ANTI-GRAVITY MODELS FOR EPIDEMIC SPREAD OF INFECTIOUS DISEASES ON LONG DISTANCE TRAVEL NETWORKS

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Based on the joint work with G. Röst (U of Szeged) and J. Wu (York U)

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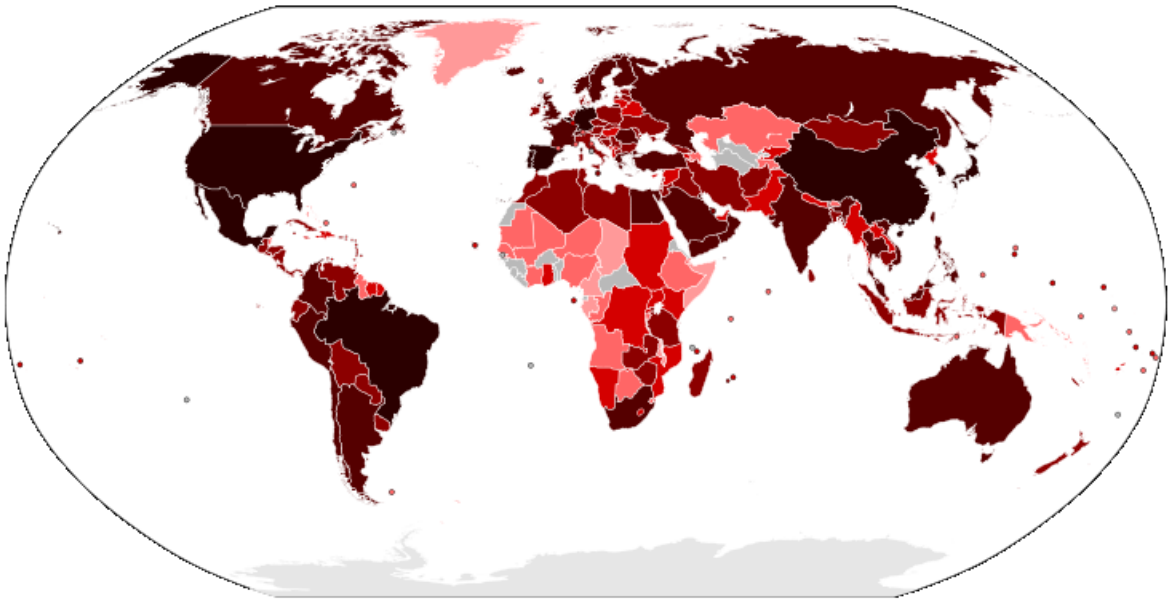
Outline

1. Introduction
   modeling disease spread on travel networks
2. Model formulation
   for influenza and global airline transportation
3. DDE with dynamically defined delay feedback
   fundamental properties
4. Reproduction number
   dependence on key model parameters
5. Simulations, datafit
   influence of heterogenity

Pandemic spread of infectious diseases

- Infectious diseases cross national boundaries
- Increased speed of spread to distant territories (air transportation)
- SARS 2002-2003, H1N1 influenza 2009



Modeling on travel networks

- Meta-population models in connecting regions (Arino (2009), Arino & Van den Driessche (2003), Ruan et al (2006), etc)
- Cui et al (2006), Takeuchi et al (2007): Passengers contract the disease while traveling – ODE models

