Efficient coupling of within- and between-host infectious disease dynamics

Cameron Smith
University of Oxford

Outline

Hybrid method

Introduction

Applications

Introduction

Introduction

Seven challenges in modeling pathogen dynamics within-host and across scales
Gog *et al.* (2015)

Introduction

In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently (Mideo *et al.*, 2008)?

Seven challenges in modeling pathogen dynamics within-host and across scales
Gog *et al.* (2015)

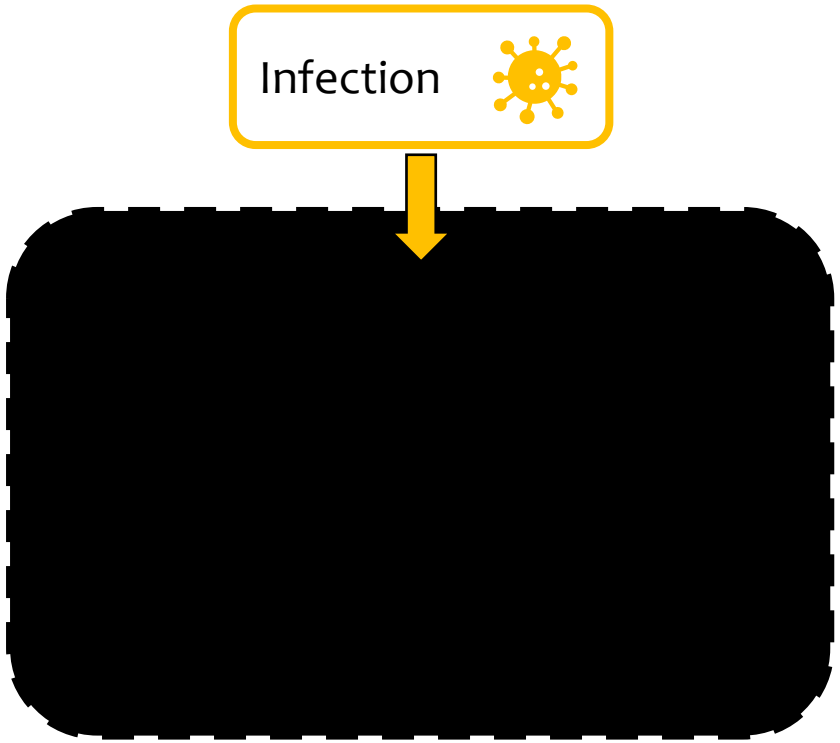
N. Mideo *et al.* (2008) Linking within- and between-host dynamics in the evolutionary epidemiology of infectious diseases, *Trends in Ecology and Evolution*

