Modeling vector-borne diseases

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Learning objectives

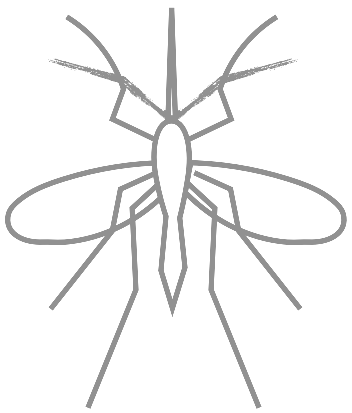
- Understand the utility and development of mathematical models to study the transmission dynamics of vector-borne infectious diseases
  Comprendre l'utilité et le développement de modèles mathématiques pour étudier la dynamique de transmission des maladies infectieuses à vecteur

- Compare and contrast epidemiological and life history features of vector-borne diseases versus directly-transmitted diseases
  Comparer et comparer les caractéristiques épidémiologiques et biologiques des maladies à vecteur par rapport aux maladies directement transmises

- SIRS model structure

- Incorporate environmental variables into vector populations
  Incorporer des variables environnementales dans les populations de vecteurs

- Understand the implications for disease elimination and control
  Comprendre les implications pour l'élimination et le contrôle de la maladie



0. Introduction

Vector-borne diseases
maladie transmise par des vecteurs

Pathogens transmitted among hosts by an intermediate species, primarily arthropods such as mosquitos or ticks
Agents pathogènes transmis parmi les hôtes par une espèce intermédiaire, principalement des arthropodes tels que les moustiques ou les tiques

Examples: malaria, dengue, chikungunya, Crimean-Congo hemorrhagic fever, west nile virus, Japanese encephalitis
paludisme, dengue, chikungunya, fièvre hémorragique de Crimée-Congo, virus du Nil occidental, encéphalite japonaise

What makes vector-borne diseases different to model and study than directly-transmitted diseases?

Two sets of population dynamics — demography, transmission, interactions, etc.

Environmental factors and abiotic conditions

Transmission depends on both the human and vector compartments

Vector	Disease	Estimated or reported annual number of cases	Estimated annual number of deaths	Estimated annual disability-adjusted life years
Mosquitoes	Malaria[1]	212 000 000 (148 000 000–304 000 000) [1]	429 000 (235 000–639 000) [1]	NA
	Dengue	96 000 000 (67 000 000–136 000 000) [2]	9 110 (5630–10 842) [3]	1 892 200 (1 266 700–2 925 500) [5]
	Lymphatic filariasis	38 464 000 (31 328 000–46 783 000) [6]	NA	2 075 000 (1 120 500–3 311 500) [5]
	Chikungunya (Americas)	693 000 [7] suspected, 2015	NA	NA
	Zika virus disease (Americas)	500 000 [8] suspected, 2016	NA	NA
	Yellow fever (Africa)	130 000 (84 000–170 000) [9]	500* (400–600) [3]	31 000* (25 000–37 000) [3]
	Japanese encephalitis	42 500* (35 000–50 000) [10]	9 250* (3500–15 000) [10]	431 552* (107 435–755 670) [10]
	West Nile fever	2 588 [11]	111 [11]	NA

~17% of all infectious diseases, more than 700k deaths (WHO, 2017)

1. The basic model

Compartmental models (Mechanistic Models)

Populations are divided into compartments

Les populations sont subdivisées en compartiments

Compartments and transition rates are determined by biological systems

Les compartiments et les taux de transition sont déterminés par les systèmes biologiques

Rates of transferring between compartments are expressed mathematically

Taux de transition entre les compartiments sont exprimés mathématiquement

Individuals within a compartment are homogeneously mixed

Les individus d'un compartiment sont mélangés de manière homogène

How are these different from statistical models?

En quoi sont-ils différents des modèles statistiques?

Make explicit hypotheses about biological mechanisms that drive dynamics (may not be realistic, but still explicit)

Faire des hypothèses explicites sur les mécanismes biologiques qui régissent la dynamique (peut ne pas être réaliste, mais toujours explicite)

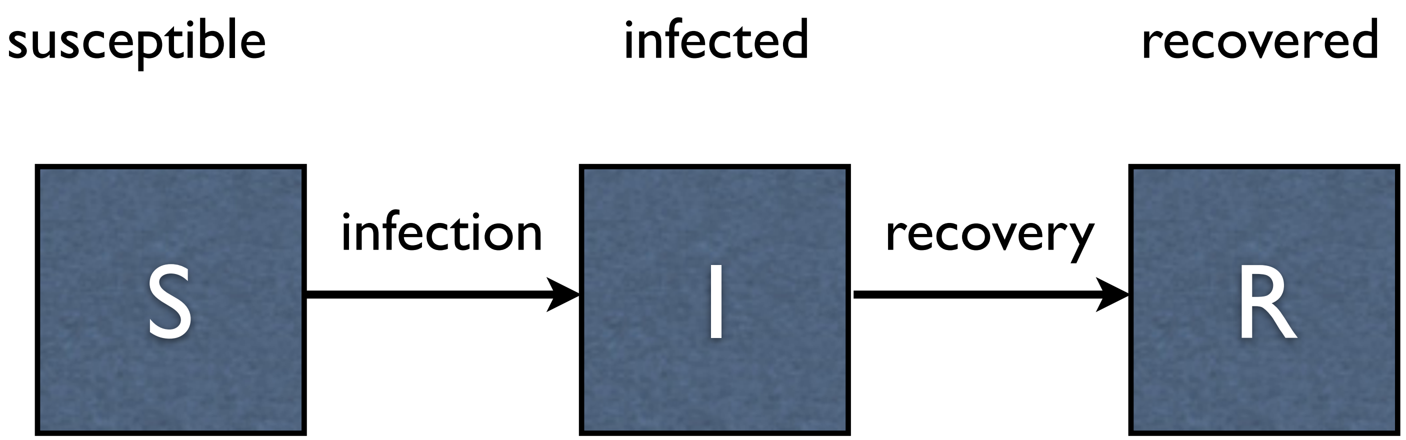
The basic vector model

susceptible infected recovered

everyone is either:

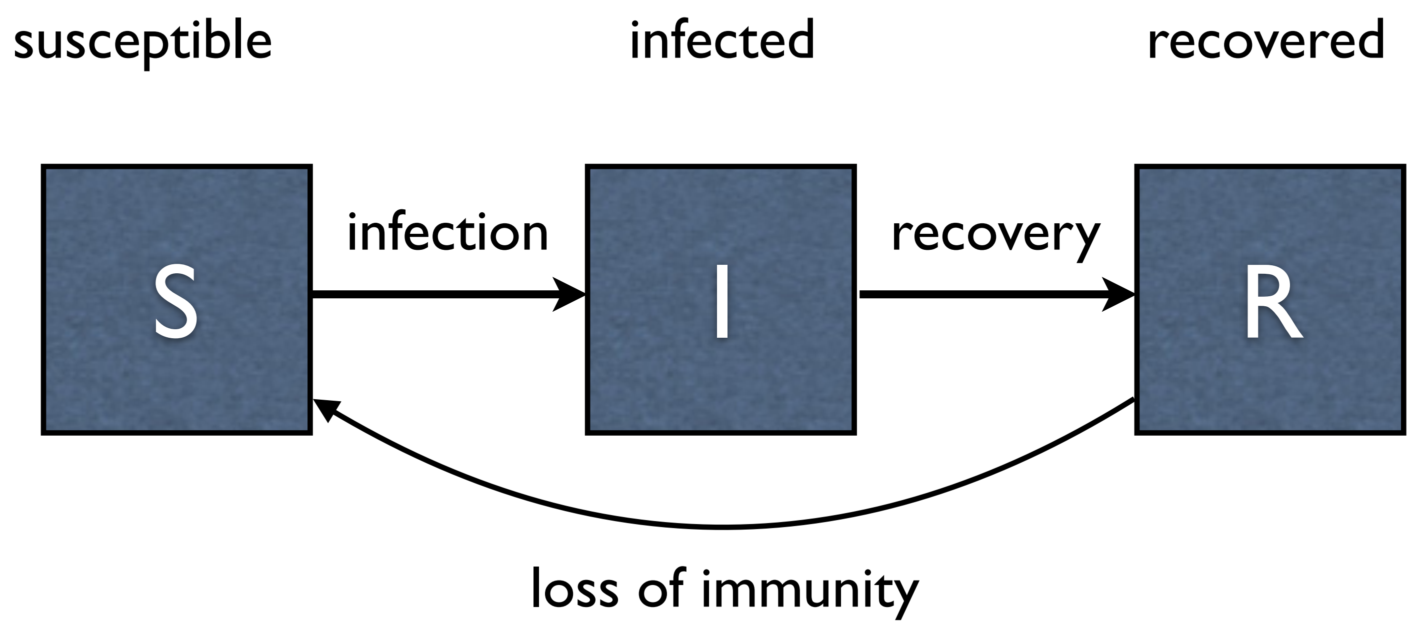
The basic vector model

everyone is either:



The basic vector model

everyone is either:



The basic vector model

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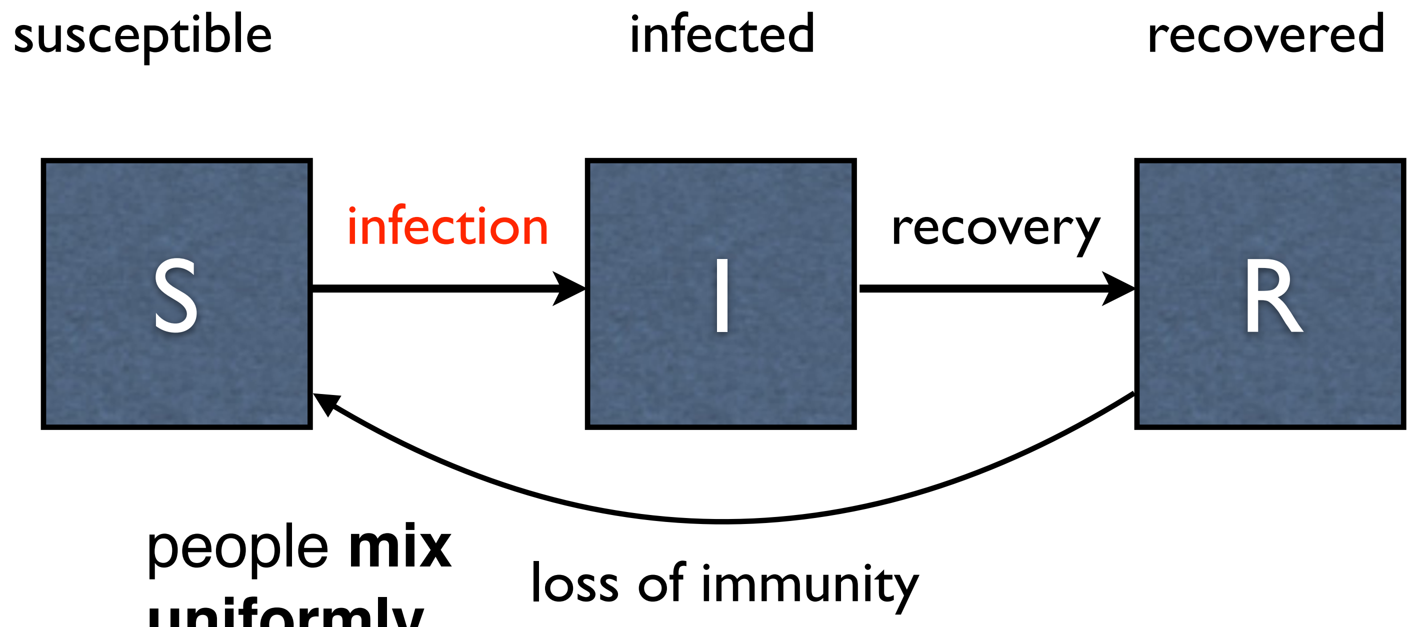
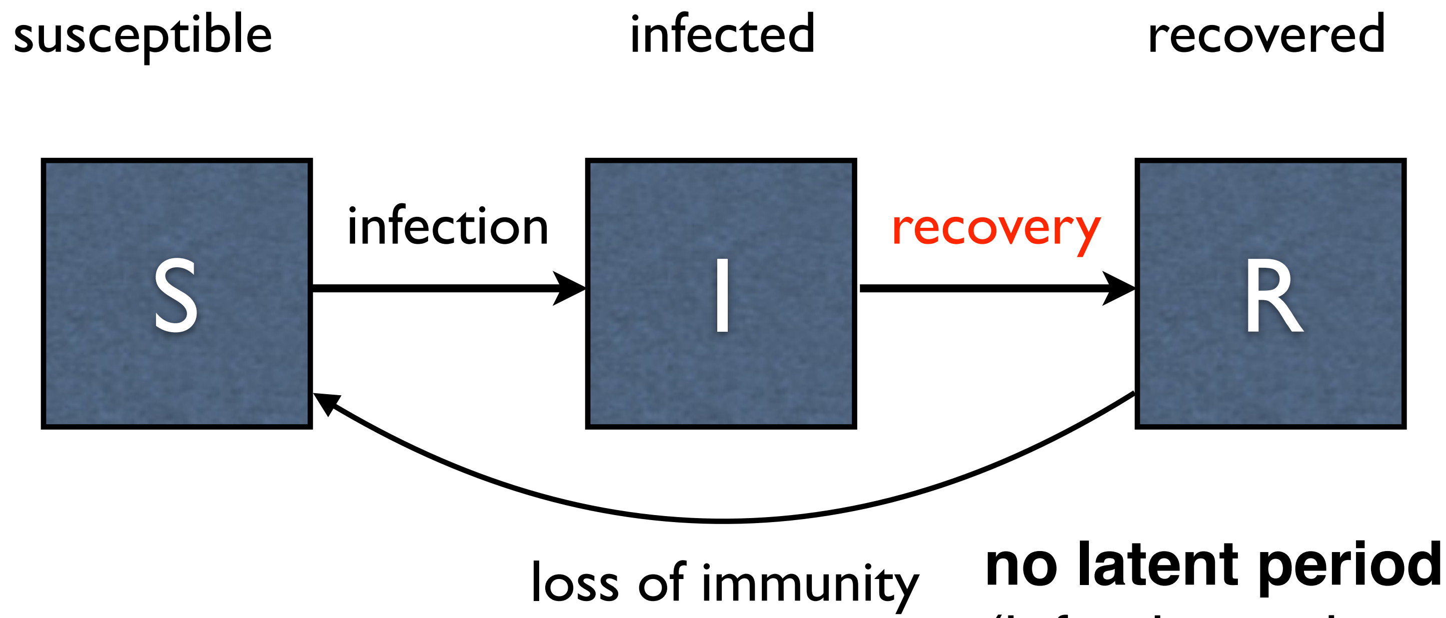


people **mix uniformly**

The basic vector model

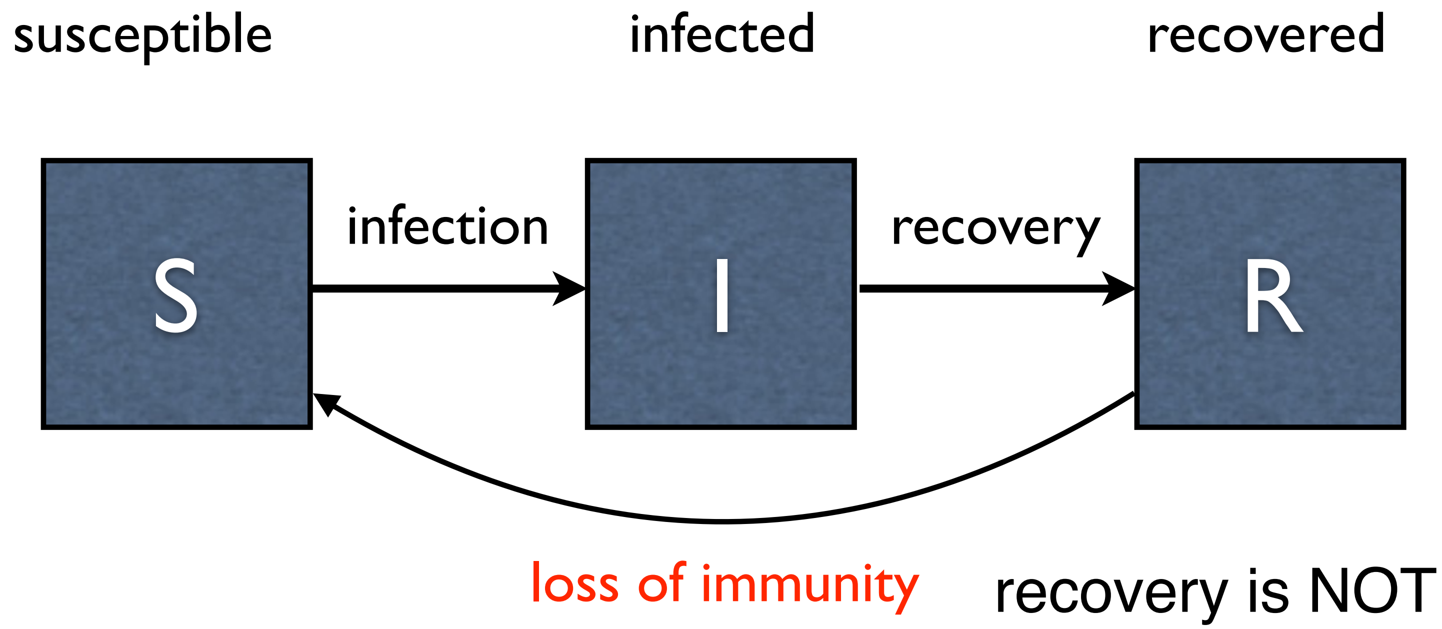
everyone is either:



no latent period
(infectious when infected)

The basic vector model

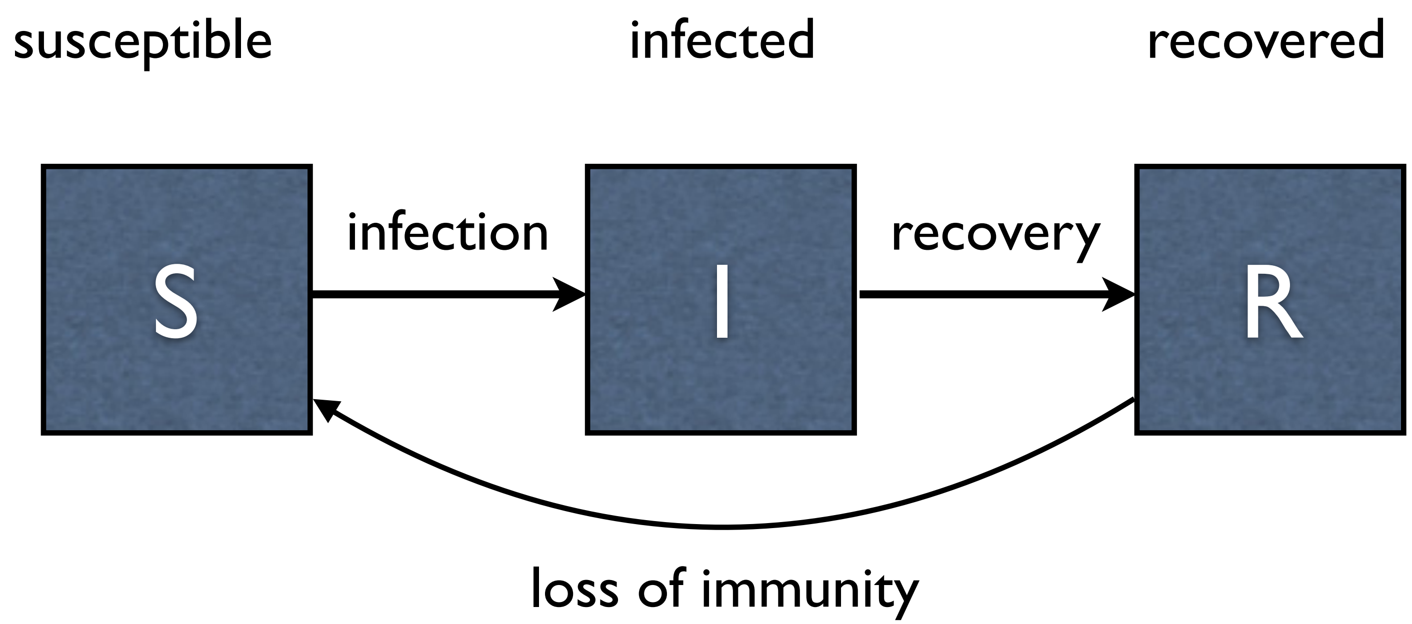
everyone is either:



recovery is NOT **permanent**

The basic vector model

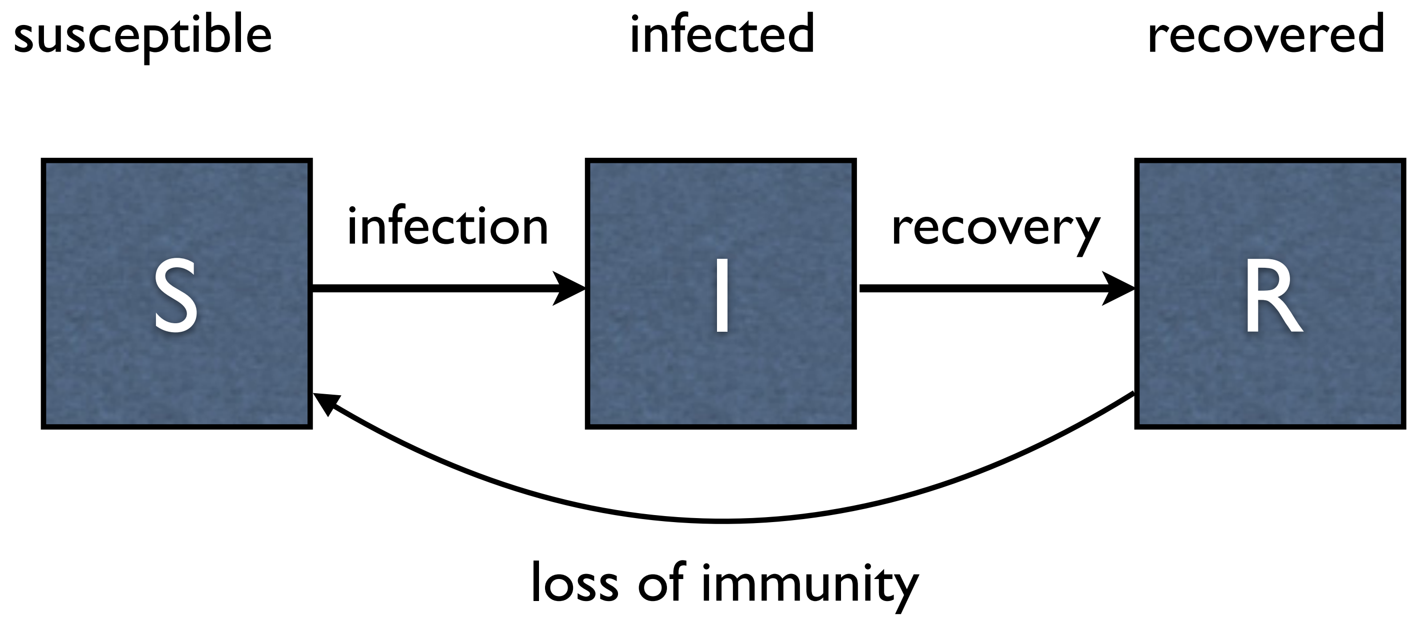
everyone is either:



population size **constant** - no births or deaths, migration

The basic vector model

everyone is either:



