Modeling vector-borne diseases

'Modeling' aretina avy amin'ny moka

Modélisation des maladies transmise par des vecteurs

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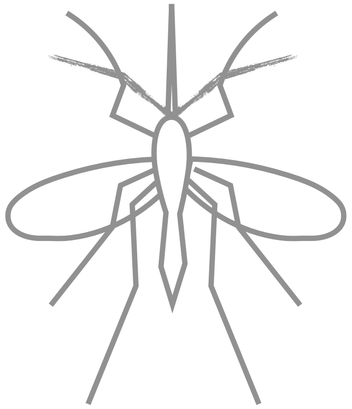
Ino no asantsika niany?
Learning objectives

- Understand the development of mathematical models to study the transmission dynamics of vector-borne infectious diseases
  Comprendre le développement de modèles mathématiques pour étudier la dynamique de transmission des maladies transmise par des vecteurs

- SIRS Model Structure
  La structure des modèles SIRS

- Incorporate environmental variables into models of vector populations
  Incorporer des variables environnementales dans modèles des 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 / Sasin-teny

What are vector-borne diseases?

Aretina avy amin'ny moka (na biby kely hafa)

Maladies 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

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Ohatra?

Examples: Chikungunya, Dengue fever, Lymphatic filariasis Rift Valley fever, Yellow fever, **Malaria**, Japanese encephalitis, **West Nile fever**, Leishmaniasis, Sandfly fever (phelebotomus fever), Crimean-Congo haemorrhagic fever, Lyme disease, Relapsing fever (borreliosis), Rickettsial diseases (spotted fever and Q fever), **Zika**, Tick-borne encephalitis, Tularaemia, Chagas disease (American trypanosomiasis), Sleeping sickness (African trypanosomiasis), **Plague**, Rickettsiosis, Onchocerciasis (river blindness), **Schistosomiasis (bilharziasis)**, Typhus and louse-borne relapsing fever, Ehrlichiosis, Bourbon virus, Colorado tick fever, O'nyong-o'nyong virus, Heartland virus, Powassan virus, Saint Louis Encephalitis, Anaplasmosis, Babesia

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

Qu'est-ce qui différencie les maladies à transmission vectorielle des modèles et des études des maladies à transmission directe?

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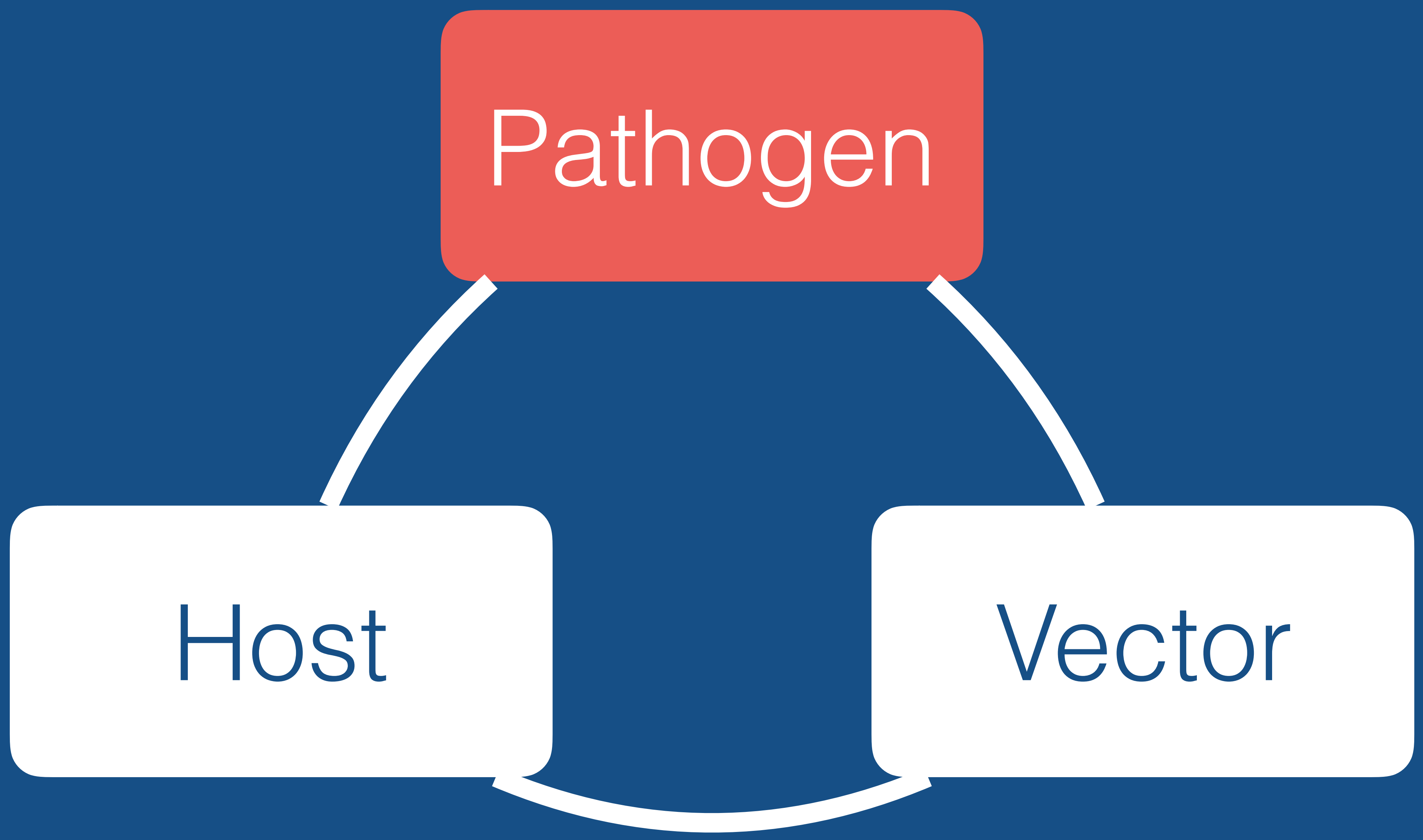
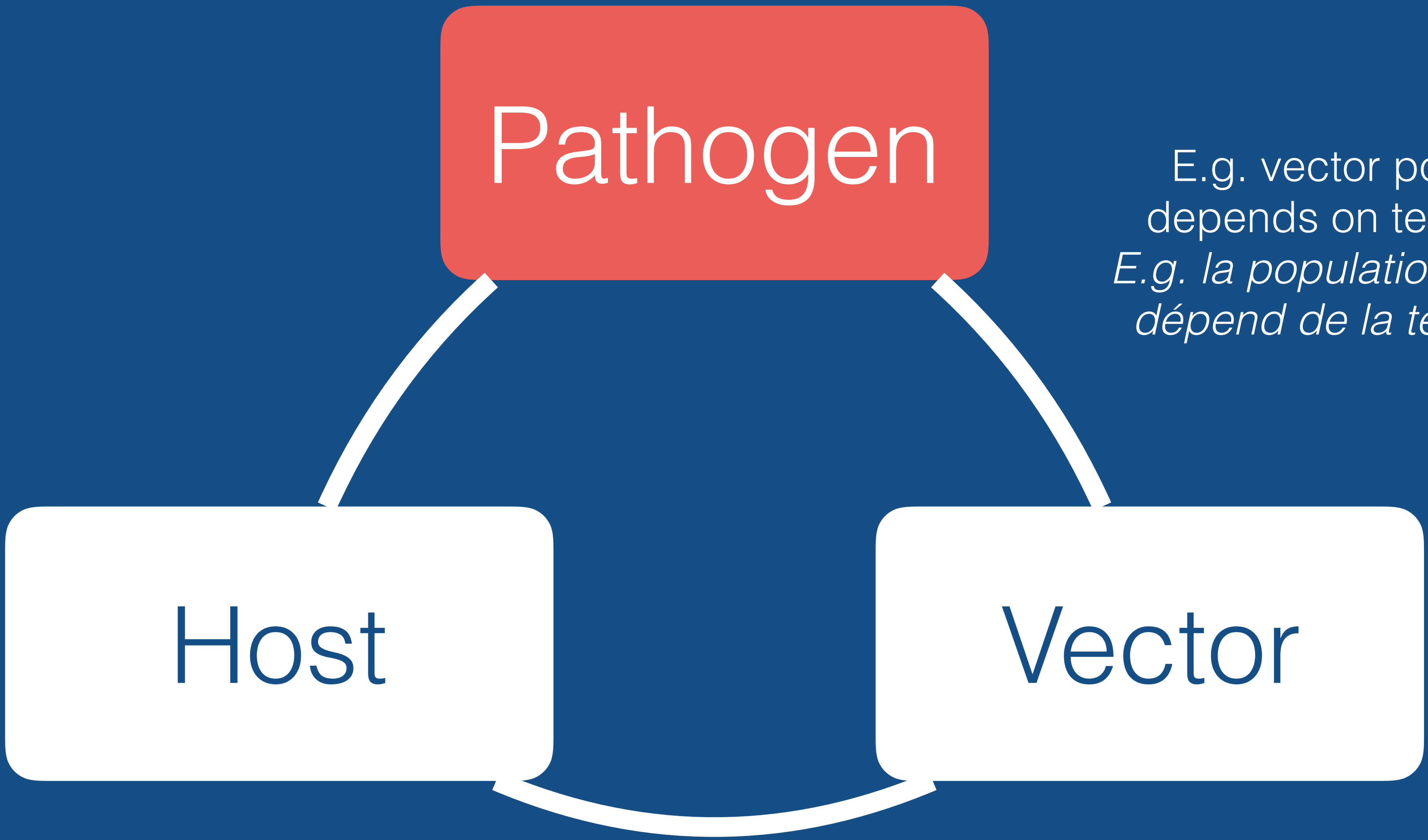
Two sets of population dynamics —
demography, transmission, interactions, etc.

Deux ensembles de dynamiques de population

Environmental factors and abiotic conditions

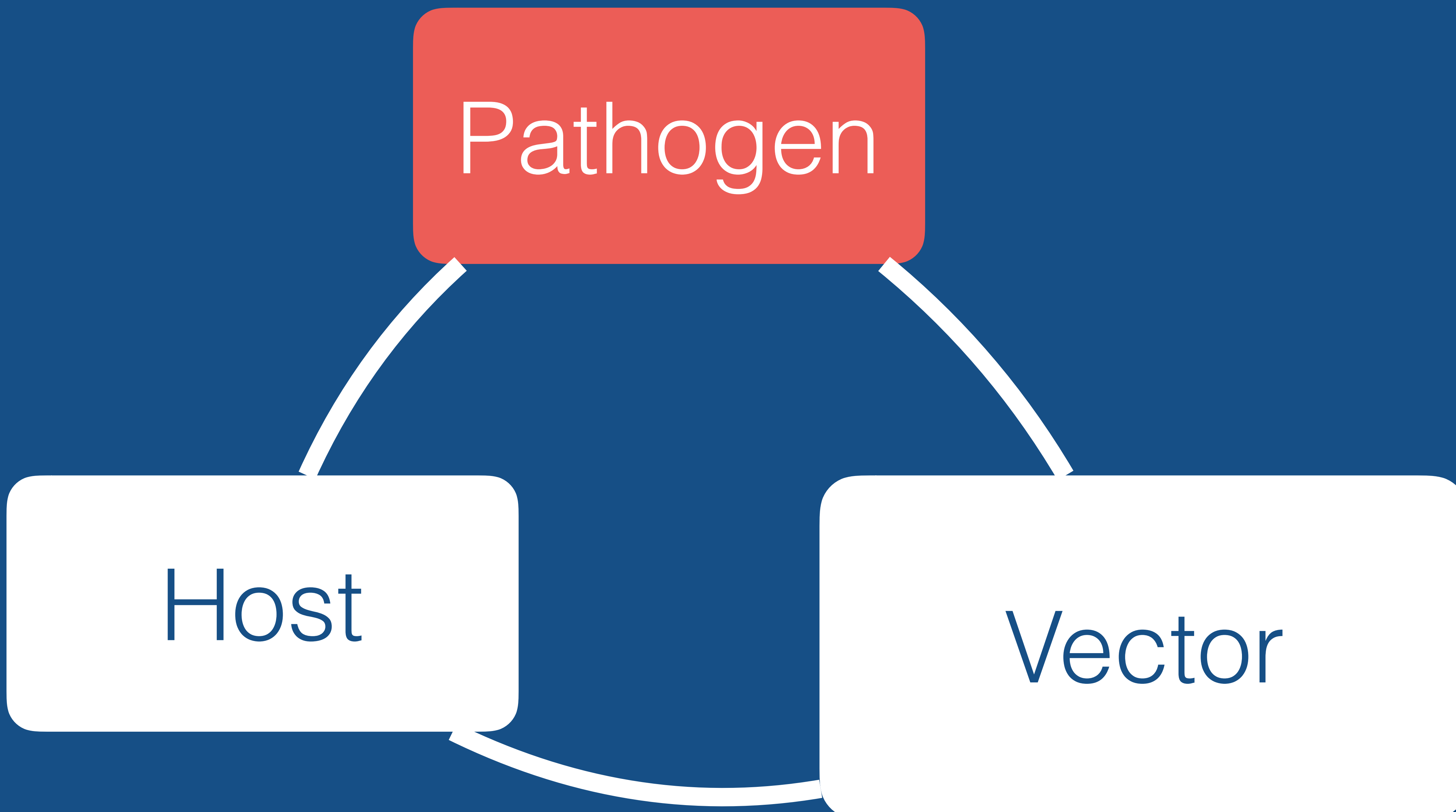
Facteurs environnementaux et conditions abiotiques


Pathogen
Host
Vector



E.g. vector population depends on temperature

E.g. la population vectorielle dépend de la température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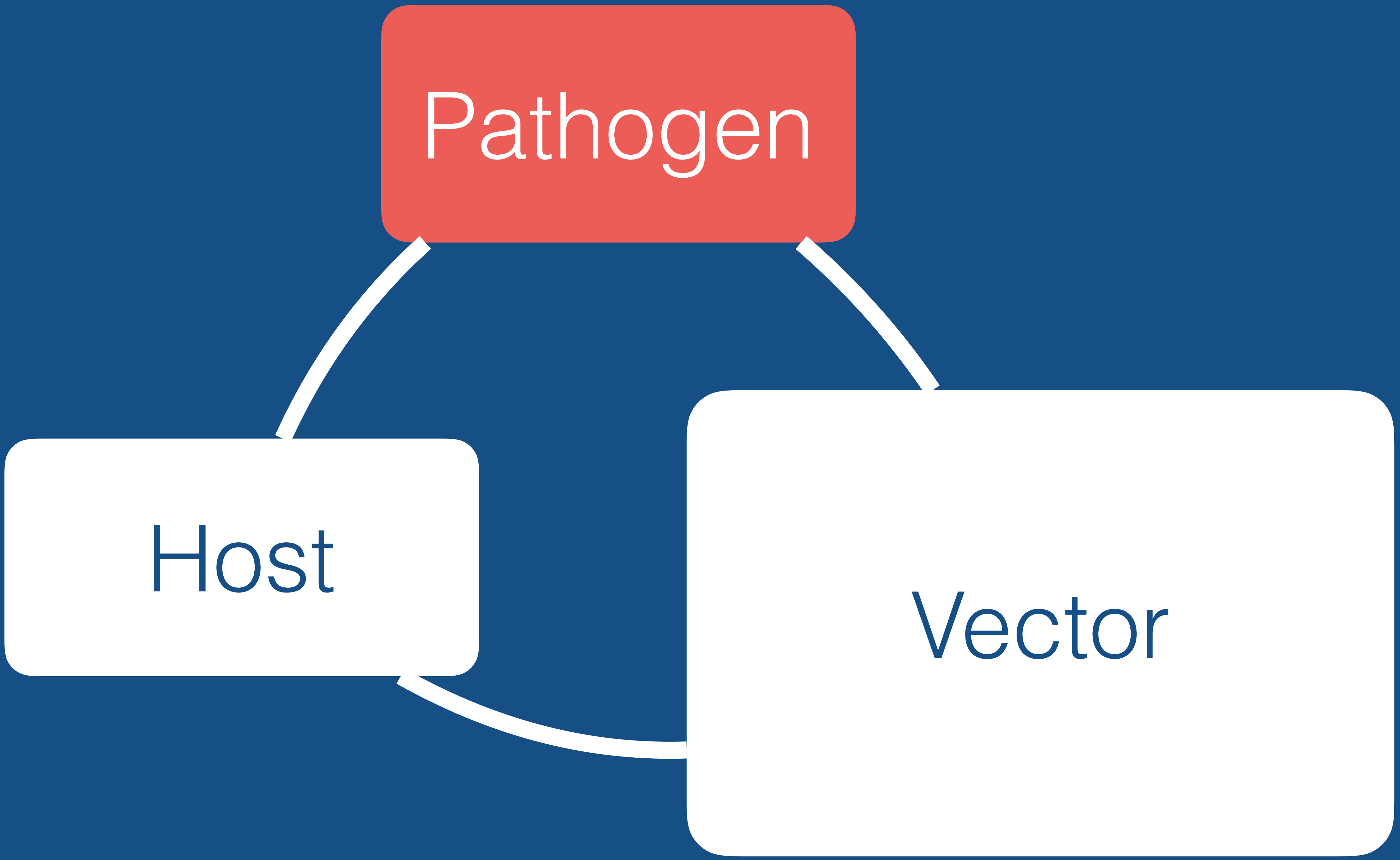
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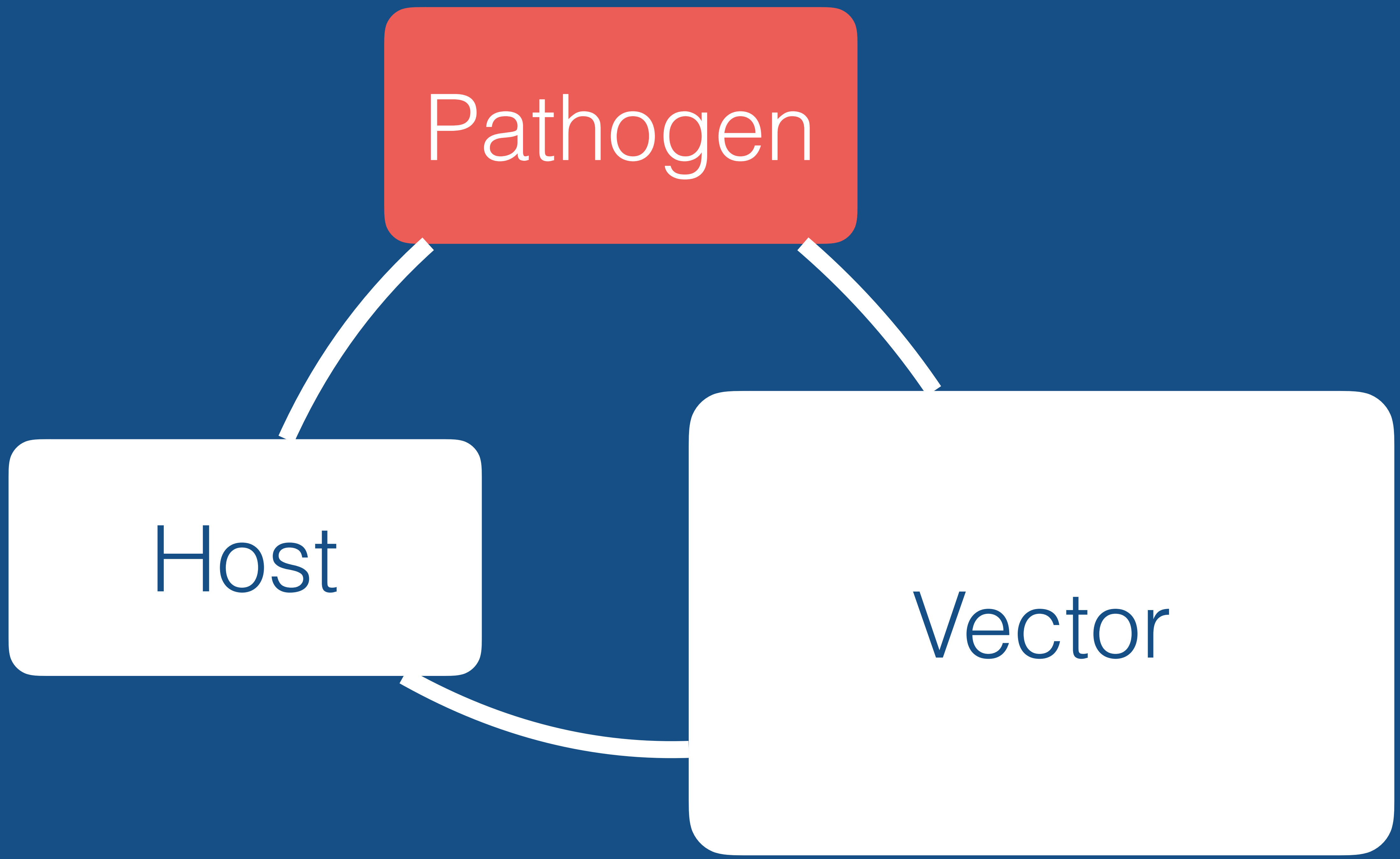
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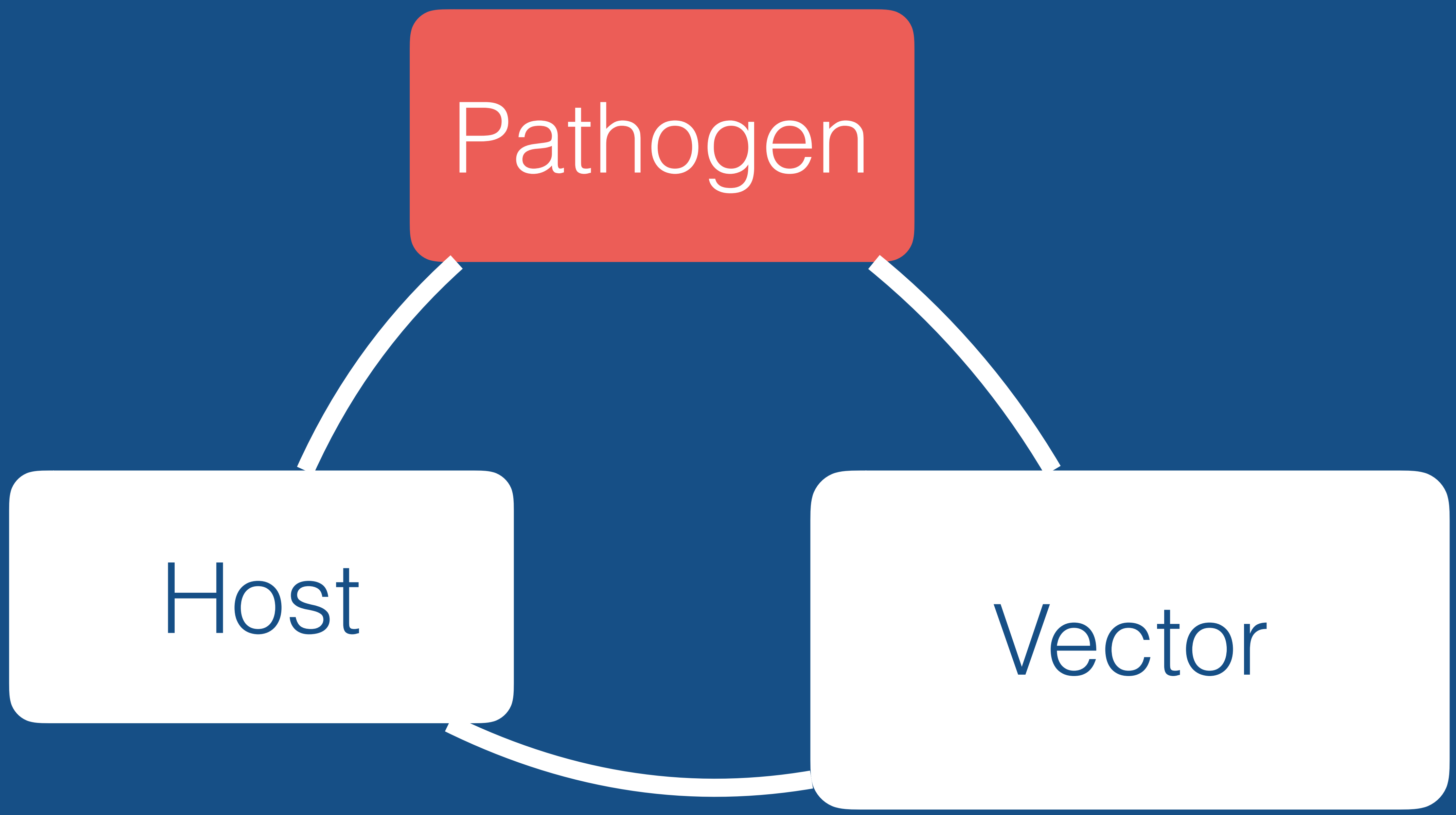
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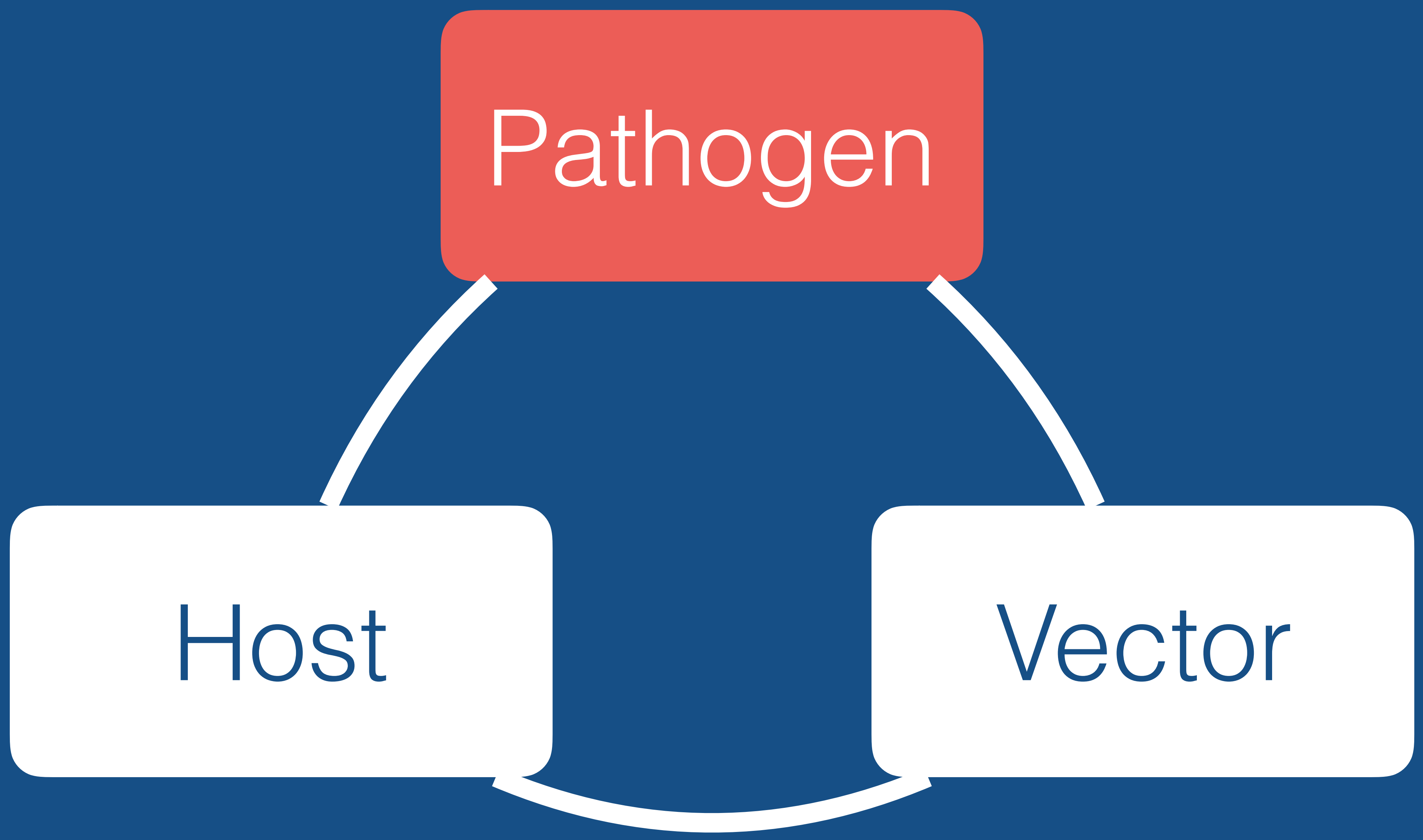
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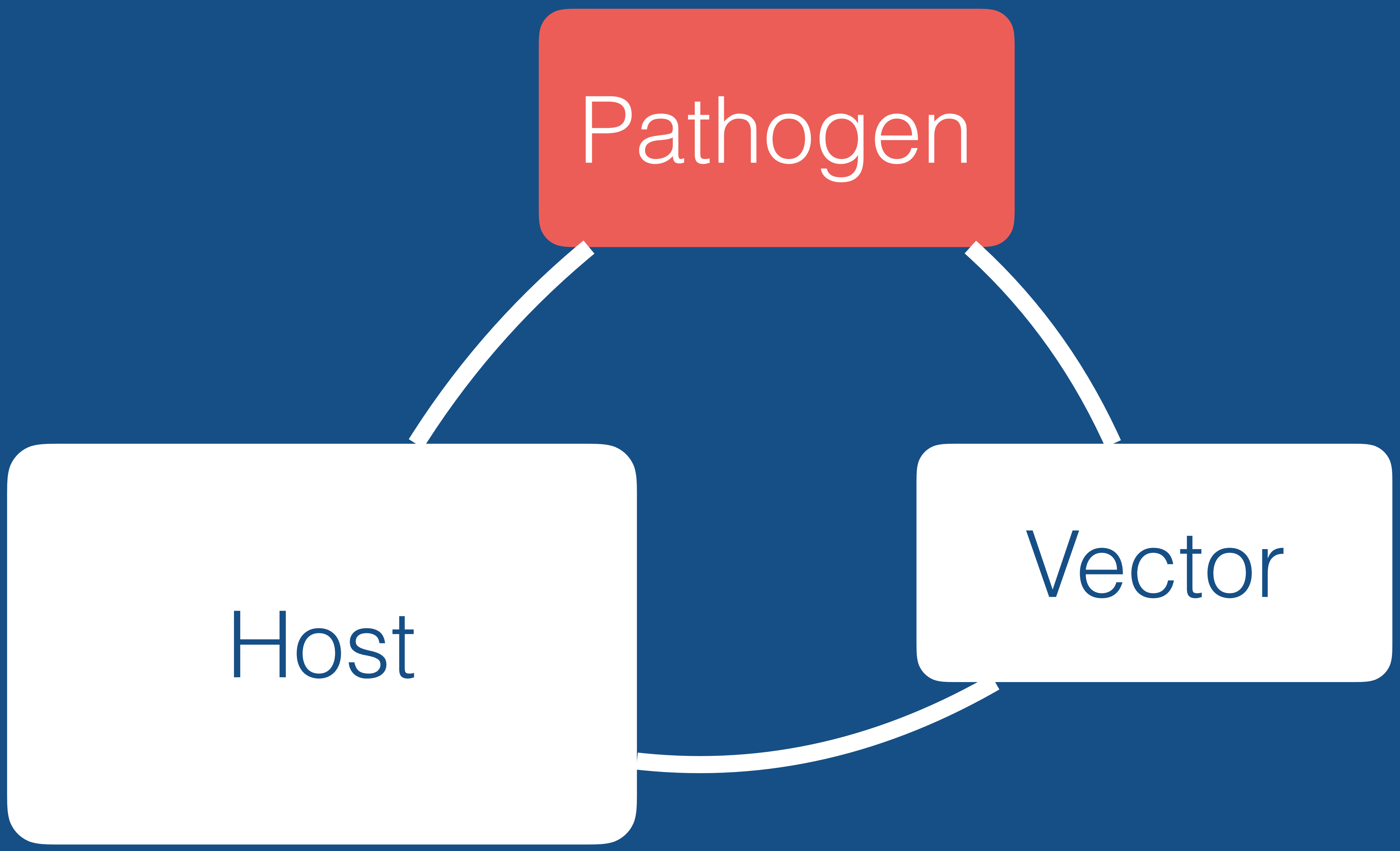
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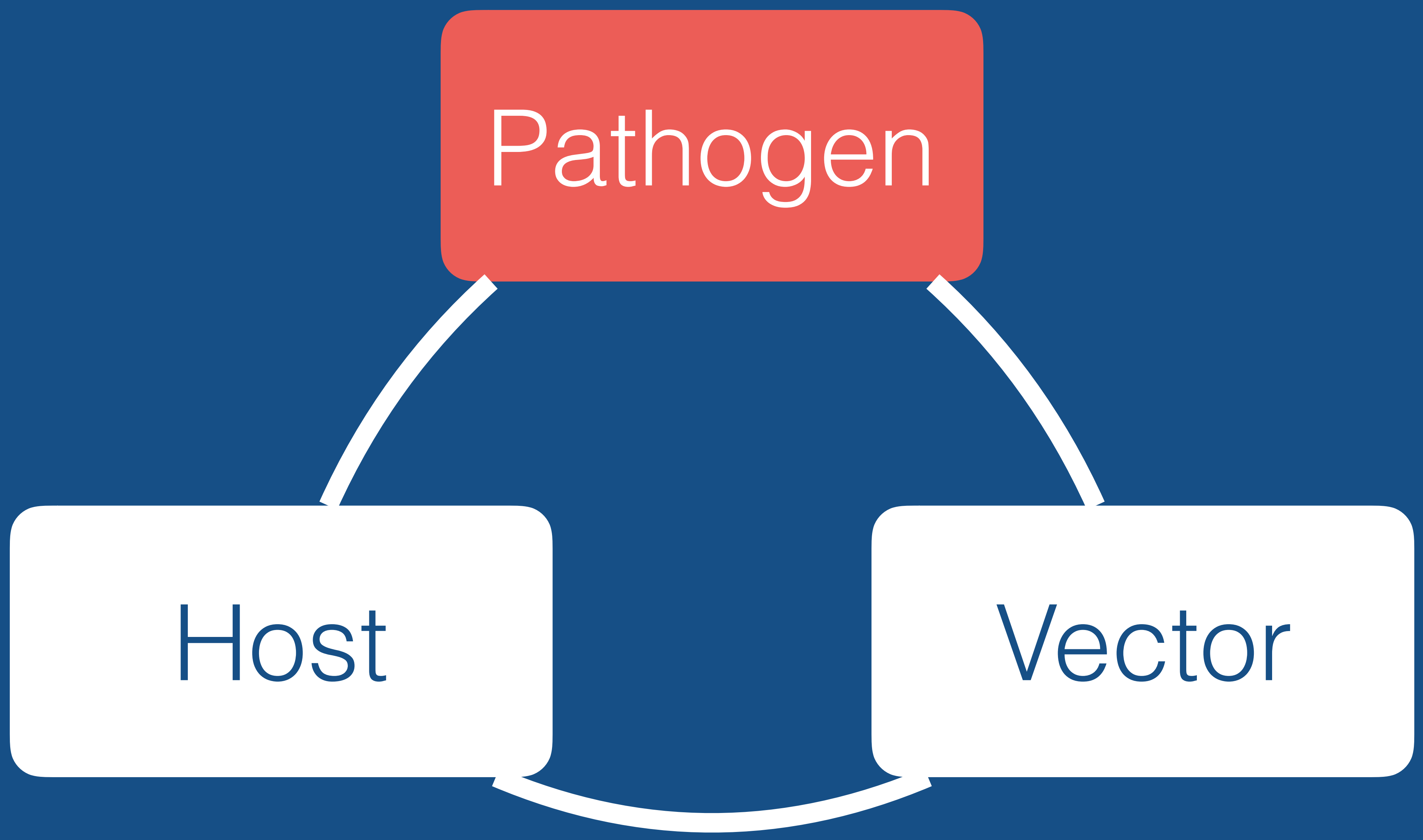
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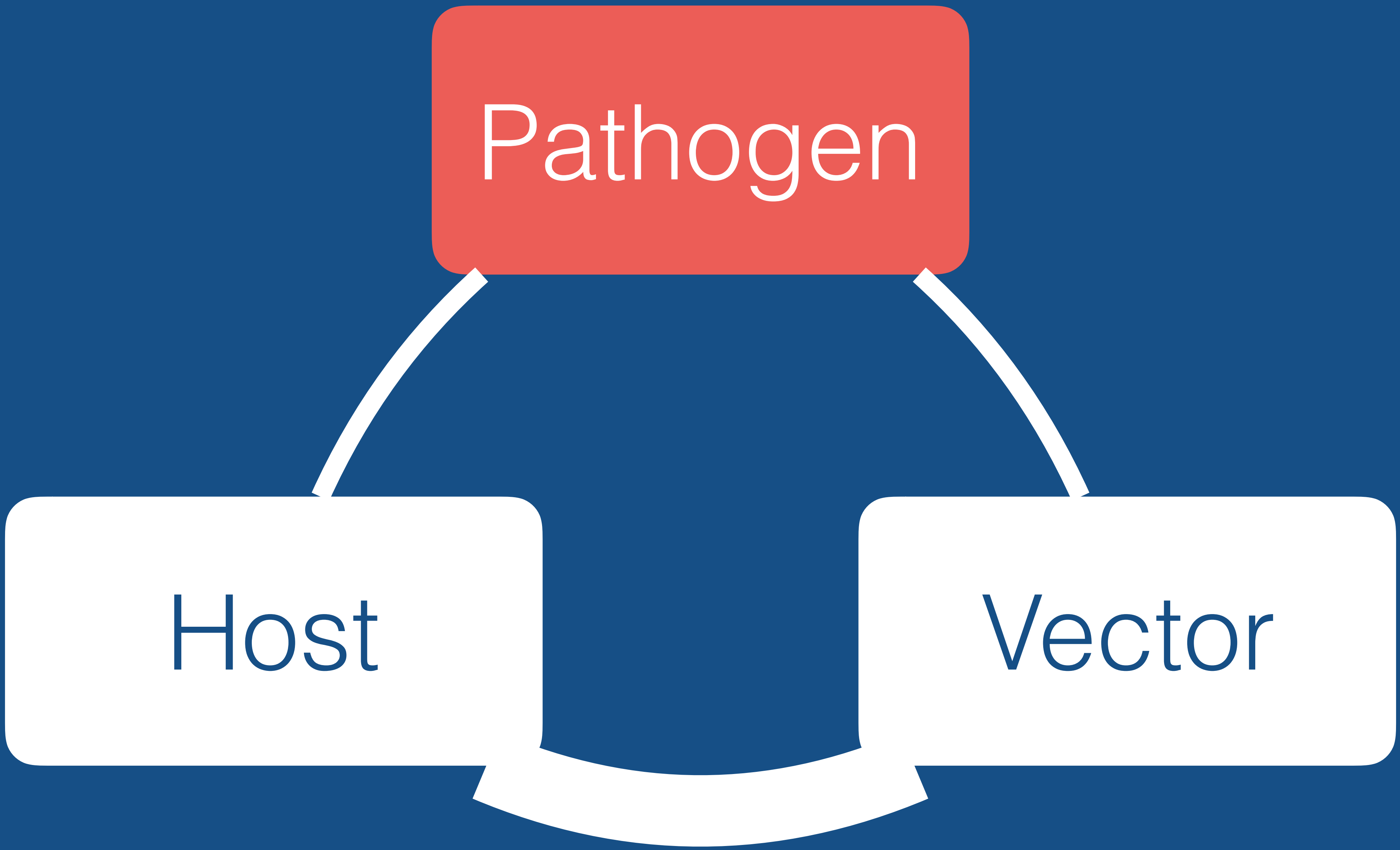
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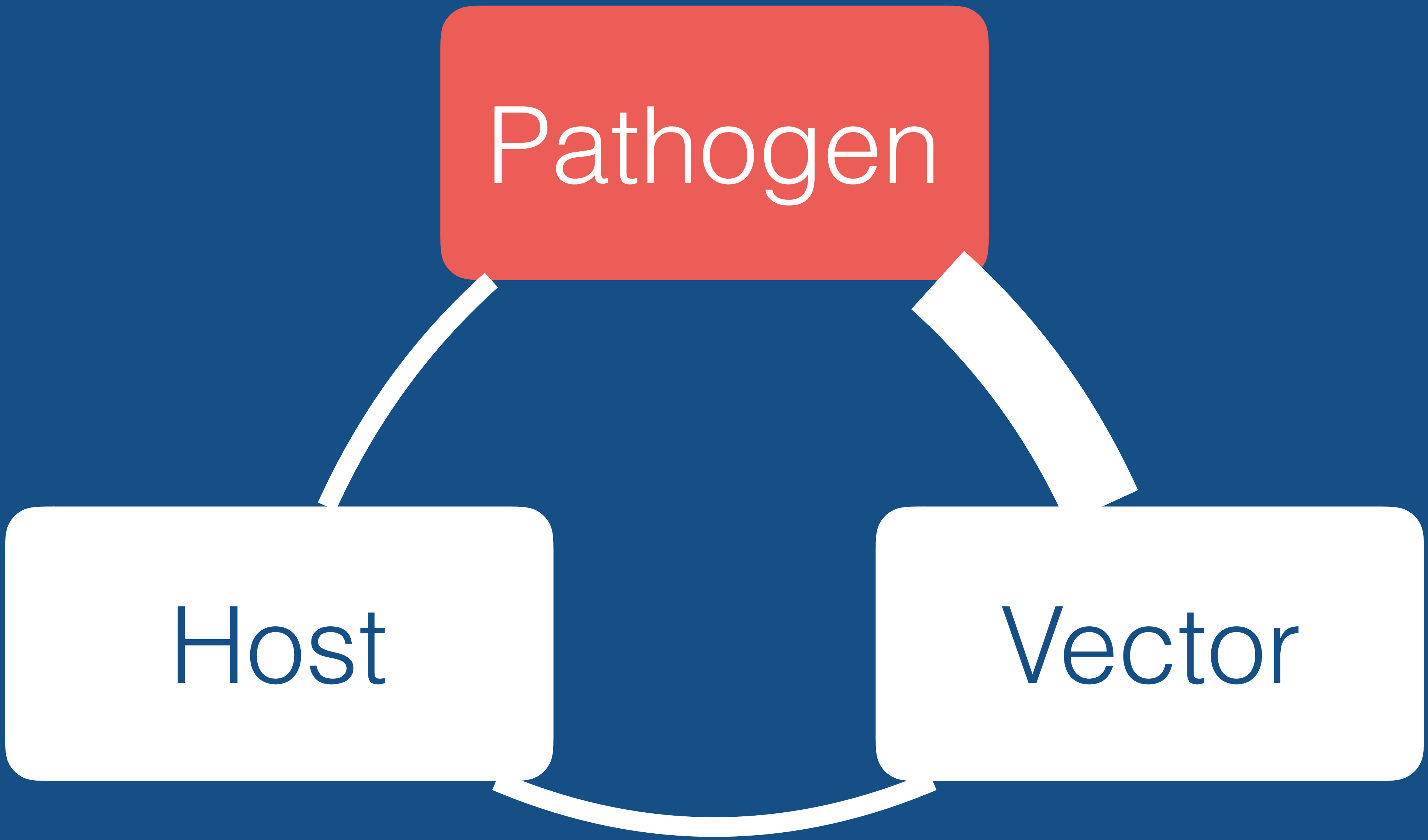
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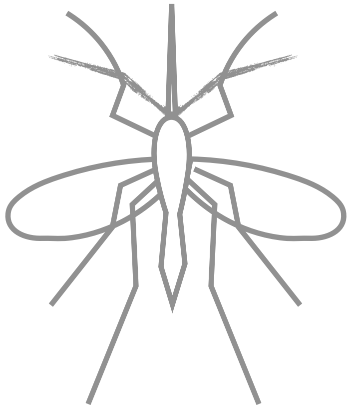
Facteurs environnementaux et conditions abiotiques

