Exam Biological Modeling (B-B2THEC05 & B-MBIMOD) **11 January 2024**

Question 1. Basic skills (10 points)

a. Compute the non-trivial steady state of the following model,

$$\frac{\mathrm{d}X}{\mathrm{d}t} = a - bX - cXY \quad \text{and} \quad \frac{\mathrm{d}Y}{\mathrm{d}t} = cXY - dY \ .$$

$X = d/c$ and $Y = a/d - b/c$.

b. Define $f(X,Y) = \mathrm{d}X/\mathrm{d}t = a - bX - cXY$. What are the partial derivatives of $f(X,Y)$ with respect to X and Y?

$\partial_X f() = -b - cY$ and $\partial_Y f() = -cX$

c. Sketch the nullcline of $\mathrm{d}X/\mathrm{d}t = a - bX - cXY$ in the positive domain. Help yourself by searching for horizontal and vertical asymptotes, and intersection points with the axes (show these results).

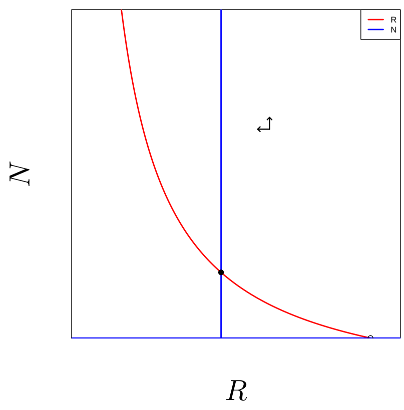
See the resource nullcline in Fig. 5.1. The vertical axis is a vertical asymptote. The horizontal asymptote is $Y = -b/c$, and the nullcline intersects the horizontal axis at $X = a/b$.

d. Sketch the output of the following script:

```
model <- function(t, state, parms) {
  with(as.list(c(state,parms)), {
    dx <- a*x + b*y
    dy <- c*x + d*y
    return(list(c(dx, dy)))
  })
}
p <- c(a=-2,b=1,c=1,d=-2)
s <- c(x=0,y=0)
plane()
```

The plot shows a red line with slope $2x$ and a blue line with slope $0.5x$, both originating in the origin.

e. Determine the stability of the steady state indicated by the bullet in the following resource, R, consumer, N, model using a graphical Jacobian. **Don't forget to show this Jacobian!**



The signs of the Jacobian are $J = \begin{pmatrix} - & - \\ + & 0 \end{pmatrix}$.

Question 2. Essential resources (10 points)

For a consumer requiring sufficient consumption of two resources for its reproduction we have written:

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \left(\beta \ \frac{c_1 R_1}{h_1 + c_1 R_1} \ \frac{c_2 R_2}{h_2 + c_2 R_2} - \delta\right) N \ ,$$

where β is a maximum birth rate per day, δ defines the daily death rate, and the $c_i R_i$ terms define the daily amount of resource ingested per consumer.

a. What is the parameter h_1 representing in biological terms?

When $c_1 R_1 = h_1$ (and $c_2 R_2 \gg h_2$) the birth rate is $\beta/2$. In other words, h_1 is the daily consumption of R_1 required for a half-maximal birth rate.

b. What is the minimum concentration of R_1 that this species requires to maintain itself?

Sending $R_2 \to \infty$ and solving

$$\beta \frac{c_1 R_1}{h_1 + c_1 R_1} - \delta > 0 \quad \text{yields} \quad R_1 > \frac{h_1}{c_1(\beta/\delta - 1)} \ .$$

c. Would it be possible for a second species with a lower fitness, $R_{0_2} = \beta_2/\delta_2 < R_{0_1} = \beta/\delta$, to invade into the non-trivial steady state of R_1, R_2 and N_1? Explain your answer in less than 50 words.

Yes, this is possible when the second species had higher consumption rates and/or lower saturation constants.

