

# **Adaptive cross-level modeling of infectious diseases in wild mammals**

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# Outline

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## **Introduction**

Mathematical modeling of infectious diseases  
in human vs. wild animals  
Bat species as viral hosts

## **Cross-level immuno-epizootic approach**

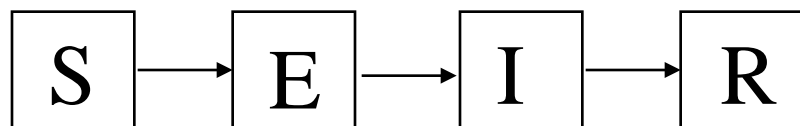
Within-host and between-host models  
Theoretical framework and cross-level integration  
Advantages and challenges

# Modeling infectious diseases

## Infectious diseases in humans and domestic animals:

- Individuals are strictly identifiable
- The disease progression is recorded and studied
- Vaccination and treatment programs are readily available
- Available data – case histories, vaccination and treatment records

## Traditional compartmental framework:



S – susceptibles

E - exposed

I – infected

R – removed (recovered)

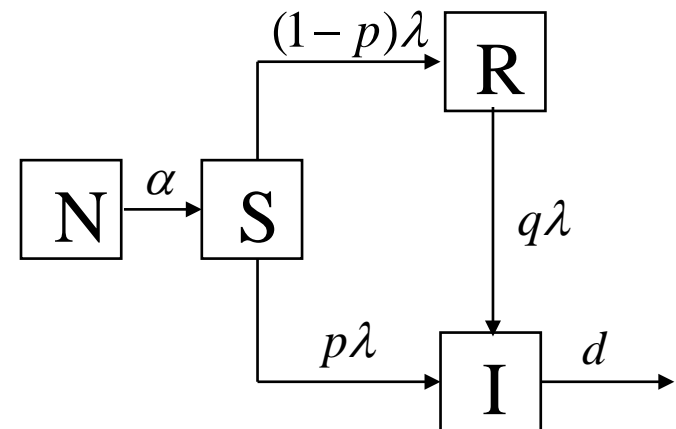
## Infectious diseases in wild animals:

- Trackability of individual animals is often infeasible
- Impossible to distinguish all phases of a disease progression
- Vaccination and treatment programs are rarely used
- Available data - snapshot field data, experimental infections

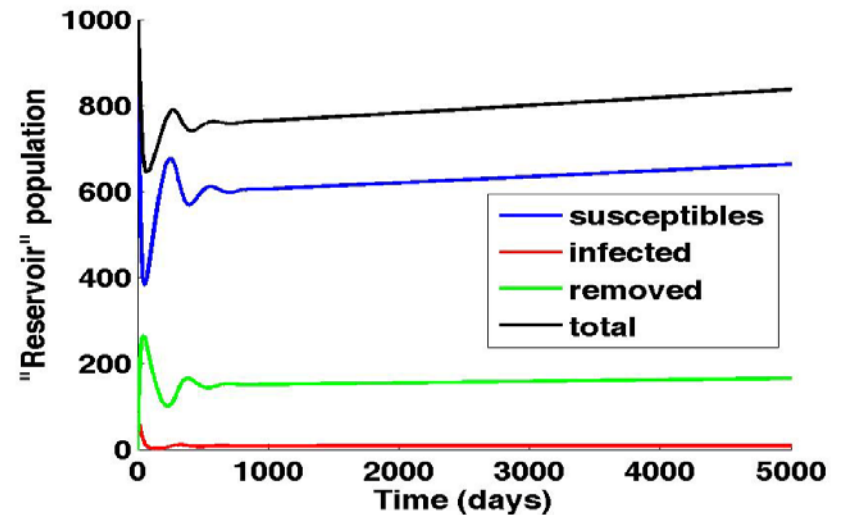
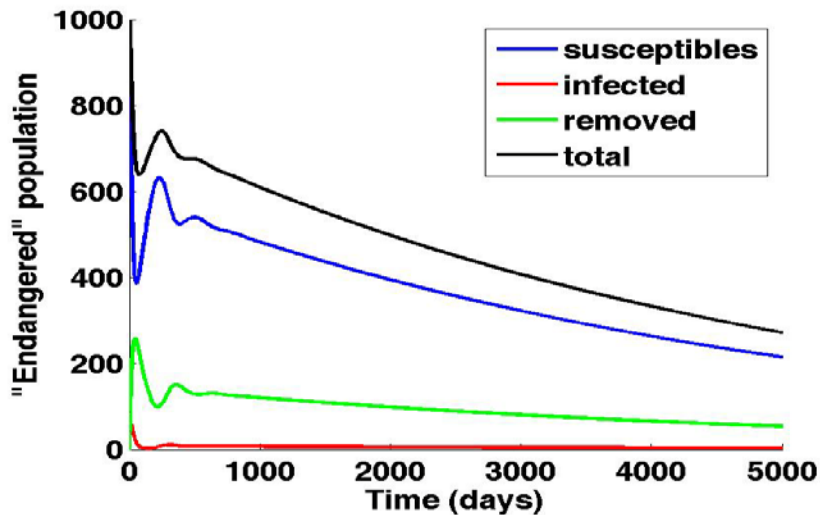
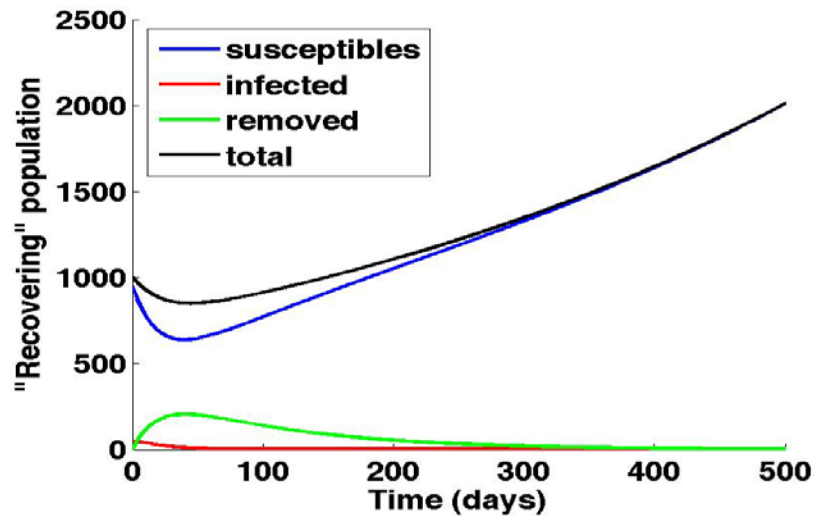
# Inter-host models