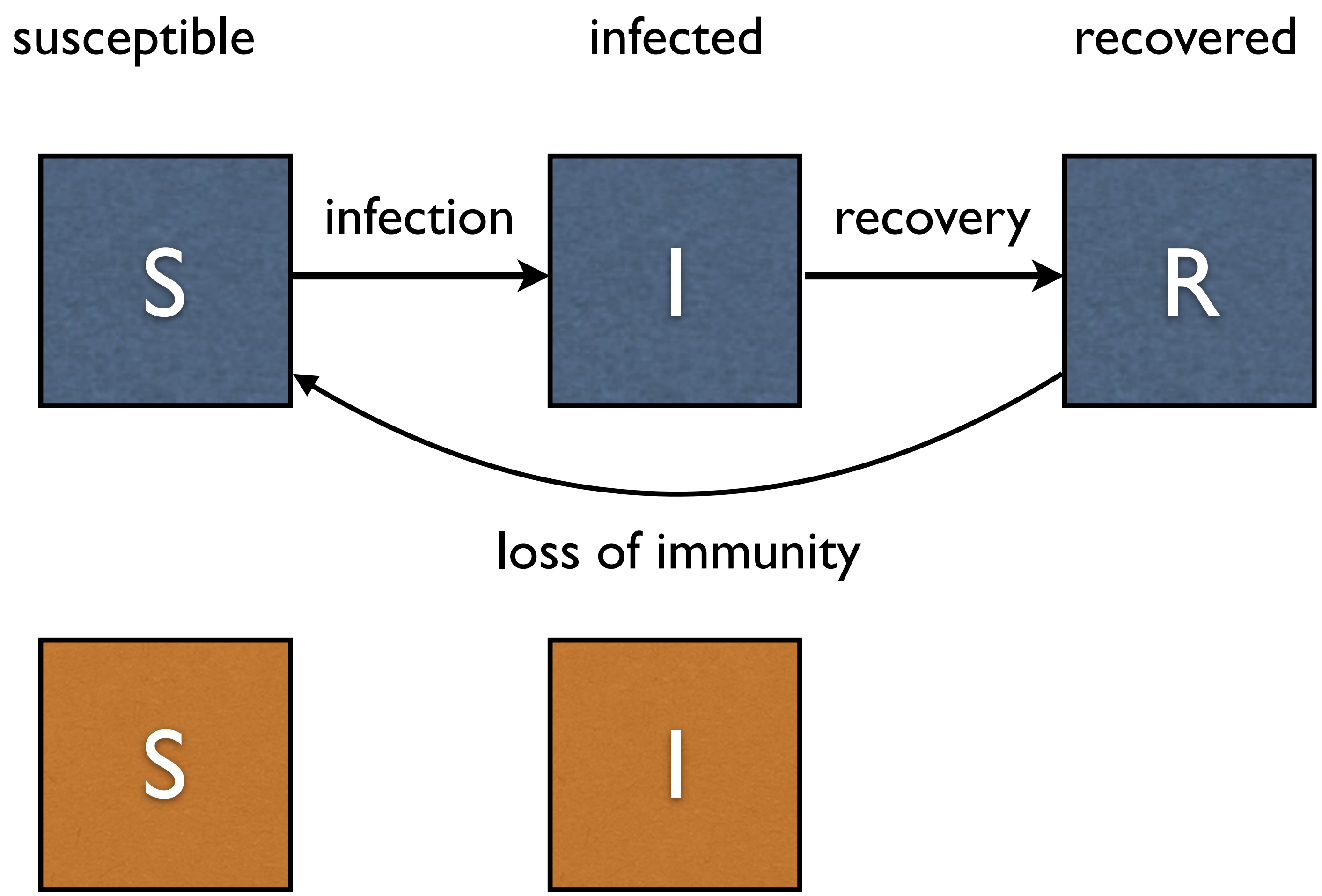
Human compartments…

Individuals can be susceptible, infected, or recovered. After recovery they can then become susceptible here.

Similar to an SIR model, but now an SIRS model.

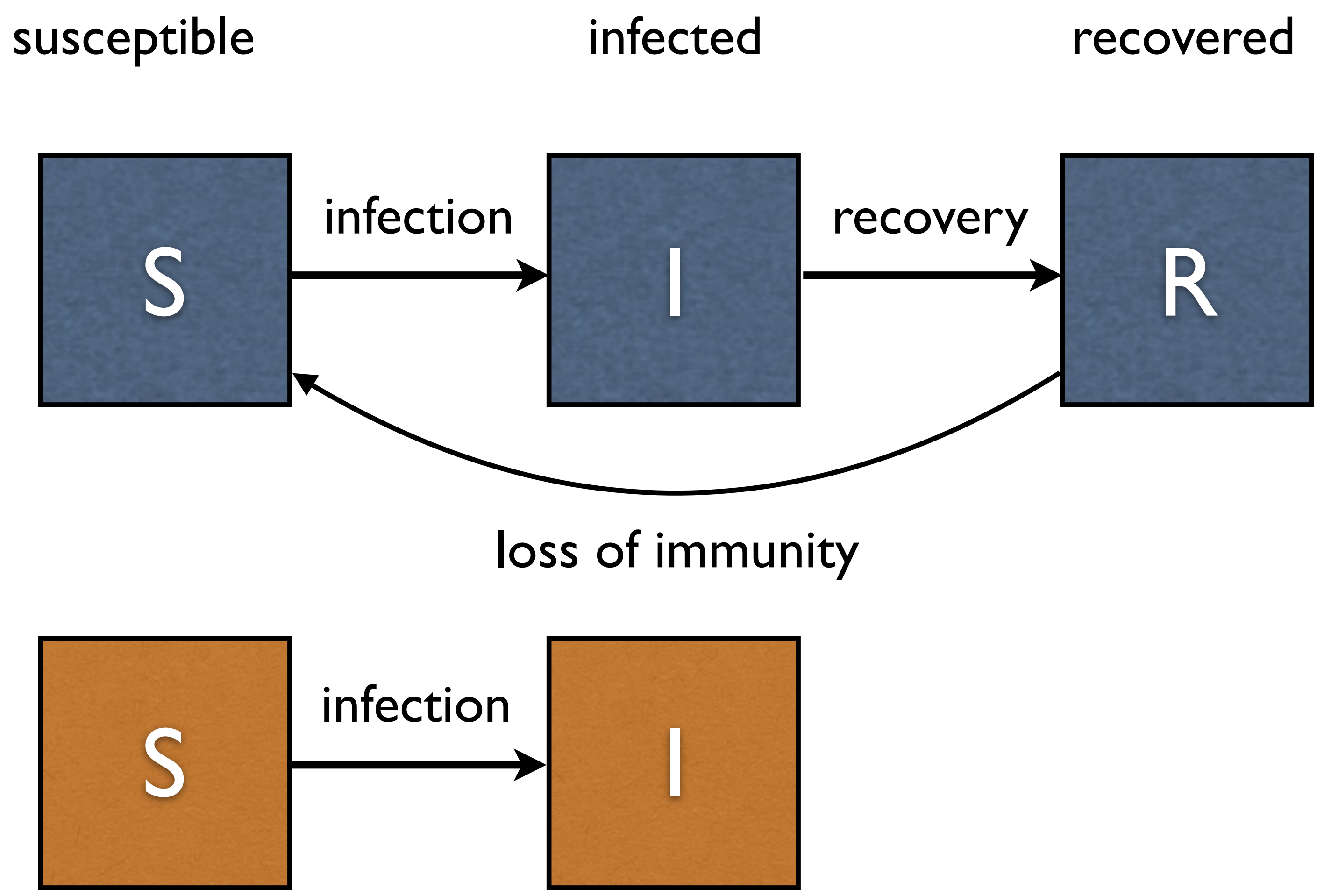
What is the assumption about immunity here?

The basic vector model



Vector compartments…

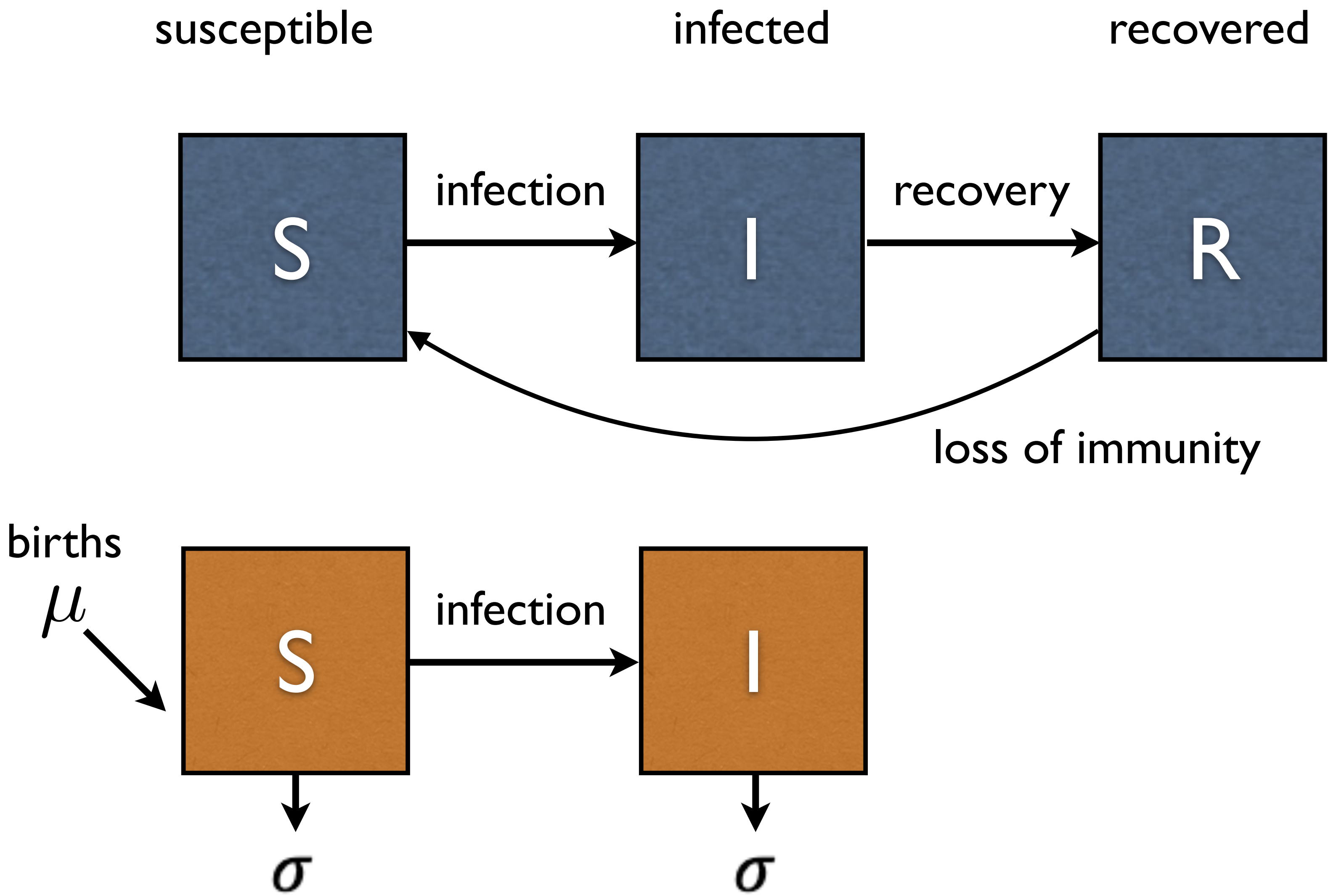
The basic vector model



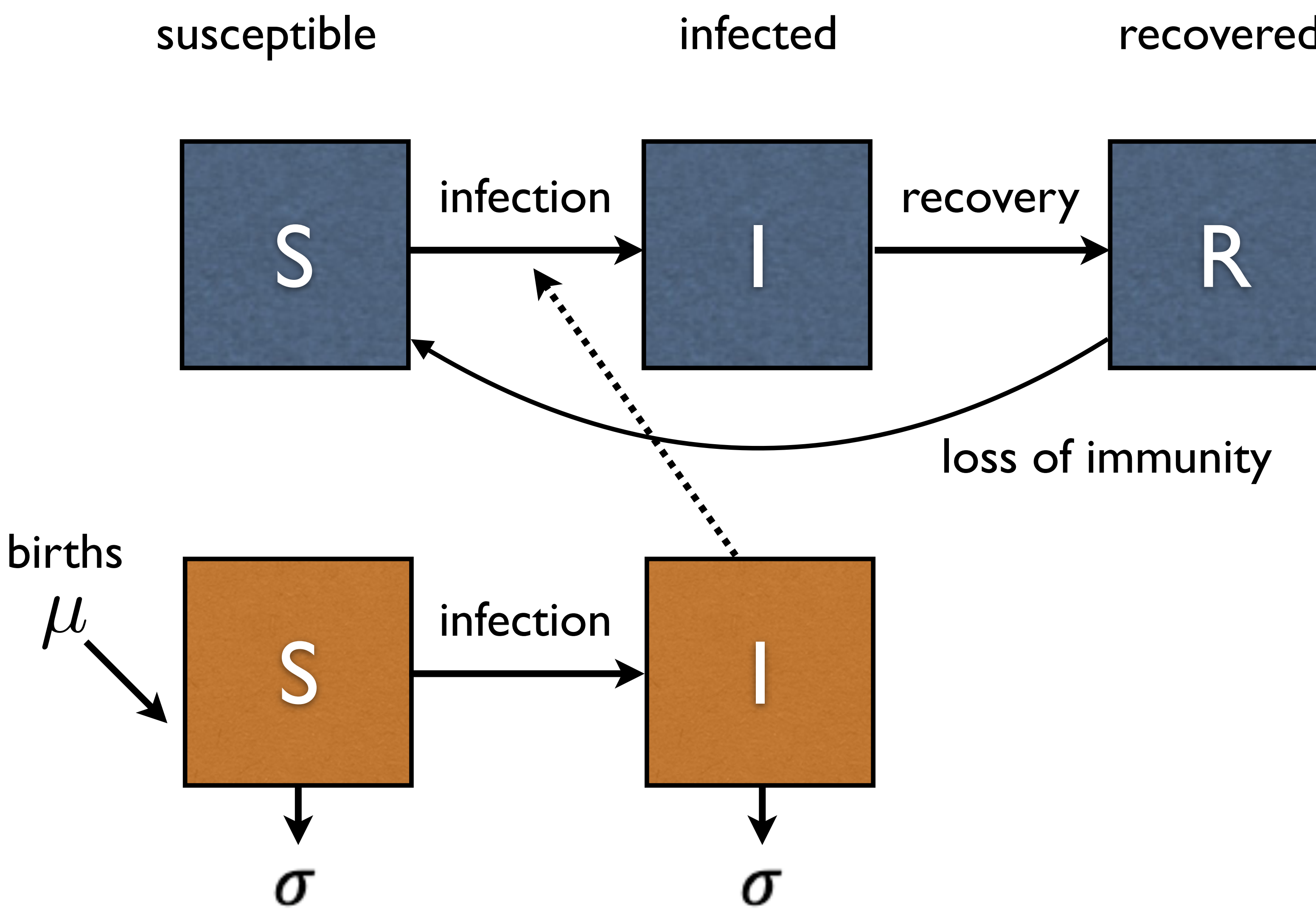
Vector compartments…

Vectors can either be susceptible or infected (assumes death after infection = no recovery).

