Reinfecciones de una enfermedad infecciosa sobre una red regional: el caso de dengue

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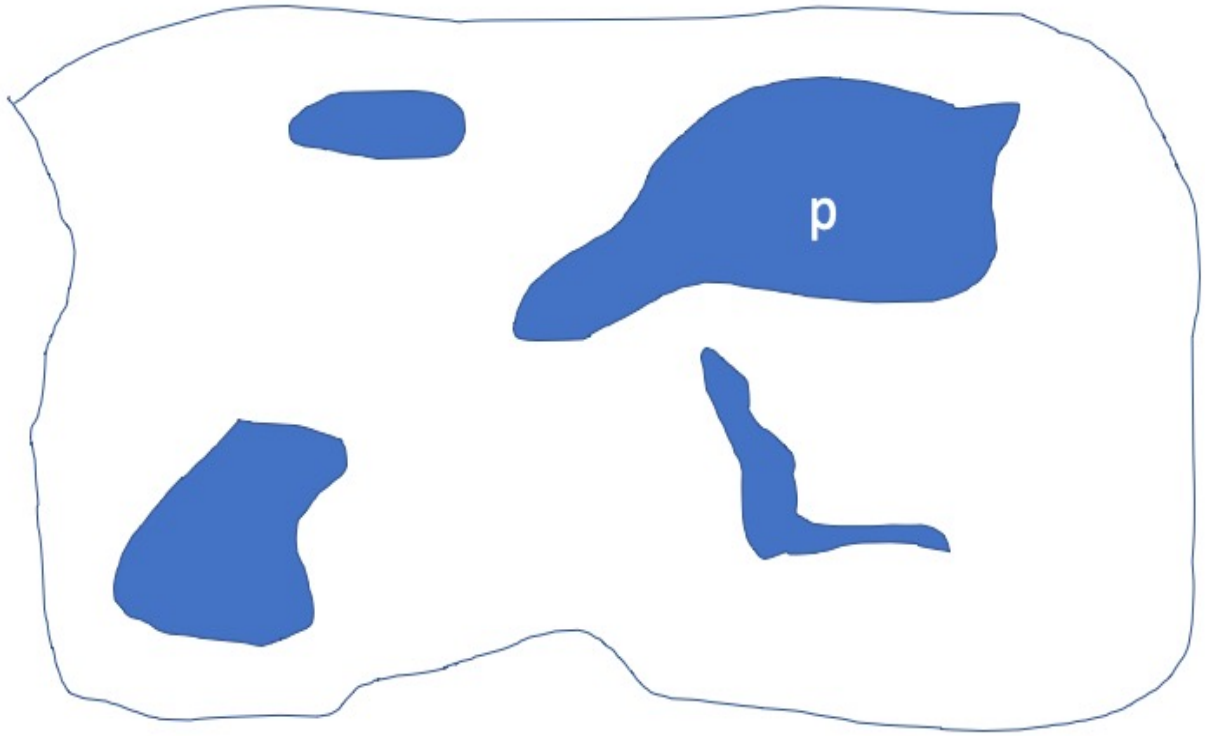
Background

Patch dynamics: colonization-extinction trade-off. Quintaessential model: Richard Levins.

$$p'(t) = \beta p(t)(1 - p(t)) - \epsilon p(t), \tag{1}$$

- $p(t)$ proportion of occupied patches at time t
- β propagule production rate
- ϵ extinction rate

Interpretation



Assume no propagule production, only extinction

$$p' = -\epsilon p, \qquad p(0) = p_0.$$

Solution

$$p(t) = p_0 e^{-\epsilon t}$$

Looking at it from another perspective:

$$\frac{p(t)}{p_0} = e^{-\epsilon t}$$

LHS: proportion of occupied patches remaining after t units of time. Therefore

$$1 - \frac{p(t)}{p_0} = 1 - e^{-\epsilon t} = G(t)$$

proportion of empty patches after t units of time have passed. $F(t)$ is the distribution function of times before extinction.

Therefore, expected time before extinction ($G'(t) = g(t) =$ density function of times before extinction).

$$\int_0^\infty tg(t)dt = \frac{1}{\epsilon}.$$

On the other hand the colonization term

$$\beta p(t)(1 - p(t))$$

is proportional to the variance of the binomial distribution.

Suppose $p(t)$ is very small (initial colonization of a previously empty habitat). Expand Eq (1):

$$p'(t) = (\beta - \epsilon)p(t) - \beta p(t)^2.$$

then

$$p'(t) \approx (\beta - \epsilon)p(t)$$

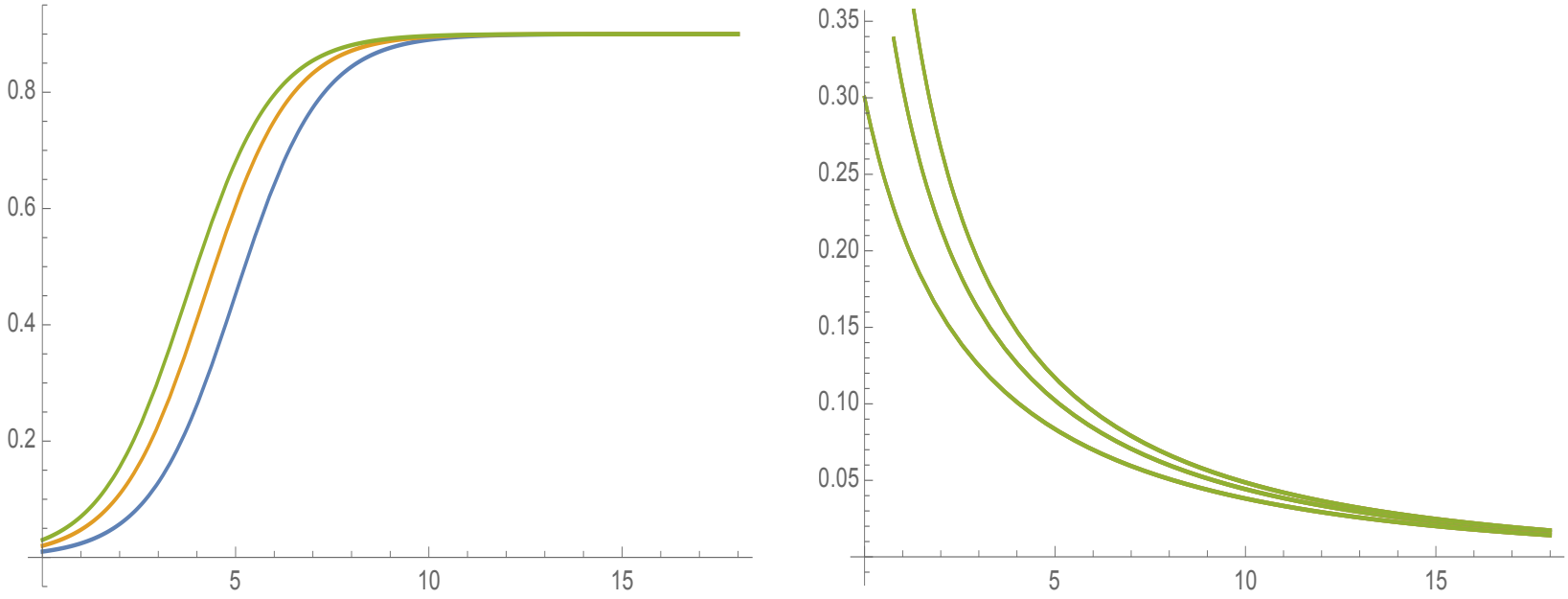
which satisfies $p(t) > 0$ if and only if $\beta - \epsilon > 0$ or equivalently, if

$$R_0 = \frac{\beta}{\epsilon} > 1.$$

Threshold numbers

R_0 : the number of new colonized patches from a small number of original colonizers in an otherwise empty habitat.

