Spatial Patterns of Infection

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March 26, 2013

Dispersal and Disease Dynamics

Some important Contributors

The role of dispersal in the evolution of communities has been a central topic in population biology.

Pioneer mathematical work includes:

- Fisher and Kolmogoroff (1937) Genetics, Travelling Waves
- Skellam (1951) Muskrats Dispersal
- Kendall (1965) Epidemic Models
- Mollison (1977) Epidemic Spread

- Okubo (1980) Biological Work
- Weinberger, Li et al. (1978, 1982, 2008) Mathematical Contributions
- Levin (1986) Significant Impact in Ecology and Evolutionary Biology
- Kot (1992, 1996) Major contributions to Ecology
- Hastings (2005), Invasion
- and others (Lewis, Wang, ...).

Reaction-Diffusion Equations

- Coupling of reaction kinetics gives rise to reaction diffusion equations

$$\frac{\partial u}{\partial t} = f(u) + D\frac{\partial^2 u}{\partial x^2}.$$

- u is concentration of a chemical (or population density), $f(u)$ kinetics (local population growth) and D diffusion coefficient (in this example a case constant).

- Growth and spread of the populations occur simultaneously.

Traveling Waves

- A traveling wave is a bounded solution that travels *without changing it shape* at a fixed speed.

- If $u(x, t)$ represents a traveling wave solution then its *shape* will be the same for all time, with speed of propagation constant (c). Hence,

$$u(x, t) = u(x - ct) = U(z), \qquad z = x - ct$$

  is a traveling wave that moves in the positive *x*-direction, if $c > 0$ and negative direction, if $c < 0$, here assume $c > 0$.

Fisher-Kolmogorov (FK) Equation

- Most famous nonlinear reaction diffusion equations is the FK equation given by

$$\frac{\partial u}{\partial t} = ku(1-u) + D\frac{\partial^2 u}{\partial x^2}.$$

  k growth rate of the local population and D diffusion coefficient, both positive parameters.

- Rescaling by $t^* = kt$ and $x^* = x(\frac{k}{D})^{\frac{1}{2}}$ gives

$$\frac{\partial u}{\partial t} = u(1-u) + \frac{\partial^2 u}{\partial x^2}.$$

- Spatially homogeneous situation, the steady states are $u = 0$ and $u = 1$, which are unstable and stable, respectively.

- Substitution of the traveling waveform $u(x, t) = u(x - ct) = U(z)$, implies that

$$U'' + cU' + U(1 - U) = 0$$

  where $\left(' = \frac{d}{dz}\right)$.

- Solution of the wavefront U will exist and typically satisfy:

$$\lim_{z \to \infty} U(z) = 0, \qquad \lim_{z \to -\infty} U(z) = 1.$$

- Studying U in the $(U, U' = V)$ phase plane means studying

$$U' = V, \qquad V' = -cV - U(1 - U).$$

The phase plane trajectories are solutions of

$$\frac{dV}{dU} = \frac{-cV - U(1 - U)}{V}.$$

- Two singular points in (U, V) plane are $(0, 0)$ and $(1, 0)$, steady states.
- Linear stability analysis shows that the eigenvalues λ for the steady states are $(\lambda_\pm = \tau \pm (\tau^2 - 4\Delta)^{1/2})$:

$(0, 0)$: $\lambda_\pm = \frac{1}{2}\left[-c \pm (c^2 - 4)^{\frac{1}{2}}\right] \implies \begin{cases} \text{st. node} & \text{if } c^2 > 4 \\ \text{st. spiral} & \text{if } c^2 < 4 \end{cases}$

$(1, 0)$: $\lambda_\pm = \frac{1}{2}\left[-c \pm (c^2 + 4)^{\frac{1}{2}}\right] \implies$ saddle point.

- If $c \geq c_{\min} = 2$ then the origin is a stable node. In terms of the original

$$c \geq c_{\min} = 2\sqrt{kD}.$$

- For the original equation $\frac{\partial u}{\partial t} = u(1-u) + \frac{\partial^2 u}{\partial x^2}$ Kolmogoroff et al. (1937) proved that if $u(x, 0)$ (initial conditions) has compact support, that is,

$$u(x, 0) = u_0(x) \geq 0, \qquad u_0 = \begin{cases} 1 & \text{if } x \leq x_1, \\ 0 & \text{if } x \geq x_2 \end{cases}$$

  where $x_1 < x_2$ and $u_0(x)$ is continuous in $x_1 < x < x_2$, then the solution $u(x, t)$ evolves into a travelling wavefront solution.

- Therefore, a travelling wavefront solution $U(z)$ with $z = x - 2t$, will exist for speeds greater than or equal to a *minimum* speed $c_{min} = 2$.
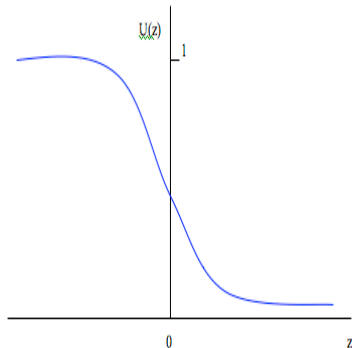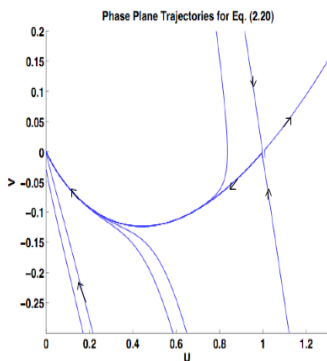
Phase Plane Trajectories for Eq. (2.20)

Recipe

1. Two or more densities.
2. Different rates of diffusion for the participants.
3. Interactions between the two densities

$$\frac{\partial c_1}{\partial t} = a_{11}c_1 + a_{12}c_2 + D_1\frac{\partial^2 c_1}{\partial x^2}$$

$$\frac{\partial c_2}{\partial t} = a_{21}c_1 + a_{22}c_2 + D_2\frac{\partial^2 c_2}{\partial x^2}$$

$$a_{i,j} = \frac{\partial R_i}{\partial C_j}\big|_{c_i,c_j}.$$

$$\frac{\partial C_1}{\partial t} = R_1(C_1, C_2) + D_1\frac{\partial^2 C_1}{\partial x^2}$$

$$\frac{\partial C_2}{\partial t} = R_2(C_1, C_2) + D_2\frac{\partial^2 C_1}{\partial x^2}$$

Instructions

- Positive *spatial steady state*

$$R_i(\bar{C}_1, \bar{C}_2) = 0$$

- Linearization

Superposition and Instability

- $c_i(x, t) = \alpha_i \cos(qx)e^{\sigma t}$
- values of q s.t. $\mathrm{Re}(\sigma) > 0$

$$\frac{\partial c_1}{\partial t} = a_{11}c_1 + a_{12}c_2 + D_1 \frac{\partial^2 c_1}{\partial x^2}$$

$$\frac{\partial c_2}{\partial t} = a_{21}c_1 + a_{22}c_2 + D_2 \frac{\partial^2 c_2}{\partial x^2}$$

$$\alpha_1(\sigma - a_{11} + D_1 q^2) - \alpha_2 a_{12} = 0$$

$$-\alpha_1 a_{21} + \alpha_2(\sigma - a_{22} + D_2 q^2) = 0$$

...Necessary and Sufficient Conditions

1. $a_{11} + a_{22} < 0$
2. $a_{11}a_{22} - a_{12}a_{21} > 0$
3. $a_{11}D_2 + a_{22}D_1 > 2\sqrt{D_1 D_2(a_{11}a_{22} - a_{12}a_{21})}$

Stage model with diffusion

Model

Two kind of infected:

- I_2 symptoms.
- I_1 no symptoms.

$$\frac{\partial S}{\partial t} = -\frac{\beta}{1 + I_2}SI_1 + \alpha I_2 + D_S\frac{\partial^2 S}{\partial x^2}$$

$$\frac{\partial I_1}{\partial t} = \frac{\beta}{1 + I_2}SI_1 - \delta I_1 + D_{I_1}\frac{\partial^2 I_1}{\partial x^2}$$

$$\frac{\partial I_2}{\partial t} = \delta I_1 - \alpha I_2 + D_{I_2}\frac{\partial^2 I_2}{\partial^2 x}$$