- Describe the dynamics of a viral infection into a population
- Connect with the possible outcomes of viral exposures at population level including vanishing infections, coexistence, and population death
- Could potentially address questions about:
  - Transmission routes and contact rates;
  - Survival probabilities and conditions (for the population);
  - Conditions for disease eradication.
- Data sources for parameterization – field studies

Bats as viral reservoirs: relatively long life span, strong parental care, flight and migratory behavior, dense aggregation.

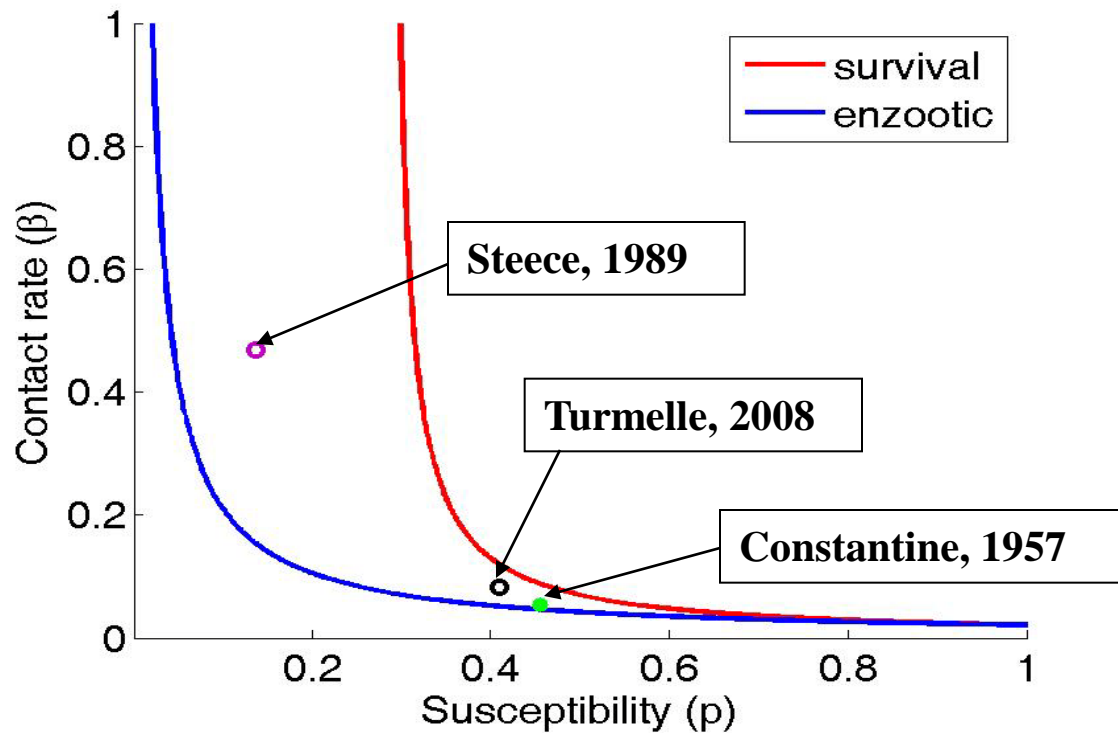


# Dynamic alternatives



# Parameter estimates

$d = 0.02$





# Intra-host models

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- Describe the dynamics of a viral infection into a individual host
- Connect with the observed outcomes of viral exposures including asymptomatic infections, development of immunity, death
- Could potentially address questions regarding:
  - Pathogenesis of the disease;
  - Survival probabilities and survival conditions;
  - Duration and strength of acquired immunity.
- Data sources for parameterization – experimental infections

## Immune Response Model

B – B cells concentration

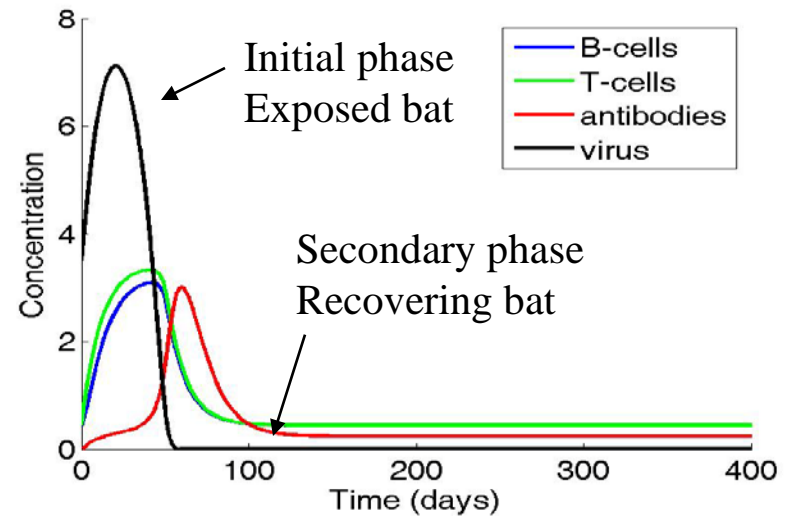
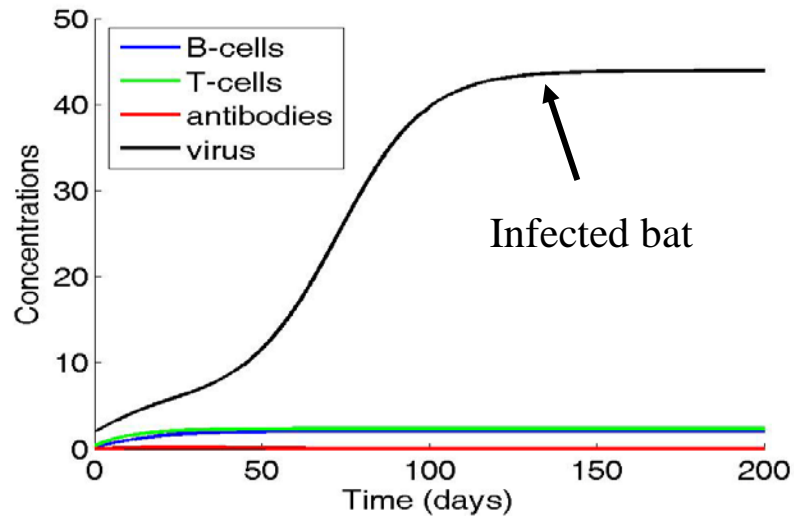
T – T cells concentration