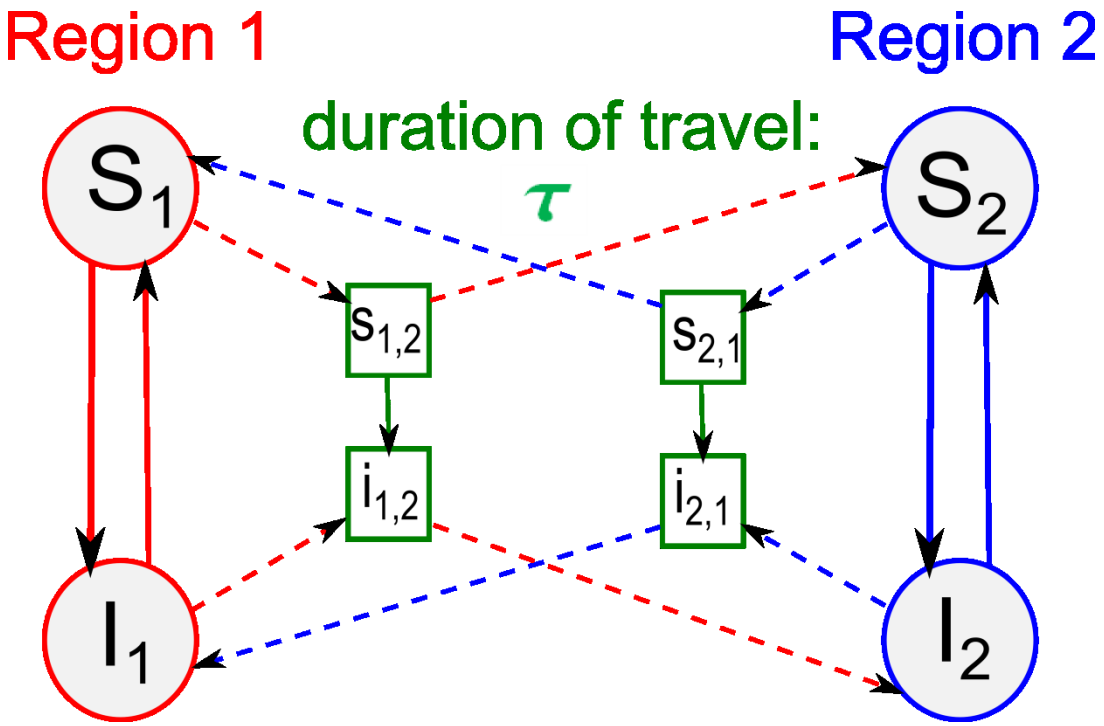
  Tuberculosis, measles, seasonal influenza are transmissable during commercial flights (ECDC)

- Liu et al (2008) introduced transporation time and the possible infections during the trip – DDE models