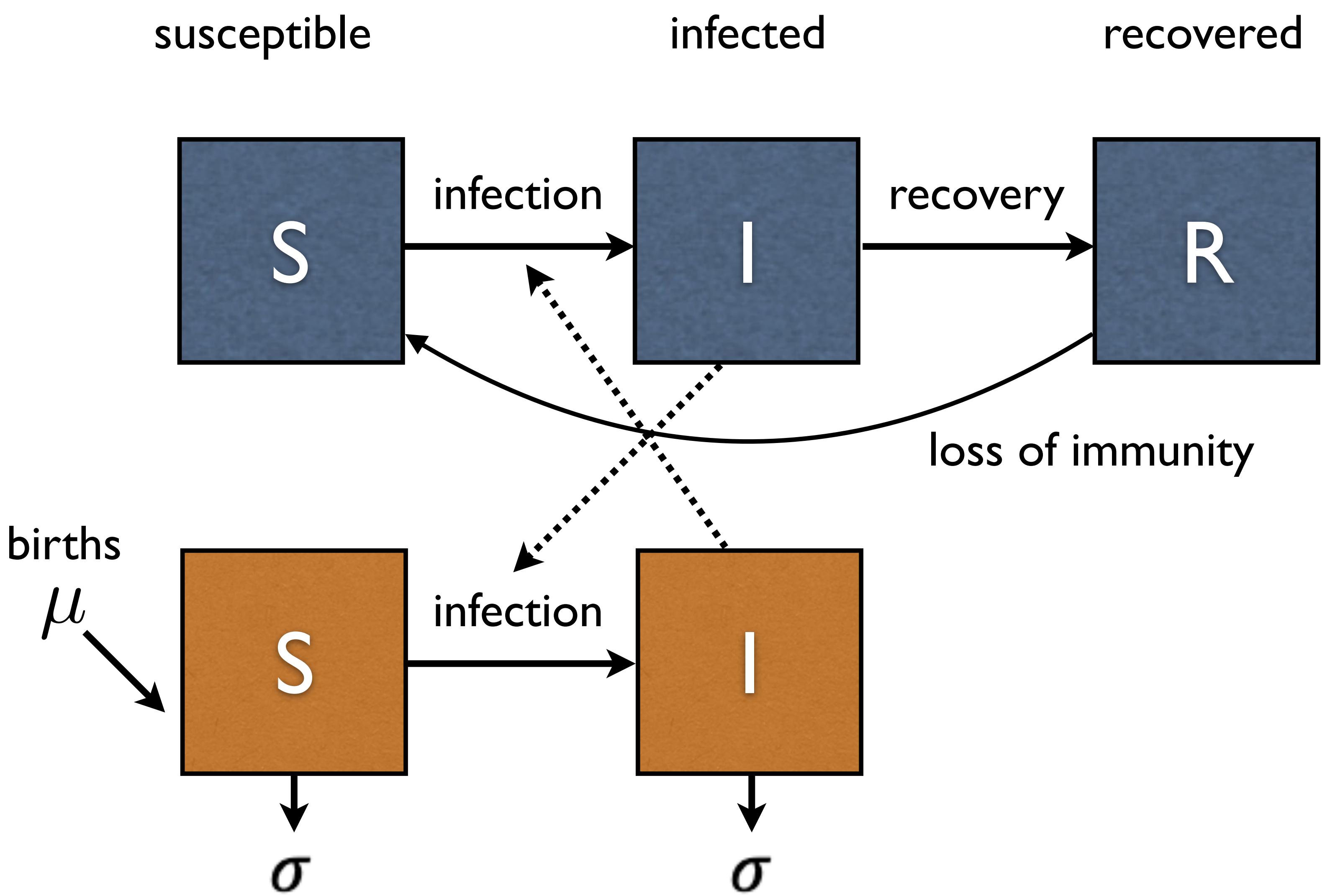
The basic vector model



The basic vector model



The basic vector model



The infectious compartment of the humans impacts the transmission for vectors! (and visa versa)