Question 3. Bacterial cross-feeding (10 points)

We discussed the following model for cross-feeding in the book. For simplicity each bacterial species feeds upon a unique resource in this model:

$$\begin{aligned}\frac{\mathrm{d}N_i}{\mathrm{d}t} &= (1-\alpha_i) b_i R_i N_i - w N_i \ , \\ \frac{\mathrm{d}R_i}{\mathrm{d}t} &= w(\hat{R}_i - R_i) - b_i R_i N_i + \sum_j S_{ij} \alpha_j b_j R_j N_j \ ,\end{aligned}$$

where R_i defines the concentration of resource i in a chemostat, N_i defines the scaled concentration of bacteria consuming resource i, b_i is a mass-action consumption rate (also defining the birth rate of the consumer), α_i defines a fractional "leakage" parameter of metabolic byproducts, and w is the wash-out rate from the chemostat. The $\hat{R}_i$ parameters define the concentration of resource i in the fluid flowing into the chemostat (where $\hat{R}_i = 0$ for the metabolic byproducts). Finally, the stoichiometric matrix S_{ij} defines whether the ith metabolic byproduct is produced when metabolite j is consumed.

Construct a specific example of this model for the situation with a single resource in the source, e.g., table sugar (saccharose), which is bi-saccharide composed of glucose and fructose, and a bacterial species using half of this sugar (e.g., glucose) for this own growth, while leaking the other (e.g., fructose) into the environment. Define a second bacterial species fully using the other component (e.g., fructose) for its growth. In the original model the contribution of compounds within a resource was scaled by their energy content, which had to be conserved, i.e., $\alpha_i < 1$. Here we can assume that the two components are equally nutritious, i.e., $\alpha_1 = 0.5$. Define the new model by writing out all equations and removing the sum term.

The equations for the resources are

$$\frac{\mathrm{d}R_1}{\mathrm{d}t} = w(\hat{R}_1 - R_1) - b_1 R_1 N_1 \quad \text{and} \quad \frac{\mathrm{d}R_2}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - b_2 R_2 N_2 - w R_2 \ ,$$

while those for the bacteria are

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - w N_1 \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = b_2 R_2 N_2 - w N_2 \ ,$$

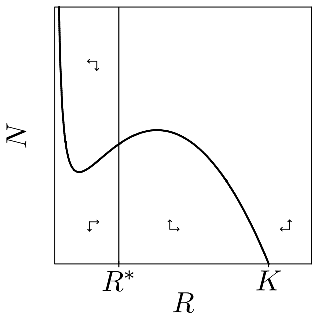
where R_1 is the bi-saccharide, R_2 is fructose, N_1 grows on glucose and N_2 grows on fructose, and $\alpha = 0.5$. Note by scaling differently we can also set $\alpha = 1$.

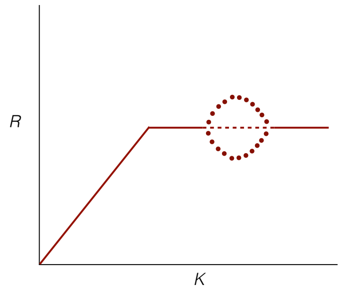
Question 4 for bachelor students (10 points)

We used the sigmoid predator-prey model to illustrate several bifurcations:

$$\frac{\mathrm{d}R}{\mathrm{d}t} = rR(1 - R/K) - \frac{aR^2 N}{h^2 + R^2} \quad \text{en} \quad \frac{\mathrm{d}N}{\mathrm{d}t} = \frac{caR^2 N}{h^2 + R^2} - dN \ .$$

An example of its nullclines are shown on the left, a bifurcation diagram is shown on the right:





We have covered the following bifurcations: Hopf, transcritical, saddle-node and pitchfork. Name all bifurcations that you see happening in the bifurcation diagram when K is increased (name them in the correct order). Shortly explain what happens for each of these bifurcations (e.g., provide little sketches).

Transcritical: the predator can invade, Hopf: the non-trivial stable spiral point becomes unstable, and Hopf: the unstable non-trivial spiral point becomes stable.

Question 4 for master students: Make a model (10 points)

Consider bacteria that are introduced into a closed well-mixed medium. The medium contains K μg of an essential compound that is incorporated when bacteria divide. This division rate is limited by this compound, and obeys a conventional Monod saturation. Each bacterium contains $c \ll K$ μg of this compound and all of this is released when they die. The bacteria produce a toxin that increases their own death rate. Write a natural model for the concentration of the compound, the bacteria, and the toxin in the medium.

Free nutrients: $F = K - cB$. Toxin: $\mathrm{d}T/\mathrm{d}t = pB - \delta T$. Bacteria: $\mathrm{d}B/\mathrm{d}t = \frac{bBF}{h+F} - dB(1 + eT)$