A – virus specific antibodies

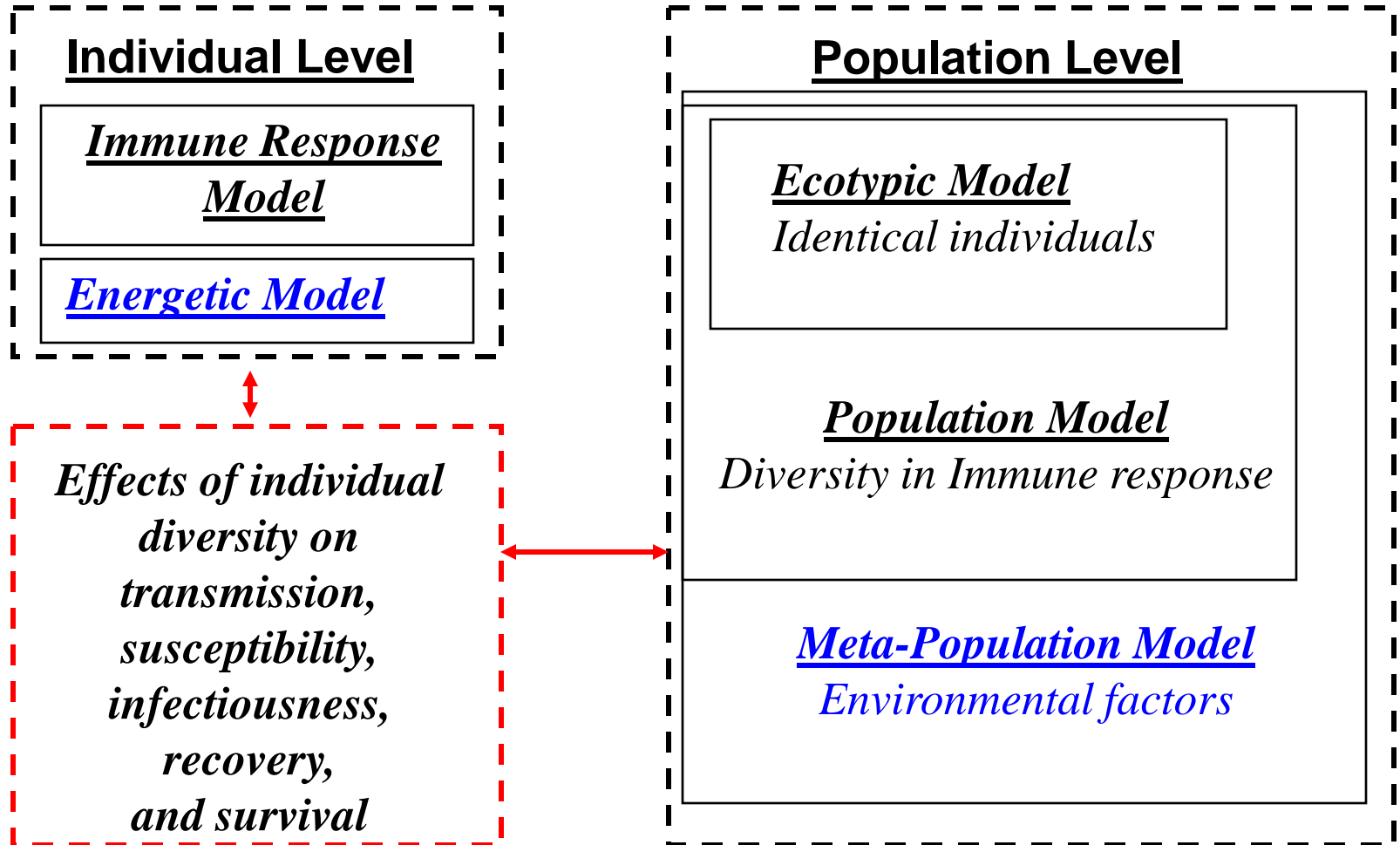
V – viral concentration



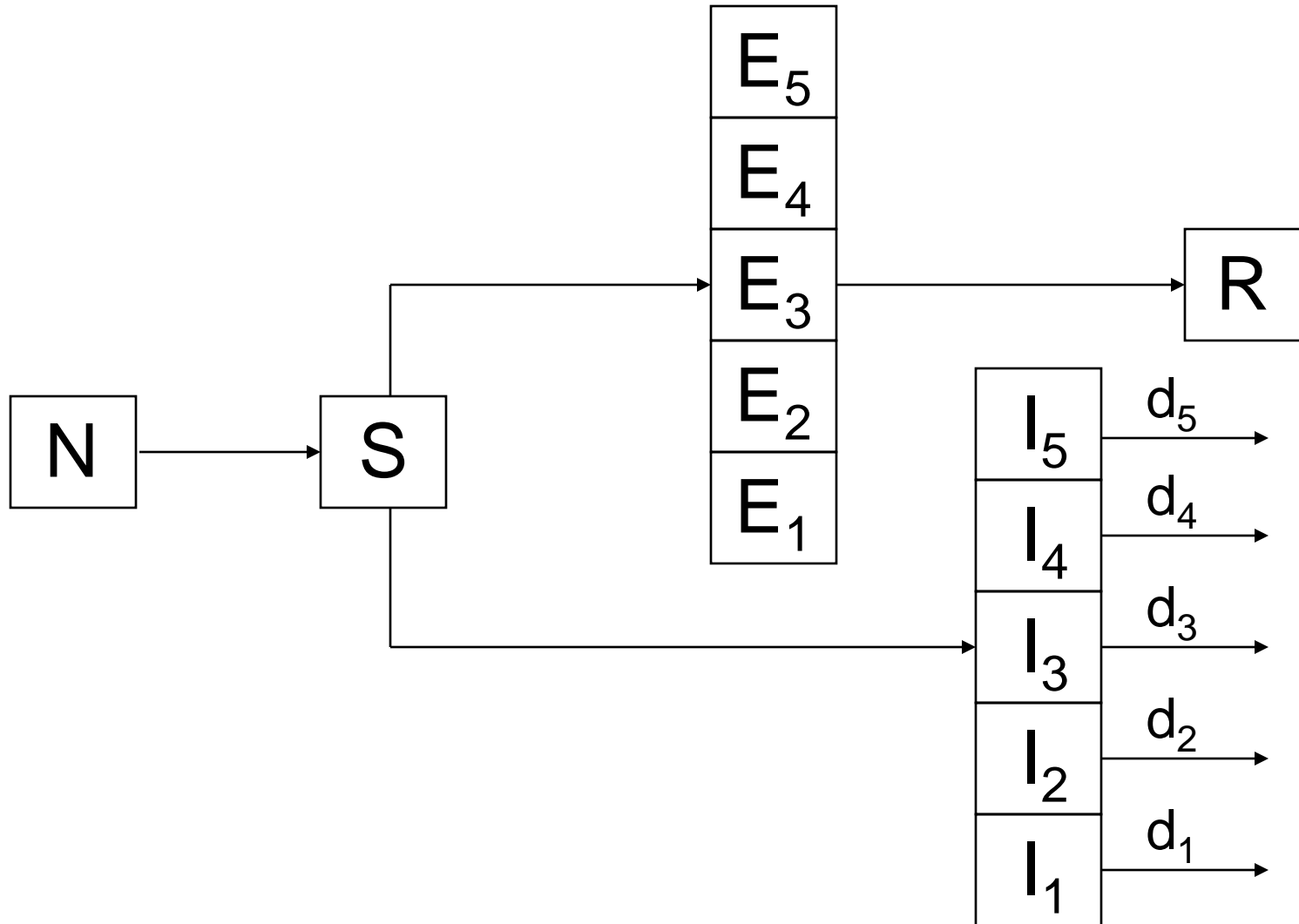
# Dynamic alternatives



# Theoretical framework



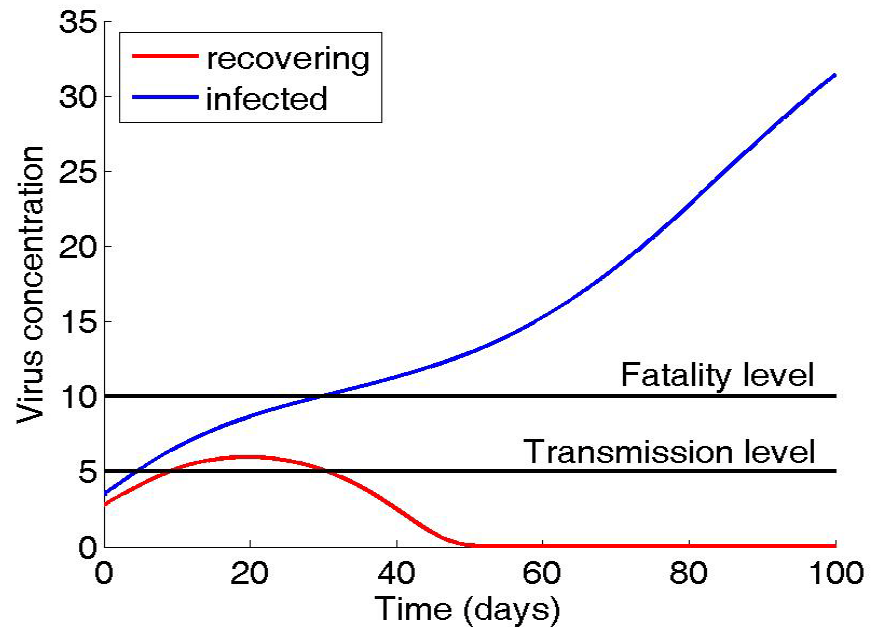
# Ecotypic Model (Immunotypes)



# Cross-level integration

Define mechanisms at intra-host level based on results from inter-host model:

- **Threshold-based infectiousness**
- **Conditional transmission**
- **Infective-dose-dependence**
- **Threshold-based mortality**
- **Complete or partial immunity upon survival**