  Long travel times (~6 – 14 h) are not negligible

  Fast progressing diseases, even a small delay is significant

SIS-based model for 2 regions with time delay



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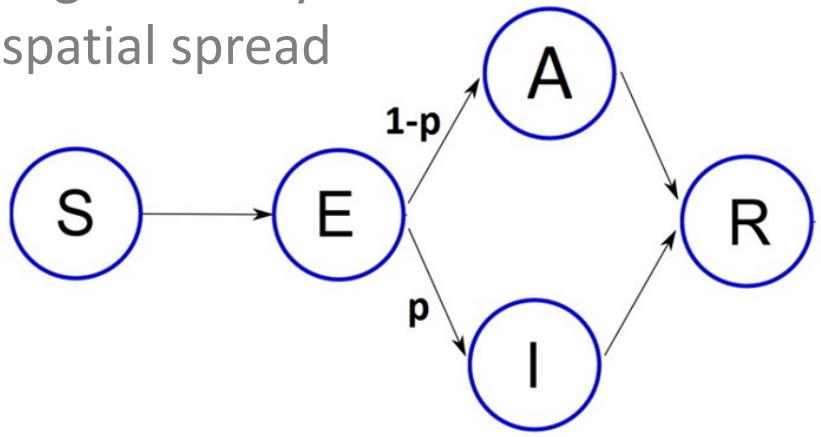
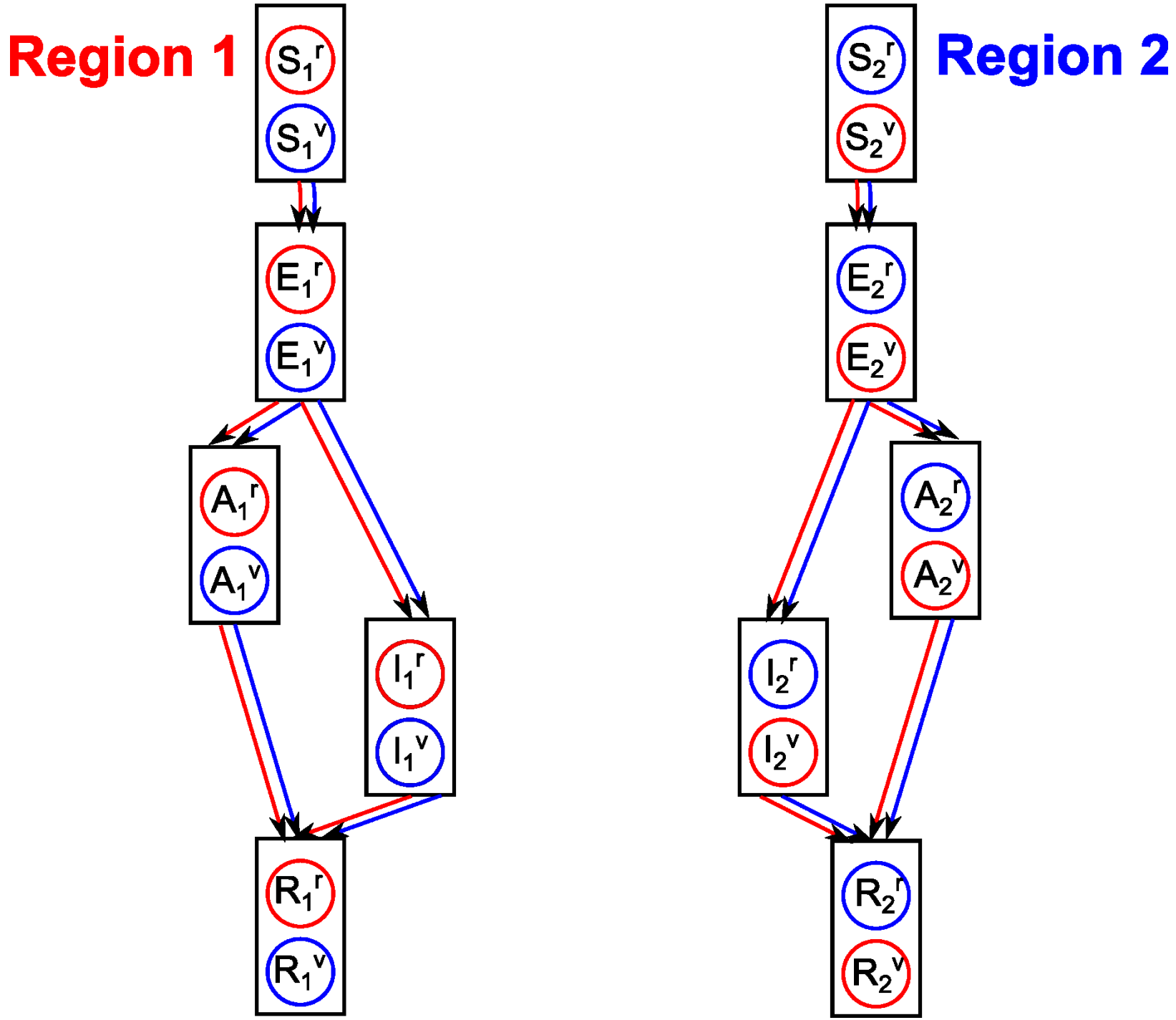
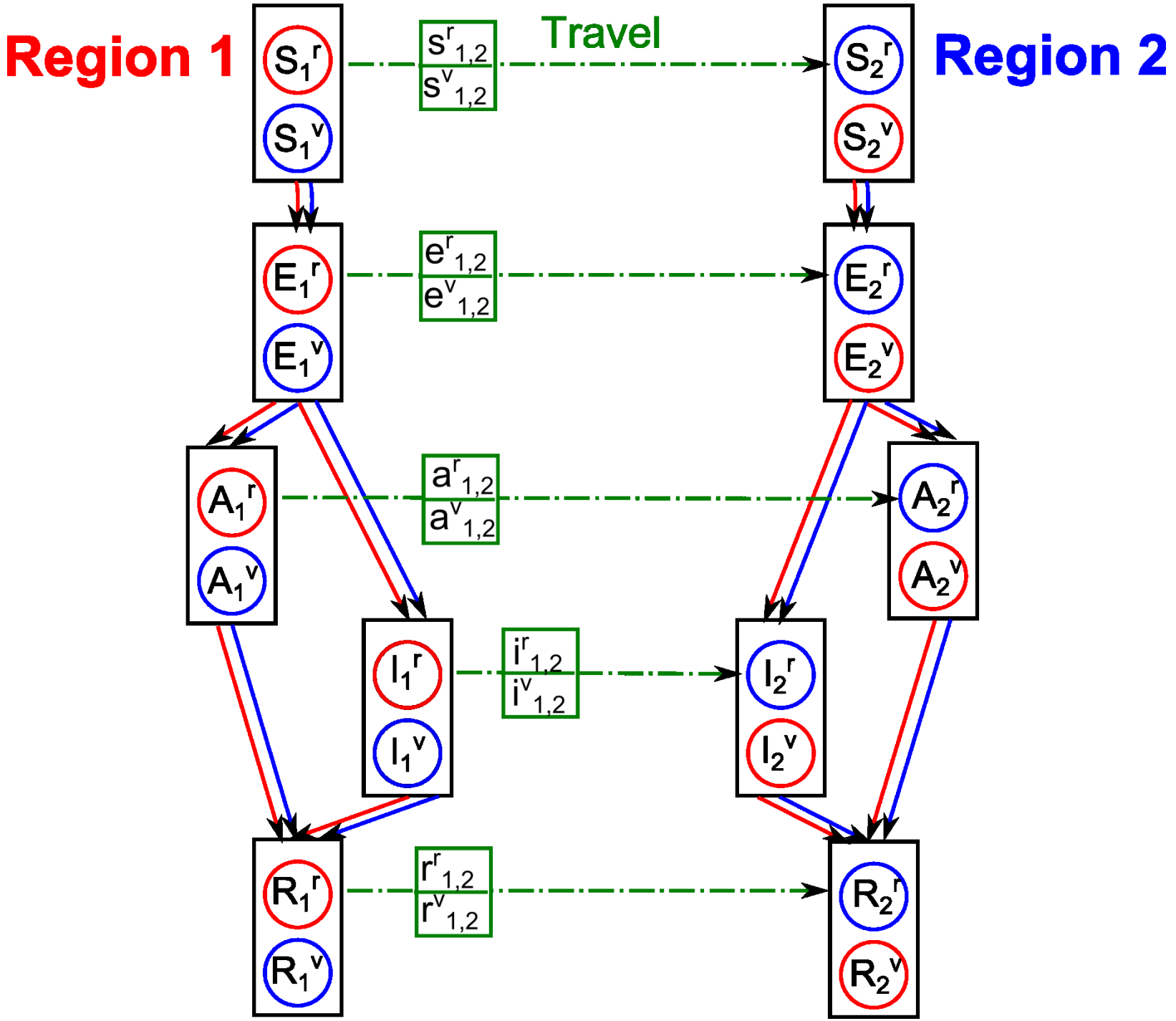
Adapting the model to influenza