- $R_0 > 1$ successful invasion
- $R_0 < 1$ extinction



(a) (b)

Figure: a) Asymptotic colonization to a positive equilibrium; b) asymptotic extinction ($p = 0$)

There are essentially two kinds of equilibrium points: those with positive proportion of occupied patches, and one with no colonization, namely the empty habitat (or trivial) equilibrium point.

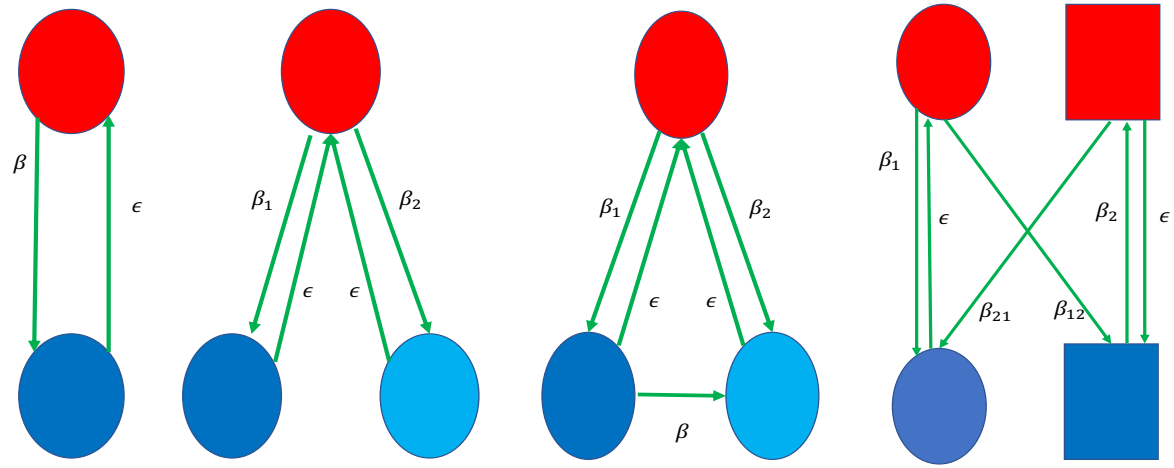


Figure: Different patch arrangements give different forms of the reproductive number

1. R_0 is unique
2. $R_0 = \max\{R_{01}, R_{02}\}$, extinction of species with lower R_{0j}.
3. $R_0 = \max\{R_{01}, R_{02}\}$, coexistence if $R_{0j} > 1$.
4. $R_0 \approx \frac{1}{2}(R_{01} + R_{02})$.

How to compute the reproductive number

This is a general procedure. In practice, the task can be much much simpler or much more complicated! There may be many kinds of colonized patches.

- Set up the model. Roughly, if X denotes the proportion of (all kinds of) colonized patches then

$$X' = \mathcal{F}(X) - \mathcal{V}(X)$$

  is the equation that describes the dynamics of patch colonization (highly non-linear).

- Linearizing around the empty habitat equilibrium point, we obtain

$$x' = (F - V)x$$

  where now F and V are matrices (linear system).

The number of secondary colonizations produced by a single colonized patch can be expressed as the product of the expected duration of the reproductive period and the propagule production rate.

- As done with the Levins model, taking $F = 0$, the solution of

$$x' = -Vx, \qquad x(0) = x_0,$$

gives the proportion of patches that remain occupied after time t;

$$x(t) = e^{-Vt} x_0.$$

- The expected time of patch occupancy is then

$$\int_0^\infty e^{-Vt} x_0 \, dt = V^{-1} x_0.$$

- The (i, j) entry of F, is the rate of secondary colonizations produced in compartment i by an index case in compartment j. Hence, the expected number of secondary colonizations produced by the index case is given by

$$\int_0^\infty Fe^{-Vt}x_0\,dt = FV^{-1}x_0,$$

where the matrix

$$FV^{-1}$$

is the so-called *next-generation matrix*.

