Modelling Host-Parasite Relationships with Multiple Infection

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Introduction

- In 2021, Scientists in Brazil reported evidence of SARS-CoV-2 multiple infection by distinct strains.

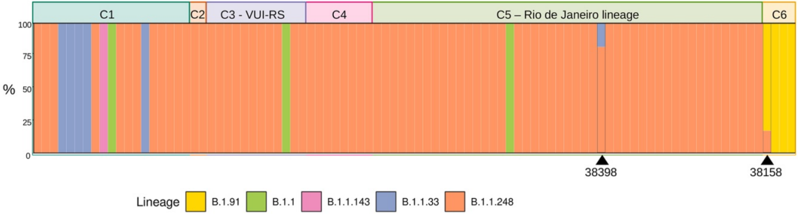


Figure 1: Population structure and intra-host variation amended from Francisco Jr et al., Pervasive transmission of E484K and emergence of VUI-NP13L with evidence of SARS-CoV-2 co-infection events by two different lineages in Rio Grande do Sul, Brazil, 2021, p.198345-198345. Used under a UK Copyright Exception.

Introduction

- **Strain** here refers to a parasite population with a particular characteristic (known as trait).
- Naturally, humans and animals (known as hosts) tend to be infected by different strains of the same parasite species, resulting from separate infecting events or a high mutation rate.

Multiple Infection

- Multiple infection: (in my work it is defined to be) infection caused by multiple strains of the same parasite species.
- Three basic theoretical frameworks have been used to study multiple infection:
  - **Superinfection**: a parasite strain infects hosts alone but can be displaced by one another based on strain traits,
  - **Co-infection**: two or more parasite strains can infect each host simultaneously,
  - **Kin Selection**: the relatedness of strains and the fact that the collective action of co-infecting strains may affect overall virulence are considered.

Virulence

- Virulence: the damage to host fitness caused by infection.
- In the model, virulence is measured as host mortality rate caused by the infection.

Notations

μ	Baseline mortality rate
S	Density of susceptible hosts
I_1	Density of hosts being singly infected
D_{11}	Density of hosts being co-infected
ρ	Host input (birth rate)
α_1	Virulence of a host being singly infected
α_{11}	Virulence of a host being co-infected
β_1	Transmission rate in single infection
β_{11}	Transmission rate of the strain in a host being co- infected
σ_S	Vulnerability of susceptible hosts to infection
σ_I	Vulnerability of infected hosts to a new infection
λ_1	The force of infection of the strain

- the force of infection of the strain, λ_1, is defined as $\lambda_1 = \beta_1 I_1 + \beta_{11} D_{11}$.

The Model

- The population dynamics of the strain in a co-infection situation can be governed by the following equations:

$$\frac{dS}{dt} = \rho - \mu S - \sigma_S \lambda_1 S, \tag{1}$$

$$\frac{dI_1}{dt} = \sigma_S \lambda_1 S - (\mu + \alpha_1 + \sigma_I \lambda_1) I_1, \tag{2}$$

$$\frac{dD_{11}}{dt} = \sigma_I \lambda_1 I_1 - (\mu + \alpha_{11}) D_{11}, \tag{3}$$

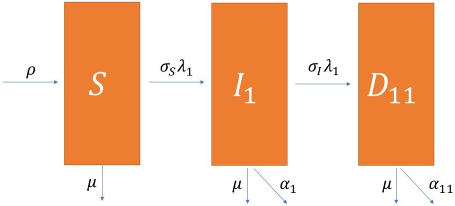


Figure 2: Schematic diagram of the model.

The Trade-off

- **The trade-off between transmission and virulence**: increasing parasite abundance can increase transmission but also may increase host death.
- Mathematically, mortality rate caused by infection can be made an increasing function of transmission rate.

