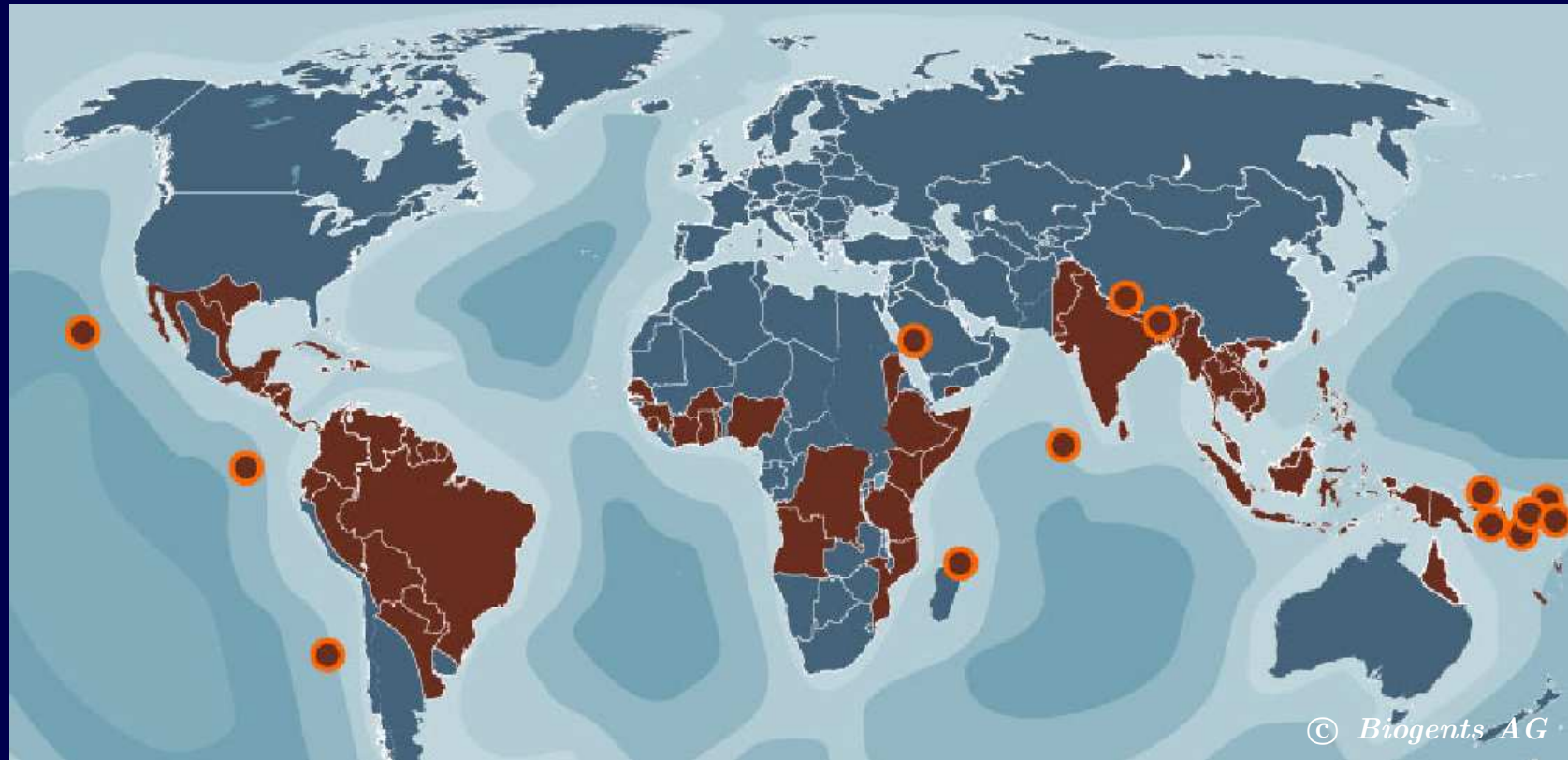


*Descriptive and Predictive models  
of dengue epidemiology: an overview*



*Maíra Aguiar*

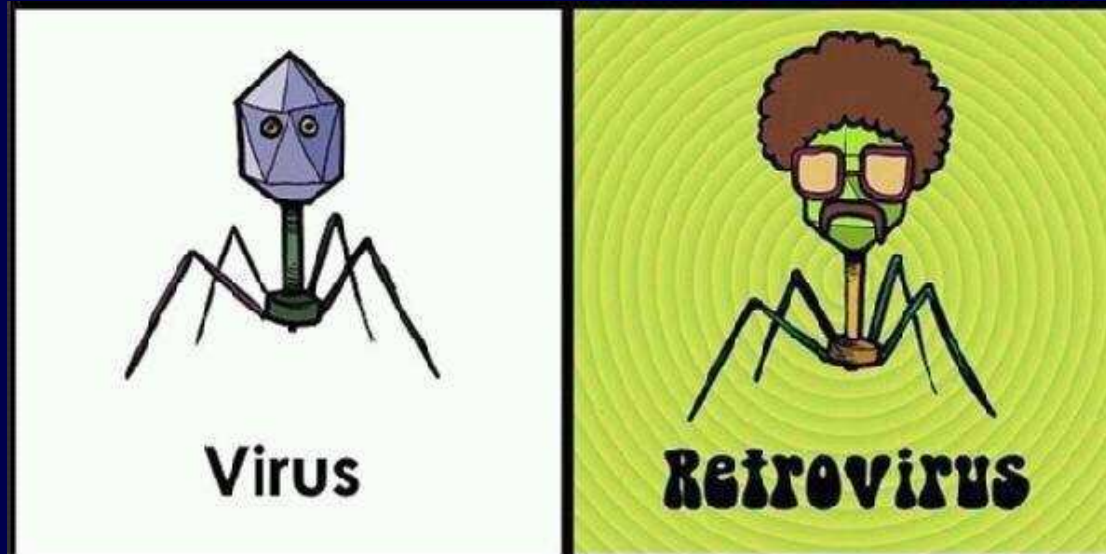
*Mathematical Biology Working Group*

*Centro de Matemática e Aplicações Fundamentais (CMAF)*

*Lisbon University, Portugal*

## Talk Outline

- ✧ *Dengue cases in the Autonomous Region of Madeira, Portugal.*
- ✧ *Dengue fever epidemiology.*



- ✧ *Epidemiological models that captures the essential differences between primary and secondary infections.*
- ✧ *Qualitative study in order to show how much complexity we need to describe the fluctuations observed in empirical dengue hemorrhagic fever incidence data.*

# *Madeira: Autochthonous Dengue Cases in Portugal*

*October 2005:*

*“MADEIRA: Praga de mosquitos no Funchal.”  
in Diário de Notícias.*

*“Mosquito da febre amarela e do dengue em Santa Luzia.”  
in Madeira On-line.*

*“Insecto identificado por Rúben Capela, entomologist UMa.”  
in Madeira On-line.*

*“ O mosquito foi detectado em 2005 na freguesia de Santa Luzia,  
no Funchal, e ter-se-á registrado após a importação de palmeiras  
para um jardim público.”, in Madeira On-line.*

## *Madeira: Autochthonous Dengue Cases in Portugal*

*November 2007:*

*“Vector monitoring of Aedes aegypti in the Autonomous Region of Madeira, Portugal.”, in Eurosurveillance.org.*

*April 2008:*

*“Portugal montará rede para enfrentar doenças tropicais.”, in BBC.*

*May 2008:*

*“Mosquito da dengue se espalha por países não-tropicais.”, in BBC.*

*“Aedes albopictus agora prolifera no sul da Europa e até na França e na Suíça.”, in BBC.*



## *Madeira: Autochthonous Dengue Cases in Portugal*

*July 2008:*

*“Portugal regista cinco casos de dengue.”, in RTP Notícias.*

*“Doença contraída por cidadãos portugueses quando estes viajavam pela América do Sul.”, in RTP Notícias.*

*August 2008:*

*“ Mais mosquitos do dengue na Madeira ”, in Revista Visão .*

*“O tempo quente está a favorecer o aumento do número de mosquitos que transmitem a doença.”, in Madeira On-line.*

*October 2008:*

*“ Dengue: Madeira toma medidas de prevenção. Todos os aviões e navios com origem na Madeira serão analisados e desinfectados. Medidas entram em vigor no dia 1 de Novembro”, in Diário de Notícias.*

# *Madeira: Autochthonous Dengue Cases in Portugal*

## *Outbreak Assessment in Autonomous Region of Madeira:*

*Onset on 3 October 2012: 2 confirmed cases.*

*10 October 2012: 18 confirmed cases, 191 probable cases, 26 hospitalized.*

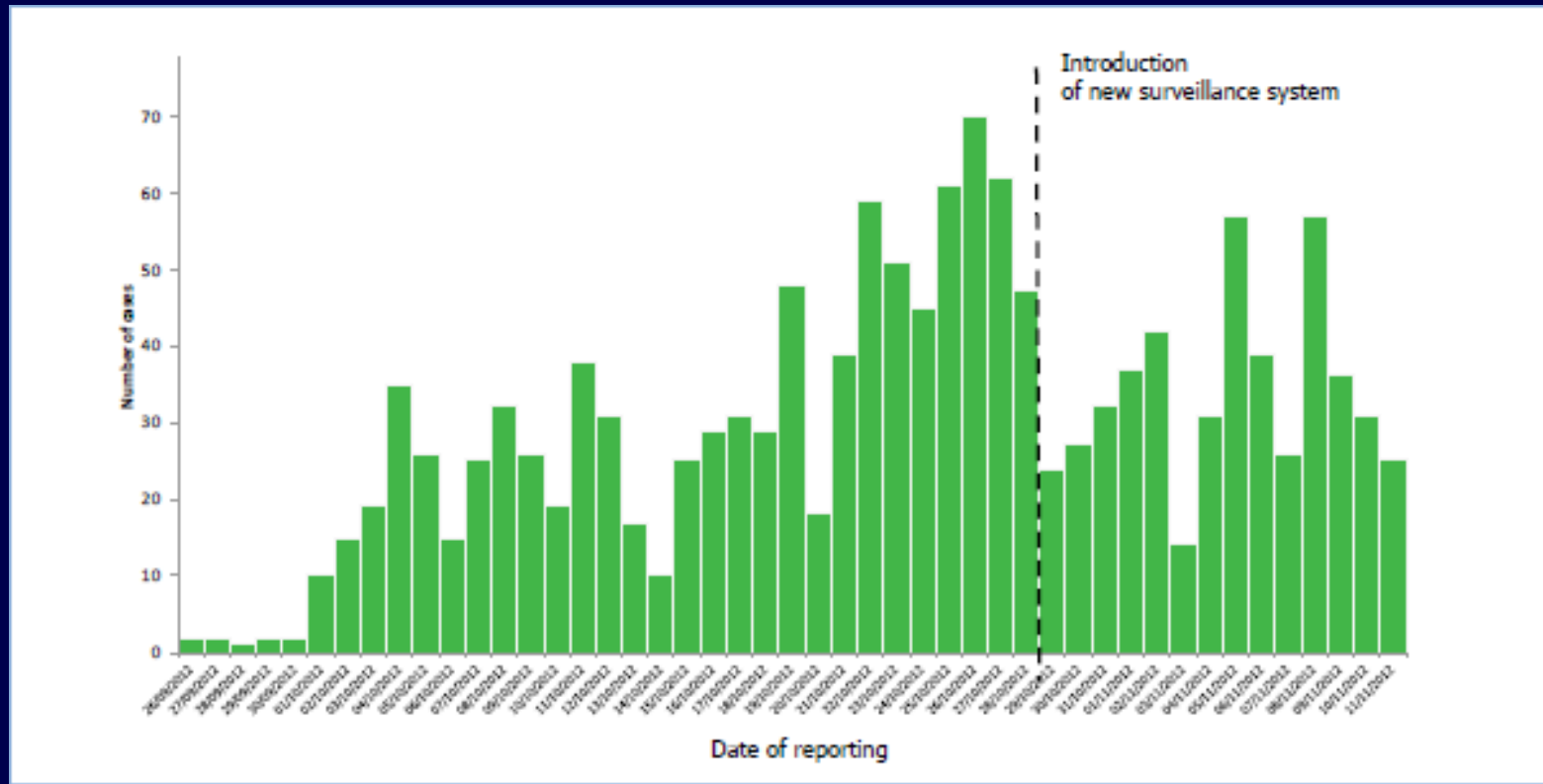
*24 October 2012: 52 confirmed cases, 404 probable cases, 5 hospitalized.*

*28 October 2012: 62 confirmed cases, 463 probable cases, 6 hospitalized.*

*07 November 2012: 537 confirmed cases, 631 probable cases, 57 hospitalized.*

# *Madeira: Autochthonous Dengue Cases in Portugal*

## *Outbreak Assessment in Autonomous Region of Madeira:*



**28 November 2012:** 1891 confirmed cases, 111 hospitalized, 32 imported cases in Continental Europe.

## *Madeira: Autochthonous Dengue Cases in Portugal*

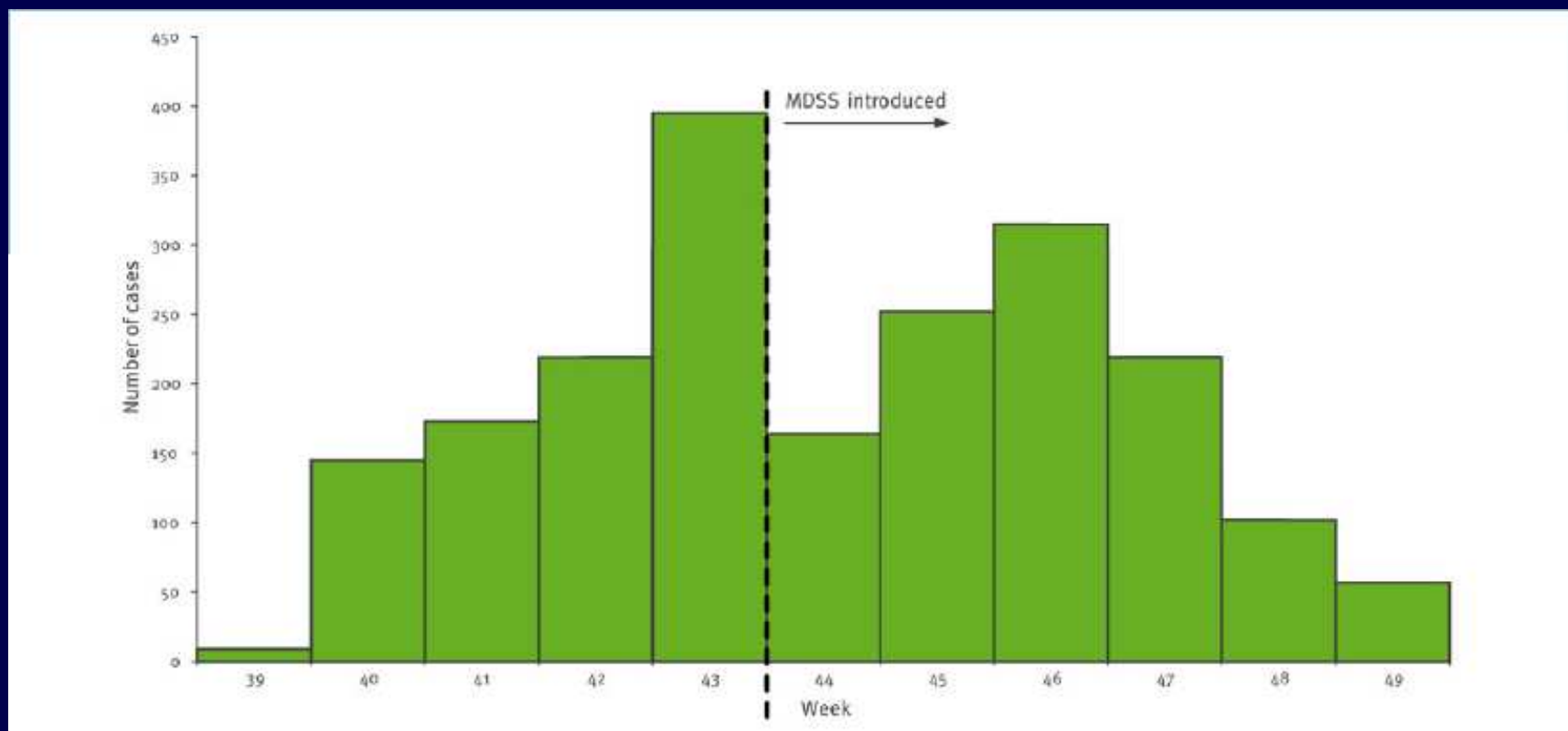
*05 Dezember 2012: 1993 confirmed cases, 118 hospitalized, 42 imported cases in Continental Europe.*

*9 Dezember 2012: 2050 confirmed cases, 122 hospitalized, 58 imported cases in Continental Europe.*

*16 Dezember 2012: 2103 confirmed cases, 122 hospitalized, 72 imported cases in Continental Europe.*

# *Madeira: Autochthonous Dengue Cases in Portugal*

*Rapid Risk Assessment ECDC: European Center for Disease Control  
From September to December 2012*



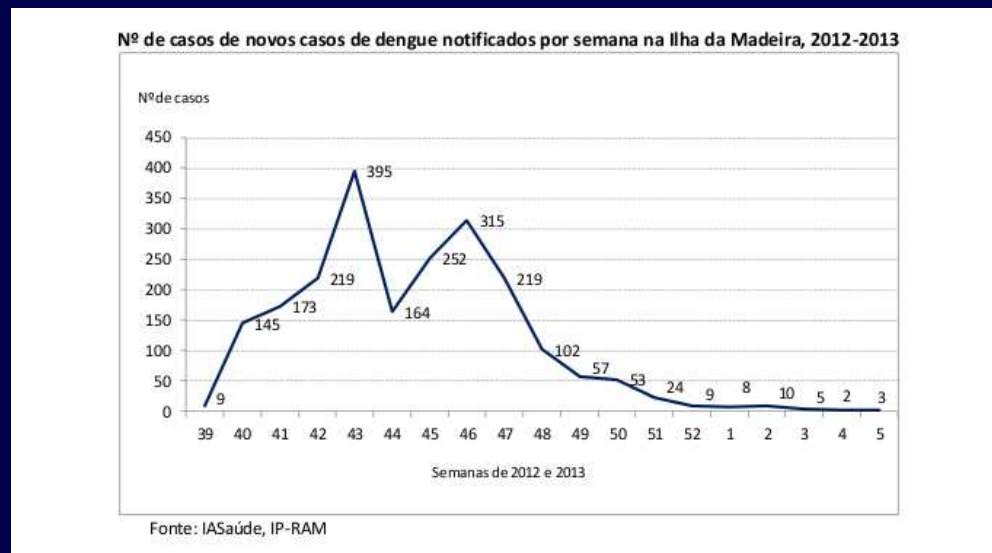
*“The LARGEST outbreak in Europe since the 1920th.”*

## *Madeira: Autochthonous Dengue Cases in Portugal*

*21 January 2013: 2144 confirmed cases, 122 hospitalized, 74 imported cases in Continental Europe.*

*28 January 2013: Communicable Disease Threats Report (CDTR ): Sporadic cases are still being reported in Madeira.*

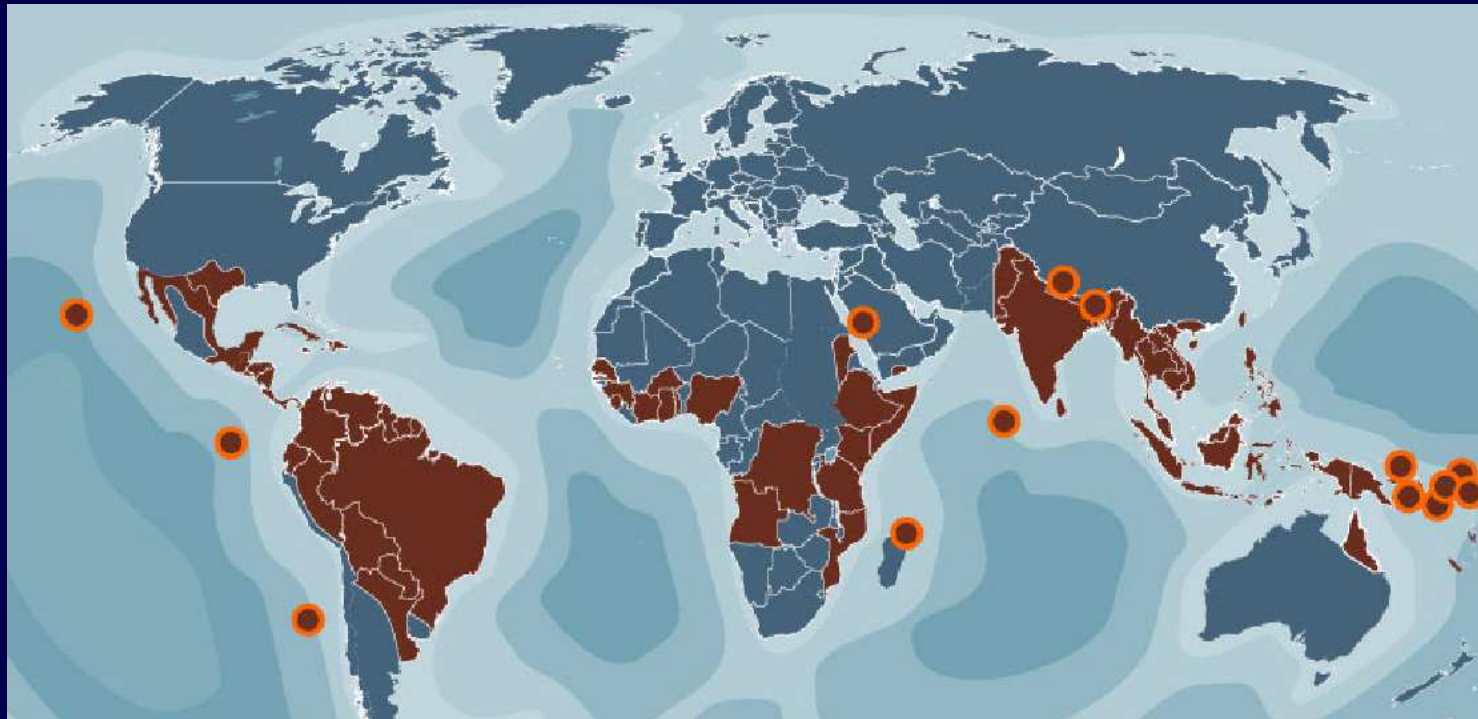
*3 February 2013: 2164 confirmed cases, 78 imported cases in Continental Europe (11 in Main Land Portugal and 66 in 12 European Countries ).*