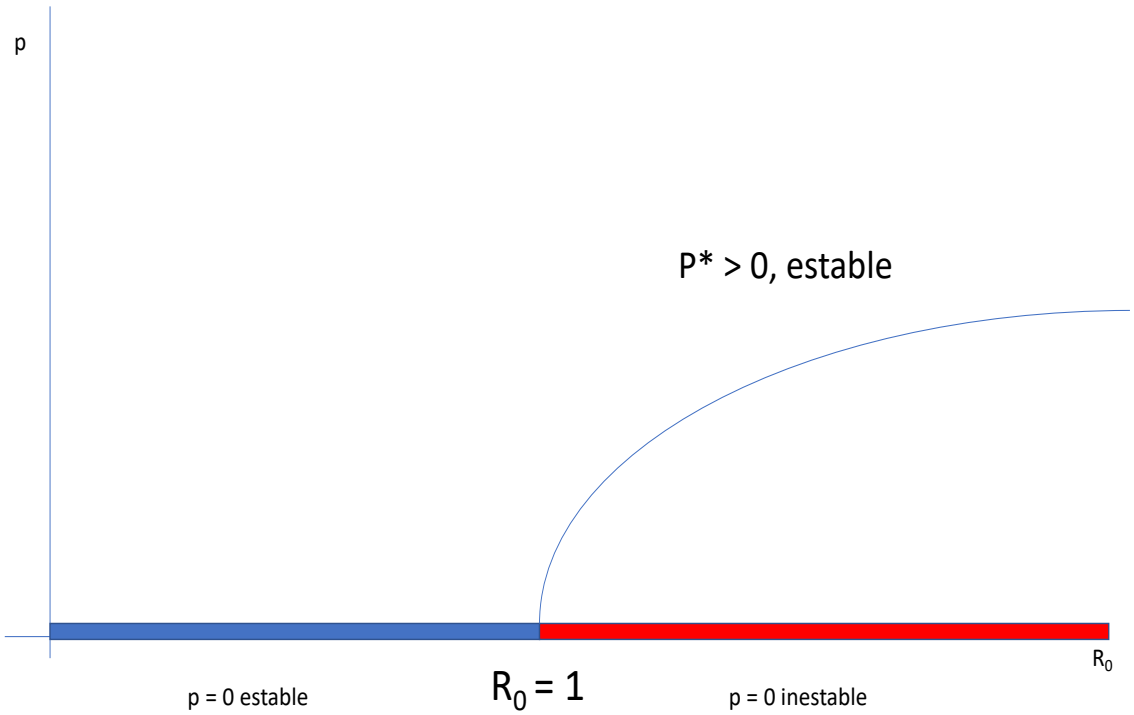
- We have that

$$R_0 = \rho(FV^{-1})$$

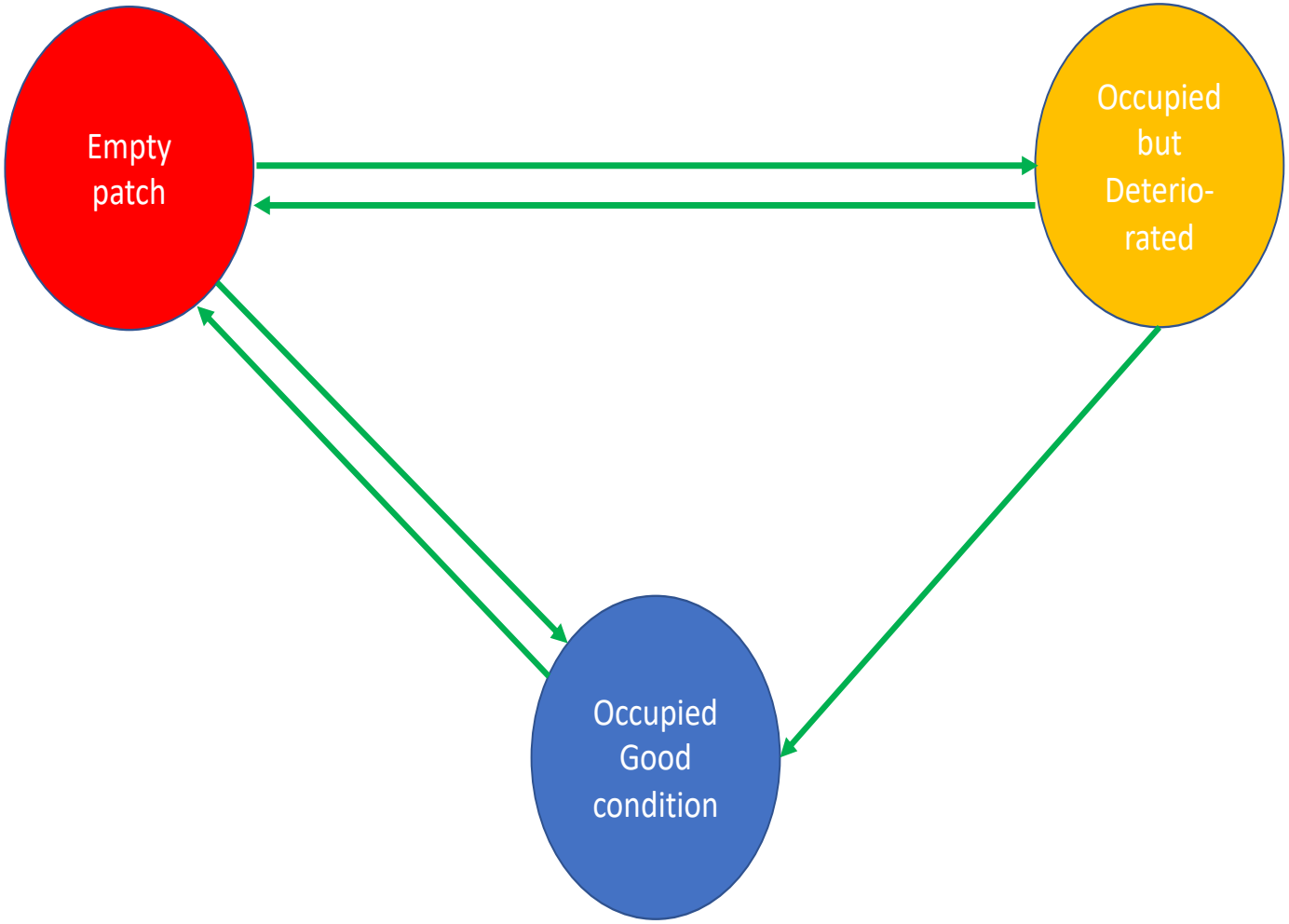
that is, R_0 is the spectral radius of the next-generation matrix.

Bifurcation diagrams

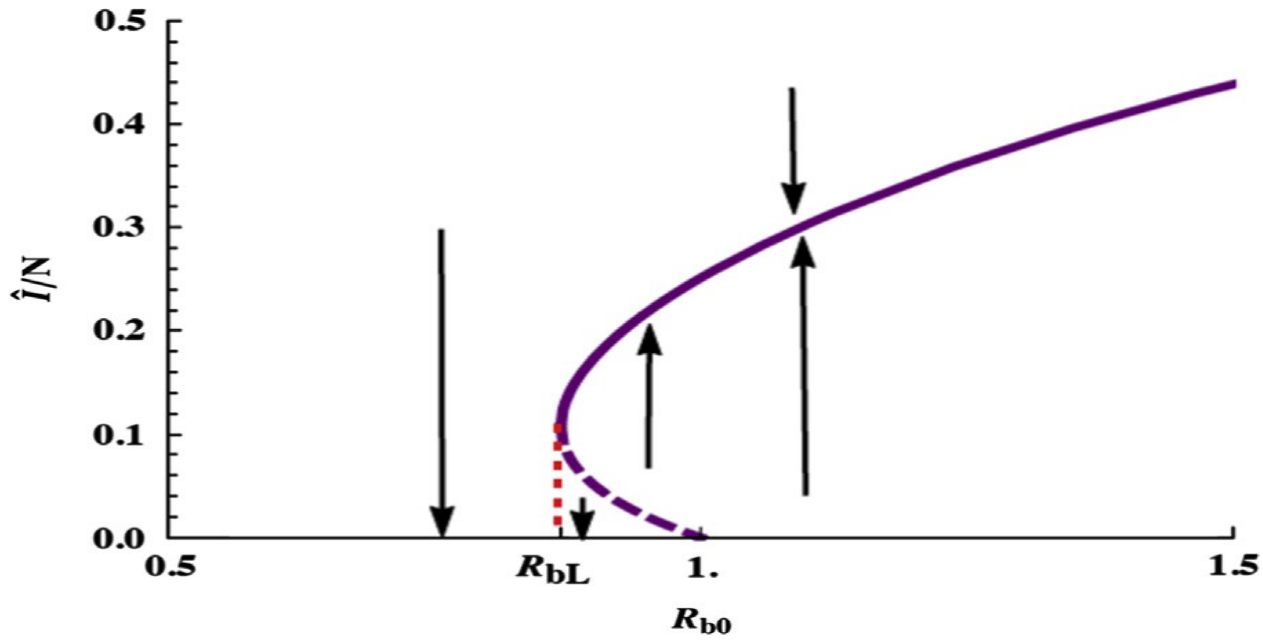
Typical behavior of equilibria as we move R_0.



Habitat deterioration



Atypical behavior of equilibria as we move R_0: hysteresis



Depends on:

- Deterioration rate ϕ.
- Propagule production rate of colonizer β.
- Degree of decrease or increase of propagule production in deteriorated habitat σ.
- Habitat recovery rate θ

Target reproduction numbers

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Target reproduction number T_C, controls only certain infection/transition terms (Shuai et al., 2013).
$K = C + (K - C)$ where C target matrix, subject to change;
$K - C$ residual matrix, not subject to change.

$P = T + F$ nonnegative irreducible population projection matrix (e.g., a Lefkovitch matrix or a Leslie matrix), with T transition probabilities, F fertilities.

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The controlled population growth rate for the controlled population matrix $\frac{1}{\lambda}T + \frac{1}{\lambda}F$ is one. In contrast, the net reproductive value R_0 determines the effort needed to scale only fertility and the resulting projection matrix $T + \frac{1}{R_0}F$ has growth rate one.

