

# Population Dynamics of Bacteria inside Humans

Battle of Bacteria, Antibiotics and Immune system

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# Outline

- 1 Introduction
- 2 Dynamic Model
- 3 Equilibria
- 4 Stability Analysis
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- Bacteria lives inside us
- Some of them unwanted
- Antibiotics to get rid of them
- interactions lead to different equilibria

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# Variable Definitions

$A$  : Concentration of Antibiotics

$S$  : Biomass of Non-Antibiotic-Resistant Bacteria

$R$  : Biomass of Antibiotic-Resistant Bacteria

$P$  : Immune Cell Population

$N$  :  $S + R$  total bacteria

$\Psi$  and  $\Phi$  : functions in  $\mathcal{C}^1(\mathbb{R}_+)$

# Model Equations

## Modified Logistic Model

$$\dot{A}(t) = \Lambda - \mu A,$$

$$\dot{S}(t) = \eta_s \left(1 - \frac{S+R}{K}\right) S - \bar{\alpha} AS - \beta \frac{SR}{N} - \Gamma SP,$$

$$\dot{R}(t) = \eta_r \left(1 - \frac{S+R}{K}\right) R + \beta \frac{SR}{N} - \Gamma RP,$$

$$\dot{P}(t) = \Phi(N)P \left(1 - \frac{P}{P_{\max}}\right) - \Psi(N)P,$$

# Parameter and Term Definitions

$\Lambda$  : administration rate of Antibiotics

$\mu$  : absorption rate of Antibiotic

$\eta_S$  and  $\eta_R$  : reproduction rate of  $S$  and  $R$

$K$  : carrying capacity (Limiting the reproduction)

$\Gamma$  : transfer rate of resistant gene

$P_{\max}$  : limit of proliferation of immune cells

# Key Assumptions

- $\eta_S > \eta_R$  cost of resistance
- Resistance genes transfer  $\beta \frac{SR}{N}$
- Immune response  $\Gamma_{SP} \Gamma_{RP}$

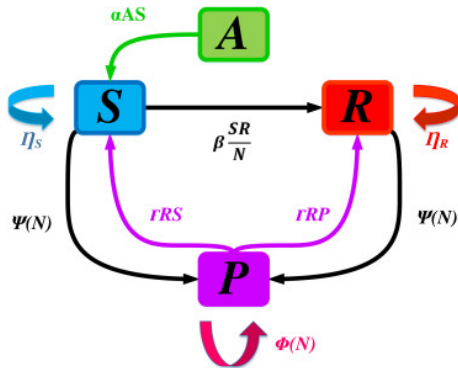


Fig. 1: Schematic Diagram [1]



# Transformation

$$a = \frac{A}{A/\mu} \quad s = \frac{S}{K} \quad r = \frac{R}{K} \quad p = \frac{P}{P_{\max}}$$
$$\alpha = \frac{\bar{\alpha}A}{\mu} \quad \gamma = \Gamma P_{\max} \quad n = s + r \quad \phi(n) = \Phi(Kn) \quad \psi(n) = \Psi(Kn)$$

$$\dot{a}(t) = \mu(1 - a)$$

$$\dot{s}(t) = \eta_s(1 - n)s - \alpha as - \beta \frac{sr}{n} - \gamma sp$$

$$\dot{r}(t) = \eta_r(1 - n)r + \beta \frac{sr}{n} - \gamma rp$$

$$\dot{p}(t) = \phi(n)p(1 - p) - \psi(n)p$$

# Boundedness

- $\mathbb{R}_+^4 = \{(a, s, r, p) \in \mathbb{R}^4 \mid a \geq 0, s \geq 0, r \geq 0, p \geq 0\}$
- Right hand side of our system  $\in \mathcal{C}^1(\text{Int}(\mathbb{R}_+^4), \mathbb{R}_+^4)$
- Unique Solution exists  $\in [0, T_{\max}]$
- $\mathcal{A} = \{(a, s, r, p) \in \text{Int}(\mathbb{R}_+^4), a \leq 1, s + r \leq 1, p \leq 1\}$
- lemma:  $\mathcal{A}$  is positively invariant with respect to 1
- hence mathematically and biologically well posed