Introduction

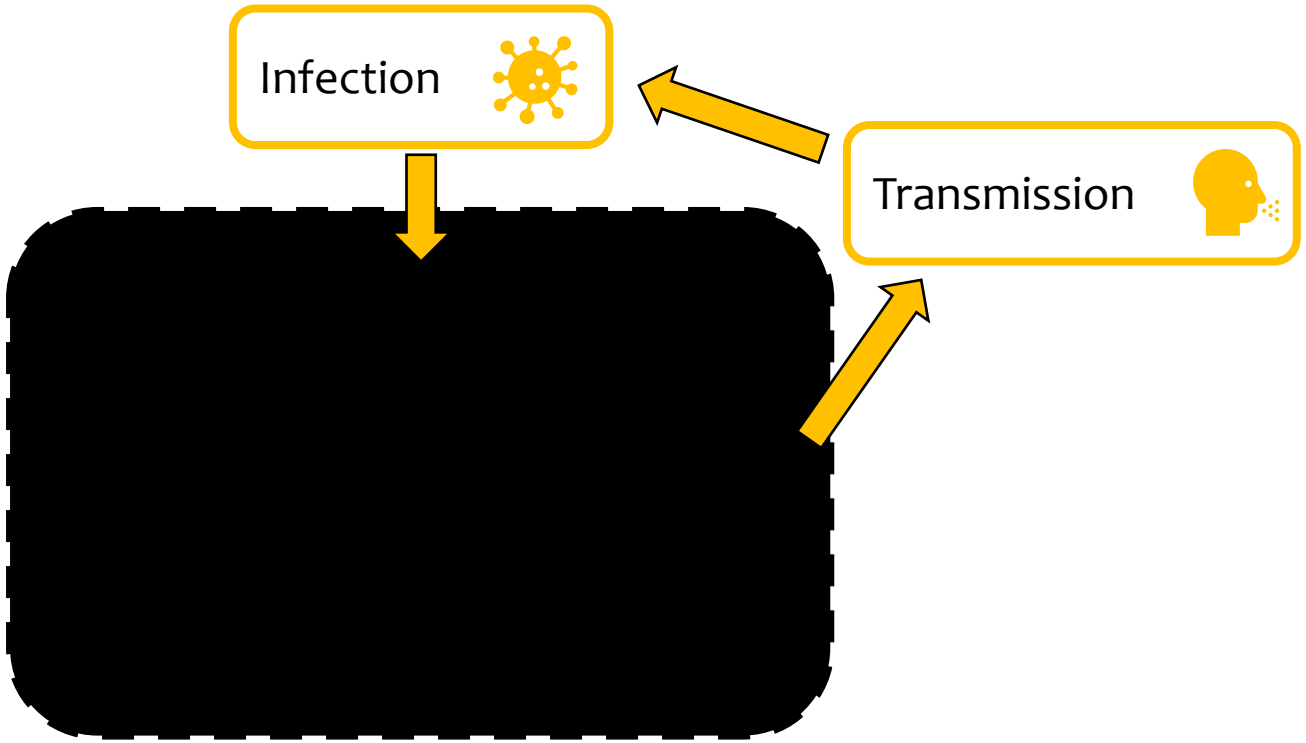
Introduction

Infection 

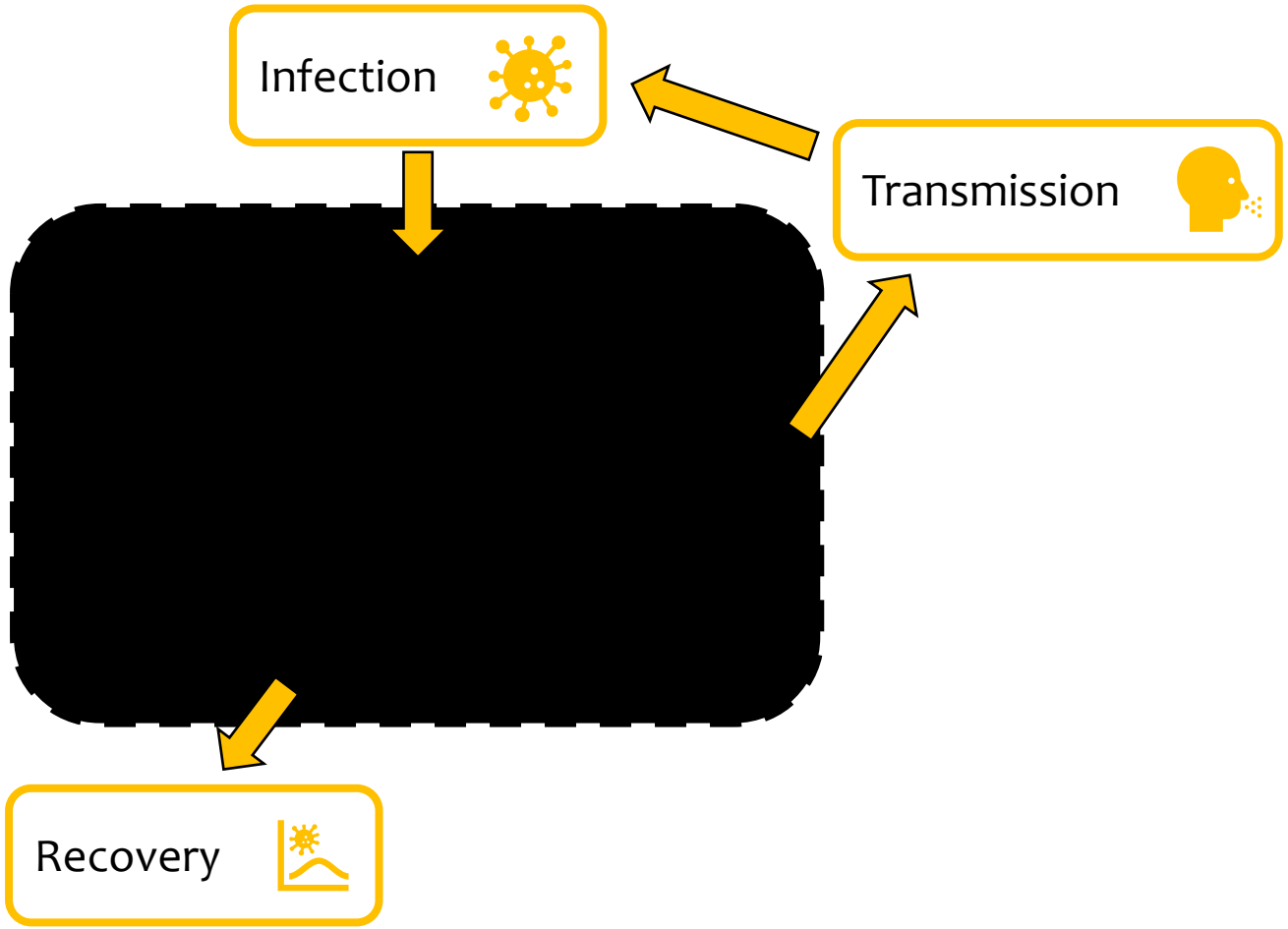
Introduction



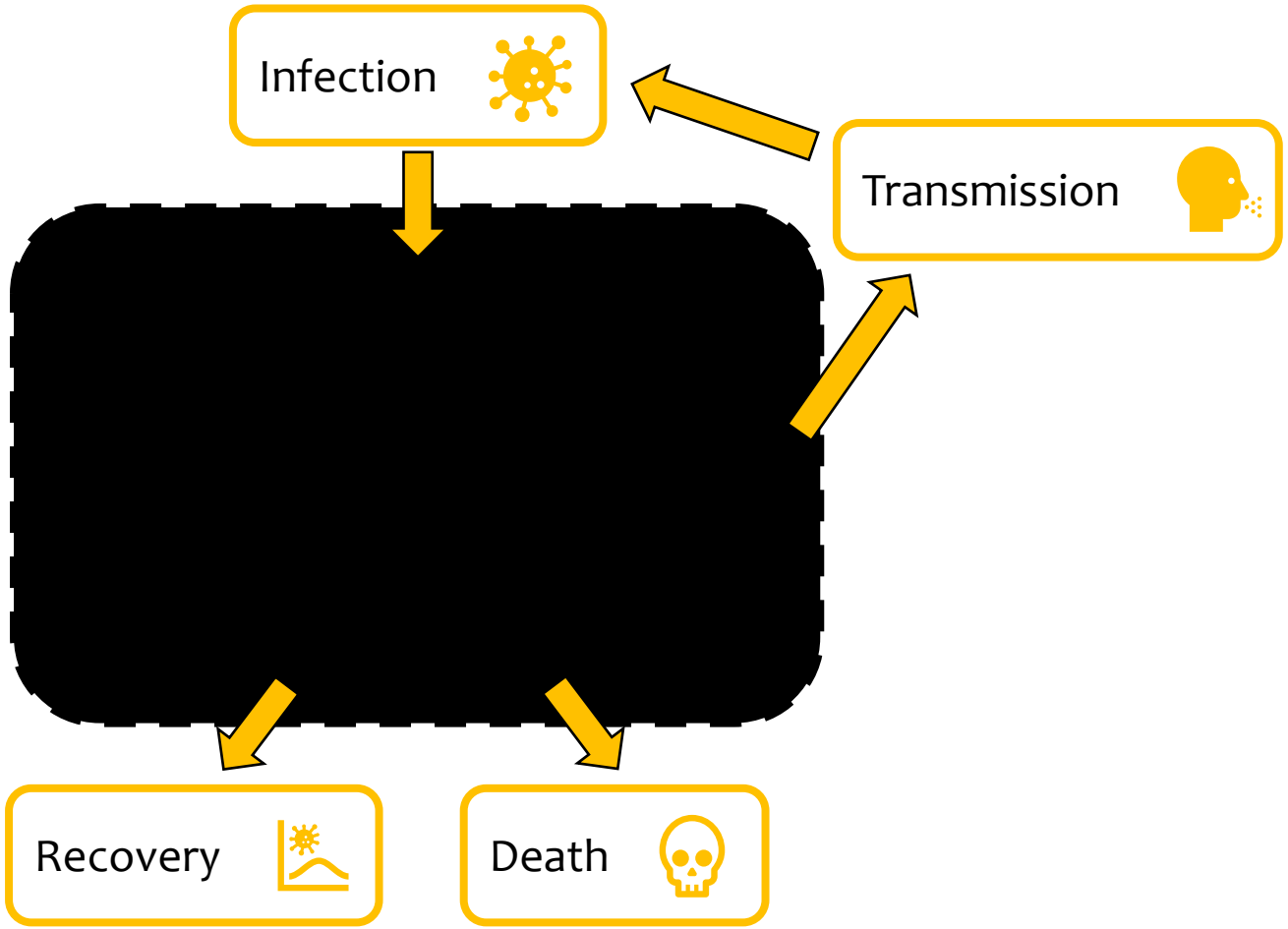
Introduction



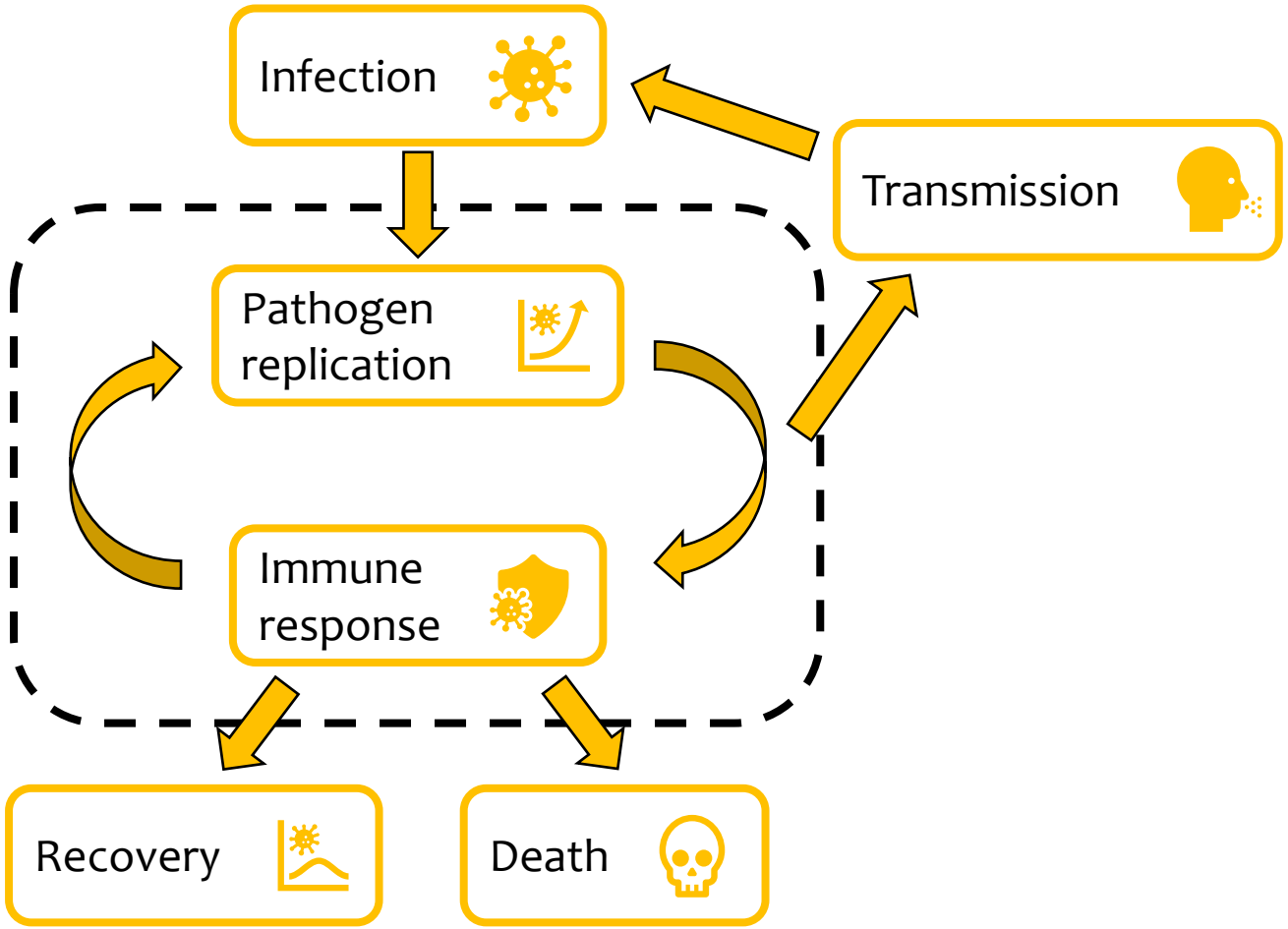
Introduction



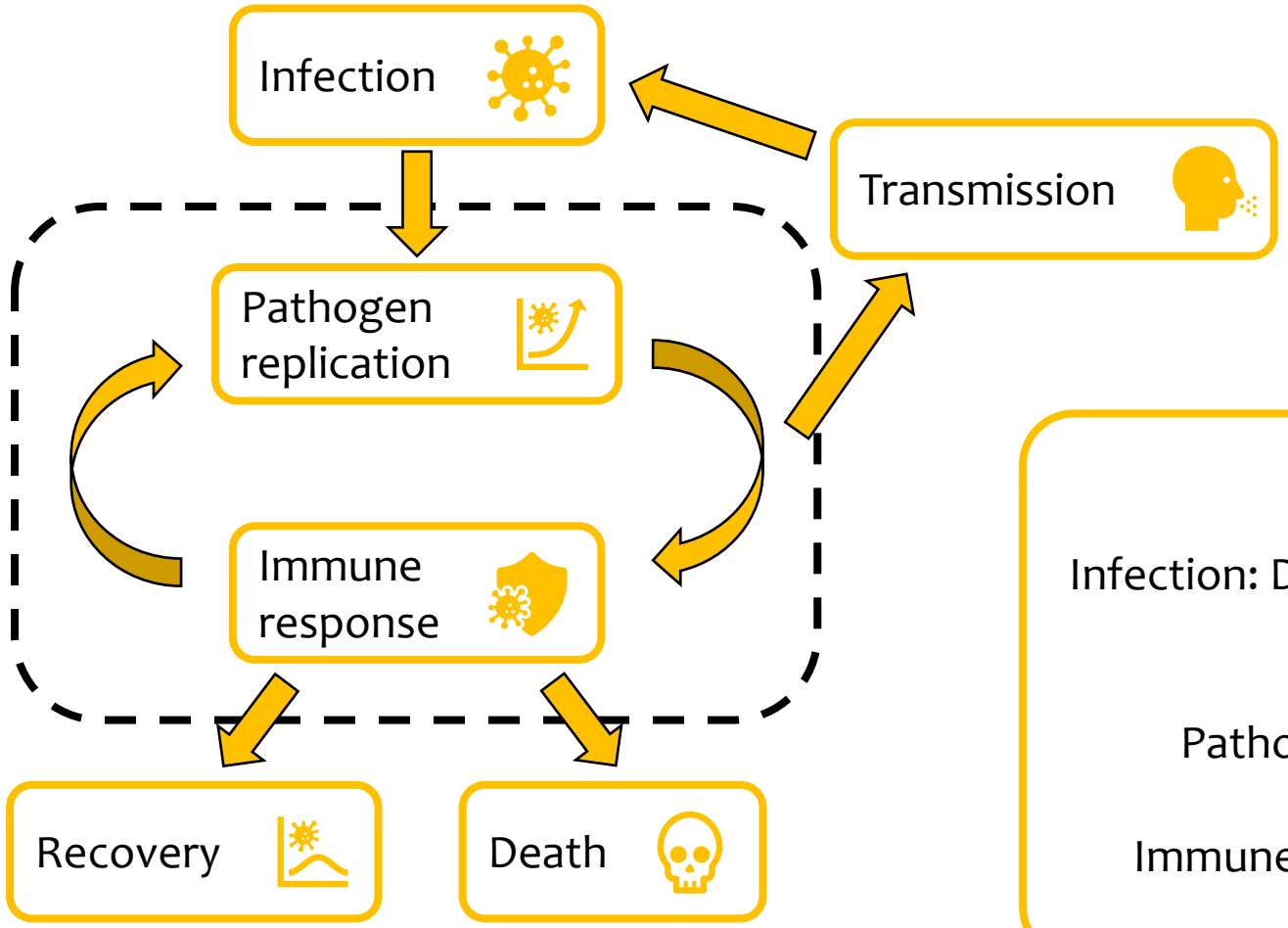
Introduction



Introduction



Introduction



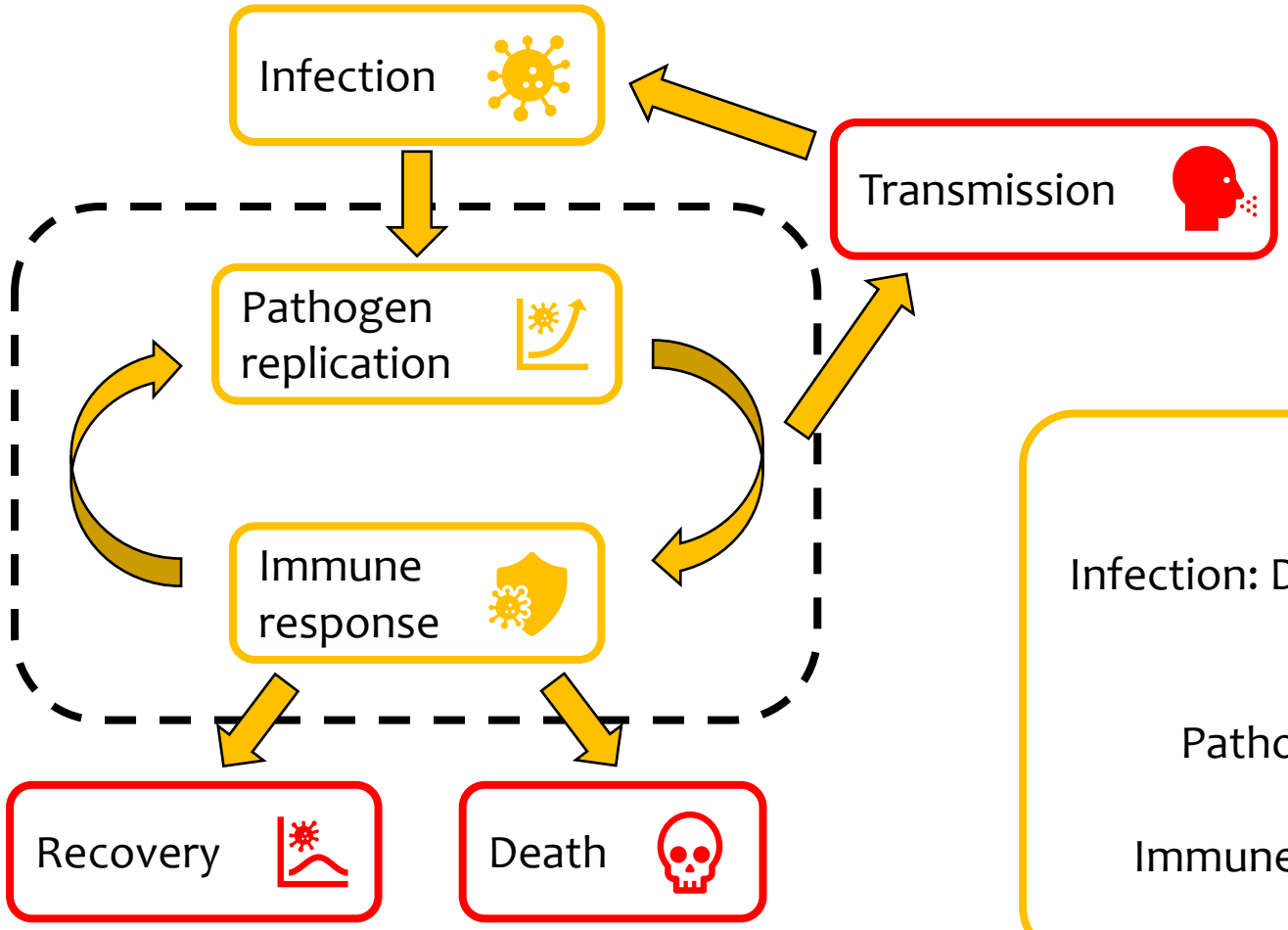