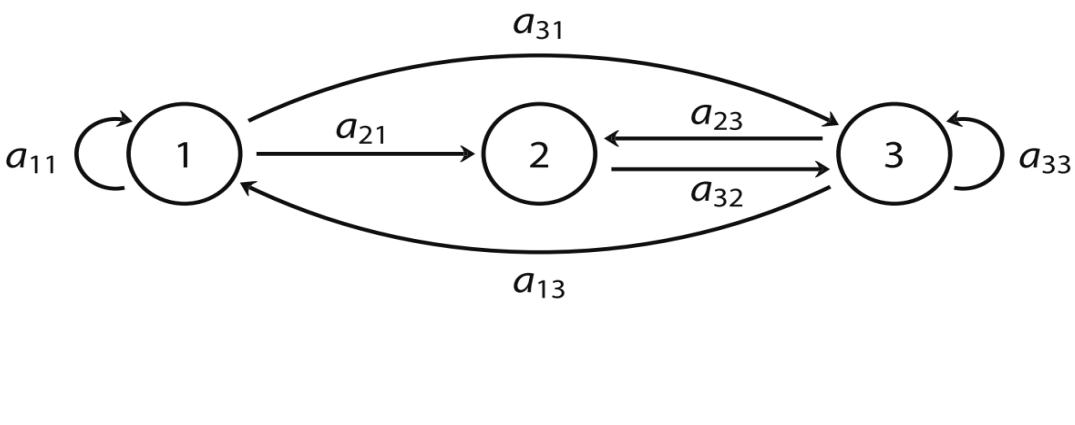
(Caswell 2001, Cushing and Zhou 1994; Li and Schneider 2002)

Example (Lewis et al, 2019)

- Scentless chamomile (Matricaria perforata) perennial, three stages: seed bank (in the ground, 1), rosettes (2), and flowering plants (3).
- Biological transitions: life-cycle graph or projection matrix.
- In a given year, seeds will remain in the seed bank with probability a_{11}.
- They will germinate into a rosette with probability a_{21}.
- Germinate into a flower with probability a_{31}.
- They will die with probability $1 - a_{11} - a_{21} - a_{31}$.
- Rosettes into flowers with probability a_{32}, and die with probability $1 - a_{32}$.

The flowers contribute to all fecundities as follows.

- In a single year, flowers will produce a_{13} seed bank seeds per flower
- will produce a_{23} rosettes per flower, and will produce a_{33} new flowers per flower.
- Then the original flower will die.



Projection matrix for chamomile (de-Camino-Beck and Lewis 2008)

$$P = \begin{bmatrix} a_{11} & 0 & a_{13} \\ a_{21} & 0 & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$$

Controls affecting seed production will reduce a_{13}, a_{23} and a_{33}.
Controls affecting plant growth will reduce a_{21}, a_{31} and a_{32}.

- *Control of off-spring production*. Target matrix C has $a_{i3} > 0$ $(i = 1, 2, 3)$ only.

$$T_C = \frac{a_{33} + a_{13}a_{31} + a_{23}a_{32} + a_{13}a_{32}a_{21} - a_{11}a_{33} - a_{11}a_{23}a_{32}}{1 - a_{11}}.$$

- *Control of survival probability at the first stage*. Target matrix C has only $a_{11} > 0$, i.e., control of the survival probability of seeds.

$$T_{11} = \frac{a_{11}(1 - a_{33} - a_{23}a_{32})}{1 - a_{33} - a_{13}a_{31} - a_{23}a_{32} - a_{13}a_{32}a_{21}}.$$

A metapopulation model for human mobility and Dengue

Joint work Mayra Nuñez-Lopez and Luis Alarcón.

- Connectivity between population centers and travel are closely related to the import/export of infectious diseases both in directly- as well as in vector-transmitted diseases.
- Patterns of human mobility are seasonal.
- Climatic conditions affect transmission since pathogens life cycles and habitat suitability for vectors, hosts or pathogens can be significatively modified by it.

We address specifically the reinfection process of whole geographical regions. In a network, each site can be reinfected (recolonized) by the movement of infectious individuals from neighboring patches and the disease in the patch may decline due to the natural disease life cycle or because of emigration of sick individuals.

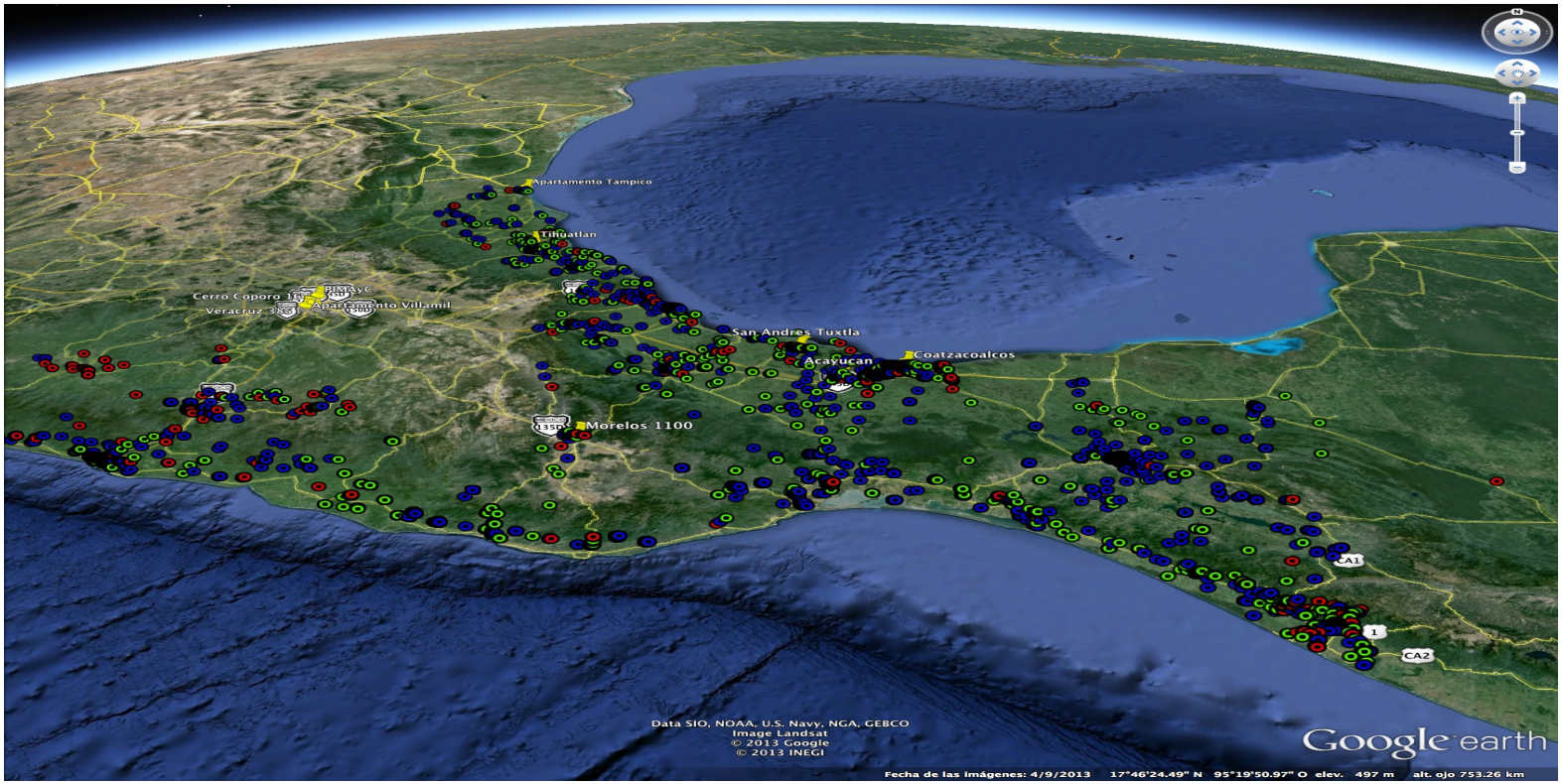


Figure: Dengue in Oaxaca, Chiapas, Veracruz y Guerrero 2002-2009.