Transmission depends on both the human and vector compartments
La transmission dépend à la fois des compartiments humain et vectoriel

Aretina avy amin'ny moka (na biby kely hafa)

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 / Le modèle de base

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:

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susceptible | infected | recovered

everyone is either: S I R

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susceptible | infected | recovered

everyone is either: $S \xrightarrow{\text{infection}} I \xrightarrow{\text{recovery}} R$

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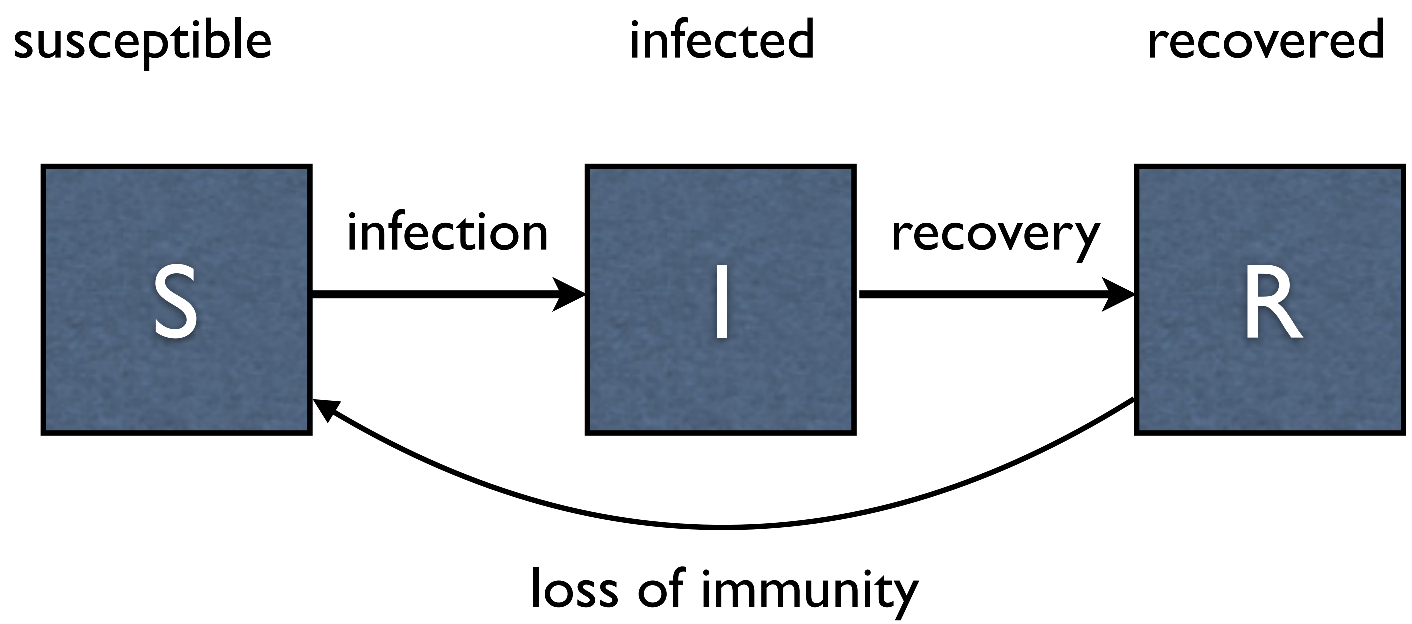
everyone is either:



- perte d'immunité

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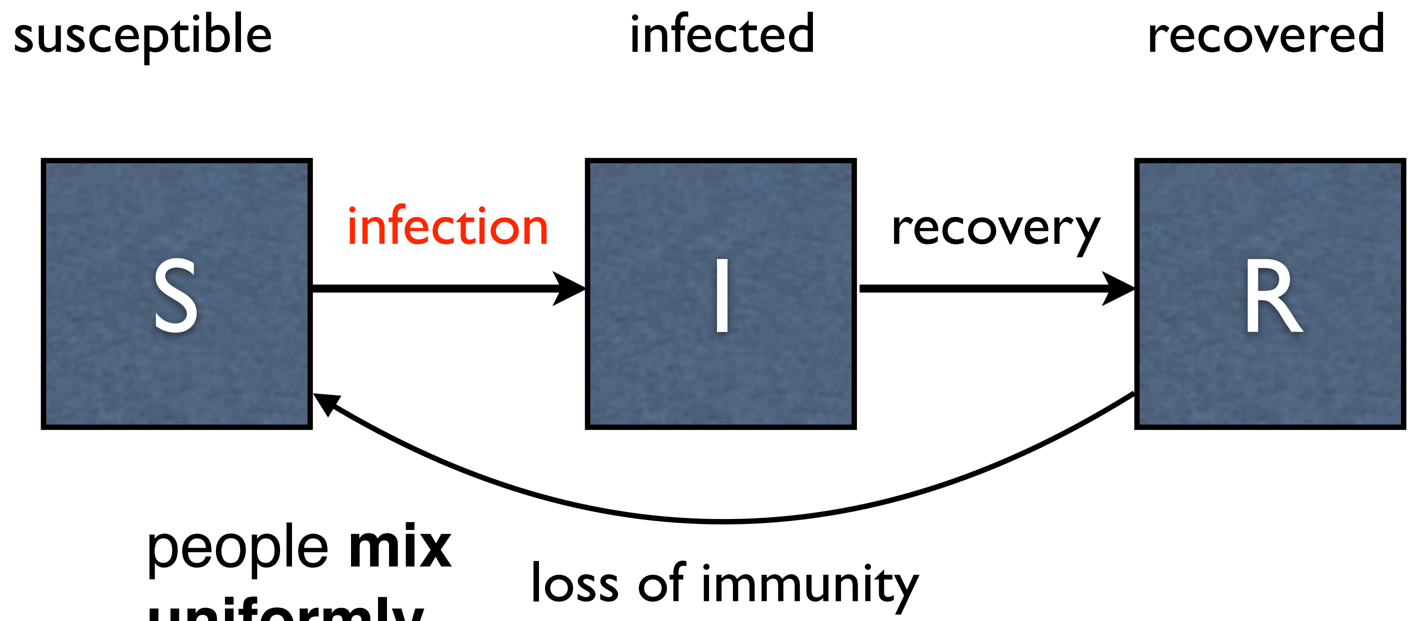
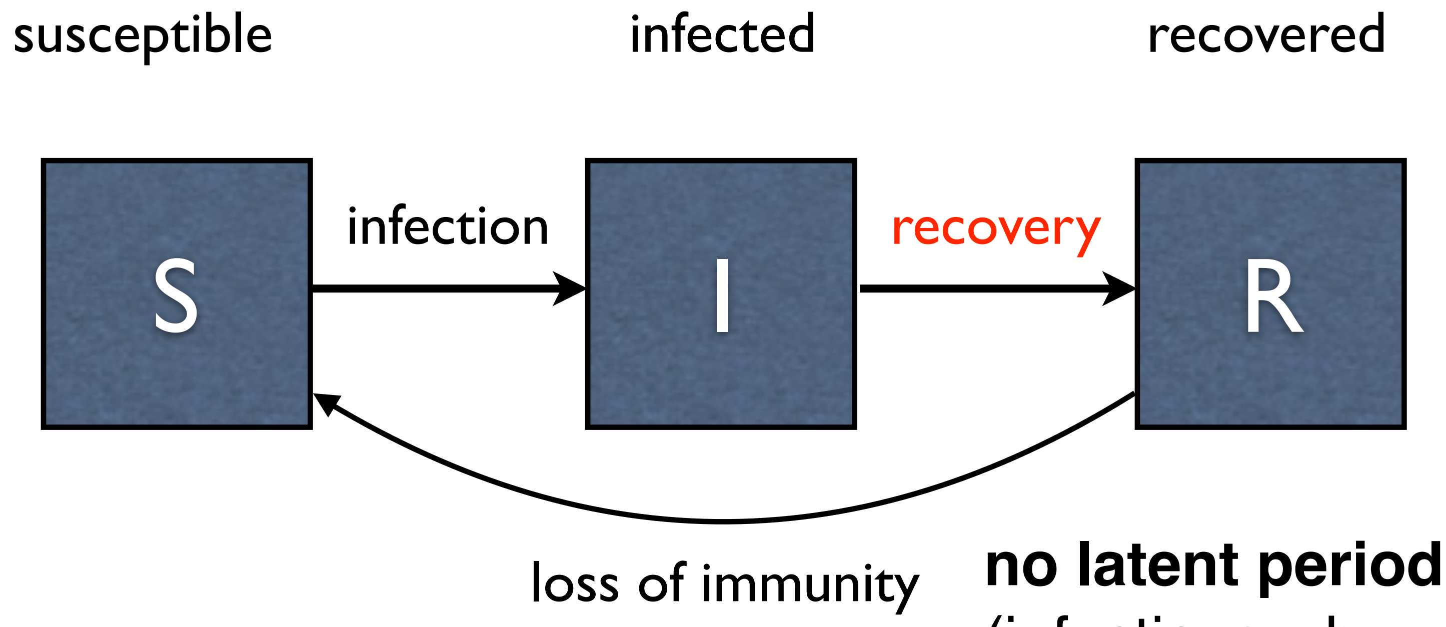


people **mix uniformly**

- perte d’immunité
- les gens se mélangent uniformément

The basic vector model

everyone is either:



no latent period
(infectious when infected)

- perte d'immunité
- les gens se mélangent uniformément
- pas de période de latence

The basic vector model

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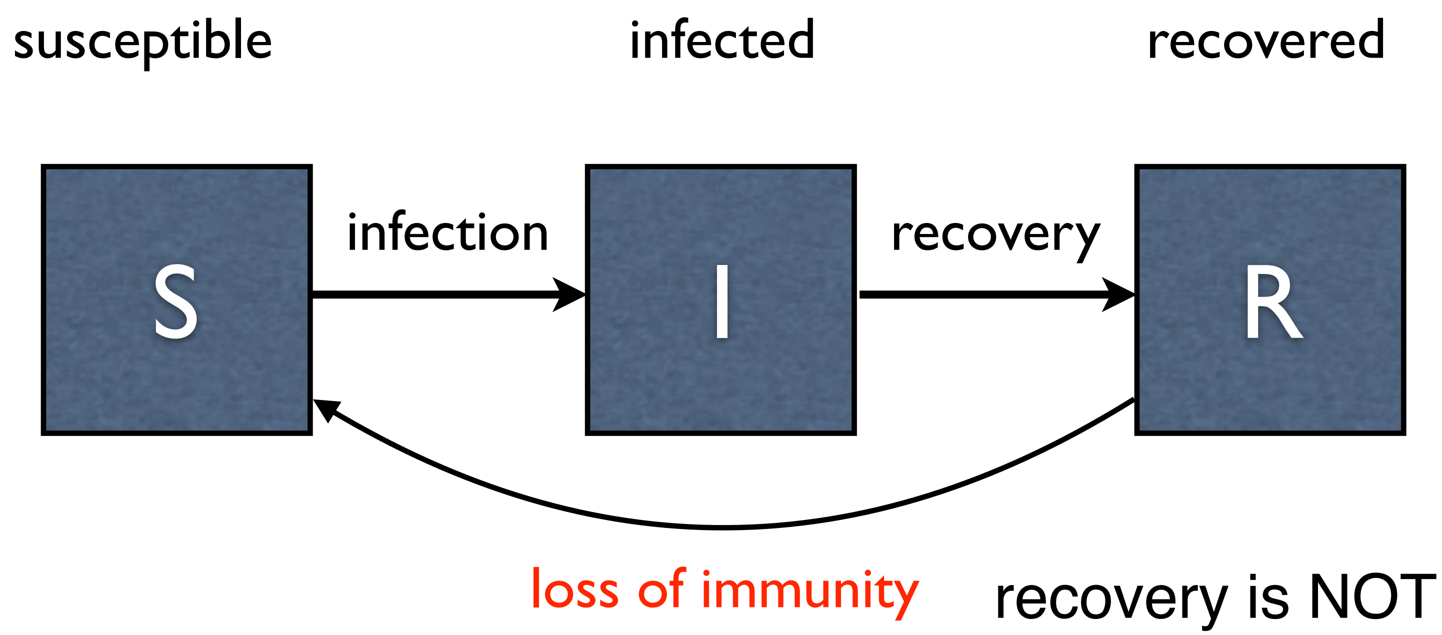
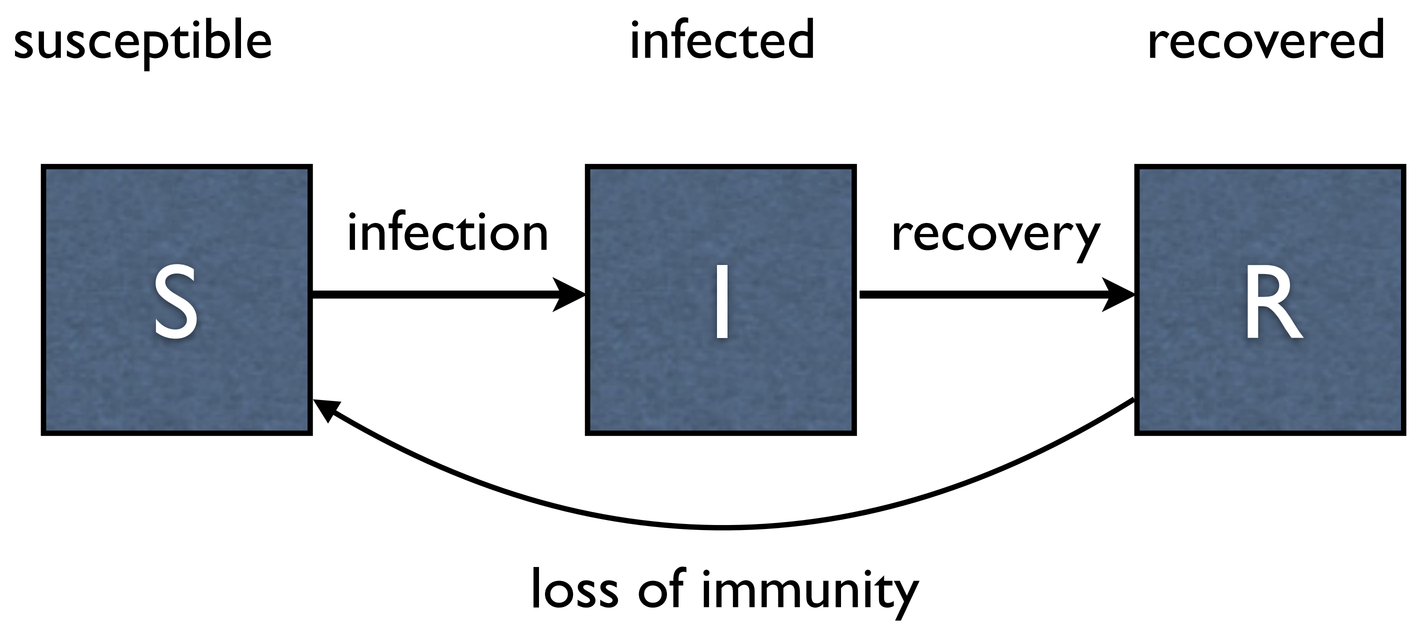


recovery is NOT **permanent**

- perte d’immunité
- les gens se mélangent uniformément
- pas de période de latence
- la récupération n’est pas permanente

The basic vector model

everyone is either:



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

- perte d'immunité
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- taille de population constante