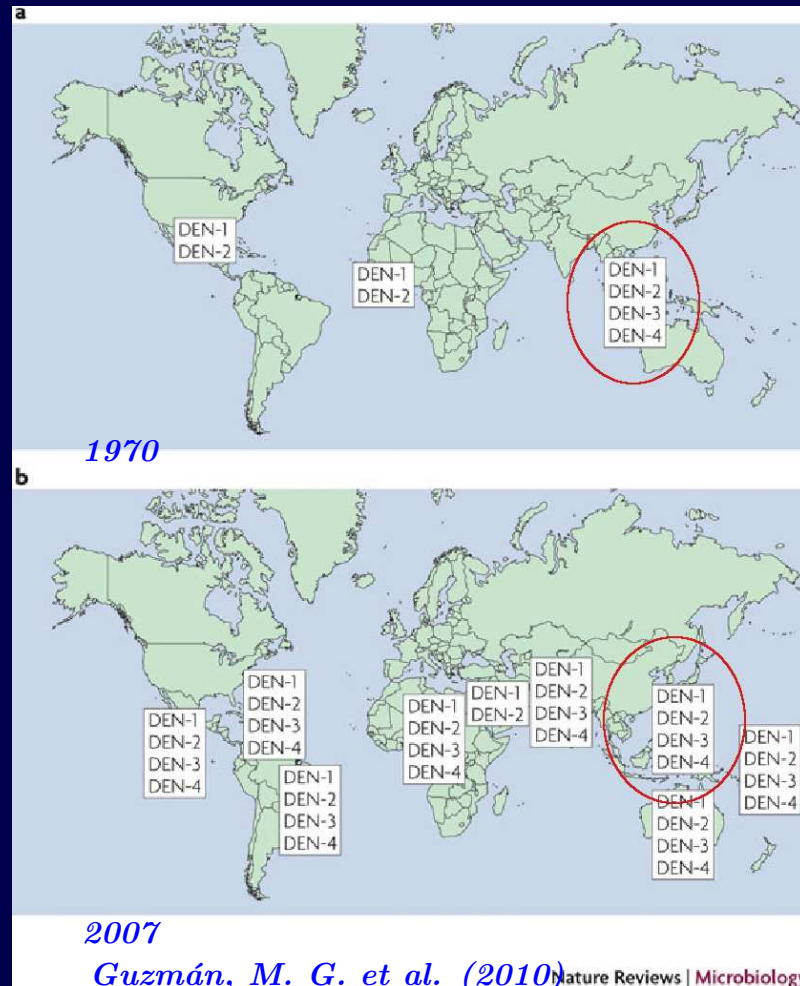
## *Dengue fever epidemiology*

- ✧ Dengue is a viral mosquito-borne infection, a leading cause of illness and death in the tropics and subtropics.*
- ✧ More than one-third of the world's population are living in areas at risk of acquiring dengue infection.*



*Worldwide dengue distribution 2008 - Source: WHO (2007) & CDC (2008)*

# *Dengue fever epidemiology*



✧ *Four antigenically distinct but closely related dengue viruses: DEN-1, DEN-2, DEN-3, DEN-4.*

## *Dengue fever epidemiology*

- ✧ Infection by one serotype confers life-long immunity to that serotype and a short period of temporary cross-immunity to other serotypes (3-9 months).*
- ✧ Two forms of the disease exist: dengue fever (DF), and dengue hemorrhagic fever (DHF).*
- ✧ Epidemiological studies support the association of DHF with secondary dengue infection, due to the antibody-dependent enhancement (ADE) process.*