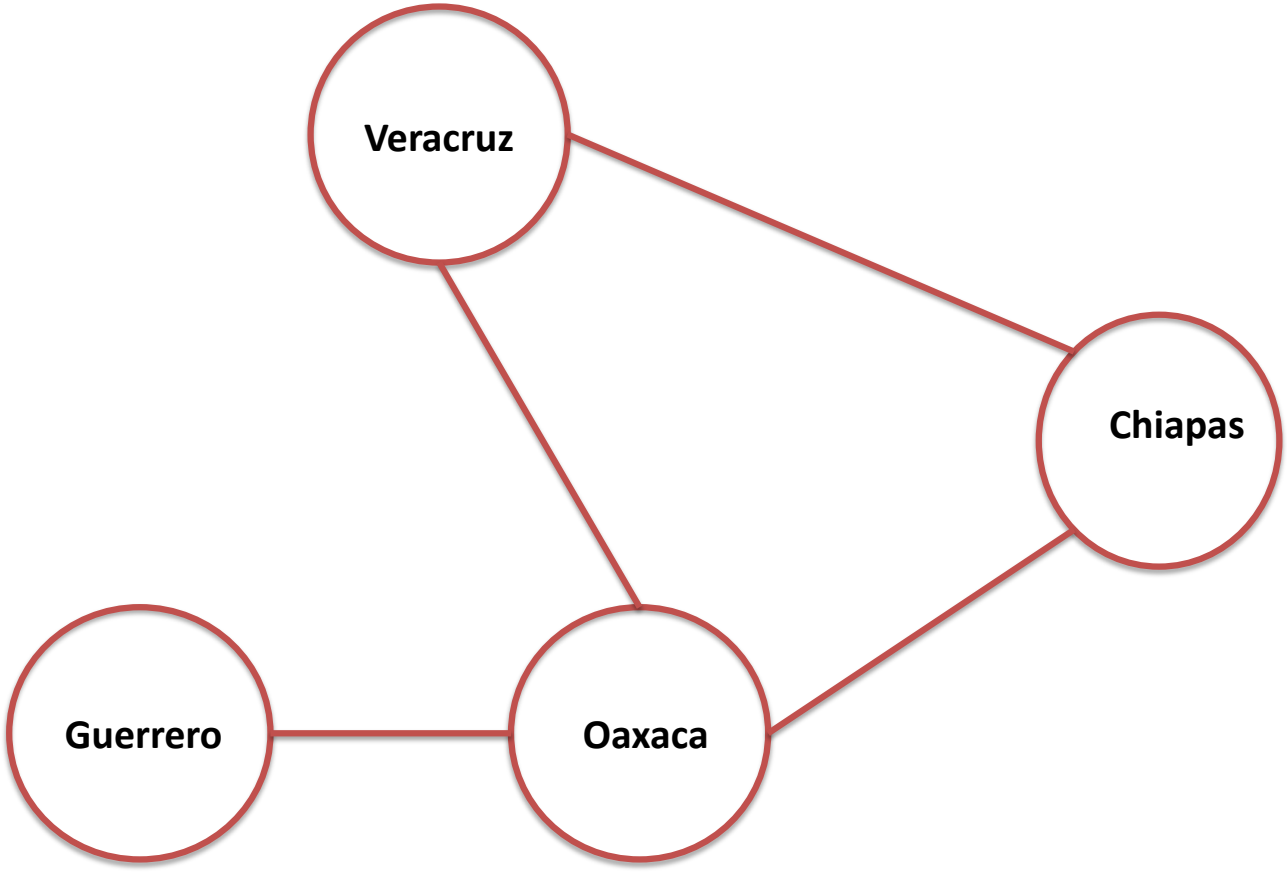


Figure: Network of locations where outbreaks are propagated.

The Model components

- Each location can be in either of two states: S suceptible (empty of infection) or I (occupied or with sick persons).
- The probability of finding an *infected* individual in location i at time t, is $p_i(t)$, with $i \in \mathbf{E} = \{$Chiapas, Guerrero, Oaxaca and Veracruz$\}$. Therefore, each location at each time t is with probability $1 - p_i(t)$ in *state* S (without outbreaks), and with probability $p_i(t)$ in *state* I (with outbreaks).
- Infections are climate sensitive, due to the dependence of the mosquito life cycle on rain and temperature. Precipitation is used as a general "proxy" of an external factor, which changes the probability of contagion.

- We assume discrete time-steps of size Δt, Δt an epidemiological week.
- Any location in state I recovers and passes to state S with probability μ (recovery rate), but it is reinfected with probability $\eta_i(P(t))$, where

$$P(t) = [p_{Chis}(t), p_{Gro}(t), p_{Oax}(t), p_{Ver}(t)]$$

  is a vector with entries $p_i(t)$ that represent the probability of outbreaks in location i at time t.

$\eta_i(P(t))$ is the probability that in ith location, the number of outbreaks will increase due to population displacement from the jth-location with $i \neq j$; this probability is affected by climatological factors (precipitation)

Effective innoculum size

Location i receives, on average from location j, $r_i N_j$ individuals, where N_j represents the population in location j and r_i the fraction of individuals that moved from j to i in each step of time. In this migrant population, there are on average $r_i N_j p_j(t)$ infected individuals with $i, j \in E$. Therefore, the effective infective innoculum size arriving to location i will be given as the sum of

- immigrant individuals that enter that location,
- plus the cases that already exist at that location
- minus the infected individuals leaving i (emmigration), given by expression

$$T_i(t) = \frac{\sum_{j \in E} r_i N_j p_j(t) a_{ij} + p_i(t) N_i - \sum_{j \in E} r_j N_i p_i(t) a_{ij}}{\sum_{j \in E} r_i N_j a_{ij} + N_i - \sum_{j \in E} r_j N_i a_{ij}}. \quad (2)$$

$\eta_i(P(t))$ is a function of three factors:

- the probability β_i of an individual in location i becoming infected (the product of the per-contact probability of infection times the per capita number of contacts per unit time for each location i);
- the effective infective inoculum size $T_i(t)$,
- average weekly precipitation in location i given by $f_i(t)$. Note that $f_i(t)\beta_i$ gives the time-dependent infection rate of location i.

The model

Our discrete model describes the colonization-extinction of cases by considering cases moving to location i, those cases that stay in location i and those that recover in location i:

$$p_i(t+1) = (1-\mu)p_i(t) + \alpha_i f_i(t)\beta_i T_i(t)(1-p_i(t)). \qquad (3)$$