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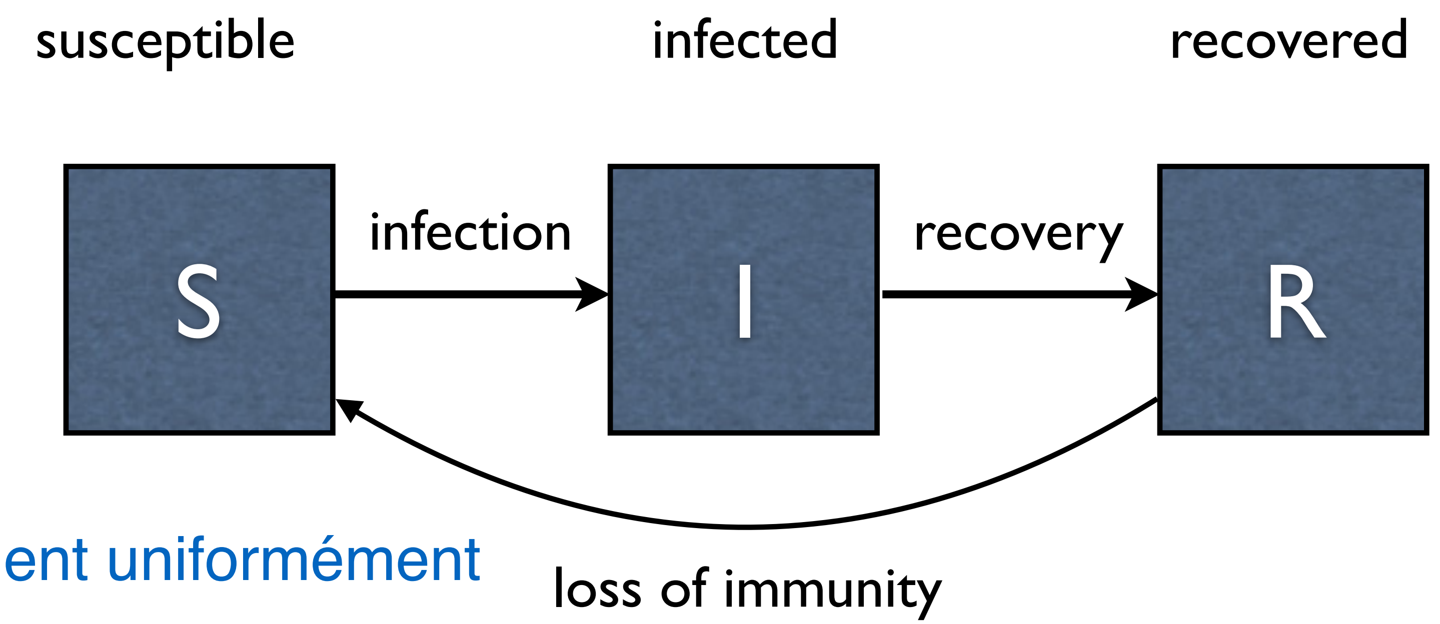

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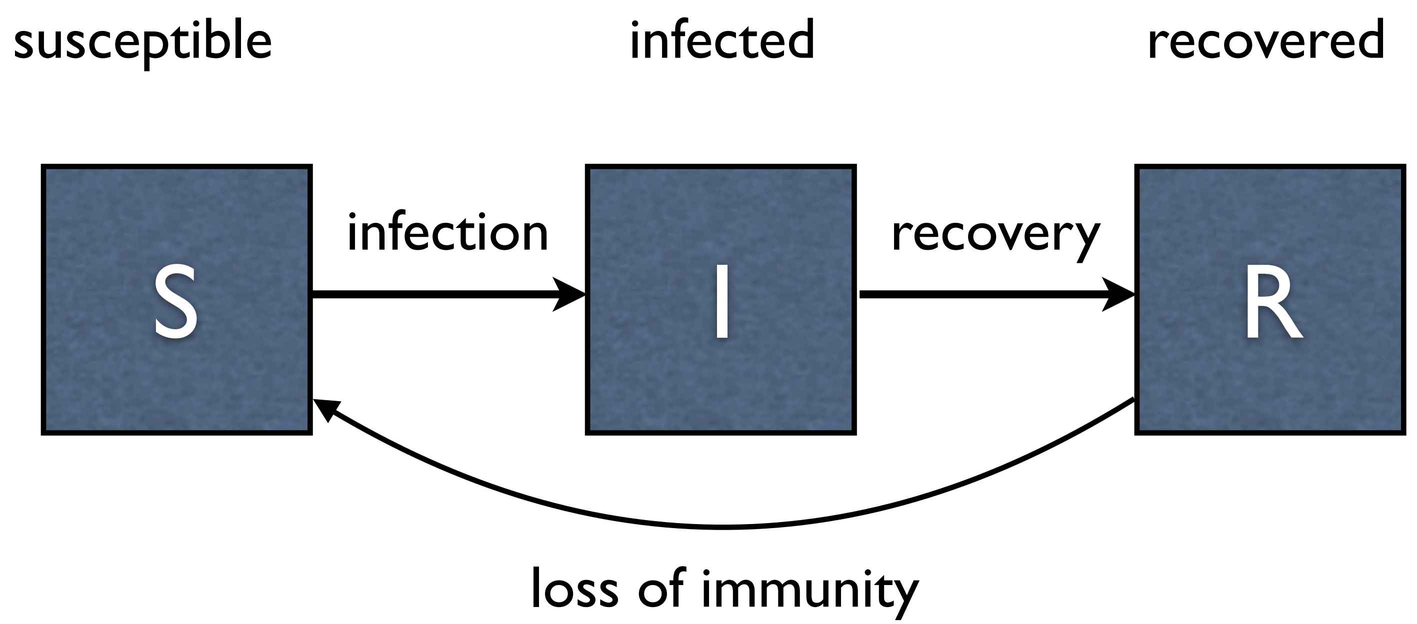

Human compartments…

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

susceptible infected recovered

everyone is either: S $\xrightarrow{\text{infection}}$ I $\xrightarrow{\text{recovery}}$ R

Compartmental models (Mechanistic Models)

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Human c

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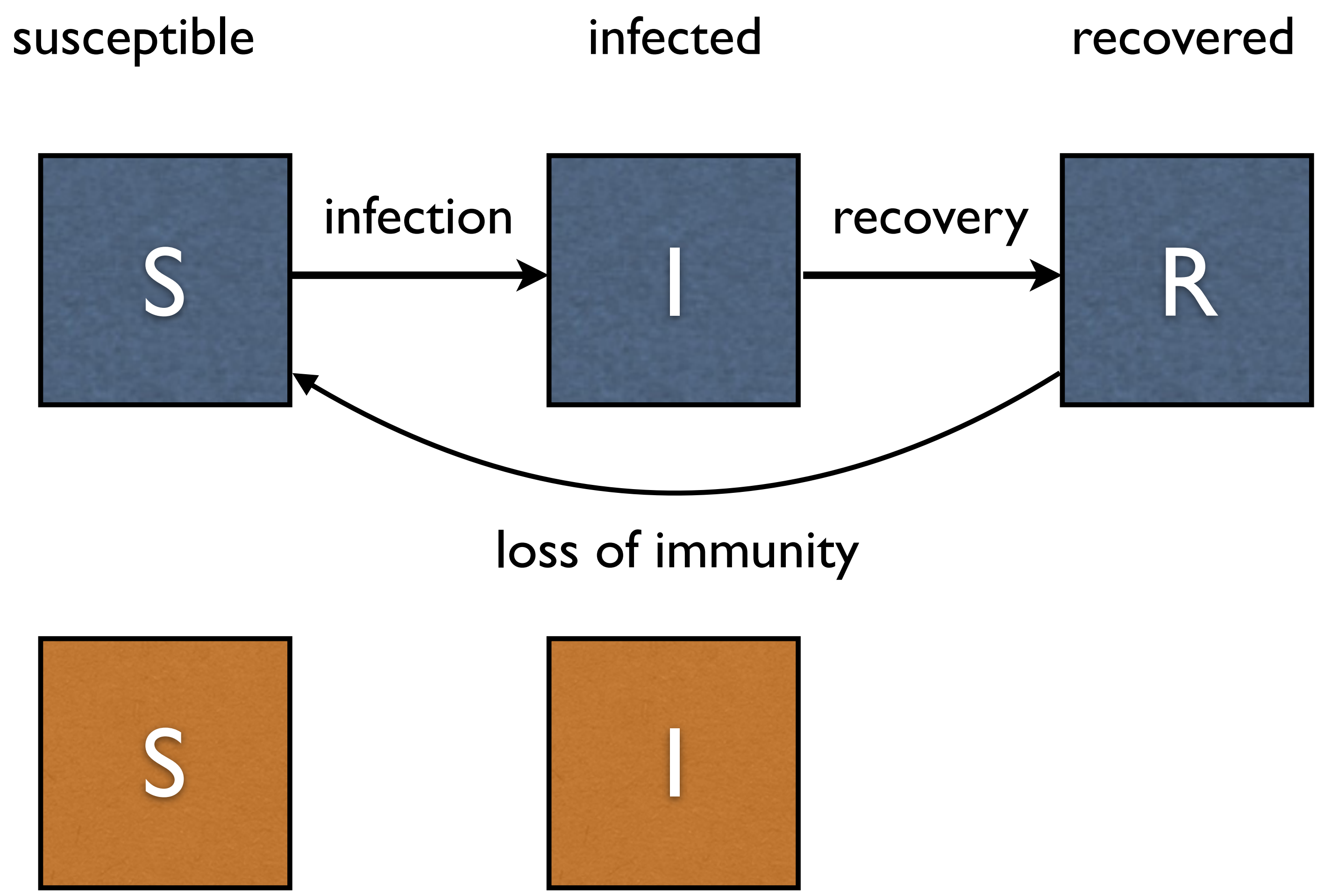

Vector compartments.

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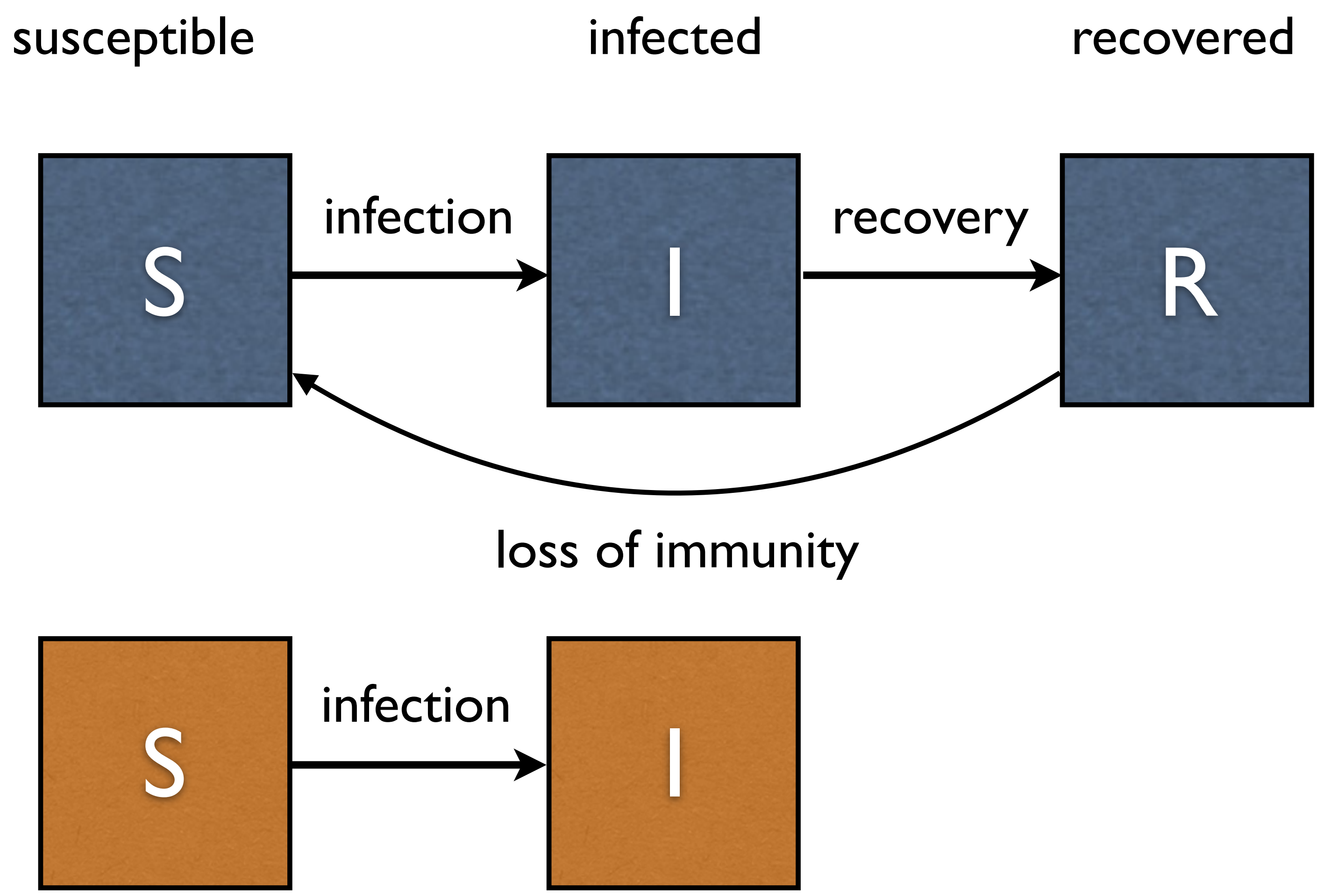
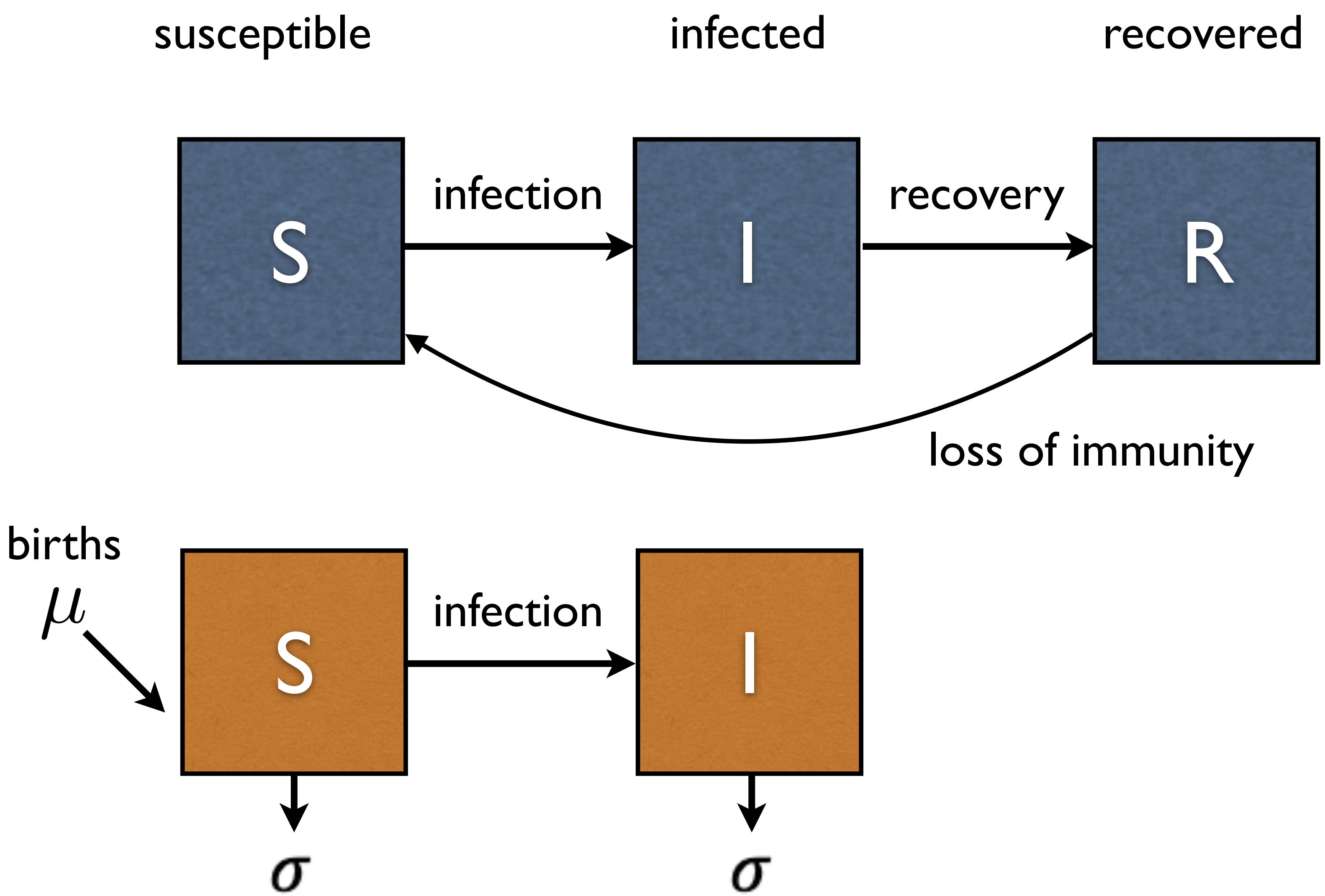
The basic vector model



Vector compartments…

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

The basic vector model



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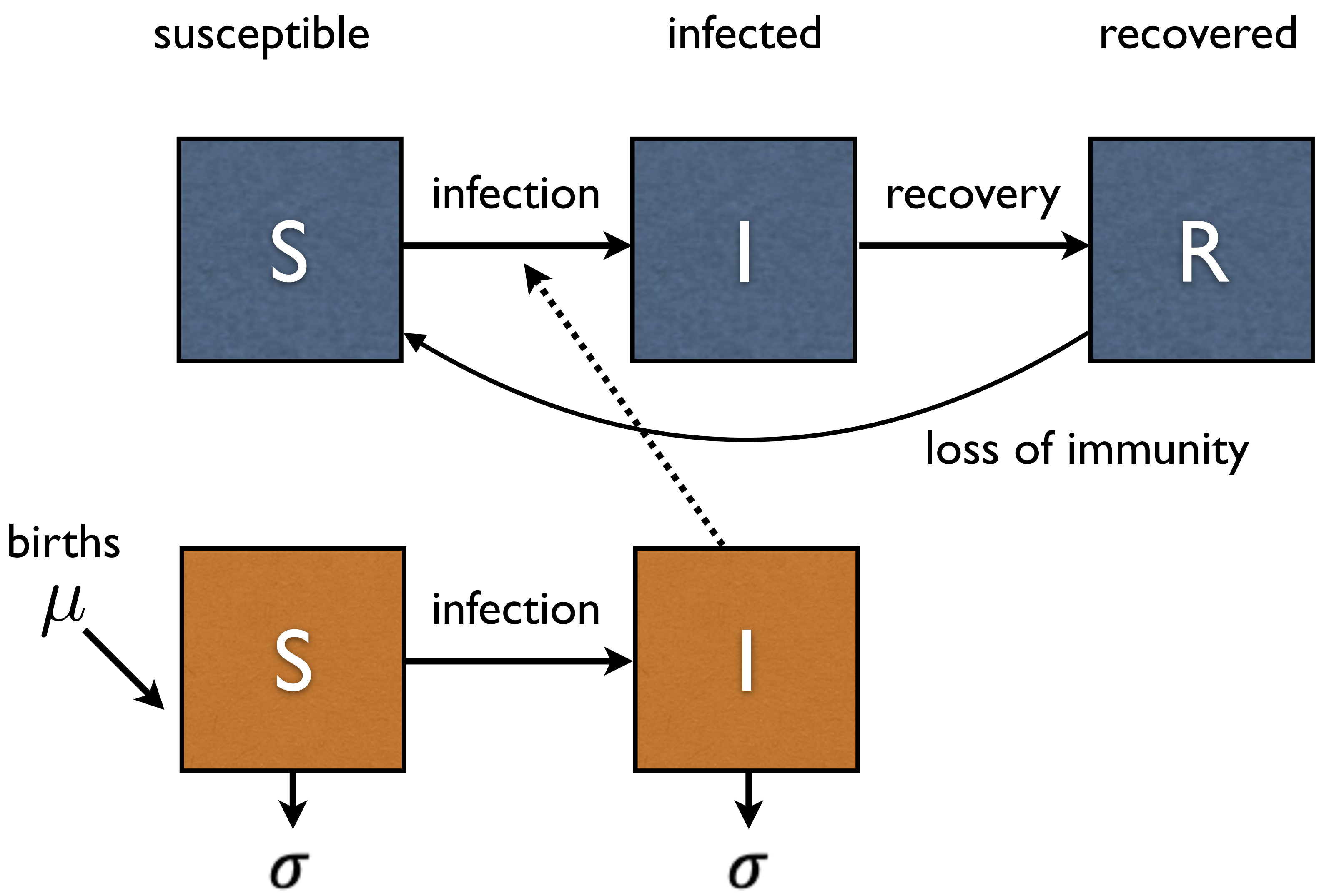
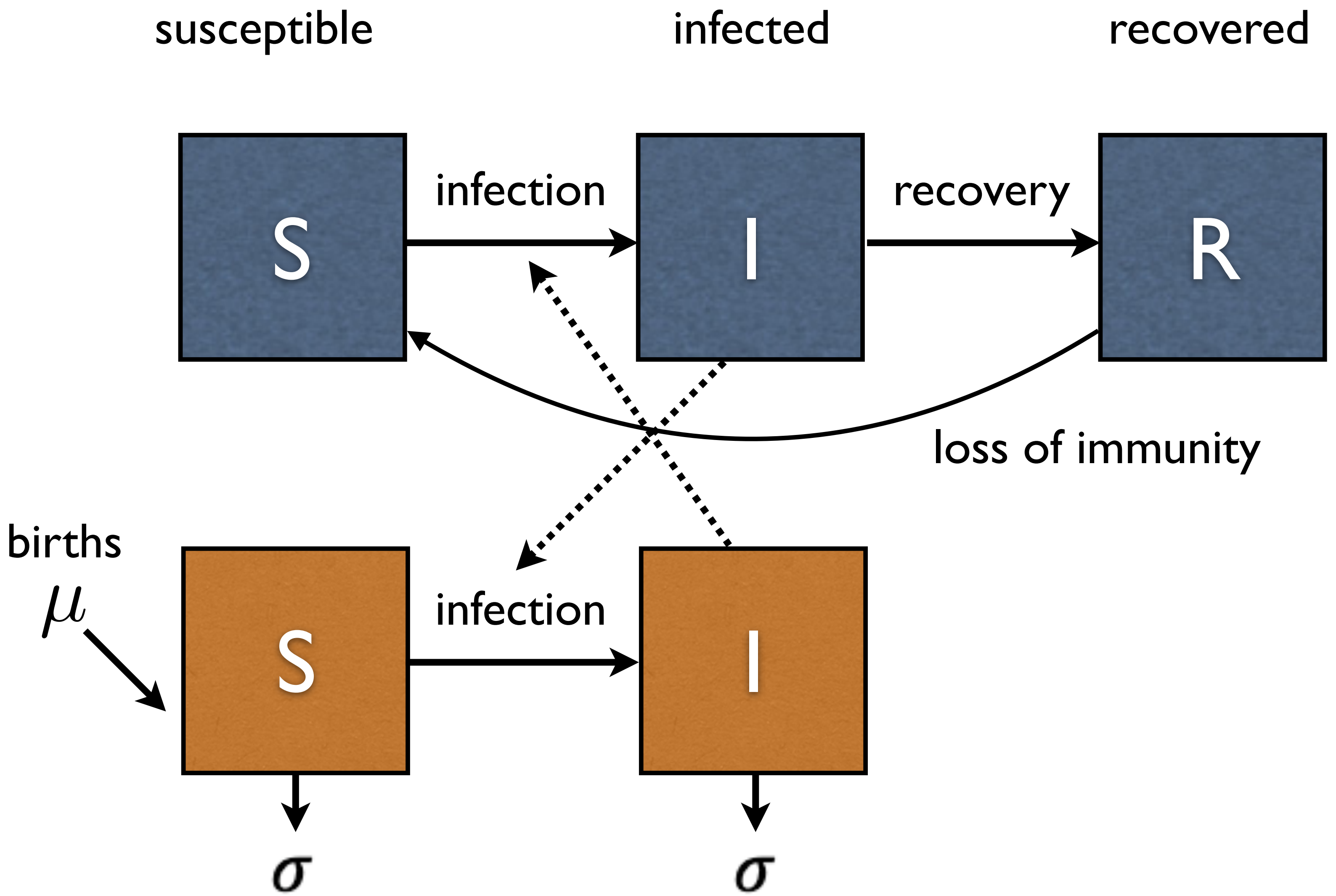


The basic vector model



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

Le compartiment infectieux des humains influe sur la transmission des vecteurs! (et vice versa)

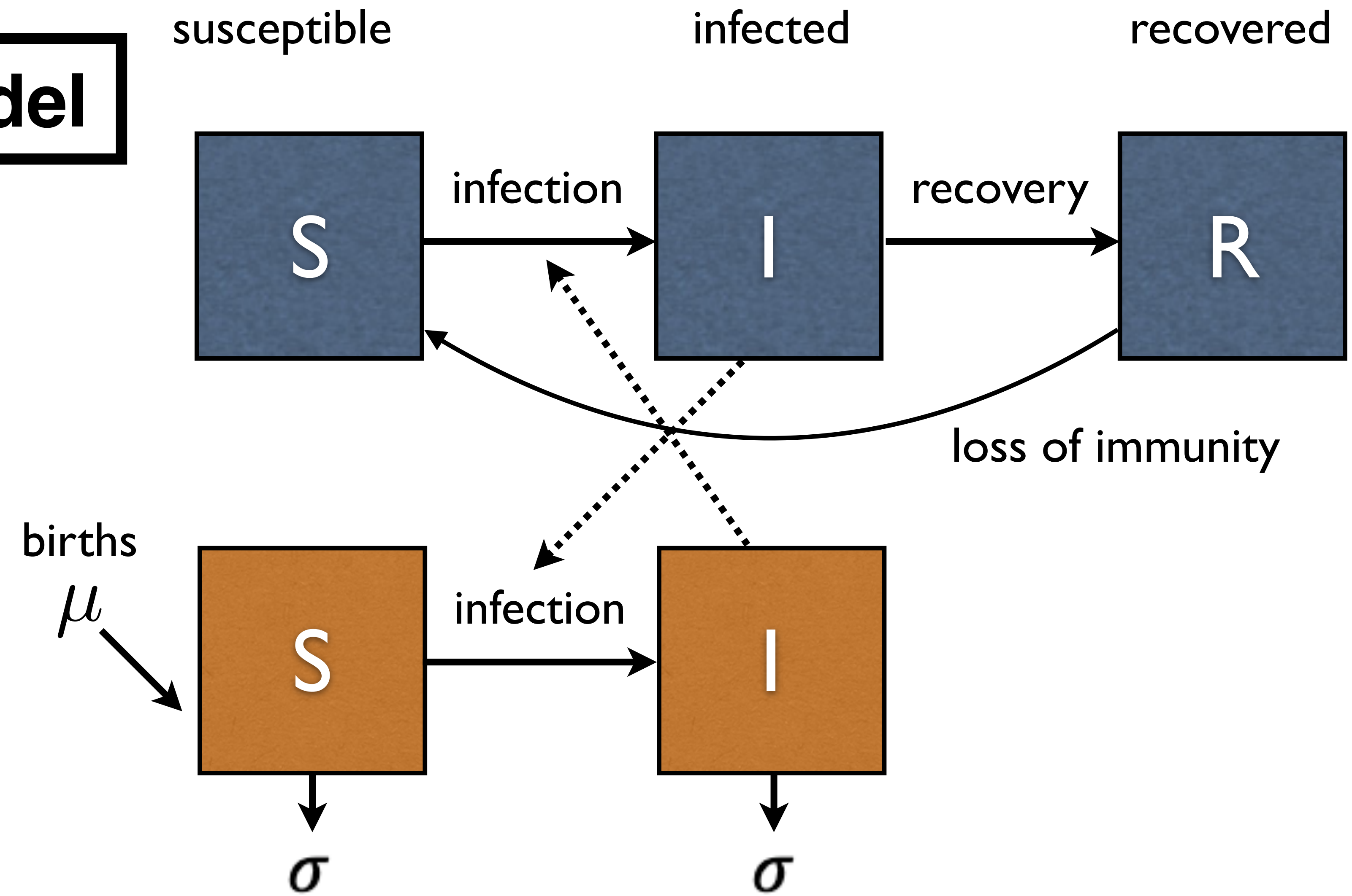
The basic vector model

Parameters

β_H: transmission rate

γ : rate of recovery

w : rate of loss of immunity



Humans

Vectors

Compartmental models (Mechanistic Models)