# *Dengue fever epidemiology*

## *ADE in recurrent infections*

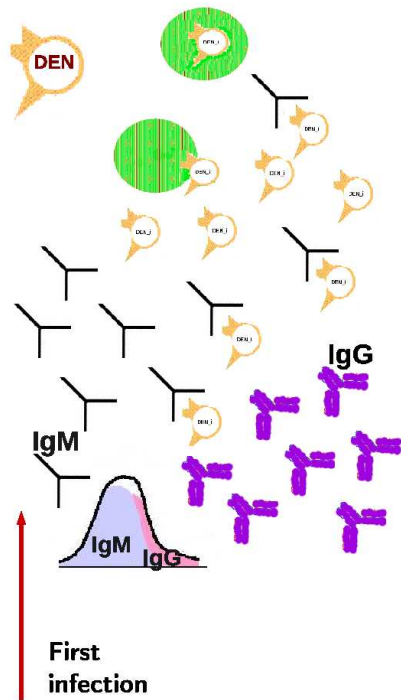


# *Dengue fever epidemiology*

## *ADE in recurrent infections*

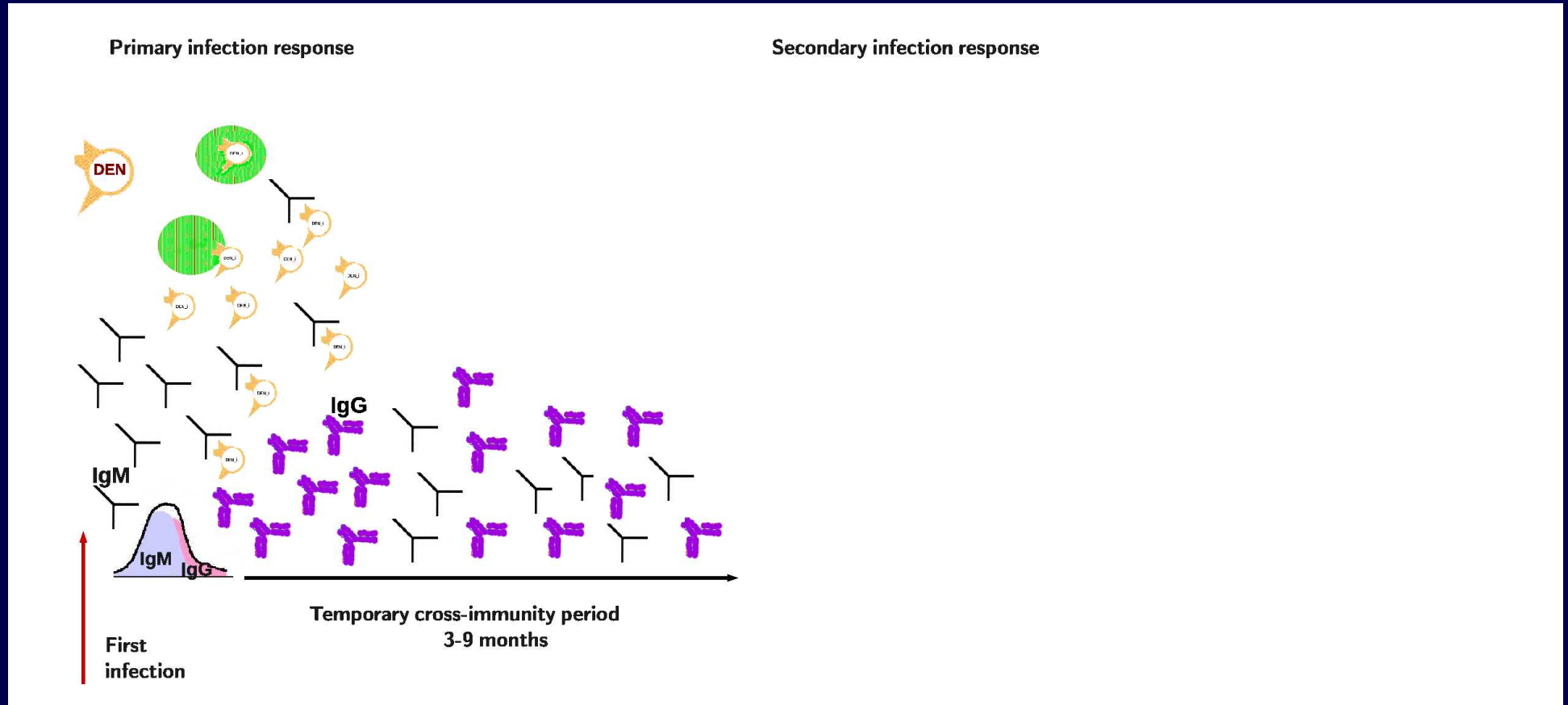
Primary infection response

Secondary infection response



# Dengue fever epidemiology

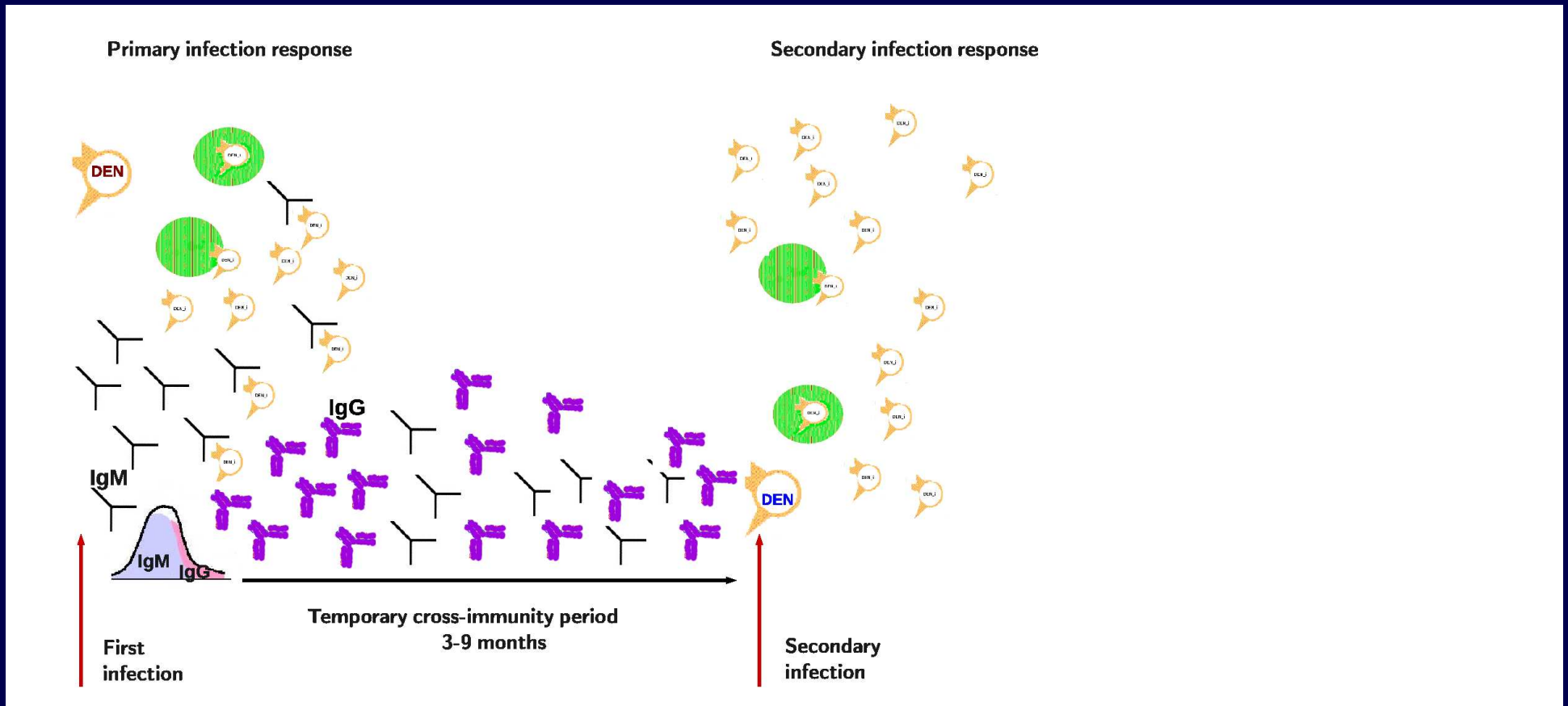
## *ADE in recurrent infections*





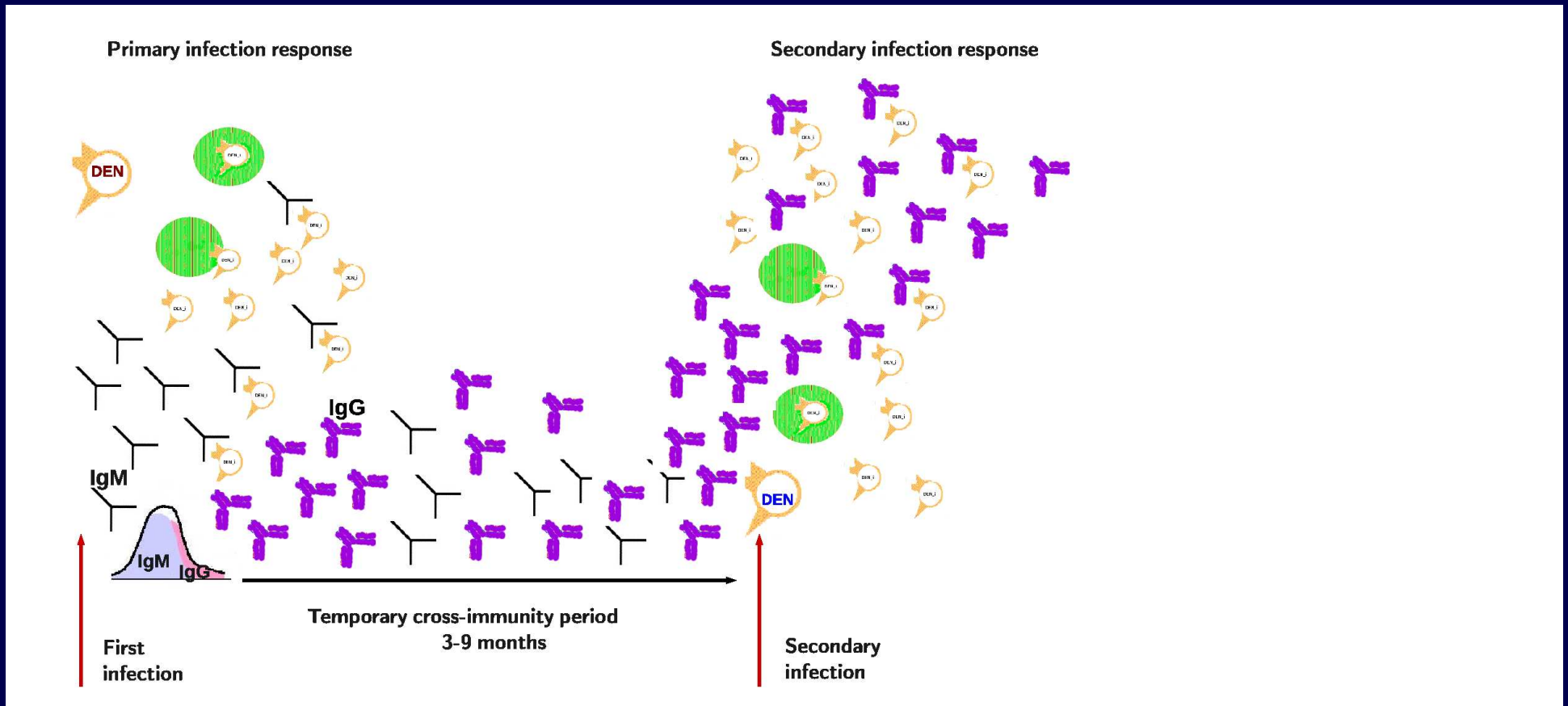
# Dengue fever epidemiology

## *ADE in recurrent infections*



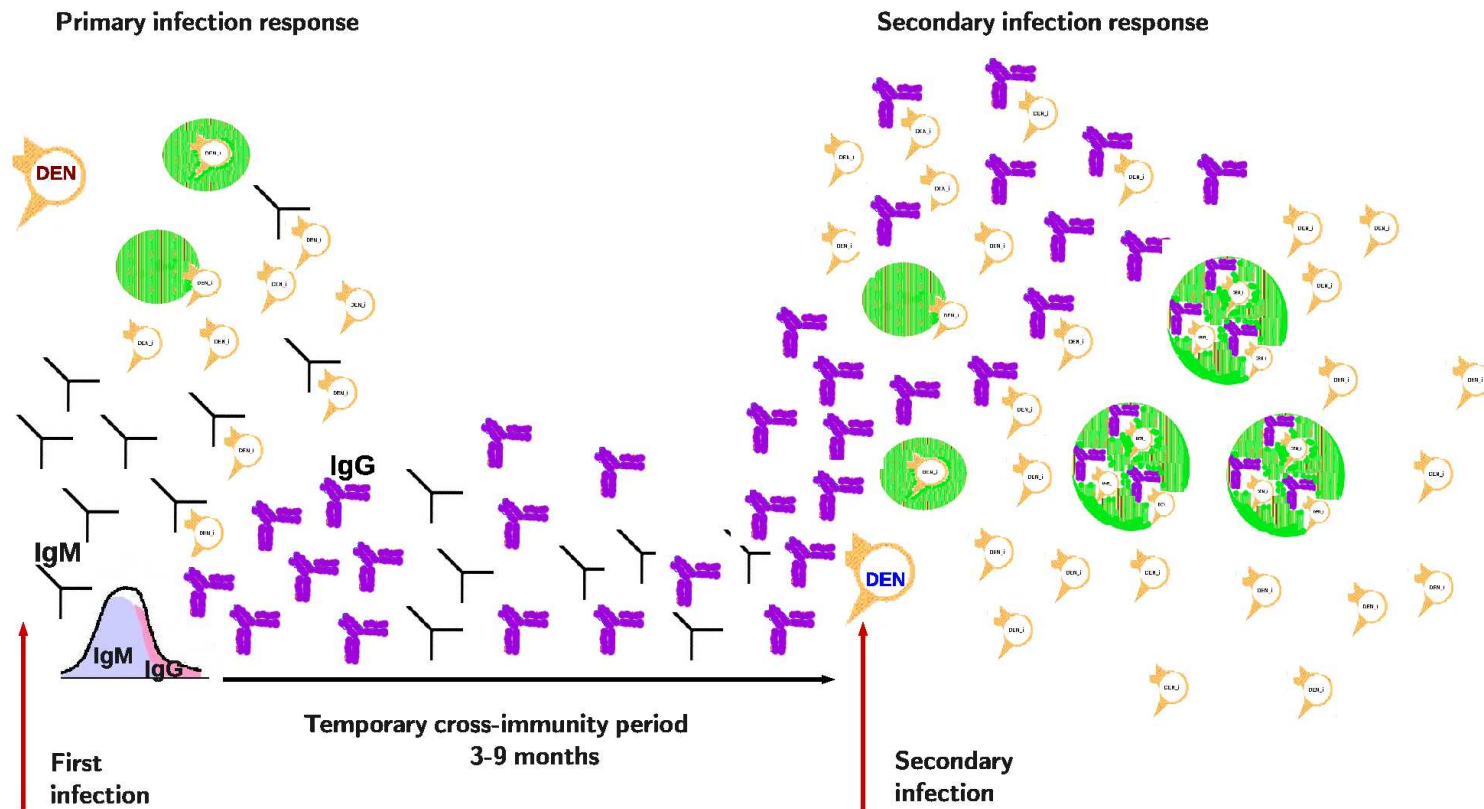
# Dengue fever epidemiology

## *ADE in recurrent infections*



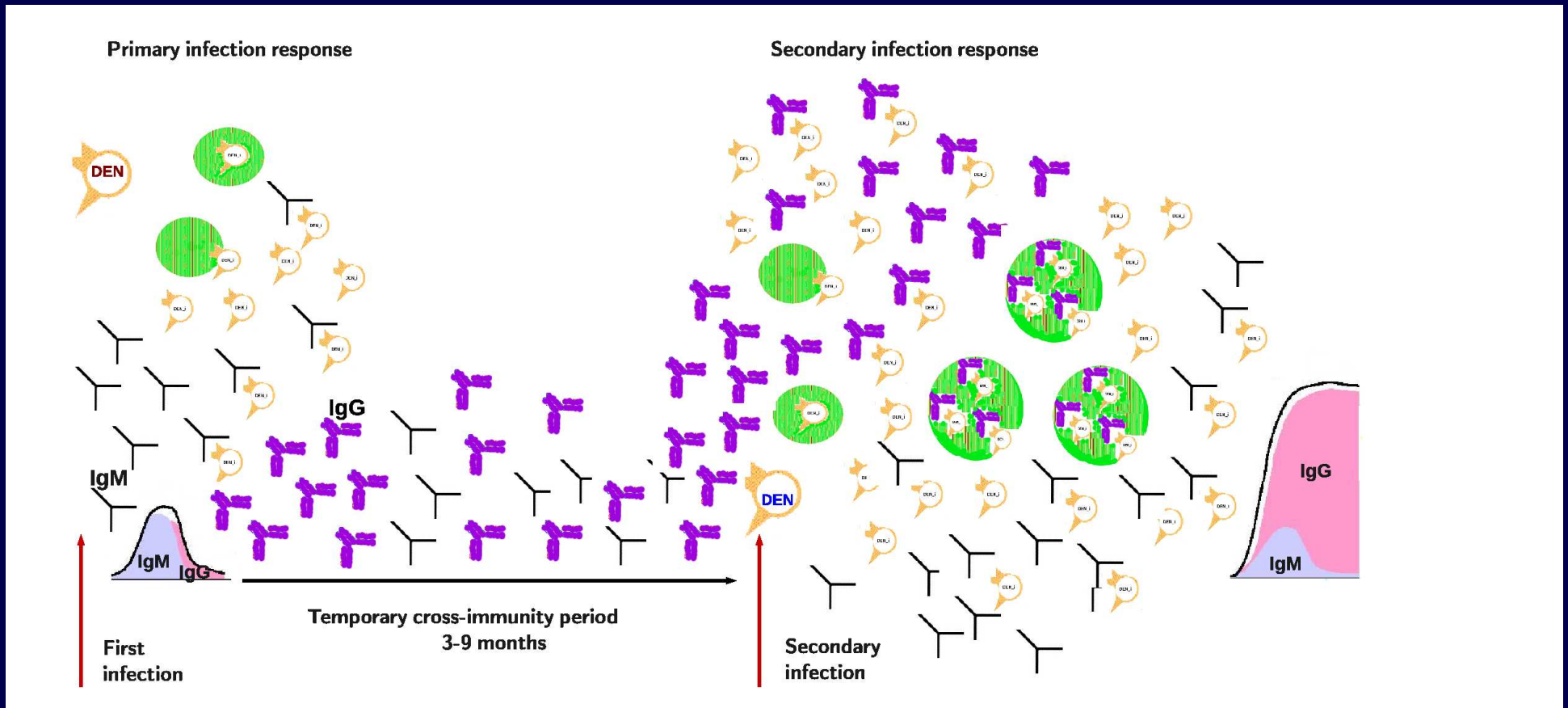
# Dengue fever epidemiology

## *ADE in recurrent infections*



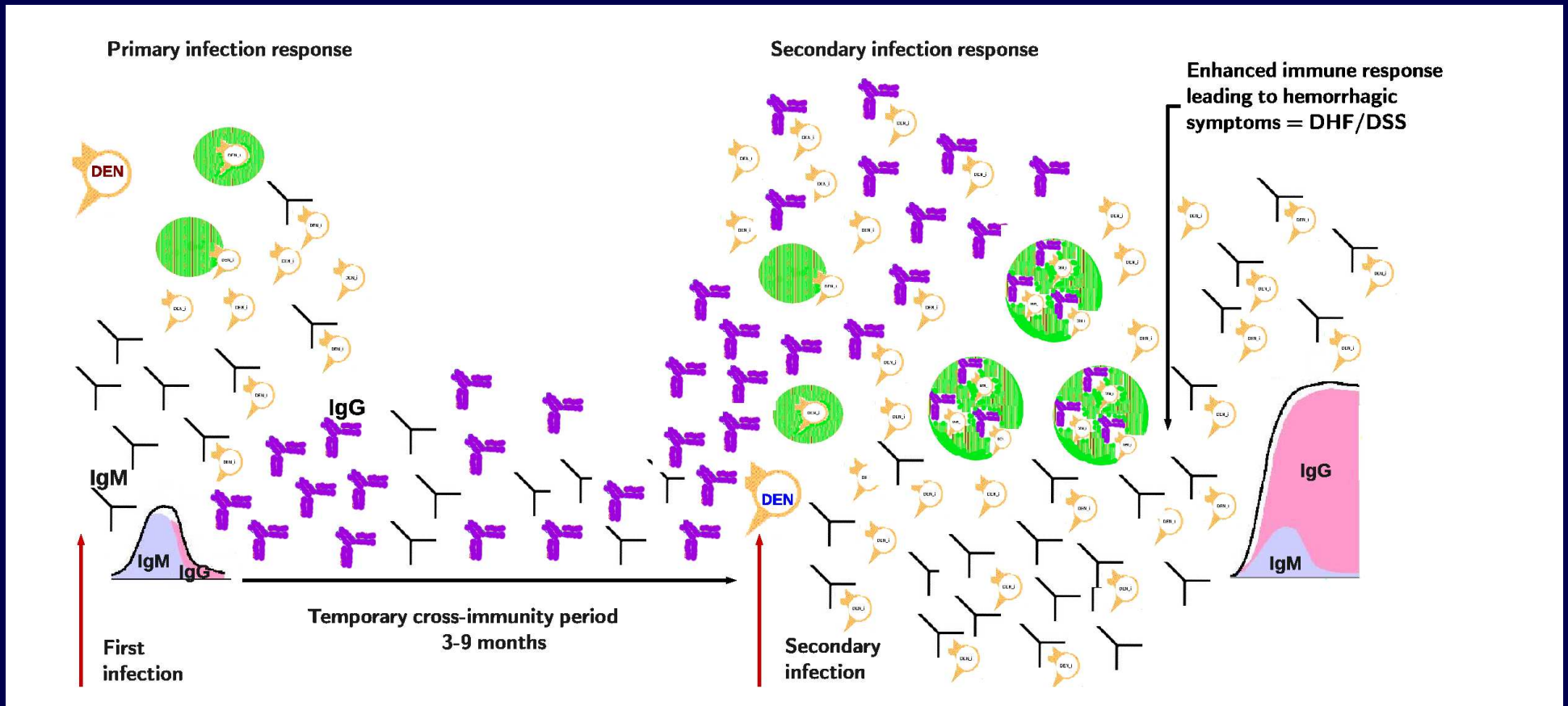
# Dengue fever epidemiology

## *ADE in recurrent infections*



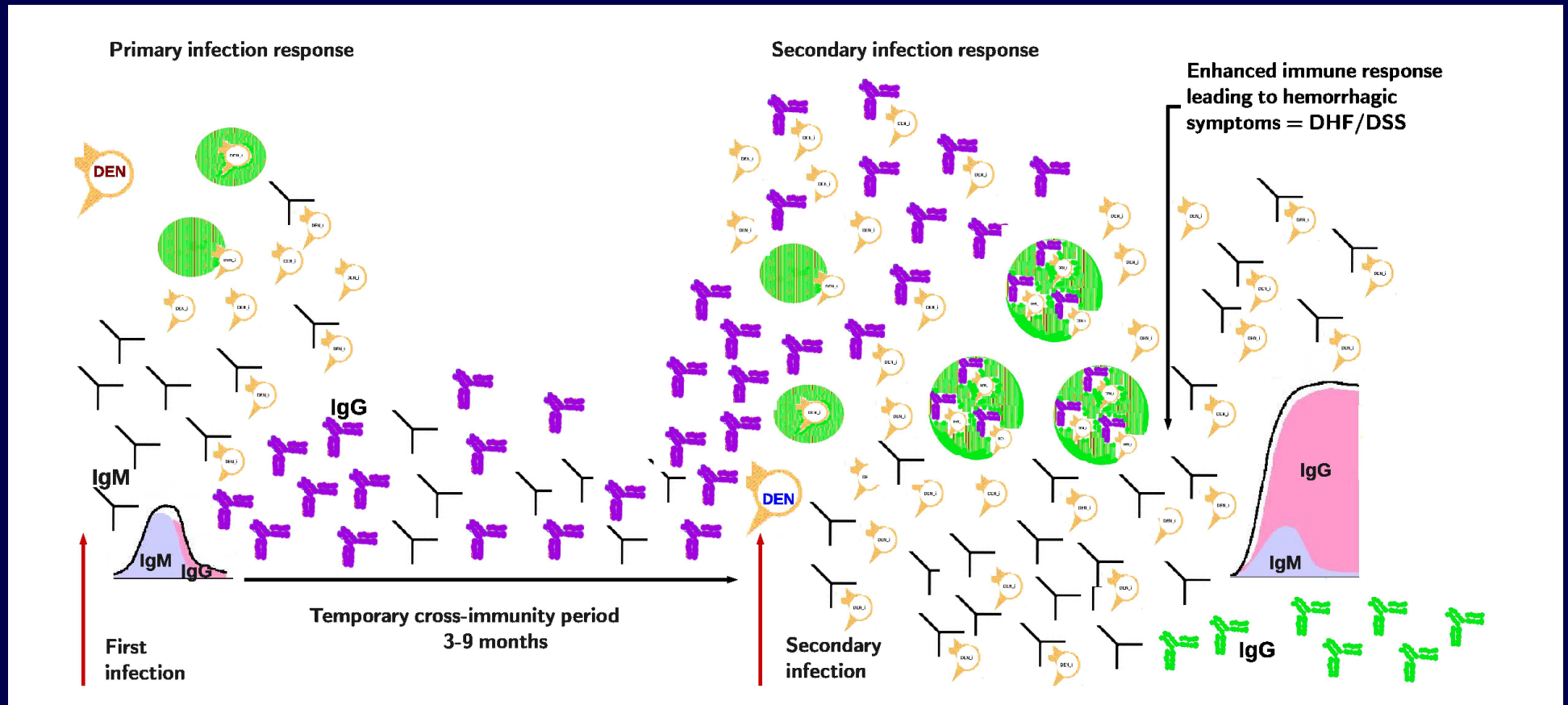
# Dengue fever epidemiology

## *ADE in recurrent infections*



# Dengue fever epidemiology

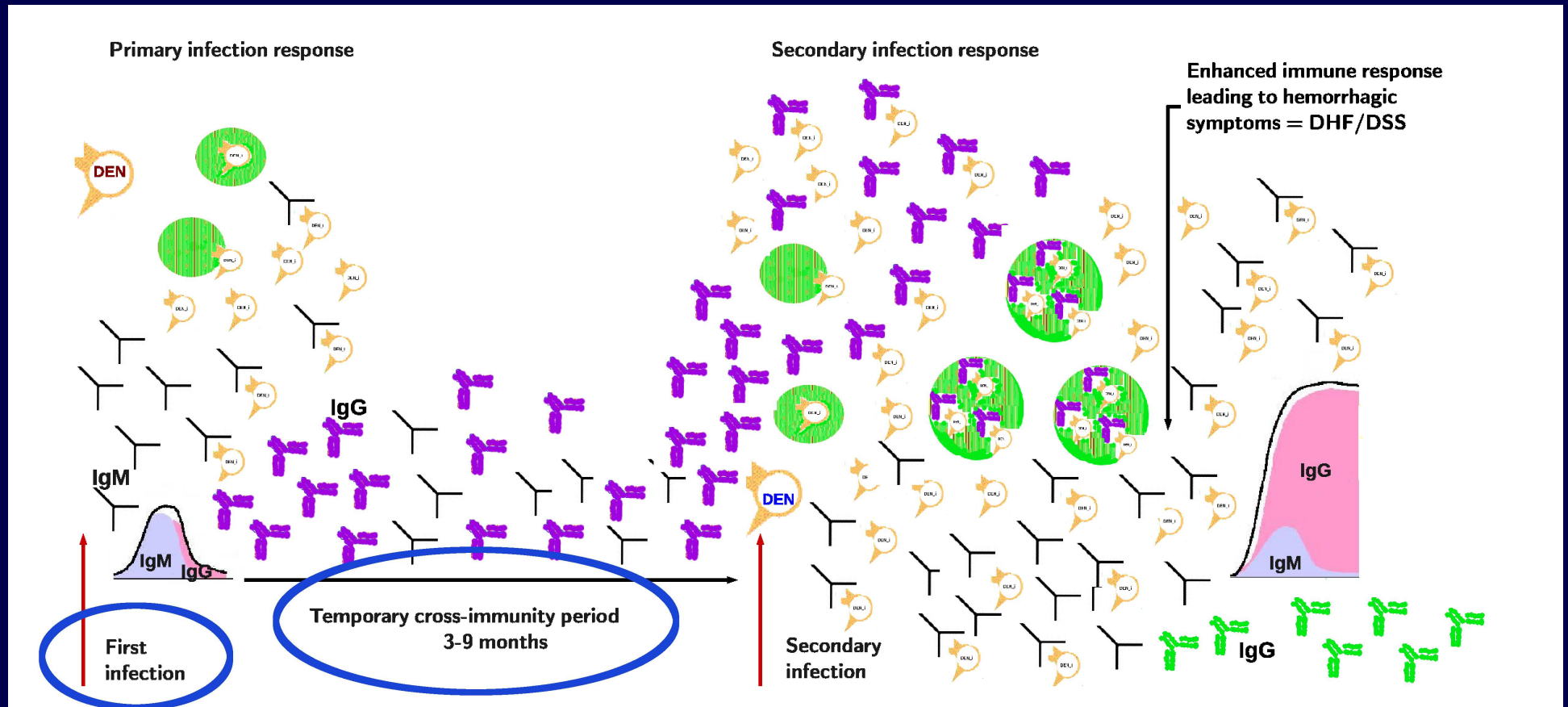
## *ADE in recurrent infections*





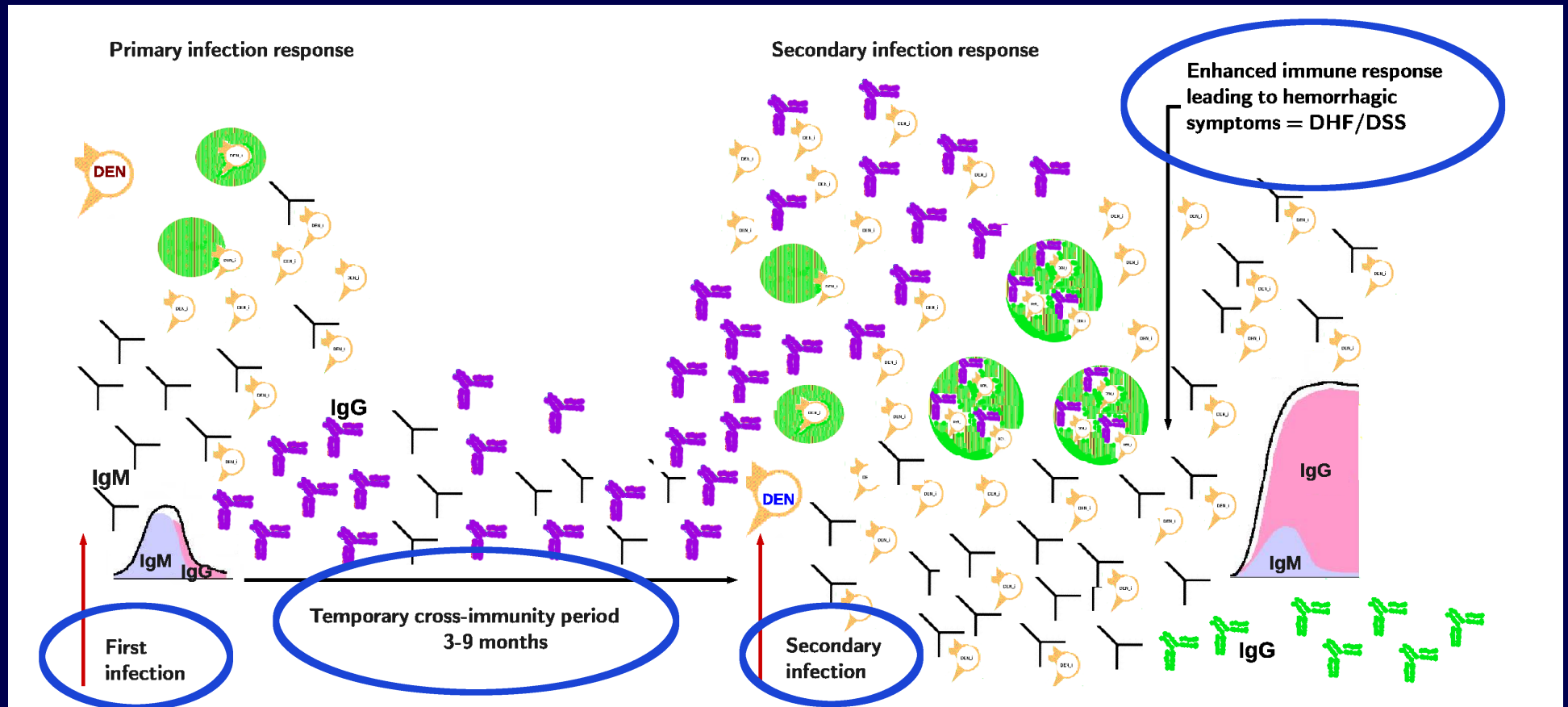
# Dengue fever epidemiology

## ADE in recurrent infections



# Dengue fever epidemiology

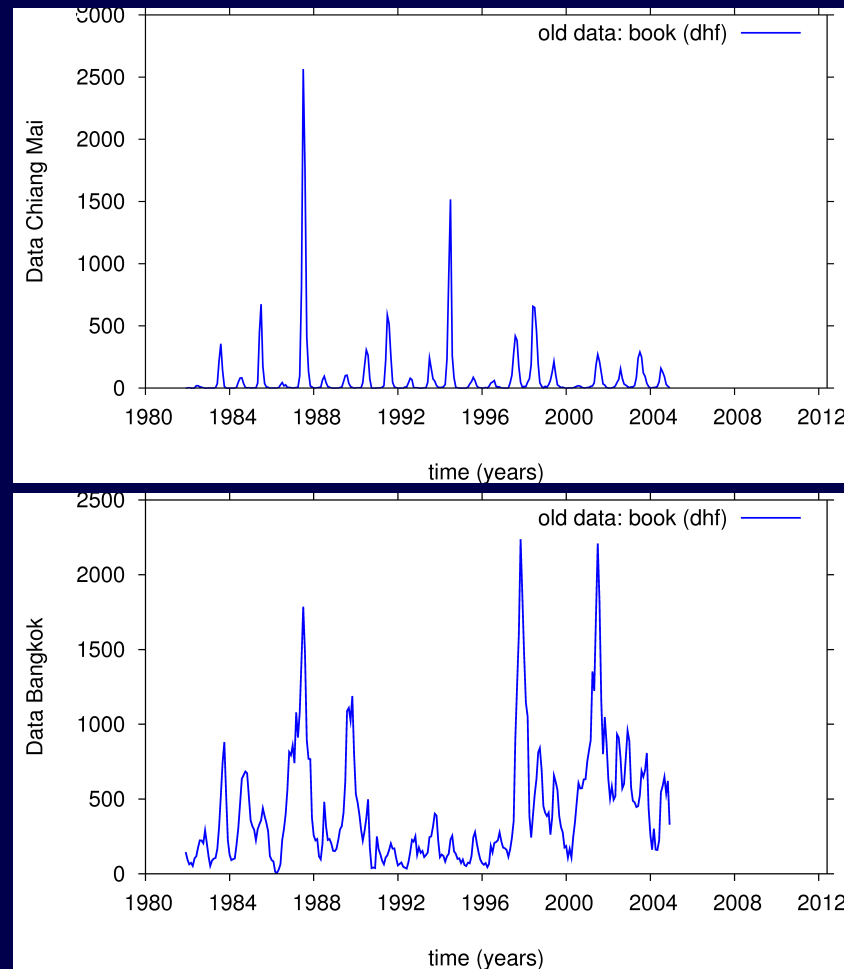
## ADE in recurrent infections



## *Dengue fever epidemiology*

- ✧ It is suggested that the majority of secondary dengue infections occur at a spacing of more than 6 months.*
- ✧ There is no specific treatment for DF, and DHF cases require hospitalization.*
- ✧ A vaccine is not yet available. Some of the candidates are in different stages of trials but so far, prevention of exposure remains the only alternative to prevent dengue transmission.*