$S = 1 - I_1 - I_2$

Steady state:

$$\bar{I}_1 = \frac{\alpha(\beta - \delta)}{\beta\alpha + \beta\delta + \delta^2} \quad \text{and} \quad \bar{I}_2 = \frac{\delta(\beta - \delta)}{\beta\alpha + \beta\delta + \delta^2}$$

$$
\begin{aligned}
\frac{\partial S}{\partial t} &= -\frac{\beta}{1+I_2}SI_1 + \alpha I_2 + D_S\frac{\partial^2 S}{\partial x^2} \qquad (0.1)\\
\frac{\partial I_1}{\partial t} &= \frac{\beta}{1+I_2}SI_1 - \delta I_1 + D_{I_1}\frac{\partial^2 I_1}{\partial x^2}\\
\frac{\partial I_2}{\partial t} &= \delta I_1 - \alpha I_2 + D_{I_2}\frac{\partial^2 I_2}{\partial^2 x}
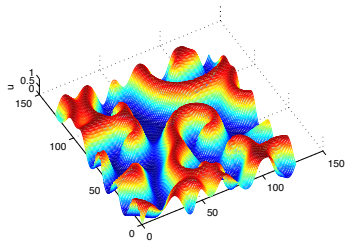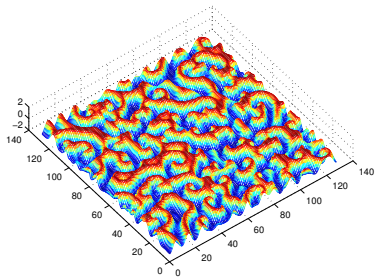\end{aligned}
$$

Theorem (Diffusive Instability in Epidemics)

The linearization of the system (0.1) satisfies the necessary and sufficient conditions for instability if and only if $\frac{\beta}{\delta} > 1$ and $\frac{\beta}{\alpha} > 1$

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From linearization
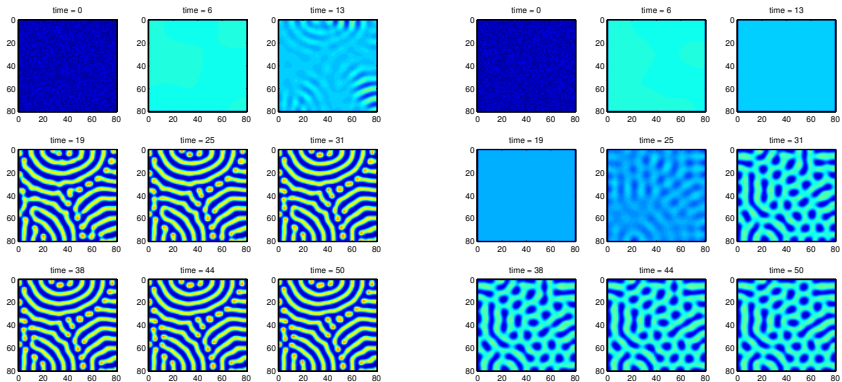
Using nonlinear model

Integrodifference Equations

Main motivation is the work of Weinberger (1978,1984) and Kot (1992,1996).

$$N_{t+1}(x) = \int_{-\infty}^{\infty} g(N_t(y))k(x - y)dy$$

where $N_{t+1} = g(N_t)$ models the local population dynamics and $k(x - y)\Delta x$ denotes the probability that an individual will disperse from location y to the interval $(x - \frac{1}{2}dx, x + \frac{1}{2}dx)$.

Traveling Waves

Weinberger (1978) showed that travelling wave solutions exist $(N_{t+1}(x) = N_t(x - c))$ for all speeds c greater than a minimum wave speed c^* if

(i) $g(N)$ is continuously differentiable on the interval $[0, N^*]$;

(ii) $g(0) = 0$ and $g(N^*) = N^*$;

(iii) $g'(N) \geq 0$, $N < g(N) \leq g'(0)N$ in $(0, N^*)$;

(iv) $k(x)$ is exponentially bounded.

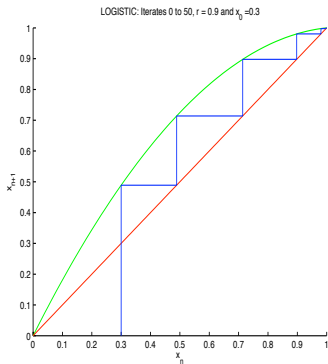He further showed, for such exponentially bounded kernels, initial conditions with compact support, that is,

$$N_0(x) > 0, \ x \in [-\delta, \delta] \text{ and } N_0(x) = 0, \ x \notin [-\delta, \delta],$$

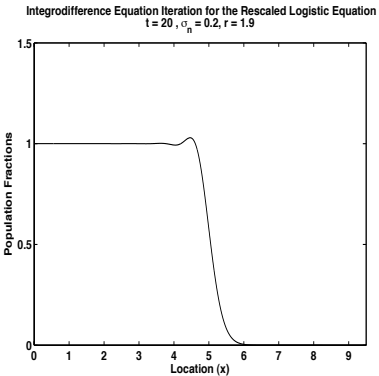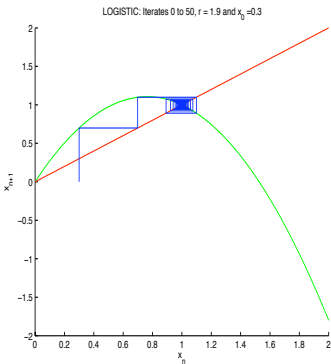converge to travelling waves with minimum speed of propagation given by

$$c^* = \min_{\rho > 0} \left\{ \frac{1}{\rho} \ln \left[g'(0) M(\rho) \right] \right\}$$

where $M(\rho) = \int_{-\infty}^{\infty} e^{\rho x} k(x) dx$, the moment generating function of $k(x)$.

Simulation with Logistic Map
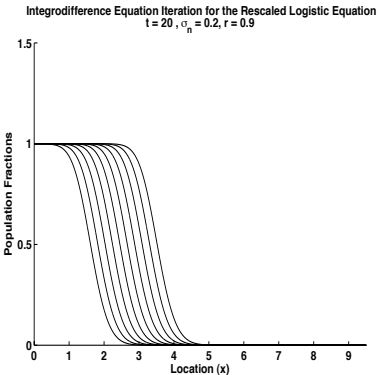
LOGISTIC: Iterates 0 to 50, r = 0.9 and x_0 =0.3

Integrodifference Equation Iteration for the Rescaled Logistic Equation
t = 20 , σ_n = 0.2, r = 0.9

Simulation with Logistic Map

LOGISTIC: Iterates 0 to 50, r = 1.9 and x_0 =0.3

Integrodifference Equation Iteration for the Rescaled Logistic Equation
t = 20 , σ_n = 0.2, r = 1.9

Discrete SIS model with overlapping generations:

$$
\begin{aligned}
S_{t+1} &= \varphi(S_t, I_t) = Q(z_t)f(P_t) + \gamma Q(z_t)S_t + \gamma(1-\sigma)I_t, \\
I_{t+1} &= \psi(S_t, I_t) = (1 - Q(z_t))f(P_t) + \gamma(1 - Q(z_t))S_t + \gamma\sigma I_t,
\end{aligned}
$$

where $P_{t+1} = S_{t+1} + I_{t+1}$ and $Q(z_t) = e^{-\alpha z_t}$ is the probability of not becoming infected in t to $t+1$ when the disease prevalence is $z_t = \frac{I_t}{f(P_t) + P_t}$.

- σ gives the fraction of infected individuals that remain infected from one time step to the next.

- The function $Q(z_t)$ denotes the proportion of susceptible individuals that do not become infected at time t given disease prevalence z_t.

- In general, $Q : [0, \infty) \to [0, 1)$ is a monotone concave function with $Q(0) = 1$; $Q'(u) < 0$ and $Q''(u) \geq 0$ for all $u \in [0, \infty)$.

- As is common, we model the "probability" of not becoming infected as

$$Q(z_t) = e^{-\alpha z_t}.$$

That is encounters that lead to infection are modeled via a Poisson process.

Adding Dispersal

Assuming that dispersal occurs after mortality, and that the disease does not affect the dispersal process, we can add dispersal to the SIS model to give

$$S_{t+1}(x) = \int_{-\infty}^{\infty} \varphi(S_t(y), I_t(y)) \, k(x - y) \, dy,$$

$$I_{t+1}(x) = \int_{-\infty}^{\infty} \psi(S_t(y), I_t(y)) \, k(x - y) \, dy,$$

a system of integrodifference equations.

$\Lambda = 500, \gamma = 0.98$, thus $\Lambda^* = \Lambda/(1 - \gamma) = 25000$
IDE iterated on the domain $-15 \leq x \leq 15$ with initial data
$I_0(x) = 750$ on $-1 \leq x \leq 1$ and $I_0(x) = 0$ elsewhere.