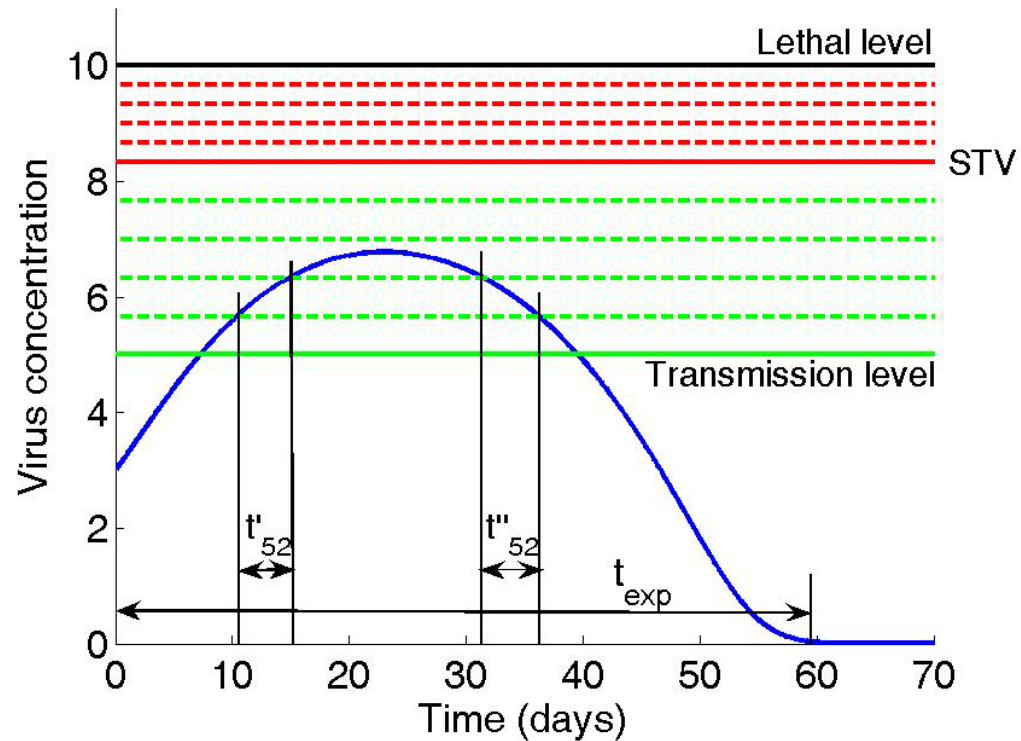
# Cross-level integration

$$\frac{1}{\gamma_i} = \text{Duration of the class } E_i$$

$$\frac{1}{d_i} = \text{Lifespan of the class } I_i$$

$$p_{ij}, q_{ij}$$

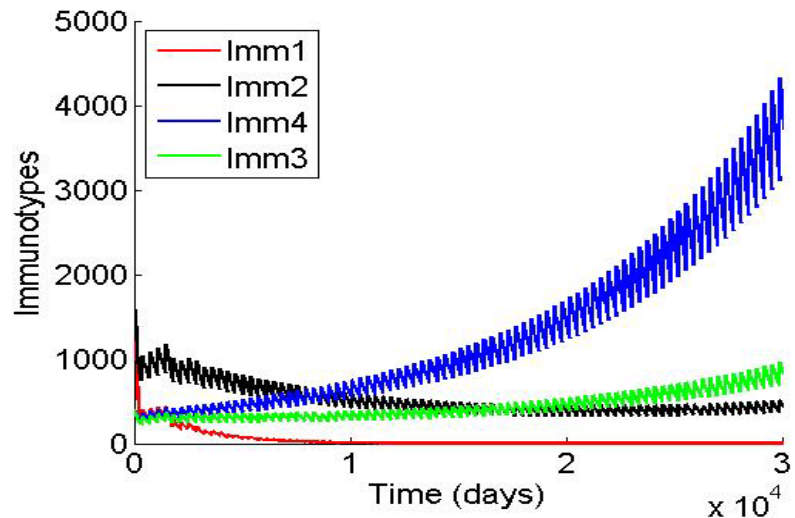
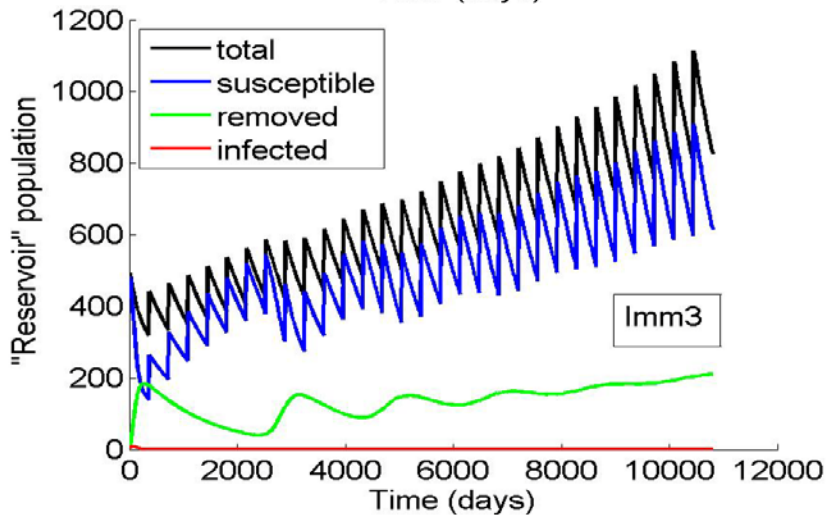
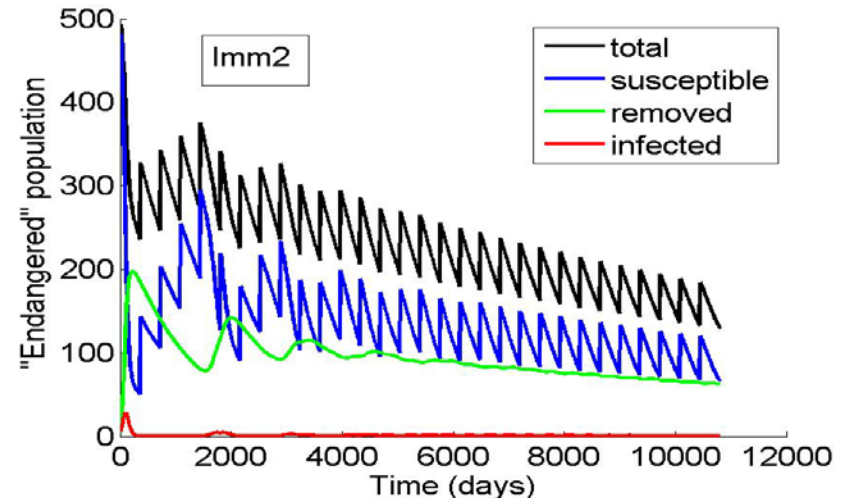
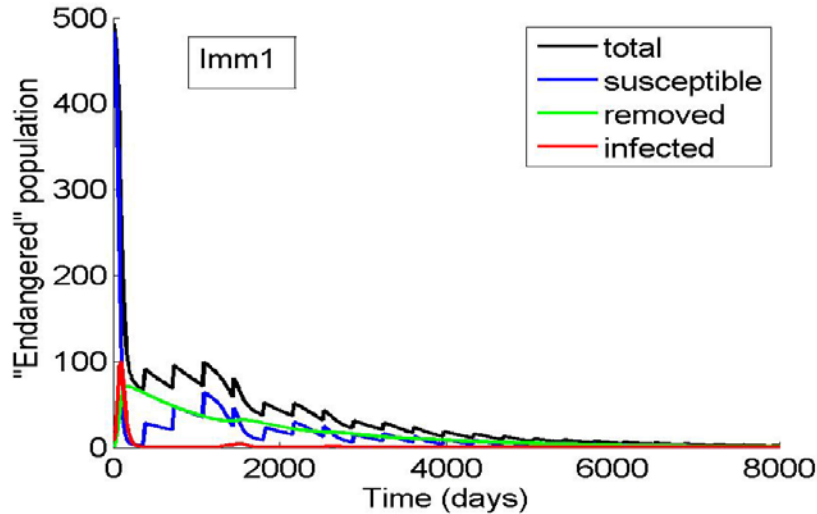
Probabilities that infectious bats have viral concentrations in the ranges initiating transfers to different infected and recovered classes