The infection process is individual

Infection: Depends on transmission bottlenecks, how infectious was the infector.

Pathogen replication: Multiple strains, initial dosage.

Immune response: Cross-immunity, vaccination, immuno-compromised.

Introduction



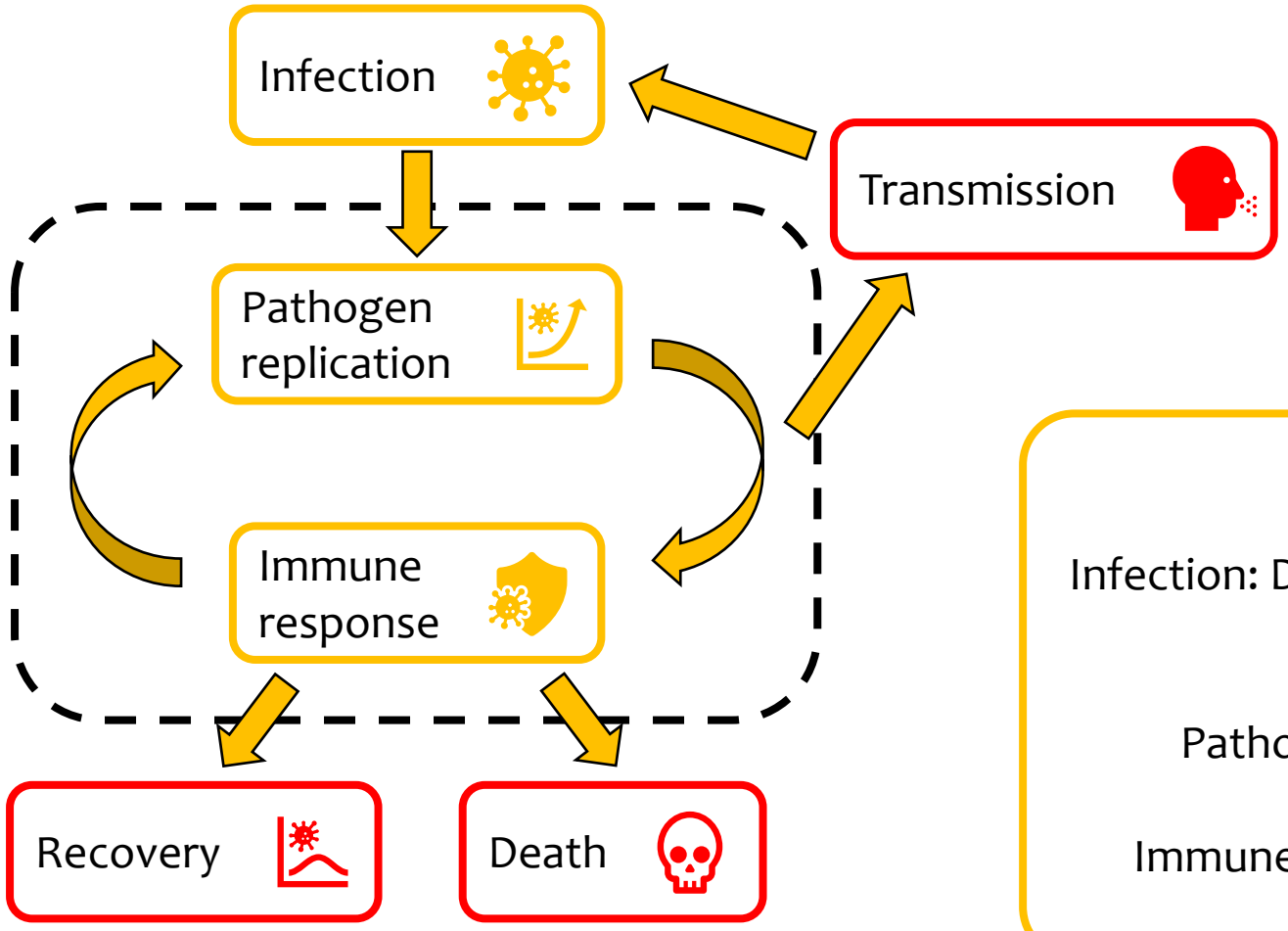
The infection process is individual

Infection: Depends on transmission bottlenecks, how infectious was the infector.