The trade-off function

- The trade-off function takes the form

$$\alpha(\beta) \;=\; \alpha(\beta^*) - \frac{\alpha'(\beta^*)^2}{\alpha''(\beta^*)}\left[1 - \exp\left(\frac{\alpha''(\beta^*)(\beta-\beta^*)}{\alpha'(\beta^*)}\right)\right]. \qquad (4)$$

The trade-off function

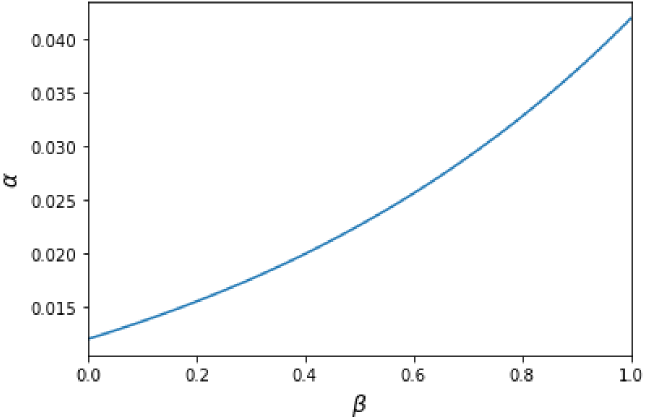


Figure 3: Graph of the trade-off function, with parameters fixed as follows: $\beta^* = 0.4$, $\alpha(\beta^*) = 0.02$, $\alpha'(\beta^*) = 0.025$, $\alpha''(\beta^*) = 0.03$.

Results

- When the population dynamics reach equilibrium, there are 3 scenarios of interest: **existence of both infected host types**, **disease-free** and **single infection only**.

Scenario I: Existence of both infected host types

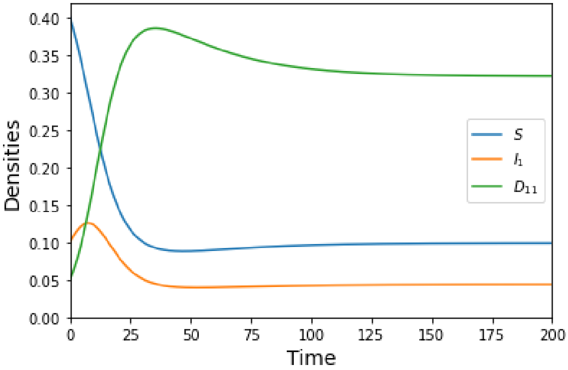


Figure 4: Coexistence of singly infected and co-infected hosts, with parameters $\rho = \mu = 0.012$, $\beta_1 = \beta_{11} = 0.3$, $\sigma_S = 1$, $\sigma_I = 2$.

Scenario II: Disease-free

- The disease-free case may occur when the transmission rate is too low or,

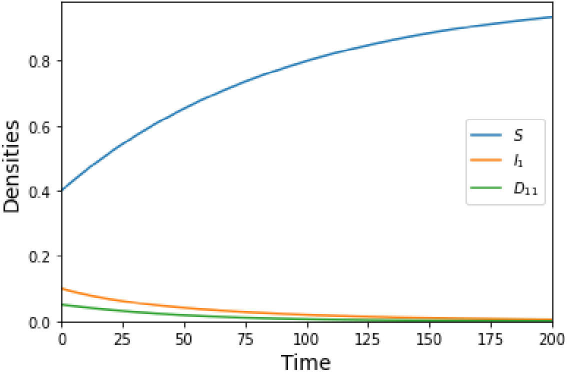


Figure 5: Disease-free case with low transmission rate, with parameter $\rho = \mu = 0.012$, $\beta_1 = \beta_{11} = 0.01$, $\sigma_S = 1$, $\sigma_I = 2$.

Scenario II: Disease-free

- when the background mortality rate is too high or,

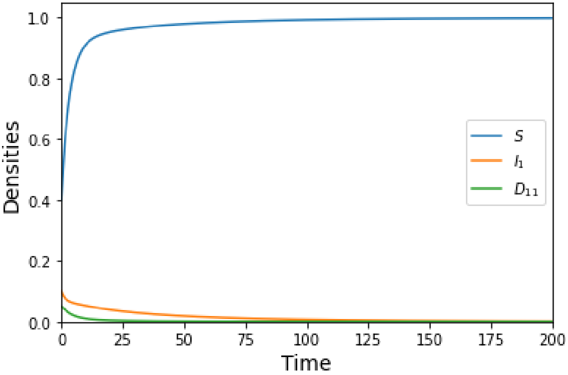


Figure 6: Disease-free case with high background mortality rate, with parameter $\rho = \mu = 0.3$, $\beta_1 = \beta_{11} = 0.3$, $\sigma_S = 1$, $\sigma_I = 2$.

