Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Department of Epidemiology and Public Health
Infectious Disease Modelling Unit

Modelling competition dynamics of drug resistant malaria

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Objectives

Via a theoretical model: What **dynamics** have the strongest influence on the frequency of resistance within a population?

↓ *Recombination* ↓ *Suppression* ↑ *Competitive release*

How does this vary by **setting** and **strategy**?

∼ 3%, ∼ 15%, ∼ 40% *prevalence (all ages)*
5%, 40%, 80% *probability of being treated in two weeks*

Overview

The model

The dynamics

Sensitivity analysis

The model

Adapted SIS model to include within host dynamics (not an explicit within-host model). Hosts carry a mix of sensitive and resistant parasitaemia.

Input: Parameters for key dynamics

Output: The proportion of resistant parasitaemia in the whole population

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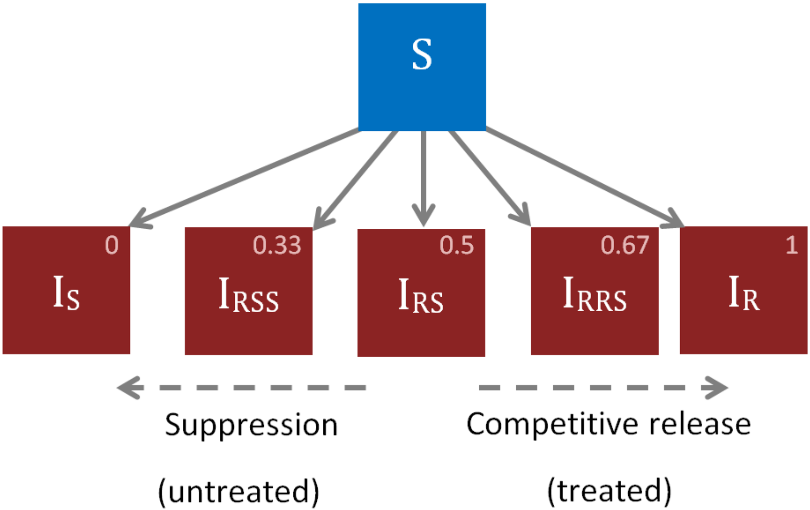
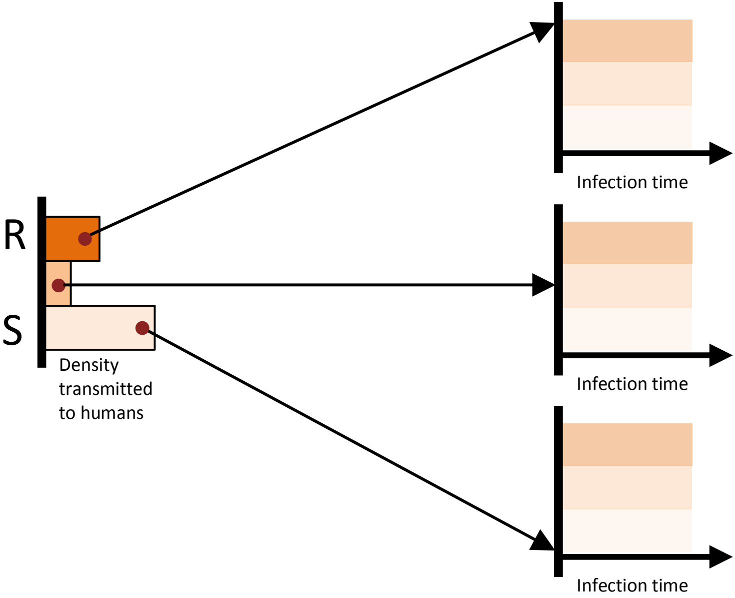
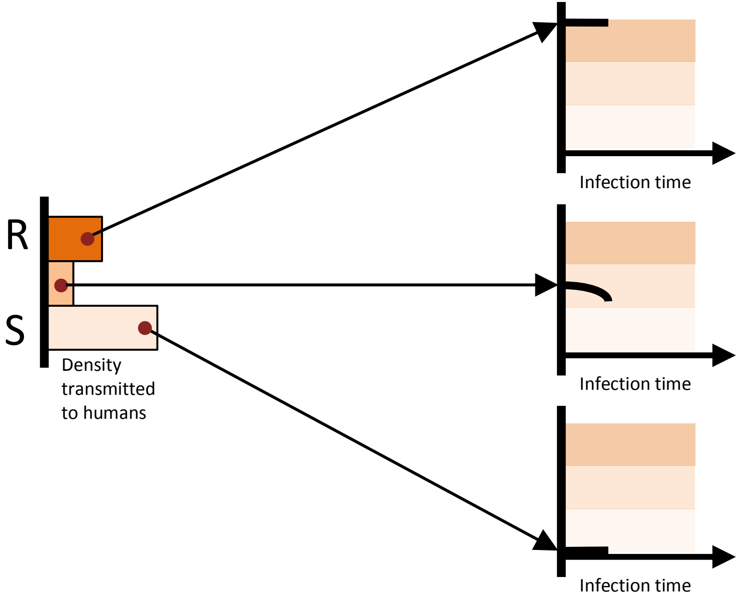
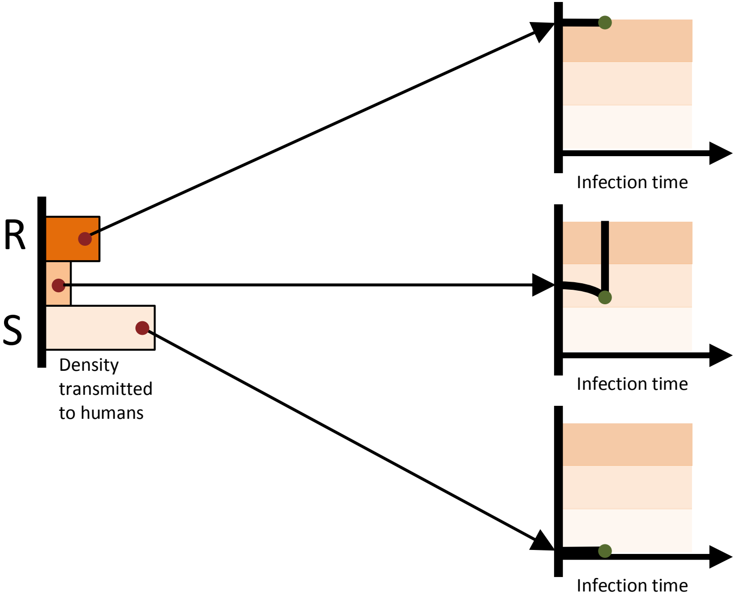