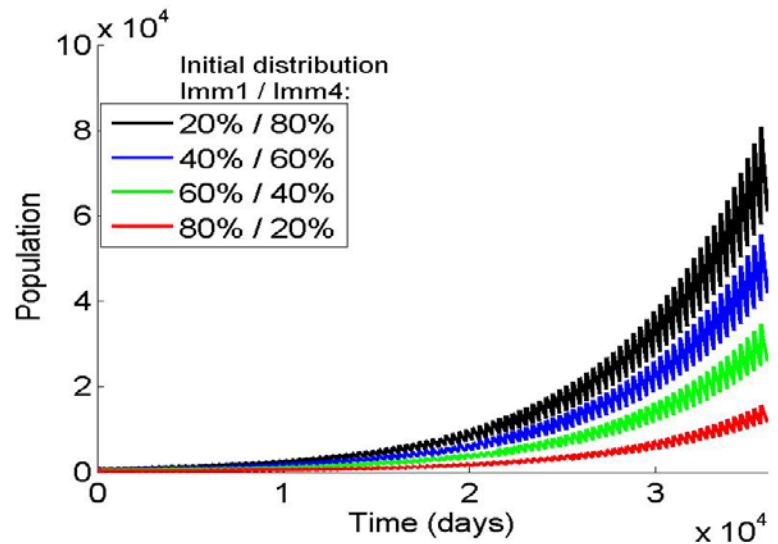
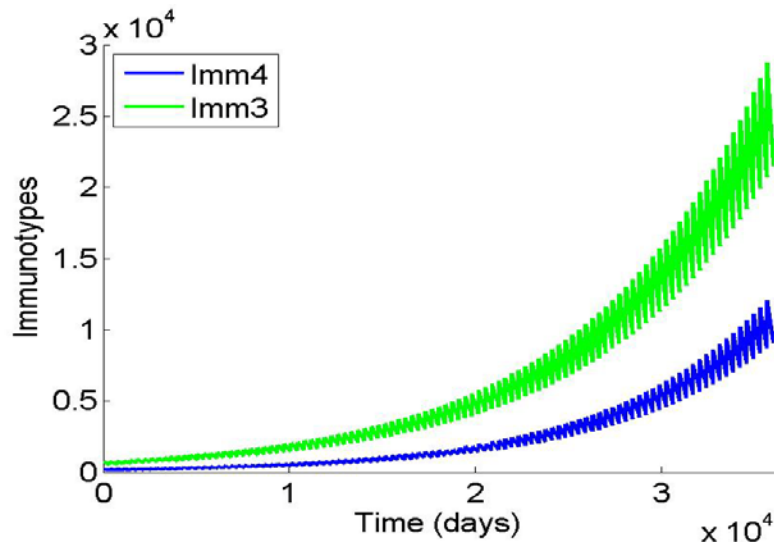
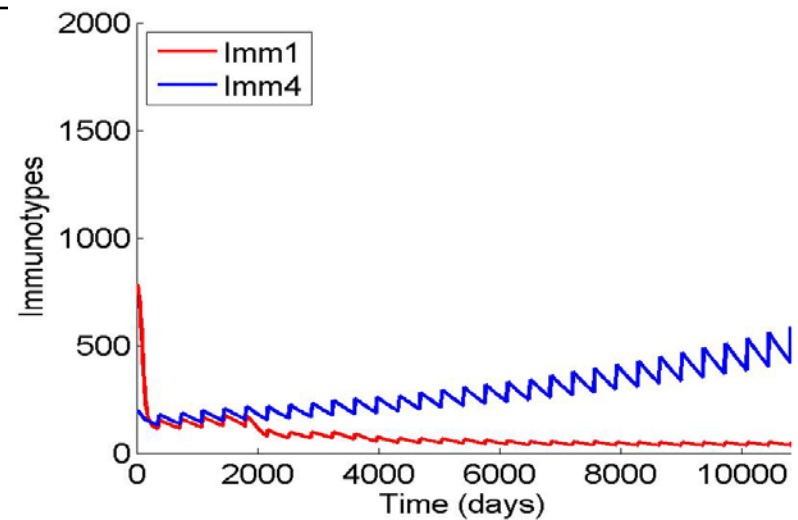
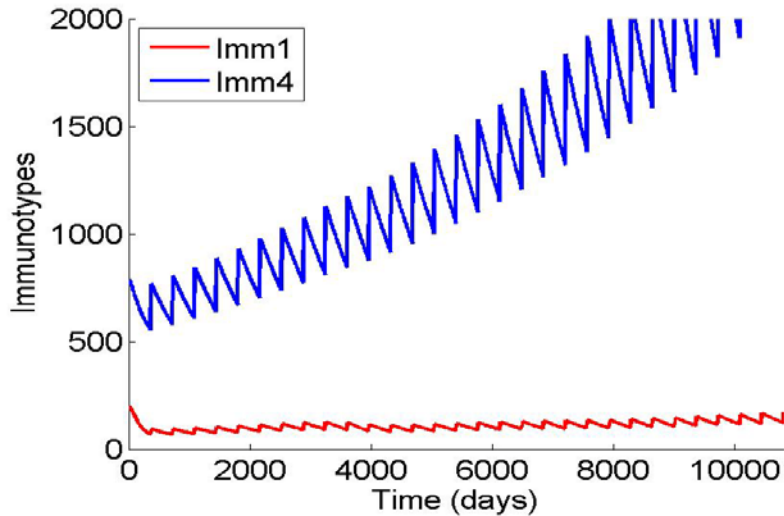
$$\gamma_5 = \frac{1}{t_{exp}}, \quad q_{52} = \frac{t'_{52} + t''_{52}}{t_{exp}}$$