Scenario II: Disease-free

- when the vulnerability of susceptible hosts is too low.

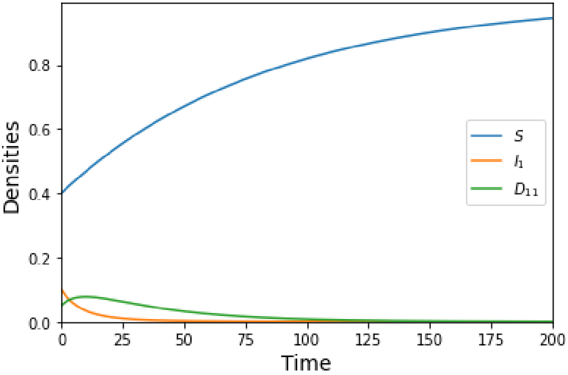


Figure 7: Disease-free case with low vulnerability of susceptible host, with parameter $\rho = \mu = 0.012$, $\beta_1 = \beta_{11} = 0.3$, $\sigma_S = 0.001$, $\sigma_I = 2$.

Scenario III: Single infection only

- The single-infection-only case may occur when it is hard for singly infected hosts to be infected again, i.e. the vulnerability of infected hosts is low.

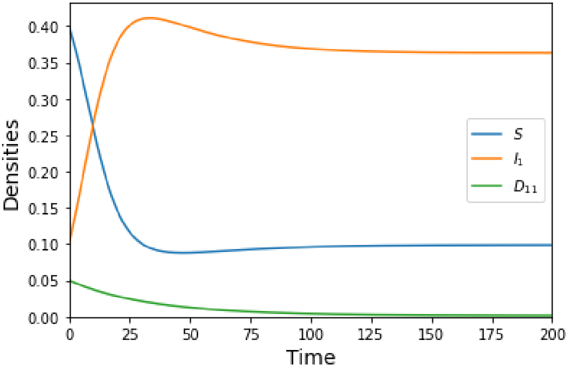


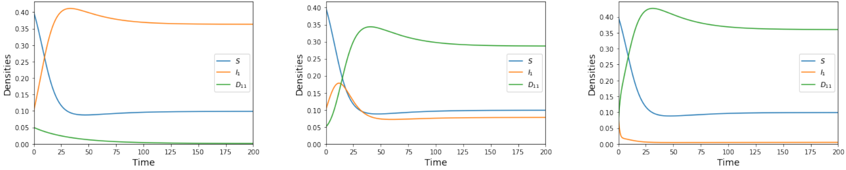
Figure 8: Single-infection-only case, with parameter $\rho = \mu = 0.012$, $\beta_1 = \beta_{11} = 0.3$, $\sigma_S = 1$, $\sigma_I = 0.001$.

Extension: Hosts vulnerability

- σ_S and σ_I: two new parameters which quantify the vulnerability of susceptible and infected hosts to a new infection.

Extension: Hosts vulnerability

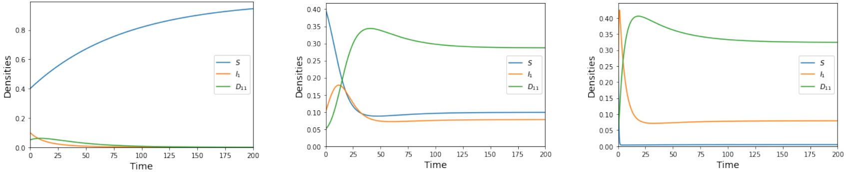
- The proportion of co-infected hosts decreases (increases) if the infected hosts are less (more) vulnerable to further infection.



(a) (b) (c)

Figure 9: (a): $\sigma_S = 1$, $\sigma_I = 0.001$; (b): $\sigma_S = 1$, $\sigma_I = 1$; (c): $\sigma_S = 1$, $\sigma_I = 20$.

- The fraction of susceptible hosts increases (decreases) as the vulnerability of susceptible hosts decreases (increases).