The basic vector model

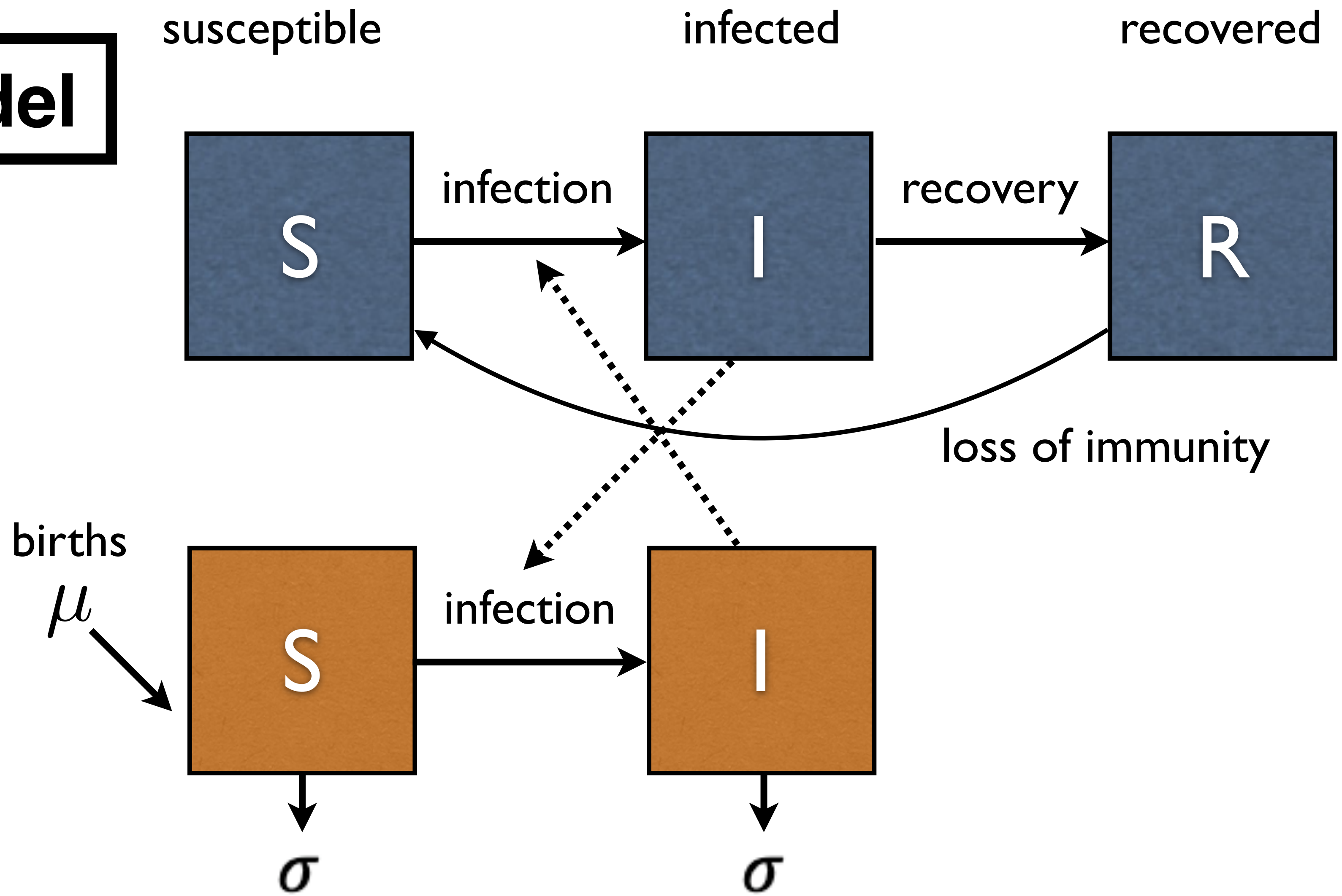
Parameters

β_H: transmission rate

γ : rate of recovery

w : rate of loss of immunity

Humans



Vectors

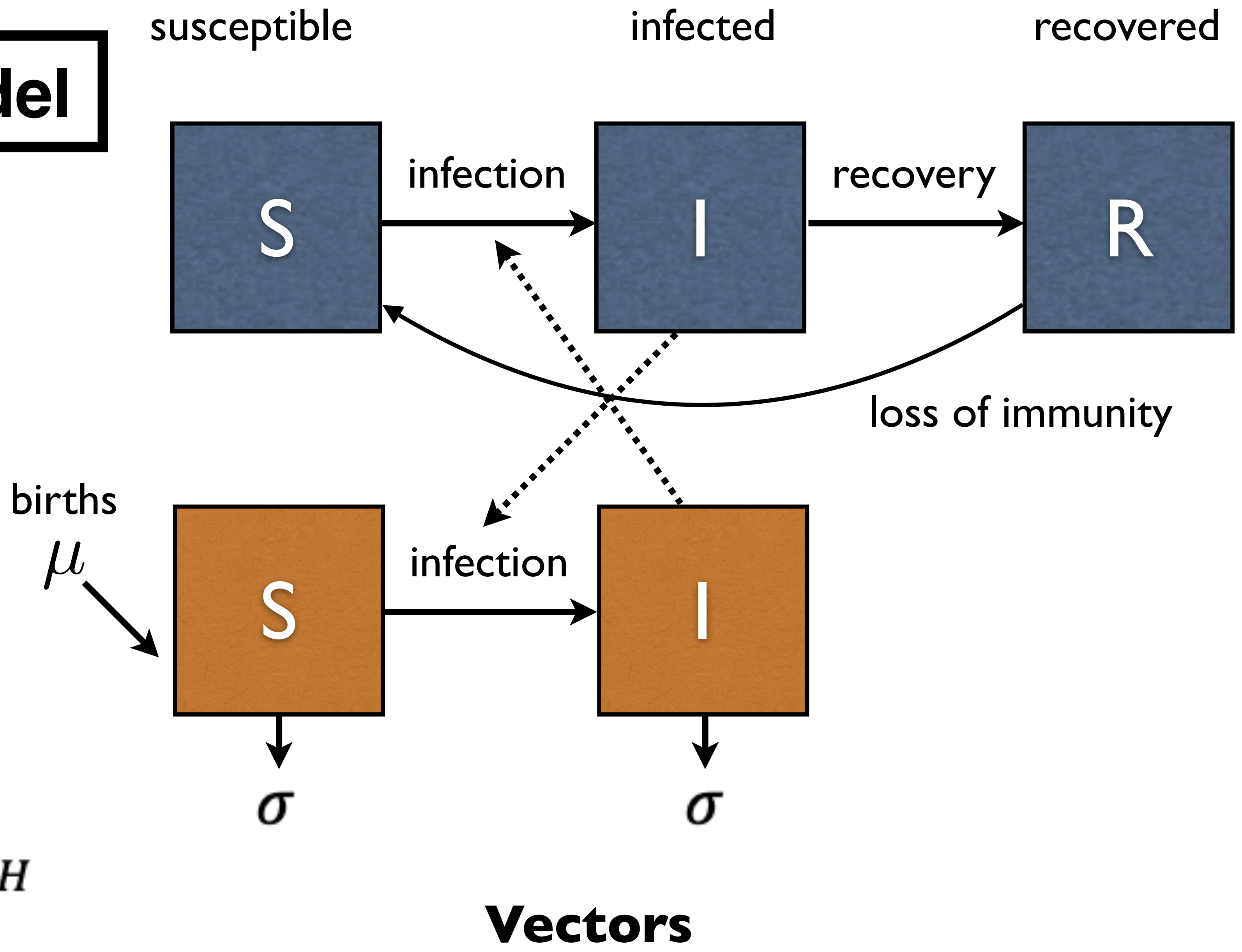
The basic vector model

Parameters

β_H: transmission rate

γ : rate of recovery

w : rate of loss of immunity



Humans

$$\frac{dS_H(t)}{dt} = -\beta_H S_H I_V + wR_H$$

$$\frac{dI_H(t)}{dt} = \beta_H S_H I_V - \gamma I_H$$

$$\frac{dR_H(t)}{dt} = \gamma I_H - wR_H$$

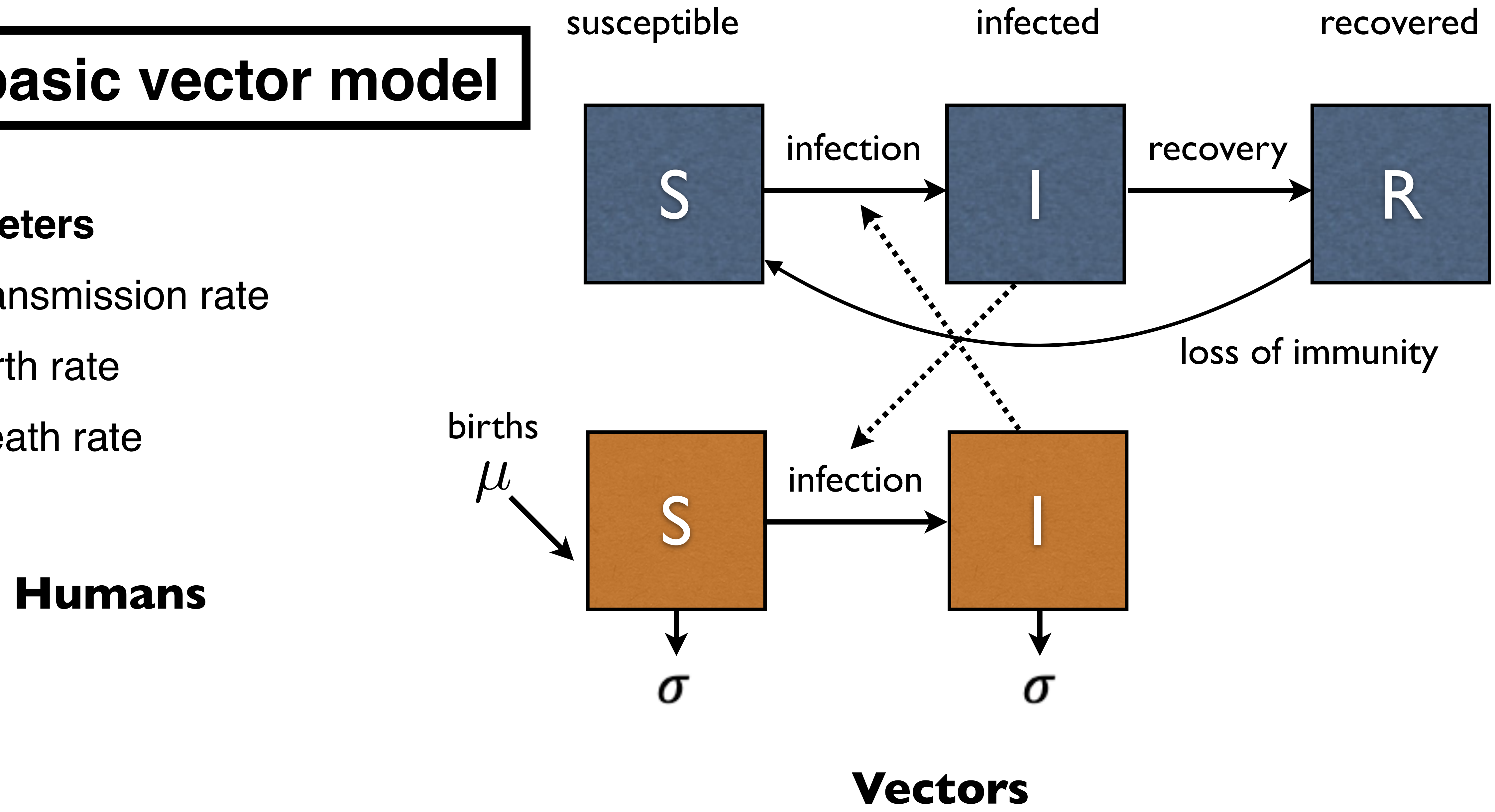
The basic vector model

Parameters

β_V : transmission rate

μ : birth rate

σ : death rate



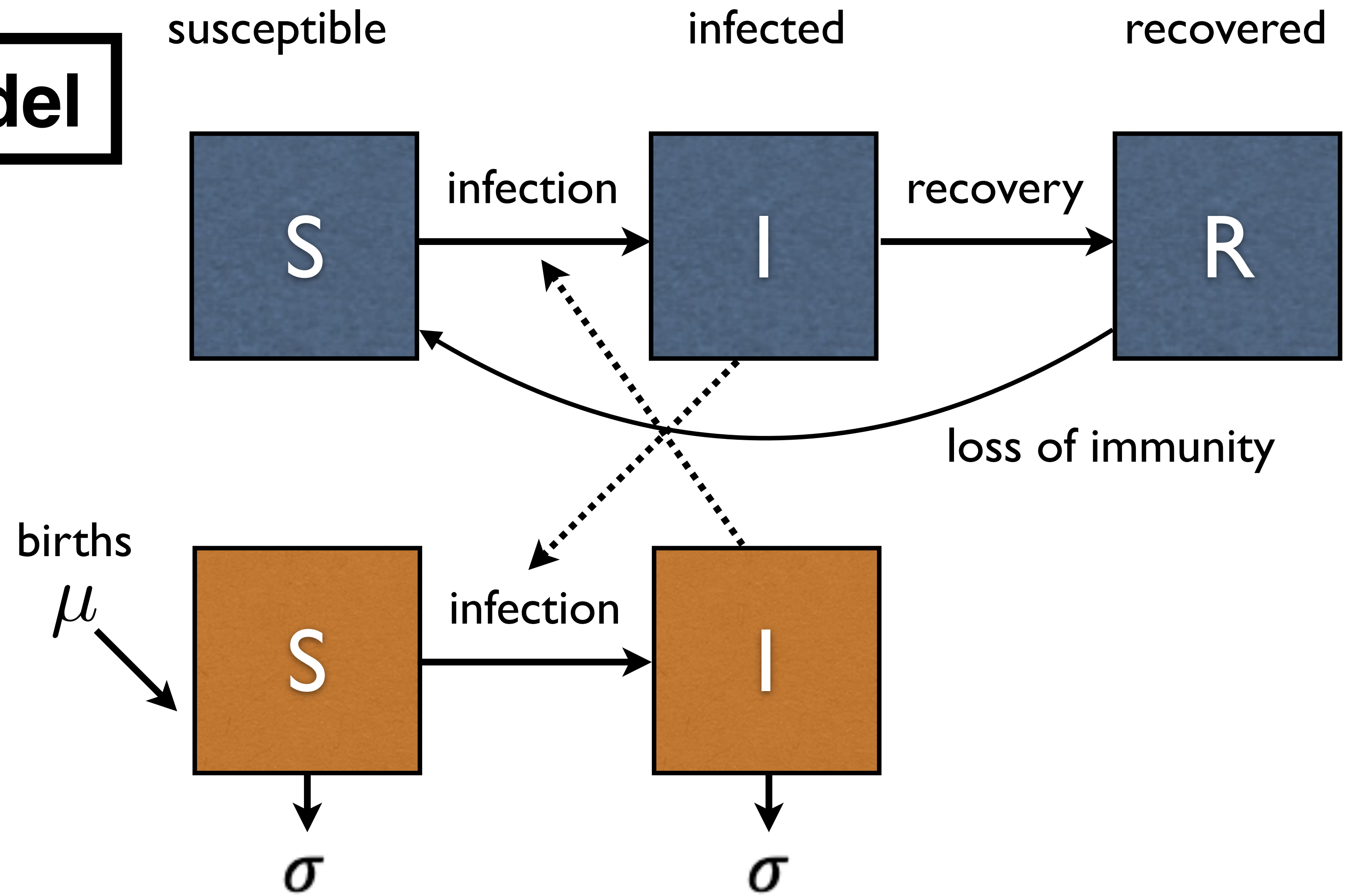
The basic vector model

Parameters

β_V : transmission rate

μ : birth rate

σ : death rate



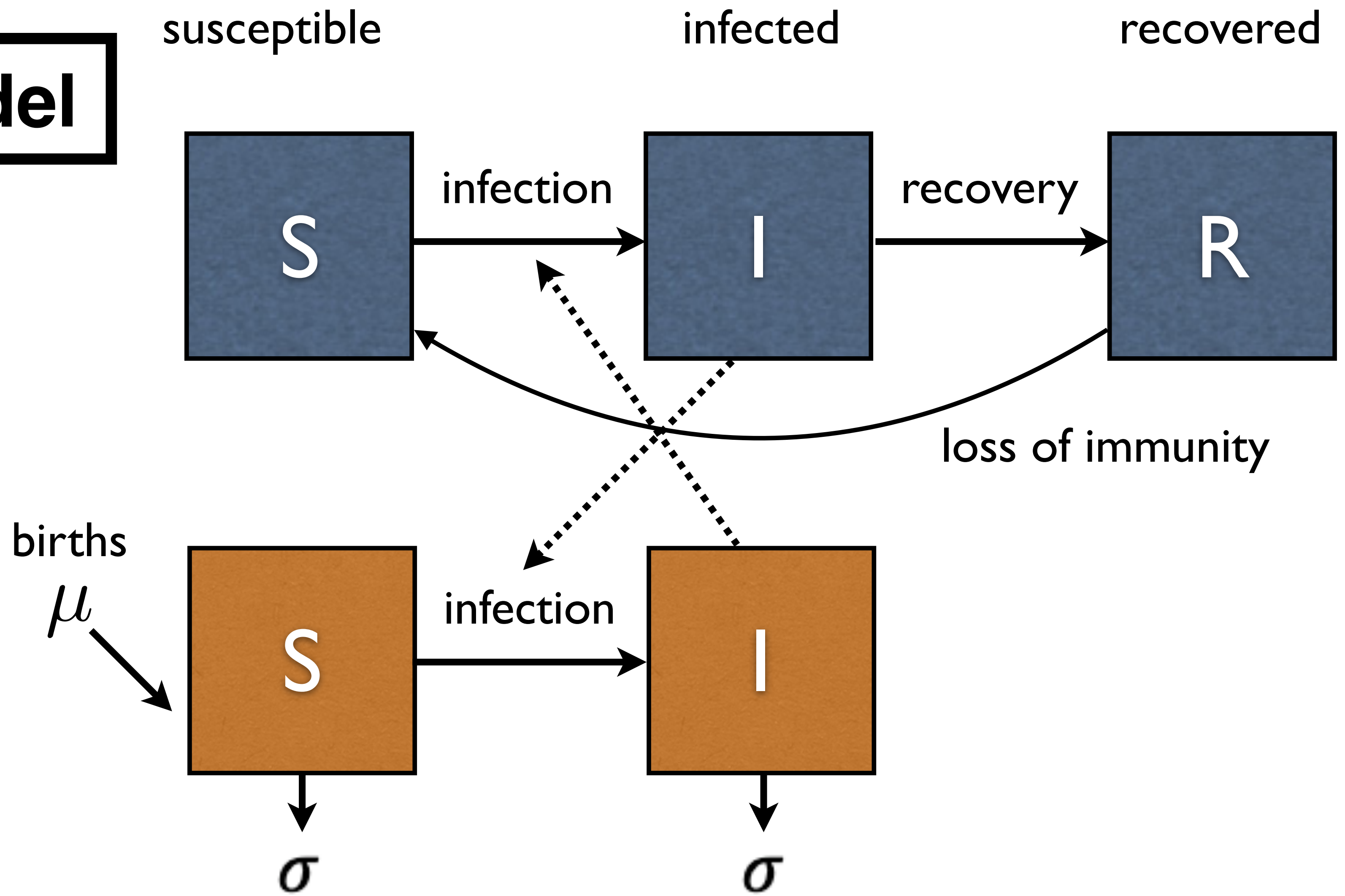
Humans

Vectors

$$\frac{dS_V(t)}{dt} = \mu - \beta_V S_V I_H - \sigma S_V$$

$$\frac{dI_{V(t)}}{dt} = \beta_V S_V I_H - \sigma I_V$$

The basic vector model



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Vectors

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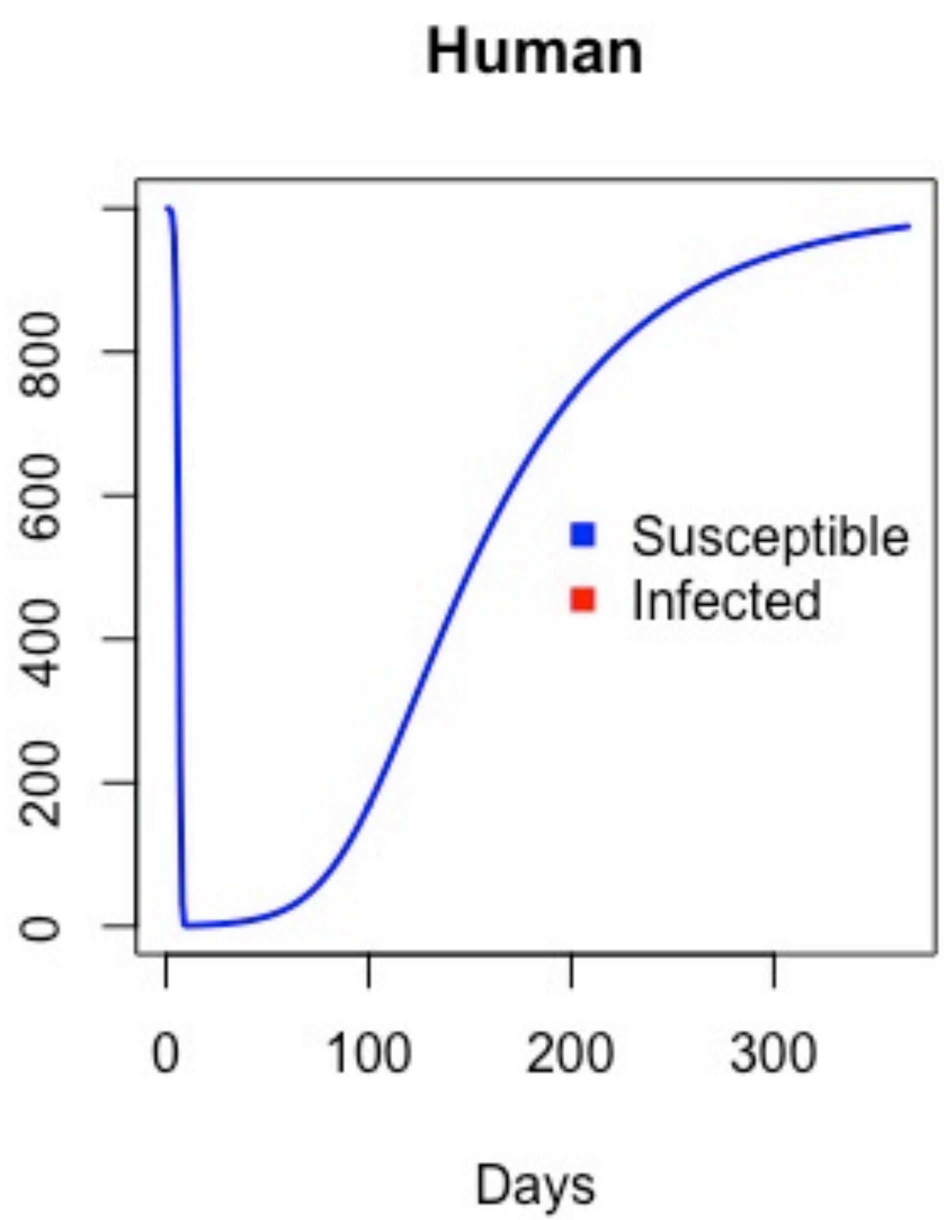
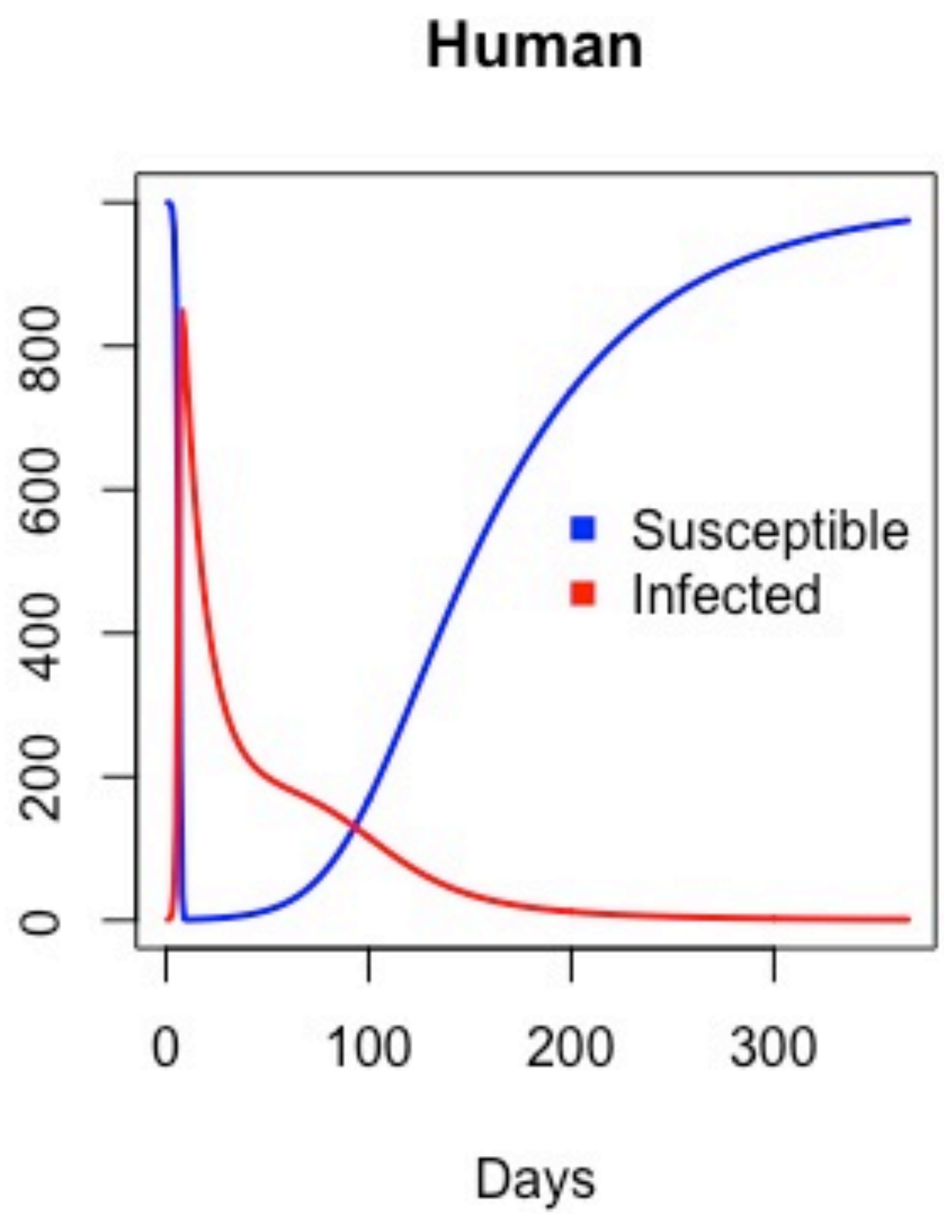
The basic vector model: dynamics



The basic vector model: dynamics



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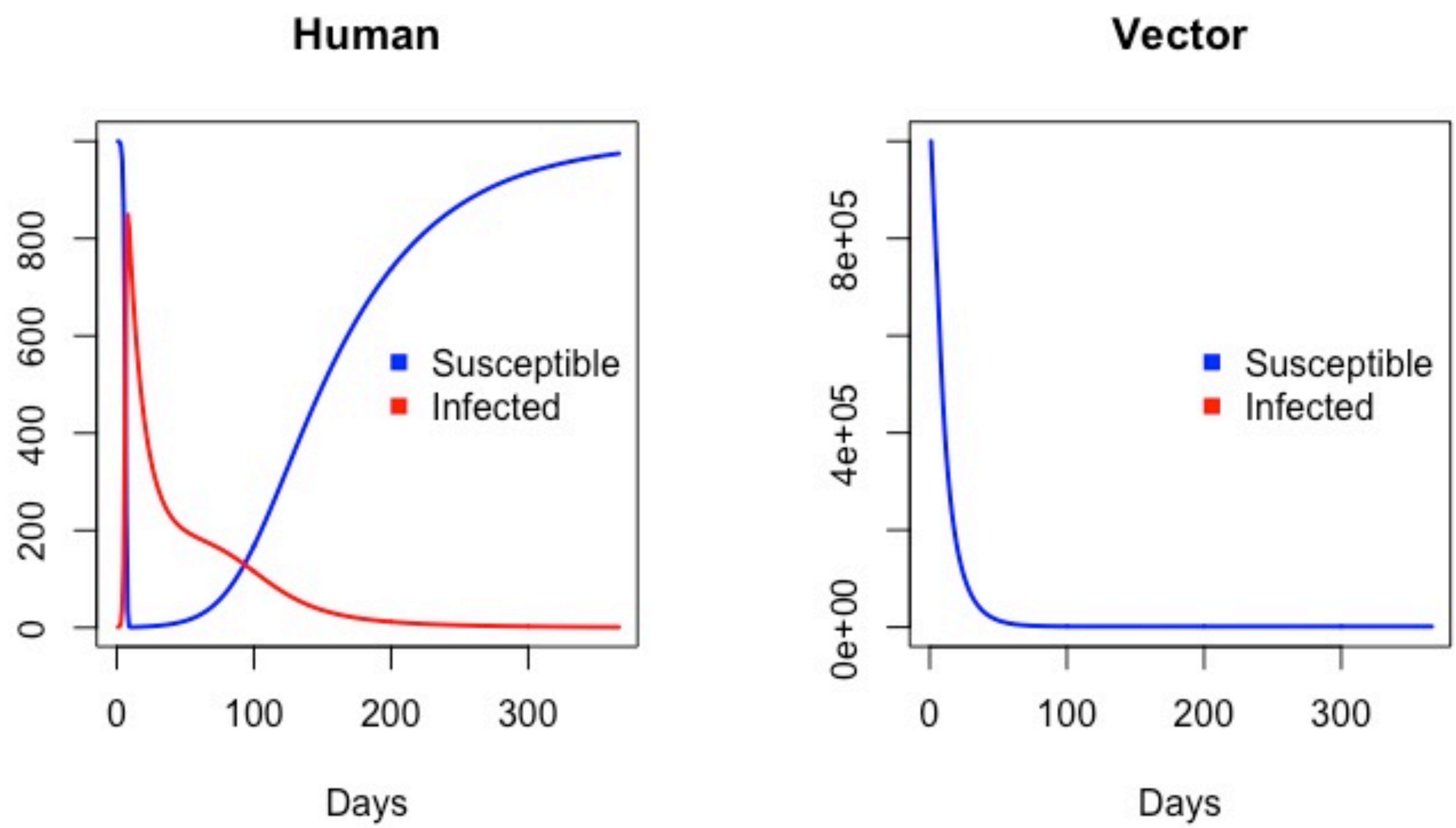
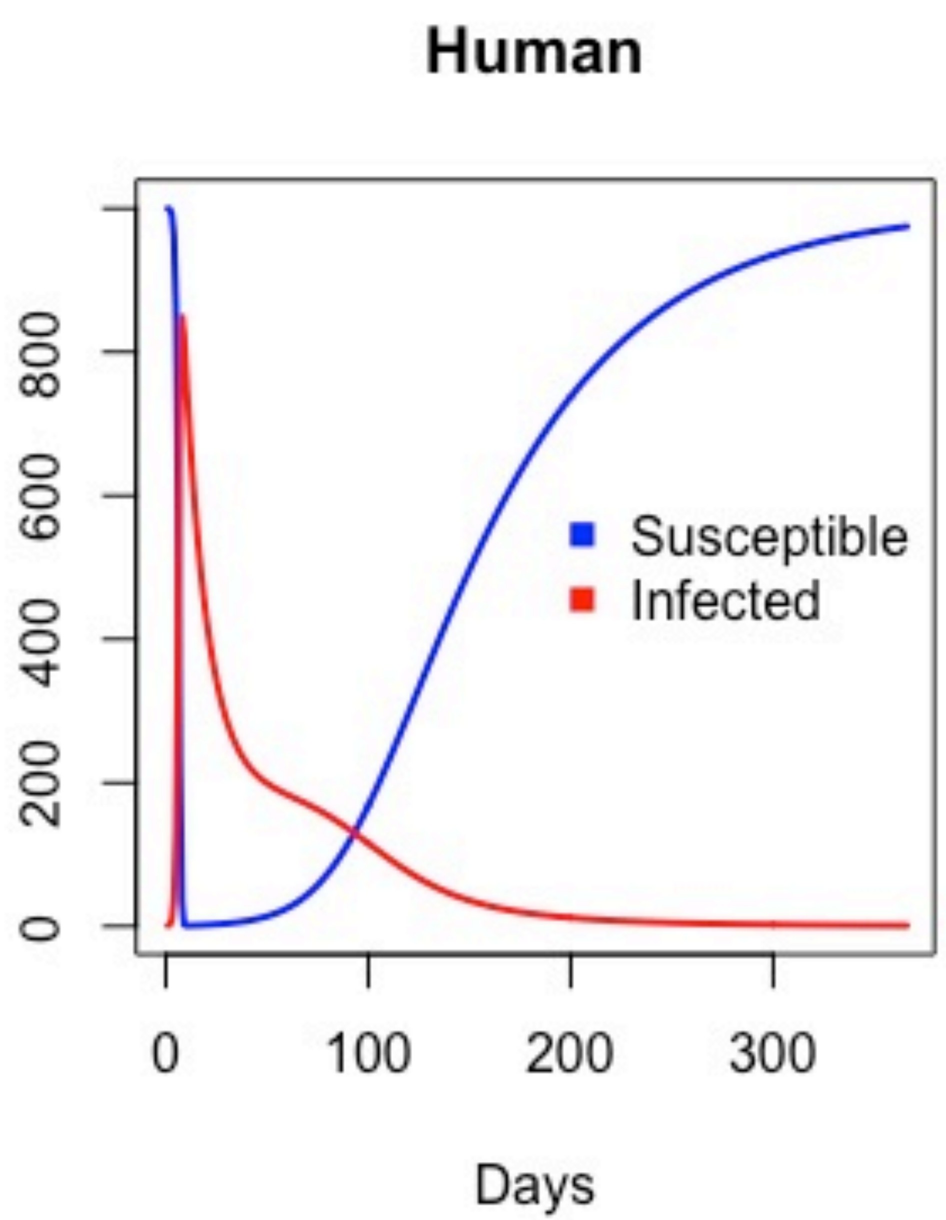
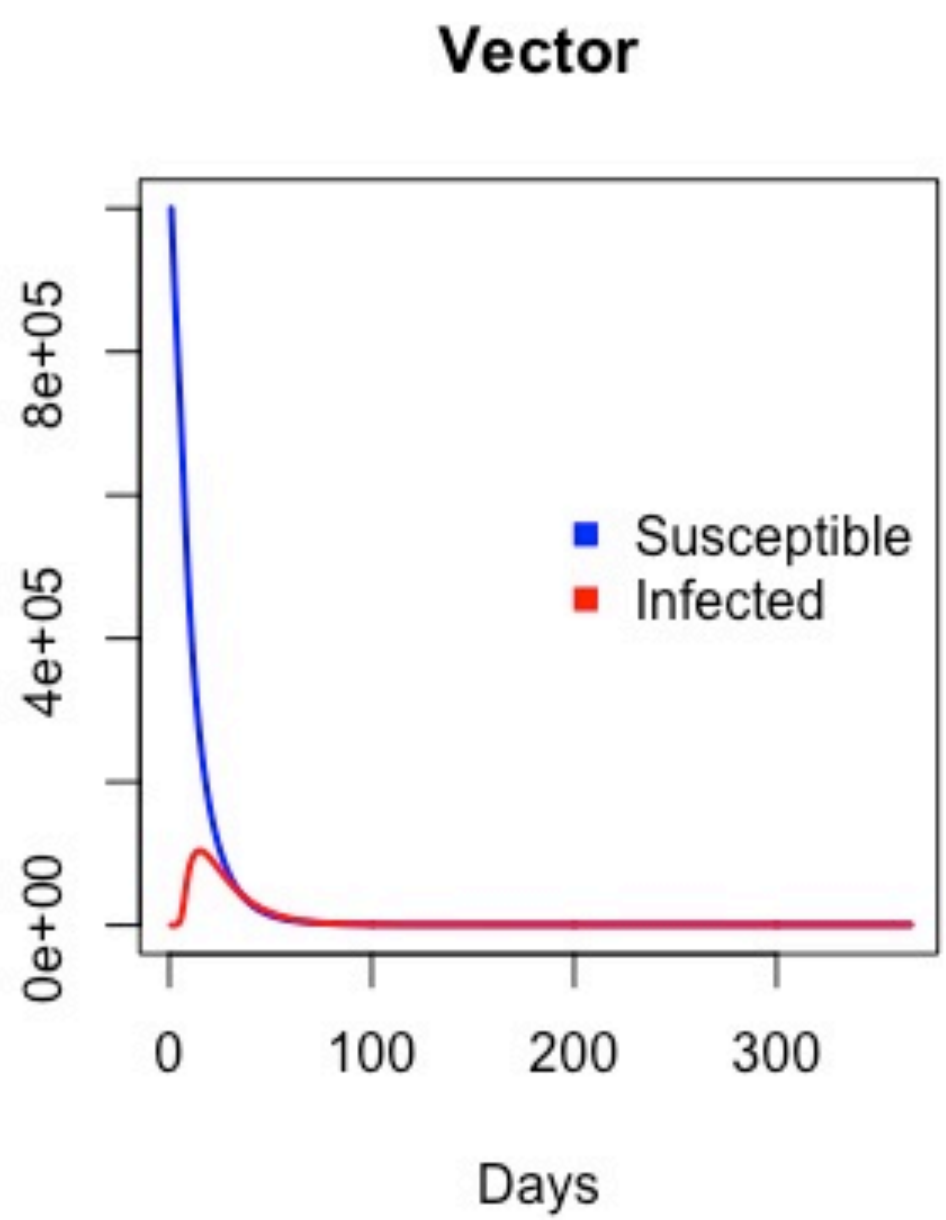
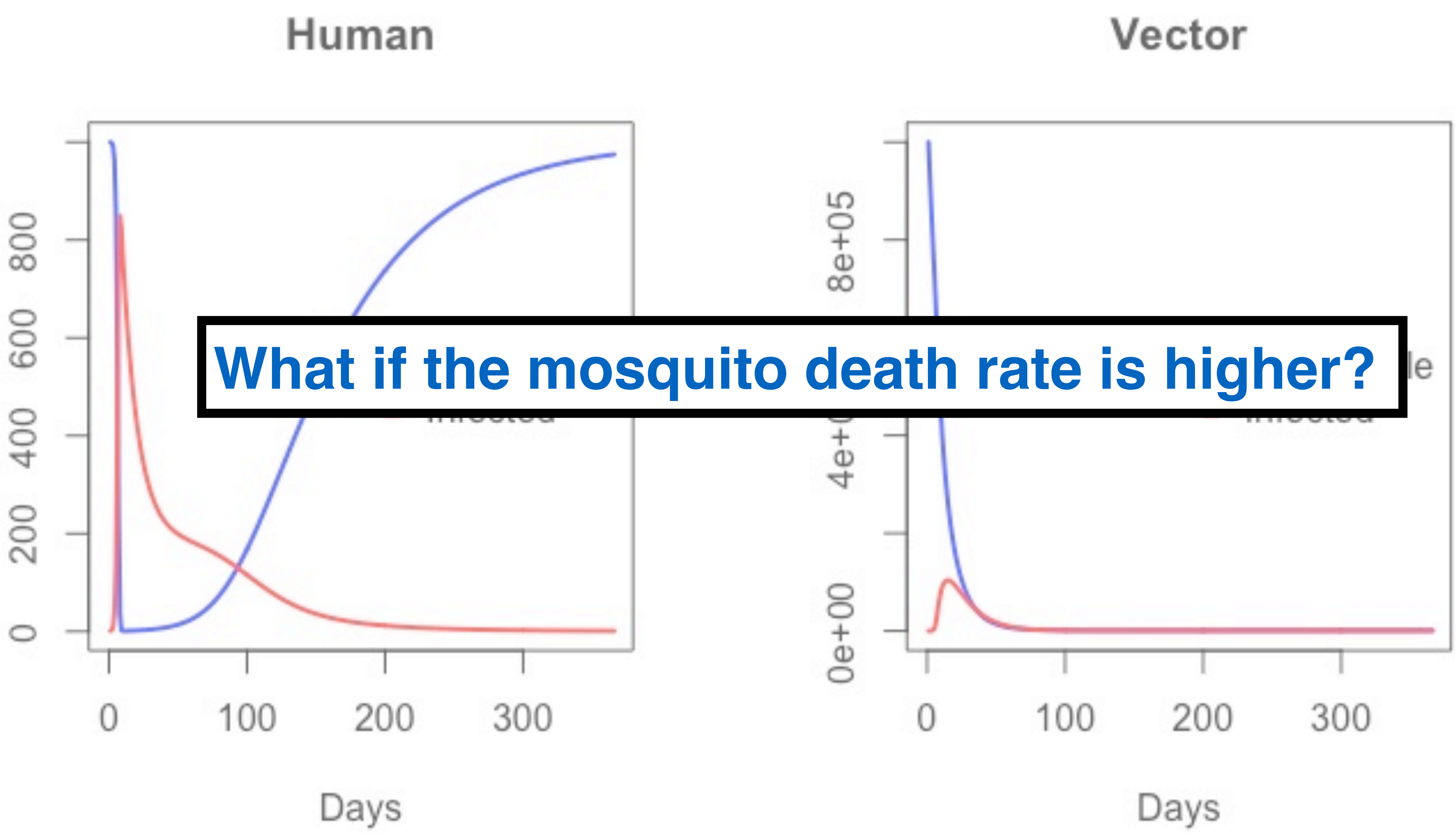