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Analysing reveals 4 Equilibria - biologically meaningful

- clearance of infection
- infection under  $S$
- infection under  $R$
- infection under both

# deriving Equilibria

- Equilibria  $\equiv$  Zero Change  $\equiv \dot{\mathbf{X}} = \vec{0}$
- let  $f(n) = 1 - \frac{\psi(n)}{\phi(n)}$  with  $f(0) > 0$  and simplify
- we want  $f \uparrow$  for small  $n$  and  $f \downarrow$  for large  $n$  (How Immunity works)
- $f$  either remains  $+$  or after a threshold drops  $< 0$
- we focus on 2nd scenario (remember  $n$  is bounded )

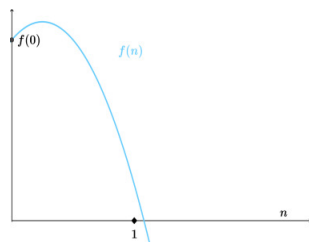


Fig. 2: Schematic Rep. of what  $f$  can be [1]

$$\mu(1 - a) = 0$$

$$a = 1$$

$$\eta_s(1 - n)s - \alpha as - \beta \frac{sr}{n} - \gamma sp = 0$$

$\Rightarrow$

$$s = 0 \quad \text{or} \quad \eta_s(1 - n) - \alpha - \beta \frac{r}{n} - \gamma p = 0$$

$$\eta_r(1 - n)r + \beta \frac{sr}{n} - \gamma rp = 0$$

$$r = 0 \quad \text{or} \quad \eta_r(1 - n) + \beta \frac{s}{n} - \gamma p = 0$$

$$\phi(n)p(f(n) - p) = 0$$

$$p = 0 \quad \text{or} \quad p = f(n)$$

# Equilibria

## 7 Cases

- Case 1:  $E_0(1, 0, 0, 0)$   $r = s = p = 0$
- Case 2:  $E_1(1, 0, 0, f(0))$   $r = s = 0$  ,  $p \neq 0$
- Case 3:  $E_2(1, 0, 1, 0)$   $s = p = 0$  ,  $r \neq 0$

# Case 4

Case 4:  $E_+ s = 0$  ,  $r \neq 0$  ,  $p \neq 0$

$$r = \lambda_+ \quad p = f(\lambda_+) \Rightarrow f(r) = \eta_r \frac{1-r}{\gamma}$$

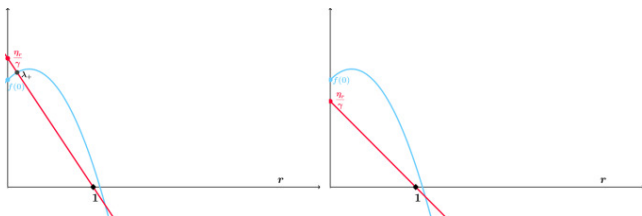


Fig. 3:  $f$  and  $\lambda_+$  [1]

if  $f(0) < \frac{\eta_r}{\gamma}$  exists Unique  $0 < \lambda_+ < 1$

## Case 5 an 6

- Case 5  $E_3(1, 1 - \frac{\alpha}{\eta_s}, 0, 0)$   $s \neq 0$  ,  $r = 0$  ,  $p = 0$
- Case 6  $E_-$   $s \neq 0$  ,  $r = 0$  ,  $p \neq 0$

$$s = \lambda_- \quad , \quad p = f(\lambda_-) \Rightarrow f(s) = \frac{\eta_s - \alpha}{\gamma} - \frac{\eta_s}{\gamma}s$$

Like Case 4 if  $f(0) < \frac{\eta_s - \alpha}{\gamma}$  exists Unique  $0 < \lambda_- < 1$



