1 Introduction

This Document goes through the work for the research done for this project

2 Model Assumptions

- **Logistic Growth for Pathogens:** The pathogen population grows logistically, meaning that its growth rate slows as the population approaches a maximum carrying capacity.
- **Abiotic Growth for Macrophages:** Macrophages are generated at a constant rate, regardless of the pathogen population.
- **One-to-One Killing:** It is assumed that each interaction results in one macrophage killing one pathogen, and thus one macrophage dying in the process.
- **Interaction Term:** The interaction between macrophages and pathogens is quantified by the term $\mu\, M\, P$, where μ is a constant representing the hunting rate at which macrophages hunt and kill pathogens, and $\mu\, M\, P$ represents that the macrophages hunt pathogens at a rate proportional to each others population.

3 Mathematical Model

$$\frac{dM}{dt} = \delta - \sigma\, M - \mu\, M\, P, \tag{1}$$

$$\frac{dP}{dt} = \alpha\, P \left(1 - \frac{P}{\beta}\right) - \mu\, M\, P, \tag{2}$$

4 Parameter Definitions

The model includes five parameters, defined as follows:

δ The constant rate at which macrophages are generated

σ The natural death rate of macrophages.

α The growth rate of pathogens.

β The carrying capacity of pathogens.

μ The rate at which macrophages hunt pathogens

5 Scaling to two dimensions

Introduce the dimensionless variables

$$p = \frac{P}{\beta}, \quad g = \frac{G}{\delta/\sigma}, \quad t = \alpha\, T,$$

so that

$$P = \beta\, p, \quad G = \frac{\delta}{\sigma}\, g, \quad \frac{d}{dT} = \alpha\, \frac{d}{dt}.$$

Substitute into the original system

$$\frac{dP}{dT} = \alpha\, P\Big(1 - \frac{P}{\beta}\Big) - \mu\, P\, G, \quad \frac{dG}{dT} = \delta - \sigma\, G - \mu\, P\, G,$$

to obtain

$$\beta\, \alpha\, \frac{dp}{dt} = \alpha\, \beta\, p\,(1-p) - \mu\, \beta\, p\, \frac{\delta}{\sigma}\, g,$$

$$\frac{\delta}{\sigma}\, \alpha\, \frac{dg}{dt} = \delta - \sigma\, \frac{\delta}{\sigma}\, g - \mu\, \beta\, p\, \frac{\delta}{\sigma}\, g.$$

Divide through by the variables on the left and define

$$r = \frac{\mu\, \delta}{\alpha\, \sigma}, \quad b = \frac{\sigma}{\alpha}, \quad m = \frac{\mu\, \beta}{\alpha},$$

to arrive at the scaled two–dimensional system:

$$\boxed{\begin{aligned} \frac{dp}{dt} &= p\,(1-p) - r\, p\, g, \\ \frac{dg}{dt} &= b\,\big(1 - g - m\, p\, g\big). \end{aligned}}$$

6 2D Scaled Equations

$$\boxed{\frac{dp}{dt} = p\,(1 - p - r\, g)}$$

$$\boxed{\frac{dg}{dt} = b(1 - g - m\, g\, p).}$$

7 Analysis of the 2D System

7.1 Number of Solutions

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

$$\frac{dg}{dt} = b(1 - g - mpg)$$

With our given nullclines

$$g = \frac{1-p}{r}$$

$$g = \frac{1}{1+mp}$$

Setting them equal to each other and solving, we get this equation

$$mp^2 - (m-1)p + (r-1) = 0$$

Looking at the discriminant, we find these conditions for a certain number of solutions.

$$\#\{\text{equilibria}\} = \begin{cases} 2, & r > 1 \text{ and } r < \dfrac{(m+1)^2}{4m}, \\ 1, & r = 1 \text{ or } r = \dfrac{(m+1)^2}{4m}, \\ 0, & r < 1 \text{ or } r > \dfrac{(m+1)^2}{4m}. \end{cases}$$

7.1.1 Two Solutions

Parameters

$$a = 2, \quad b = 2, \quad k = 8$$

Condition check:

$$b > 1 \quad \Longrightarrow \quad 2 < \frac{(8+1)^2}{4 \cdot 8} = \frac{81}{32} \approx 2.53$$

7.1.2 One Solution

Parameters

$$a = 1, \quad b = \tfrac{16}{7}, \quad k = 7$$

Condition check:

$$b \neq 1 \quad \Longrightarrow \quad \frac{16}{7} = \frac{(7+1)^2}{4 \cdot 7} = \frac{64}{28} = \frac{16}{7} \approx 1.56$$

7.1.3 No Solutions

Parameters

$$a = 1, \quad b = 2, \quad k = 4$$

Condition check:

$$b > 1 \quad \Longrightarrow \quad 2 > \frac{(4+1)^2}{4 \cdot 4} = \frac{25}{16} \approx 1.56$$

7.2 Jacobian and Equilibria

The Jacobian for the 2D system

$$J(p,g) = \begin{pmatrix} (1-p-rg)-p & -rp \\ -bmg & -b(1+mp) \end{pmatrix}.$$

7.2.1 Disease-free equilibrium

At $(p,g) = (0,1)$

$$J(0,1) = \begin{pmatrix} 1-r & 0 \\ -bm & -b \end{pmatrix}, \quad \lambda_1 = 1-r,\ \lambda_2 = -b.$$

Stable if $r > 1$ (so both eigenvalues are negative).