- For most diseases which cause global pandemics, an SIS-type model is not adequate -> SEAIR model
- Antygravity-type model

  the longer the flight, the more infections on-board
- Distinguish local residents from temporary visitors
  1. Number of visitors, average visiting time may significantly affect the speed of spatial spread
  2. Visitors and residents can have different mixing patterns, contact rates




Region 1
S_1^r
S_1^v
E_1^r
E_1^v
A_1^r
A_1^v
I_1^r
I_1^v
R_1^r
R_1^v
Region 2
S_2^r
S_2^v
E_2^r
E_2^v
A_2^r
A_2^v
I_2^r
I_2^v
R_2^r
R_2^v


Region 1
Travel
Region 2
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S_2^v
E_1^r
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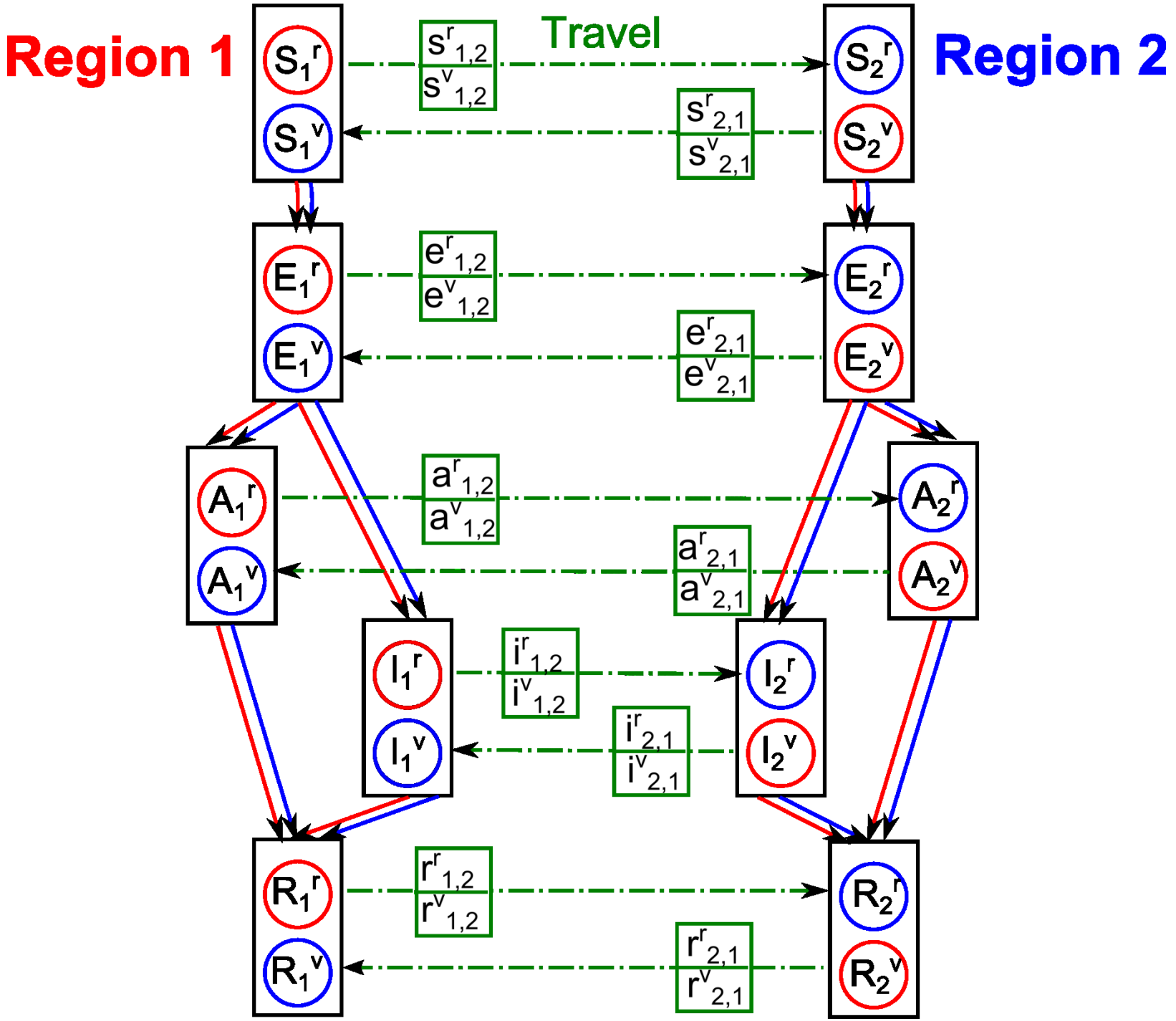
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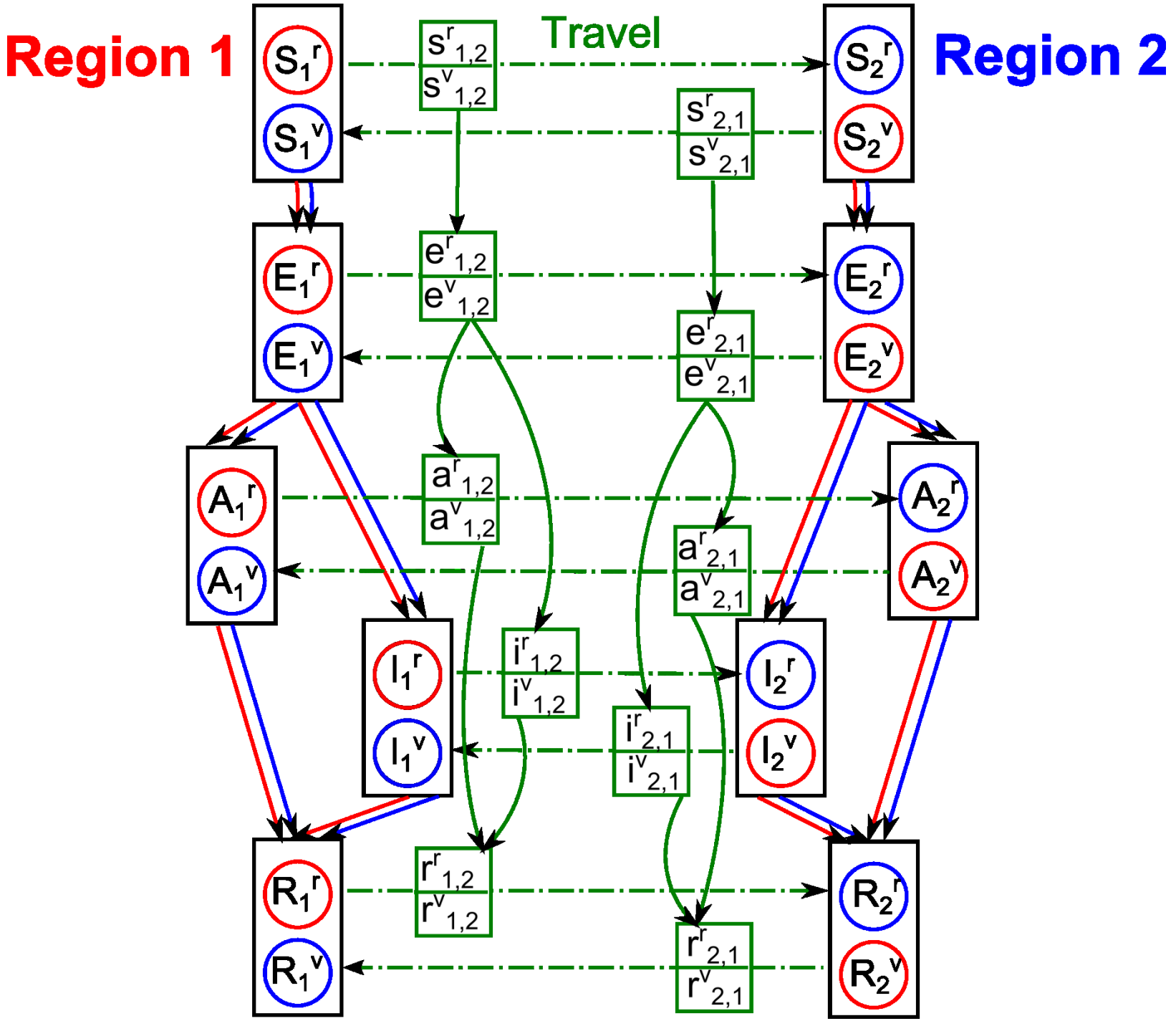
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$r^r_{2,1}$
$r^v_{2,1}$
R_2^r
R_2^v