S
0
I_S
0.33
I_{RSS}
0.5
I_{RS}
0.67
I_{RRS}
1
I_R
Suppression
(untreated)
Competitive release
(treated)

Demonstration

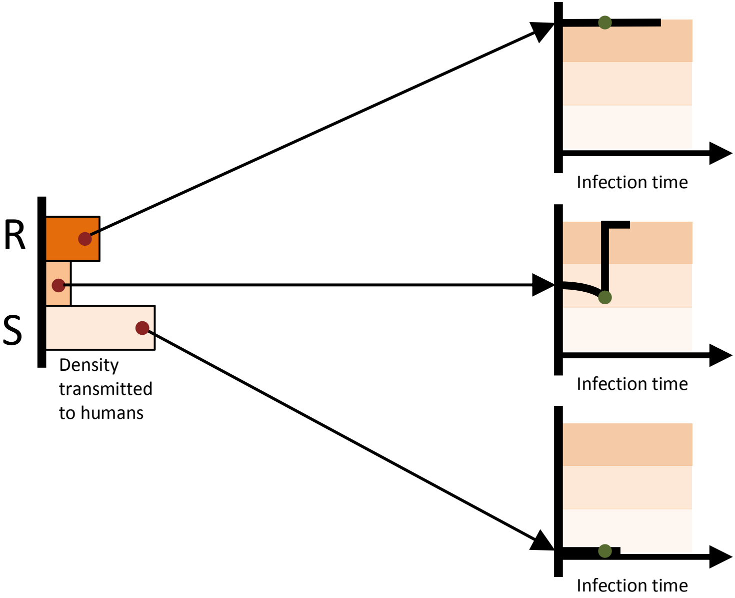


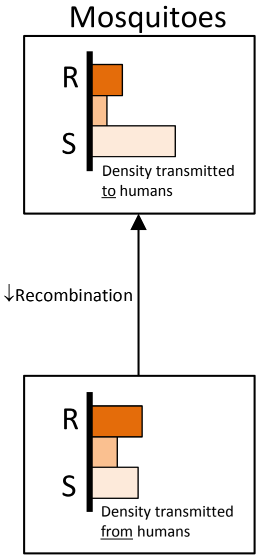

R
S
Density
transmitted
to humans
Infection time
Infection time
Infection time

Demonstration

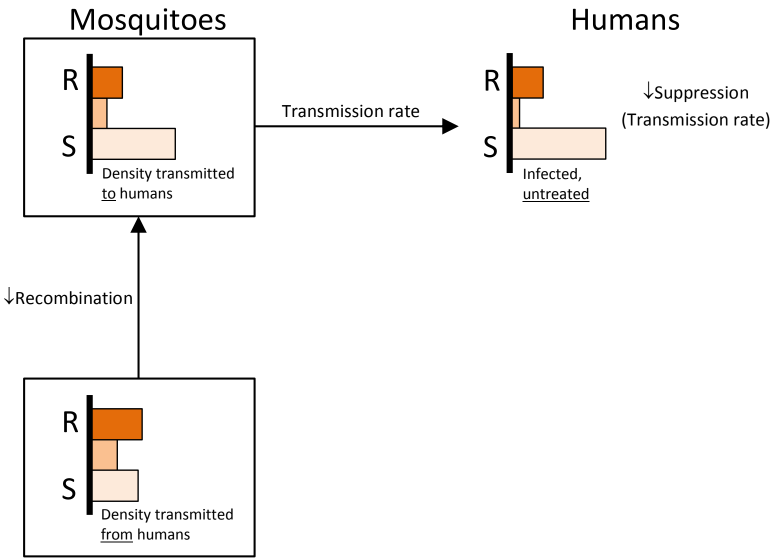


Demonstration

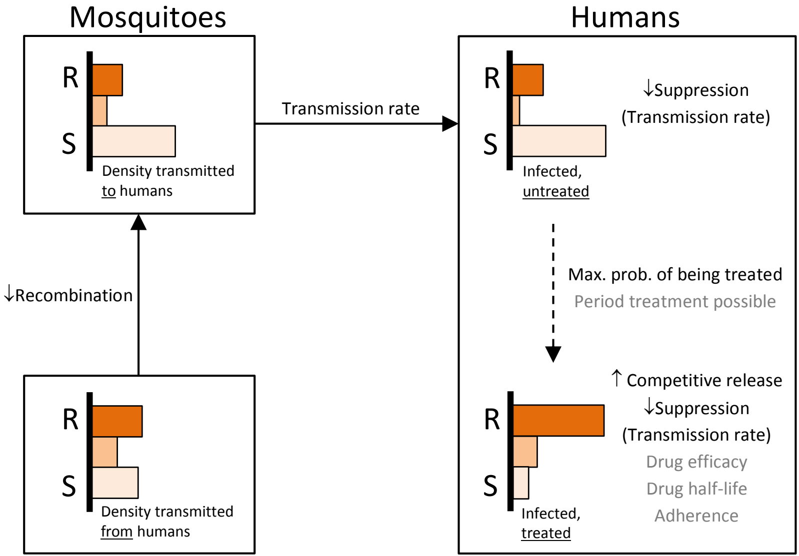


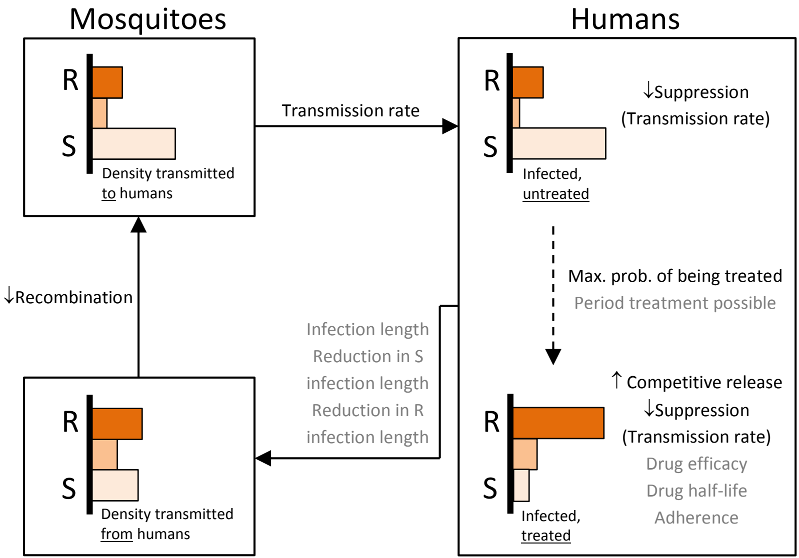


Mosquitoes
R
S
Density transmitted
to humans
↓Recombination
R
S
Density transmitted
from humans



Mosquitoes
R
S
Density transmitted to humans
Transmission rate
Humans
R
S
Infected, untreated
↓Suppression
(Transmission rate)
↓Recombination
R
S
Density transmitted from humans


Mosquitoes
Humans
R
S
Density transmitted to humans
Transmission rate
R
S
Infected, untreated
↓Suppression
(Transmission rate)