The basic vector model: dynamics



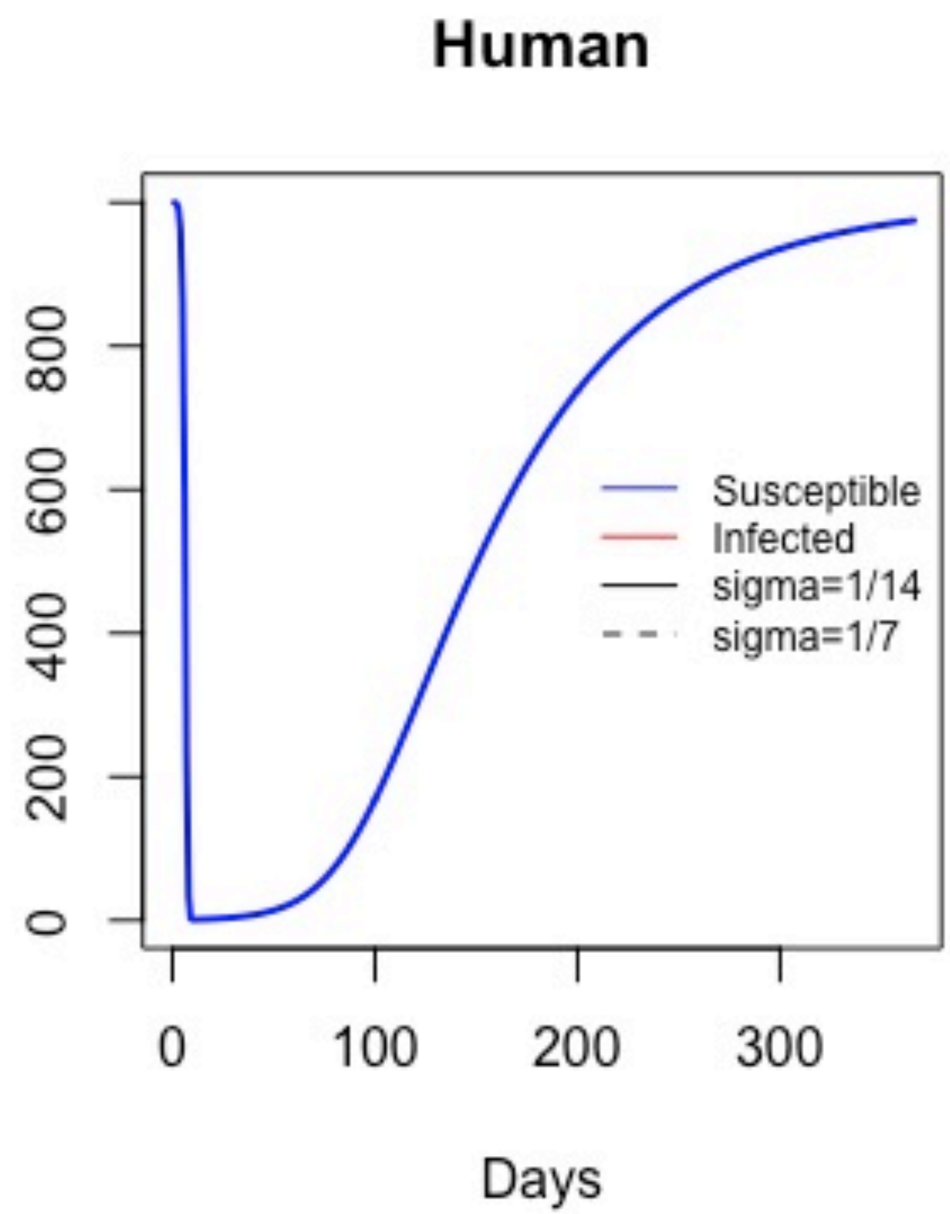


The basic vector model: dynamics

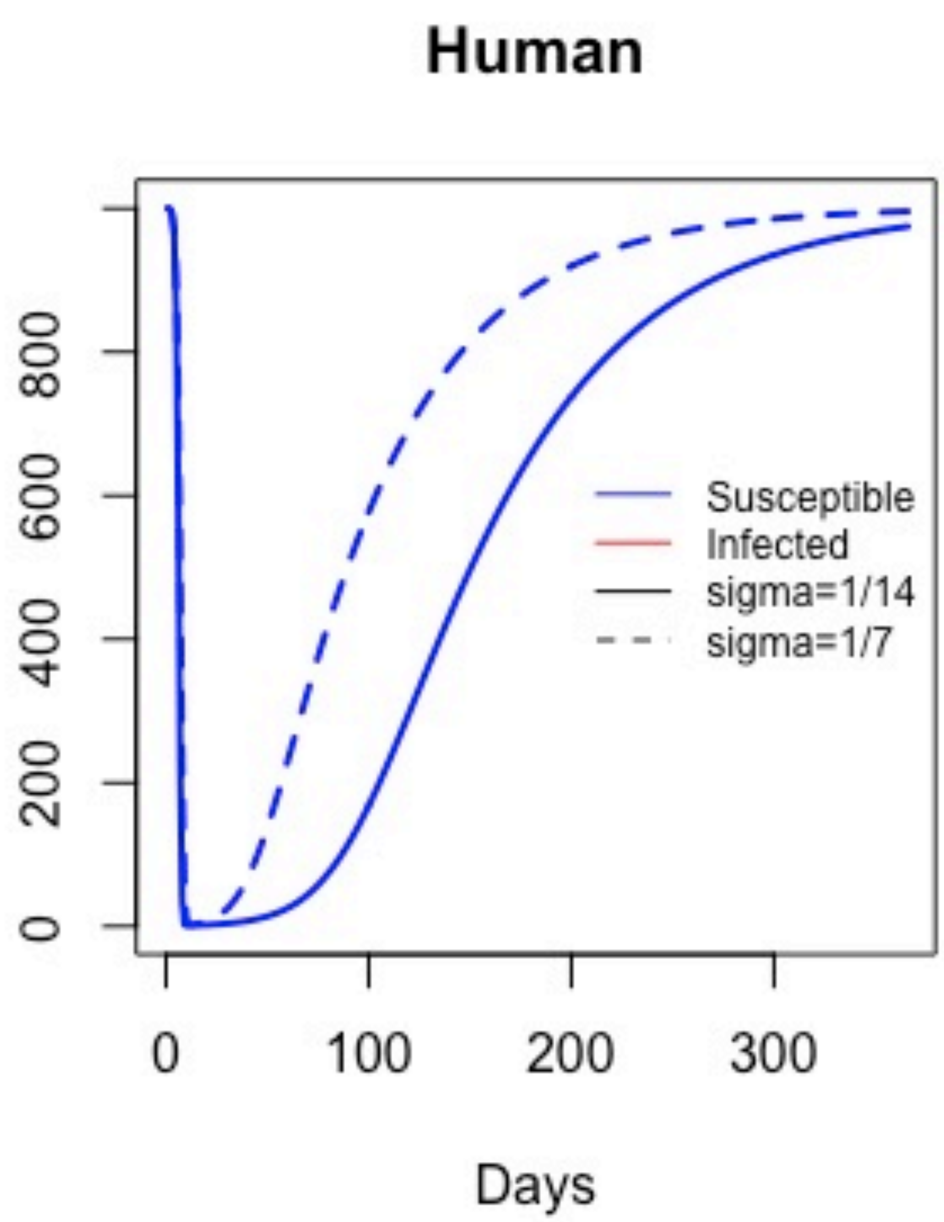


What if the mosquito death rate is higher?