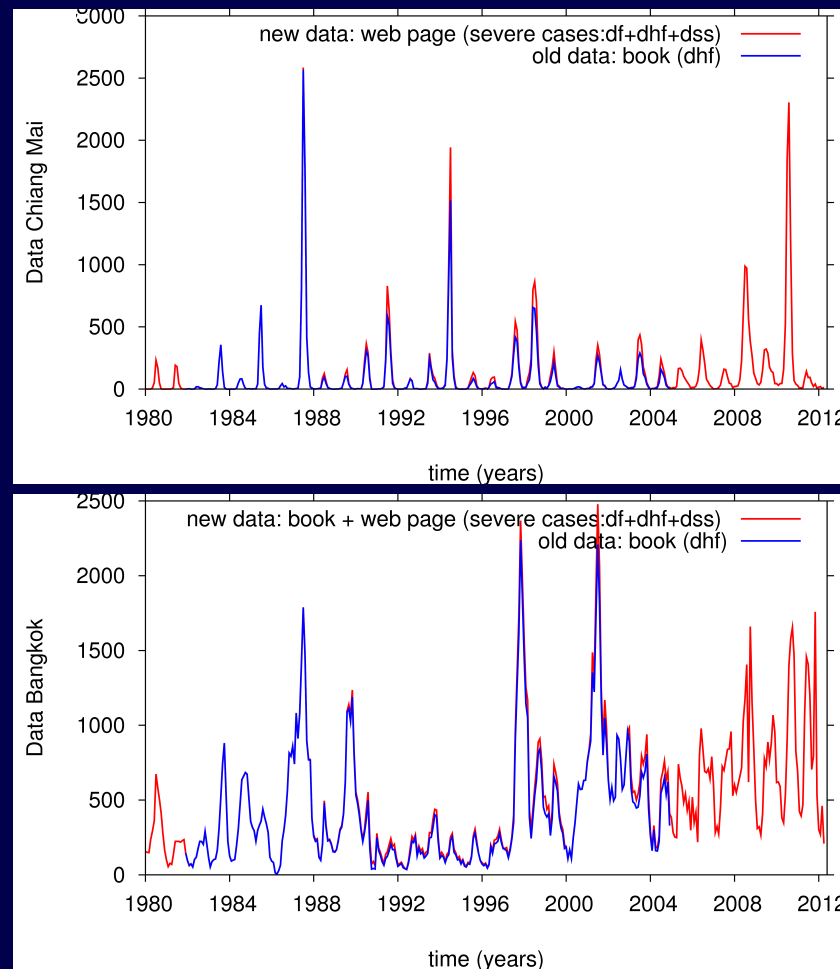
# *Dengue fever notification data in Thailand*



*Source: Ministry of Public Health, Thailand. Bureau of Epidemiology (2012)*

*Note the yearly fluctuations.*

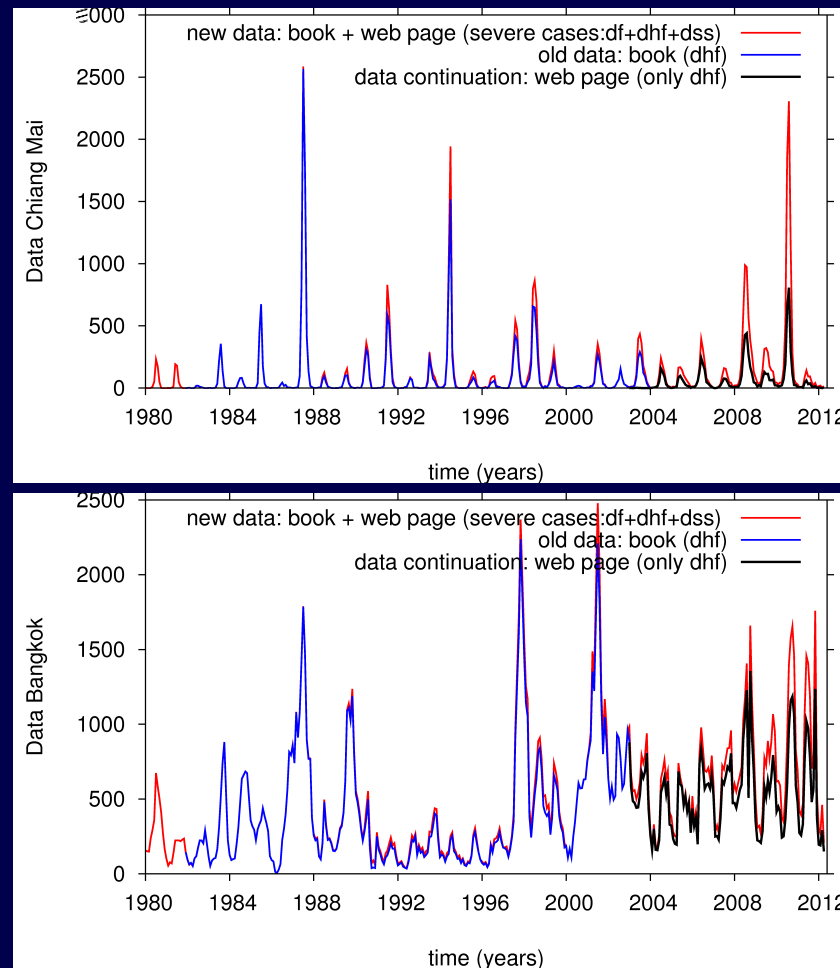
# *Dengue fever notification data in Thailand*



*DENFREE EU project under FP7:*

*Dengue Research Framework for Resisting Epidemics in Europe*

# *Dengue fever notification data in Thailand*

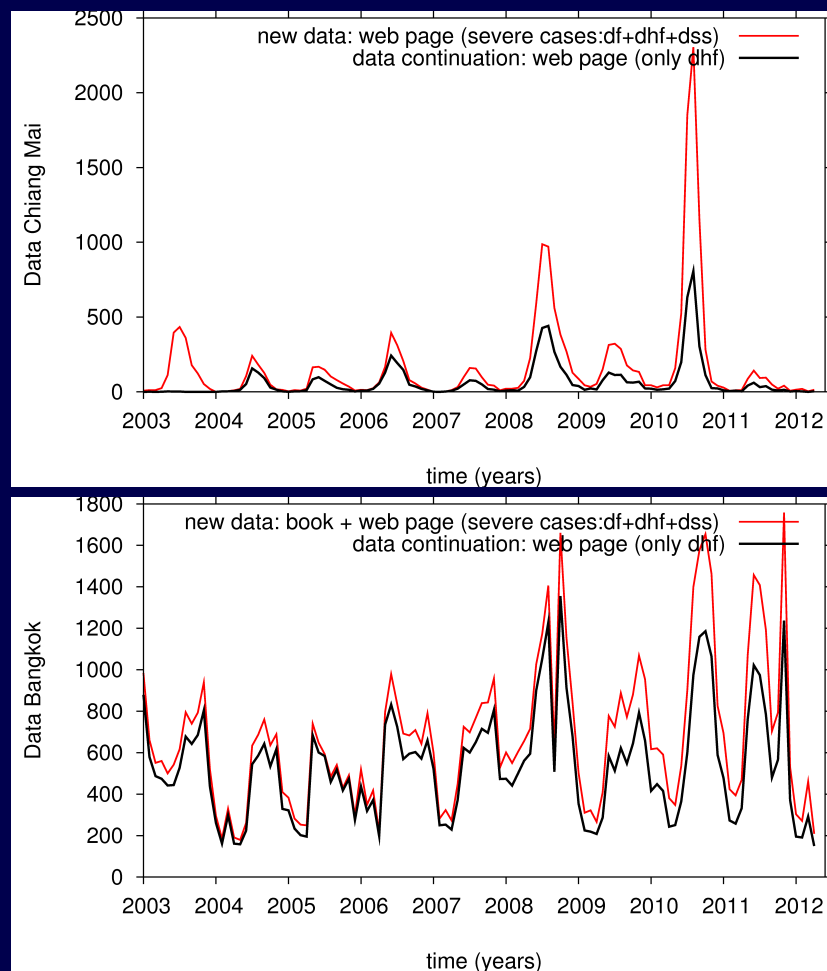


*DENFREE EU project under FP7:*

*The continuation of the data does not match!*



# *Dengue fever notification data in Thailand*



*DENFREE EU project under FP7:*

*Official data is the sum up of “severe cases” ( $DF+DHF+DSS$ )!*

# *Modeling dengue fever epidemiology*

$\beta$  - Infection rate

$\phi$  - Second. infection contribution  
to the force of infection (*ADE ratio*)

$\alpha$  - Cross-immunity period

$\gamma$  - Recovery rate

$\mu$  - Demographic rate

# Modeling dengue fever epidemiology

## The $n$ -strain epidemiological model

$$\dot{S} = \mu (N - S) - \sum_{i=1}^n \frac{\beta}{N} S \left( I_i + \rho \cdot N + \phi \left( \sum_{j=1, j \neq i}^n I_{ji} \right) \right)$$

and for  $i = 1, \dots, n$

$$\dot{I}_i = \frac{\beta}{N} \left( I_i + \rho \cdot N + \phi \left( \sum_{j=1, j \neq i}^n I_{ji} \right) \right) - (\gamma + \mu) I_i$$

$$\dot{R}_i = \gamma I_i - (\alpha + \mu) R_i$$

$$\dot{S}_i = \alpha R_i - \sum_{j=1, j \neq i}^n \frac{\beta}{N} S_i \left( I_j + \rho \cdot N + \phi \left( \sum_{k=1, k \neq j}^n I_{kj} \right) \right) - \mu S_i$$

and for  $i = 1, \dots, n$  and  $j = 1, \dots, n$  with  $j \neq i$

$$\dot{I}_{ij} = \frac{\beta}{N} S_i \left( I_j + \rho \cdot N + \phi \left( \sum_{k=1, k \neq j}^n I_{kj} \right) \right) - (\gamma + \mu) I_{ij}$$

and finally

$$\dot{R} = \gamma \left( \sum_{i=1}^n \sum_{j=1, j \neq i}^n I_{ij} \right) - \mu R$$

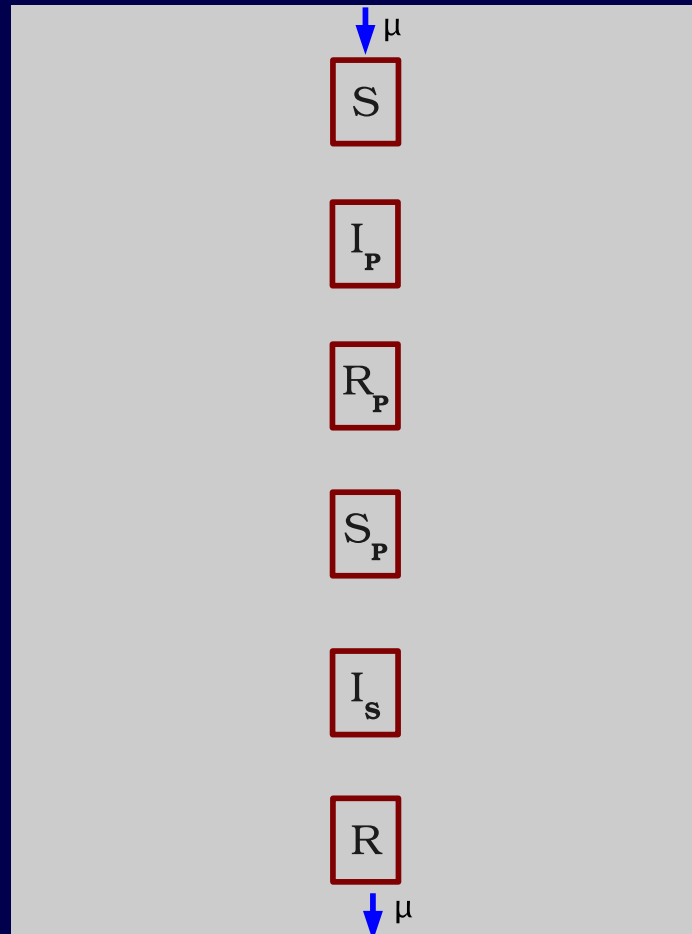
## *Modeling dengue fever epidemiology*

*The n-strain epidemiological model can be written as:*

- ✧ One-strain epidemiological model, an Eq. system with 6 ODE's*
- ✧ One-strain epidemiological + vector, an Eq. system with 8 ODE's*
- ✧ Two-strain epidemiological model, an Eq. system with 10 ODE's*
- ✧ Four-strain epidemiological model, an Eq. system with 26 ODE's*

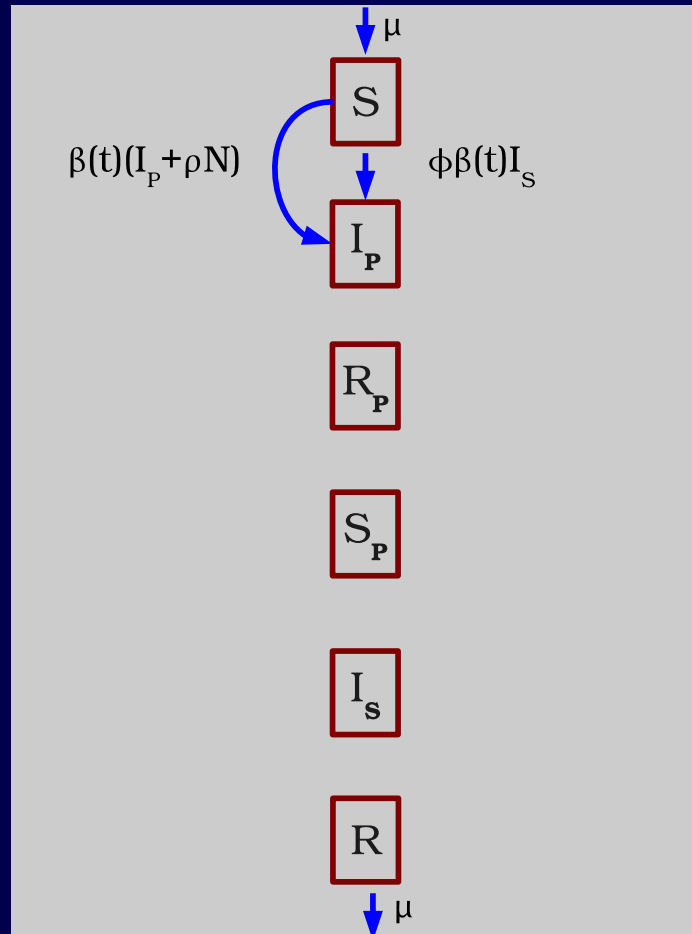
# *Modeling dengue fever epidemiology*

*The two-infections model  
without strain structure of the pathogens*



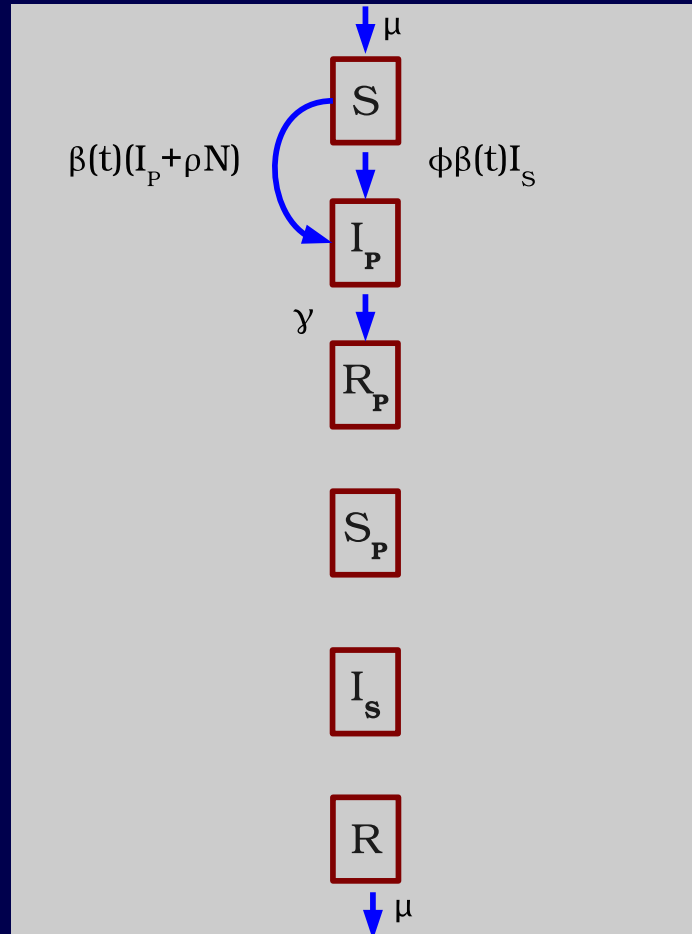
# *Modeling dengue fever epidemiology*

## *The two-infections model without strain structure of the pathogens*



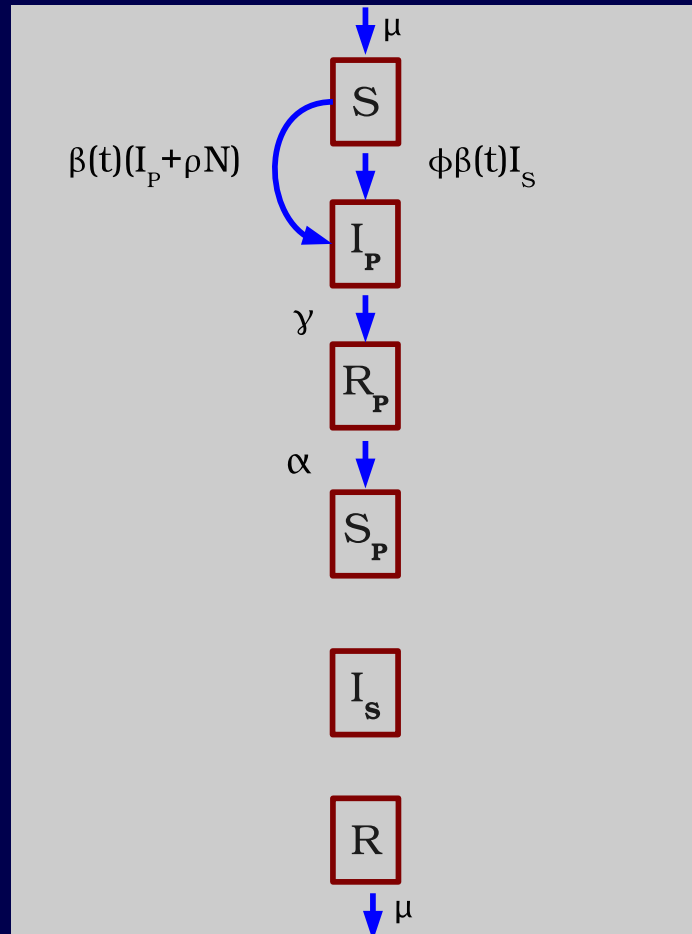
# *Modeling dengue fever epidemiology*

## *The two-infections model without strain structure of the pathogens*



# *Modeling dengue fever epidemiology*

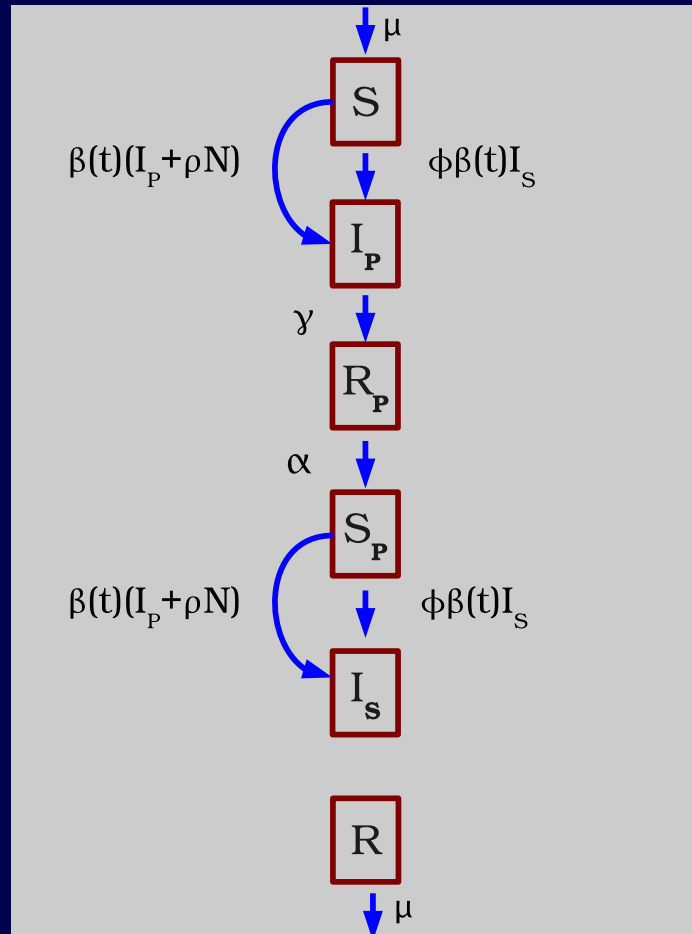
## *The two-infections model without strain structure of the pathogens*