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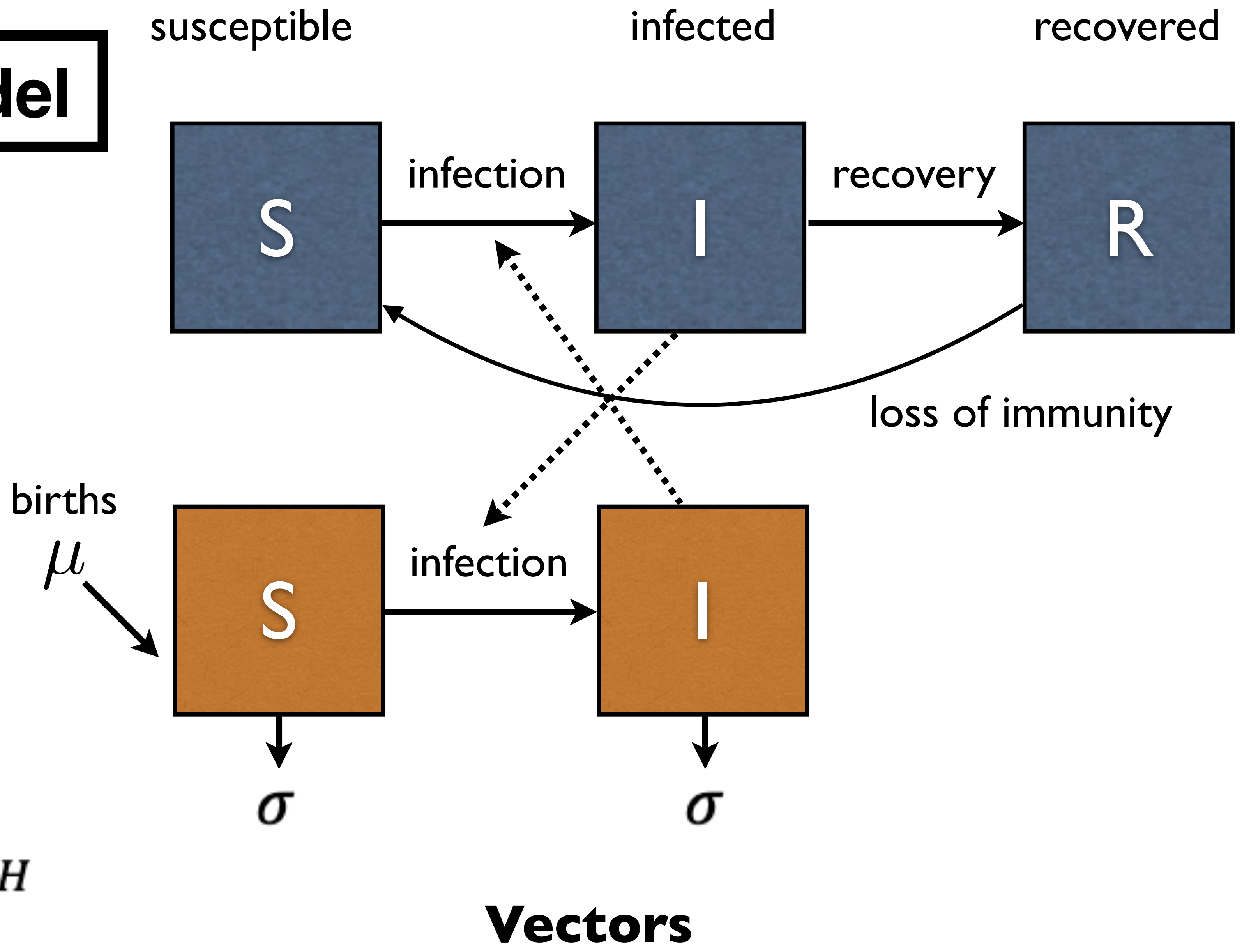


Humans

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

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

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

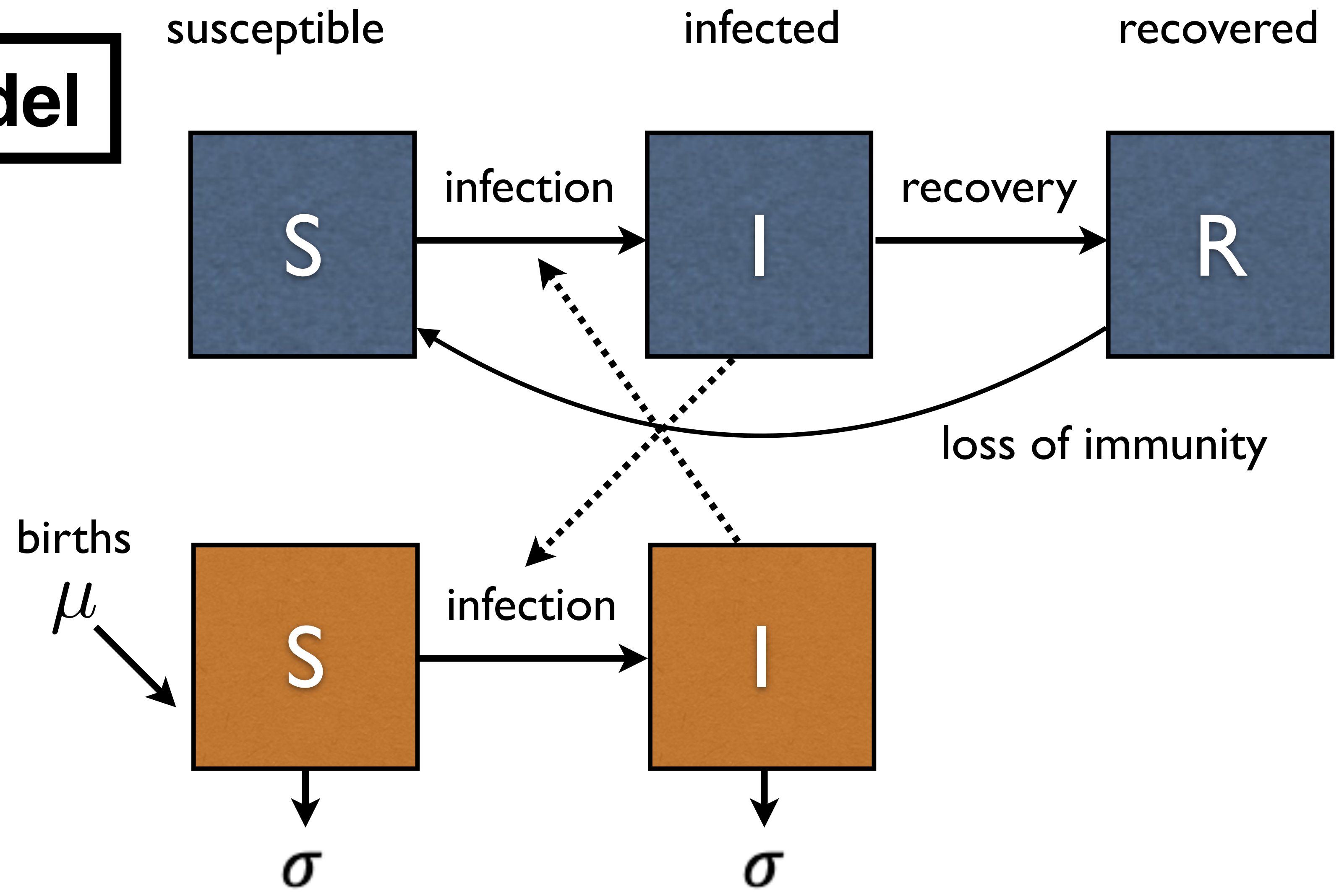
The basic vector model

Parameters

β_V : transmission rate

μ : birth rate

σ : death rate



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Vectors

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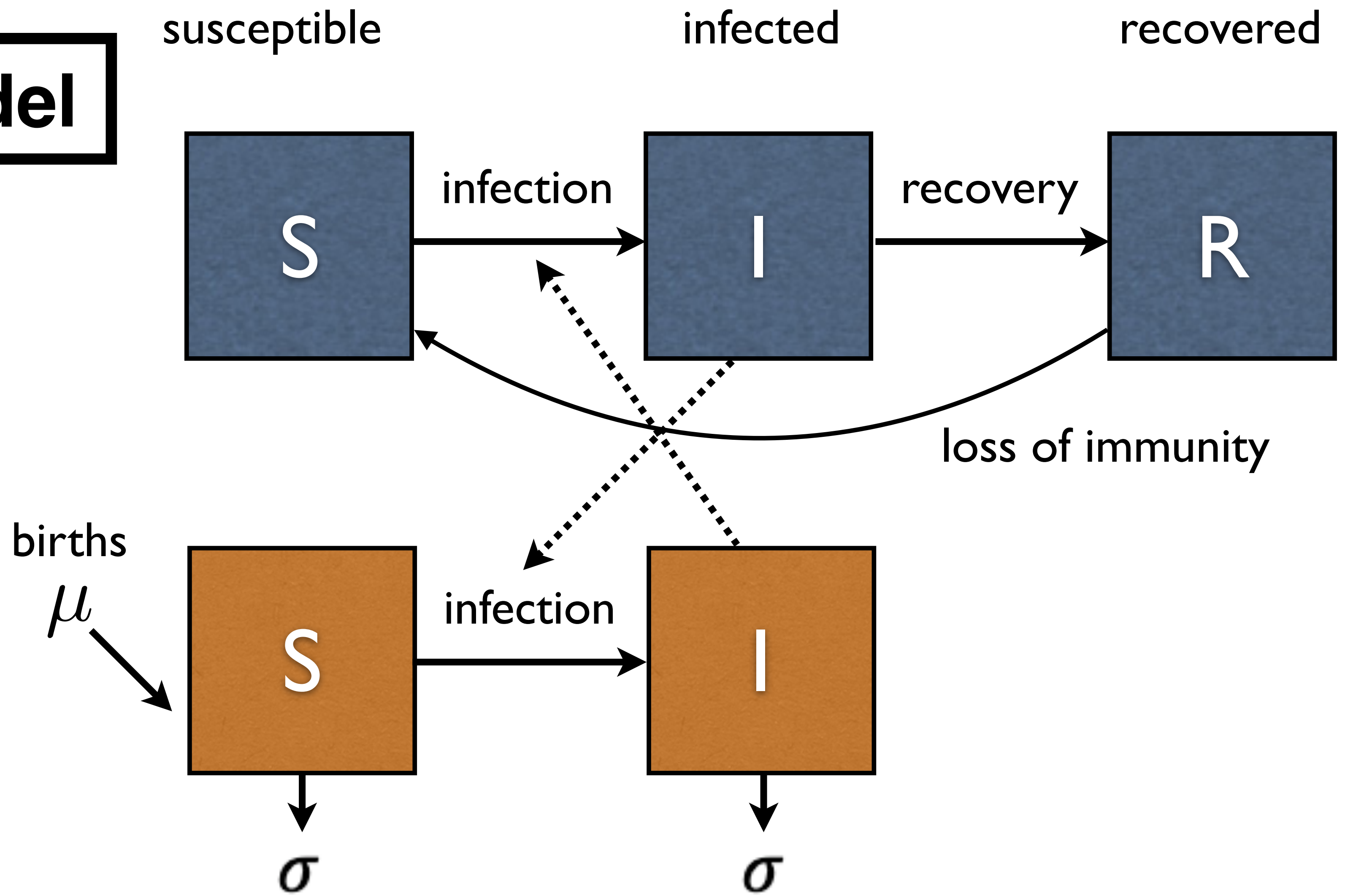

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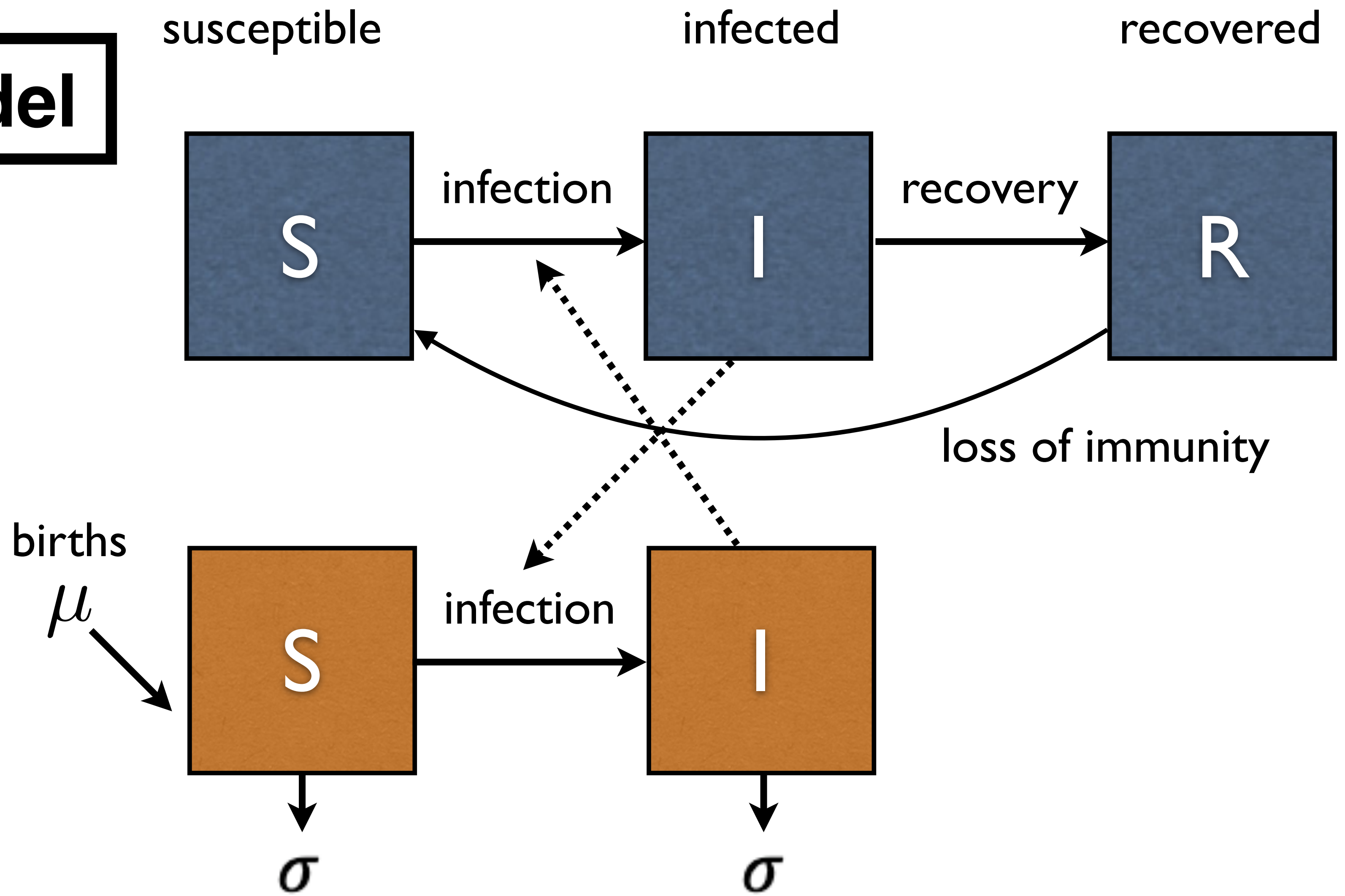
Vectors

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

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

The basic vector model



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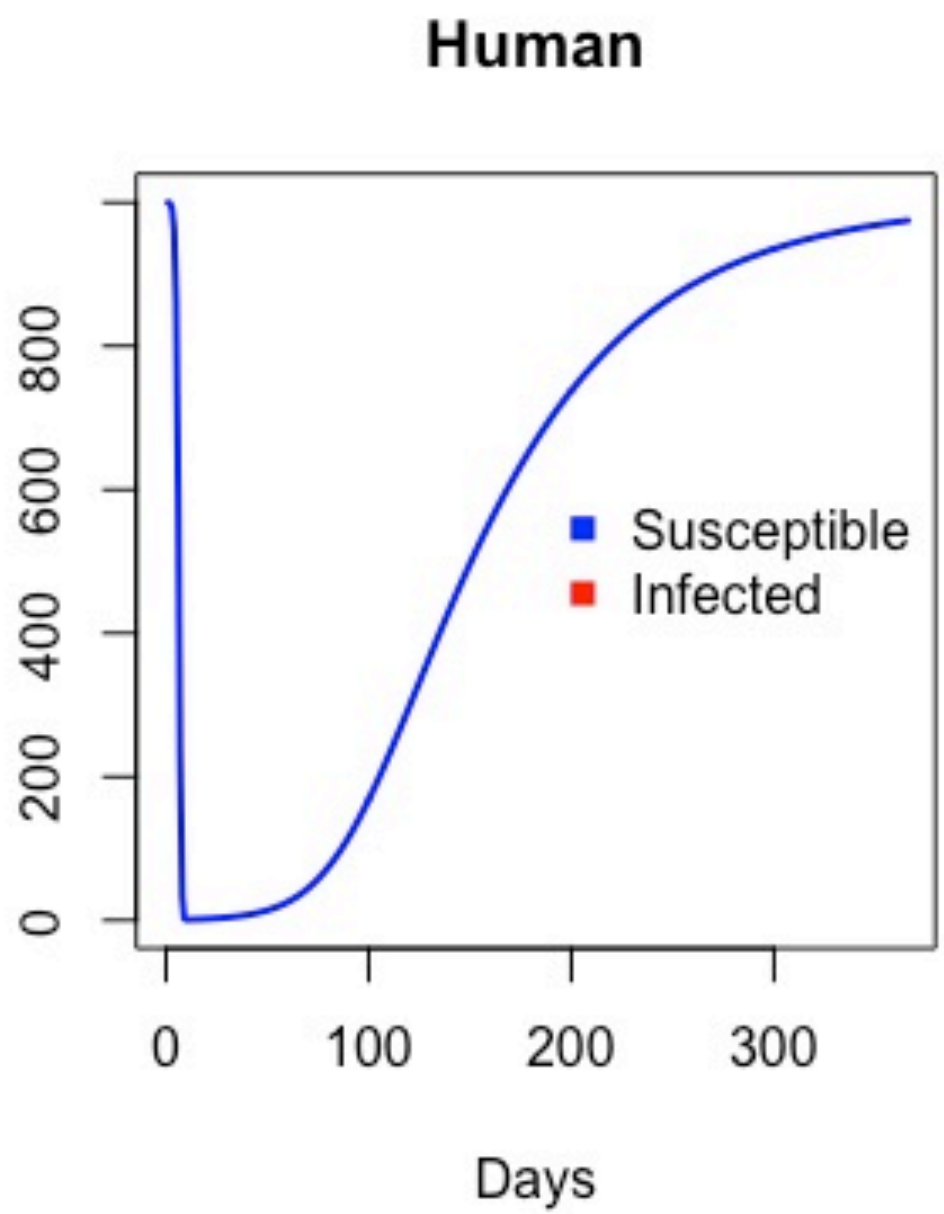
The basic vector model: dynamics



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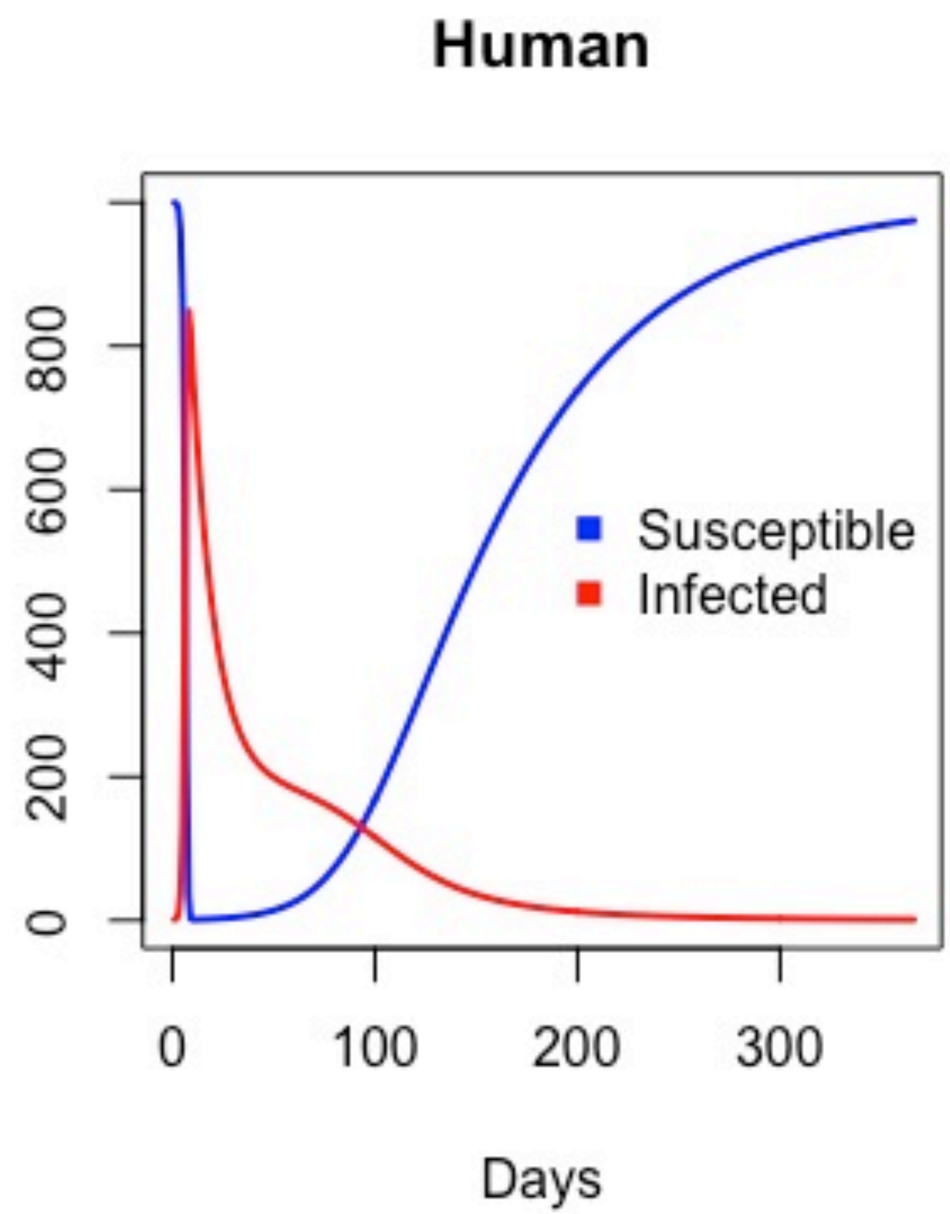

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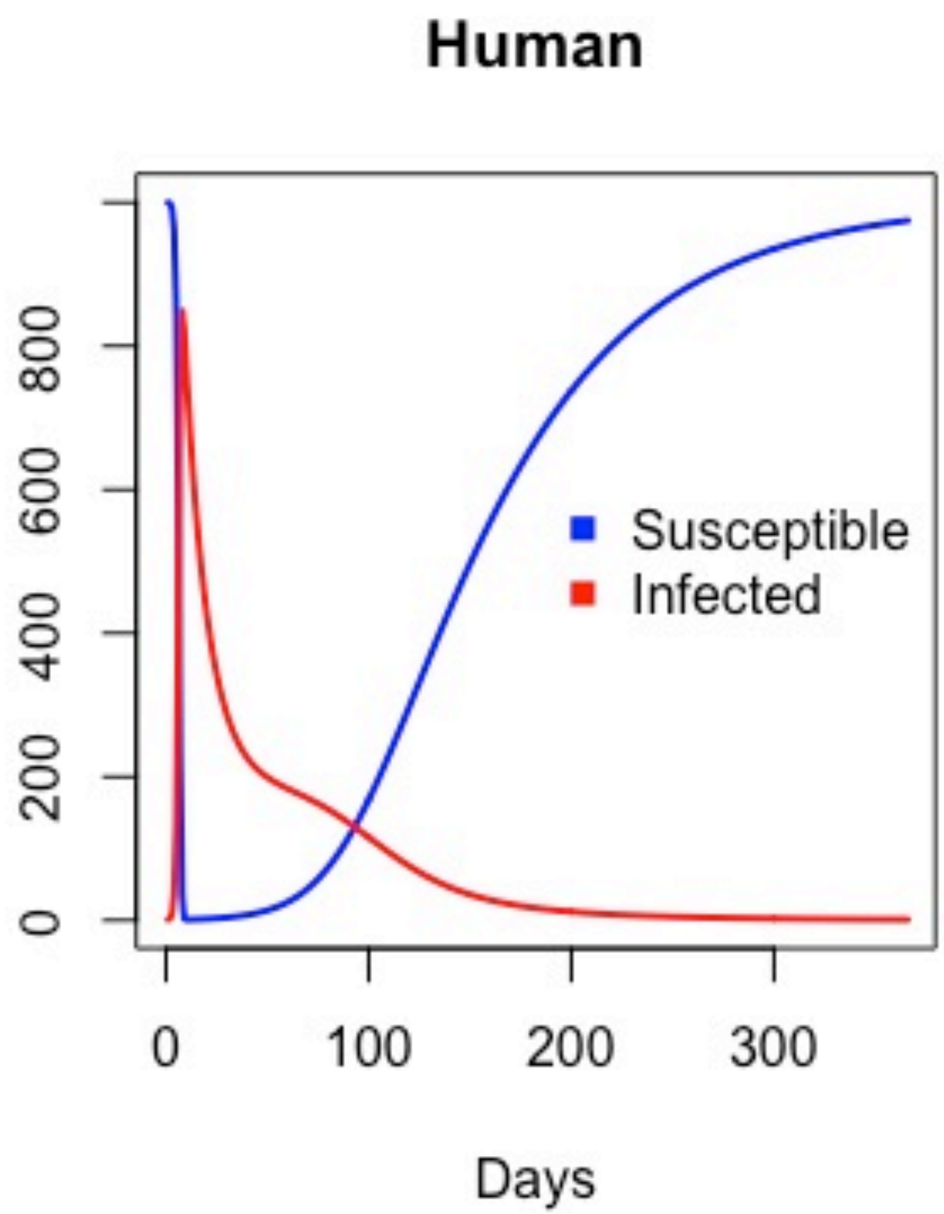

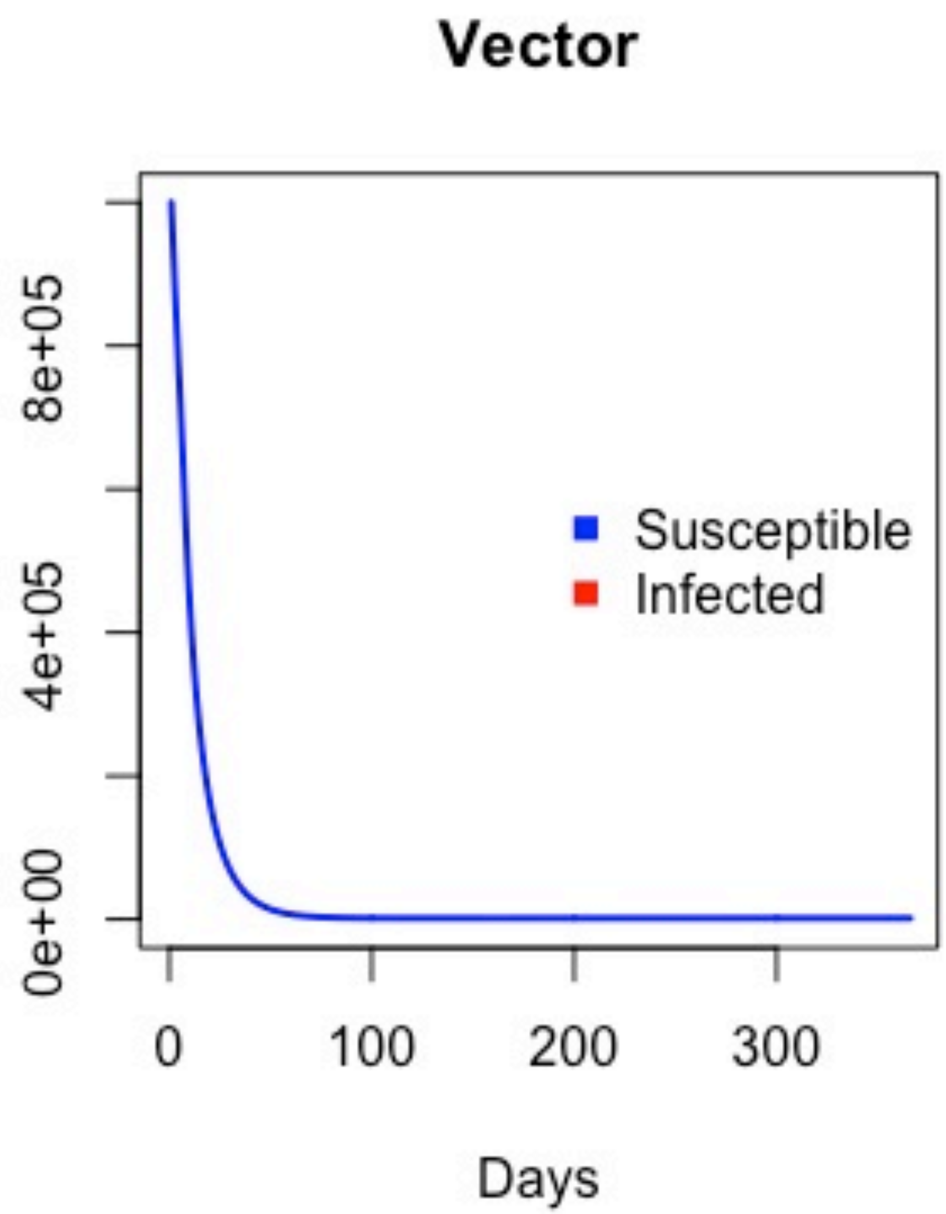

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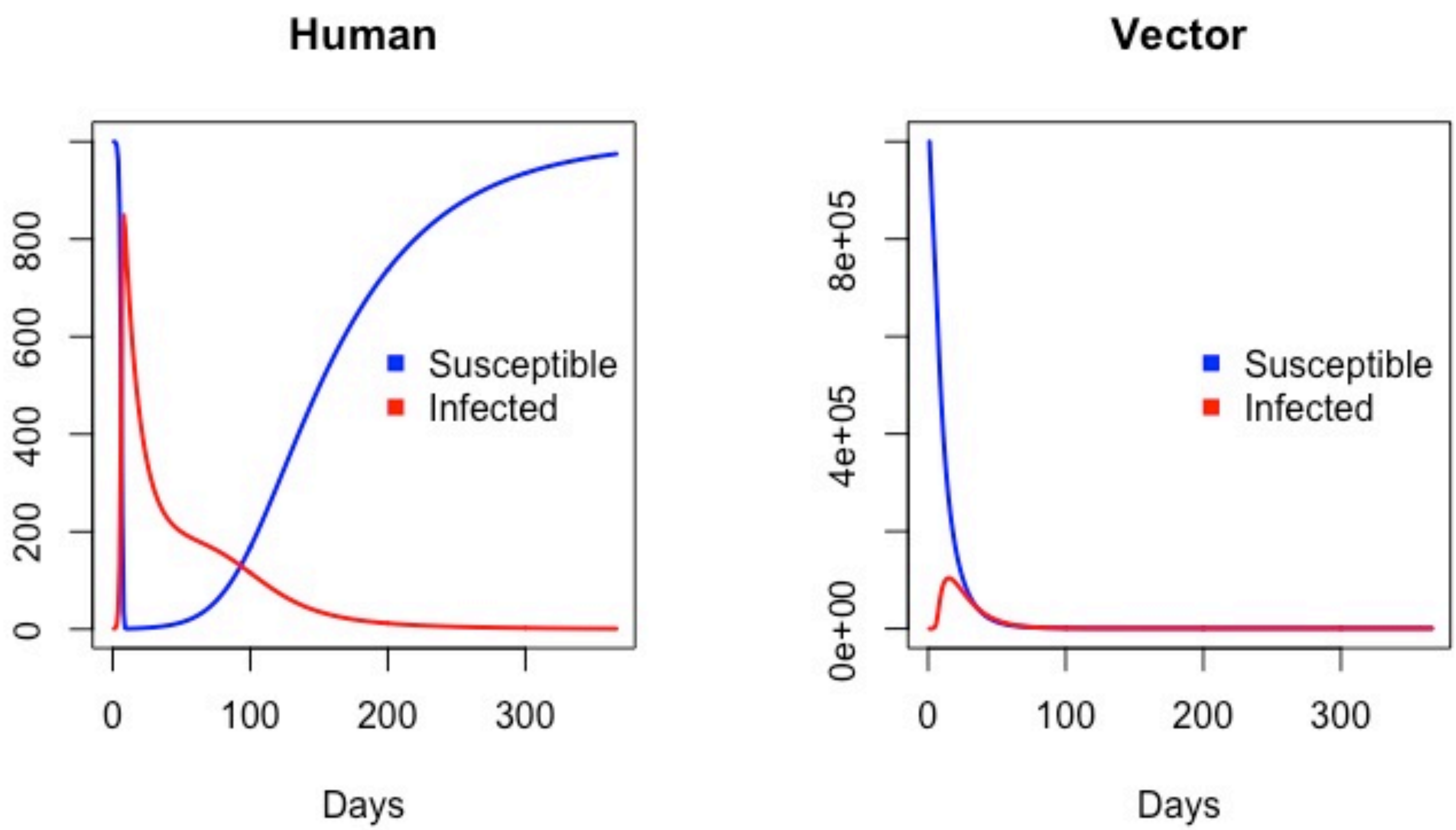