Pathogen replication: Multiple strains, initial dosage.

Immune response: Cross-immunity, vaccination, immuno-compromised.

Introduction



These are "outcomes"

They are functions of an individual, not a universal measure of everyone.

They impact population level dynamics and will be different for each individual.

The infection process is individual

Infection: Depends on transmission bottlenecks, how infectious was the infector.

Pathogen replication: Multiple strains, initial dosage.

Immune response: Cross-immunity, vaccination, immuno-compromised.

Outline

Hybrid method

Introduction

Applications

Hybrid method

Hybrid method

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Each individual has their own ODE system;

Internal state determines transmission, recovery, virulence;

Contains a complete disease history, including who has infected who.

$$\frac{d\boldsymbol{W}_i}{dT_i} = \boldsymbol{f}_W(\boldsymbol{W}_i, \boldsymbol{\theta}_W, T_i)$$

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Each individual has their own ODE system;

Internal state determines transmission, recovery, virulence;

Contains a complete disease history, including who has infected who.

$$\frac{d\boldsymbol{W}_i}{dT_i} = \boldsymbol{f}_W(\boldsymbol{W}_i, \boldsymbol{\theta}_W, T_i)$$

Transmission

$$\beta(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Recovery

$$\gamma(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Virulence

$$\alpha(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Each individual has their own ODE system;

Internal state determines transmission, recovery, virulence;

Contains a complete disease history, including who has infected who.

$$\frac{d\boldsymbol{W}_i}{dT_i} = \boldsymbol{f}_W(\boldsymbol{W}_i, \boldsymbol{\theta}_W, T_i)$$

Transmission

$$\beta(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Recovery

$$\gamma(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Virulence

$$\alpha(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$$

Natural mortality

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Let $P_i(T_i)$ be the pathogen count of individual i for an infection of age T_i. Then:

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Transmission

$\beta(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$

Recovery

$\gamma(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$

Virulence

$\alpha(\boldsymbol{W}_i, \boldsymbol{\theta}_C, T_i)$

Natural mortality

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Let $P_i(T_i)$ be the pathogen count of individual i for an infection of age T_i. Then:

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Transmission

$$\beta(P_i) = \beta_1 P_i$$

Recovery

$$\gamma(P_i) = 0$$

Virulence

$$\alpha(P_i) = \alpha_1 P_i^2$$

Natural mortality

Host demographics

All host demographics calculated here;

At their simplest, they might be:

$$\dot{S} = N(a - qN) - bS,$$
$$\dot{I} = -bI,$$
$$\dot{R} = -bR.$$

Hybrid method

Within-host dynamics

Let $P_i(T_i)$ be the pathogen count of individual i for an infection of age T_i. Then:

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Transmission

$$\beta(P_i) = \beta_1 P_i$$

Recovery

$$\gamma(P_i) = 0$$

Virulence

$$\alpha(P_i) = \alpha_1 P_i^2$$

Natural mortality

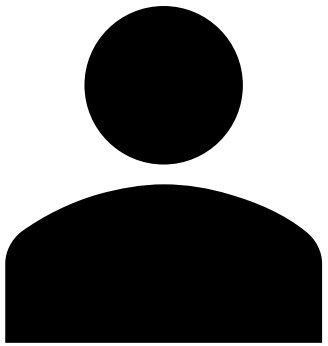
Host demographics

Let $S(t)$ and $I(t)$ be the proportion of susceptible and infected individuals respectively, t days after initial infection. Then:

$$\frac{dS}{dt} = N(a - qN) - bS$$

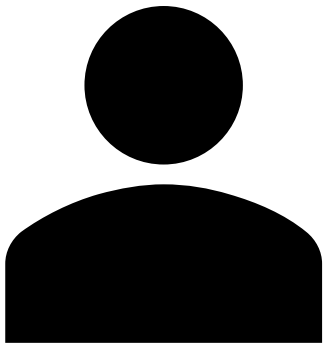
$$\frac{dI}{dt} = -bI$$

Hybrid method

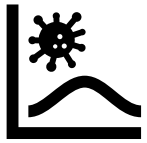


What can we track for each individual?

Hybrid method

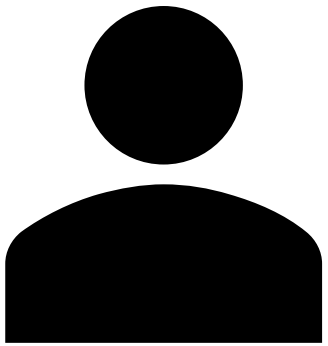


What can we track for each individual?

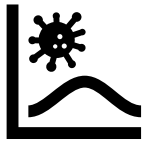


Within-host state

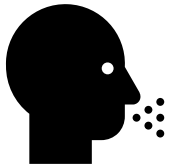
Hybrid method



What can we track for each individual?

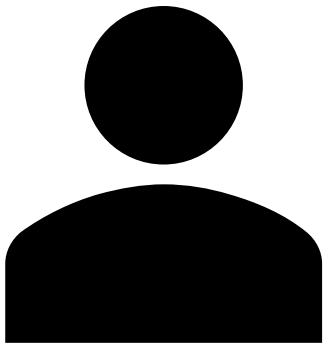


Within-host state

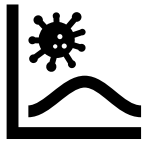


Infection history

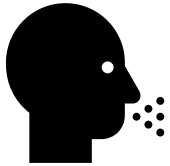
Hybrid method



What can we track for each individual?



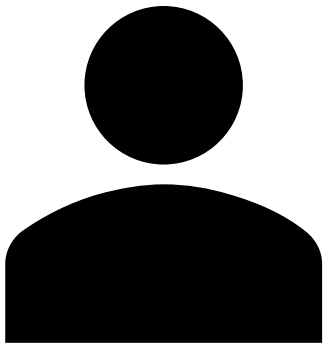
Within-host state



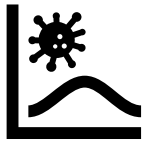
Infection history

Who infects who?

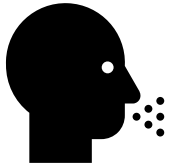
Hybrid method



What can we track for each individual?



Within-host state

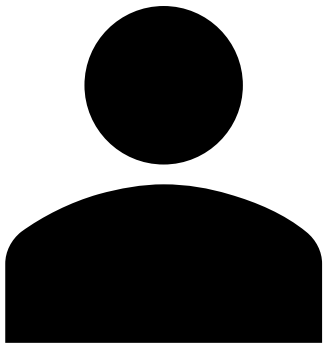


Infection history

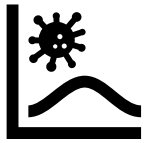
Who infects who?

Timings of infection

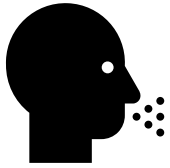
Hybrid method



What can we track for each individual?



Within-host state



Infection history

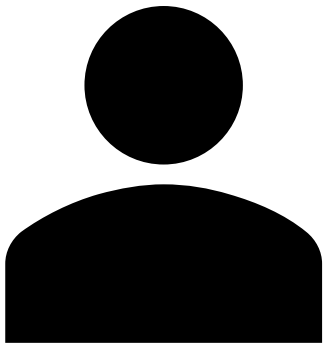
ACGTCAA
ACGTGAA

Mutation history

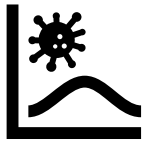
Who infects who?

Timings of infection

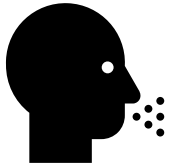
Hybrid method



What can we track for each individual?



Within-host state



Infection history

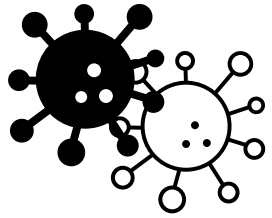
ACGTCAA
ACGTGAA

Mutation history

Who infects who?

Timings of infection

Which variant?