Max. prob. of being treated
Period treatment possible
↓Recombination
R
S
Density transmitted from humans
↑ Competitive release
↓Suppression
(Transmission rate)
Drug efficacy
Drug half-life
Adherence
R
S
Infected, treated


Mosquitoes
Humans
R
S
Density transmitted
to humans
Transmission rate
R
S
Infected,
untreated
↓Suppression
(Transmission rate)
↓Recombination
Max. prob. of being treated
Period treatment possible
Infection length
Reduction in S
infection length
Reduction in R
infection length
R
S
Density transmitted
from humans
R
S
Infected,
treated
↑ Competitive release
↓Suppression
(Transmission rate)
Drug efficacy
Drug half-life
Adherence

Number of infected hosts (without dynamics)

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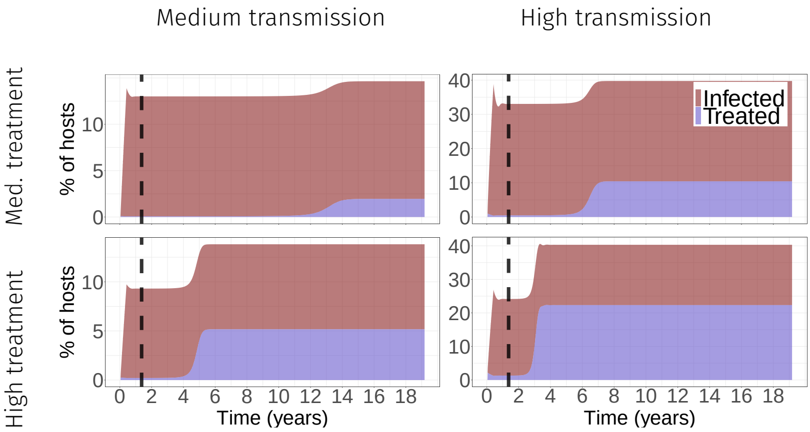
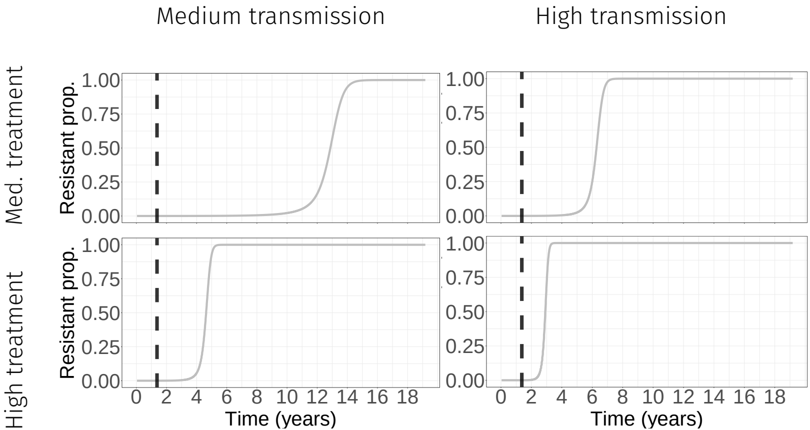
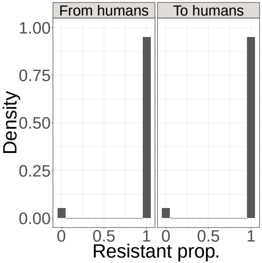