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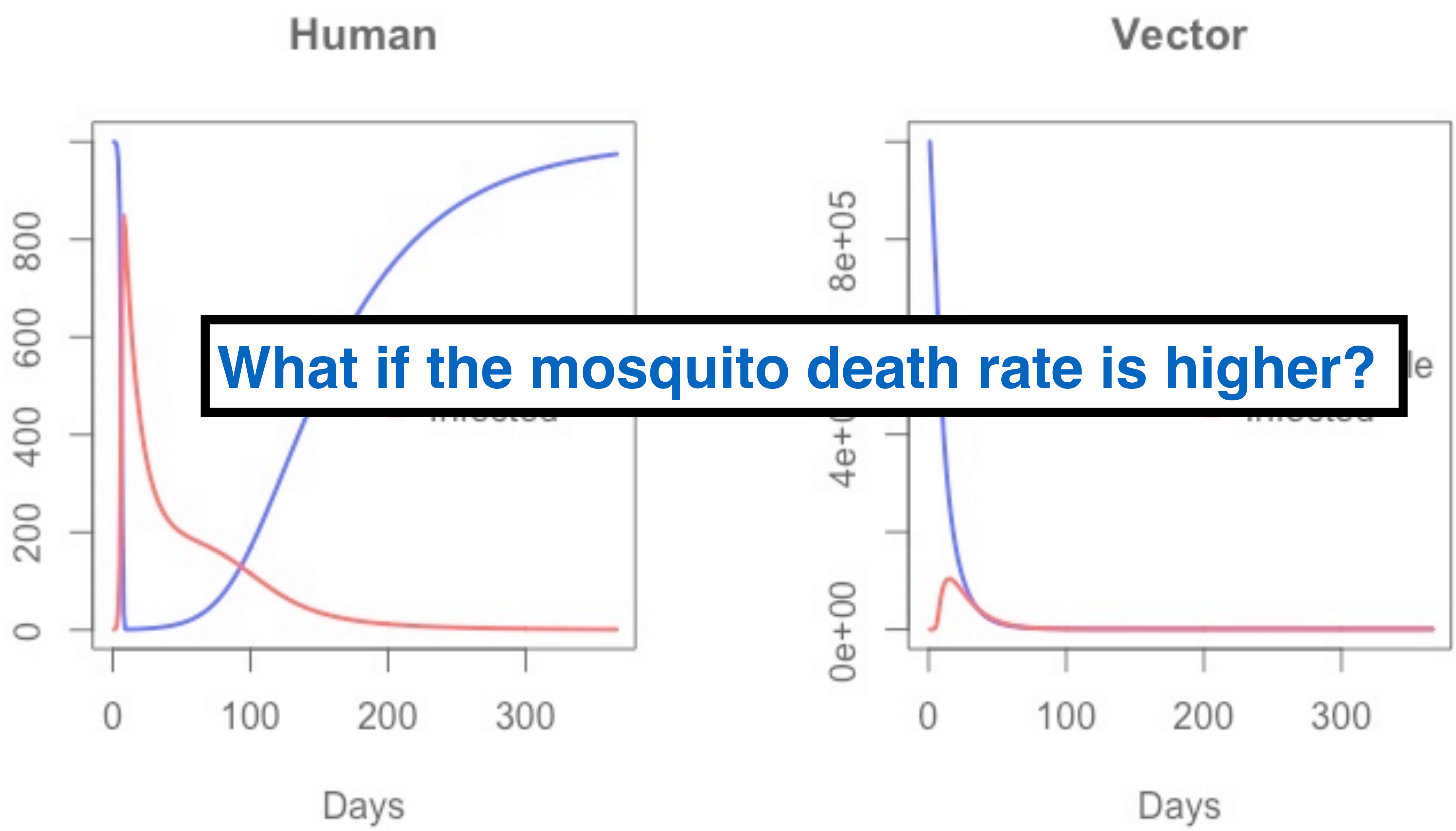
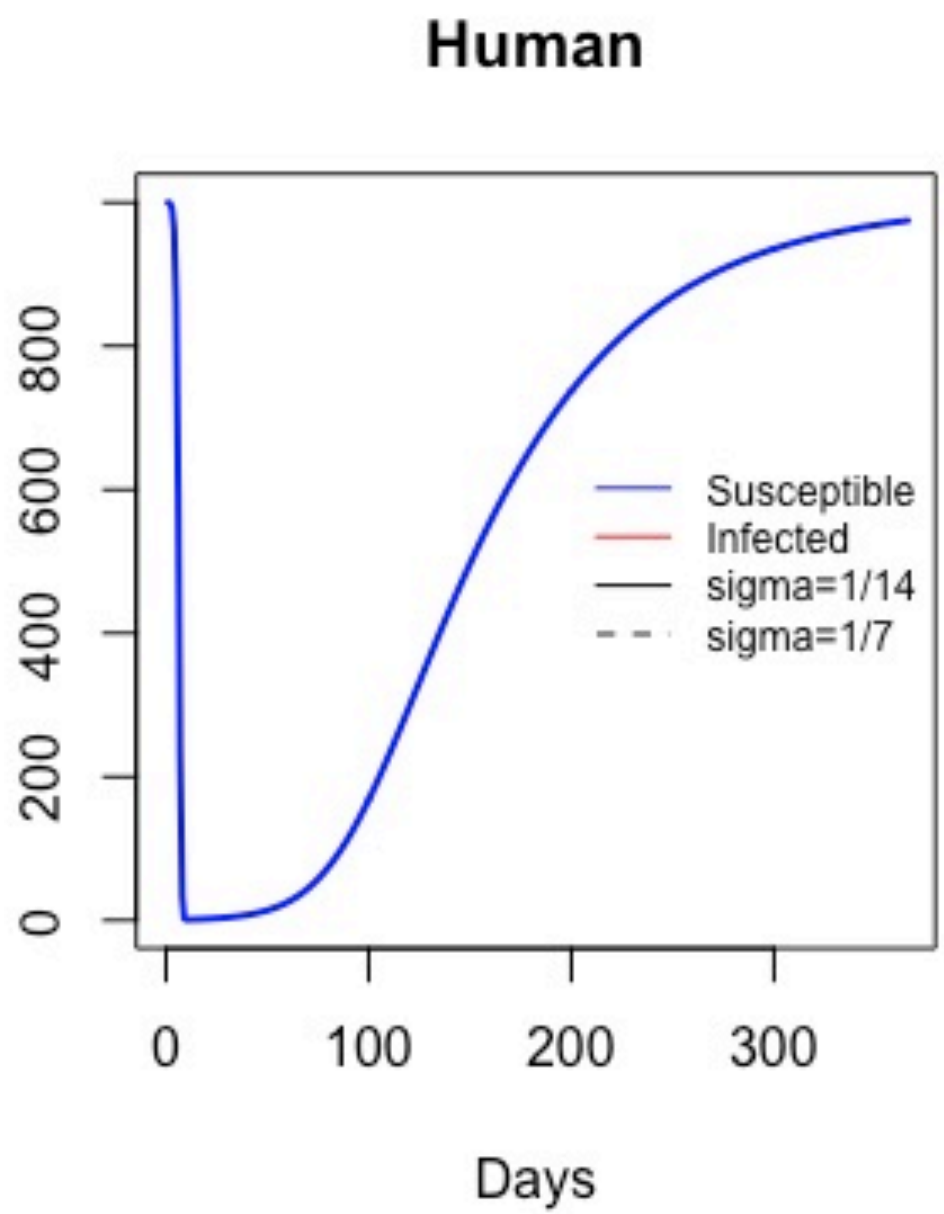


What if the mosquito death rate is higher?

The basic vector model: dynamics



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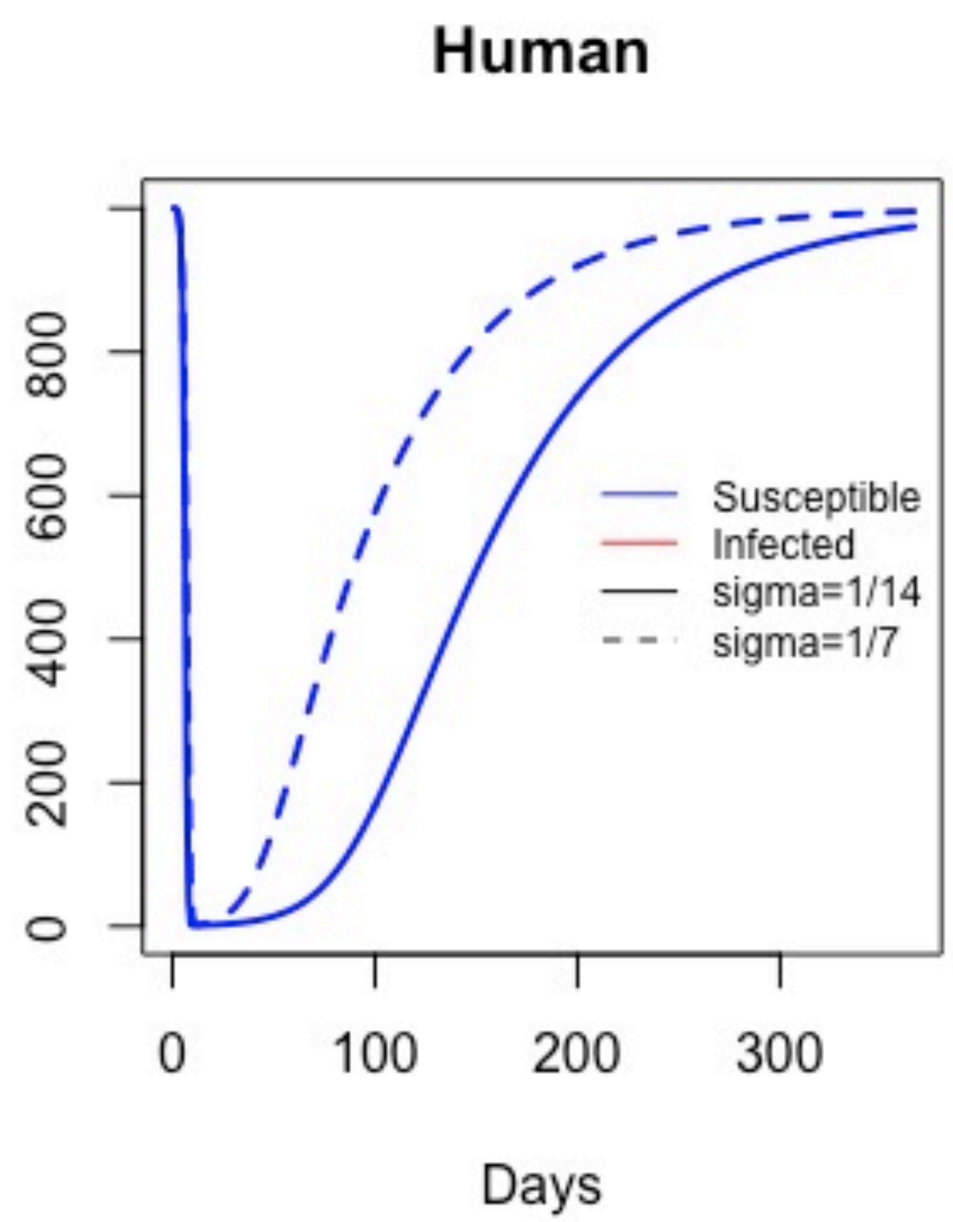

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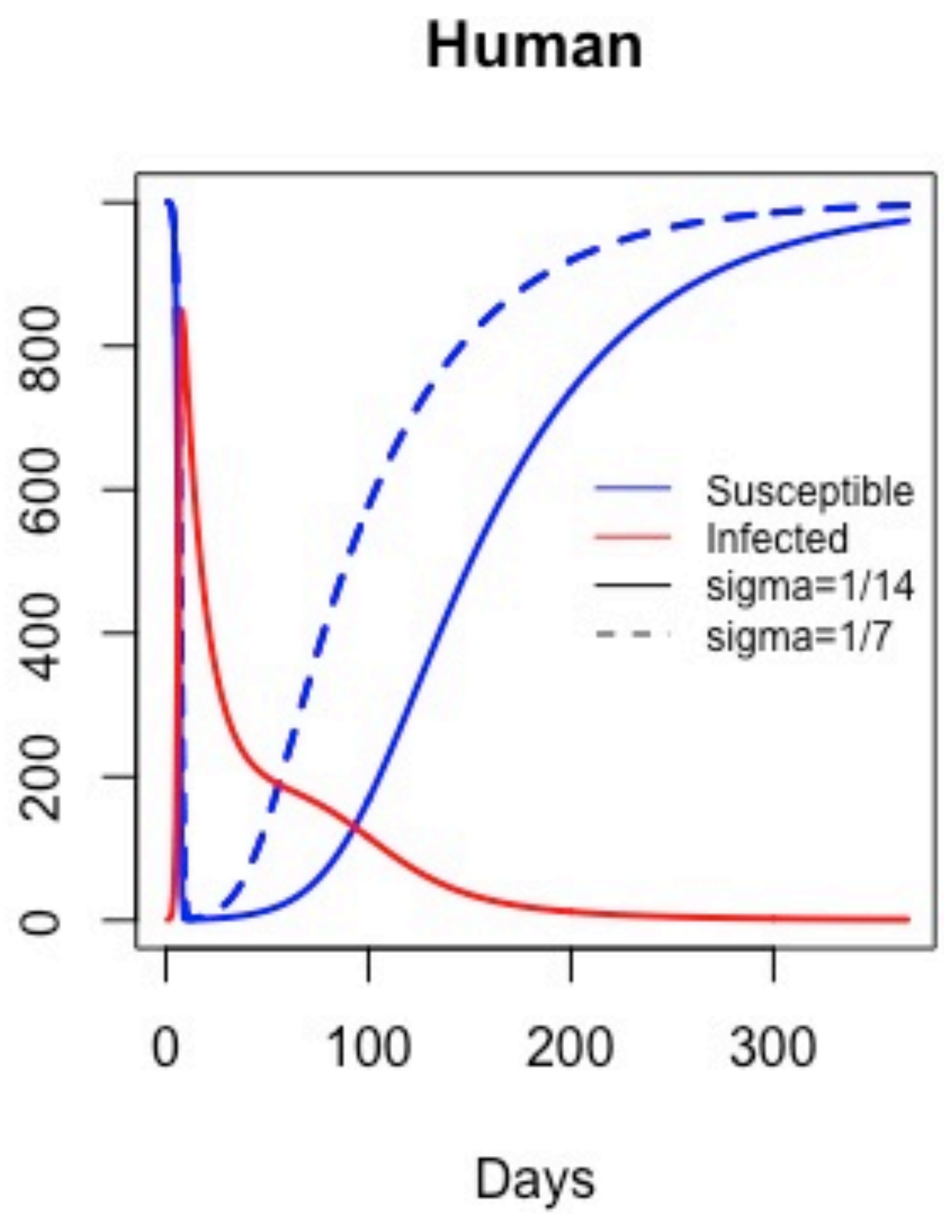

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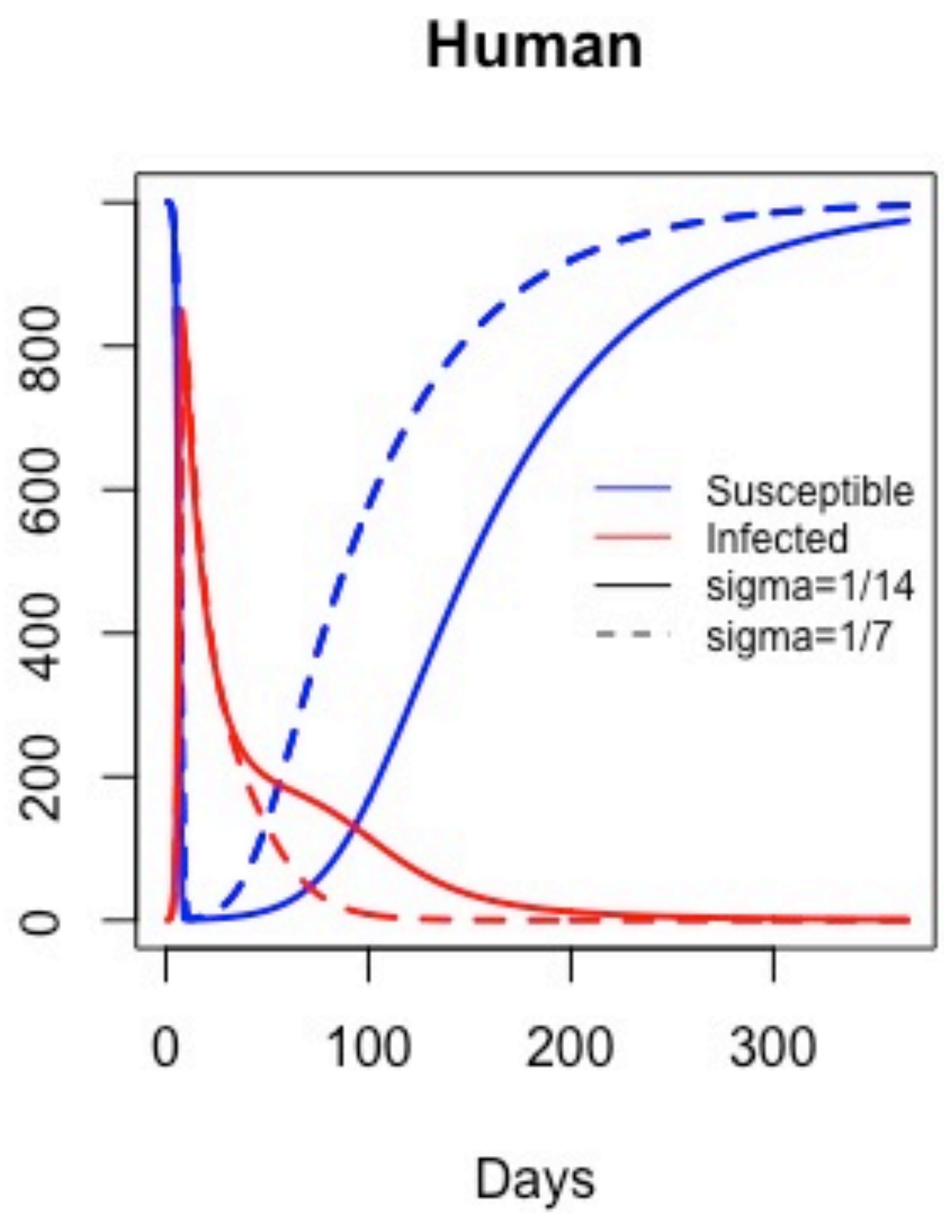

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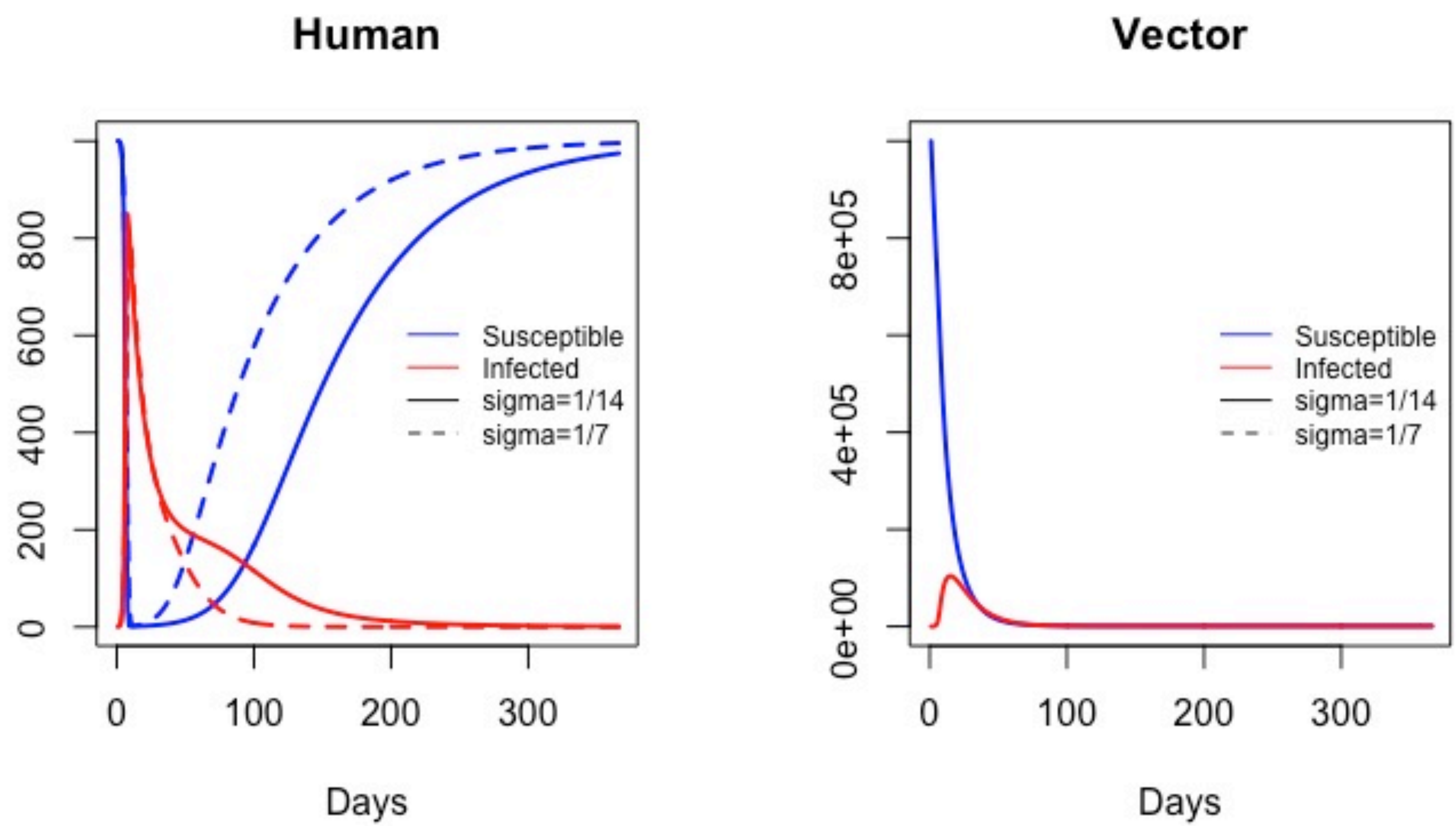

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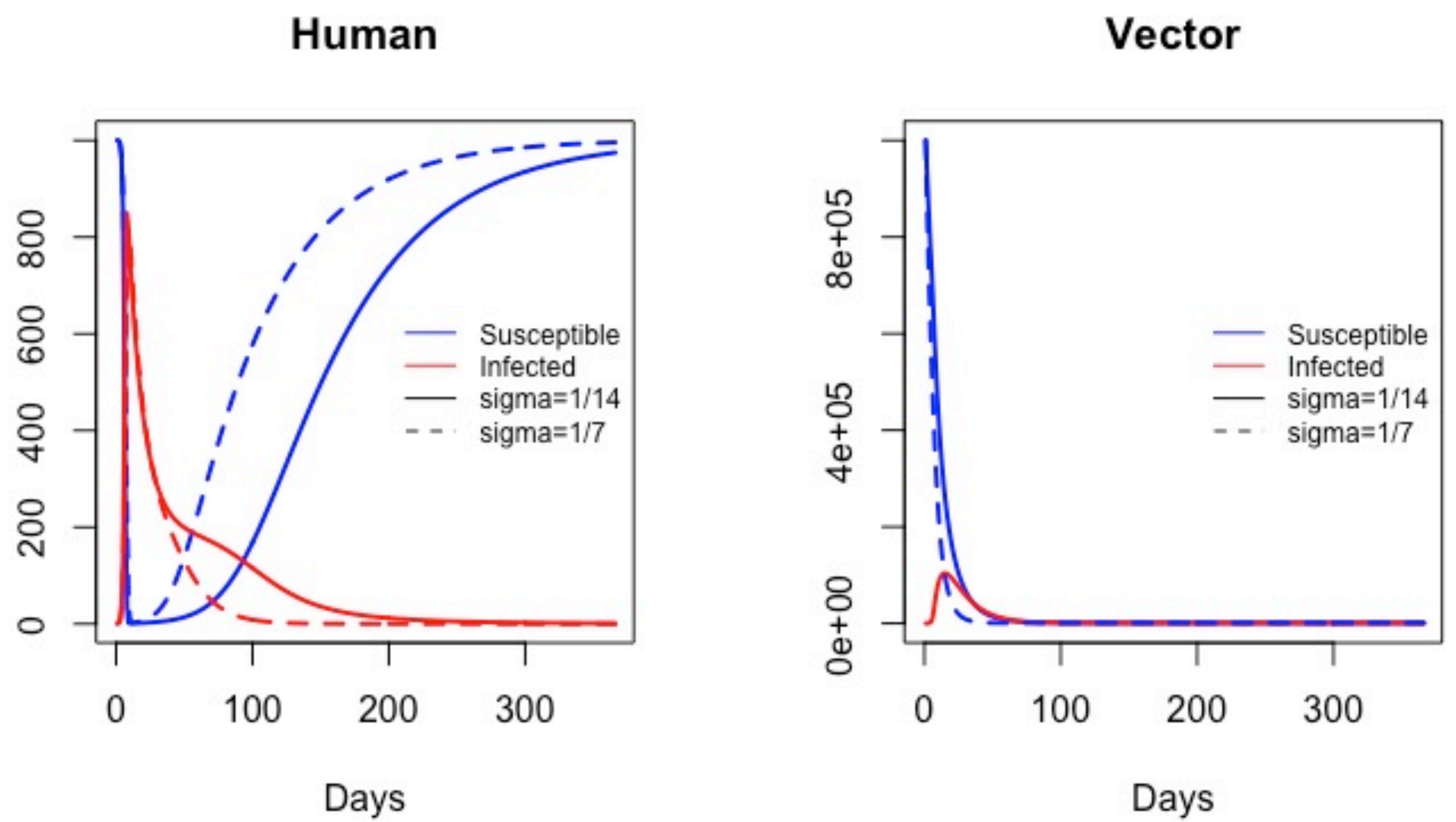
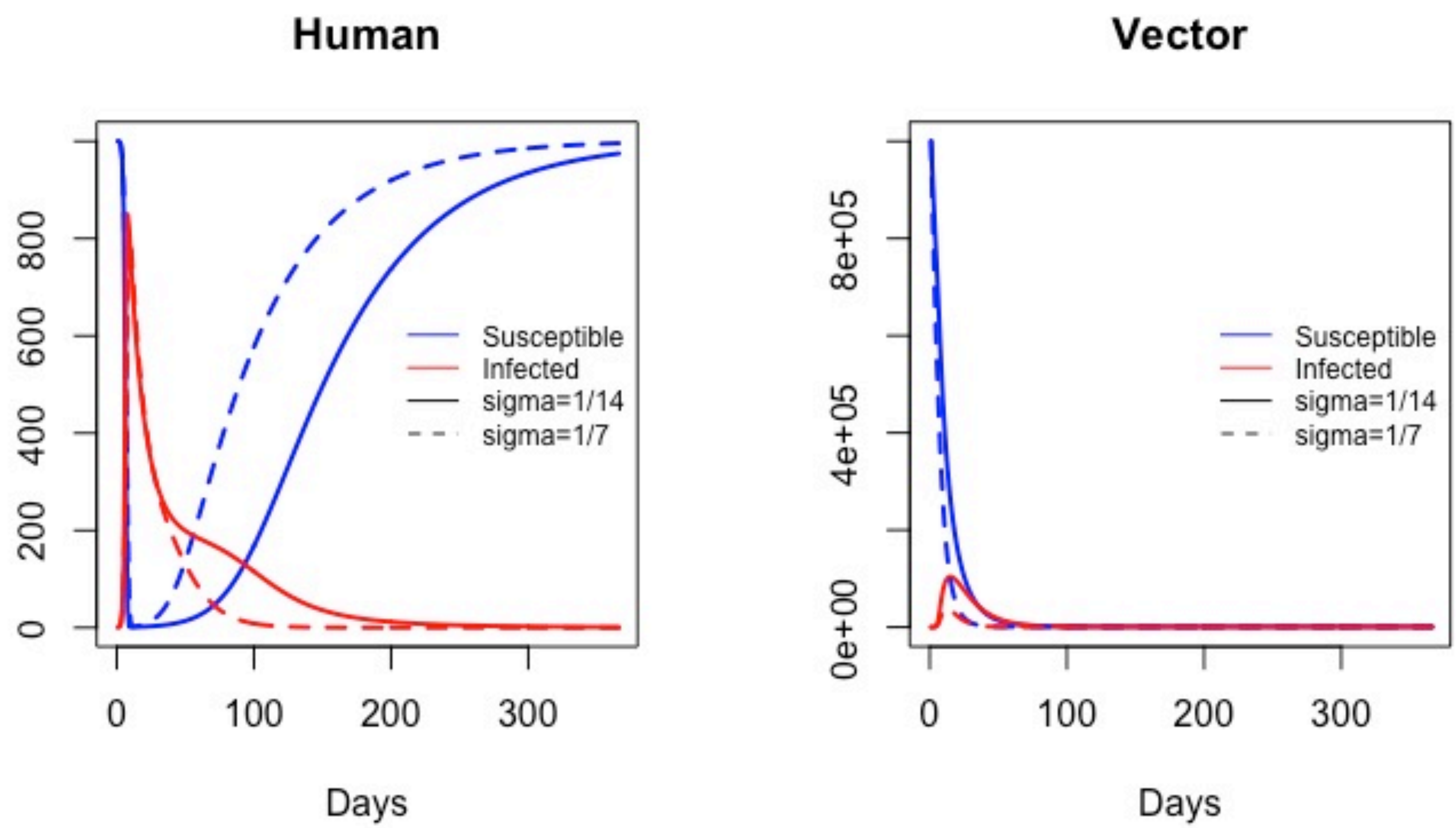
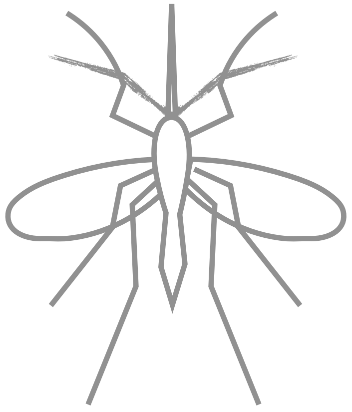