Outline

Hybrid method

Introduction

Applications

Applications

<u>CASE STUDY:</u> Slow-clearing pathogen

Prevalence

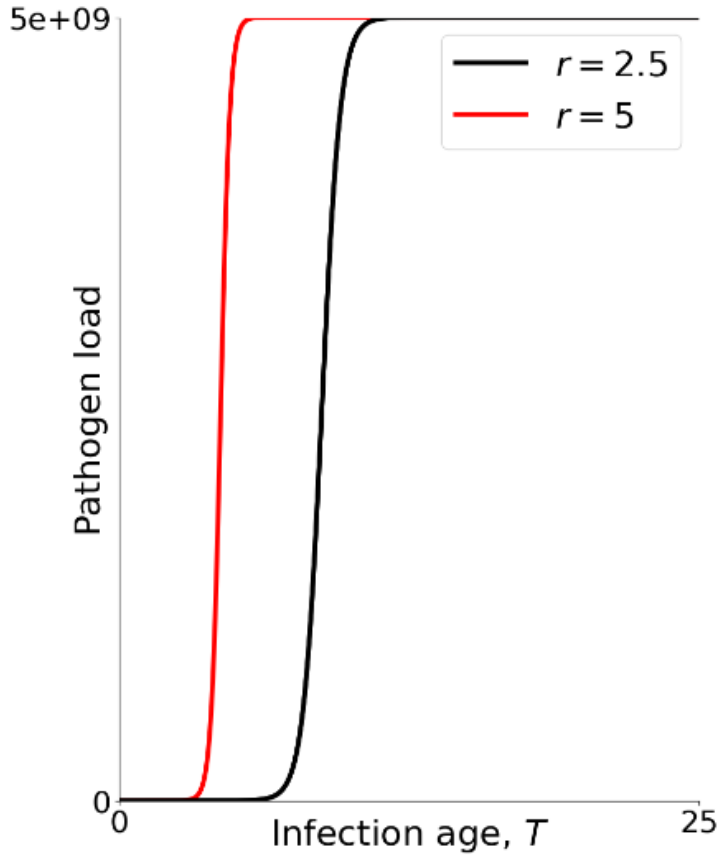
$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Applications

CASE STUDY: Slow-clearing pathogen

Prevalence

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

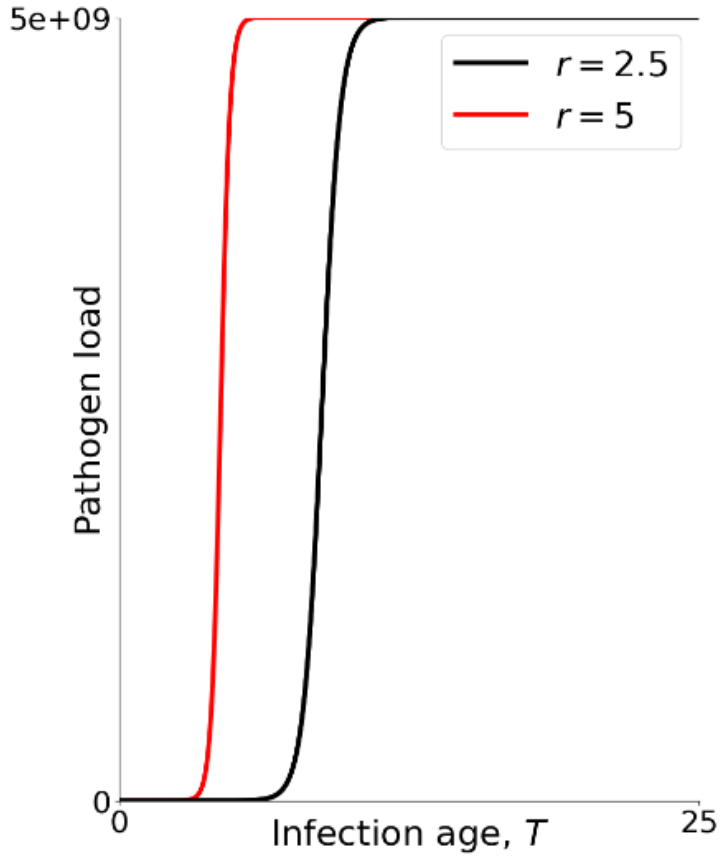


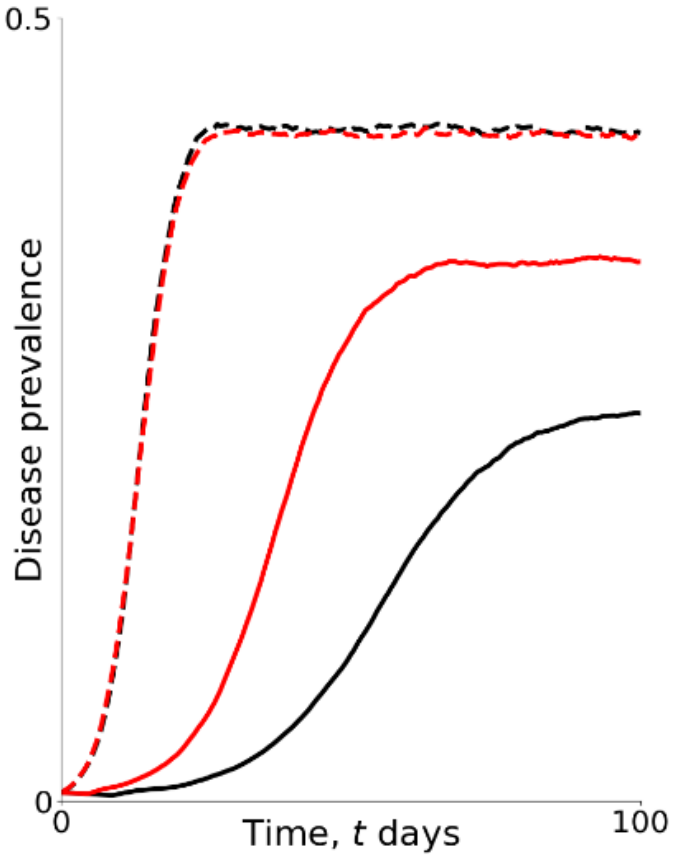
Applications

CASE STUDY: Slow-clearing pathogen

Prevalence

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$





Applications

CASE STUDY: Slow-clearing pathogen

Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Applications

CASE STUDY: Slow-clearing pathogen

Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Evolve the growth rate, r

Applications

CASE STUDY: Slow-clearing pathogen

Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Evolve the growth rate, r

At equilibrium, $P^* = K$, independent of r – (A)

Applications

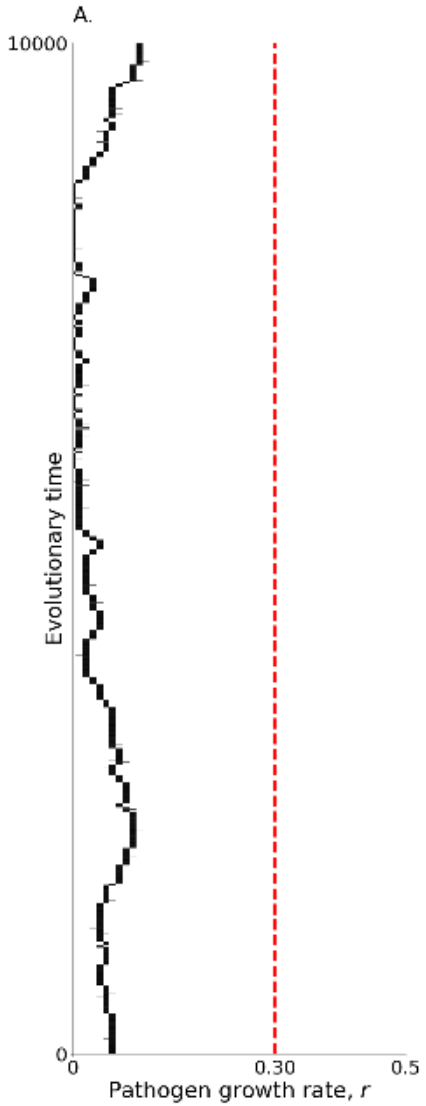
CASE STUDY: Slow-clearing pathogen

Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Evolve the growth rate, r

At equilibrium, $P^* = K$, independent of r – (A)



Applications

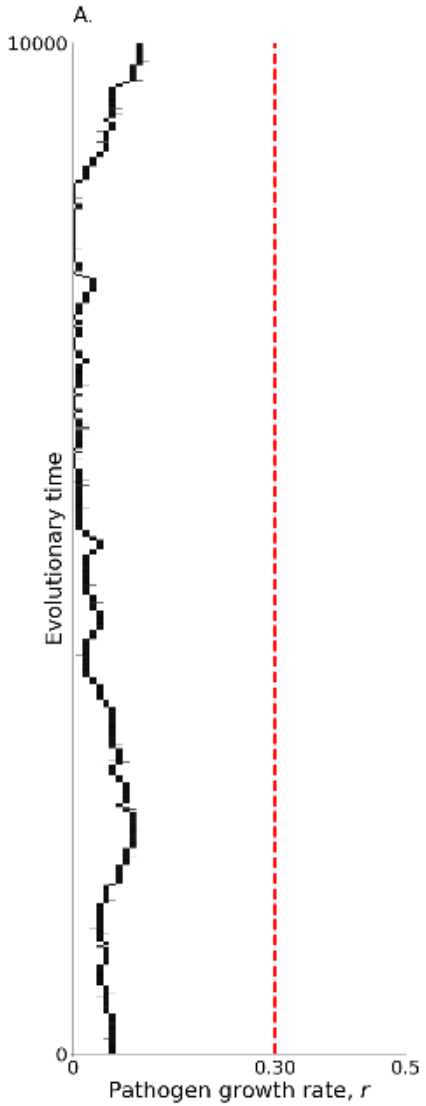
CASE STUDY: Slow-clearing pathogen
Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Evolve the growth rate, r