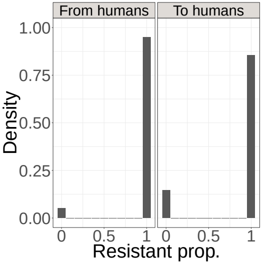
Resistance added after 500 days (dashed line).

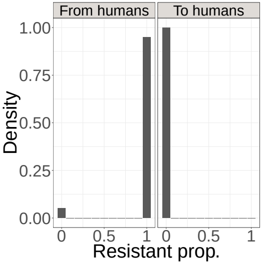
Proportion of resistant infections (without dynamics)



The dynamics

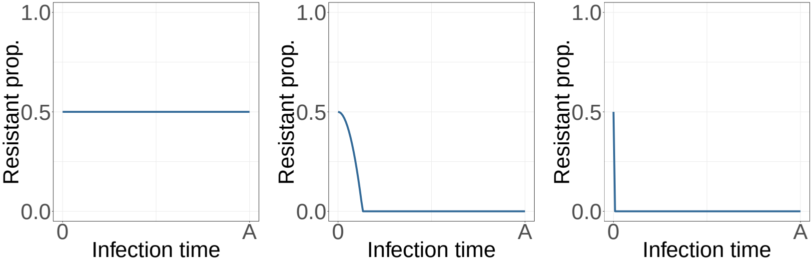






None $\{0\}$ $\longrightarrow$ $\{0.1\}$ $\longrightarrow$ Maximum $\{1\}$

↓ Suppression



None {0} $\longrightarrow$ {0.004} $\longrightarrow$ Maximum {1}

↓ Suppression

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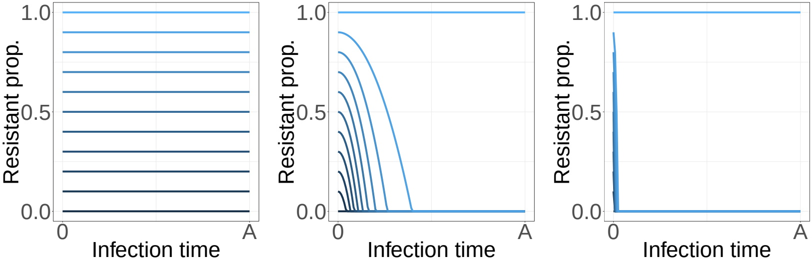
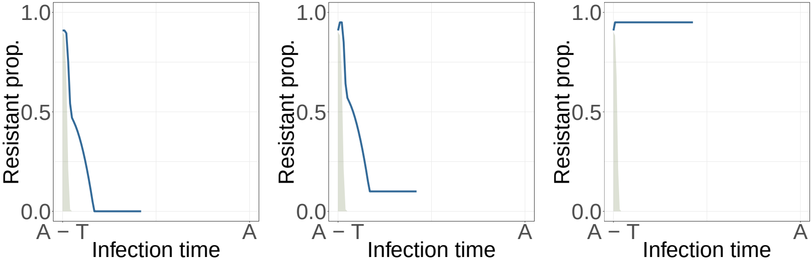