The basic vector model: dynamics





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http://www.parasitesandvectors.com/content/4/1/153

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We can really go down the rabbit hole on each parameter

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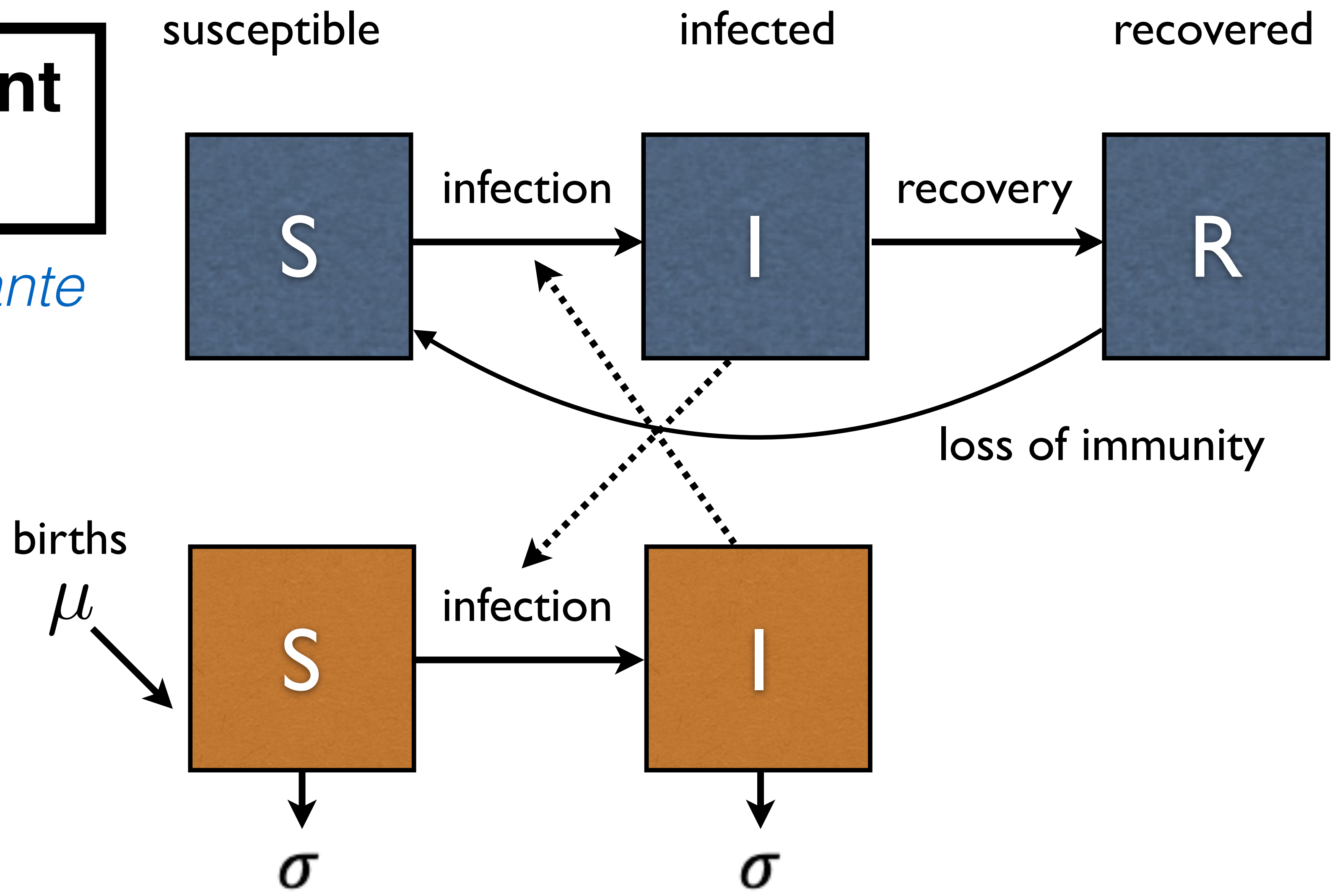
Ino dikany "down the rabbit hole" @ tony gasy?

We can really go down the rabbit hole on each parameter

Temperature dependent vector mortality

Mortalité vectorielle dépendante de la température



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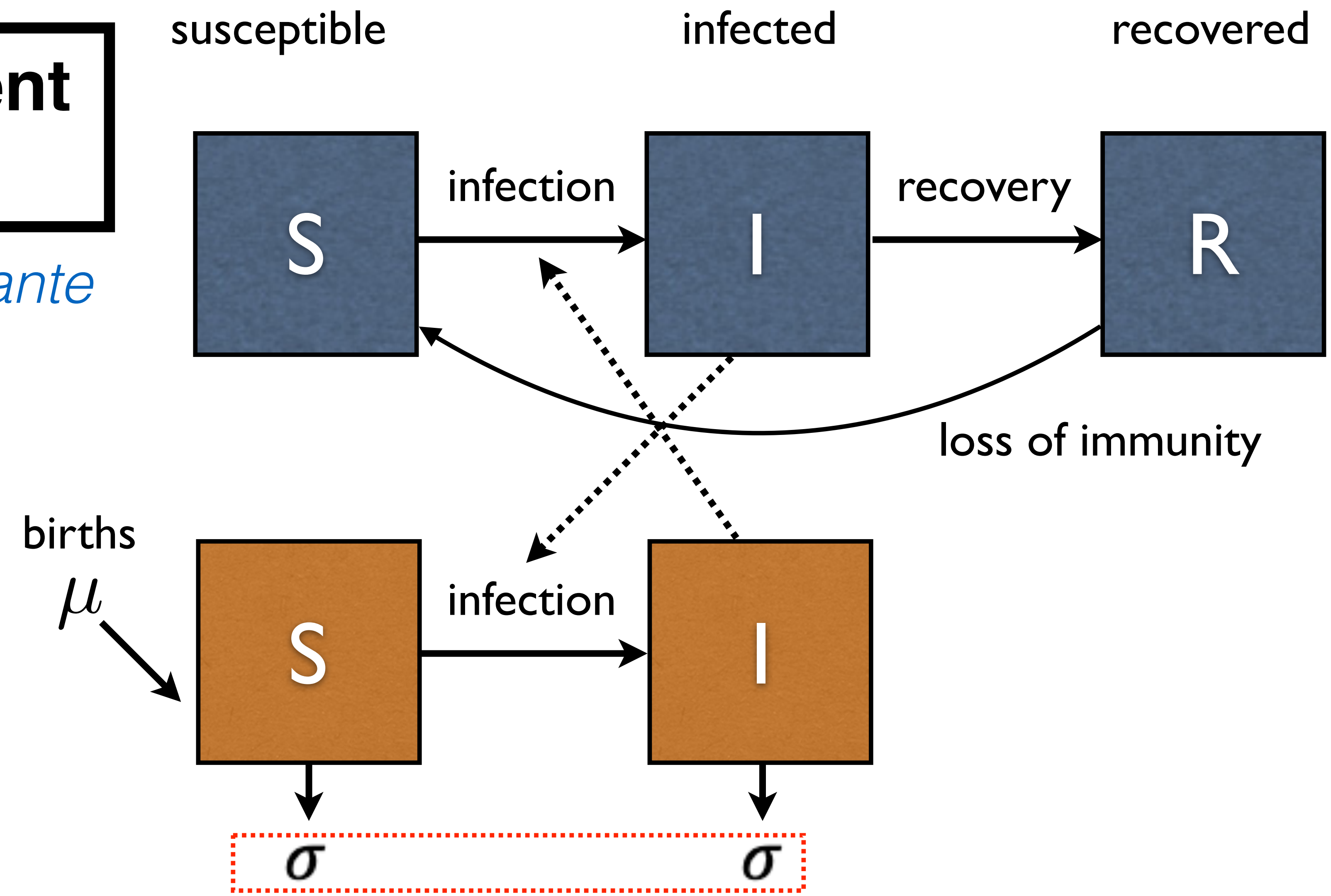

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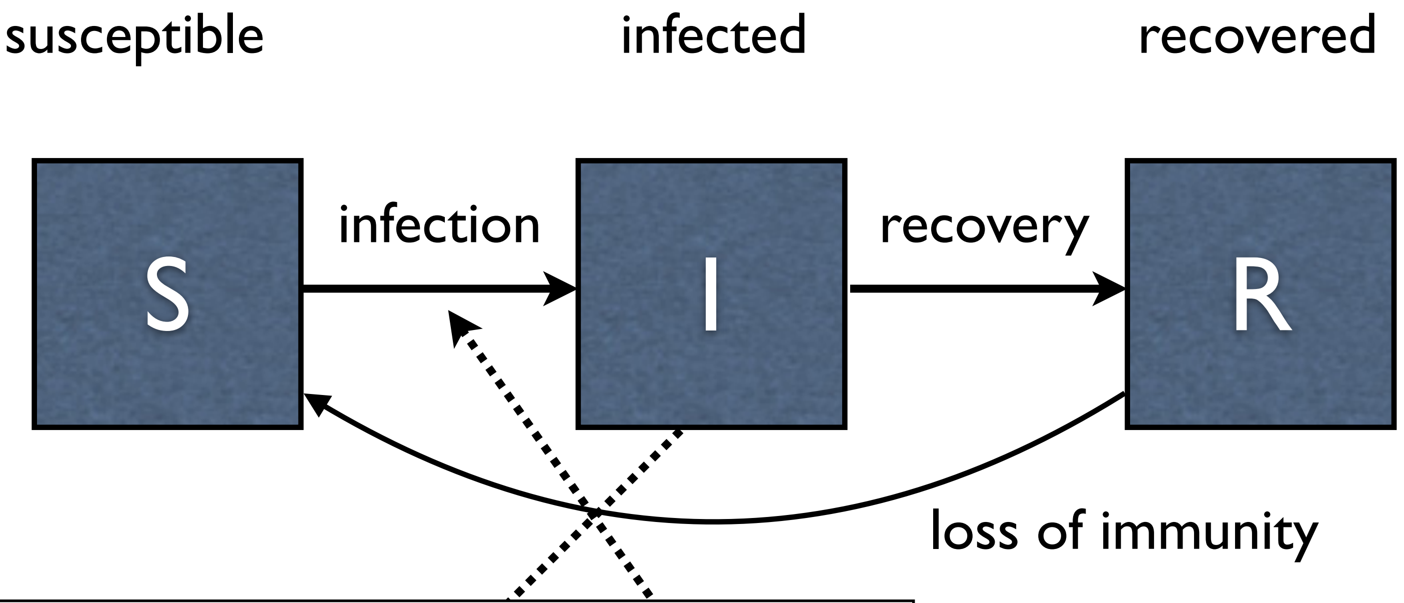

Shaprio LLM. *et al.* (2... Quantifying the eff... temperature on mo... parasite traits that ... the transmission po... human malaria. *PL... Bio*, **15**(10): e2003...

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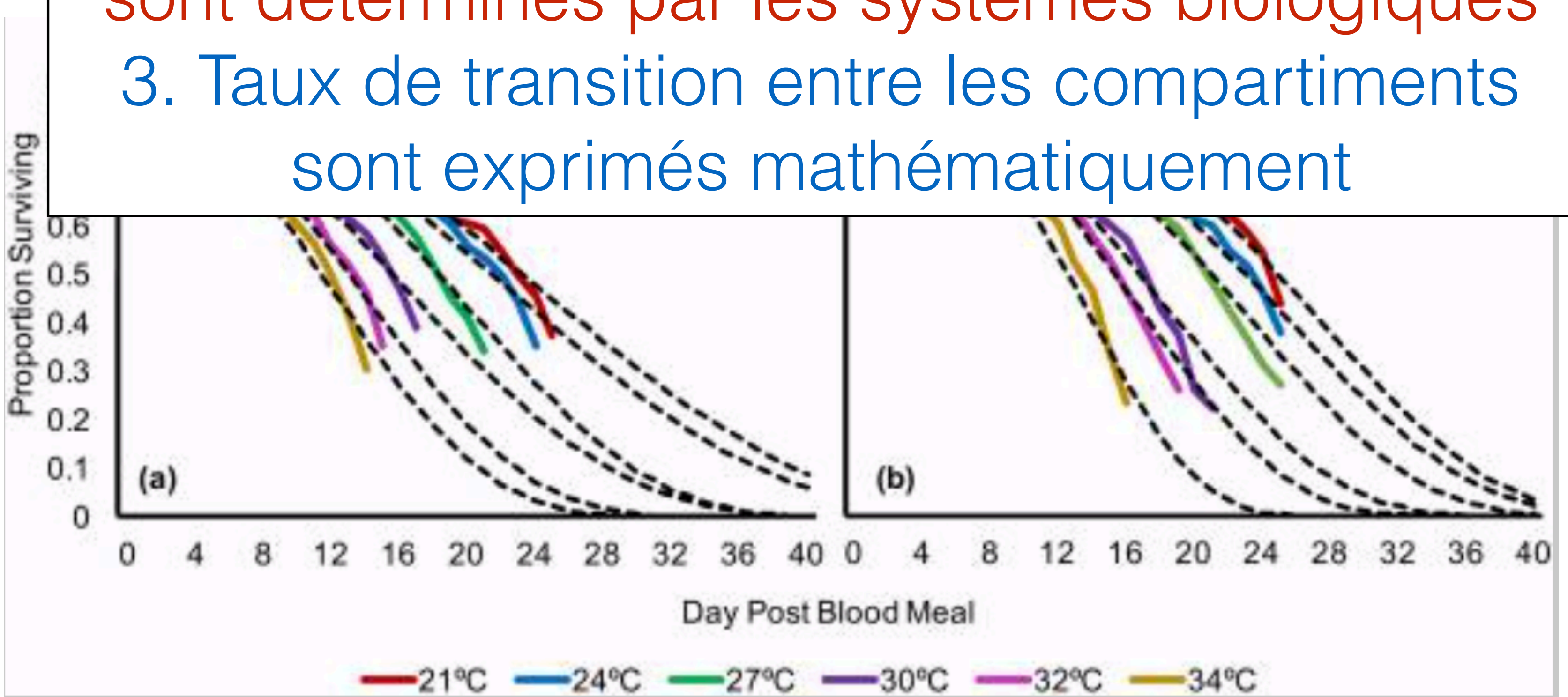

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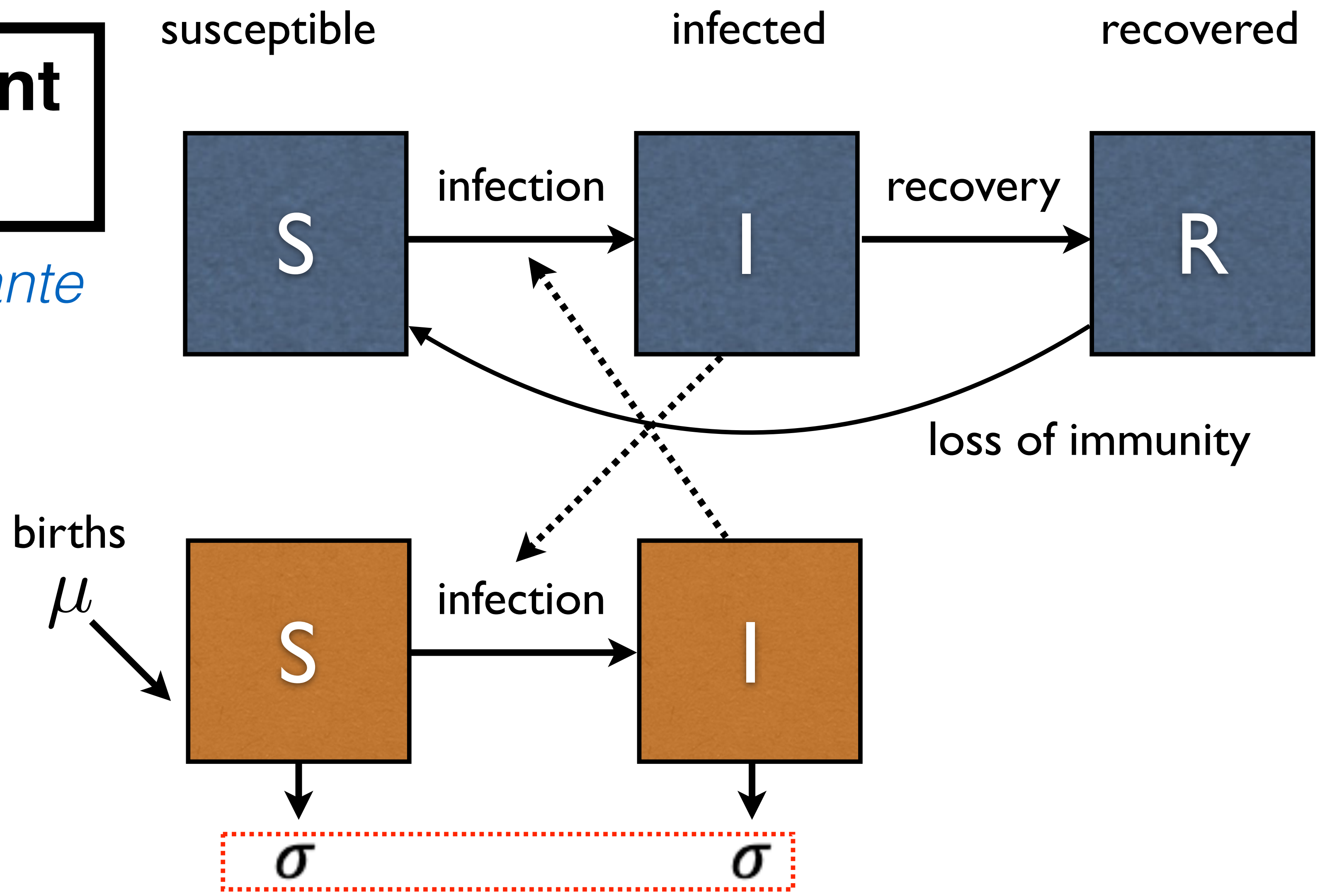

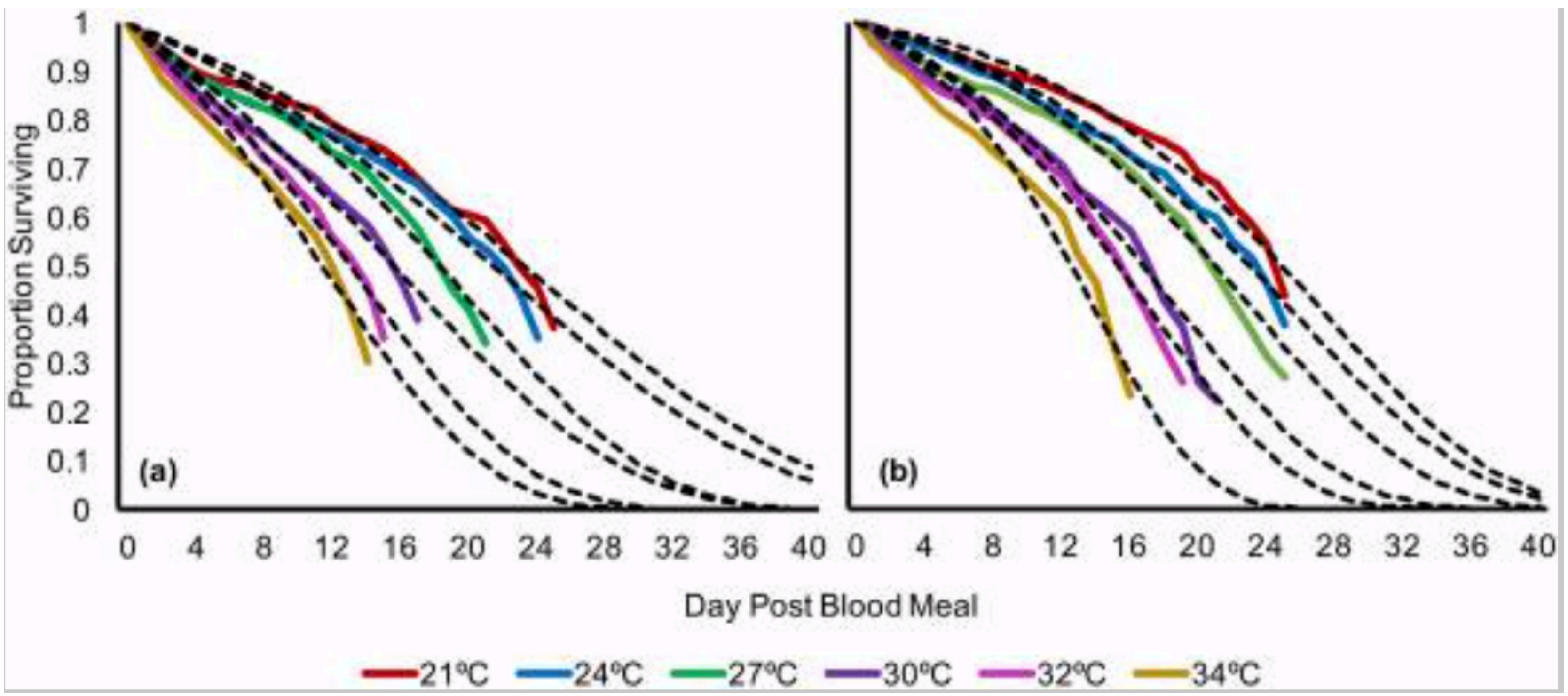

Modèle de base → *Modèle avec incorporation de température*

Sigma (σ): *valeur fixe, constant, statique* → Sigma (σ): *la valeur change avec le temps, dynamique*

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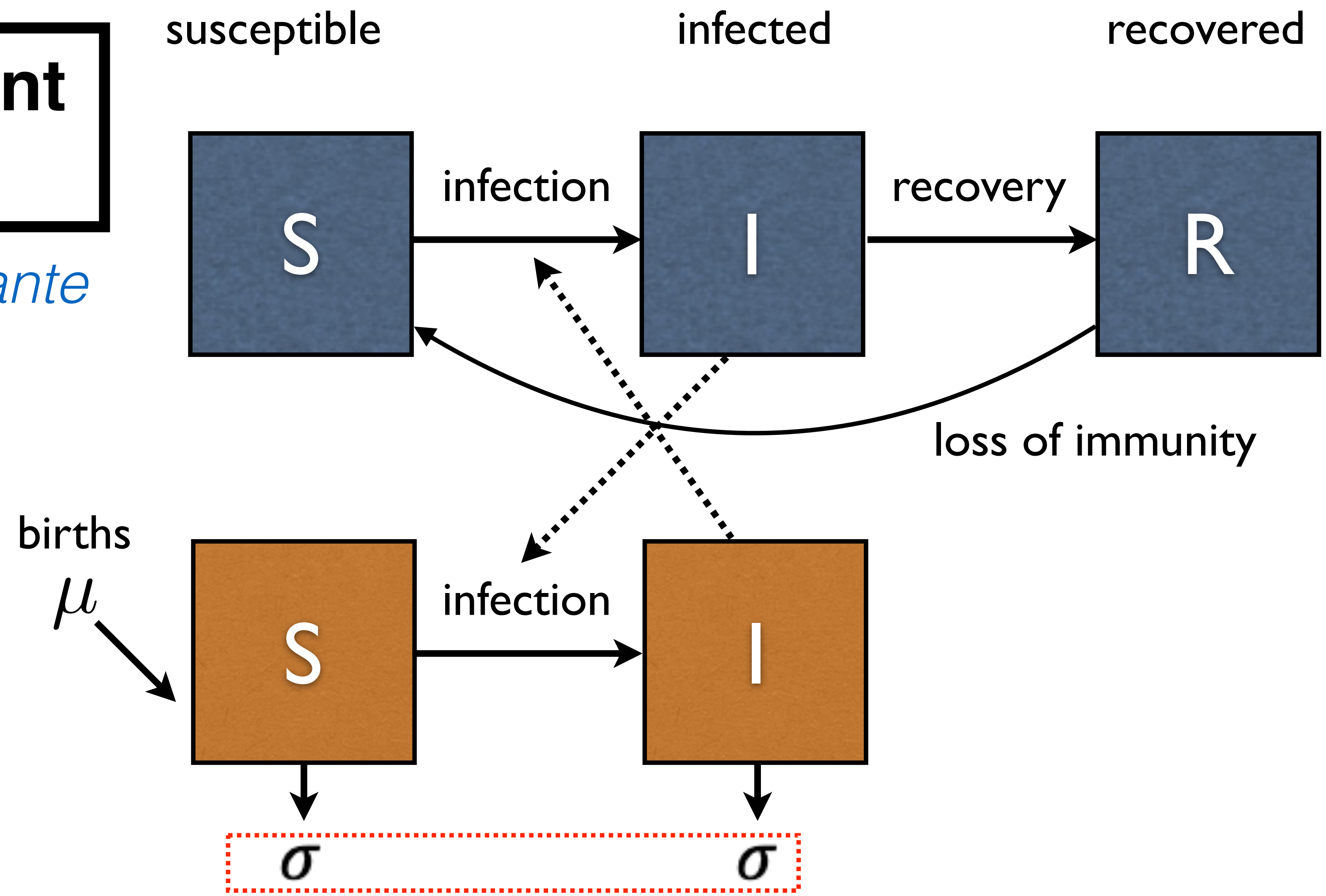
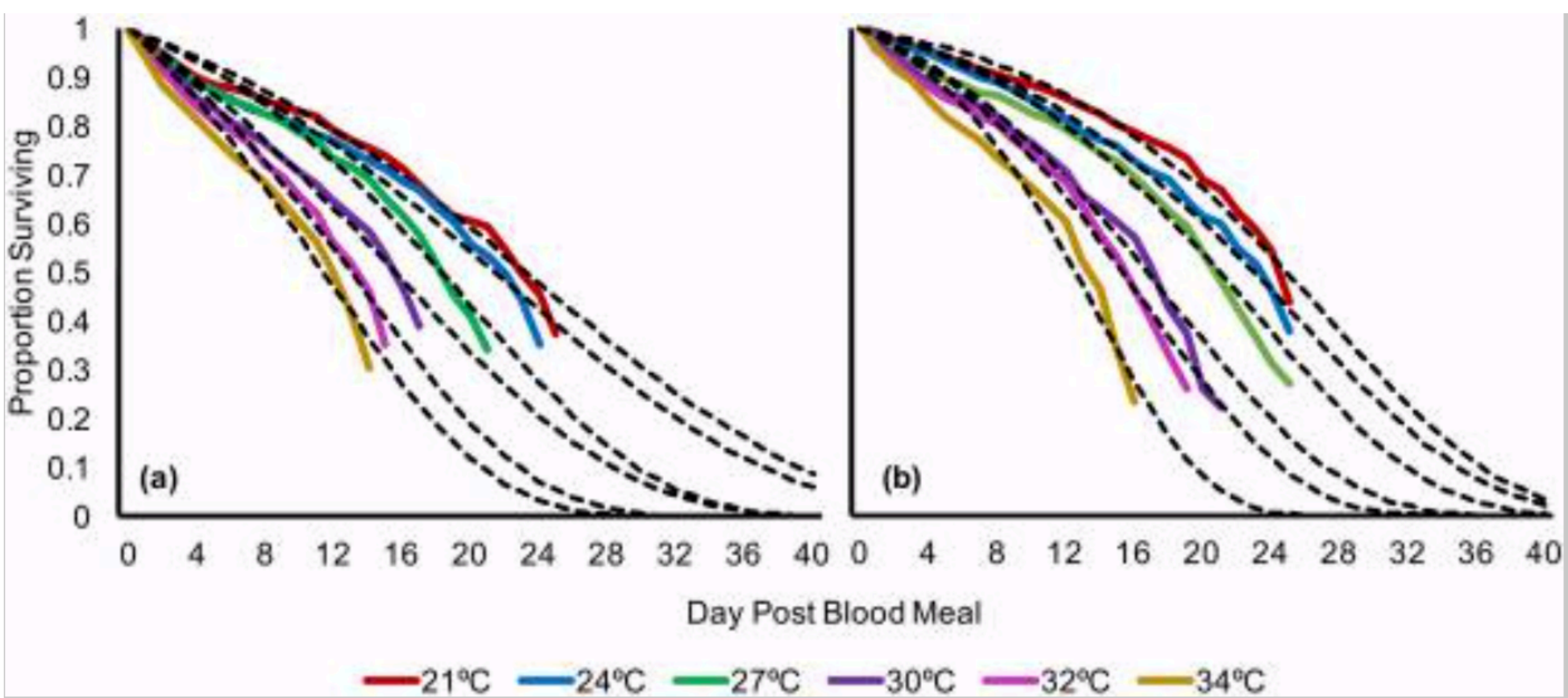
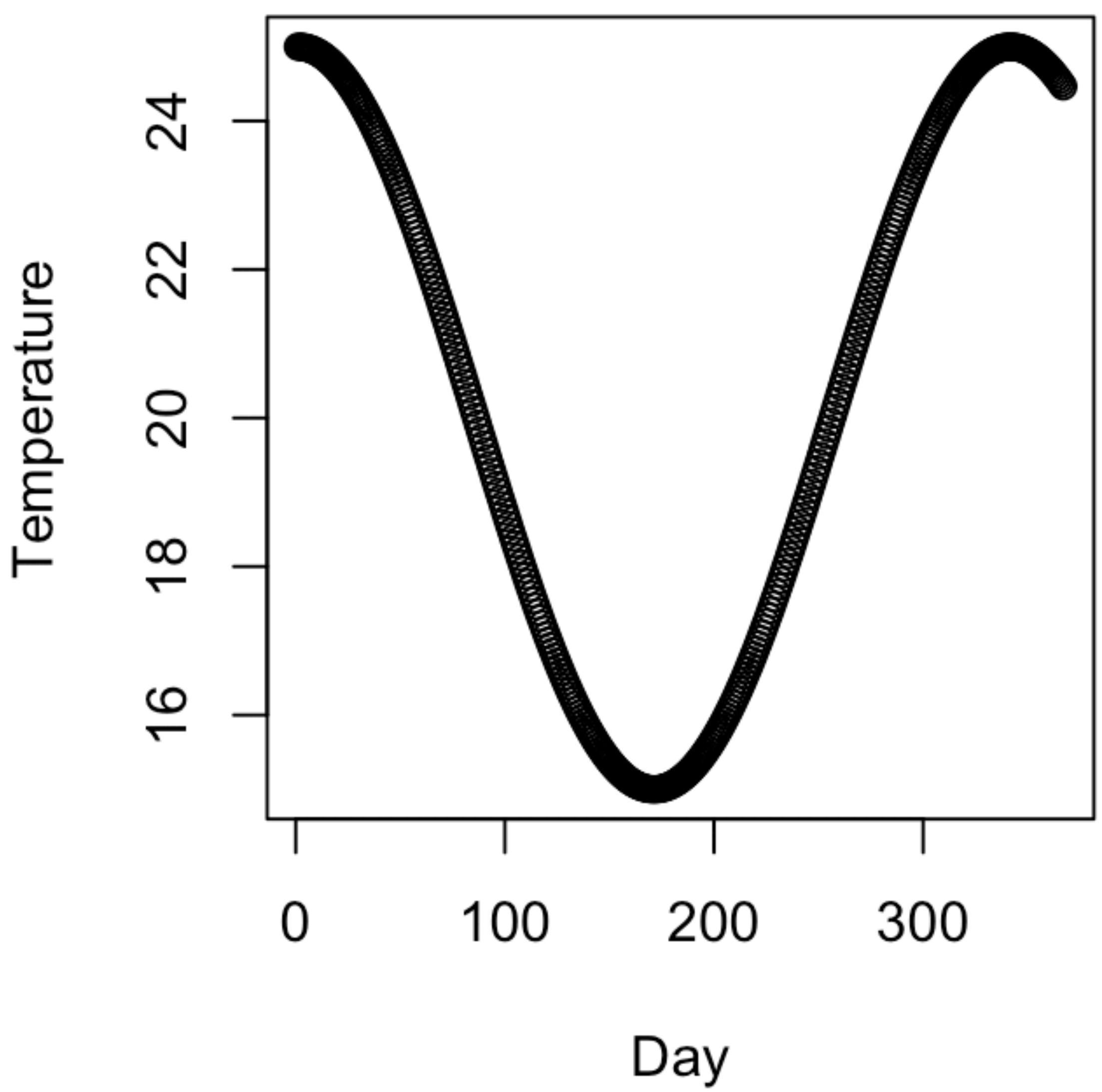