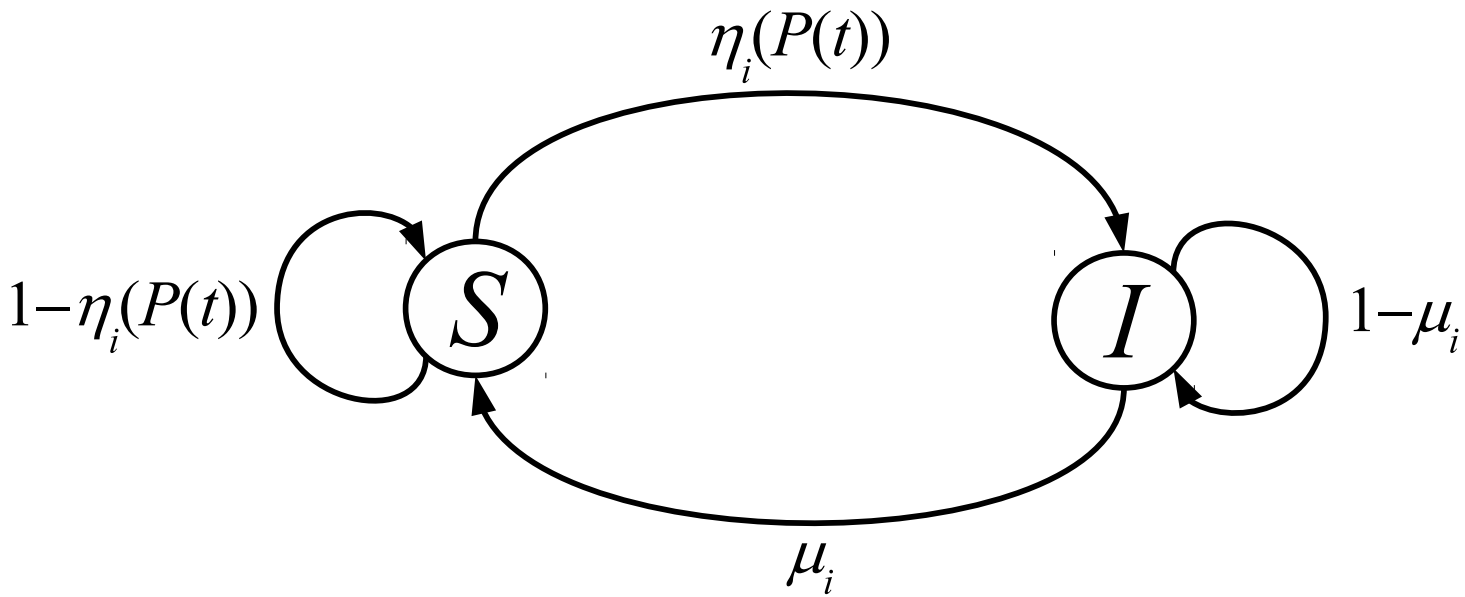


Figure: Transitions for each node showing the two possible states for each location, and the transition probabilities between states S and I.

Model parametrization

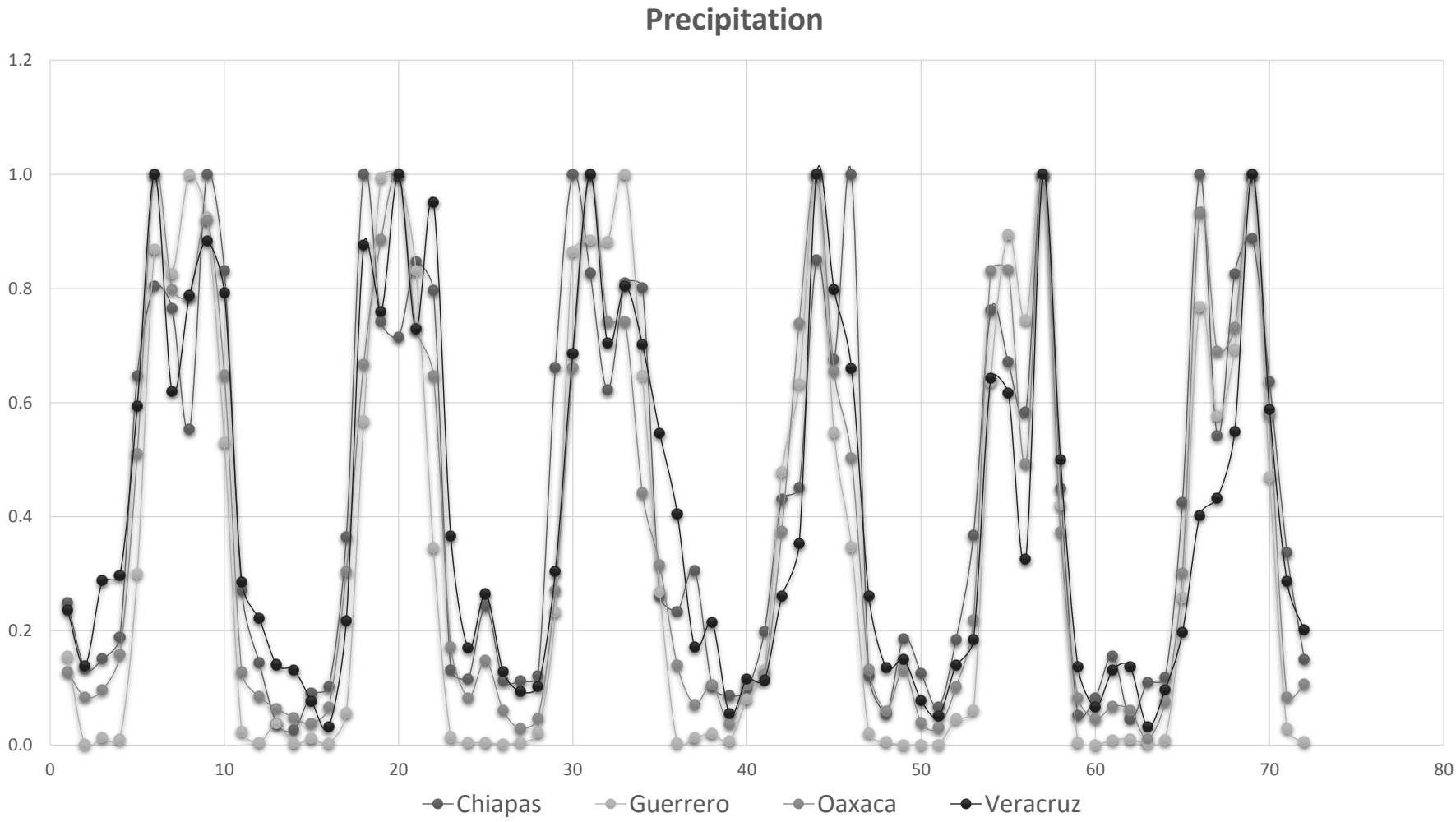


Figure: Standardized precipitation data during 2004-2009.

Data on mobility through public transportation in the roads and highways of Mexico is scarce and very incomplete. We have information on the total population and the economic status of each of the Mexican states, thus r_i the fraction of individuals that move to location i can be roughly approximated assuming that individuals migrate in higher proportions to Veracruz State due to its economic, political and social characteristics

State	r_i	α_i
Chiapas	0.0009	0.680
Guerrero	0.0090	0.790
Oaxaca	0.0010	0.730
Veracruz	0.0100	0.735

Table: Mobility rate r_i and precipitation weight of each State.