# Alternatives and population profile

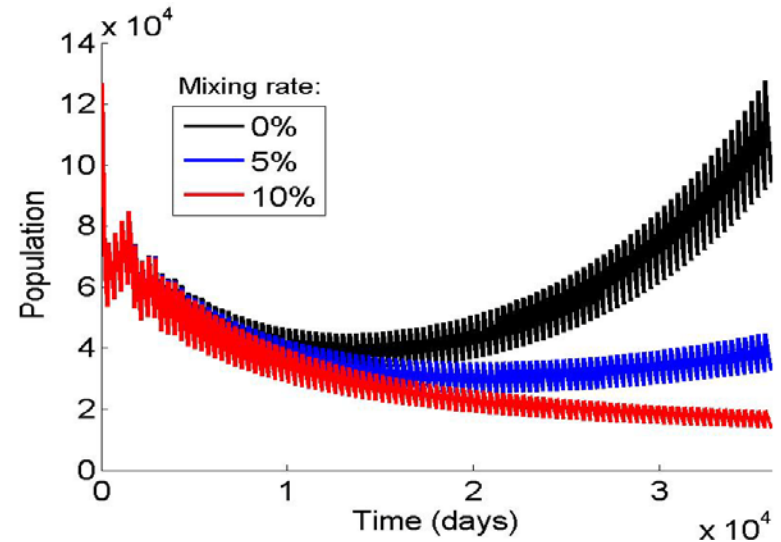
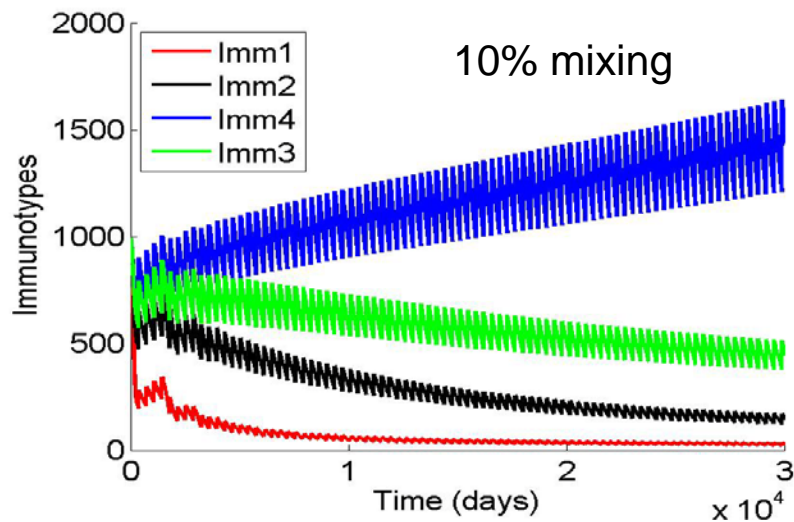
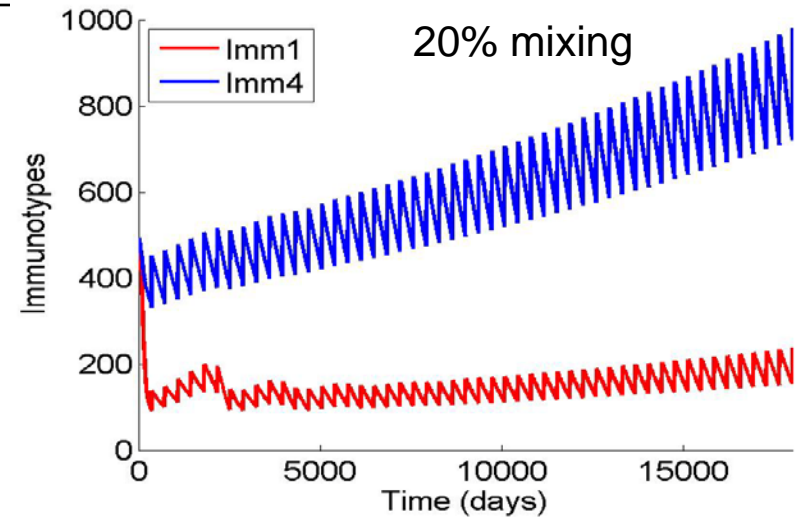
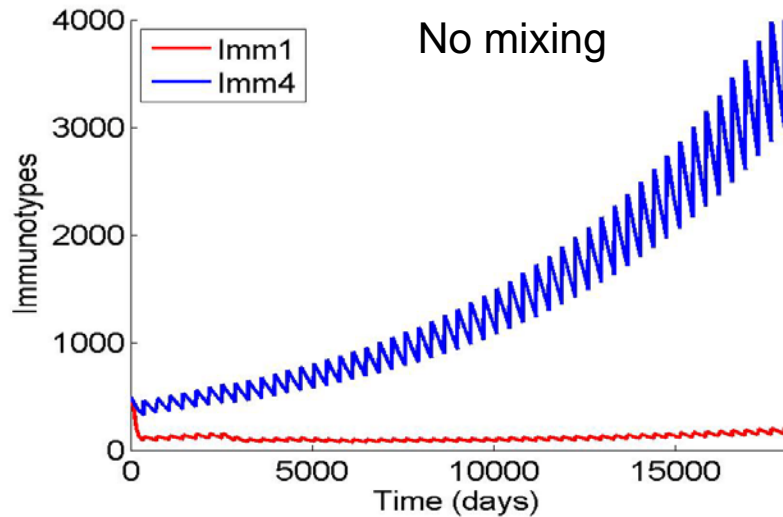
Immunosuppression   Imm1 >>> Imm2 >>> Imm3 >>> Imm4   Immunocompetence