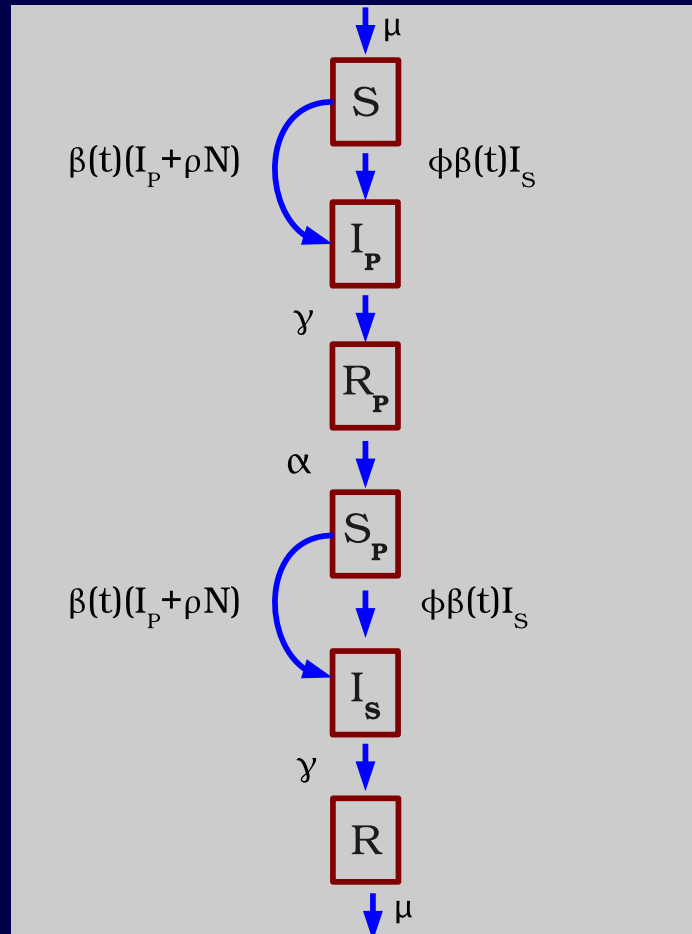
# *Modeling dengue fever epidemiology*

## *The two-infections model without strain structure of the pathogens*



# *Modeling dengue fever epidemiology*

## *The two-infections model without strain structure of the pathogens*



# *Modeling dengue fever epidemiology*

## *The two-infections model*

*without strain structure of the pathogens*

$$\dot{S} = -\frac{\beta(t)}{N}S(I_P + \rho \cdot N + \phi I_S) + \mu(N - S)$$

$$\dot{I}_P = \frac{\beta(t)}{N}S(I_P + \rho \cdot N + \phi I_S) - (\gamma + \mu)I_P$$

$$\dot{R}_P = \gamma I_P - (\alpha + \mu)R_P$$

(1)

$$\dot{S}_P = -\frac{\beta(t)}{N}S_P(I_P + \rho \cdot N + \phi I_S) + R_P\alpha - S_P\mu$$

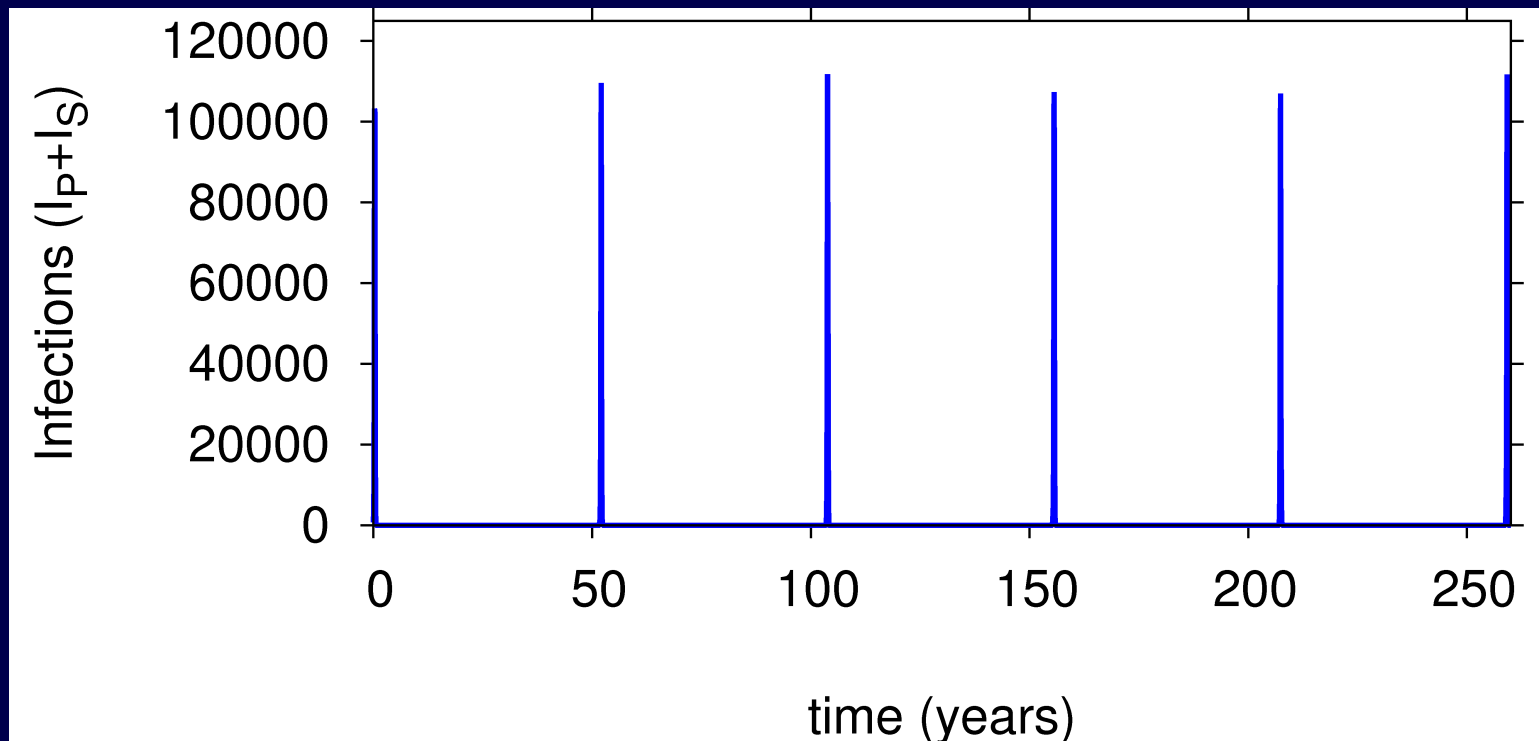
$$\dot{I}_S = \frac{\beta(t)}{N}S_P(I_P + \rho \cdot N + \phi I_S) - (\gamma + \mu)I_S$$