SIS with Overlapping Generations and Constant Recruitment
$t = 22$, $\sigma_n = 0.5$, $\alpha = 1.5$, Ro = 1.9478
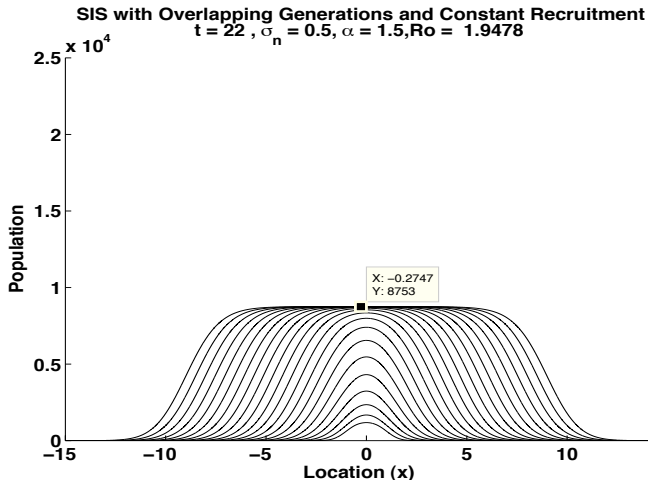
Karen Rios-Soto PhD Thesis
Epidemic Spread With Non-monotone Epidemic Functions

- Simulations of the integrodifference equations in two spatial dimension are carried out using the bivariate normal kernel.

$$k(x_1, x_2) = \frac{1}{2\pi\sigma_1\sigma_2\sqrt{1-\rho^2}} \exp\left[\frac{1}{2(1-\rho^2)}\left(\frac{x_1^2}{\sigma_1} + \frac{x_2^2}{\sigma_2} - \frac{2\rho x_1 x_2}{\sigma_1\sigma_2}\right)\right.$$

with mean $(0, 0)$. Here, ρ is the correlation coefficient between x_1 and x_2. That is, $\rho = cor(x_1, x_2) = \frac{\sigma_{12}}{\sigma_1\sigma_2}$ with covariance matrix

$$\Sigma = \begin{bmatrix} \sigma_1^2 & \rho\sigma_1\sigma_2 \\ \rho\sigma_1\sigma_2 & \sigma_2^2 \end{bmatrix}.$$

Simulations for SIS Epidemic Model with Constant Recruitment in 2D Spatial Dimensions

SIS with Overlapping Generations in Two Spatial Dimensions
with t=23, α =1.5 and Ro = 1.9478
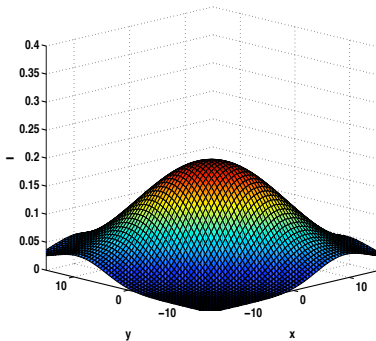
SIS with Overlapping Generations in Two Spatial Dimensions
with t=10, α =4.5 and Ro = 5.8434
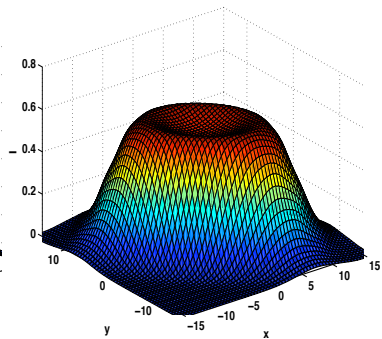
- (H1). $f(0) = 0$ and $f(1) = 1$. f is nondecreasing on $(0, 1)$ and $f(x) > x$ for $x \in (0, 1)$.
- (H2). $f'(0) > 1$ and $D > 0$, for $0 \le u \le 1$,

$$f'(0)(x - Dx^2) \le f(x) \le f'(0)x.$$

nonmonotone growth functions

- overcompensation may occur by cannibalism (eating oneself) or predation from other species. High density of a population may also induce overcompensation as it may happen that no one sequesters enough resources to reproduce

nonmonotone growth functions

- The Ricker growth function

$$f(u) = ue^{r-u}, \quad r > 0. \tag{0.6}$$

Systems of discrete-time integro-difference models

-
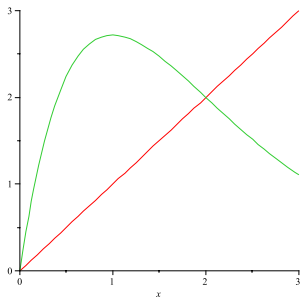
$$X_{n+1}(x) = X_n(x)e^{r_1 - X_n(x) - \sigma_1 Y_n(x)}$$
$$Y_{n+1}(x) = Y_n(x)e^{r_2 - Y_n(x) - \sigma_2 X_n(x)} \tag{0.7}$$

  where $r_1, r_2, \sigma_1, \sigma_2$ are all positive constants.

- Hassell and Comins, 1976

Systems of discrete-time integro-difference models

-
$$X_{n+1}(x) = \int_{\mathbb{R}} k_1(x - y) X_n(y) e^{r_1 - X_n(y) - \sigma_1 Y_n(y)} dy$$
$$Y_{n+1}(x) = \int_{\mathbb{R}} k_2(x - y) Y_n(y) e^{r_2 - Y_n(y) - \sigma_2 X_n(y)} dy \tag{0.8}$$

Example

- Hassell and Comins' model has four equilibria $(0, 0), (0, r_2), (r_1, 0)$ and $(\frac{r_1 - \sigma_1 r_2}{1 - \sigma_1 \sigma_2}, \frac{r_2 - \sigma_2 r_1}{1 - \sigma_1 \sigma_2})$.

Example

- The change of variables $p = X, q = r_2 - Y$ allows to convert system (0.8) into the following coupled system of integrodifference equations

-
$$
\begin{aligned}
p_{n+1}(x) &= \int_{\mathbb{R}} k_1(x - y) f(p_n(y), q_n(y)) dy \\
q_{n+1}(x) &= \int_{\mathbb{R}} k_2(x - y) g(p_n(y), q_n(y)) dy.
\end{aligned}
\tag{0.12}
$$

where

$$
\begin{aligned}
f(p, q) &= h(p) e^{r_1 - \sigma_1 r_2 + \sigma_1 q} \\
g(p, q) &= r_2 - (r_2 - q) e^{q - \sigma_2 p} \\
h(p) &= p e^{-p}
\end{aligned}
$$

- The biological interpretation of these conditions is straightforward. For an invasion to be successful, the overall dispersal of the invader (X) is relatively larger than the overall dispersal of the out-competed resident (Y). Further competition favors the invader whenever σ_1 is sufficiently small (invader less affected by competition) and σ_2 is sufficiently large (a relatively fragile resident, that is, more susceptible to interference competition).

- $$\int_{\mathbb{R}} k_1(s)e^{\mu s}ds \geq \int_{\mathbb{R}} k_2(s)e^{\mu s}ds$$

  for $\mu > 0$

- the overall dispersal of the invader (X) is relatively larger than the overall dispersal of the out-competed resident (Y).

- There are traveling wave solutions of (0.12) "loosely" connecting its two equilibria $(0, 0)$ and (r_1, r_2). Equivalently, there are traveling wave solutions of (0.8) "loosely" connecting its two boundary states $(0, r_2)$ and $(r_1, 0)$. Here the term "loosely" means the traveling waves may oscillate around the equilibria since they are not necessarily monotone.

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Influenza and Transportation
HPI
Tuesday, March 26.

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3/26/13   Arizona State University

Challenges in Mathematical Epidemiology

1. Transportation/internal travel alone **cannot** entirely explain the three different waves of the AH1N1 epidemic that have been observed in Mexico.

2. Social distancing measures (school closures and more), vacations and travel within the network help account for the characteristics and spatial tendencies observed in the reported data: **three waves, delays in some states, and the third (longer lasting) wave**.

