i.e. the points $(h(t), h(t+1))$, you'll get a line, or in other words $h(t+1)$ depends solely on $h(t)$) (this is not really obvious, but is similar to saying that $\frac{dh}{dt}$ depends only on the value of h at time t, i.e. is a function of h). If you had a three-way interaction, e.g. a system of the kind you might use in this article

$$\begin{aligned}
\frac{dh}{dt} &= f_1(h, g, p) \\
\frac{dp}{dt} &= f_2(h, g, p) \\
\frac{dg}{dt} &= f_3(h, g, p),
\end{aligned}$$

where p and g are predator population and food amount, then $h(t+3)$ will be a function of $(h(t), h(t+1), h(t+2))$, or in other words knowing the values at time t of h, $\frac{dh}{dt}$, $\frac{d^2h}{dt^2}$ determines uniquely the value of $\frac{d^3h}{dt^3}$.

9 Disparate Rate of Molecular Evolution in Cospeciating Hosts and Parasites

This is an example of interaction between systems with different speeds. In other words, a fast system (lice) interacting with a slow one (gopher). The speed here refers to the production a new generations (or turnover rate of generations). The gopher generation is approximatelly three times longer (slower) than the louses. For that reason, the louse has a time to evolve to perfect adaptation to its host every time the gopher changes before there is any new change by the gopher. The system could be modeled perhaps using a competing species model, however instead of having population abundances as variables, we can consider allele frequencies. For example, if we consider a mutation in the gopher, which makes his skin harder (to endure the lice better) and denote the percentage of gophers with such allele by g, then we can consider an adaptive mutation in the lice, which makes say their teeth sharper and longer to bite the hard skin of the gopher, denote the abundance of this allele by l. Then we can model g and l similarly to competing species (since the mutation in one species is bad for the other).

The authors however do not model this situation. Instead they try to show evidence to what they see by correlating the perfect adaptation of the lice to the genome of the gopher. A phylogenetic analysis is made to relate the adaptation of a protein that has a high rate of variability among gophers to lice, and it is found in almost all cases that the genome of the louse is highly correlated with the genome of its host. In fact the phylogenetic trees of hosts and parasites have similar topology (structure) which shows the correlation between mutations. This is one evidence that the fast paced evolution of a system with shorter generation time is able to adapt quickly to changes in the long paced one.