## Case 7: $E_*$

$$s \neq 0, r \neq 0, p \neq 0$$

$$n_* = s + r = 1 - \frac{\alpha + \beta}{\eta_s - \eta_r}$$

$$n_* > 0 \text{ if } \alpha + \beta + \eta_r < \eta_s$$

$$p_* = f(n_*)$$

$$s_* = \frac{n_*}{\beta} \left( \gamma f(n_*) - \eta_r \frac{\alpha + \beta}{\eta_s - \eta_r} \right)$$

$$r_* = \frac{n_*}{\beta} \left( \eta_s \frac{\alpha + \beta}{\eta_s - \eta_r} - \alpha - \gamma f(n_*) \right)$$

$$p_*, s_*, r_* > 0 \quad \text{if} \quad \eta_r \frac{\alpha + \beta}{\eta_s - \eta_r} < \gamma f(n_*) < \frac{\alpha \eta_r + \beta \eta_s}{\eta_s - \eta_r}$$

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# Linearinzation

- System is non linear,
- Linearinzation around fixed points  $\Rightarrow$  Jacobian Matrix

$$\begin{pmatrix} -\mu & 0 & 0 & 0 \\ -\alpha s & \eta_s(1-n) - \eta_s s - \alpha a - \beta \frac{r^2}{n^2} - \gamma p & -\eta_s s - \beta \frac{s^2}{n^2} & -\gamma s \\ 0 & -\eta_r r + \beta \frac{r^2}{n^2} & \eta_r(1-n) - \eta_r r + \beta \frac{s^2}{n^2} - \gamma p & -\gamma r \\ 0 & \phi(n)(f(n) - p) + \dot{f}(n)p\phi(n) & p\dot{\phi}(n)(f(n) - p) + \dot{f}(n)p\phi(n) & \phi(n)(f(n) - 2p) \end{pmatrix}$$

- let  $C_+ = \eta_s(1 - \lambda_+) - \alpha - \beta$ ,  $C_- = \eta_r(1 - \lambda_-) + \beta$  and

$$C_* = -\frac{(\eta_s s_* + \eta_r r_*) \beta s_* r_* (\eta_s - \eta_r)}{f(n_*)\phi(n_*)(n_*)^2 (\eta_s s_* + \eta_r r_* + f(n_*)\phi(n_*))} - \frac{\eta_s s_* - \eta_r r_*}{\eta_*}.$$

will show up for finding stability criteria

# Stability Table

Table 1: Conditions for the stability of equilibria.

Equilibrium	Biological existence	Stability
$E_0 (1, 0, 0, 0)$	Always exists	Always unstable
$E_1 (1, 0, 0, f(0))$	Always exists	$\alpha > \eta_s$ and $\gamma f(0) > \eta_r$
$E_2 (1, 0, 1, 0)$	Always exists	Always unstable
$E_3 \left(1, 1 - \frac{\alpha}{\eta_s}, 0, 0\right)$	$\eta_s > \alpha$	Always unstable
$E_+ (1, 0, \lambda_+, f(\lambda_+))$	$\eta_r > \gamma f(0)$	$\gamma f(\lambda_+) > C_+$ and $\gamma f(\lambda_+) > \eta_r$
$E_- (1, \lambda_-, 0, f(\lambda_-))$	$\eta_s - \alpha > \gamma f(0)$	$\gamma f(\lambda_-) > C_-$ and $\gamma f(\lambda_-) > \eta_s$
$E_* (1, s_*, r_*, f(n_*))$	$\left\{ \begin{array}{l} \eta_r \frac{\alpha + \beta}{\eta_s - \eta_r} < \gamma f(n_*) < \frac{\eta_r \alpha + \eta_s \beta}{\eta_s - \eta_r} \\ \text{and} \\ \eta_s > \eta_r + \alpha + \beta \end{array} \right.$	$\gamma f(n_*) > C_*$

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# References I

- [1] Imene Meriem Mostefaoui and Abdellatif Seghiour. “Modeling the dynamics of interactions between antibiotic-resistant bacteria and immune response”. In: *Communications in Nonlinear Science and Numerical Simulation* 140 (2025), p. 108412. ISSN: 1007-5704. DOI: <https://doi.org/10.1016/j.cnsns.2024.108412>. URL: <https://www.sciencedirect.com/science/article/pii/S1007570424005975>.



# For Your Attention

*Thank You!*