7.2.2 Routh–Hurwitz criterion (Endemic equilibrium)

At (p^*, m^*) satisfying nullclines

$$1-p-bm = 0, \quad 1-m-kmp = 0,$$

with

$$m^* = (1-p^*)/b, \quad g^* = 1/(1+kp^*).$$

Jacobian becomes

$$J(p^*, m^*) = \begin{pmatrix} -ap^* & -abp^* \\ -km^* & -1-kp^* \end{pmatrix},$$

trace and determinant:

$$\mathrm{tr} = -ap^* - 1 - kp^* < 0, \quad \det = ap^*(1+kp^*) - akp^*(1-p^*).$$

Stability when $\det > 0$ and $r < 0$.

8 Coefficients Explained

ϕ The growth rate of specialist macrophages

η The pathogen level at which the specialist macrophage production rate is half of its maximum

ψ The death rate of specialist macrophages

δ The growth rate of generalist macrophages

σ The death rate of generalist macrophages

μ The rate at which macrophages hunt and destroy pathogens (and themselves in the process)

α The intrinsic growth rate of the pathogen

β The carrying capacity of the pathogen population

κ The rate at which specialist macrophages hunt and destroy pathogens

9 Equations

Specialist Equation

$$\frac{dS}{dT} = \frac{\phi P}{\eta + P} - \psi S$$

Generalist Equation

$$\frac{dG}{dT} = \delta - \sigma G - \mu G P$$

Pathogen Equation

$$\frac{dP}{dT} = \alpha P\Big(1 - \frac{P}{\beta}\Big) \; - \; \mu G P \; - \; \kappa S P$$

10 Scaling to three dimensions

$$g = \frac{G}{\delta/\sigma}, \quad p = \frac{P}{\beta}, \quad s = \frac{S}{\phi/\psi}, \quad t = \alpha T$$

$$G = \frac{\delta}{\sigma} g, \quad P = \beta p, \quad S = \frac{\phi}{\psi} s, \quad T = t/\alpha, \quad dT = dt/\alpha, \quad \frac{d}{dT} = \alpha \frac{d}{dt}$$

Dimensionless equations:

$$\frac{ds}{dt} = a\Big(\frac{p}{h+p} - s\Big), \quad \frac{dg}{dt} = b(1 - g - mpg), \quad \frac{dp}{dt} = p(1-p) - rpg - kps.$$

11 3D Model Analysis

11.1 3D Nullclines

$1-g-mgp = 0 \implies g = 1/(1+mp), \quad p/(h+p)-s = 0 \implies s = p/(h+p), \quad 1-p-rg-ks = 0.$

11.2 Full cubic for p^*

Equilibrium equation becomes

$$-mp^{*3} + (m - 1 - hm - km)p^{*2} + (1 - h + hm - r - k)p^* + h(1-r) = 0.$$

12 M(p) and R(P,M)

The Nullclines

$$1 - g - mgp = 0 \implies g = \frac{1}{1 + mp}$$
$$s = \frac{p}{h + p}$$
$$1 - p - rg - ks = 0 \quad \text{or}$$

Given

From this, we can see

$$rg = 1 - p - \frac{kp}{h + p}$$
$$rg = \frac{r}{1 + mp}$$
$$(rg)' = -1 - \frac{(k(h + p) - (kp))}{(h + p)^2} = -1 - \frac{kh}{(h + p)^2}$$
$$rg' = \frac{-rm}{(1 + mp)^2}$$

r(m,p)

From combing the two rg equtaions we can see

$$\boxed{r(m, p) = (1 - p - \frac{kp}{h + p})(1 + mp)}$$

Setting up

$$rg' = \frac{-rm}{(1+mp)^2} = -1 - \frac{kh}{(h+p)^2}$$

trying now to manipulate the rg equations to get something in the equivalent form for rg'

$$\frac{r}{1+mp} = 1 - p - \frac{kp}{h+p}$$

$$\frac{-rm}{1+mp} = -m(1 - p - \frac{kp}{h+p})$$

From rg' multpling by $(1+mp)$

$$rg' = \frac{-rm}{(1+mp)} = (-1 - \frac{kh}{(h+p)^2})(1+mp)$$

Now we have

$$\frac{-rm}{(1+mp)} = -m(-1 - \frac{kh}{(h+p)^2})$$

and

$$\frac{-rm}{1+mp} = (-1 - \frac{kh}{(h+p)^2})(1+mp)$$

combing them gives

$$-m(1 - p - \frac{kp}{h+p}) = (-1 - \frac{kh}{(h+p)^2})(1+mp)$$

Solving for m(p)

$$-m + mp + \frac{kmp}{h+p} = -1 - \frac{kh}{(h+p)^2} - mp - \frac{mkph}{(h+p)^2}$$

$$-m + mp + \frac{kmp}{h+p} + mp + \frac{mkph}{(h+p)^2} = -1 - \frac{kh}{(h+p)^2}$$

$$m(-1 + 2p + \frac{kp}{h+p} + \frac{khp}{(h+p)^2}) = -1 - \frac{kh}{(h+p)^2}$$

$$m(p) = \frac{-1 - \frac{kh}{(h+p)^2}}{(-1 + 2p - \frac{kp}{h+p} + \frac{khp}{(h+p)^2})}$$

mutiplying by negative one

$$\boxed{m(p) = \frac{1 + \dfrac{k\,h}{(h+p)^2}}{1 - 2p - \dfrac{k\,p}{h+p} - \dfrac{k\,h\,p}{(h+p)^2}}}$$

Final Equations

$$r(m,p) = (1 - p - \frac{kp}{h+p})(1 + mp)$$

$$m(p) = \frac{1 + \frac{kh}{(h+p)^2}}{1 - 2p - \frac{kp}{(h+p)} - \frac{khp}{(h+p)^2}}$$