At equilibrium, $P^* = K$, independent of r – (A)

Full transient dynamics – (B)



Applications

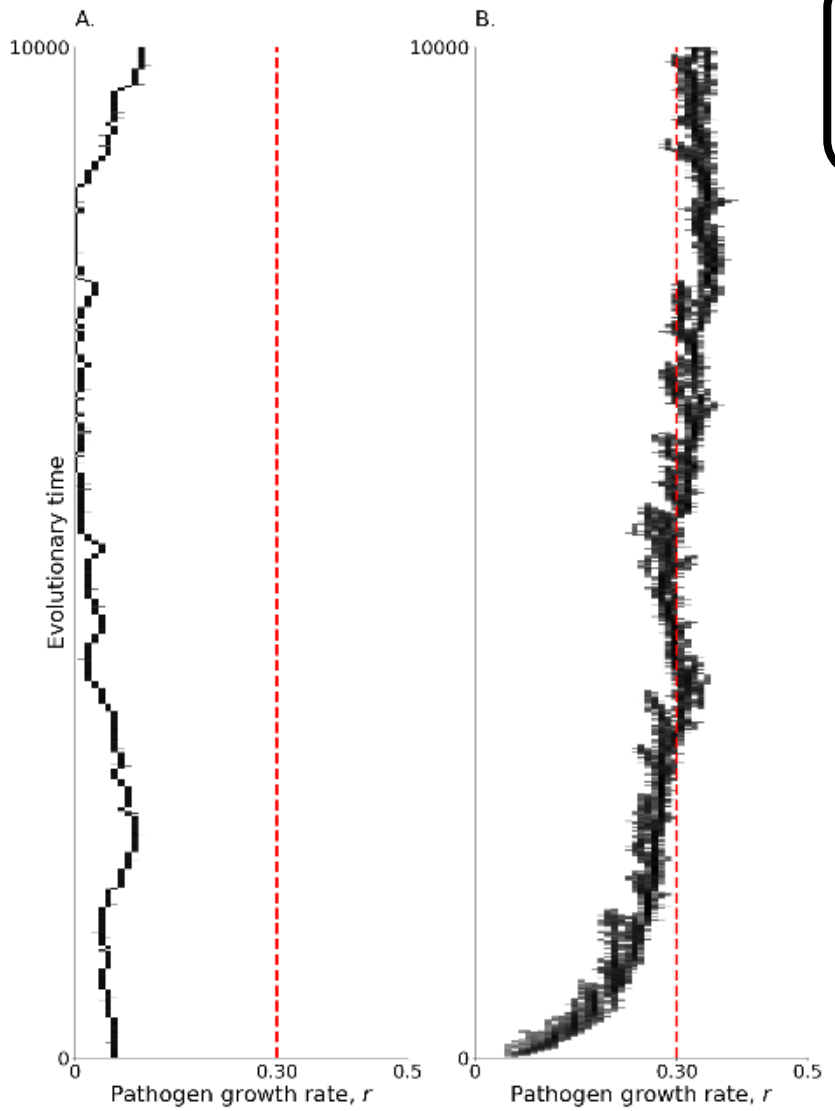
CASE STUDY: Slow-clearing pathogen
Within-host evolution

$$\frac{dP_i}{dT_i} = rP_i\left(1 - \frac{P_i}{K}\right)$$

Evolve the growth rate, r

At equilibrium, $P^* = K$, independent of r – (A)

Full transient dynamics – (B)



Applications

<u>CASE STUDY 2:</u> Possible recovery

Prevalence

Applications

<u>CASE STUDY 2:</u> Possible recovery

Prevalence

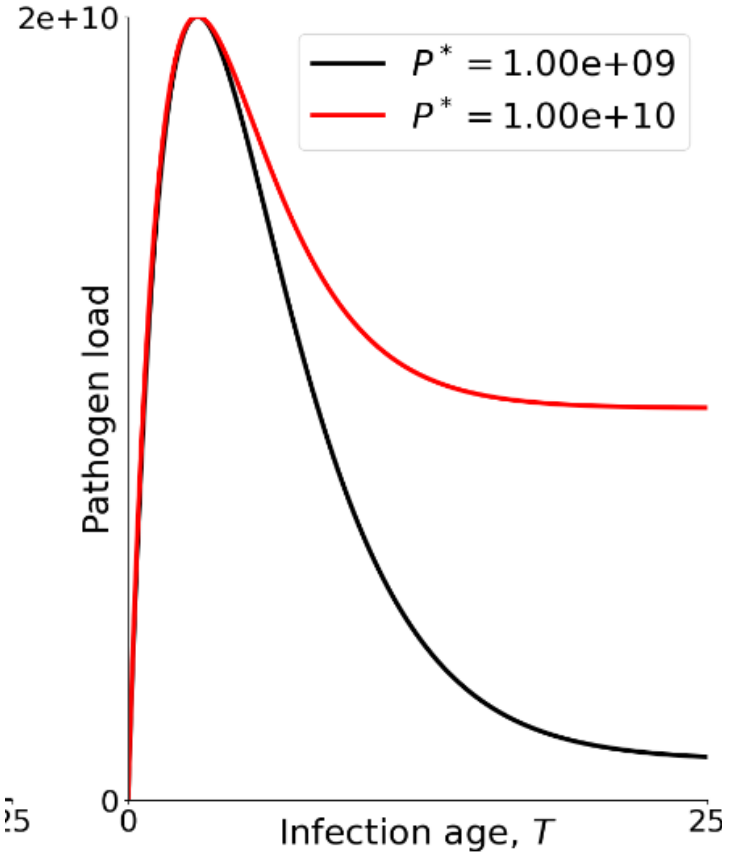
$$\frac{dP}{dT_i} = re^{-\eta T_i} + \eta(P^* - P_i)$$