$$\dot{R} = \gamma I_S - \mu R$$

# *Modeling dengue fever epidemiology*

## *The two-infections model*

*without strain structure of the pathogens*



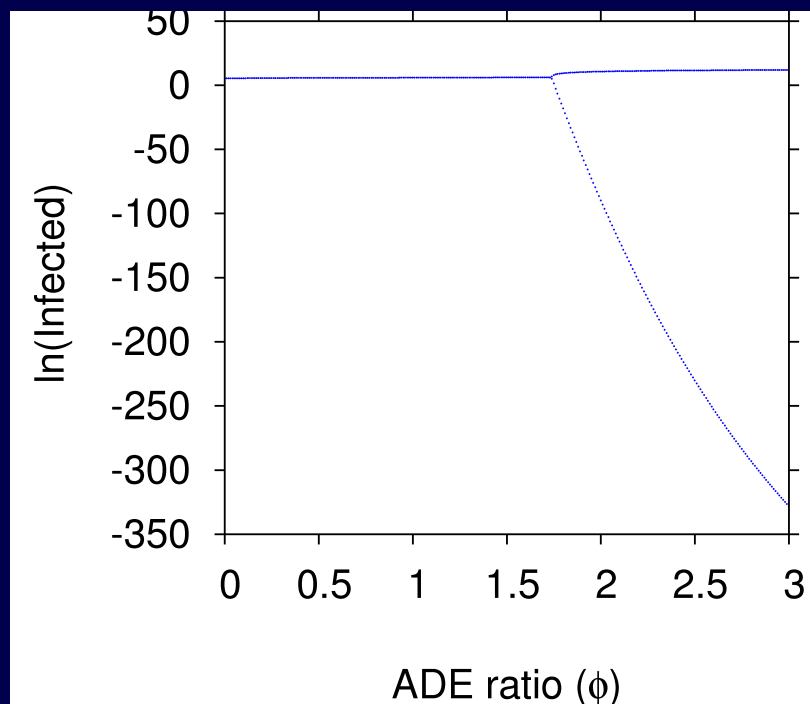
*( $\phi=2.6$ )*

*Outbreaks every 50 years.*

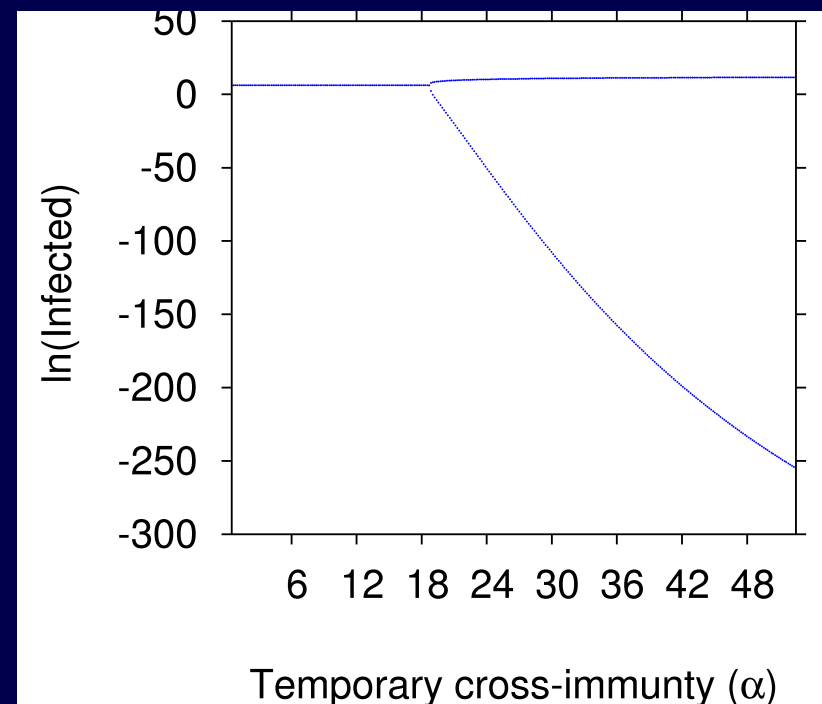
# *Modeling dengue fever epidemiology*

## *The two-infections model without strain structure of the pathogens*

*Bifurcation diagram for  $\alpha$  and  $\phi$*



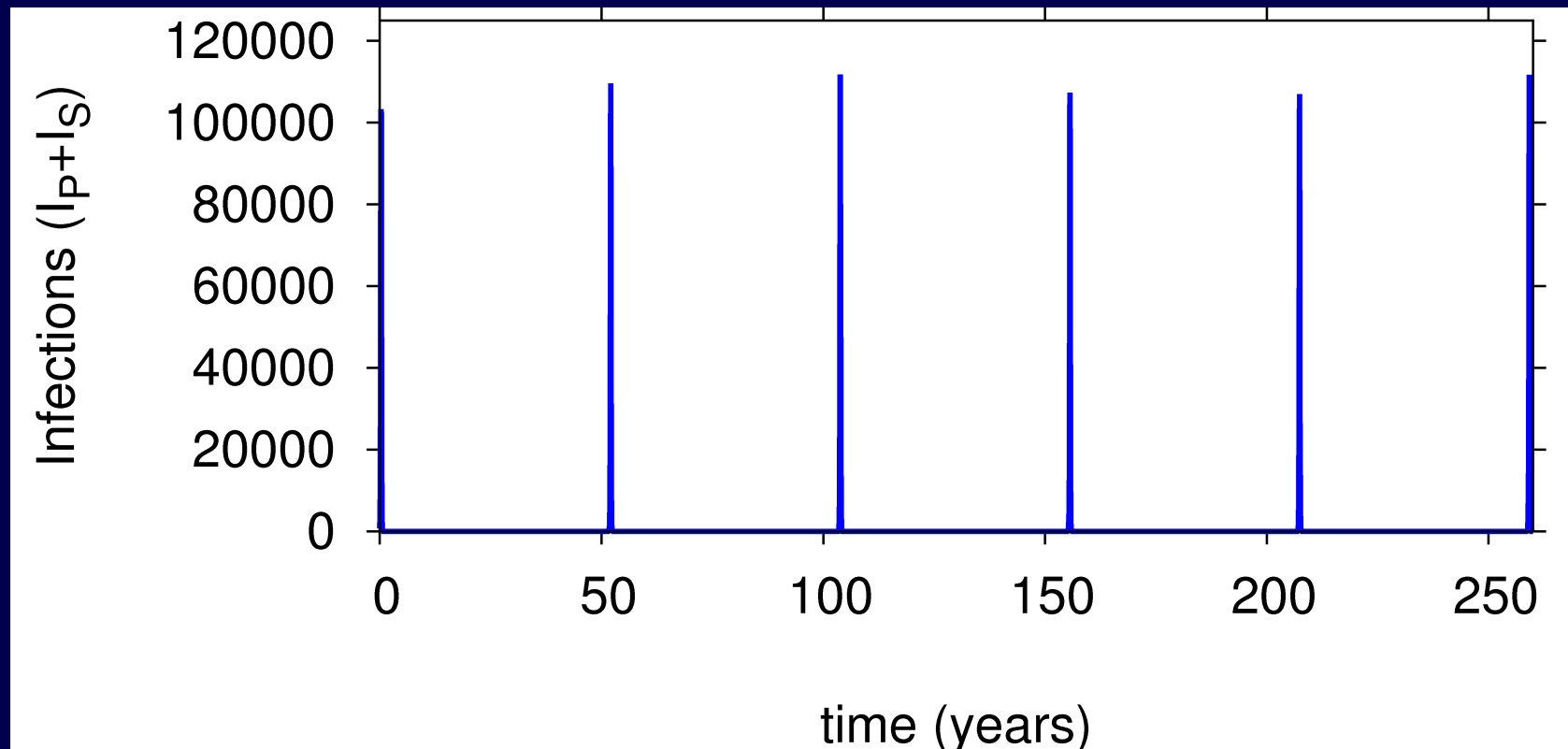
*( $\alpha=1/\text{one week}$ )*



*( $\phi=2.6$ )*

# *Modeling dengue fever epidemiology*

*The two-infections model  
without strain structure of the pathogens*

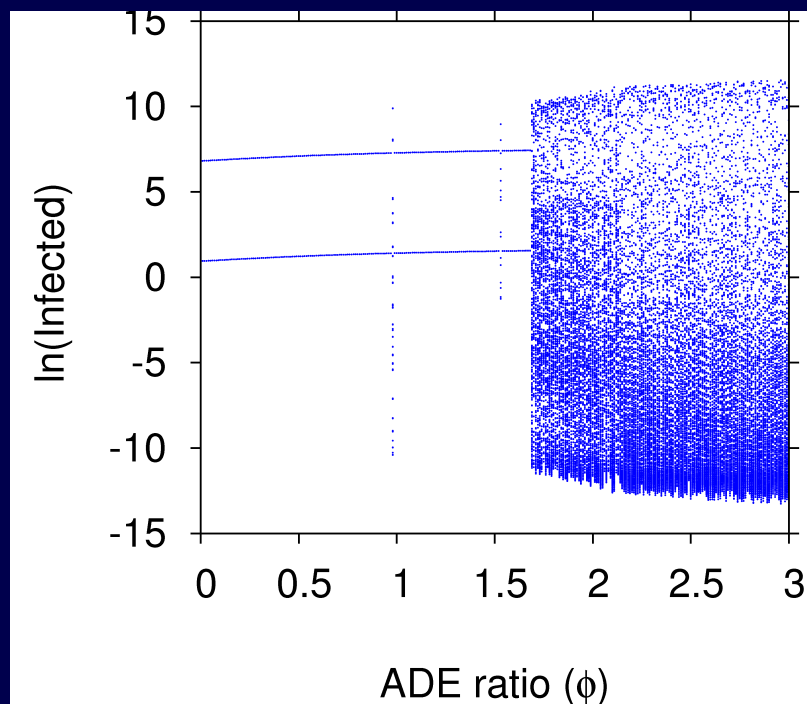


*Outbreaks every 50 years.*

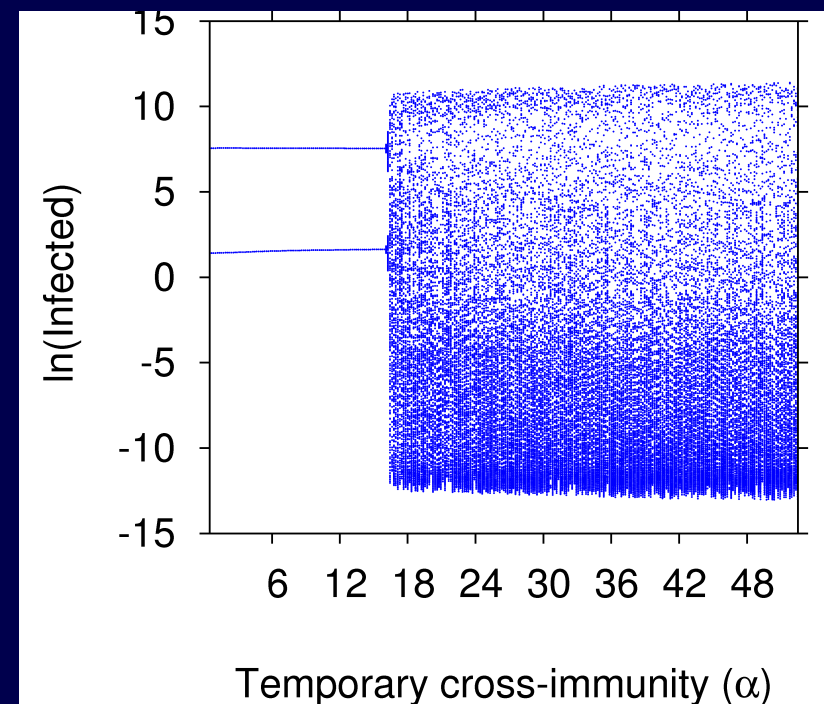
# Modeling dengue fever epidemiology

## *The two-infections model without strain structure of the pathogens*

*Bifurcation diagram for  $\alpha$  and  $\phi$*



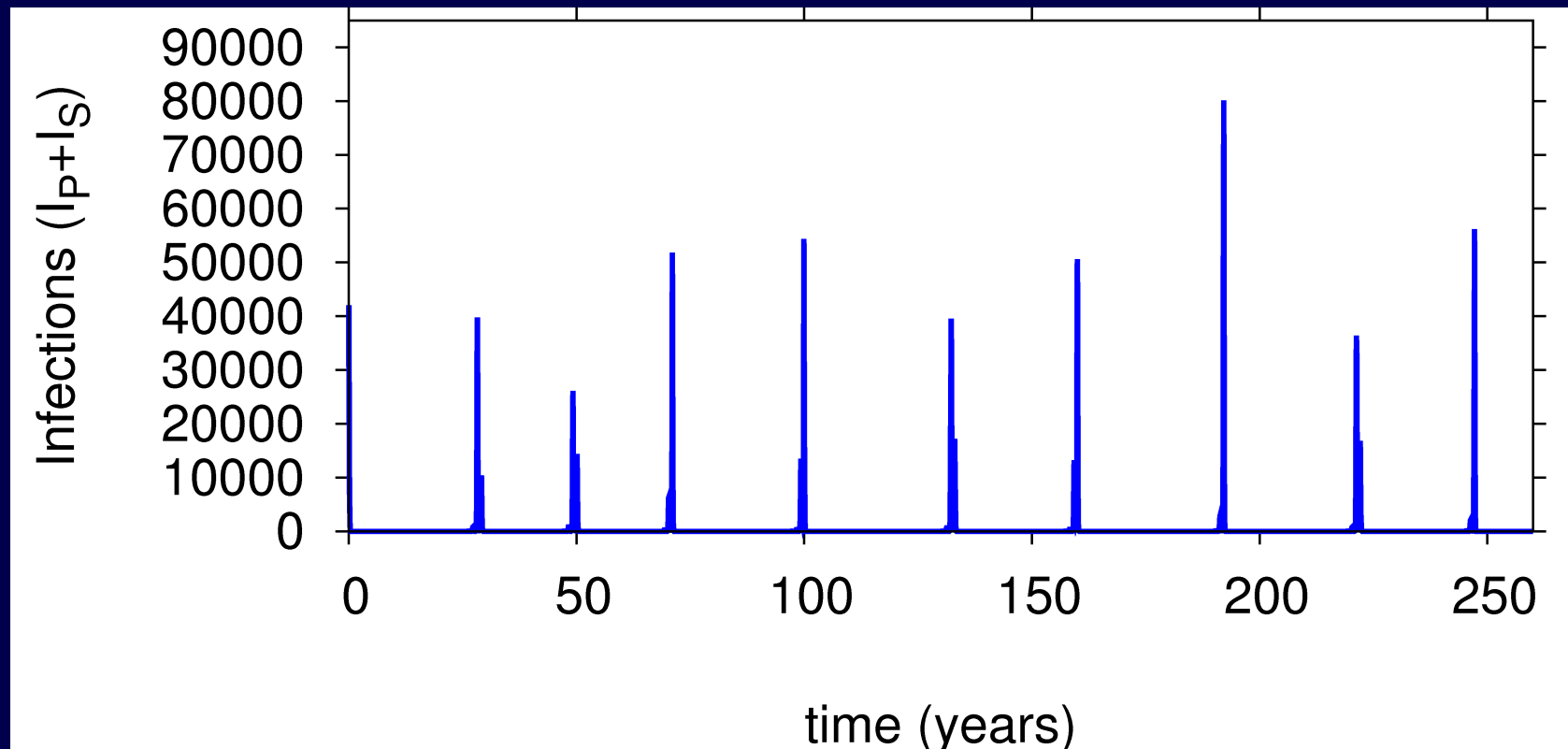
*( $\alpha=1/\text{one week}$ )*



*( $\phi=2.6$ )*

# *Modeling dengue fever epidemiology*

*The two-infections model  
without strain structure of the pathogens*

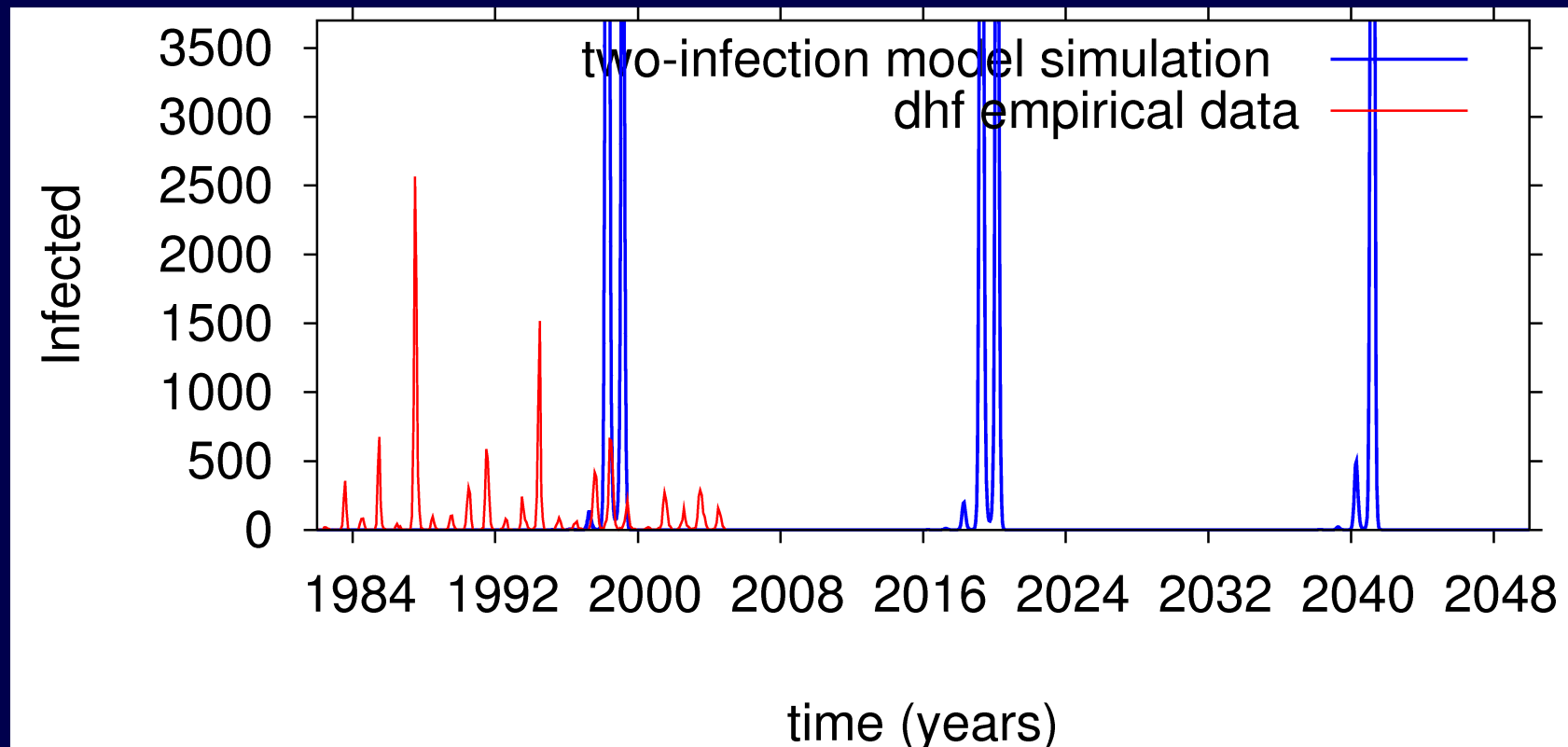


*Irregular outbreaks every 25 years...*



# *Modeling dengue fever epidemiology*

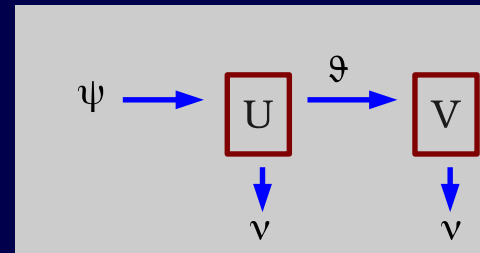
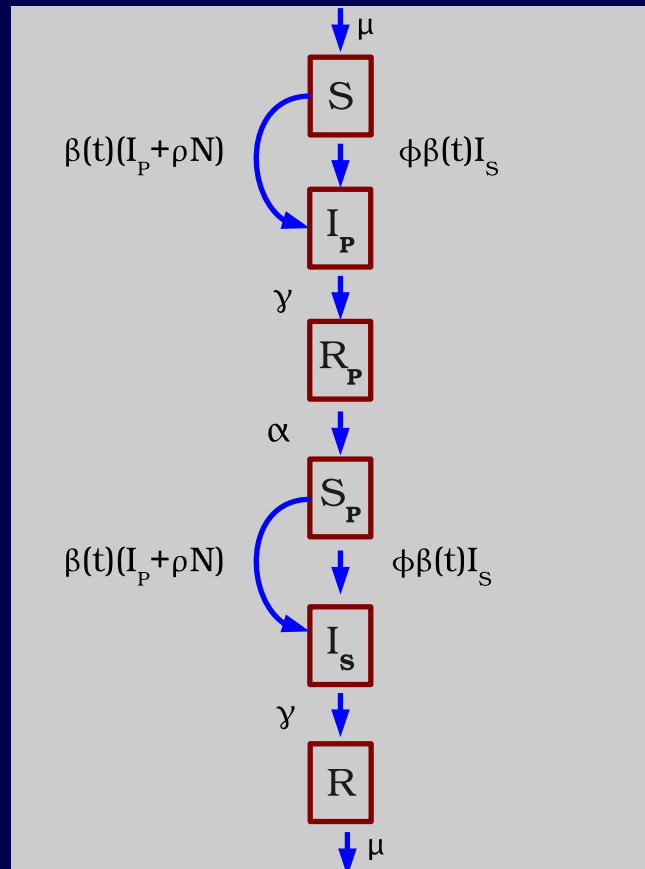
*The two-infections model  
without strain structure of the pathogens*



*... and not data alike.*

# Modeling dengue fever epidemiology

## *The two-infections model without strain structure of the pathogens*



# *Modeling dengue fever epidemiology*

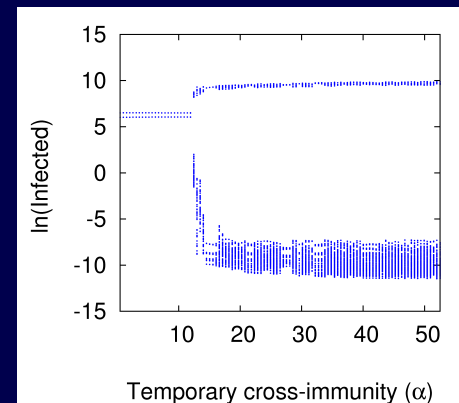
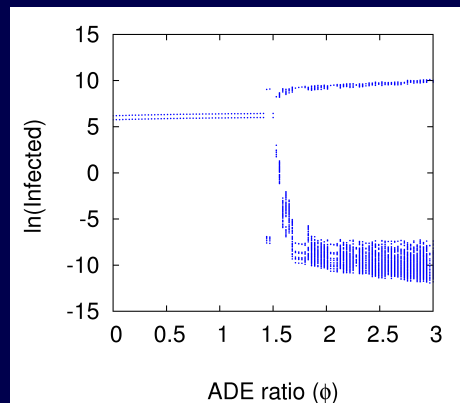
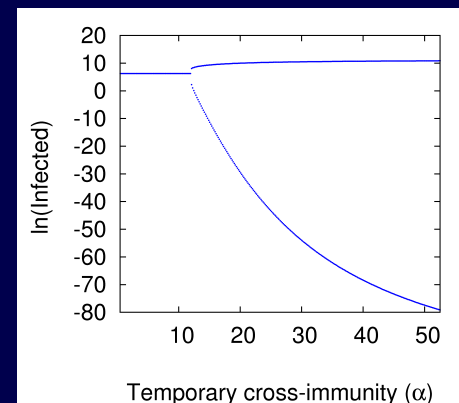
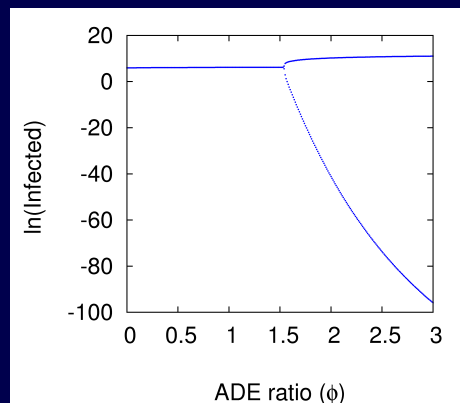
## *The two-infections model without strain structure of the pathogens*

$$\begin{aligned}\dot{S} &= -\frac{\beta}{M_0}SV + \mu(N - S) \\ \dot{I}_P &= \frac{\beta}{M_0}SV - (\gamma + \mu)I_P \\ \dot{R}_P &= \gamma I_P - (\alpha + \mu)R_P \\ \dot{S}_P &= -\frac{\beta}{M_0}S_PV + R_P\alpha - S_P\mu \\ \dot{I}_S &= \frac{\beta}{M_0}S_PV - (\gamma + \mu)I_S \\ \dot{R} &= \gamma I_S - \mu R \\ \dot{U} &= \psi - \frac{\theta}{N}(M(t) - V)(I_P + \rho \cdot N + \phi I_S) - \nu U \\ \dot{V} &= \frac{\theta}{N}(M(t) - V)(I_P + \rho \cdot N + \phi I_S) - \nu V\end{aligned}\tag{2}$$

# Modeling dengue fever epidemiology

## *The two-infections model without strain structure of the pathogens*

*Bifurcation diagram for  $\alpha$  and  $\phi$*

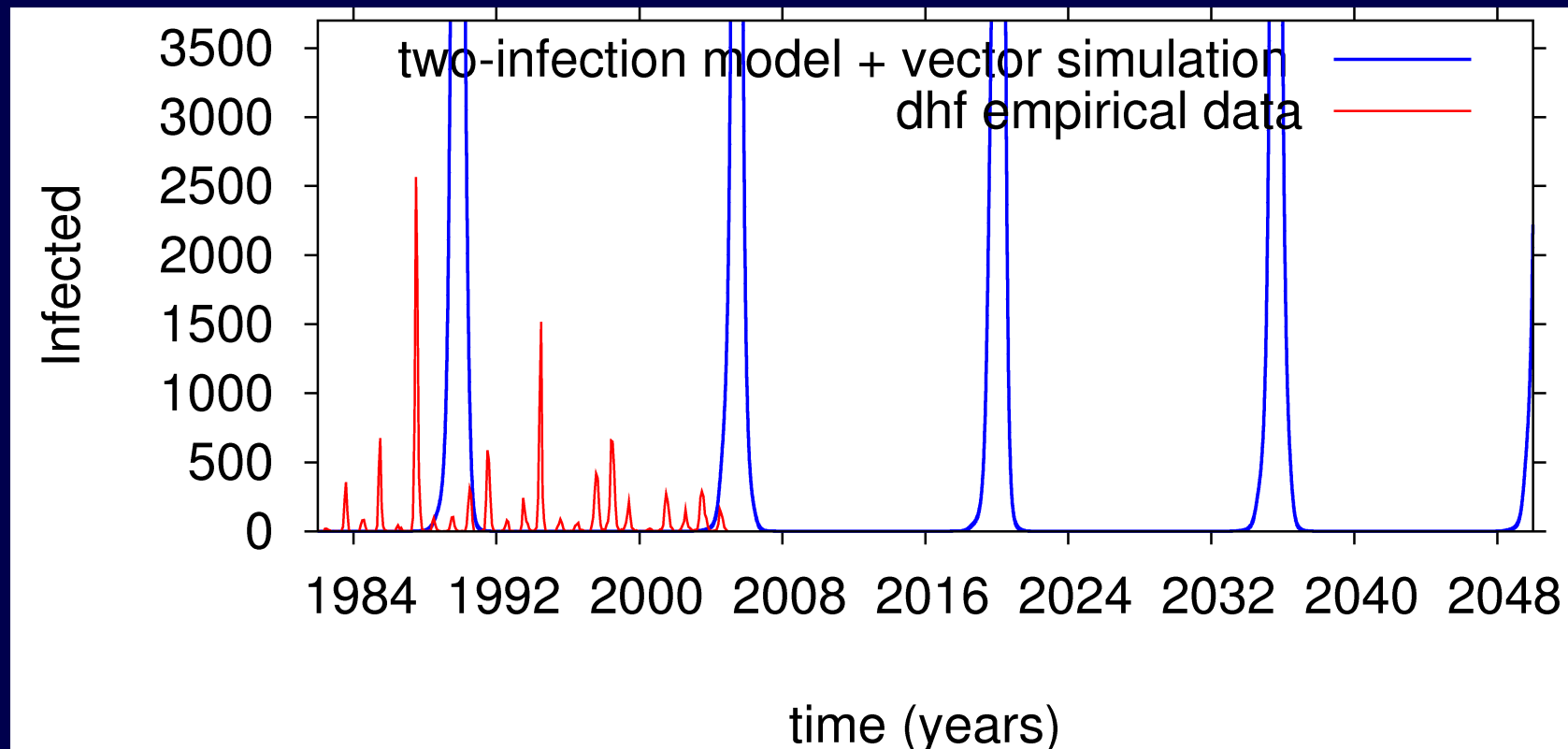


*( $\alpha = 1/\text{one week}$ )*

*( $\phi = 2.6$ )*

# *Modeling dengue fever epidemiology*

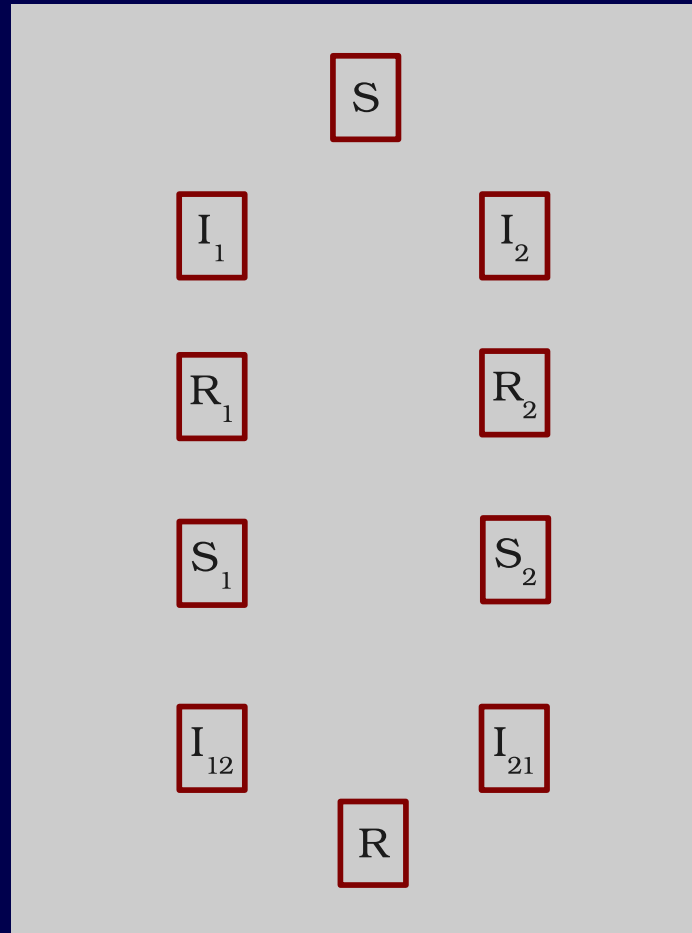
*The seasonal two-infections model  
without strain structure of the pathogens*



*Also not data alike.*

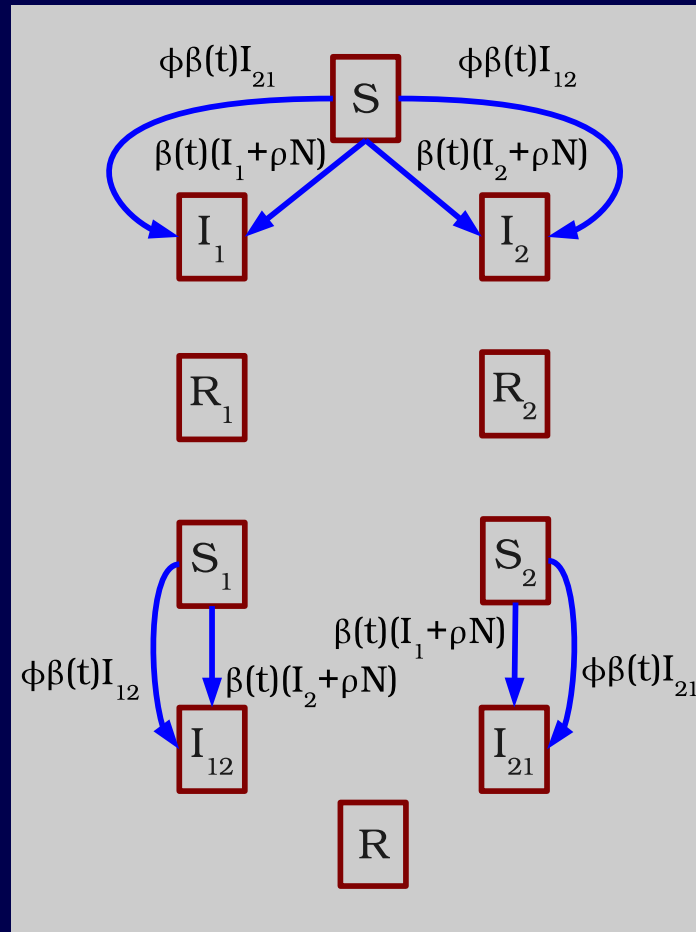
# *Modeling dengue fever epidemiology*

*The two-strain model  
with strain structure of the pathogens*



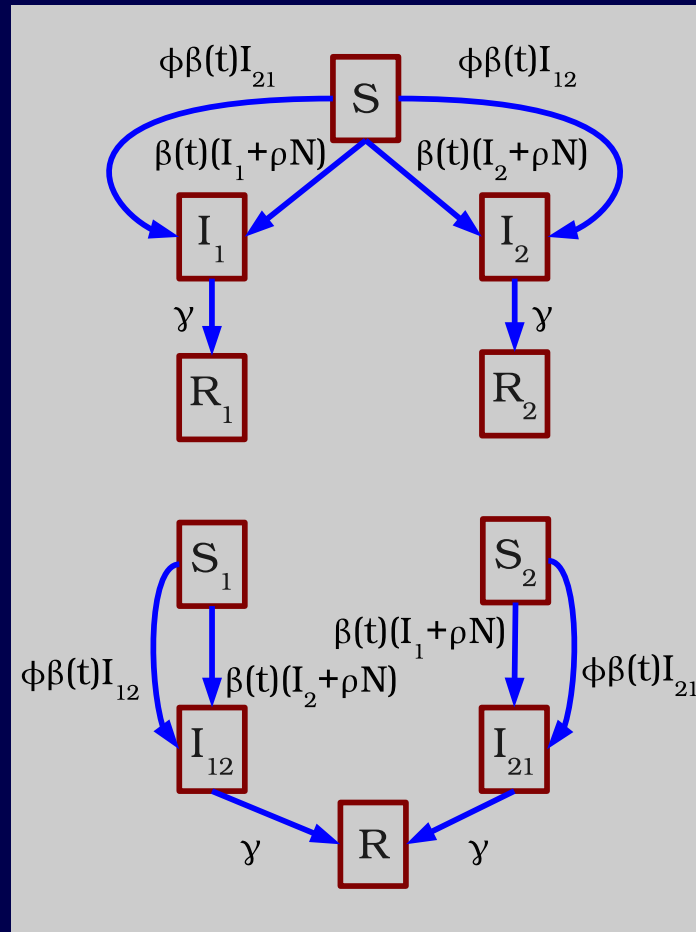
# Modeling dengue fever epidemiology

## *The two-strain model with strain structure of the pathogens*



# Modeling dengue fever epidemiology

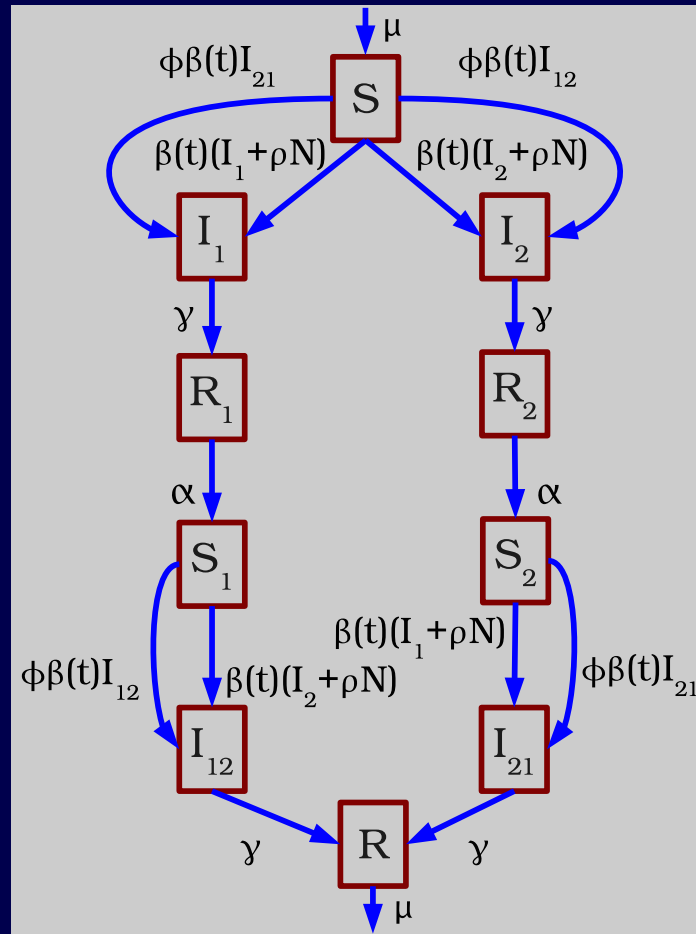
## *The two-strain model with strain structure of the pathogens*