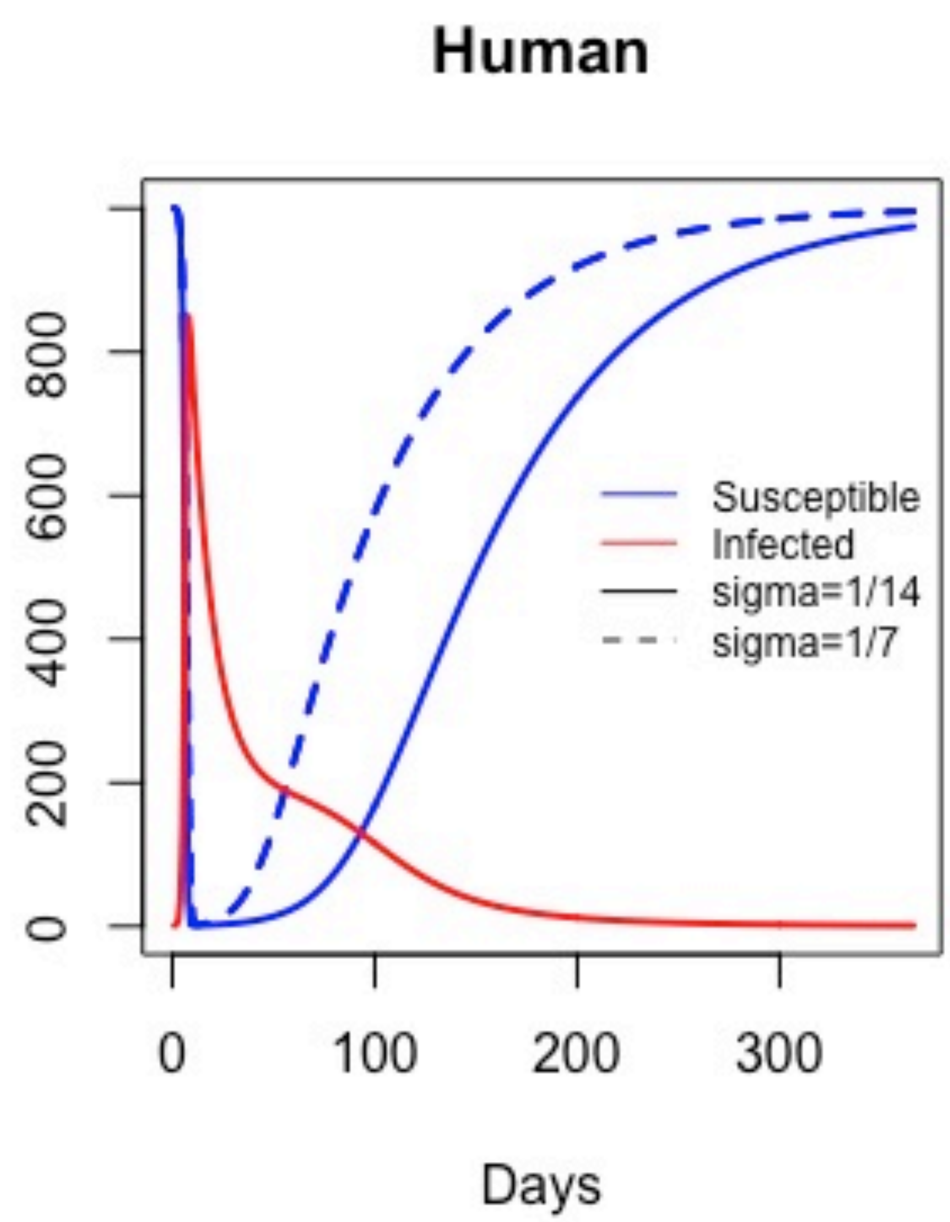
The basic vector model: dynamics



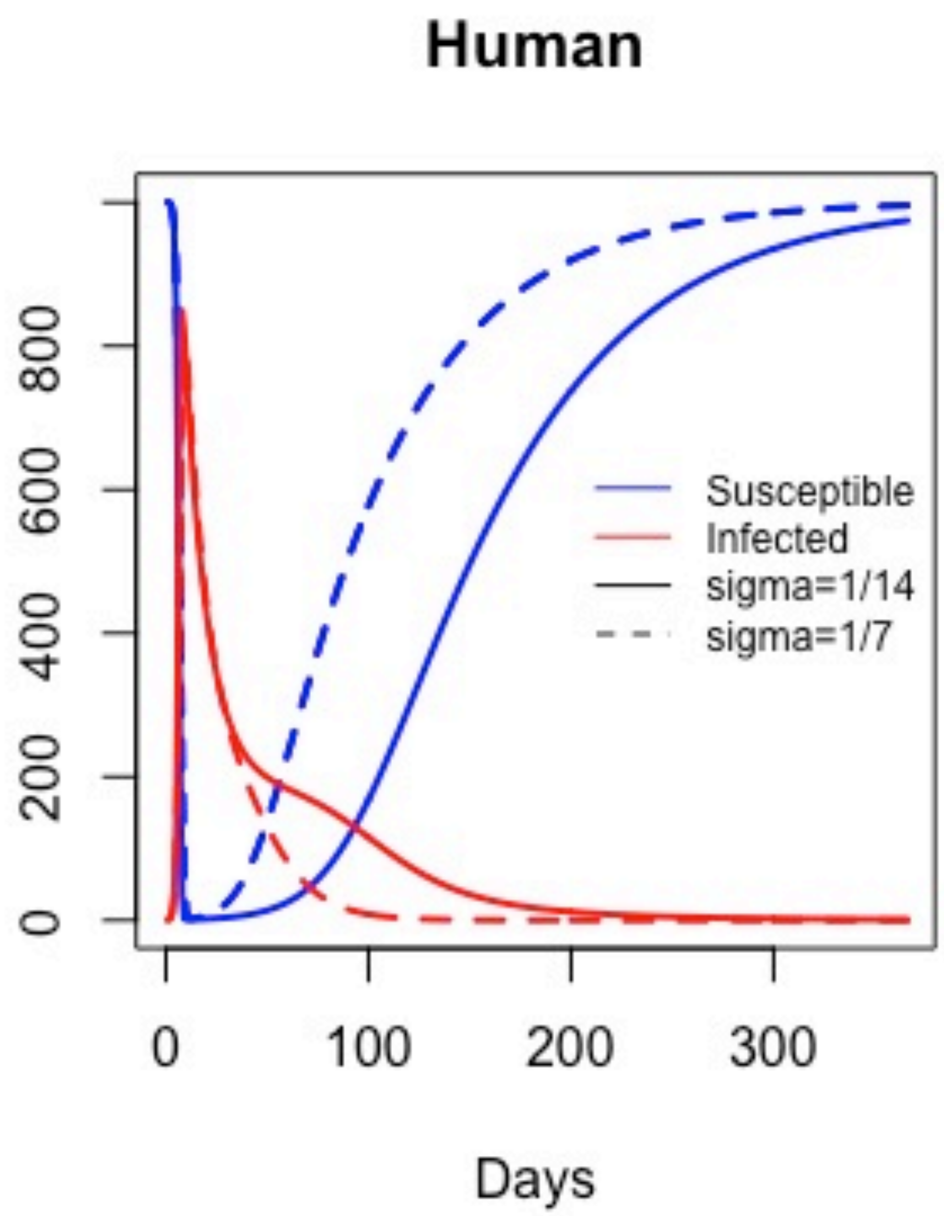
The basic vector model: dynamics



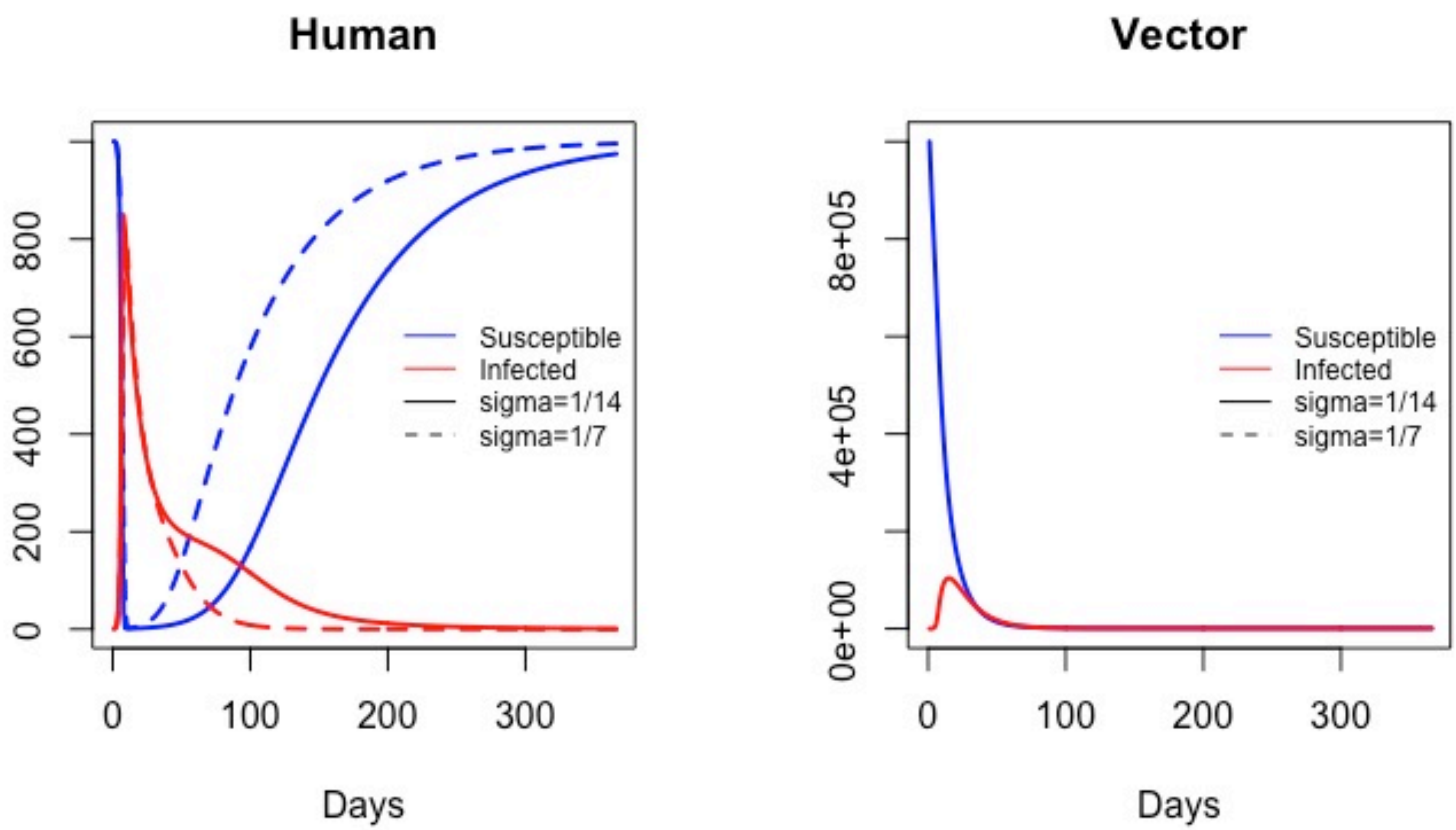
The basic vector model: dynamics



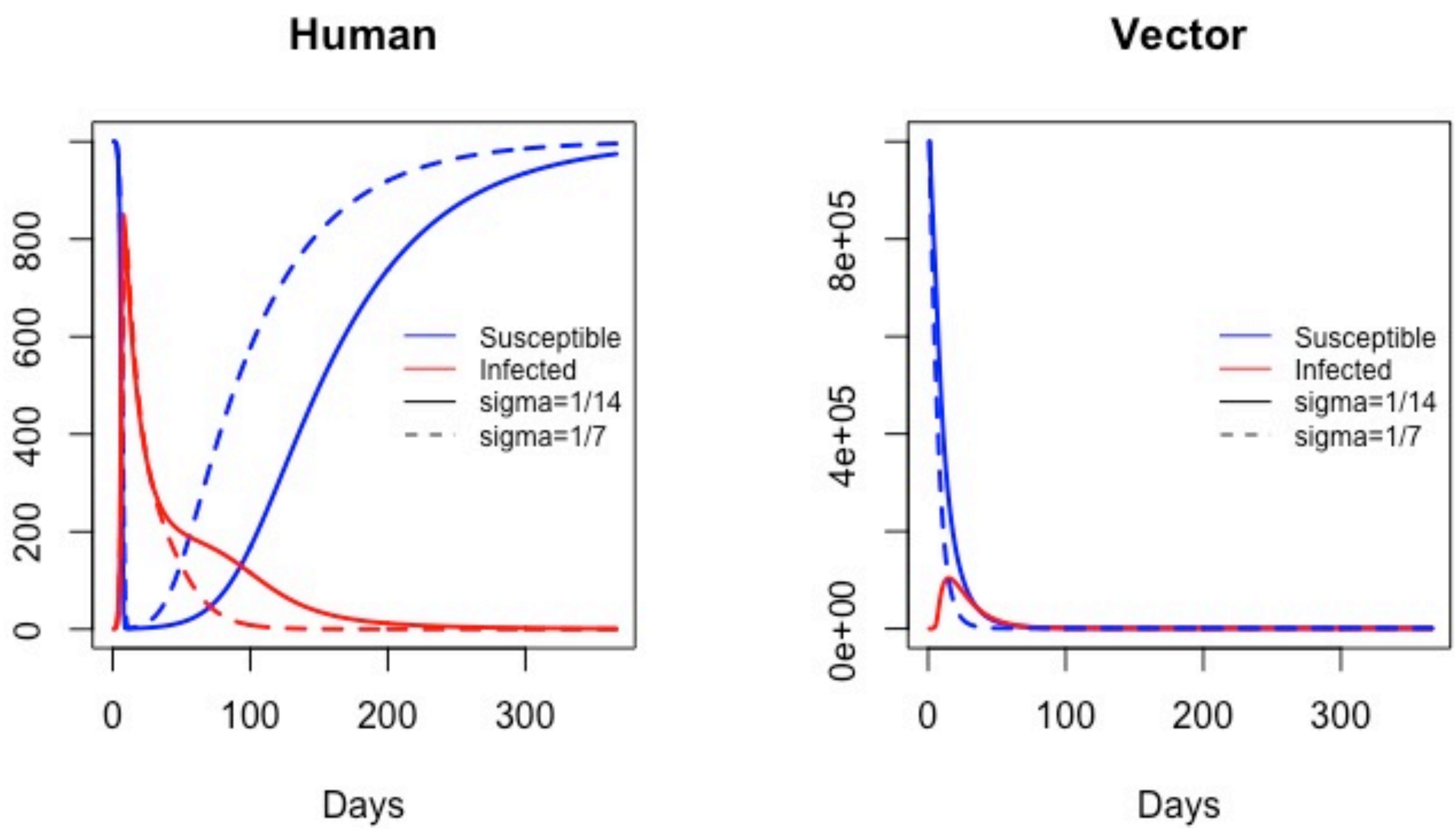
The basic vector model: dynamics



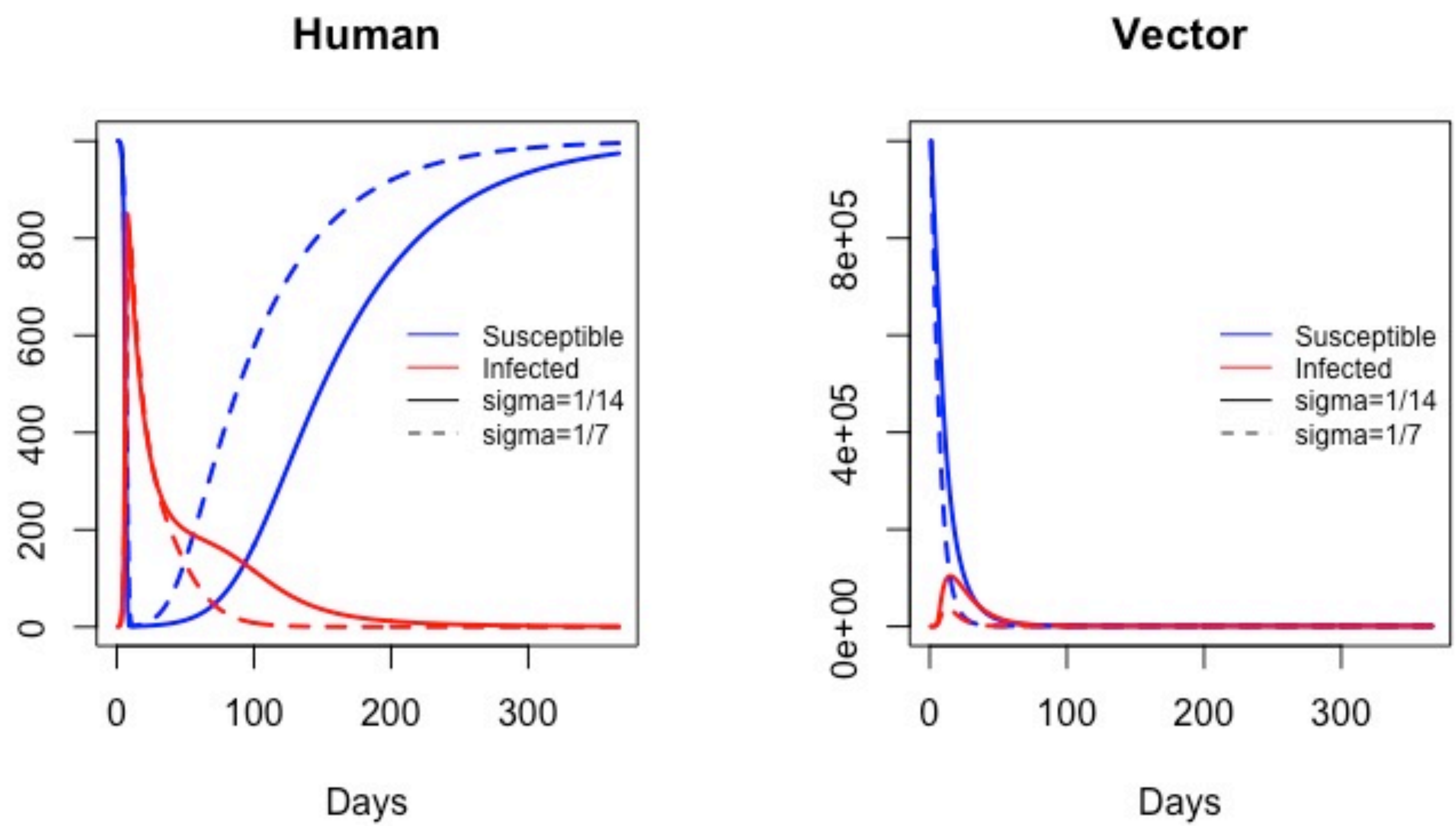
The basic vector model: dynamics



The basic vector model: dynamics

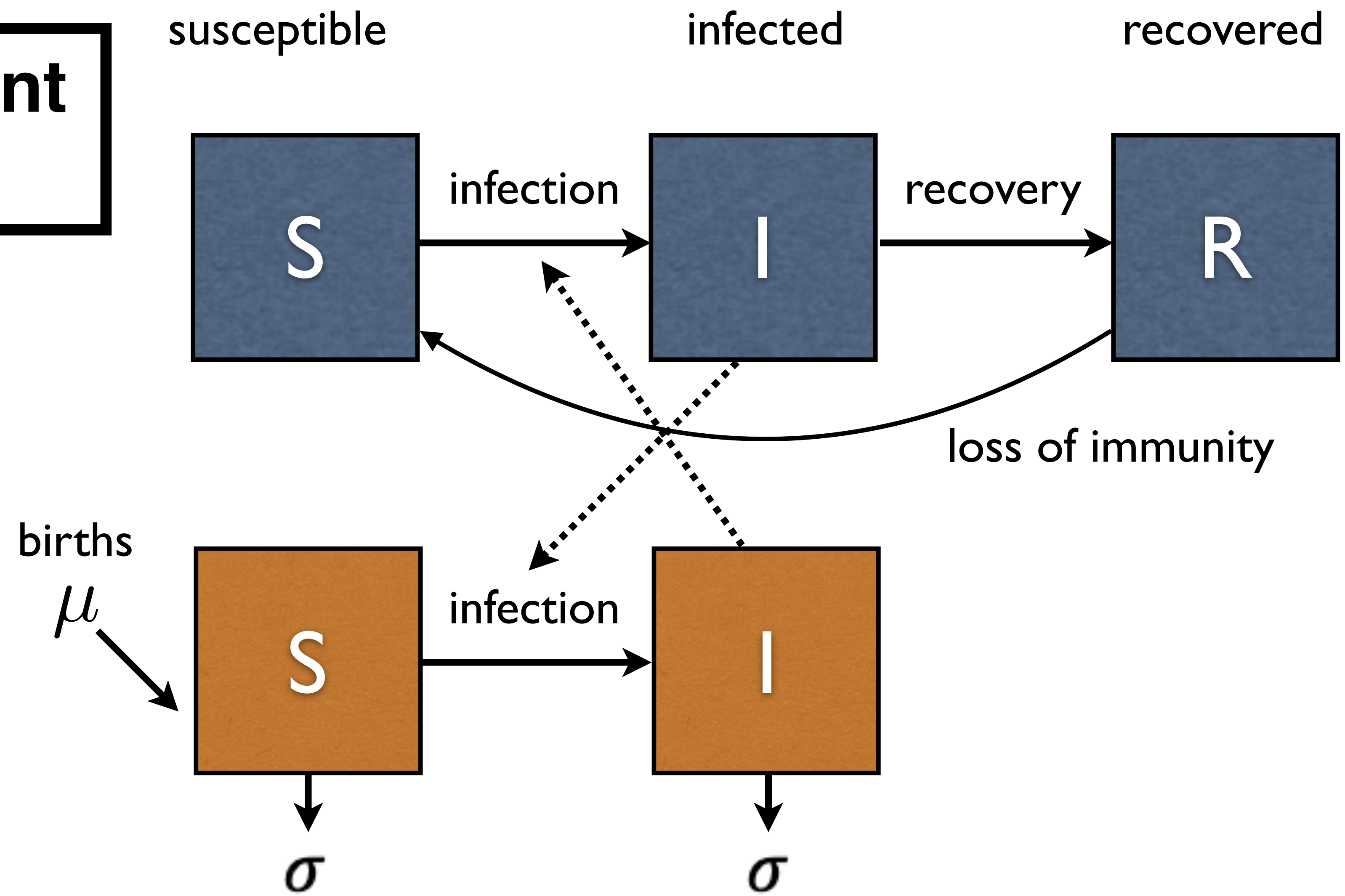


The basic vector model: dynamics

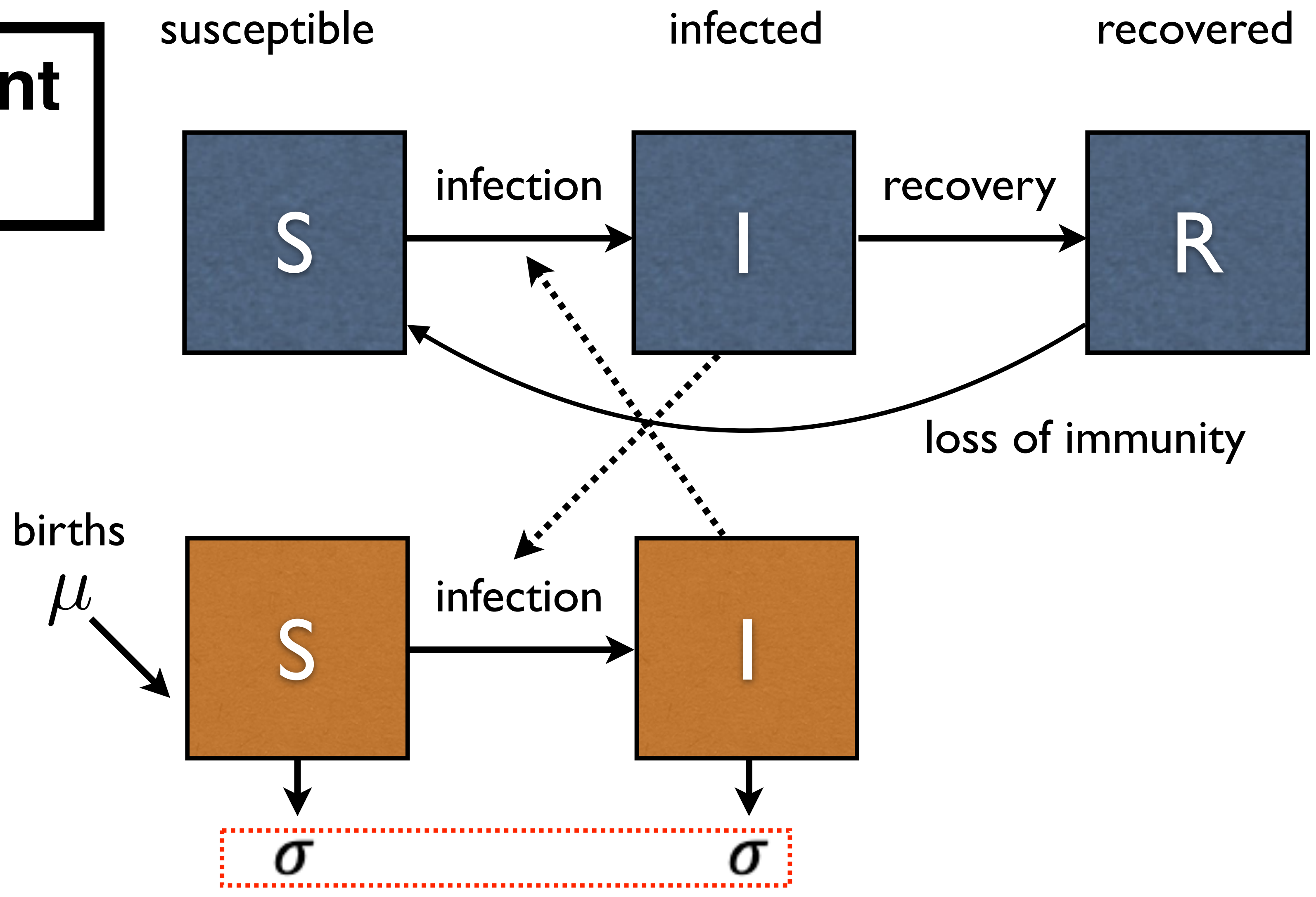


2. Incorporating temperature

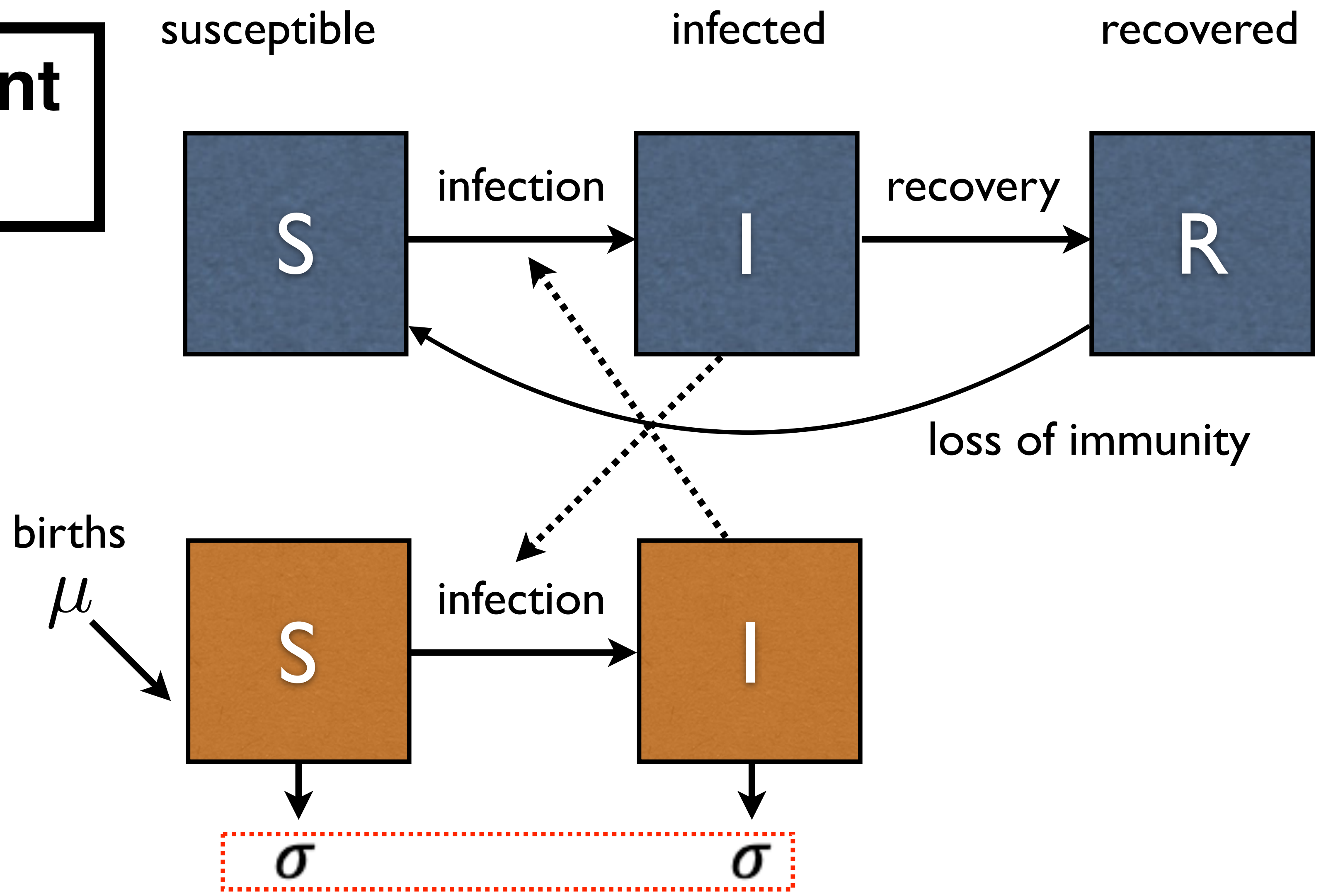
Temperature dependent vector mortality