3. School closures, summer vacations, have a strong modulating effect on the epidemic curves.

Time course of pandemic reported Mexican data up to Jan 4, 2010

First two local maxima: at times around social distancing and/or school closures.
First two local minima: at times when social distancing is relaxed or schools reopen.
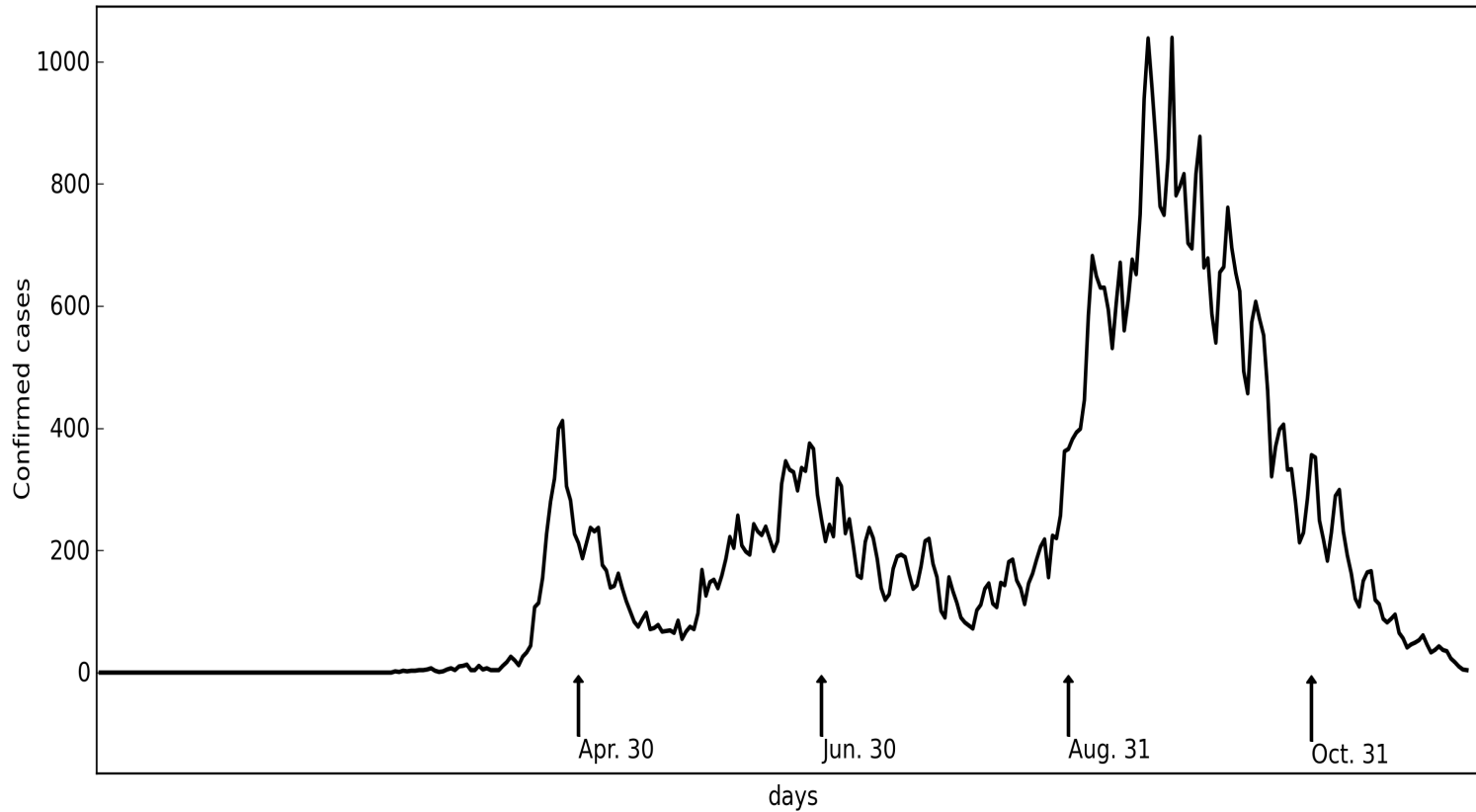
School closing and social distancing implementations impact the shape the epidemic waves.
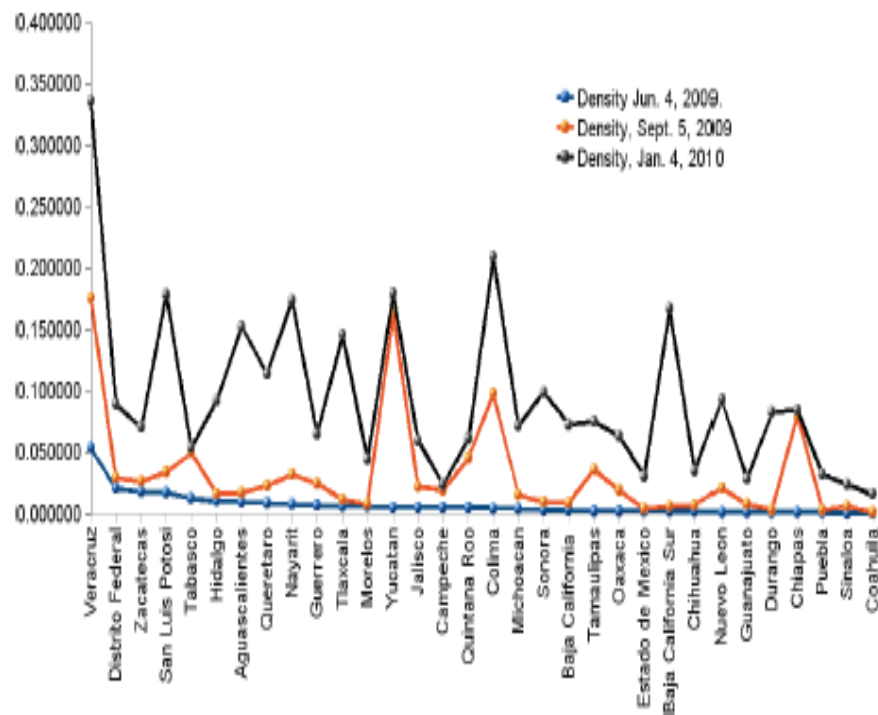**April 30 – School closures**
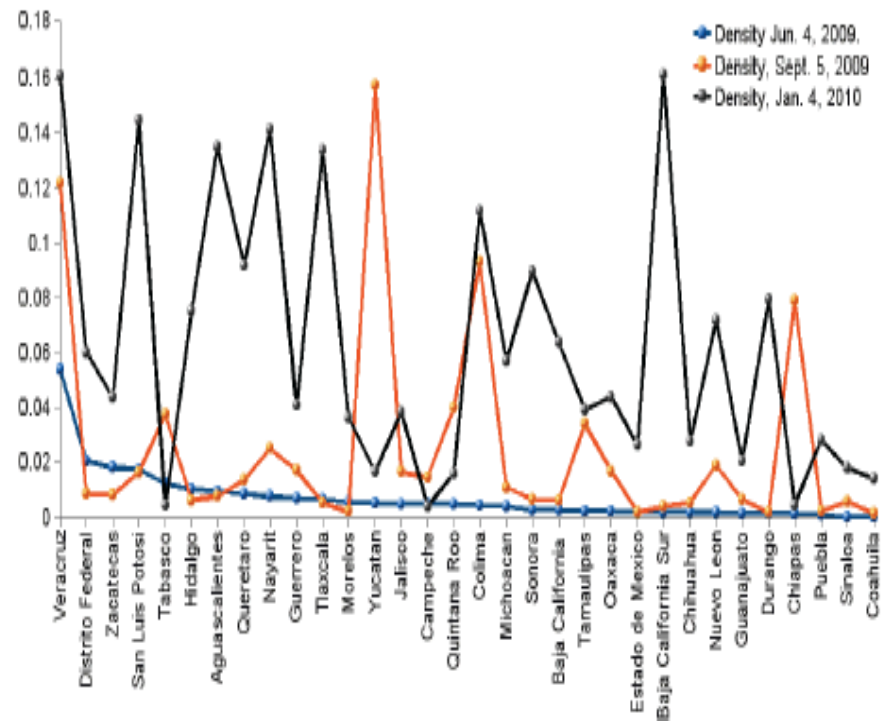**June 30 – School Vacations**
August 31 – Classes start

Confirmed cases reported by each of the Mexican States.

A. Local percentage of confirmed cases.

B. Difference between reports.

Three reports dated June 4, September 5, 2009 and January 4, 2010.
Left: cumulative, Right: Difference between reports.
Different states contribute at different times to the outbreak.

Local mass transportation by land

San Luis Potosi
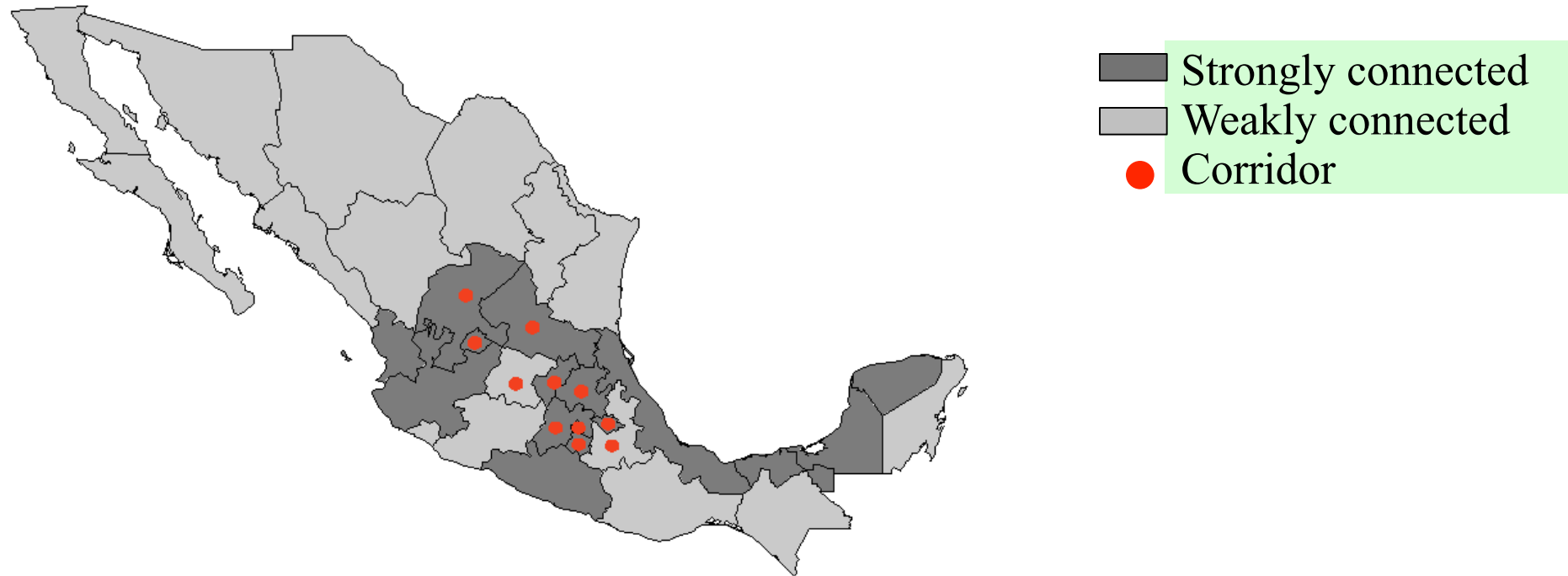
Mexico City

Hidalgo

Tlaxcala

In Mexico most traffic flow goes through Mexico City. **Did transportation drove the waves**?