None {0} ⟶ {0.004} ⟶ Maximum {1}

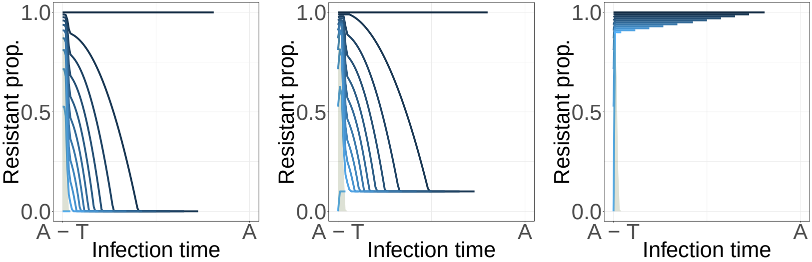
↑ Competitive release $[\cancel{S}SR] \rightarrow [SR] \Rightarrow [SRR]$



None {0} $\longrightarrow$ {0.1} $\longrightarrow$ Maximum {1}

↑ Competitive release [$\cancel{S}$SR] → [SR] ⇒ [SRR]

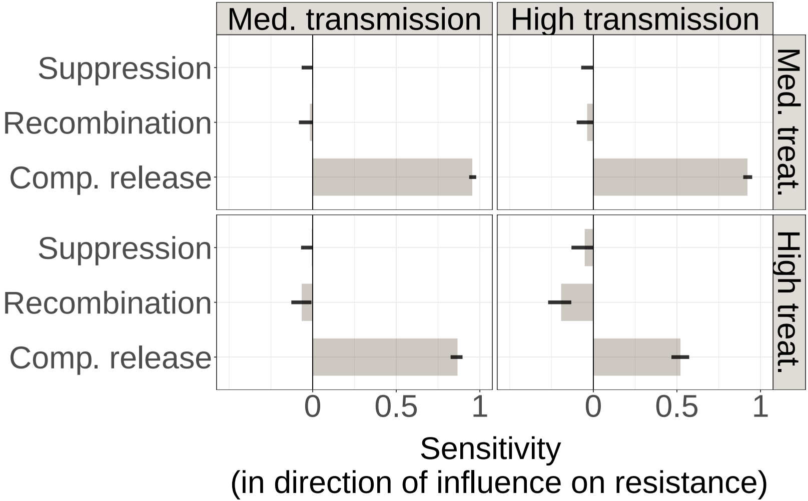
Swiss TPH



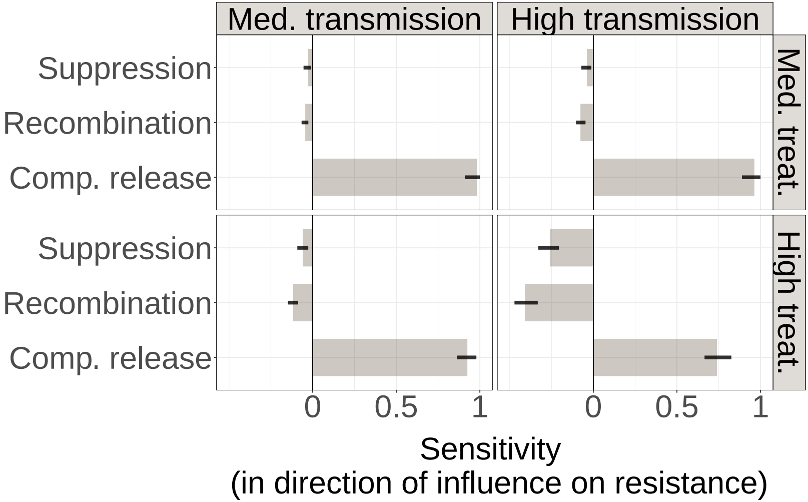
None {0} ⟶ {0.1} ⟶ Maximum {1}

Sensitivity analysis

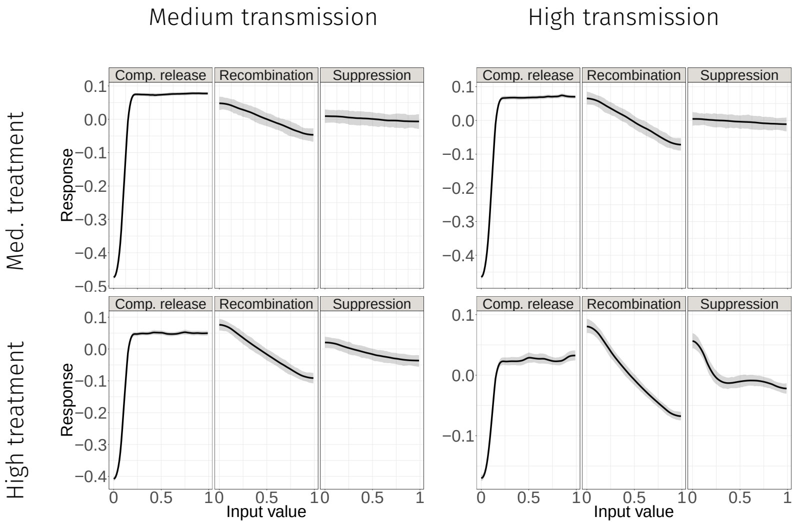
Sensitivity analysis (Single effects)



Sensitivity analysis (Total effects)



Main effects



Dynamic effects (high transmission only)

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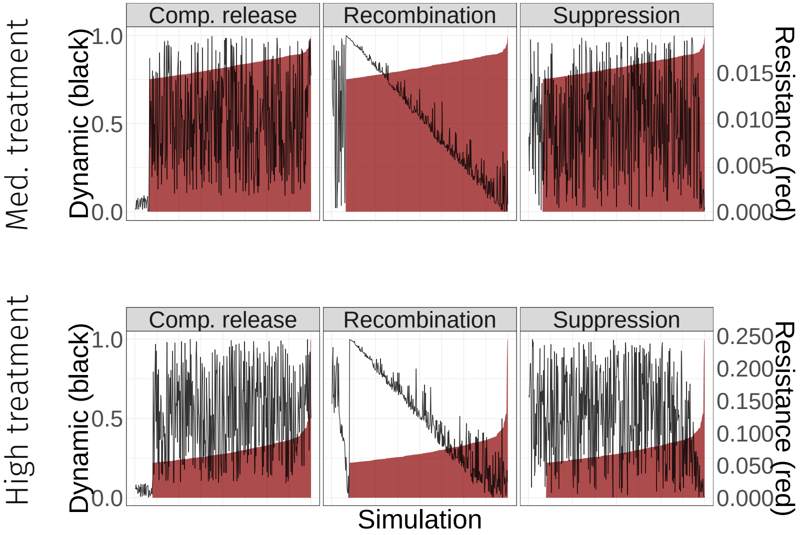

Summary

Model within-host dynamics without explicitly modelling parasite density.

Can track:

Dynamics - $\downarrow$ *recombination* $\downarrow$ *suppression* $\uparrow$ *competitive release*

Infection parameters - *Infection length (S&R)*

Treatment parameters - *Treatment rate that changes in time, reduction in infection length (S & R)*

Treatment parameters - *Drug efficacy, drug half-life, adherence*

When there is little resistance in the population, ↑ competitive release dominates and thus resistance spreads.

When there is high resistance in the population, ↓ recombination and ↓ suppression have more influence, **especially when transmission is high**.

Treatment increases the proportion of resistant parasitaemia, with or without ↑ competitive release. However, **the spread of resistance is greatly hindered by ↓ recombination, and failing that, ↓ suppression**.

Acknowledgements

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