# Variation in initial immunological profile

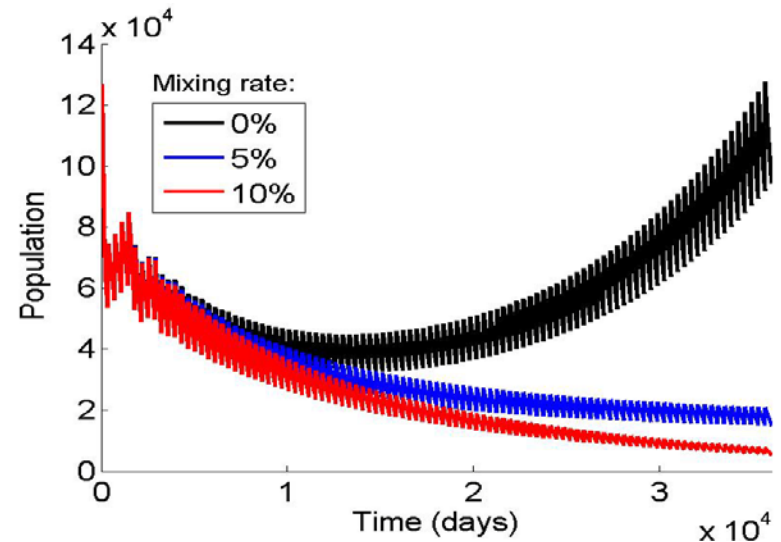
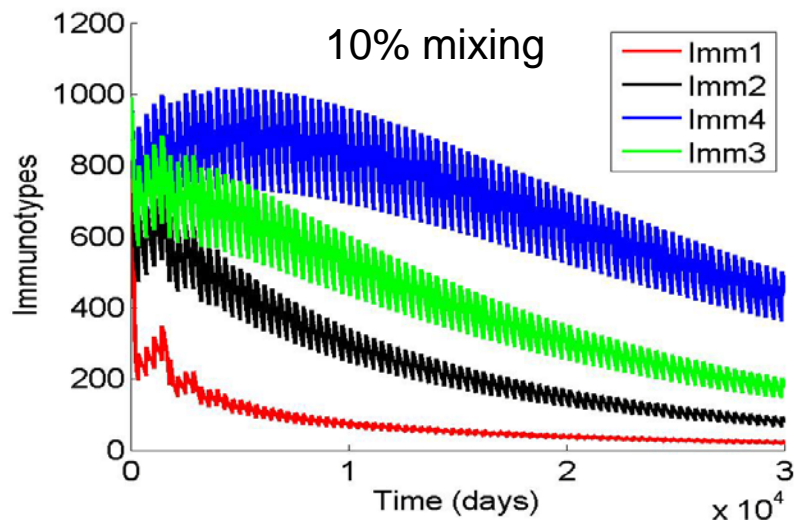
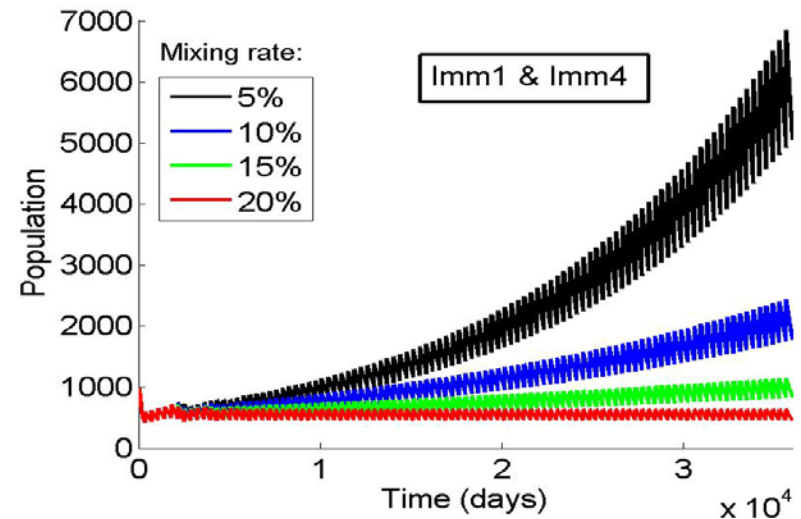
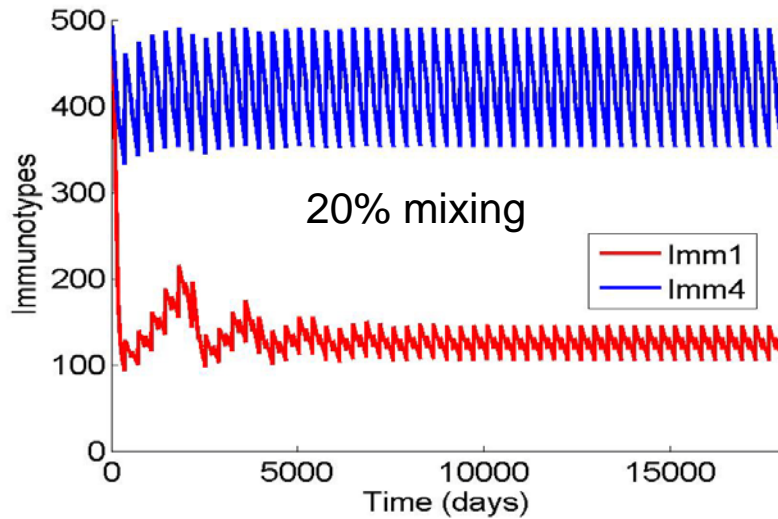


# Reproductive immunotypic mixing





# Migratory immunotypic mixing





# Summary

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- Integrative modeling technique combines the aggregating approach of traditional epidemiology with the individual diversification, based on data provided by within-host models.
- This framework allows for analysis of the effects of the individual differences in susceptibility, immune response efficiency, transmission ability, and chances of survival on the disease dynamics and the immunological profile of the population.
- The effects of different factors, such as adverse weather, climate changes, food availability, and stresses can be investigated through their influence on host physiology, and consequent population level changes.

## **Challenges:**

- To identify diversity sources and determine the optimal level of complexity of the model
- To establish feasible mechanisms of cross-level integration
- Interface with the experimental and field data
- Parameter identifiability and estimation



# Acknowledgements

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## **Collaborators:**

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