State populations of the model were modeled as nodes in a star-shaped graph with the center (hub) corresponding to the capital "El Distrito Federal or DF or Mexico City".

Cities are classified as strongly connected to México City if the in and out traffic from Mexico City is heavy. These cities form part of the historical "influenza corridor" that extends from north to south and is bounded by two mountain ranges, the east and west Sierra Madres (e.g. Morelos, D.F. State of México, Tlaxcala, Queretaro, San Luis Potosí)
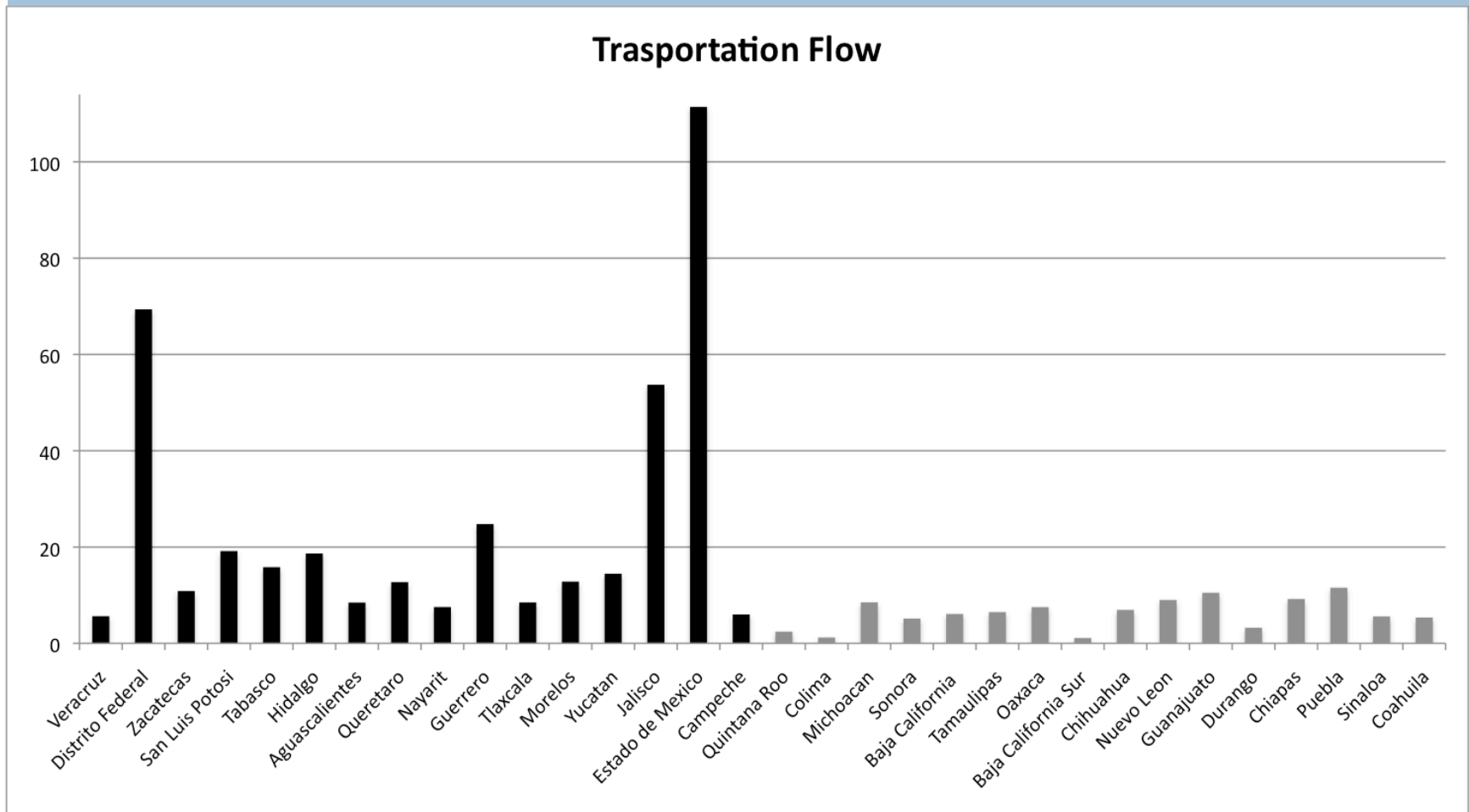
Strongly connected
Weakly connected
● Corridor

Everybody that travels from X to Y is assumed to go through Mexico City."
The Mexican States are nodes of an internal transportation network that divides them
into *strongly* and *weakly connected depending on the strength of the traffic*
***Land flow* in and out of Mexico City (The influenza corridor describe by historian**
Roberto Acuña-Soto).

Mexican population by State: The black and gray bars show, the states that are strongly and weakly connected to D.F. (Mexico City), respectively.
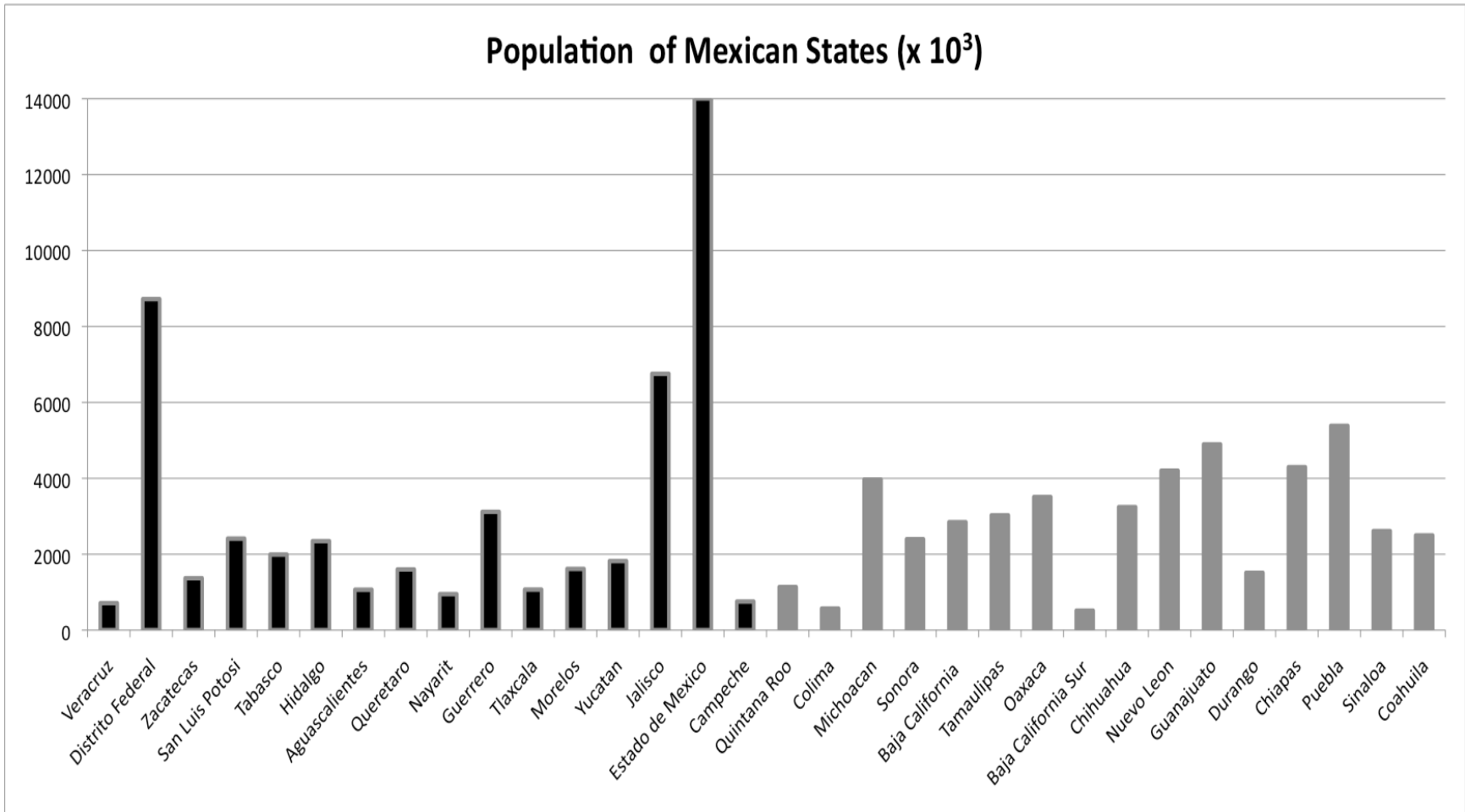
Histogram of populations(x1000) in México.