# Modeling dengue fever epidemiology

## *The two-strain model with strain structure of the pathogens*



# *Modeling dengue fever epidemiology*

## *The two-strain model*

*with strain structure of the pathogens*

$$\dot{S} = -\frac{\beta(t)}{N}S(I_1 + \rho \cdot N + \phi I_{21}) - \frac{\beta(t)}{N}S(I_2 + \rho \cdot N + \phi I_{12}) + \mu(N - S)$$

$$\dot{I}_1 = \frac{\beta(t)}{N}S(I_1 + \rho \cdot N + \phi I_{21}) - (\gamma + \mu)I_1$$

$$\dot{I}_2 = \frac{\beta(t)}{N}S(I_2 + \rho \cdot N + \phi I_{12}) - (\gamma + \mu)I_2$$

$$\dot{R}_1 = \gamma I_1 - (\alpha + \mu)R_1$$

$$\dot{R}_2 = \gamma I_2 - (\alpha + \mu)R_2$$

$$\dot{S}_1 = -\frac{\beta(t)}{N}S_1(I_2 + \rho \cdot N + \phi I_{12}) + \alpha R_1 - \mu S_1$$

$$\dot{S}_2 = -\frac{\beta(t)}{N}S_2(I_1 + \rho \cdot N + \phi I_{21}) + \alpha R_2 - \mu S_2$$

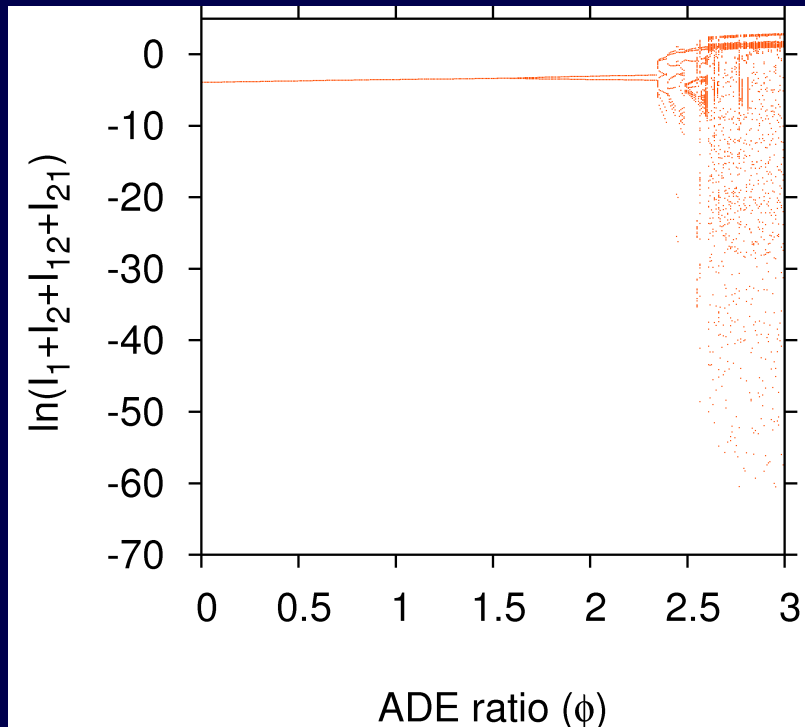
$$\dot{I}_{12} = \frac{\beta(t)}{N}S_1(I_2 + \rho \cdot N + \phi I_{12}) - (\gamma + \mu)I_{12}$$

$$\dot{I}_{21} = \frac{\beta(t)}{N}S_2(I_1 + \rho \cdot N + \phi I_{21}) - (\gamma + \mu)I_{21}$$

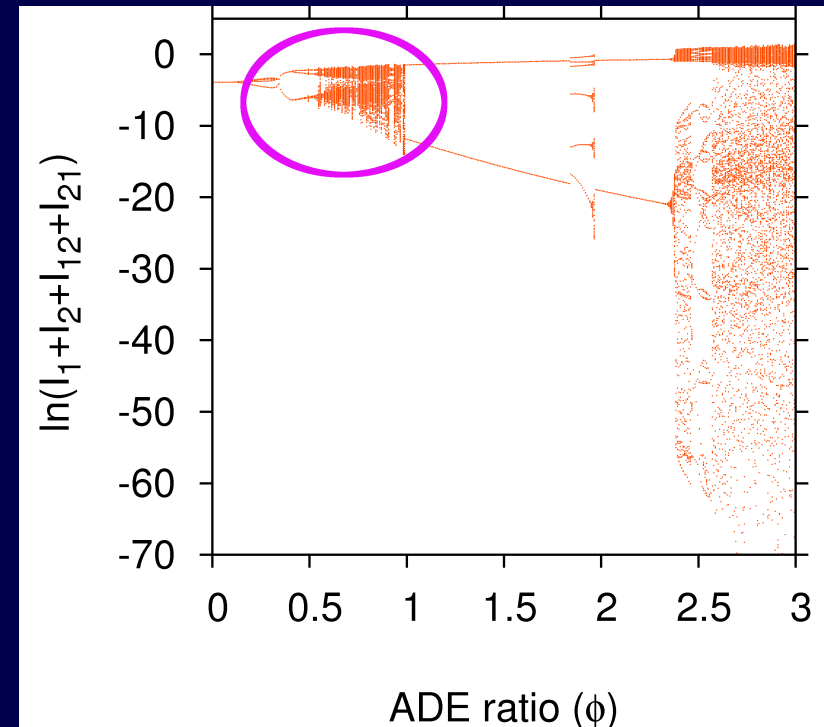
$$\dot{R} = \gamma(I_{12} + I_{21}) - \mu R$$

# Modeling dengue fever epidemiology

## *The two-strain model with strain structure of the pathogens*



*( $\alpha=1/\text{one week}$ )*



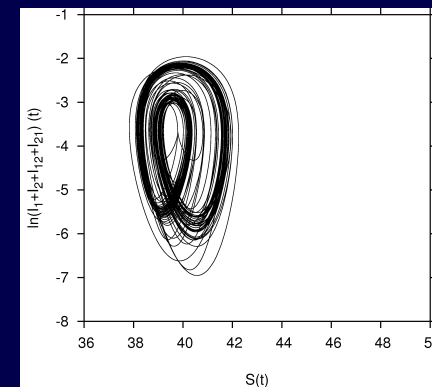
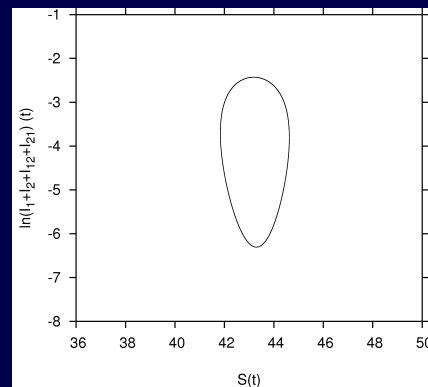
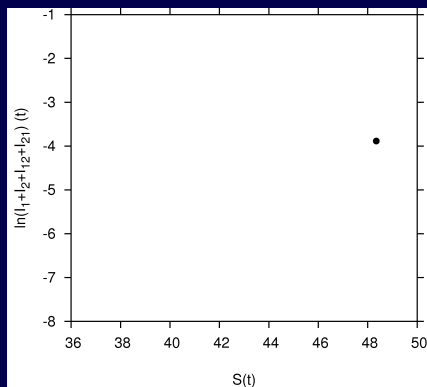
*( $\alpha=1/6 \text{ months}$ )*

*New chaotic window for  $\phi < 1$ !*

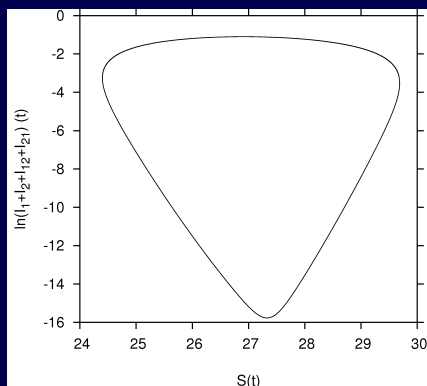
*More realistic due to hospitalization of the severe cases.*

# Modeling dengue fever epidemiology

## The two-strain model with strain structure of the pathogens

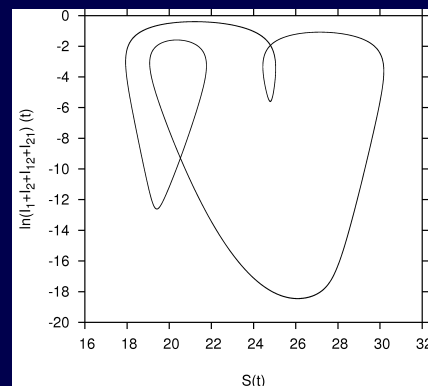


$\phi = 0.1$



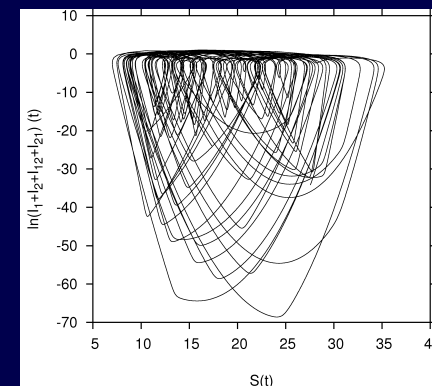
$\phi = 1.5$

$\phi = 0.4$



$\phi = 1.9$

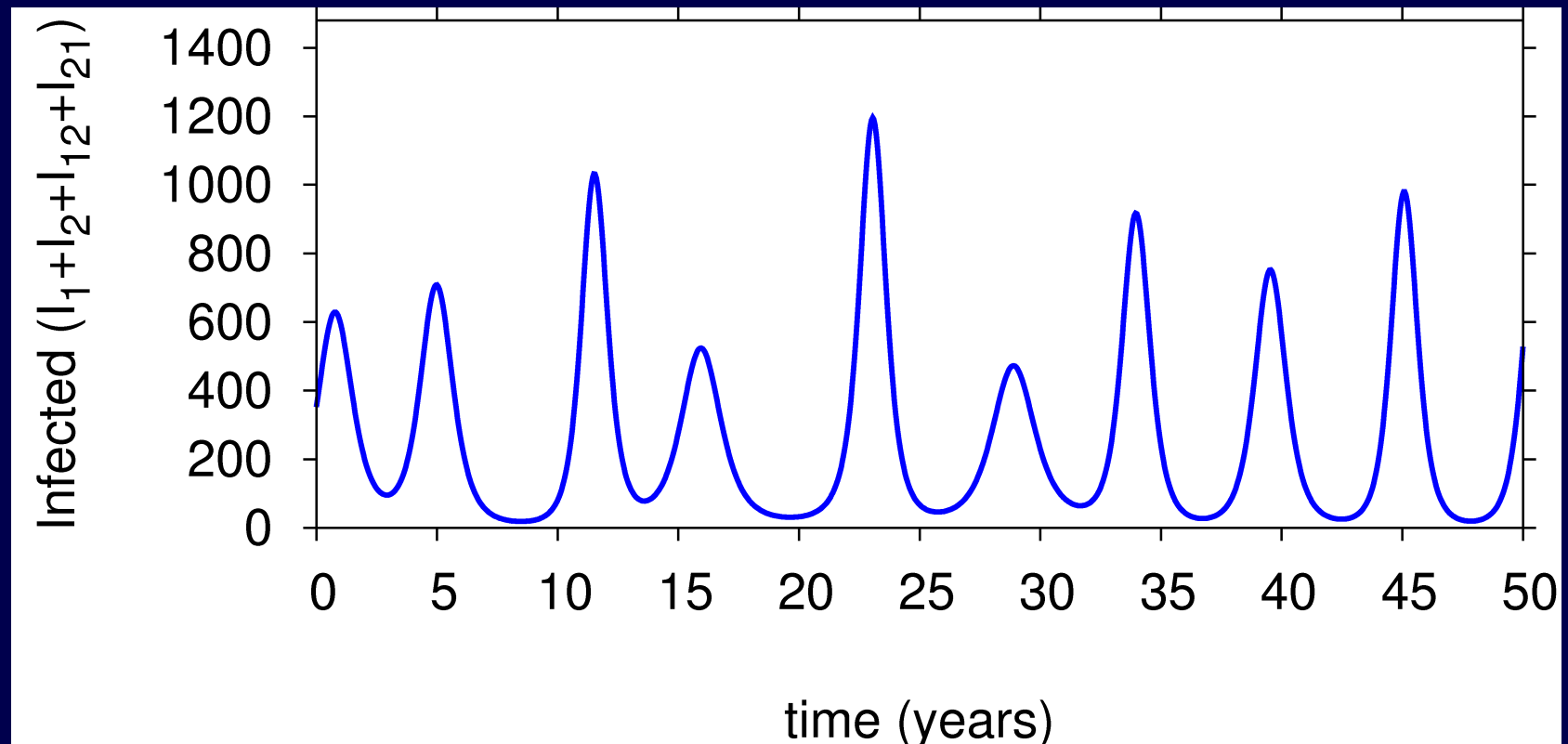
$\phi = 0.6$



$\phi = 2.7$

# *Modeling dengue fever epidemiology*

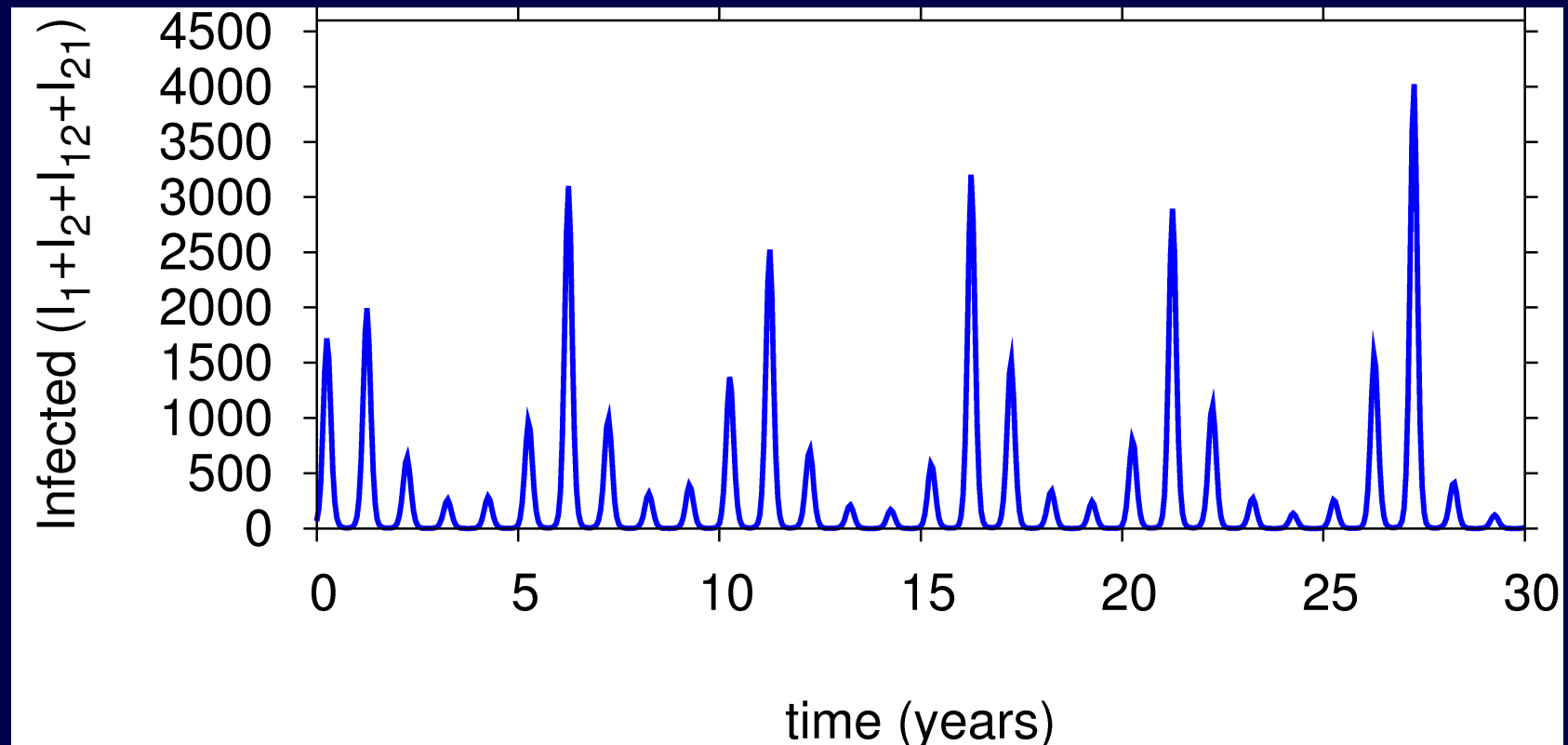
*The two-strain model  
with strain structure of the pathogens*



*Irregular pattern every 5 years.*

# *Modeling dengue fever epidemiology*

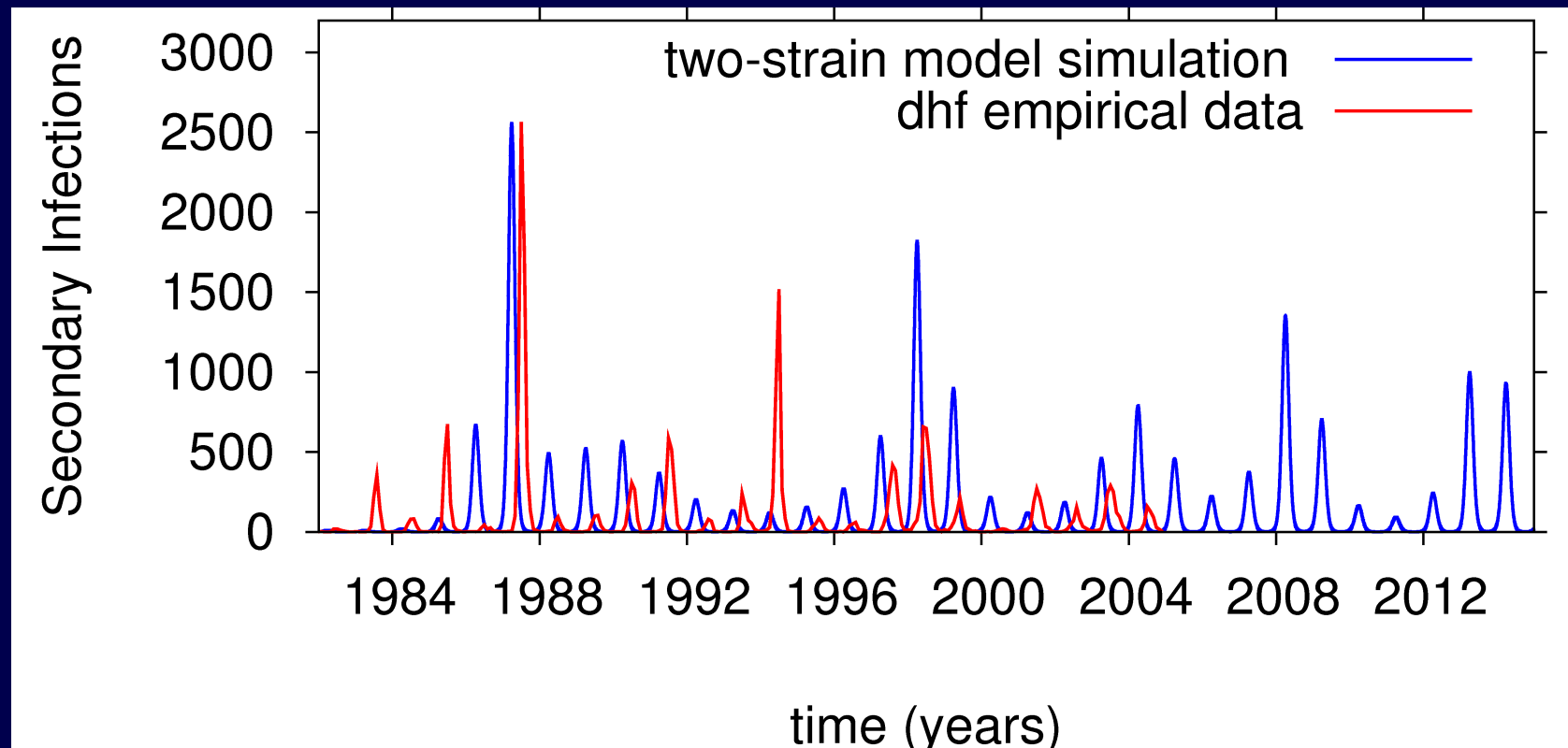
*The seasonal two-strain model  
with strain structure of the pathogens*