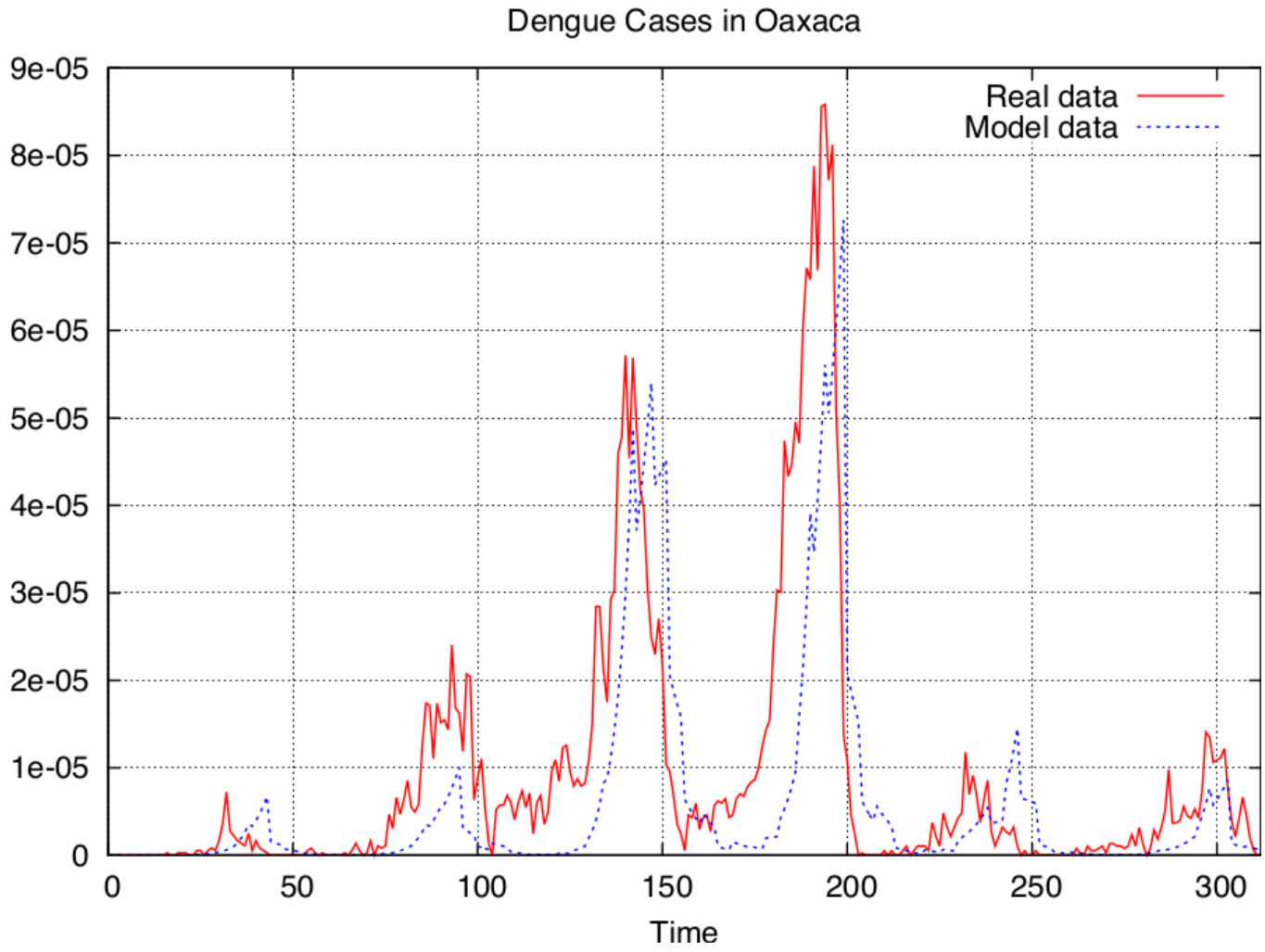
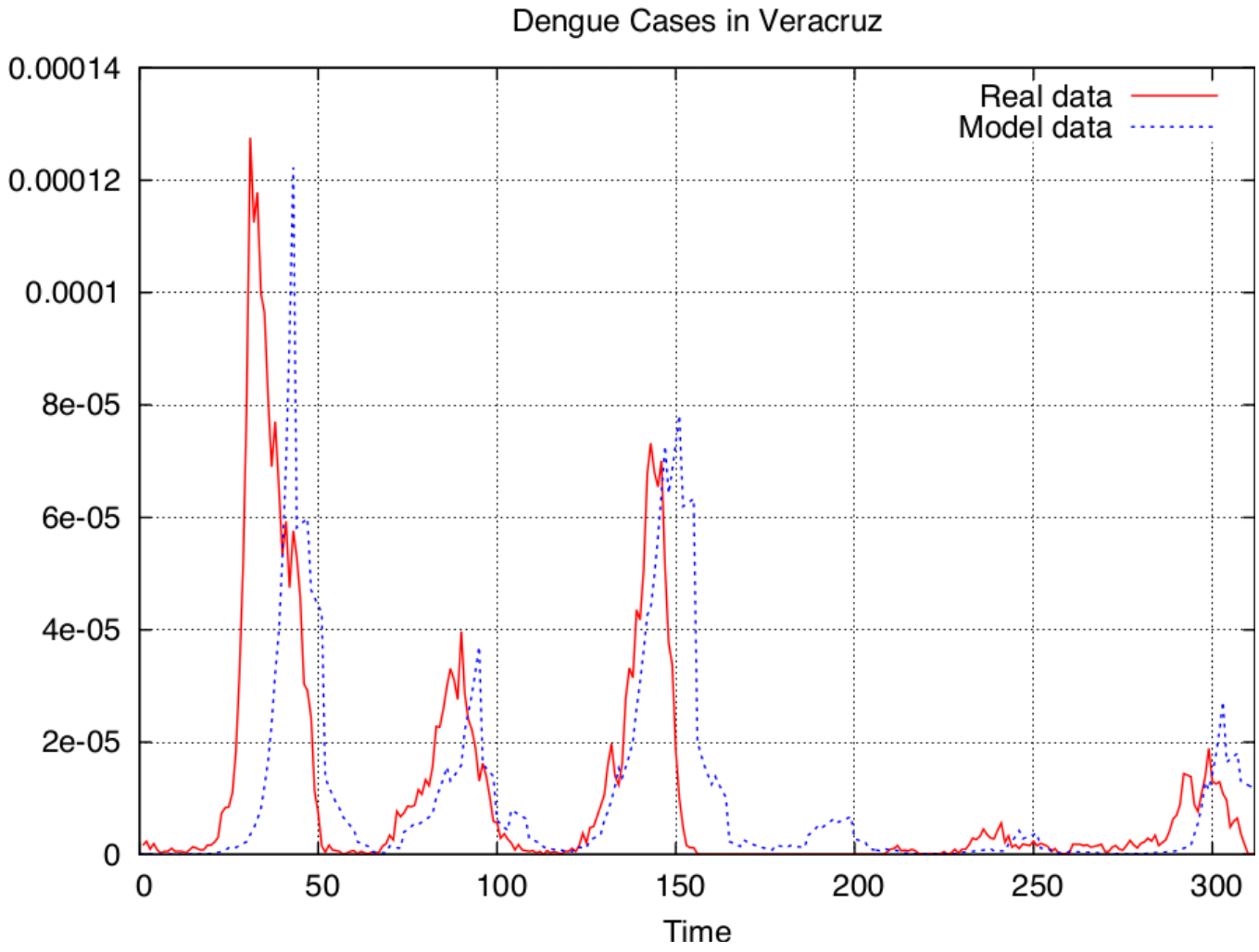


Figure: Comparative between observed outbreaks and numerical simulations data for Oaxaca State during 2004-2009 with host mobility.