Adjusted land transportation flow by state per day.


Trasportation Flow

Number of people transported every day between different states and D.F. The flow has been adjusted to reflect the strong or weak connectivity and the population size in each state.

Susceptible (S); Exposed (Incubating, E); Infected (asymptomatic and symptomatic, I); Symptomatic diagnosed (confirmed cases, J); Recovered (R) and Vaccinated (V)

**Flow between disjoint epidemiological compartments:**
The vaccines is distributed daily and it is a function of the remaining stock pile available. Stockpile size is controlled by the known maximum number of vaccines available
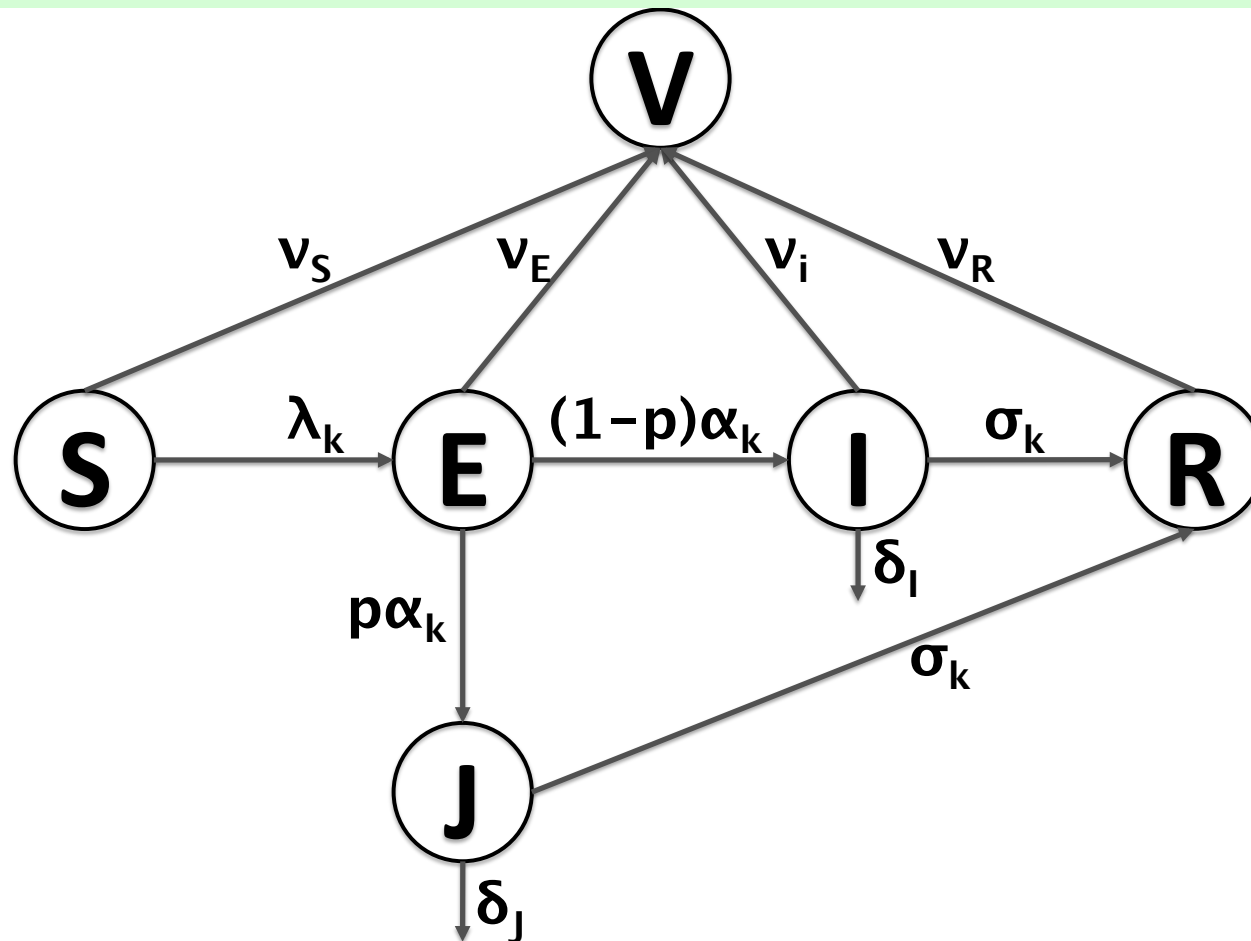
A rate of infection of about .95 gives the closest shape to the data (incubation and recovery periods of 2 and 7 days). The data (**black**) and model (**green**) curves are normalized to have peaks at 1. The infection rate is adjusted until the best fit (rate of change of **the data curve)** up to the peak is found. The start date is changed systematically until the best approximation is found.