Applications

CASE STUDY 2: Possible recovery

Prevalence

$$\frac{dP}{dT_i} = re^{-\eta T_i} + \eta(P^* - P_i)$$

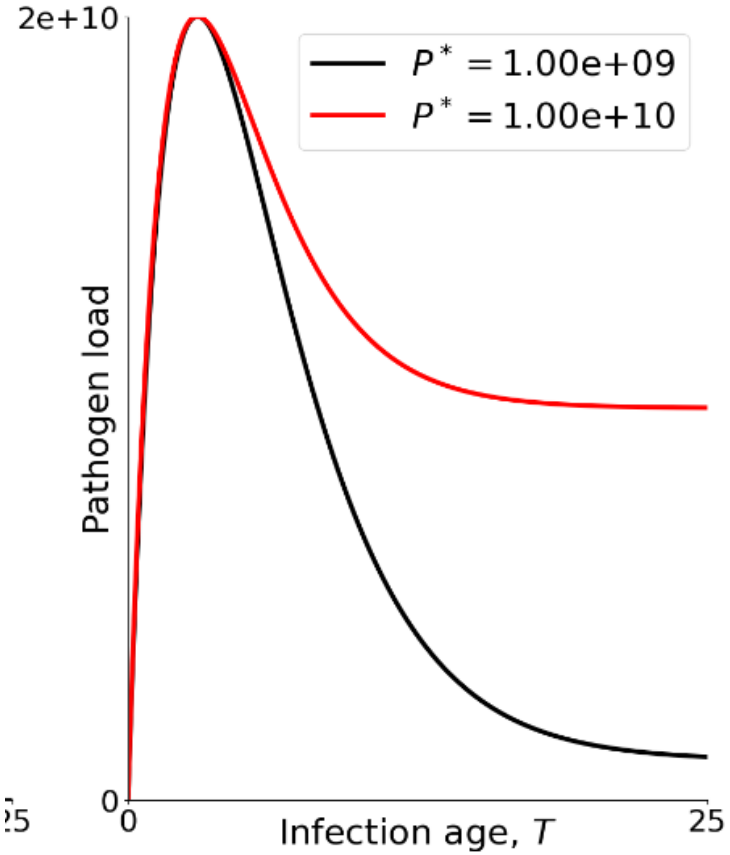


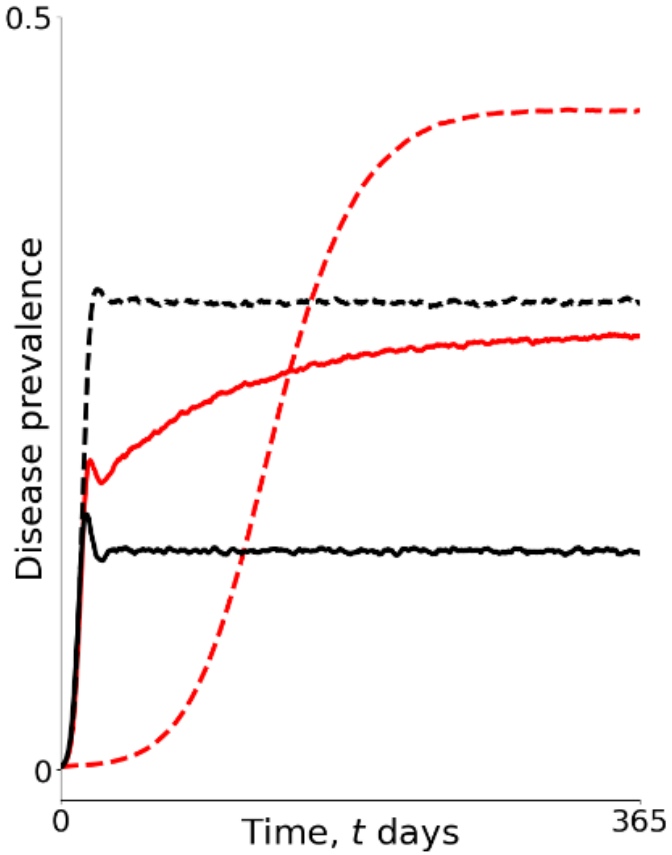
Applications

<u>CASE STUDY 2:</u> Possible recovery

Prevalence

$$\frac{dP}{dT_i} = re^{-\eta T_i} + \eta(P^* - P_i)$$





Applications

CASE STUDY 2: Possible recovery

Phylogeny

$$\frac{dP}{dT_i} = re^{-\eta T_i} + \eta(P^* - P_i)$$

150 base genotype

Neutral mutation

Applications

<u>CASE STUDY 2:</u> Possible recovery

Phylogeny

$$\frac{dP}{dT_i} = re^{-\eta T_i} + \eta(P^* - P_i)$$

150 base genotype

Neutral mutation

Recap

Recap

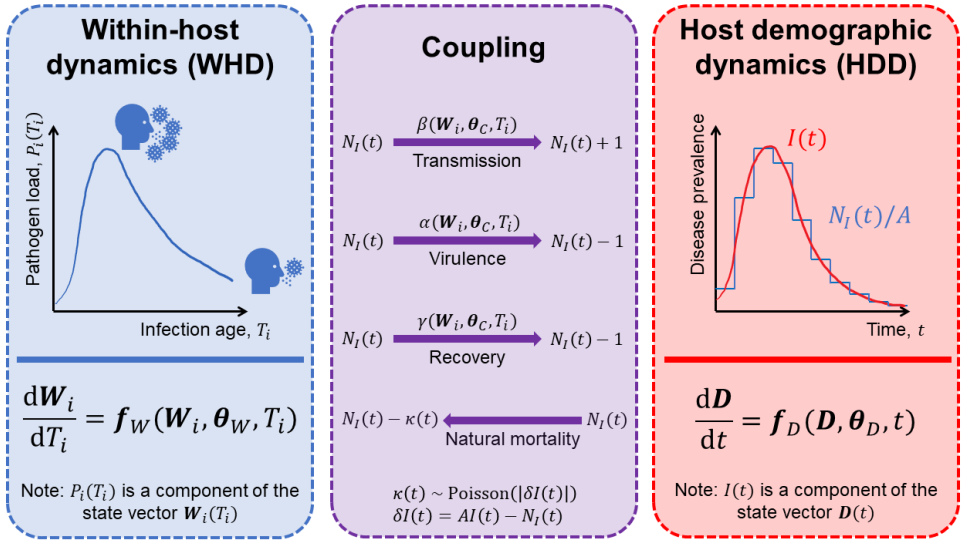
In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently (Mideo et al., 2008)?

Recap

In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. **Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently** (Mideo et al., 2008)?

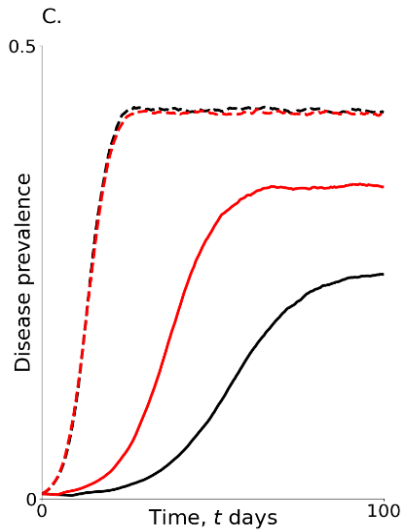
Recap

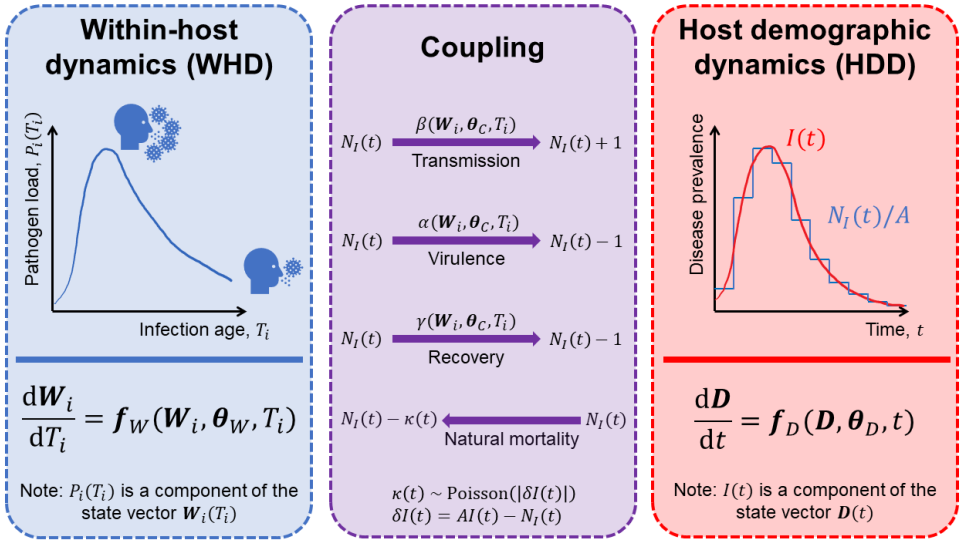
In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. **Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently** (Mideo et al., 2008)?



Recap

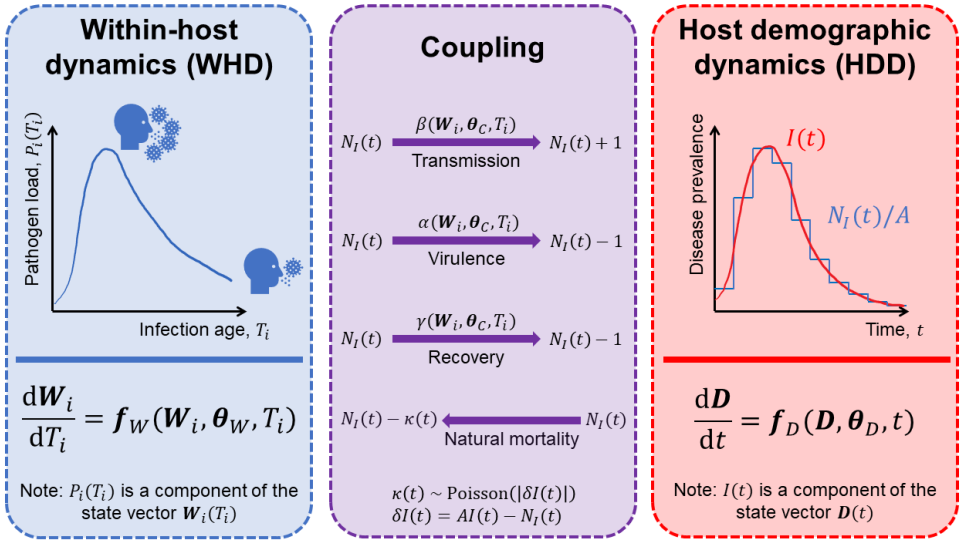
In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. **Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently** (Mideo et al., 2008)?