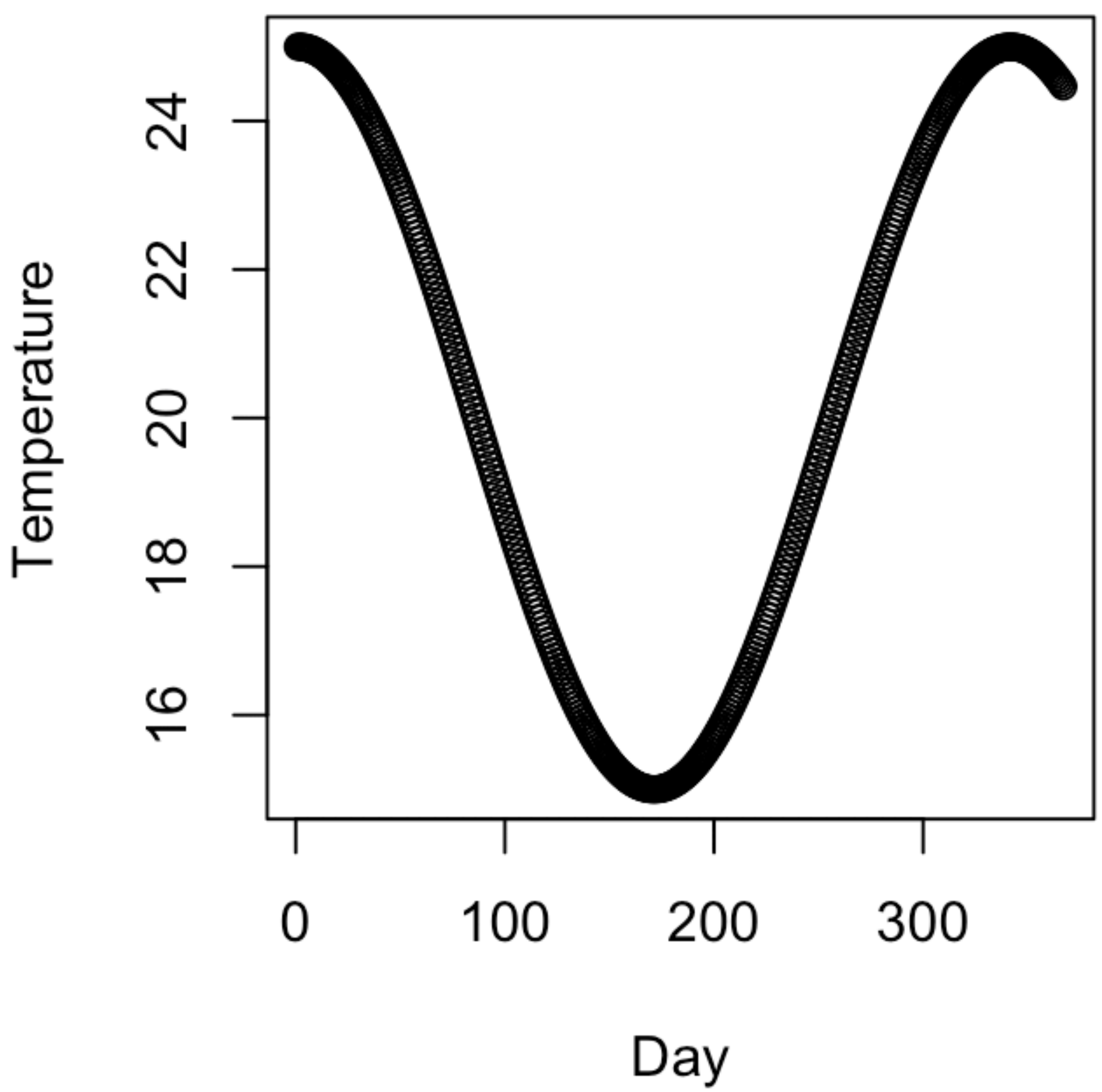


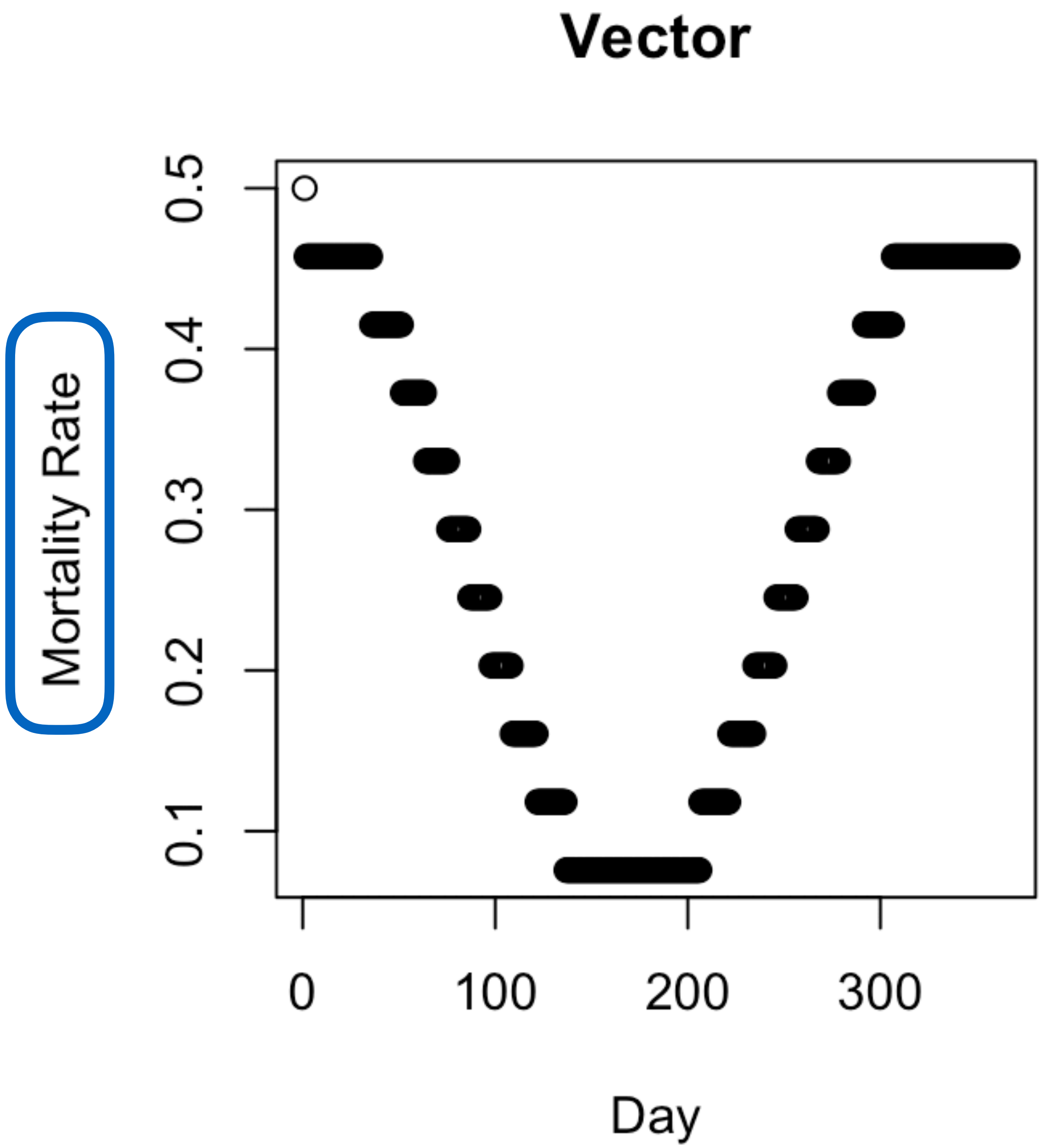
Temperature dependent vector mortality: dynamics



Temperature dependent vector mortality: dynamics

Le taux de mortalité du vecteur dépend de la température





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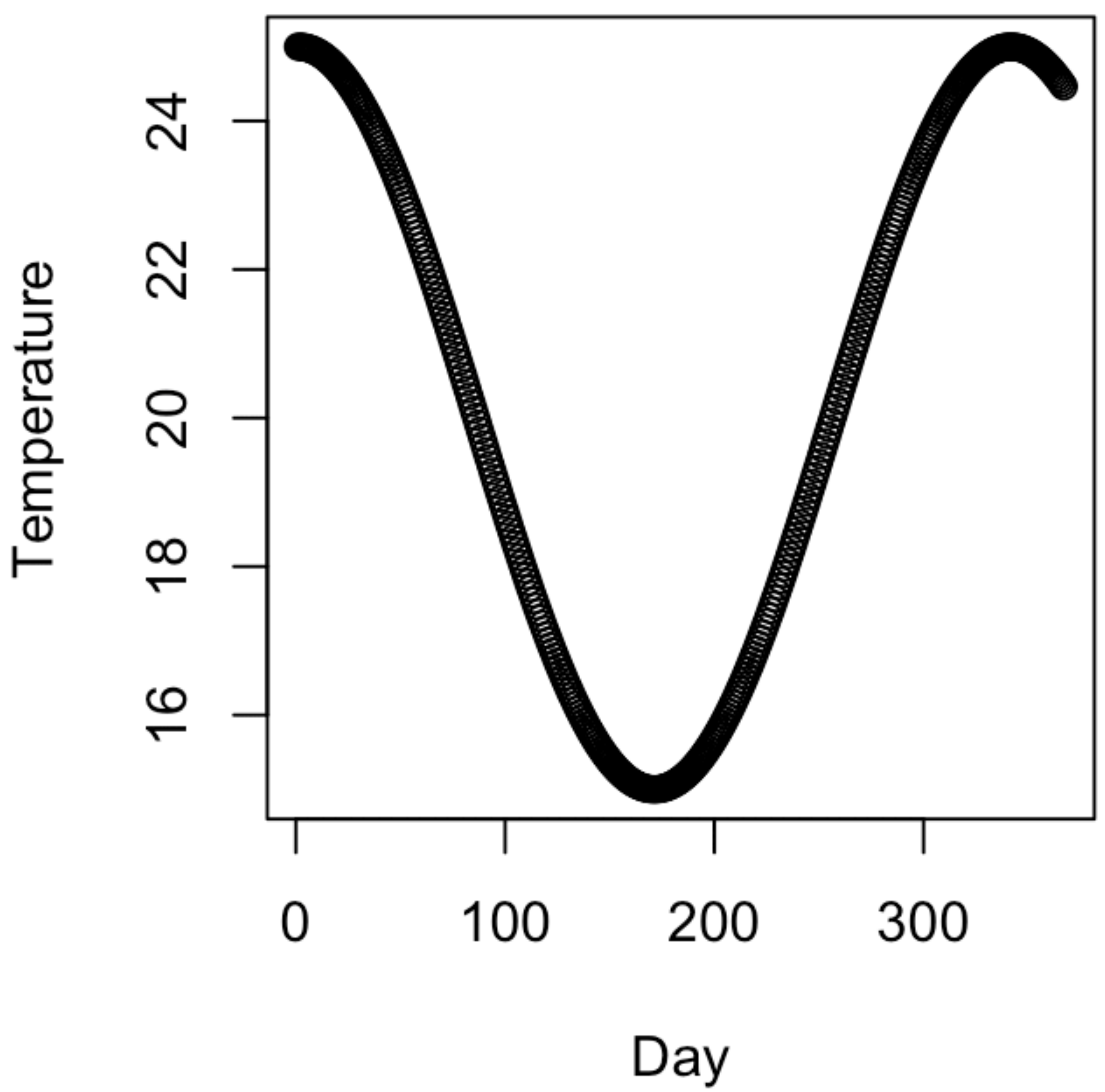

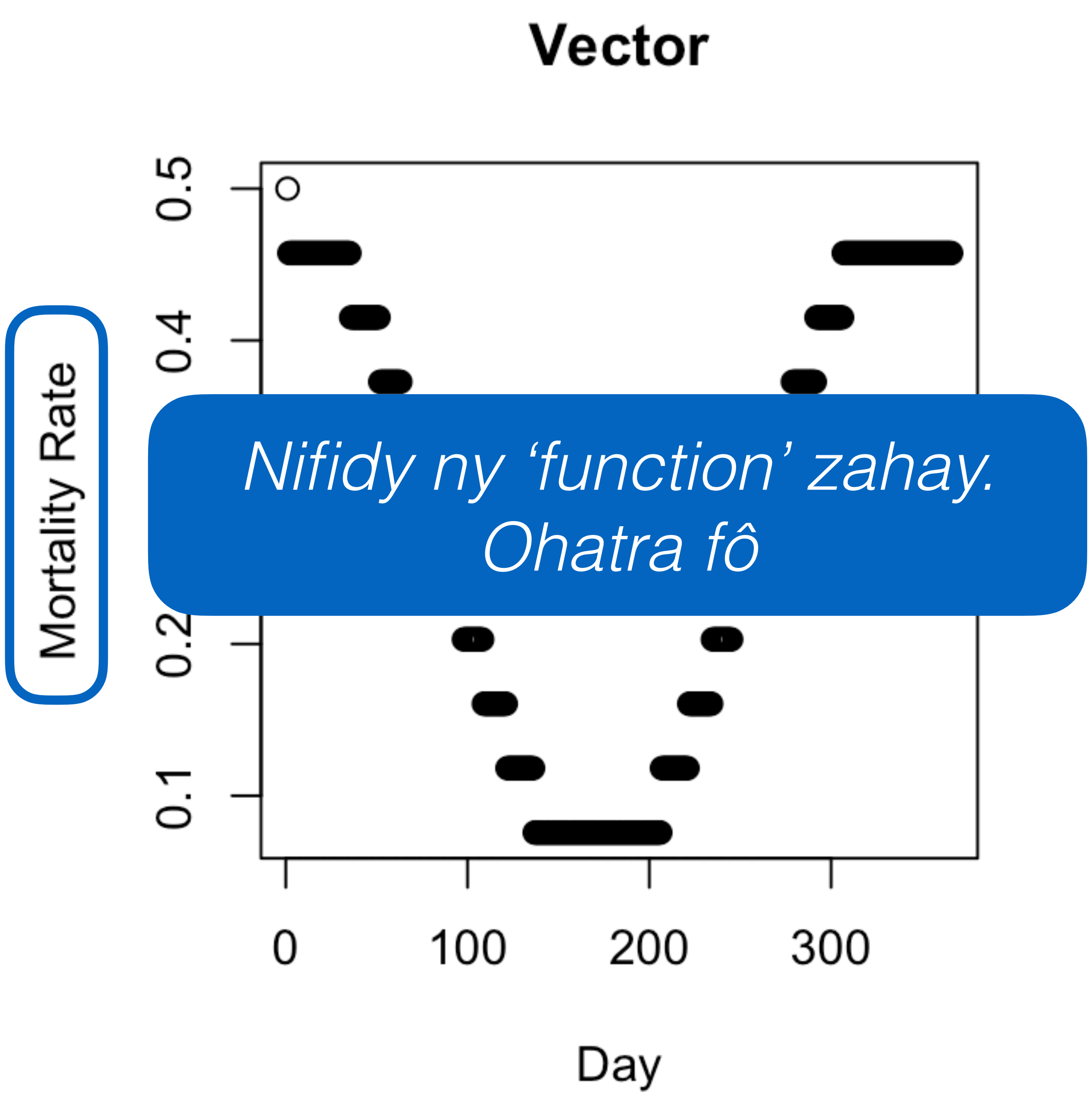

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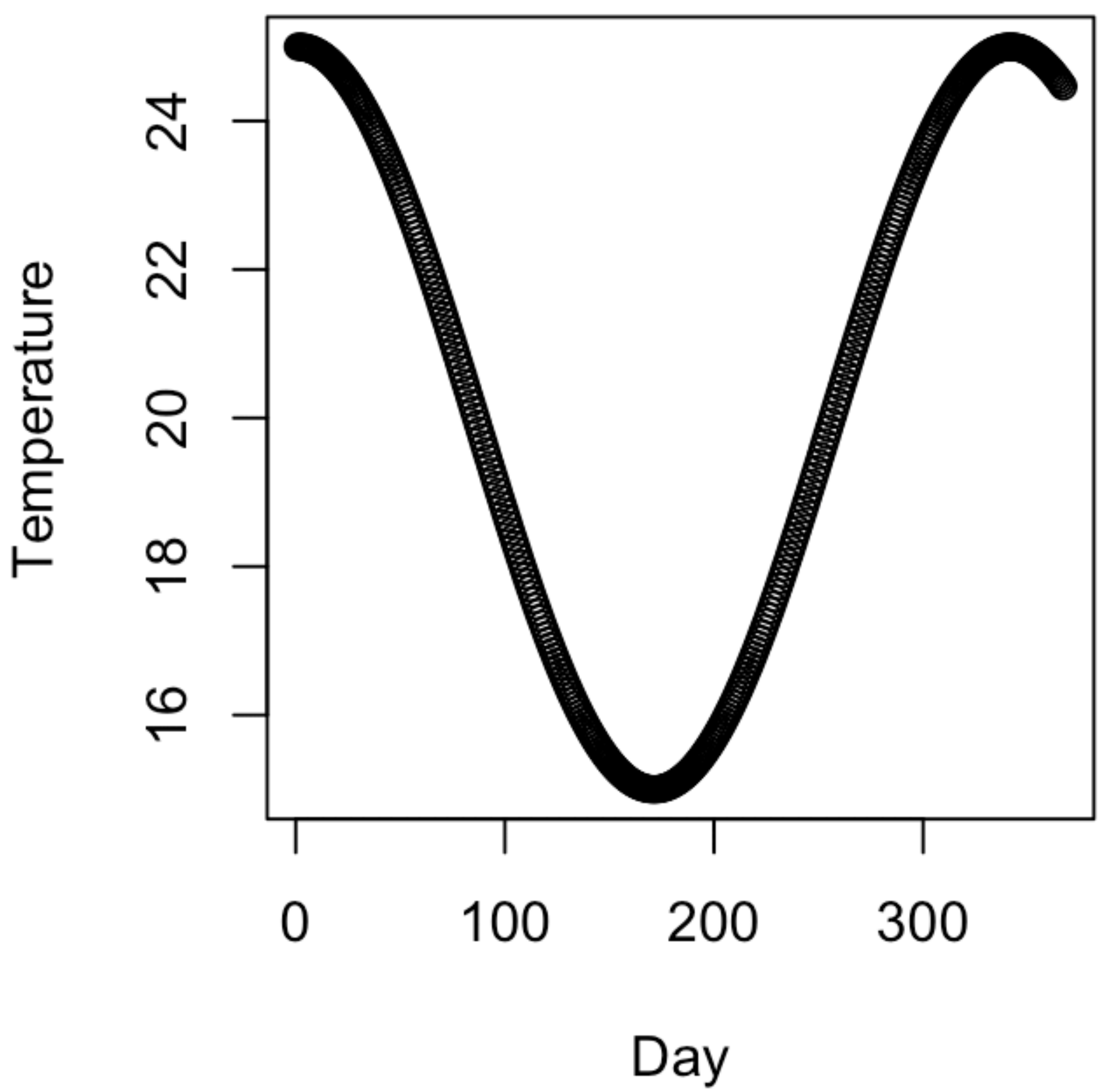