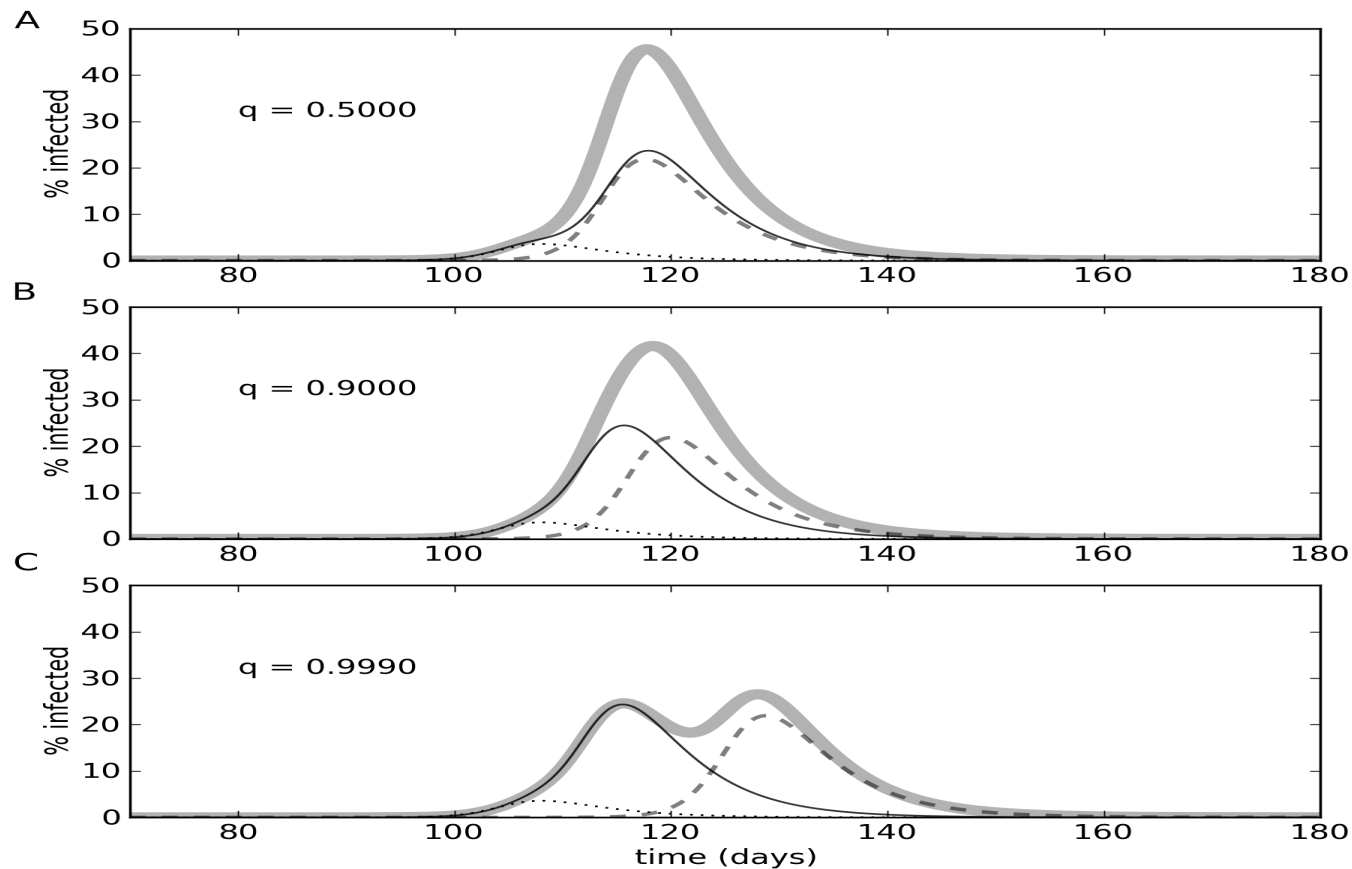r_{infec}= 0.950 , τ_{incub}= 2 , t=118

t=117

t=73
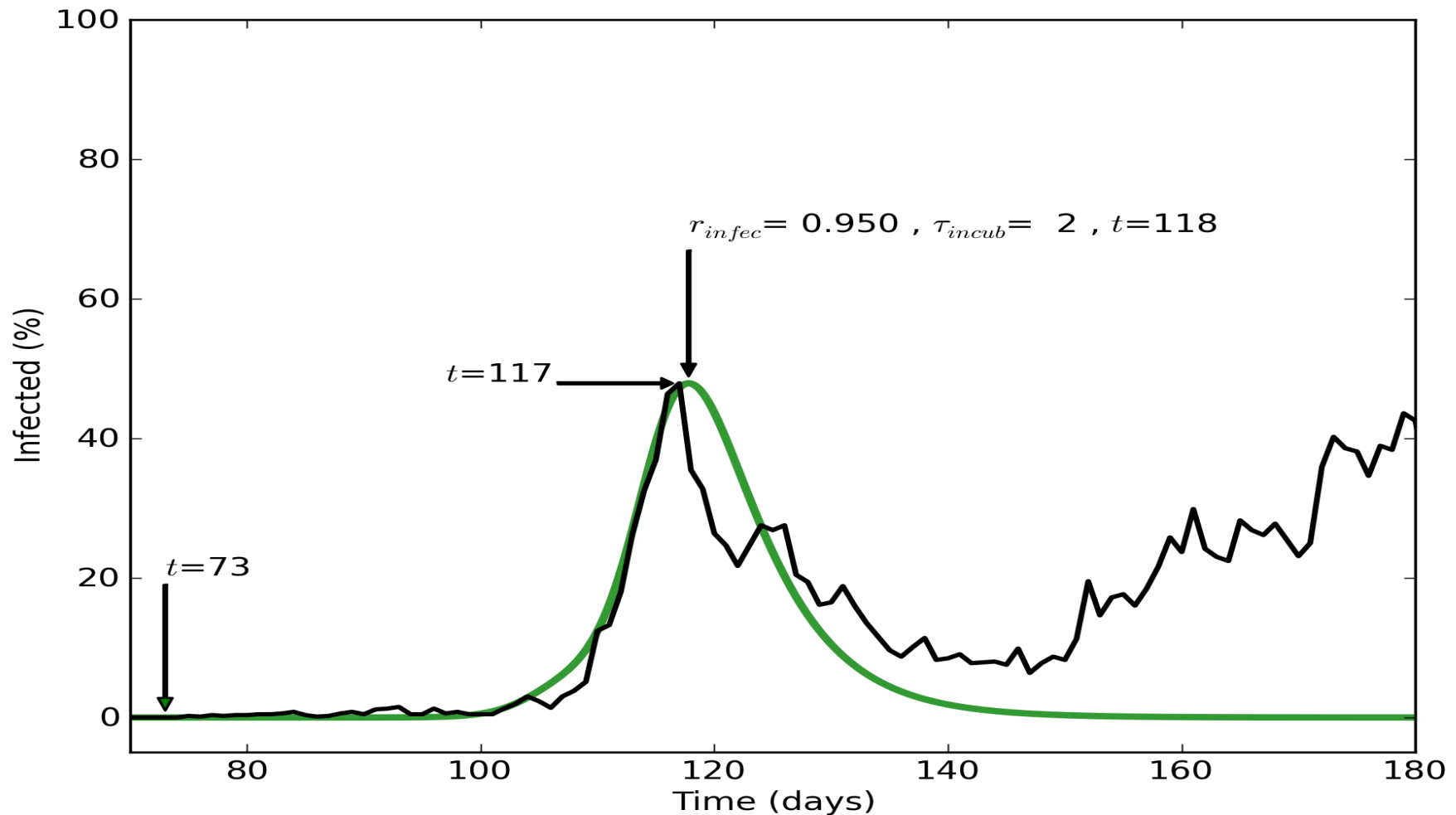
Sigmoid Modulation Function g(t), captures the changes in effective contact rates.
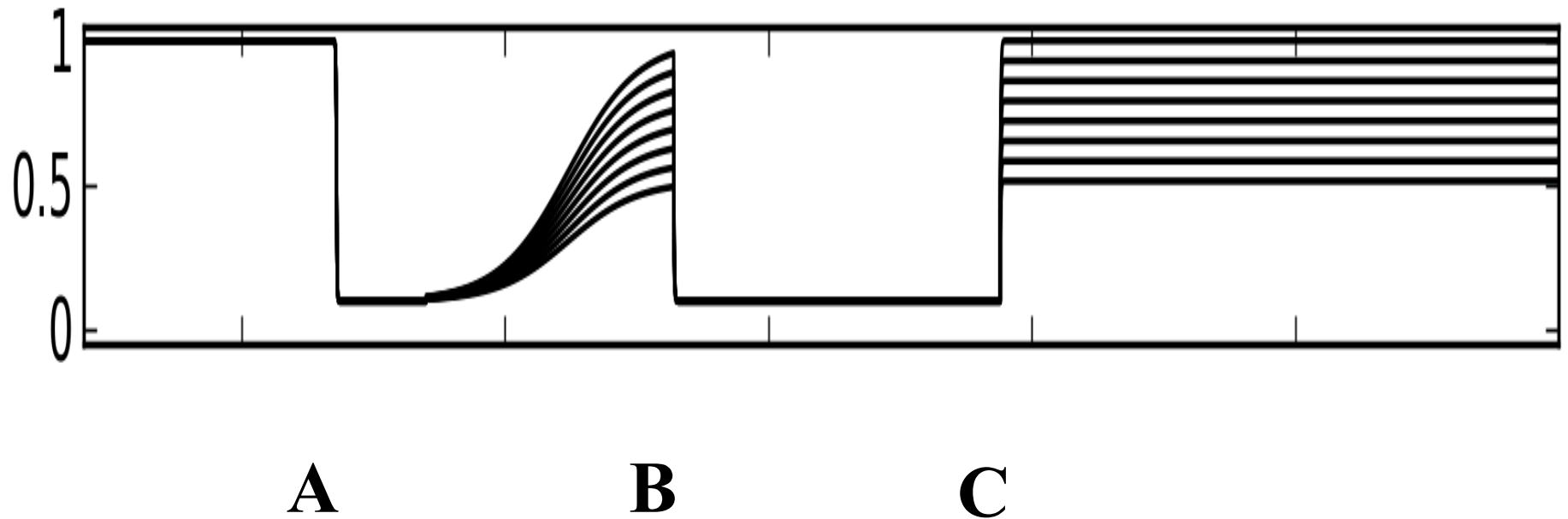
A - **School closure** (Apr 30)
B - **Vacation Starts** (Jun 30)
C - **School Classes Start** (Aug 30)

Influence of the transportation in the time course of the epidemic: q the probability that the flow originates at a strongly connected state

Thick gray: All cases. Black solid: Strongly connected. Black dashed: Weakly connected. Dotted line: Starting state, Oaxaca.