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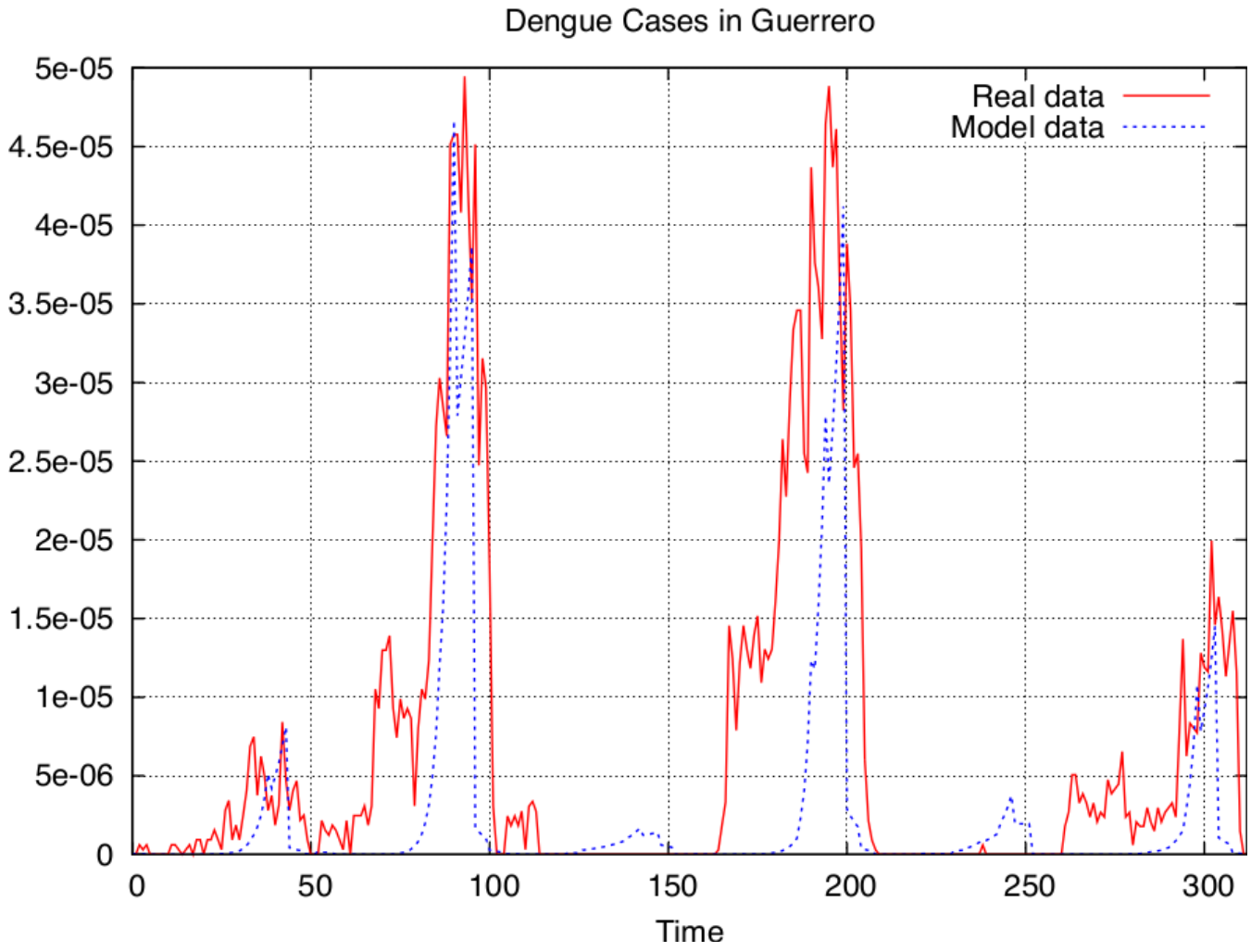

Figure: Comparative between observed outbreaks and numerical simulations data for Guerrero State during 2004-2009 with host mobility.

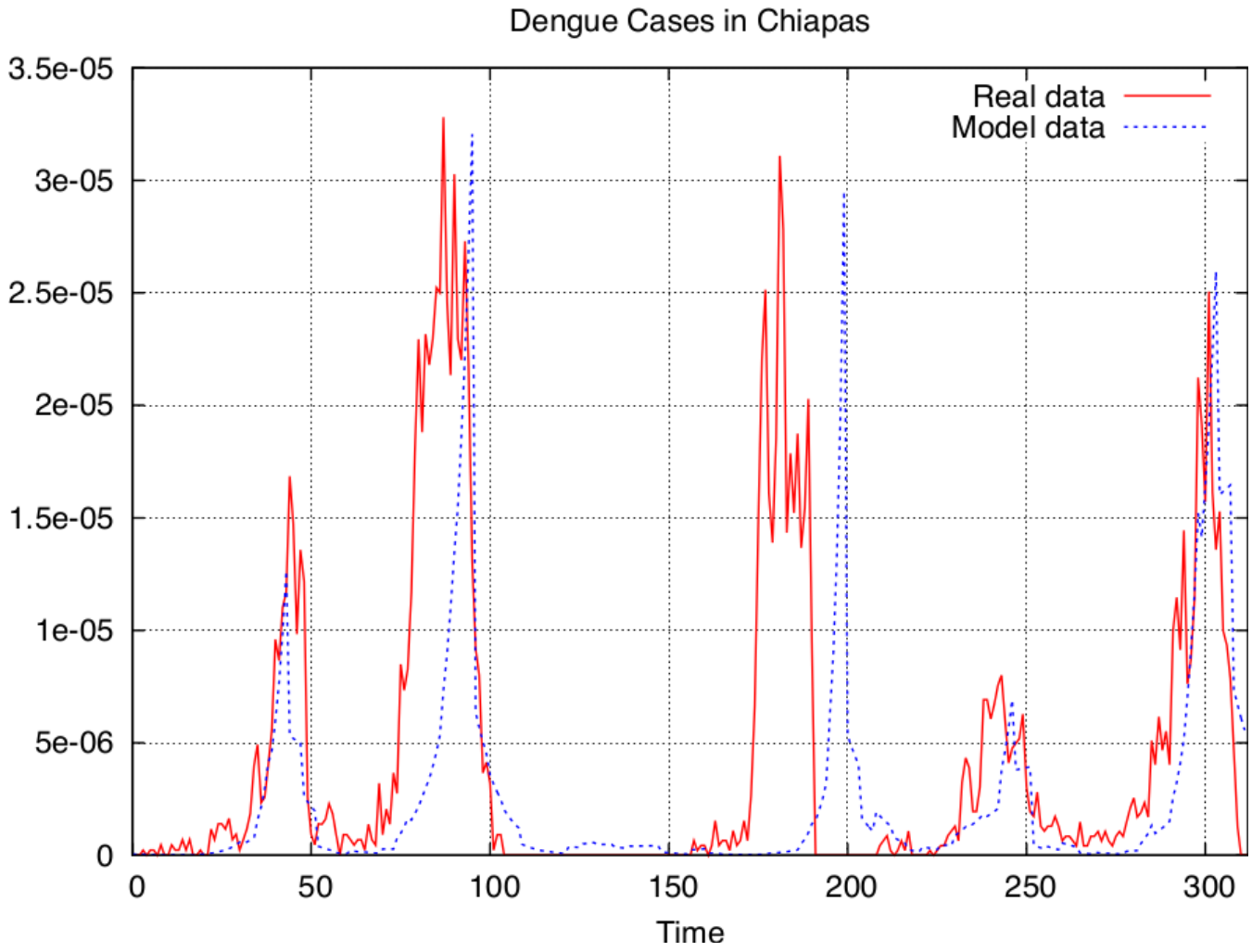

Figure: Comparative between observed outbreaks and numerical simulations data for Chiapas State during 2004-2009 with host mobility.

- Our framework, albeit simple in terms of the actual population dynamics of Dengue, concentrates on the movement patters underlying the spread of this disease in a large region of Southern and Eastern Mexico.
- $T_i(t)$ the effective infective innoculum size represents a local measure of the population size of infected hosts that arrive at a given location. This parameter can be interpreted as an indicator of outbreak risk of location i.
- Regardless of the complexity of Dengue, movement at a geographical scale is a relatively simple colonization extinction process taking place in a network that is an spatially extended system whose dynamics is dependent on its topological arrangement, and neighborhood interactions.
- During the years covered by our data, the Dengue strains that have circulated have been mainly Dengue II and I with lower prevalence of Dengue III and IV. Immunity, therefore, must play a role in the observed reinfection dynamics.

Conclusions

- Data from SINAVE data base: dengue weekly incidence, spatially distributed.
- Minimal dengue model for two strains for the evaluation of vaccination strategies.
- Constructions of incidence networks to approximate mobility between towns and regions.
- Development of methods for parameter inference and forecasting.

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