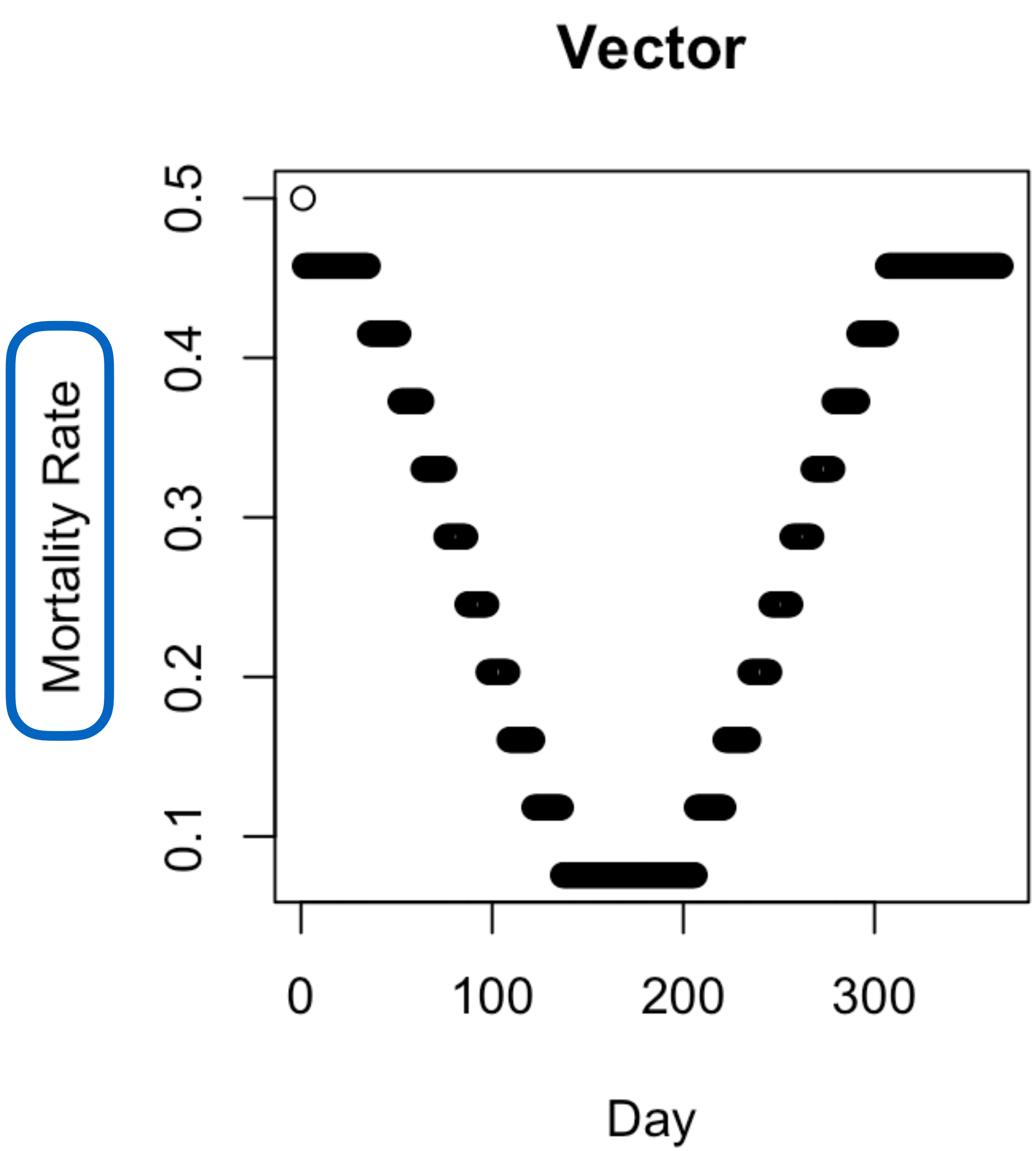

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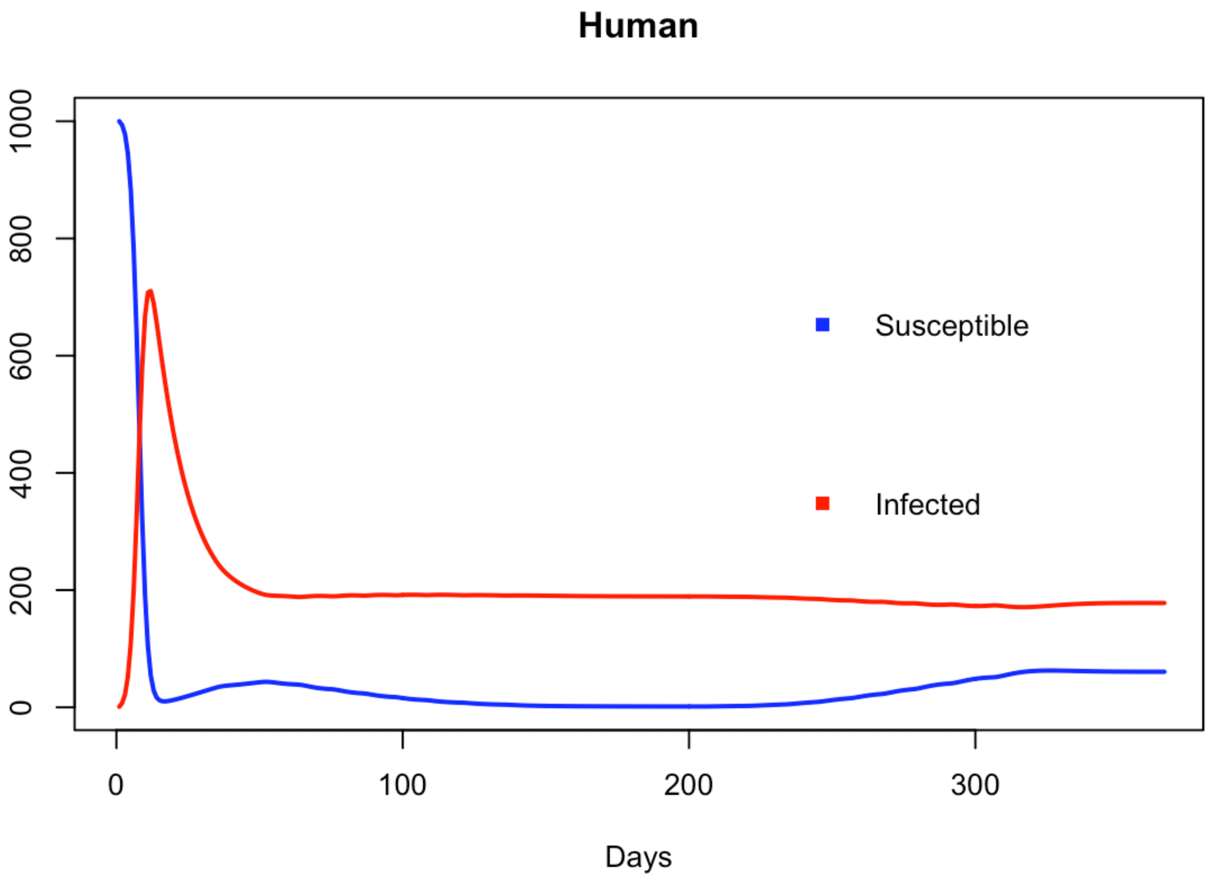
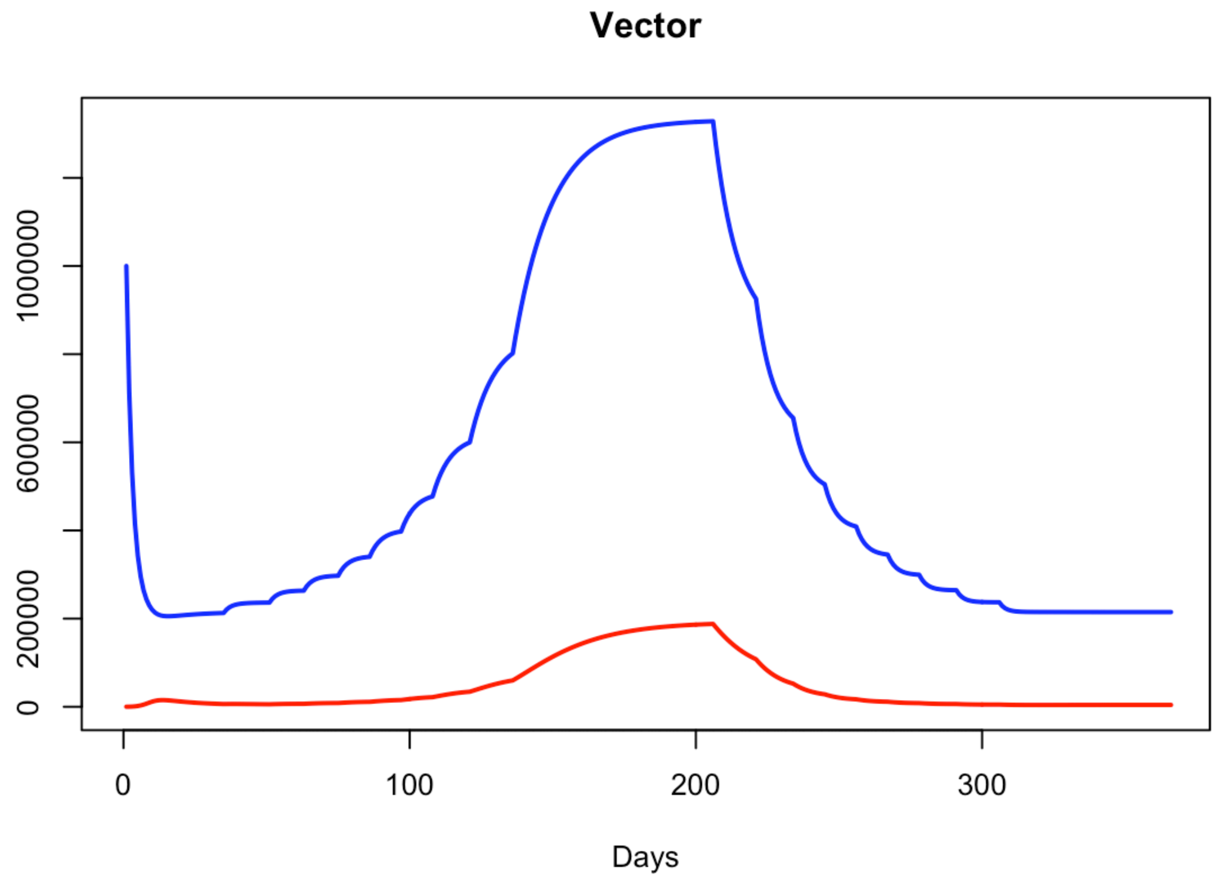




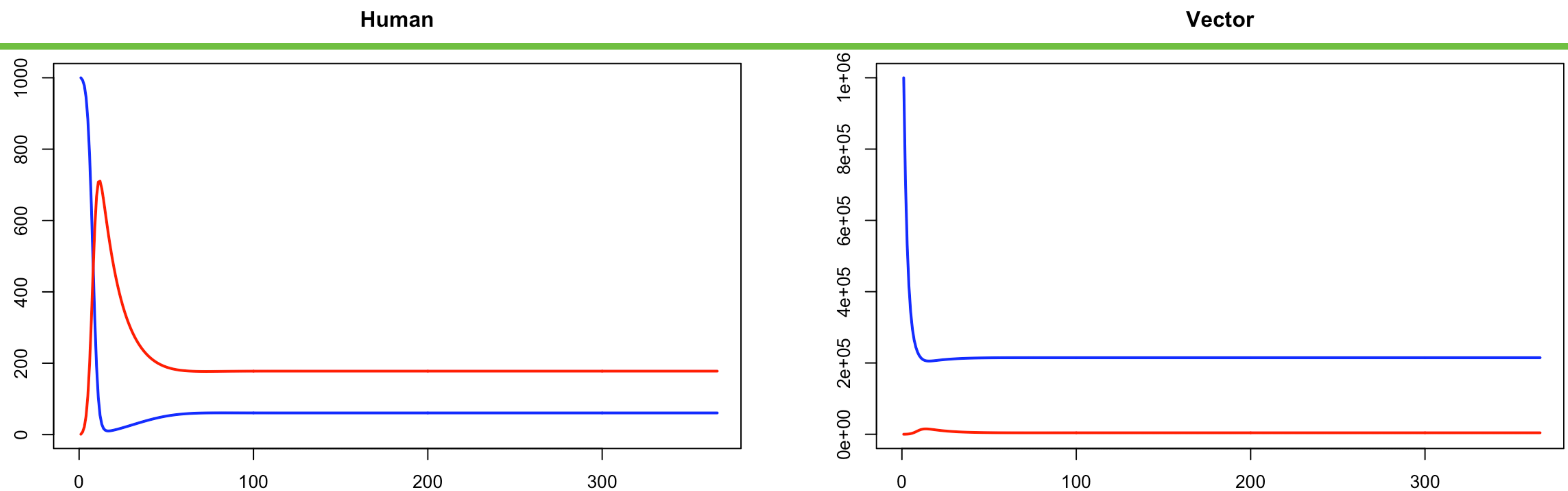
Le taux de mortalité du vecteur dépend de la température

Human

Vector

Résultat d'avant. La mortalité du taux ne dépend pas de la température

Le taux de mortalité du vecteur dépend de la température



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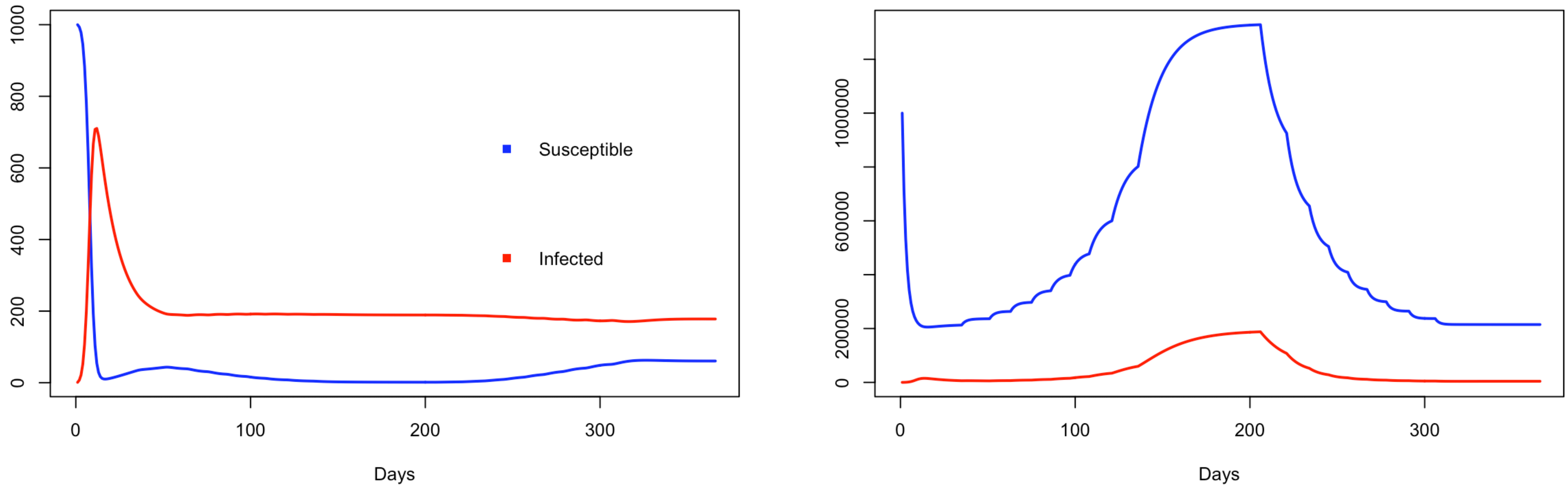

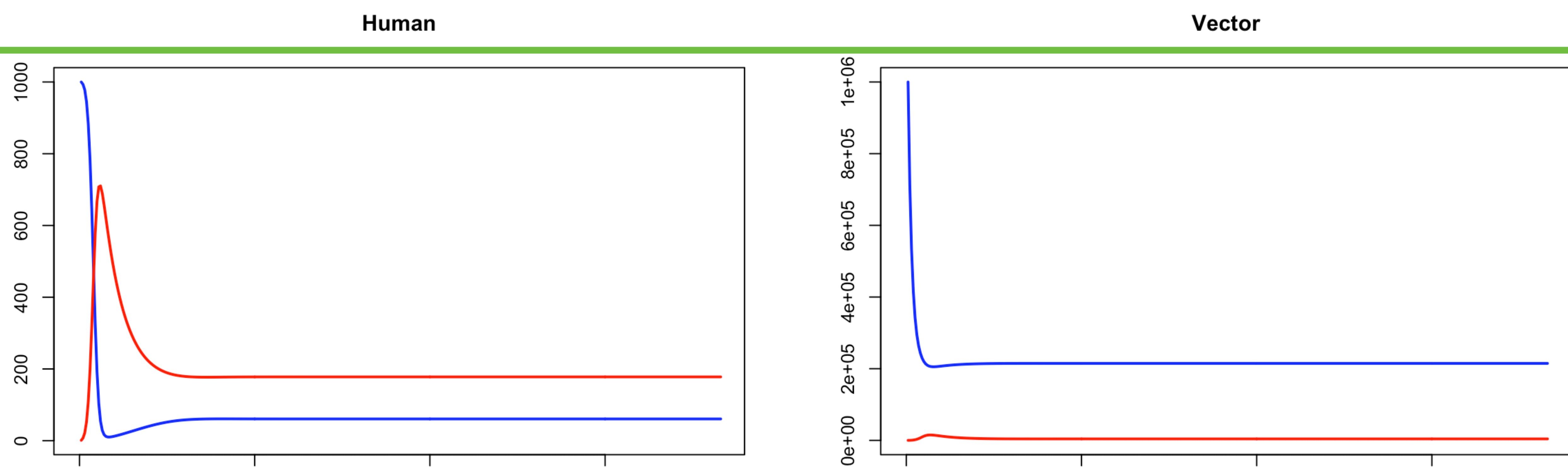

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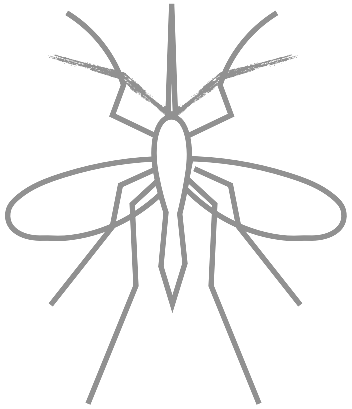

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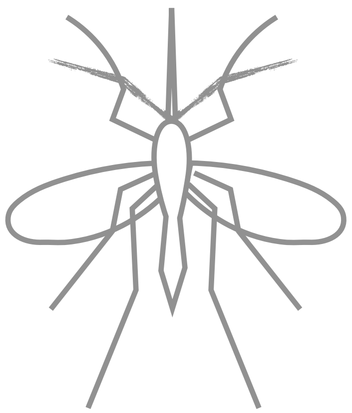
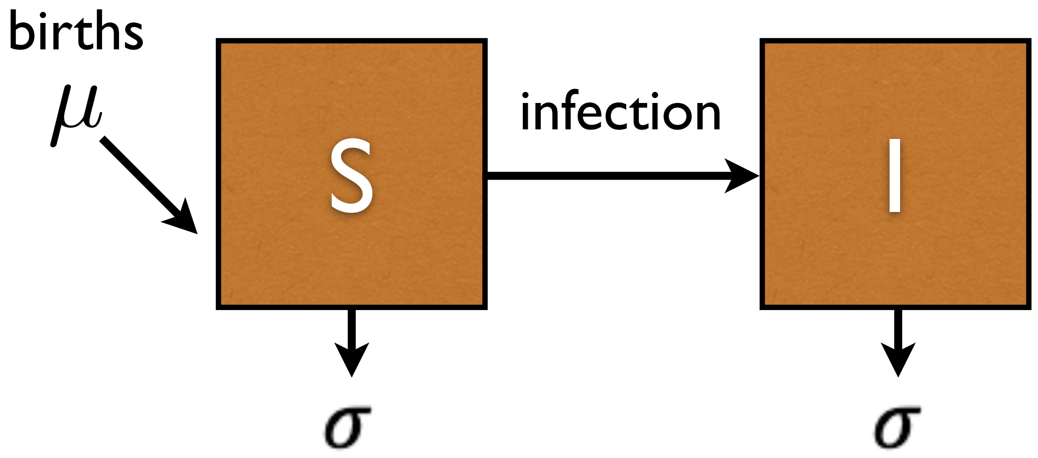


3. Increasing complexity about the vector lifecycle / Complexité croissante du cycle de vie des vecteurs

Multiple vector lifestages

Plusieurs étapes de la vie des vecteurs



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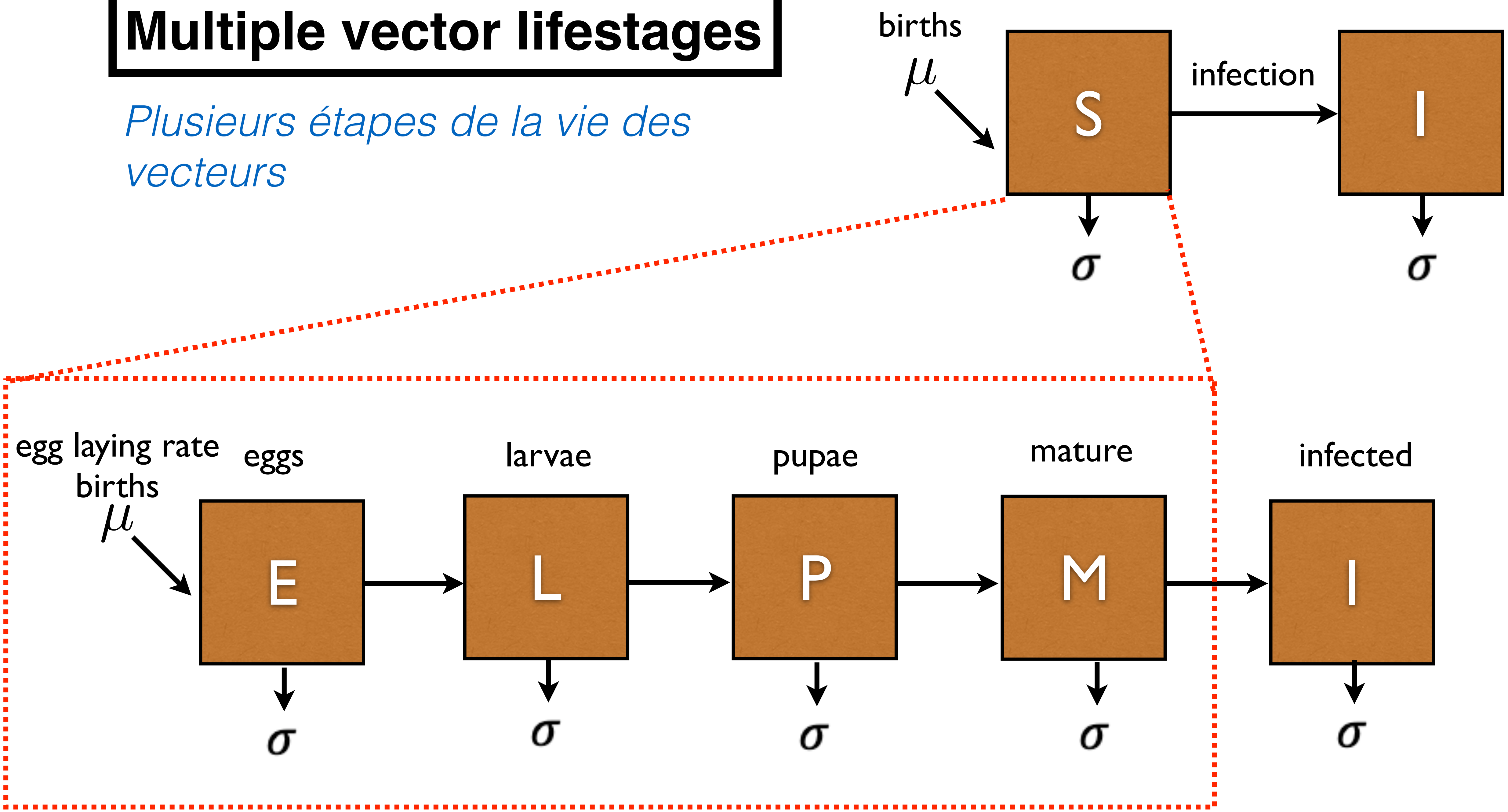

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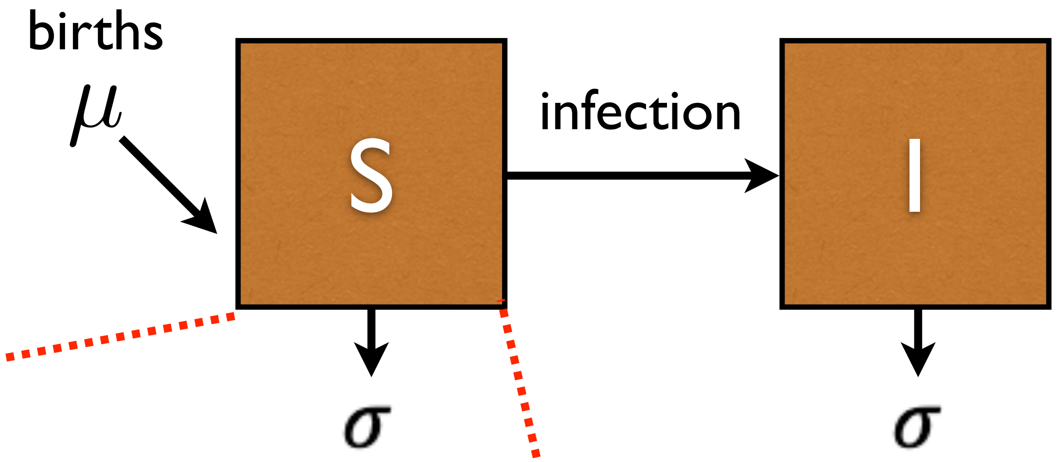

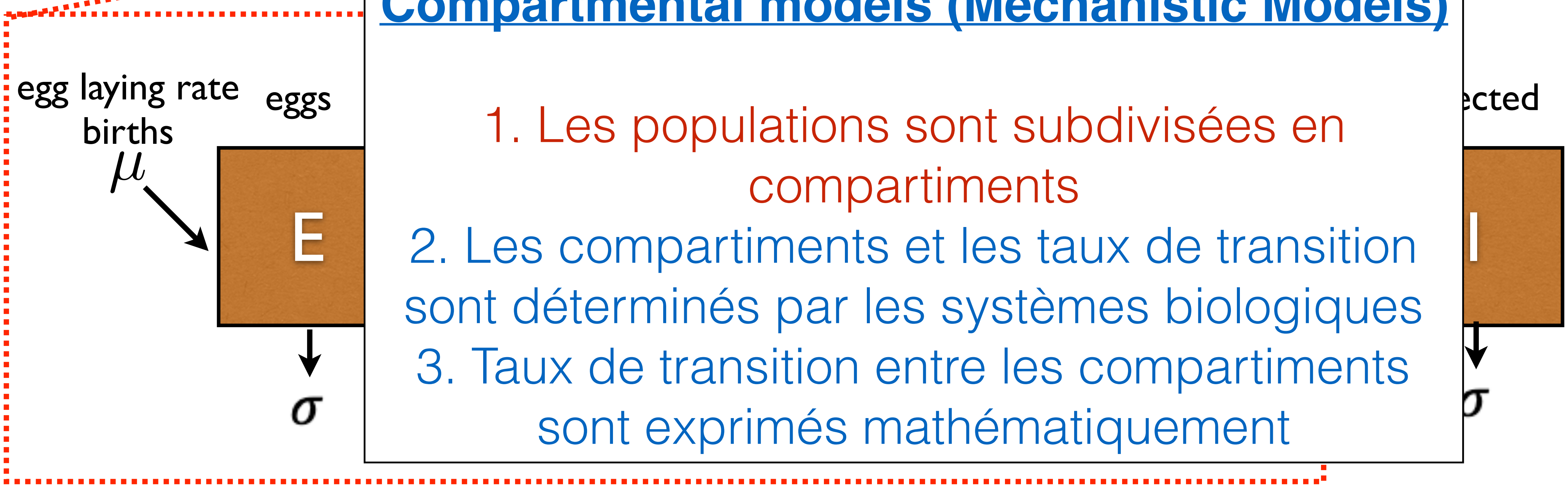

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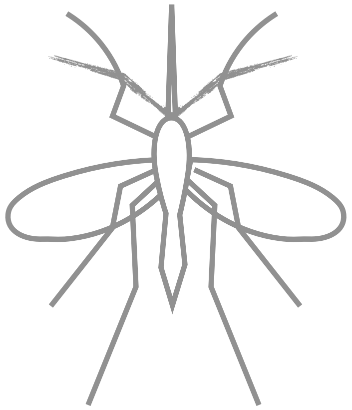
Modeling vector-borne diseases

'Modeling' aretina avy amin'ny moka

Modélisation des maladies transmise par des vecteurs

Amy Wesolowski
Department of Epidemiology
Ben Rice
Harvard University

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH



4. How can the dynamics be used for disease control? / Comment la dynamique peut-elle être utilisée pour lutter contre la maladie?

Mosquitoes and malaria

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

Ronald Ross commentaires sur les cellules à l'extérieur de l'estomac du moustique Anopheles:

"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)."

“mais ce qui a retenu l'attention maintenant, c'est que chacun de ces corps contenait quelques granules de pigment noir d'aspect absolument identique au pigment bien connu et caractéristique du parasite du paludisme (grands quartans et sphères dérivées du croissant).”

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

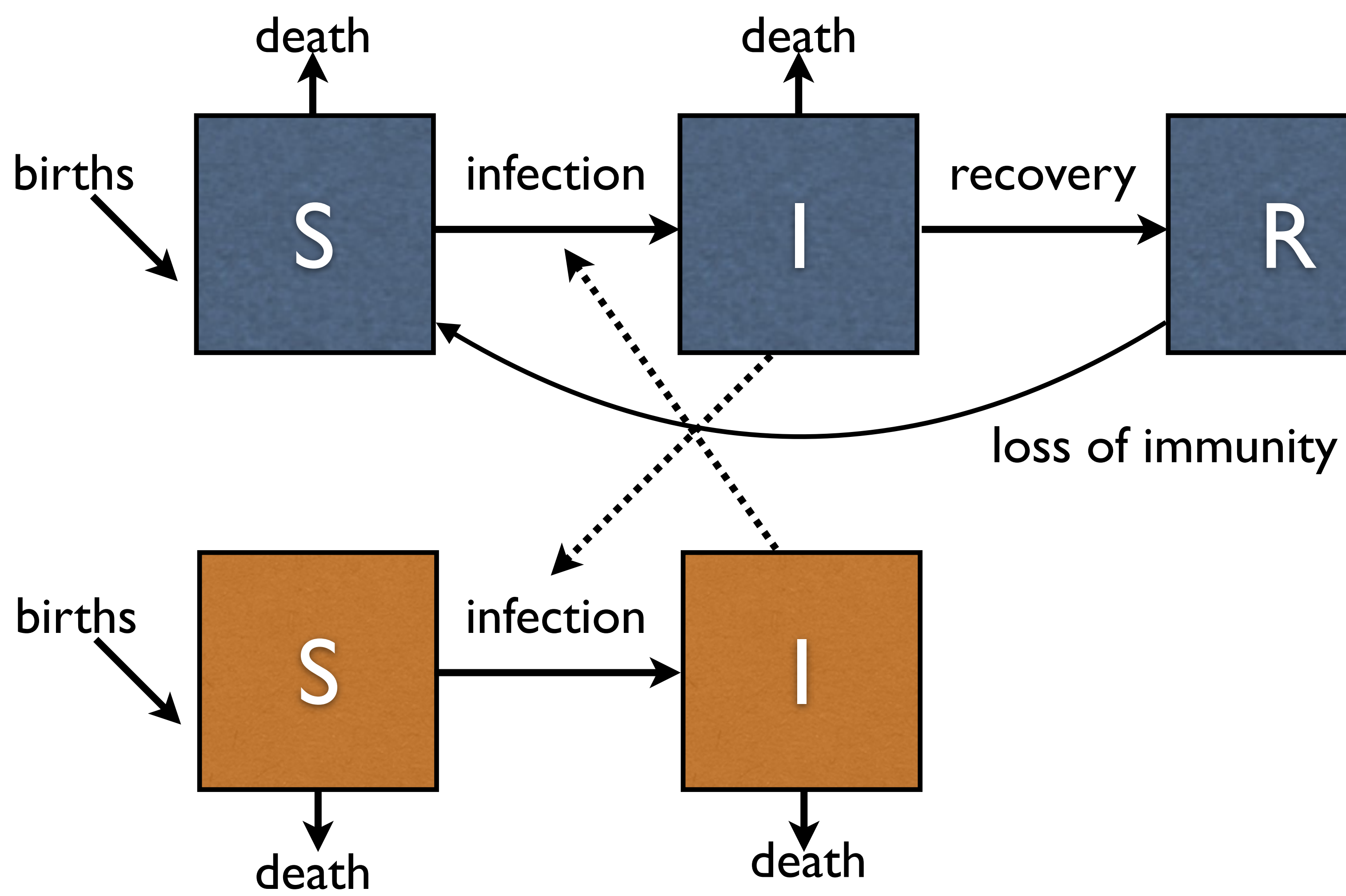
Environmental modification and species sanitation - reasonable history of success in temperate regions.
Modification de l'environnement et assainissement des espèces - historique raisonnable de succès dans les régions tempérées.

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
Médicaments et traitement - accroître l'accès au traitement et à la disponibilité des médicaments

Implications for control

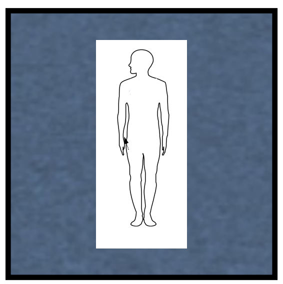
Implications pour le contrôle



Implications for control

Version of the Ross-MacDonald model

- Assumption: populations broadly at equilibrium
  - Aza miasa loha momba fiterahana sy fahafatesana
- Focus on proportions:



x = proportion of infectious humans

no. female mosquitoes per human host

prob. human infection per bite

human recovery rate

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

number of 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?

Comment interprétons-nous cela?
Peut-on estimer R_0?

R_0 *is the number of new infections for one infected human in a completely susceptible population.*
R_0 *est le nombre de nouvelles infections chez un être humain infecté dans une population totalement susceptible.*

R_0 *> 1 implies that the infection will spread - one infection will result in more than one new infection.*
R_0 *> 1 implique que l'infection se propagera - une infection entraînera plus d'une nouvelle infection.*

R_0 *< 1 implies that the infection will go extinct - and thus also represents the condition for successful control.*
R_0 *< 1 implique que l'infection va disparaître - et représente donc également la condition pour un contrôle réussi.*

Assume no infected humans (*x*=0)

Supposons qu'aucun humain ne soit infecté (x = 0)

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

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

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..