Social distancing and school closures may generate multiple waves
(Thick curves --- cumulative; solid –from strongly connected; dash—from weakly connected).
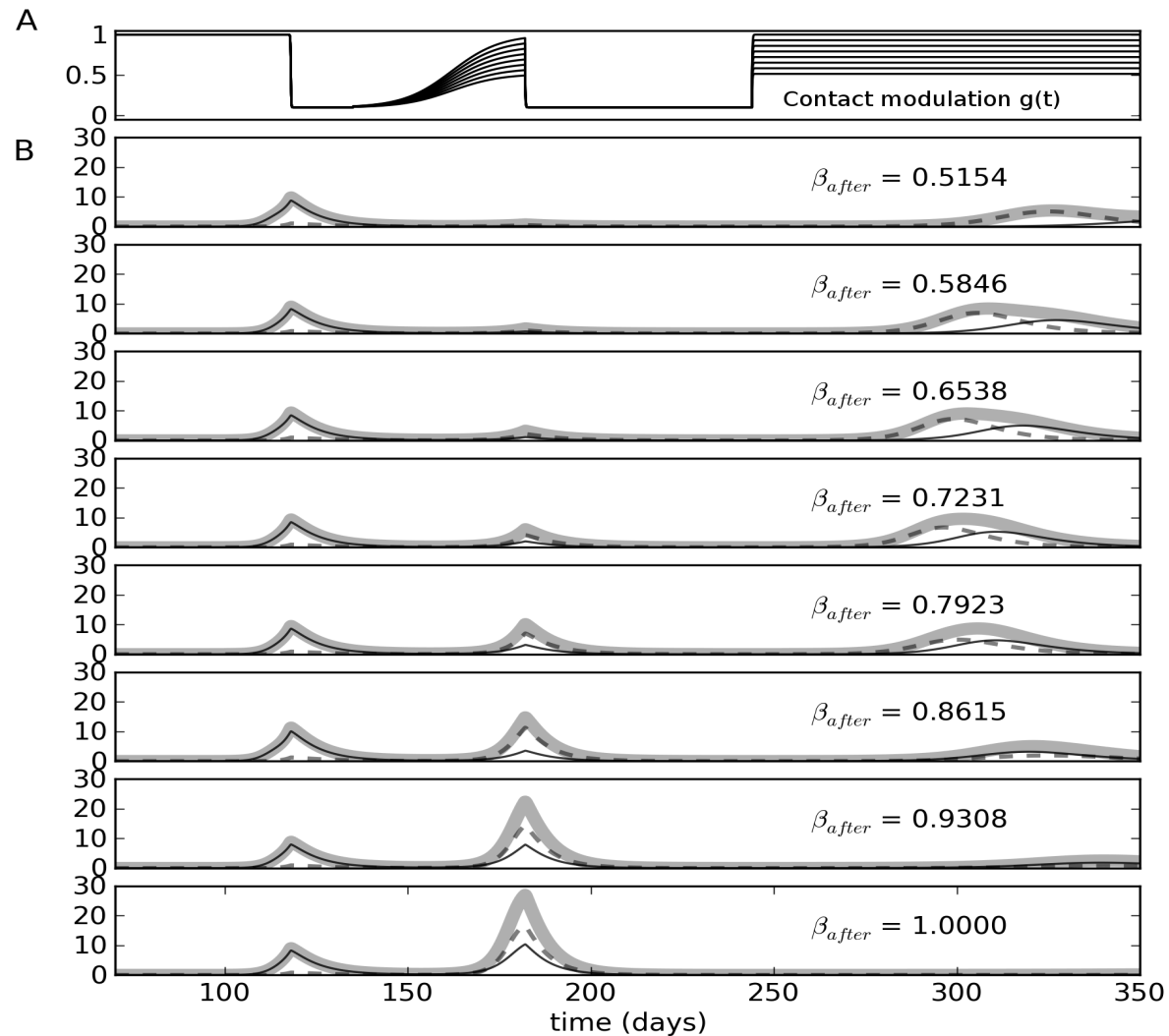
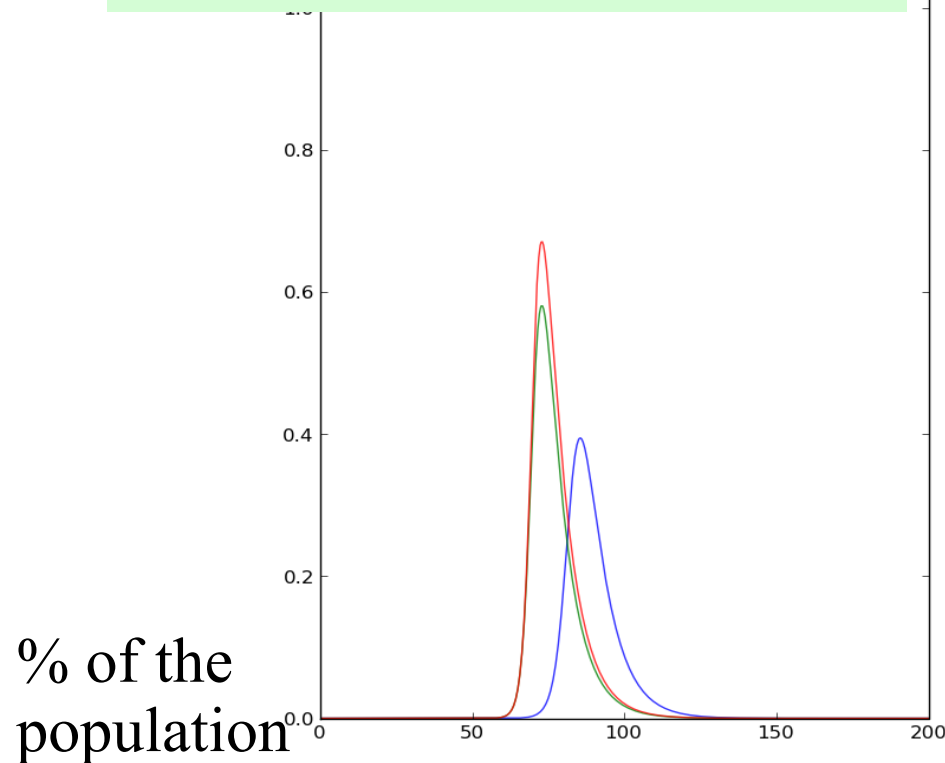Lines in panel A correspond (from top to bottom) to the different panels in B.

Wasted Vaccine: vaccinated individuals come from the unprotected, incubating, unconfirmed, or recovered groups (people not presenting symptoms)

Different epidemic outbreaks for third wave

Wasted vaccines: Day 0 is September 1st.

% of the population

Days after epidemic start

— 40 days
+ 65 days
+ 120 days
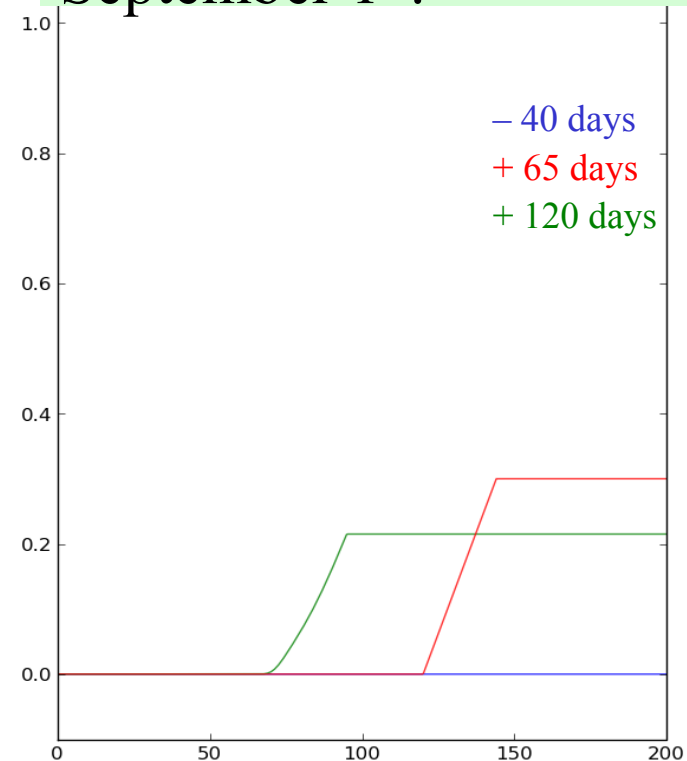
Days after epidemic start

Conclusions I: (Marco Herrera-Valdez; Maytee Cruz-Aponte; and Jose Vega-Guzman at ASU): http://mcmsc.asu.edu/

1. Transportation/internal travel alone **cannot** entirely explain the three different waves of the AH1N1 epidemic that have been observed in Mexico.

2. Social distancing measures (school closures and more), vacations and travel within the network help account for the characteristics and spatial tendencies observed in the reported data: **three waves, delays in some states, and the third (longer lasting) wave**.

3. School closures, summer vacations, have a strong modulating effect on the epidemic curves.

Conclusions II (Marco Herrera-Valdez; Maytee Cruz-Aponte; and Jose Vega-Guzman at ASU): http://mcmsc.asu.edu/

1. **Early arrival of H1N1 vaccines** (40 days before the fall start of school) before the third wave, even at 30% levels, would have reduced the number of infected people. Late arrival has been less effective.

2. The number of **wasted vaccines** increases linearly from the start of the epidemic.

3. The number of wasted vaccines turned out to be almost as large as the number of **administered vaccines** (after the start of third wave).

Conclusions A

1. Mexico did a superb job in responding to this health emergency given the high levels of uncertainty. **So far, we have had a hurricane "Rita" rather than a "Katrina"**. So what did we learn?

2. . Massive social distancing measures **cannot be sustained** for long periods of time due to economic reasons.

3. Vaccine production limitations meant that **most nations** had limited and late access to vaccines at best. **National health disparities** became **flagrantly** as the ability to secure/purchase antiviral medication, "fast" access to vaccine stockpiles, and the reductions in risks from access to modern delivery, surveillance and diagnostic systems … well are country-dependent. An issue that must be addressed (WHO or UN?).

Conclusions B

1. The importance of **global surveillance/sentinel disease-specific** systems like those in use to warn us against hurricanes, tsunamis, or earthquakes, are needed at a global scale.

2. **Timely serological accurate studies** that assess **in real time** the magnitude and severity of influenza outbreaks are missing. How many cases did we really have? We "count" the number of **severe** (reported) A-H1N1 cases but hardly know anything about the *potentially* huge number of asymptomatic or mild infections.

3. **A definition of pandemic** that incorporates severity (via fast and effective serological studies) via the ratio of severe to asymptomatic and mild infections, is needed.