(a) (b) (c)

Figure 10: (a): $\sigma_S = 0.001$, $\sigma_I = 1$; (b): $\sigma_S = 1$, $\sigma_I = 1$; (c): $\sigma_S = 20$, $\sigma_I = 1$.

Extension: Micro-parasite vs. Macro-parasite

- **Micro-parasites**: D_{11} hosts resemble singly infected host, and α_{11} is the same as virulence caused by single infection,
- **Macro-parasites**: D_{11}, the density of hosts being co-infected, can be regarded as hosts with a double parasite load.

- In the analysis above, it is assumed that the parasite is micro-parasite. For the macro-parasite, the population dynamics does not vary greatly from that in micro-parasite case, i.e. it also has the similar three scenarios.

Extension: Model with recovery

- Assume that both the singly infected and co-infected hosts can recover to susceptible class with recovery rate γ_1 and γ_{11} respectively, and can be reinfected.

Extension: Model with recovery

$$\frac{dS}{dt} = \rho + \gamma_1 I_1 + \gamma_{11} D_{11} - (\mu - \sigma_S \lambda_1) S, \tag{5}$$

$$\frac{dI_1}{dt} = \sigma_S \lambda_1 S - (\mu + \alpha_1 + \sigma_I \lambda_1 + \gamma_1) I_1, \tag{6}$$

$$\frac{dD_{11}}{dt} = \sigma_I \lambda_1 I_1 - (\mu + \alpha_{11} + \gamma_{11}) D_{11}, \tag{7}$$

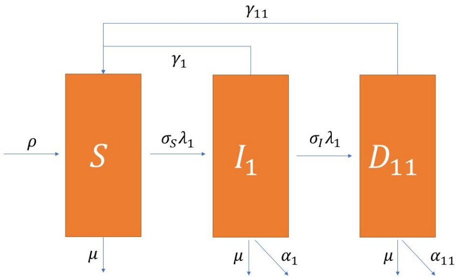


Figure 11: Schematic diagram of the model with recovery.

Extension: Model with recovery

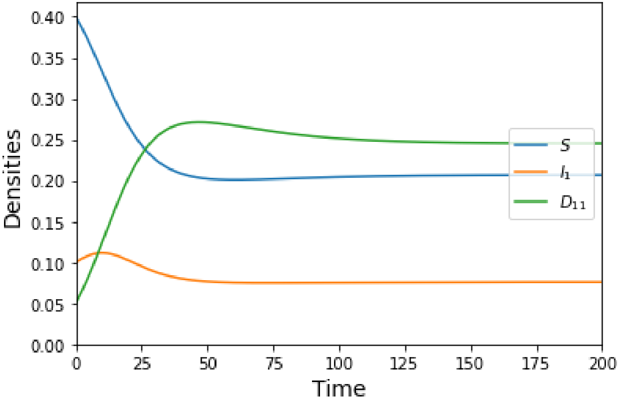
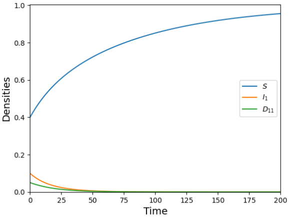
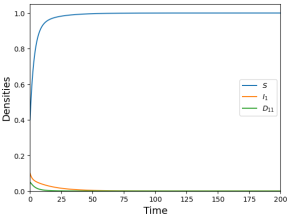


Figure 12: Population dynamics in the model with recovery.

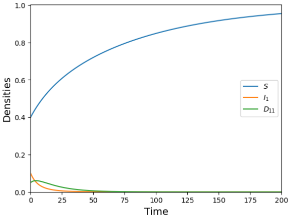
- The scenarios in equilibrium are similar to the original model.



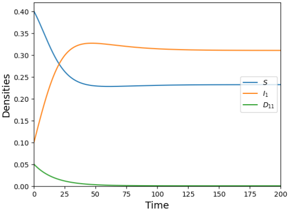
(a)



(b)



(c)



(d)

Figure 13: (a), (b), (c): disease-free case, with low transmission rate, high background mortality rate and low vulnerability of susceptible host, respectively; (d): Single-infection-only case with low vulnerability of infected hosts.

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