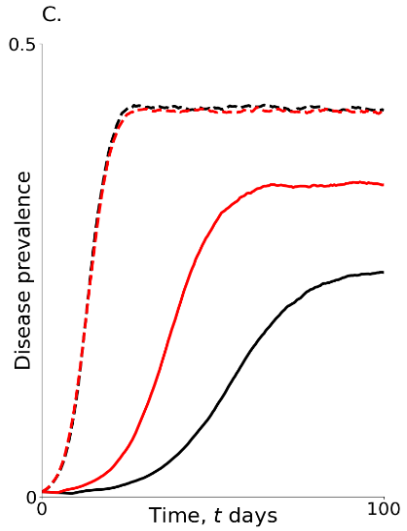


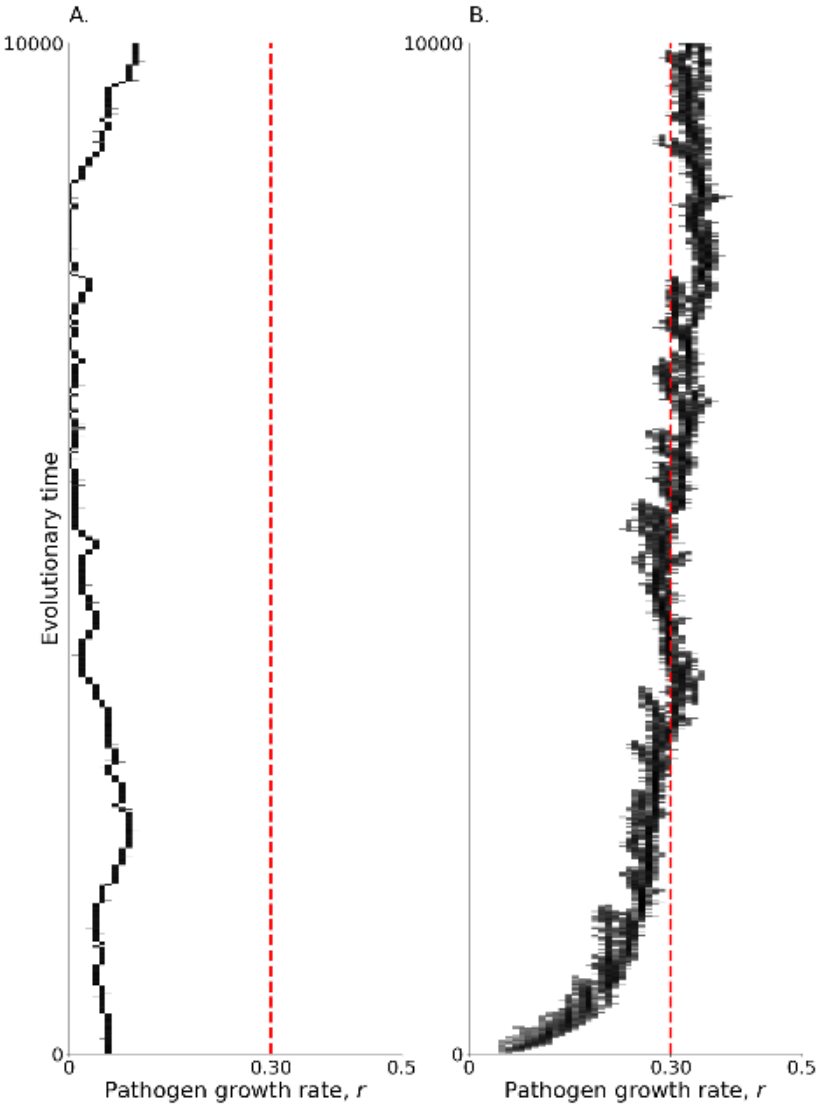


Recap

In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. **Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently** (Mideo et al., 2008)?

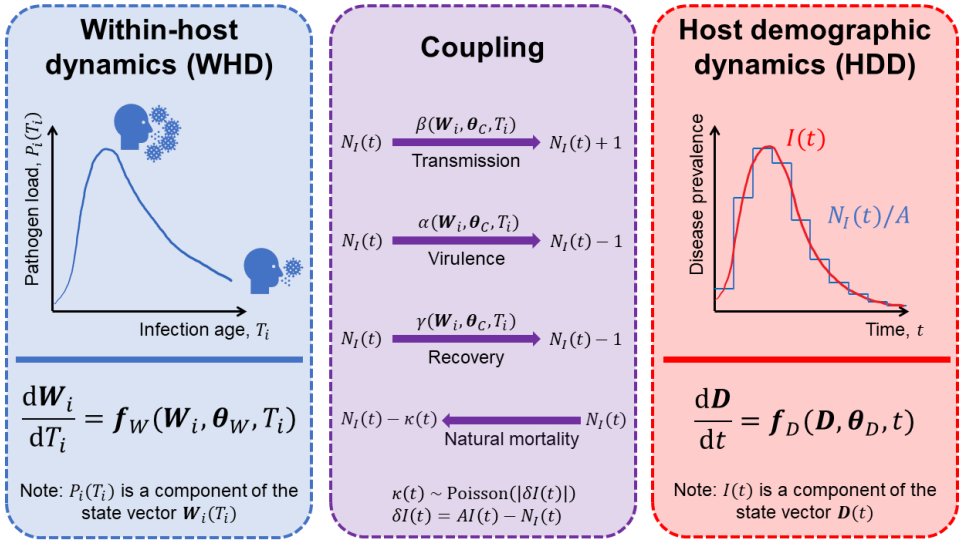


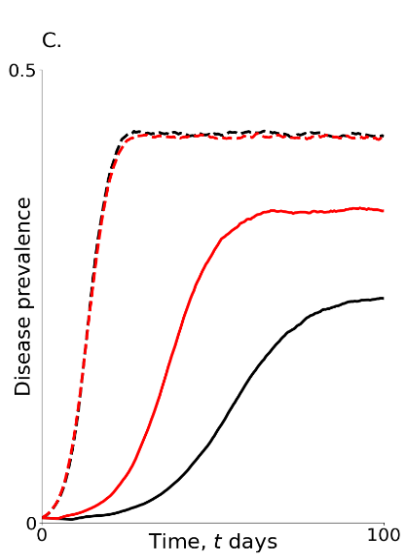


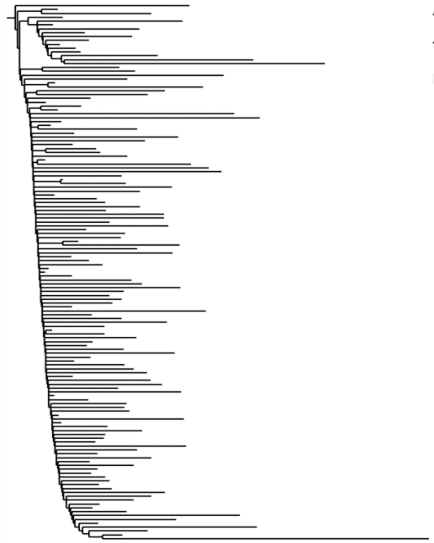


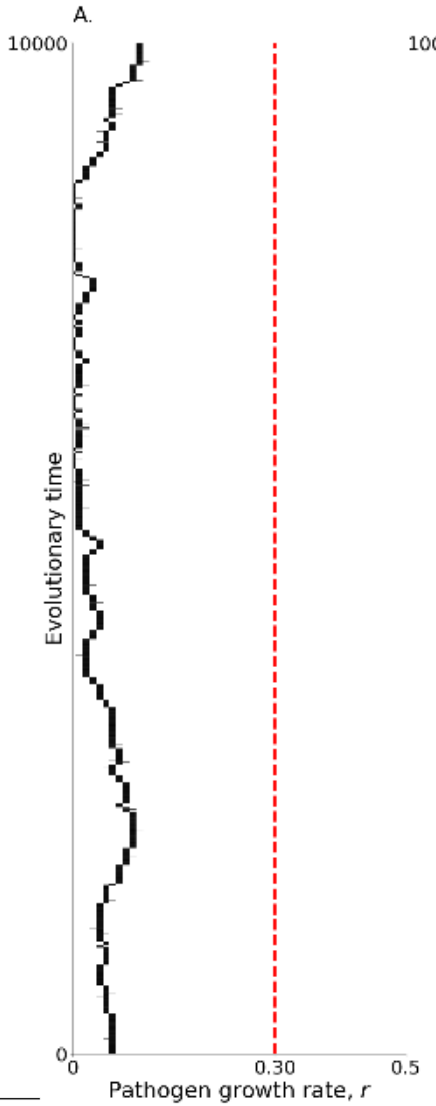
Recap

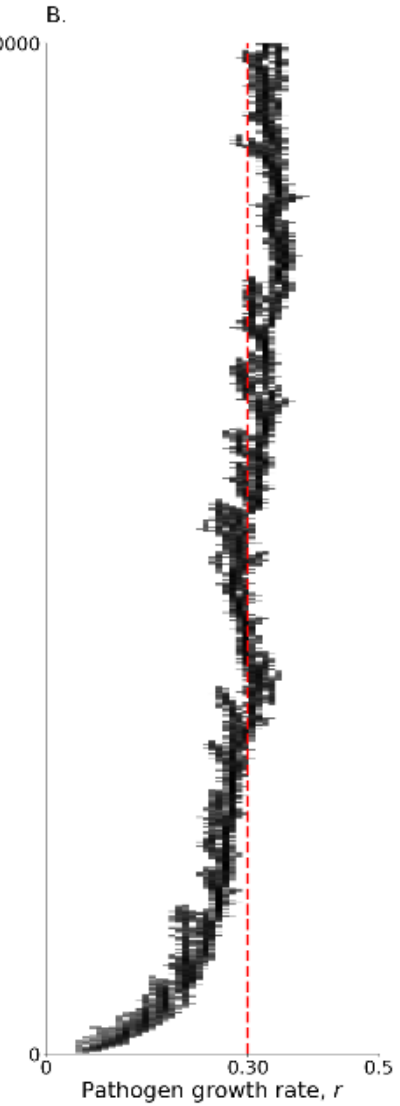
In general we cannot (or do not wish to) model multi-scale processes in full mechanistic detail, and even simulating such models becomes computationally intractable. **Can we come up with ways of extracting the essence of lower-scale models so that they can be embedded into higher-scale models efficiently** (Mideo et al., 2008)?











Thank you!

Efficient coupling of within- and between-host infectious disease dynamics
C.A. Smith and B. Ashby
Under review

Ben Ashby

Simon Fraser University

Kayla King

University of British Columbia

Get in touch!

cameron.smith@biology.ox.ac.uk

cameronsmith50.github.io

Funders/affiliations

erc

UKRI Natural Environment Research Council

University of Bath

Department of Biology

University of Oxford