Biomath 201 Comprehensive Exam (T. Chou), August 28, 2018

Show all your work *neatly*, *clearly*, and *systematically*. You are allowed all notes that you have written or typed yourself. Moreover, you are allowed to choose two textbooks after the 30min perusal period. Return this copy of the exam with your blue book(s).

1. **Mood dynamics and bipolar disorder**: Consider the following simple model for mood and expectation:

$$\frac{\mathrm{d}m(t)}{\mathrm{d}t} = a_m(m-(v-r)) - km + k_3m^3 \tag{1}$$

$$\frac{\mathrm{d}v(t)}{\mathrm{d}t} = a_v(m-(v-r)) \tag{2}$$

where $m(t)$ and $v(t)$ represent, in some suitable units, the mood and expectation of an individual. The term k_3m^3 is included simply to prevent blow-up. The function $r(t)$ represents reality and is externally determined. Henceforth, assume $r(t)=0$.

(a) Assume $a_m, k, k_3 > 0$ and find all steady states (m^*, v^*).

(b) Linearize the equations about the steady states, and solve for $m(t)$ and $v(t)$ assuming an arbitrary initial condition $m(0), v(0)$. Consider the $(0,0)$ steady state, and explicitly determine the conditions necessary for oscillations to occur.

(c) Now suppose that the coefficient $a_m > 0$ is discontinuous and takes on the value $a_m^+ > 0$ for $m > v$ and $a_m^- > 0$ for $m < v$. Develop a complete stability analysis in this case. Note that the system may be stable or unstable within each half-plane, $m > v$ or $m < v$. Explicitly describe how you would determine the overall stability of the problem. What are the criteria on the parameters, including $a_m^{\pm}$, for overall stability? Note that it is possible for the dynamics to be oscillatory in one $m-v$ half-plane while monotonic (stable or unstable) in the other. Work out as many cases as you can.

2. **Competing Birth-death-immigration process**: Consider the following deterministic model for a two-species birth-death-immigration process:

$$\frac{\mathrm{d}n_1(t)}{\mathrm{d}t} = a_1 + r_1\left(1-\frac{N(t)}{K_1}\right)n_1 \tag{3}$$

$$\frac{\mathrm{d}n_2(t)}{\mathrm{d}t} = a_2 + r_2\left(1-\frac{N(t)}{K_2}\right)n_2 \tag{4}$$

where $N(t) = n_1(t) + n_2(t)$ is the total population (dimensionless number), $a_{1,2}$ are constant immigration rates, $r_{1,2}$ are intrinsic proliferation rates, and $K_{1,2}$ are carrying capacities

(a) Find approximate analytic expressions for the steady-state populations n_1^* and n_2^*. Assume $a_{1,2}$ and $r_{1,2}$ are $O(1)$, while $K_1, K_2 \gg 1$. Describe how the steady-state values depend on the parameters. Hint: since we are concerned with steady state, nondimensionalize away a pair of rates in the two equations, derive approximations for n_1^* and n_2^* in terms of each other, and determine which roots make sense. Alternatively, express n_1^* and n_2^* in terms of $N^* = n_1^* + n_2^*$, and find a cubic equation for N^*. Use asymptotic analysis to find physical roots of N^* and then recover $n_{1,2}^*$. A simple check is to set $K_1 = K_2 = K$.

(b) Now assume that $r_1 = r_2 = r$ and $K_1, K_2 \gg 1$, $K_1 \neq K_2$, but that $K_1/K_2 = 1 \pm \varepsilon$ where $\varepsilon \ll 1$. Find an analytic approximation to $n_1(t)$ and $n_2(t)$ for small $a_{1,2}$ and initial condition $n_1(0) = n_2(0) = 0$. Hint: consider different timescales and find approximations for short and long times.

If you need to, you can assume $a_1 = a_2 = a$ to simplify. Try to work out the most general case possible. Note that qualitatively new features arise when $a_1 \neq a_2$ and when $r_1 \neq r_2$.

3. **Spherical tumor model:** Assume that there is a spherical clump of cells that takes up nutrients (such as oxygen) in order to survive and proliferate. Suppose the sphere has radius a and that the nutrient has diffusivity D_0 exterior to the sphere and is fixed far away at concentration $c(r \to \infty) \equiv c_\infty$. The nutrient inside the sphere has diffusivity D_1 (typically $D_1 < D_0$).

   (a) Assume that the consumption rate of nutrients by the cells is $kc(r)$, proportional (k is a constant) to the nutrient concentration at position r inside the clump. Derive the steady-state (static) concentration field everywhere, and draw the profile. First formulate the complete mathematical problem, define and give units to all the parameters used, and nondimensionalize if you wish. Hints: Recall the form of the solutions to Kelvin's equation in 3D are $e^{\pm\sqrt{k}r}/r$. Consider the spatial variation of the concentration profile at $r = 0$ and impose a flux conservation condition across $r = a$. Impose all physical constraints to determine the concentration at $r = a$.

   (b) The cells can proliferate if they have access to nutrient but will die if they don't. Define the effective local proliferation rate as $g[c(r)] = g_0(c(r) - c_0)$ for $c(r) > c_0$, where c_0 is a critical nutrient above which the cells divide and grow and below which the cells die (negative effective growth rate). Assume that the density of cells is constant and that each cell has volume v. Thus, the number of cells in a spherical shell with radius r and thickness dr is $4\pi r^2 v^{-1} dr$. Cells that die are quickly removed from the sphere. Assume spherical symmetry in all quantities and processes. Find the condition for static sphere size a^*. Is this clump radius stable? Hint: Assume growth or death in each spherical shell of thickness dr and integrate over the entire sphere. Keep in mind that the concentration field $c(r)$ in $g[c(r)]$ depends implicitly on a^*.