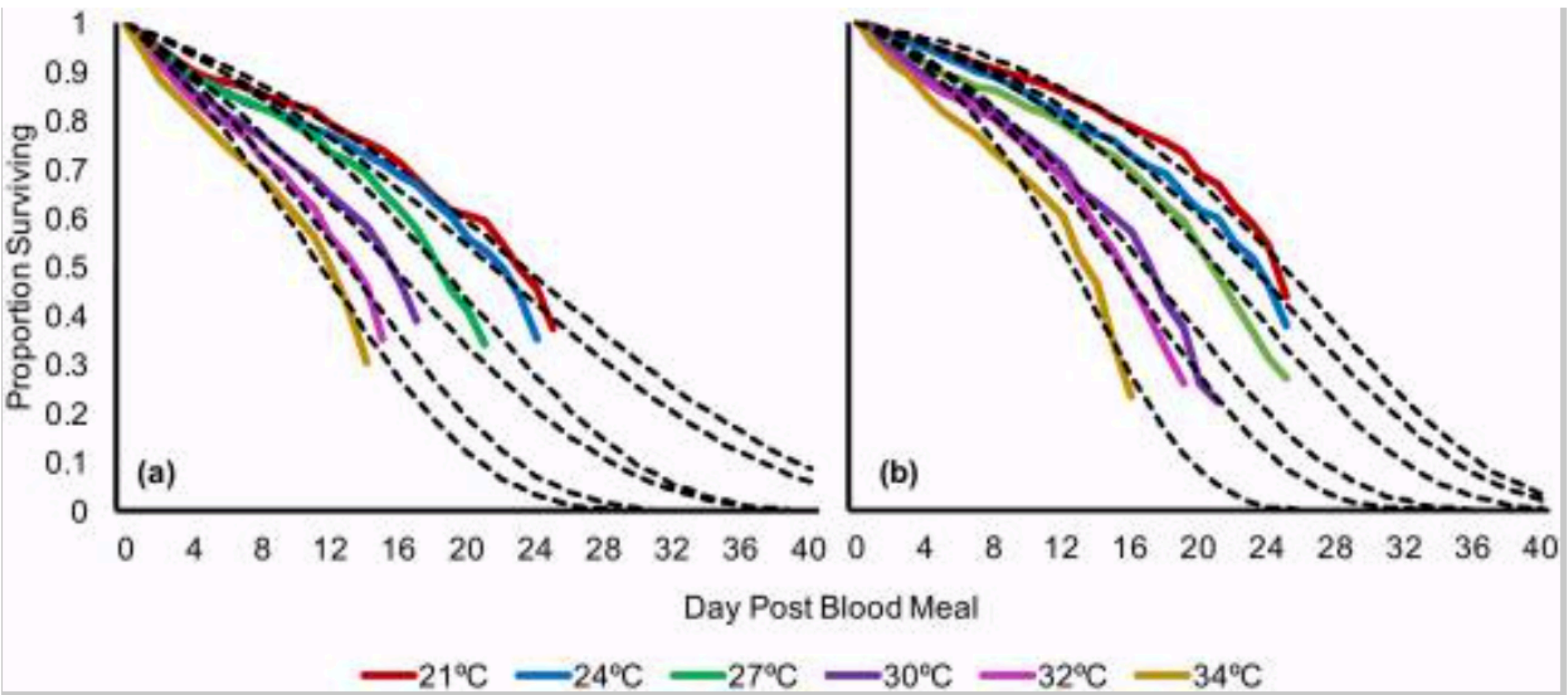
Temperature dependent vector mortality



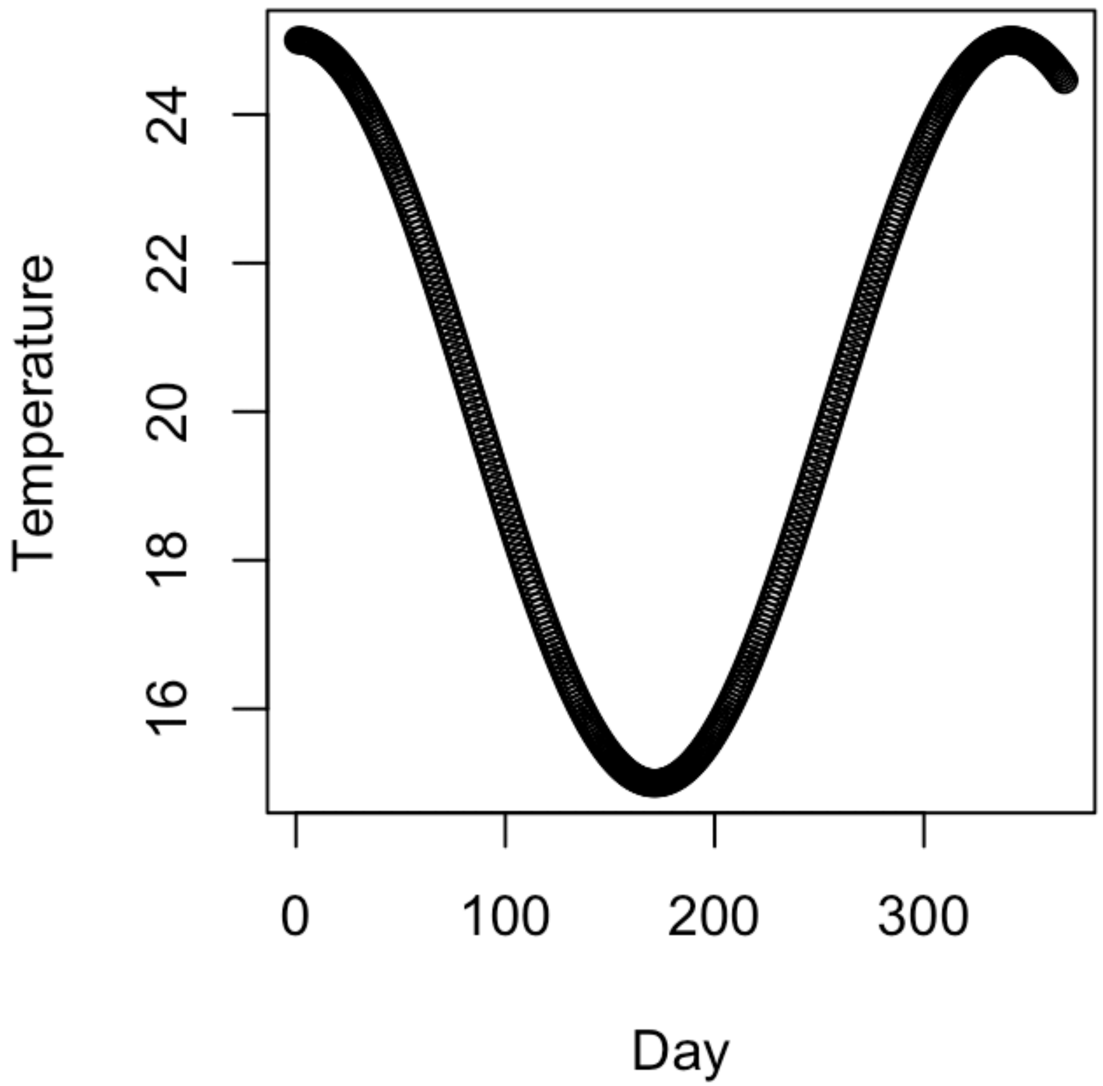
Temperature dependent vector mortality



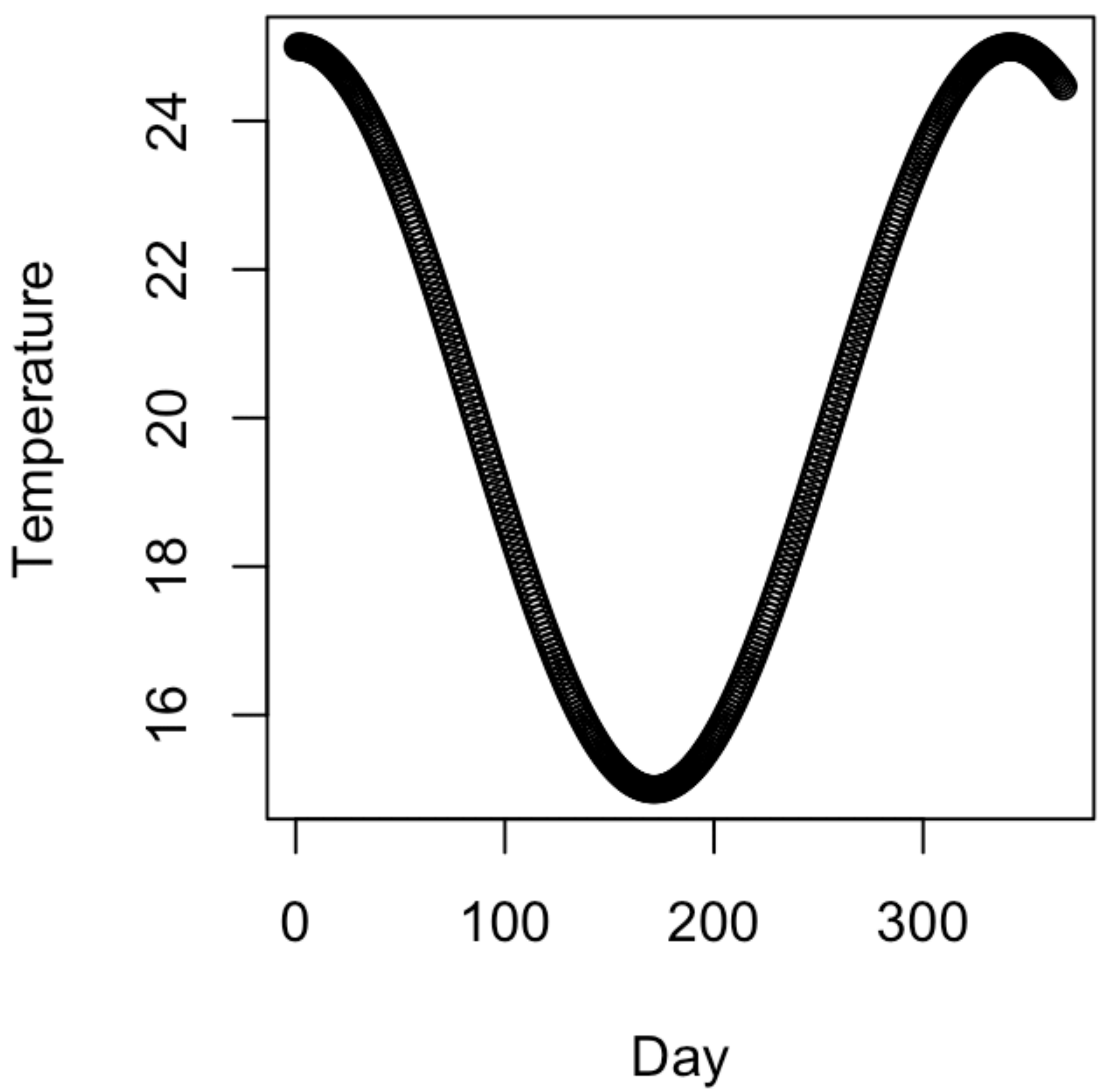
Shaprio LLM. *et al*. (2017). Quantifying the effects of temperature on mosquito and parasite traits that determine the transmission potential of human malaria. *PLoS Bio*, **15**(10): e2003489.

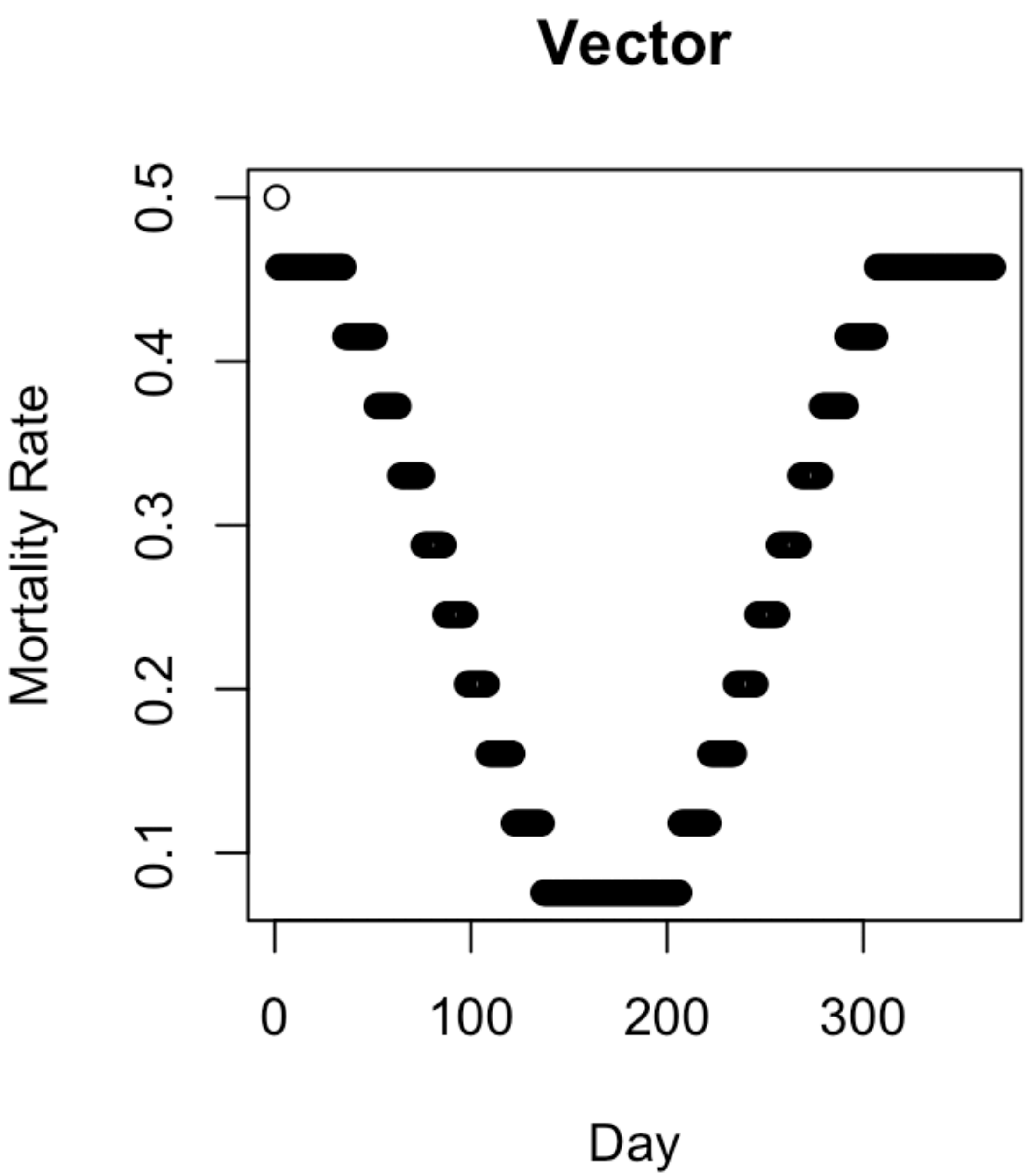


Temperature dependent vector mortality: dynamics

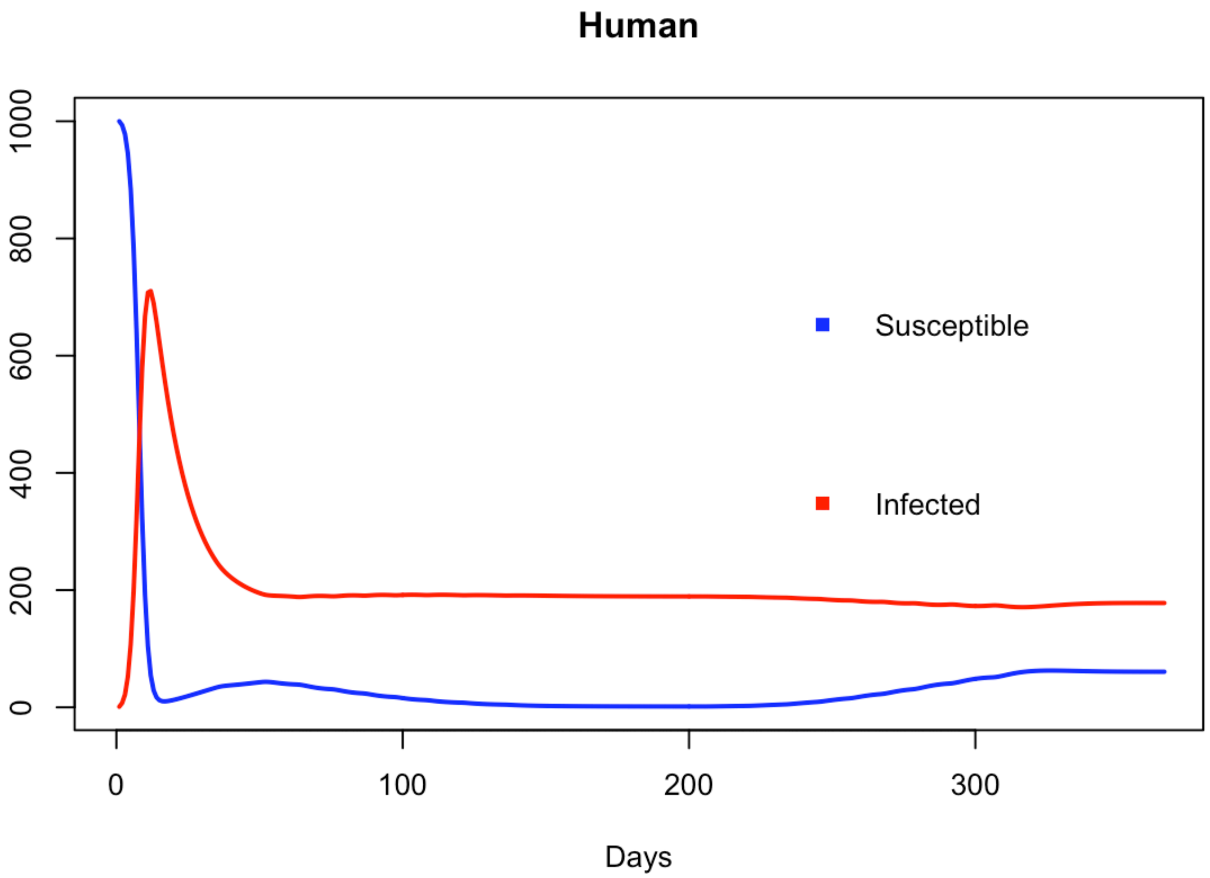


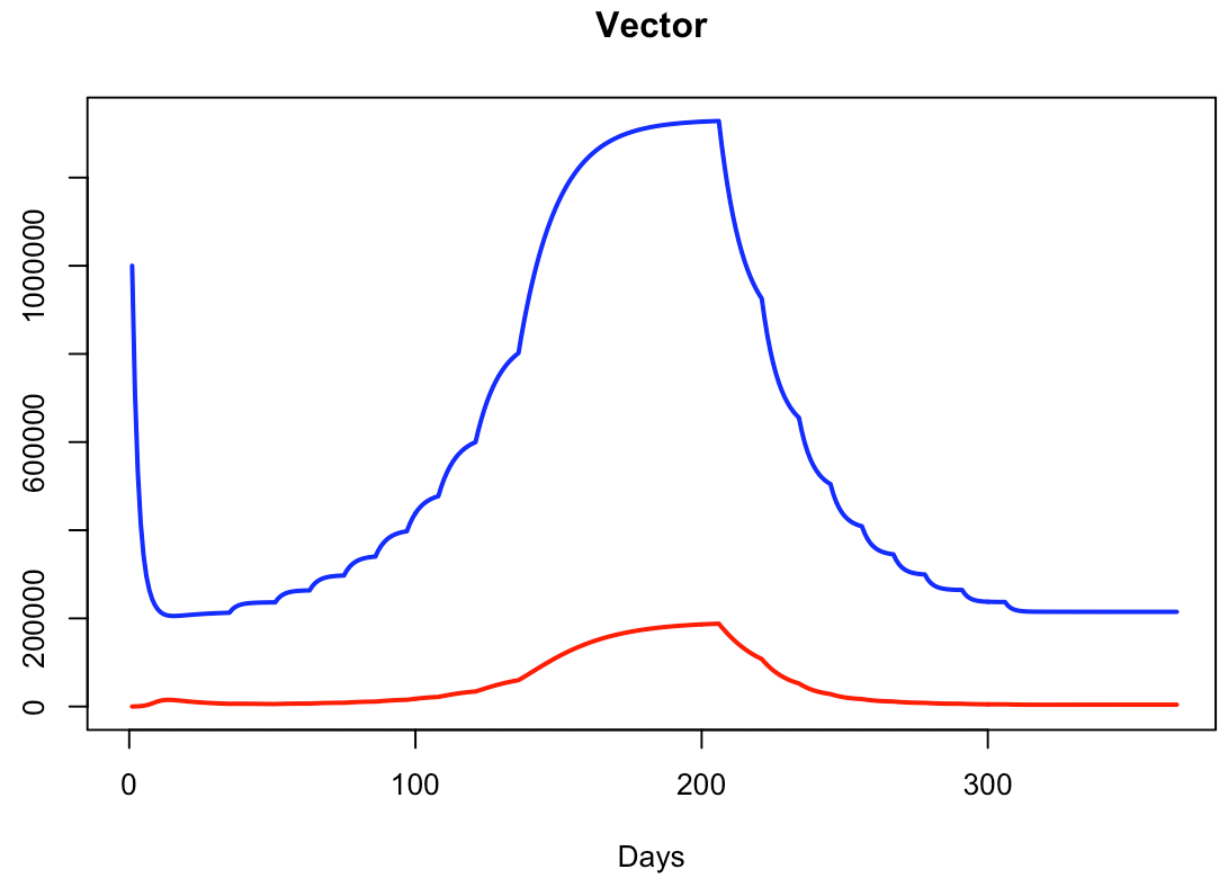
Temperature dependent vector mortality: dynamics