*Realistic pattern with irregular, yearly and smooth outbreaks.*

# *Modeling dengue fever epidemiology*

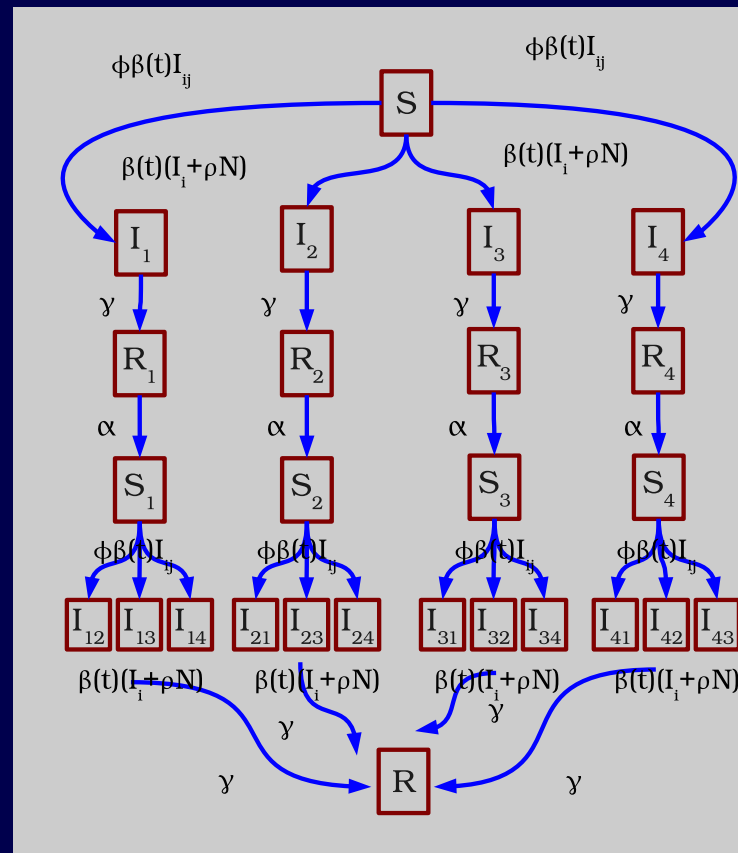
## *Implications for data analysis*



*Qualitatively a very good result when comparing empirical DHF data and model simulation.*

# Modeling dengue fever epidemiology

## The four-strain model with strain structure of the pathogens





# Modeling dengue fever epidemiology

## The four-strain model with strain structure of the pathogens

$$\dot{S} = \mu(N - S) \quad (\text{A.1})$$

$$\begin{aligned} & - \frac{\beta}{N} S(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) \\ & - \frac{\beta}{N} S(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) \\ & - \frac{\beta}{N} S(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) \\ & - \frac{\beta}{N} S(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) \end{aligned}$$

$$\dot{I}_1 = \frac{\beta}{N} S(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) - (\gamma + \mu)I_1 \quad (\text{A.2})$$

$$\dot{I}_2 = \frac{\beta}{N} S(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) - (\gamma + \mu)I_2 \quad (\text{A.3})$$

$$\dot{I}_3 = \frac{\beta}{N} S(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) - (\gamma + \mu)I_3 \quad (\text{A.4})$$

$$\dot{I}_4 = \frac{\beta}{N} S(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - (\gamma + \mu)I_4 \quad (\text{A.5})$$

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$$\dot{R}_1 = \gamma I_1 - (\alpha + \mu)R_1 \quad (\text{A.6})$$

$$\dot{R}_2 = \gamma I_2 - (\alpha + \mu)R_2 \quad (\text{A.7})$$

$$\dot{R}_3 = \gamma I_3 - (\alpha + \mu)R_3 \quad (\text{A.8})$$

$$\dot{R}_4 = \gamma I_4 - (\alpha + \mu)R_4 \quad (\text{A.9})$$

$$\dot{S}_1 = \alpha R_1 \quad (\text{A.10})$$

$$\begin{aligned} & - \frac{\beta}{N} S_1(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) \\ & - \frac{\beta}{N} S_1(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) \\ & - \frac{\beta}{N} S_1(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - \mu S_1 \end{aligned}$$

$$\dot{S}_2 = \alpha R_2 - \frac{\beta}{N} S_2(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) \quad (\text{A.11})$$

$$\begin{aligned} & - \frac{\beta}{N} S_2(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) \\ & - \frac{\beta}{N} S_2(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - \mu S_2 \end{aligned}$$

$$\dot{S}_3 = \alpha R_3 - \frac{\beta}{N} S_3(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) \quad (\text{A.12})$$

$$\begin{aligned} & - \frac{\beta}{N} S_3(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) \\ & - \frac{\beta}{N} S_3(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - \mu S_3 \end{aligned}$$

$$\dot{S}_4 = \alpha R_4 - \frac{\beta}{N} S_4(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) \quad (\text{A.13})$$

$$\begin{aligned} & - \frac{\beta}{N} S_4(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) \\ & - \frac{\beta}{N} S_4(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) - \mu S_4 \end{aligned}$$

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$$\dot{I}_{12} = \frac{\beta}{N} S_1(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) - (\gamma + \mu)I_{12} \quad (\text{A.14})$$

$$\dot{I}_{13} = \frac{\beta}{N} S_1(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) - (\gamma + \mu)I_{13} \quad (\text{A.15})$$

$$\dot{I}_{14} = \frac{\beta}{N} S_1(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - (\gamma + \mu)I_{14} \quad (\text{A.16})$$

$$\dot{I}_{21} = \frac{\beta}{N} S_2(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) - (\gamma + \mu)I_{21} \quad (\text{A.17})$$

$$\dot{I}_{23} = \frac{\beta}{N} S_2(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) - (\gamma + \mu)I_{23} \quad (\text{A.18})$$

$$\dot{I}_{24} = \frac{\beta}{N} S_2(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - (\gamma + \mu)I_{24} \quad (\text{A.19})$$

$$\dot{I}_{31} = \frac{\beta}{N} S_3(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) - (\gamma + \mu)I_{31} \quad (\text{A.20})$$

$$\dot{I}_{32} = \frac{\beta}{N} S_3(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) - (\gamma + \mu)I_{32} \quad (\text{A.21})$$

$$\dot{I}_{34} = \frac{\beta}{N} S_3(I_4 + \rho \cdot N + \phi(I_{14} + I_{24} + I_{34})) - (\gamma + \mu)I_{34} \quad (\text{A.22})$$

$$\dot{I}_{41} = \frac{\beta}{N} S_4(I_1 + \rho \cdot N + \phi(I_{21} + I_{31} + I_{41})) - (\gamma + \mu)I_{41} \quad (\text{A.23})$$

$$\dot{I}_{42} = \frac{\beta}{N} S_4(I_2 + \rho \cdot N + \phi(I_{12} + I_{32} + I_{42})) - (\gamma + \mu)I_{42} \quad (\text{A.24})$$

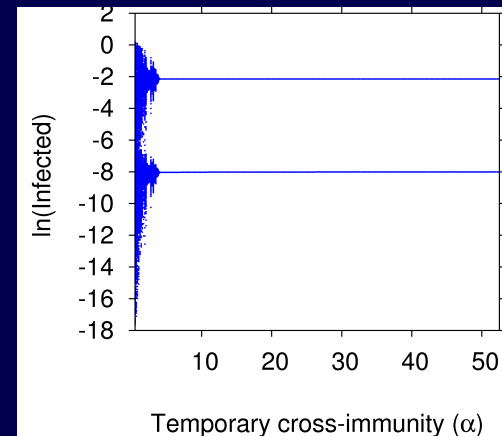
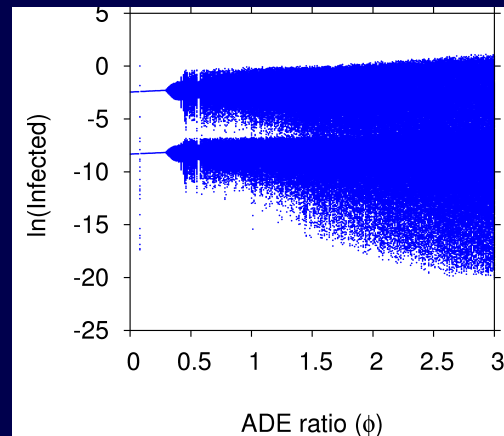
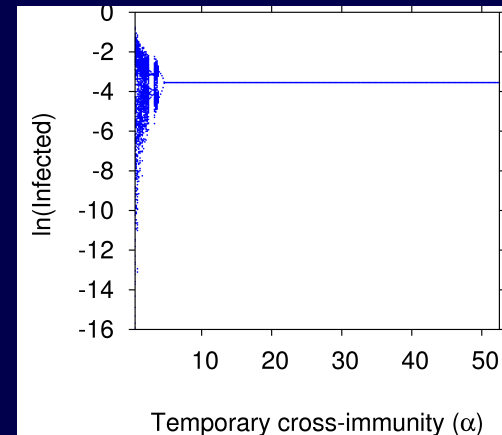
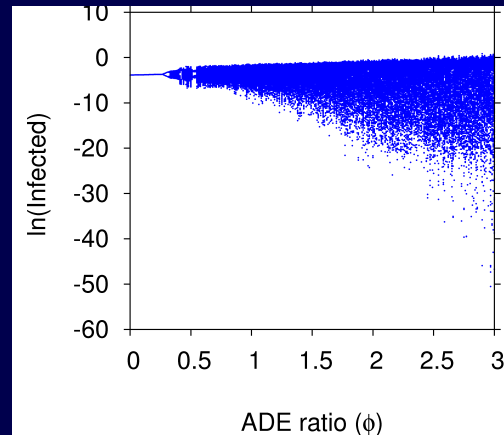
$$\dot{I}_{43} = \frac{\beta}{N} S_4(I_3 + \rho \cdot N + \phi(I_{13} + I_{23} + I_{43})) - (\gamma + \mu)I_{43} \quad (\text{A.25})$$

$$\begin{aligned} \dot{R} &= \gamma(I_{12} + I_{13} + I_{14} + I_{21} + I_{23} + I_{24} + I_{31} \\ &+ I_{32} + I_{34} + I_{41} + I_{42} + I_{43}) - \mu R \end{aligned} \quad (\text{A.26})$$

25 dimensional system!

# Modeling dengue fever epidemiology

## *The four-strain model with strain structure of the pathogens*

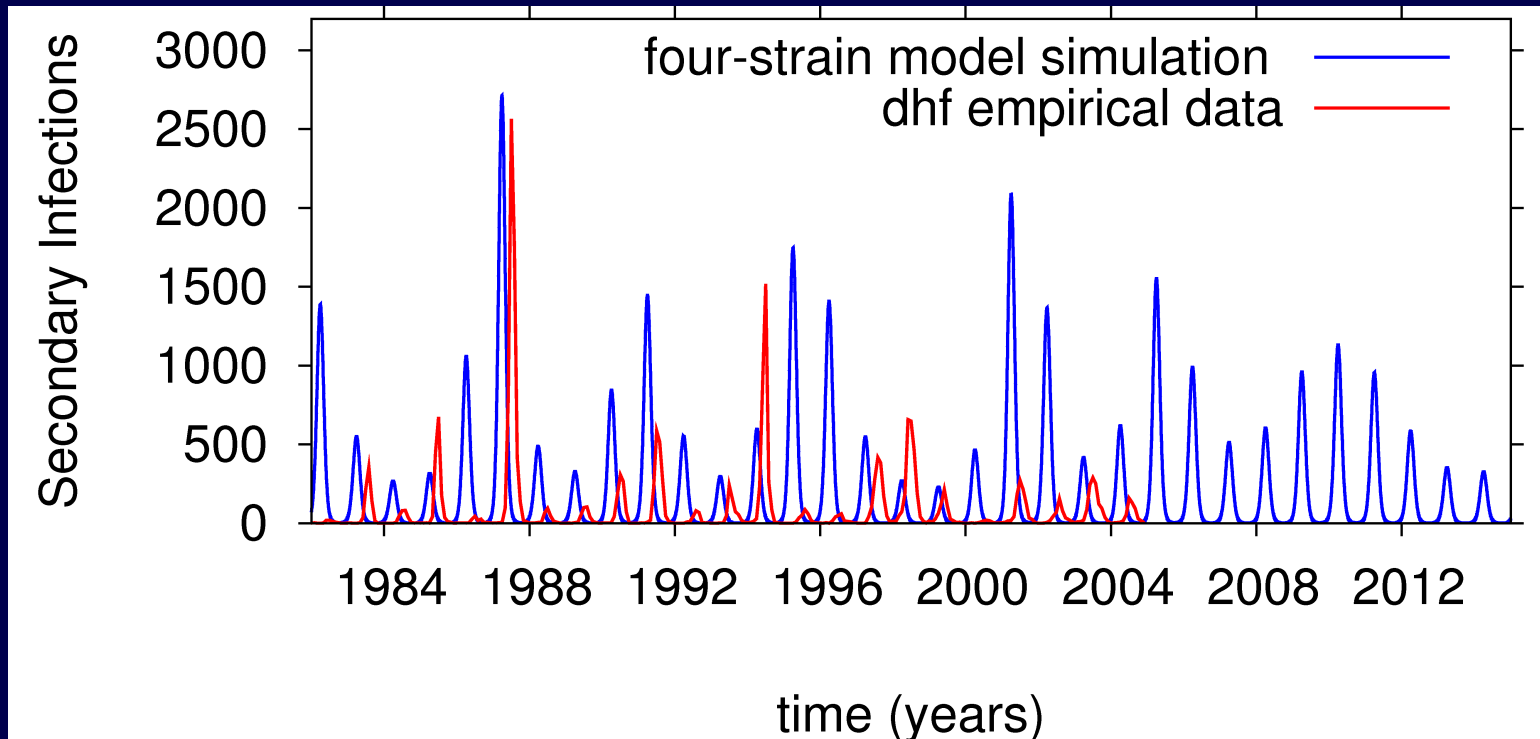


*( $\alpha = 1/6$  months)*

*( $\phi = 0.6$ )*

# *Modeling dengue fever epidemiology*

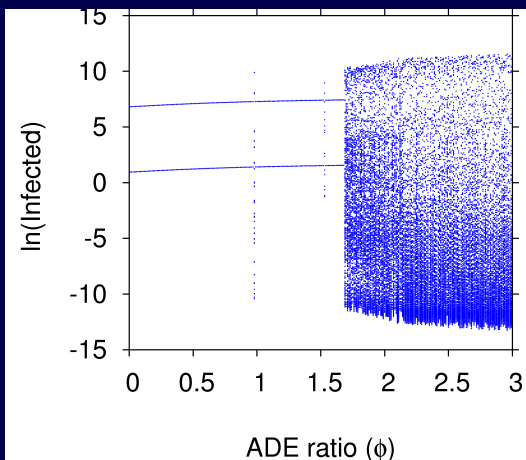
## *The four-strain model with strain structure of the pathogens*



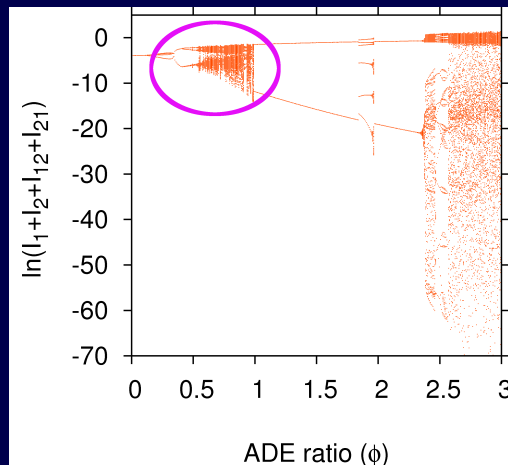
*Also qualitatively a very good result when comparing empirical DHF data and model simulation.*

## Summary

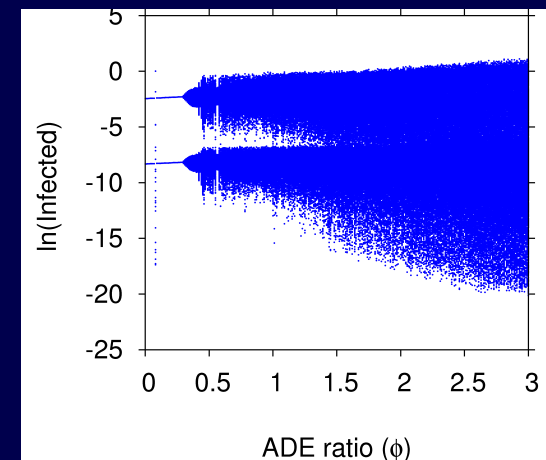
- ✧ *Basic  $n$ -strain SIR-type model for the host population, capturing differences between primary and secondary infections.*
- ✧ *Consideration of temporary cross-immunity gives bifurcations up to chaotic attractors in much wider and also unexpected (not predicted by previous models) parameter regions.*



*2-infection model*



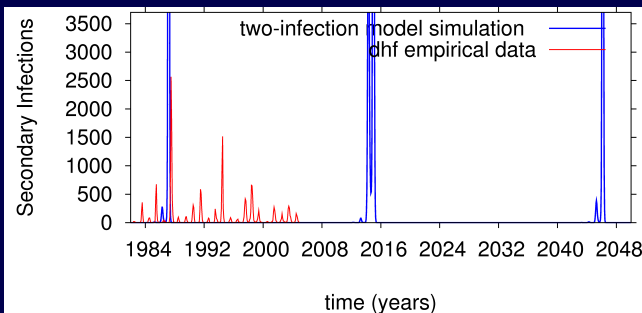
*2-strain model*



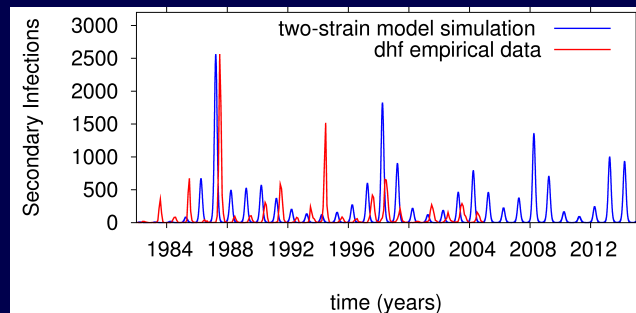
*4-strain model*

## Summary

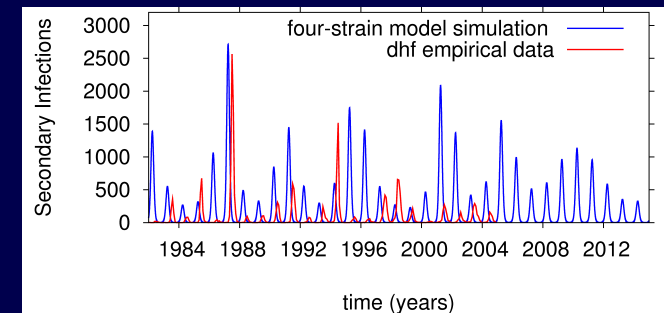
- ✧ Long term epidemiological data come from the Ministry of Public Health in Thailand and consist on monthly incidences of hospitalized cases.
- ✧ For such a data scenario, models that are able to generate both primary and secondary infection cases (with a different strain), have shown a good qualitative agreement between empirical data and model output.



*two-infection model*



*2-strain model*



*4-strain model*

*Thank you for your attention!*

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