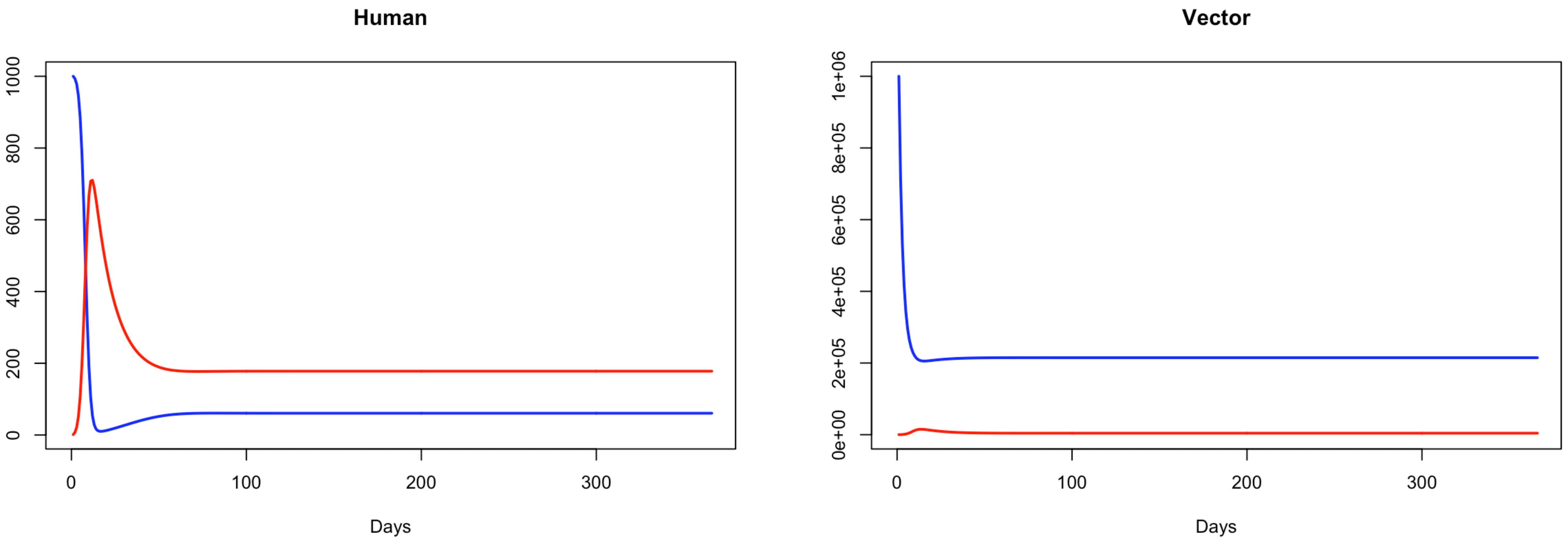


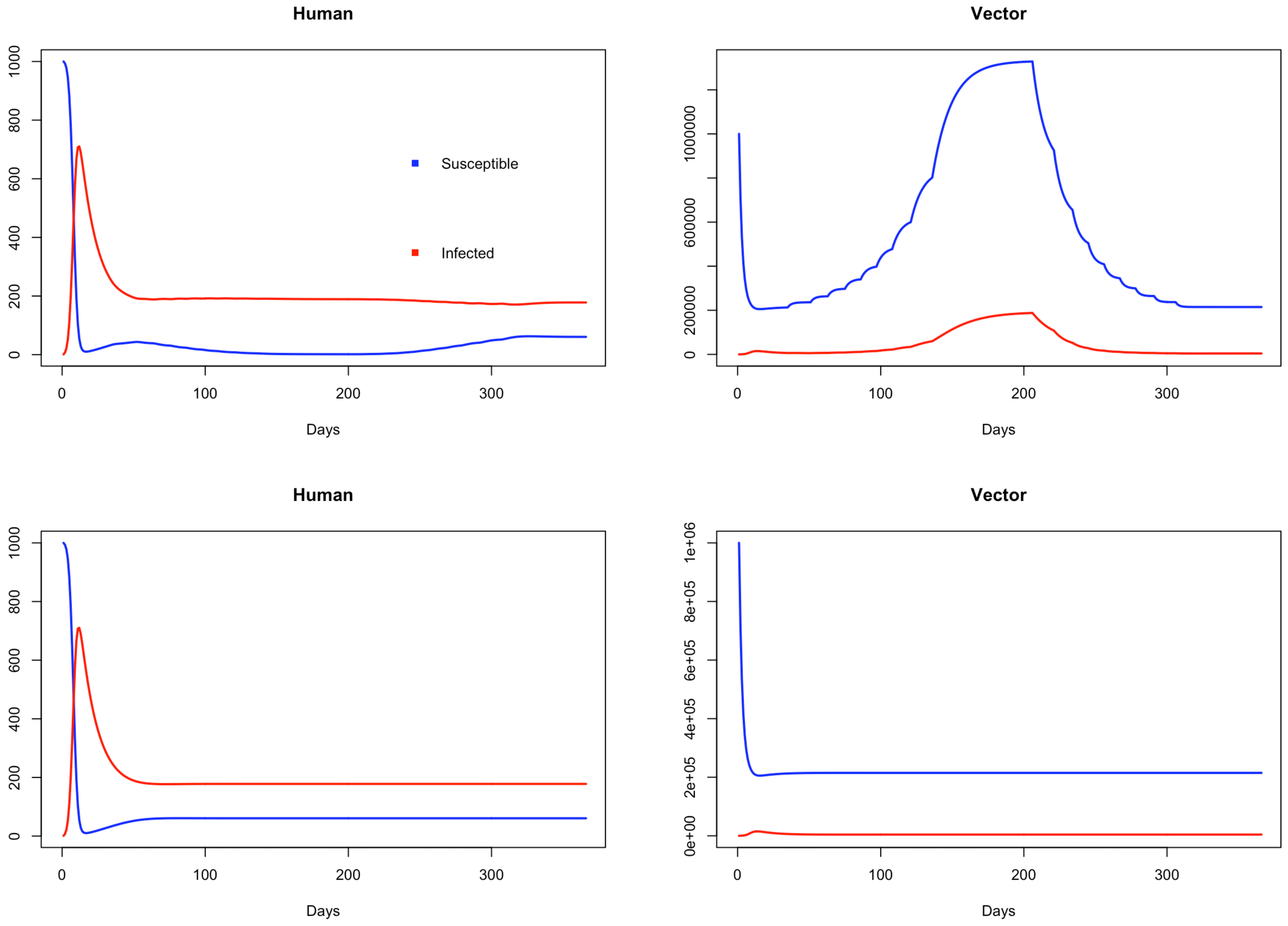
Temperature dependent vector mortality: dynamics

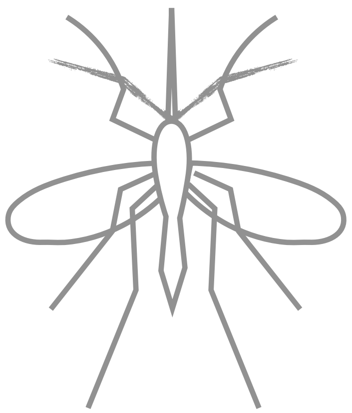




Temperature dependent vector mortality: dynamics

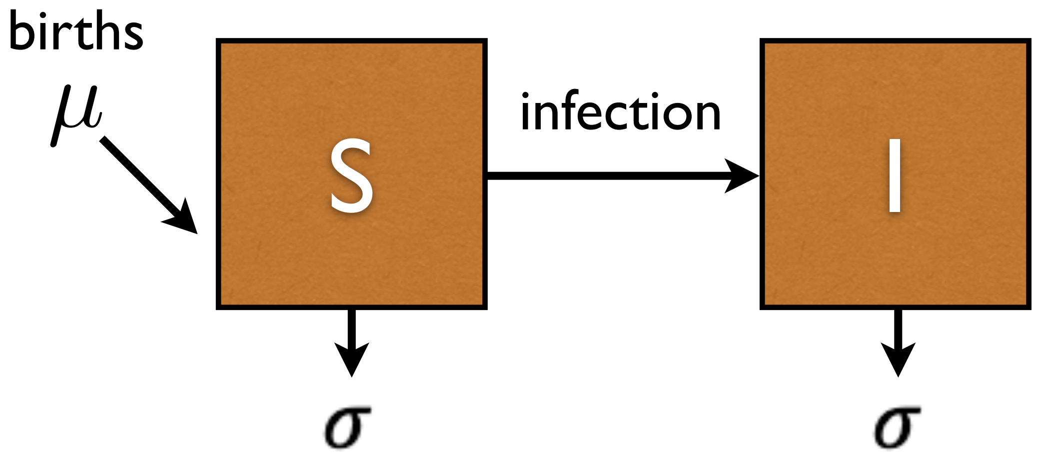



Human
Susceptible
Infected
Days
Vector
Days
Human
Days
Vector
Days

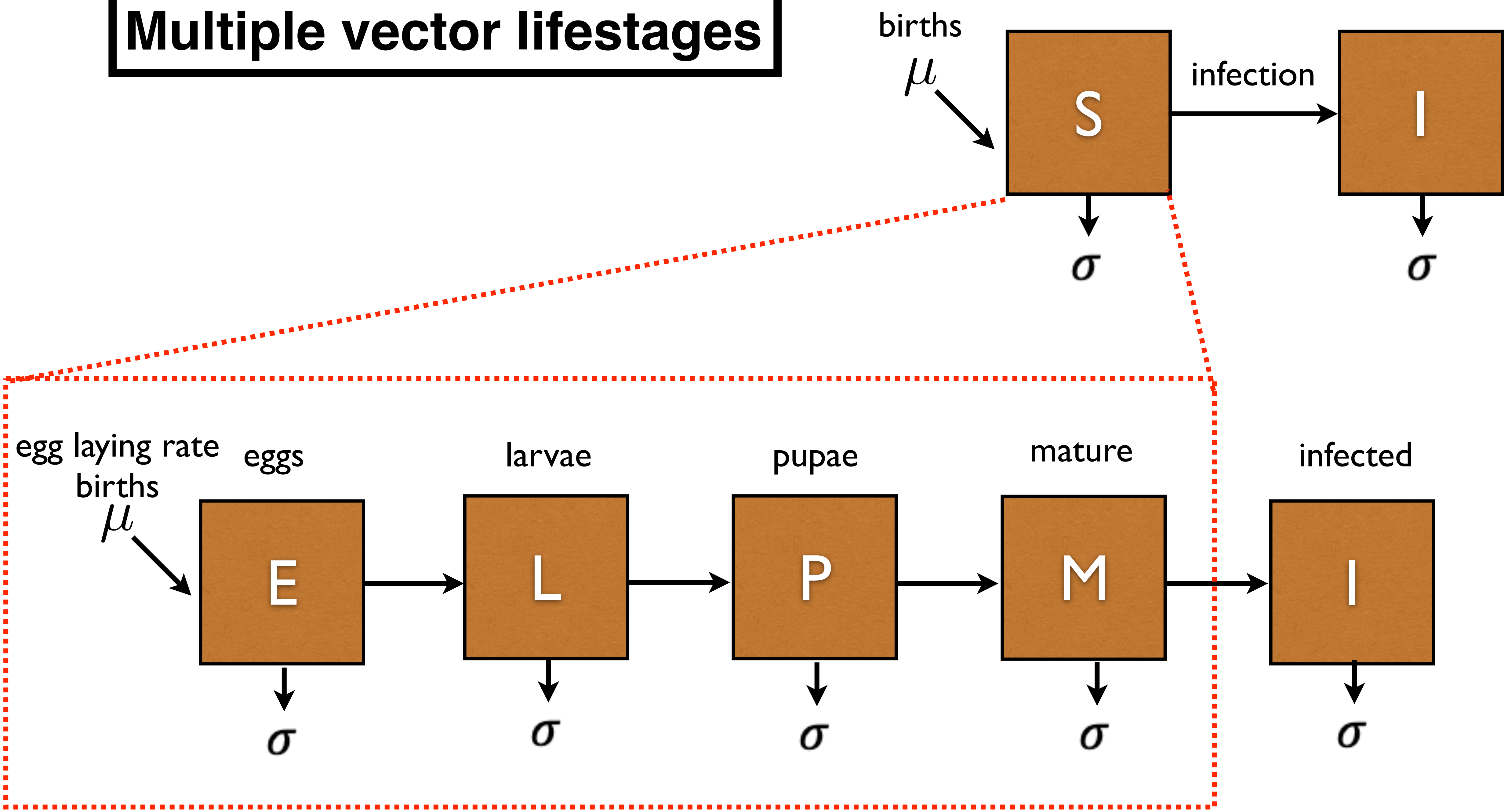


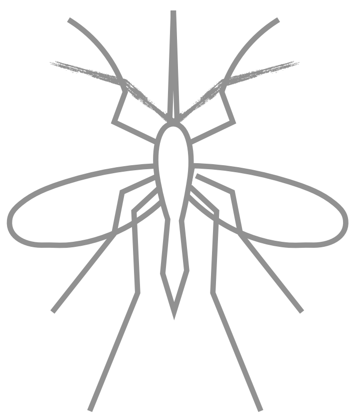
3. Increasing complexity about the vector lifecycle

Multiple vector lifestages



Multiple vector lifestages





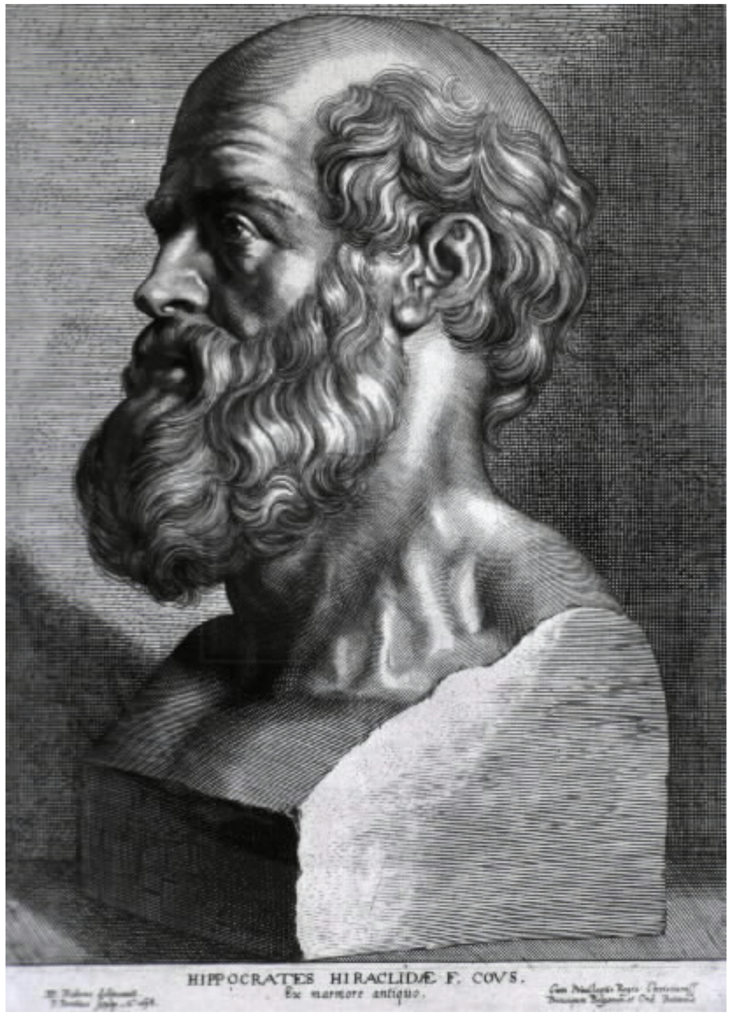
4. How can the dynamics be used for disease control?

What is malaria?

Ebers papyrus mentions fevers, rigors, splenomegaly.

1550 BC

Hippocrates connected stagnant bodies of water and occurrence of fevers in local populations.



460 BC

Romans also associated marshes with fever and pioneered efforts to drain swamps.

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Mosquitoes and malaria

Ronald Ross comments on cells outside the stomach of the Anopheles mosquito:

"but what now arrested attention was the fact that each of these bodies contained a few granules of black pigment absolutely identical in appearance with the well-known and characteristic pigment of the parasite of malaria (large quartans and crescent-derived spheres)."

Ross, Ronald British Medical Journal 1:1786-1788 (1897)

The burden of malaria

Estimated one death every 30 seconds.

Infection in pregnancy (low birth weight, pre-term delivery)
Acute febrile illness (cerebral malaria, respiratory distress, hypoglycaemia)
Chronic, repeated infection (severe anaemia)

Considerable economic impacts

Up to **40% all health expenditure**; 1.3% reduction in GDP sustained national differences; $12 billion p.a. in Africa
Poverty traps and cycles.

Sachs, J. and Malaney, P. (2002). The economic and social burden of malaria. *Nature*, **415**: 680-685.

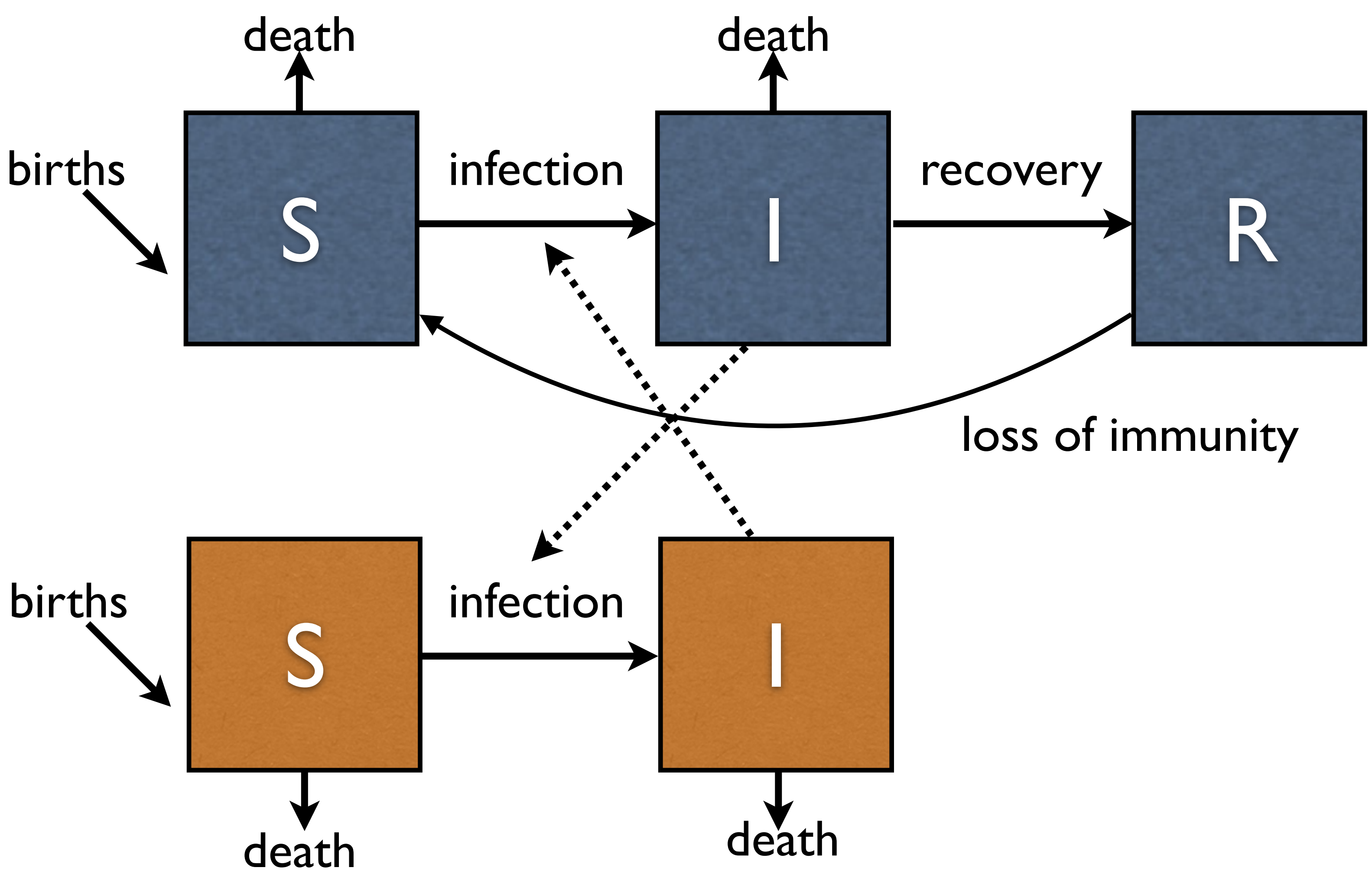
Control options

Environmental modification and species sanitation - reasonable history of success in temperate regions.

Adult vector control - current primary public health intervention - key players: indoor residual spraying (IRS), insecticide-treated mosquito nets (ITNs) and long lasting insecticide impregnated nets (LLINs)

Drugs and treatment - increasing access to drug treatment and availability

Implications for control



Implications for control

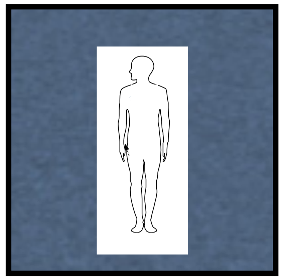
Assuming pops broadly at equilibrium – so don't worry about details of births and deaths and focus on proportions.

Version of the Ross Macdonald model

no female mosquitoes per human host

prob human infection per bite

human recovery rate



x = proportion of infectious humans

$$\frac{dx}{dt} = mabz(1-x) - rx$$

number bites per mosquito per unit time

z = proportion of infectious mosquitos

$$\frac{dz}{dt} = acx(1-z) - gz$$

prob mosquito infection per bite

mosquito death rate

How to interpret?
Can we estimate R_0?

R_0 *is the number of new infections for one infected human in a completely susceptible population.*

R_0 *>1 implies that the infection will spread - one infection will result in more than one new infection.*

R_0 *<1 implies that the infection will go extinct - and thus also represents the condition for successful control.*

Assume no infected humans (x=0)

$$\frac{dx}{dt} > 0 \quad \Longrightarrow \quad \frac{ma^2bc}{g} - r > 0$$

$$\boxed{R_0 = \frac{ma^2bc}{gr}}$$

Elimination

no female mosquitoes per human host

$R_0 = 1$ means that: $m = \frac{rg}{mba^2c}$

Using similar results, Ross identified that there is a **critical density of mosquitoes**, below which malaria cannot be sustained.

!You don't need to kill every mosquito to eliminate malaria!

Led to a huge focus on vector control..