dynamics in the region

outflow due to travel

inflow due to travel

$$
\begin{cases}
\dot{S}_1^r(t) = \Lambda_1 - S_1^r(t)F_1^r(t) - d_1^r S_1^r & -\alpha_1 S_1^r(t) + s_{2,1}^v(\tau, t-\tau), \\
\dot{E}_1^r(t) = S_1^r(t)F_1^r(t) - (d_1^r + \mu_E)E_1^r(t) & -\alpha_1 E_1^r(t) + e_{2,1}^v(\tau, t-\tau), \\
\dot{A}_1^r(t) = (1-p)\mu_E E_1 - (d_1^r + \mu_A)A_1^r(t) & -\alpha_1 A_1^r(t) + a_{2,1}^v(\tau, t-\tau), \\
\dot{I}_1^r(t) = p\mu_E E_1 - (d_1^r + \delta + \mu_I)I_1^r(t) & -\alpha_1 I_1^r(t) + i_{2,1}^v(\tau, t-\tau), \\
\dot{R}_1^r(t) = \mu_I I_1^r(t) + \mu_A A_1^r(t) - d_1^r R_1^r(t) & -\alpha_1 R_1^r(t) + r_{2,1}^v(\tau, t-\tau), \\
\\
\dot{S}_1^v(t) = -S_1^v(t)F_1^v(t) - d_1^v S_1^v(t) & -\gamma_1 S_1^v(t) + s_{2,1}^r(\tau, t-\tau), \\
\dot{E}_1^v(t) = S_1^v(t)F_1^v(t) - (d_1^v + \mu_E)E_1^v(t) & -\gamma_1 E_1^v(t) + e_{2,1}^r(\tau, t-\tau), \\
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\dot{R}_1^v(t) = \mu_I I_1^v(t) + \mu_A A_1^v(t) - d_1^v R_1^v(t) & -\gamma_1 R_1^v(t) + r_{2,1}^r(\tau, t-\tau)
\end{cases}
$$

- The dynamics during travel is described by an SEAIR-based model. No closed form solution.
- No explicit formula for the inflow terms.

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DDE system with dynamically defined delay feedback

- The model is equivalent to a large system of DDEs

$$(1)\quad \begin{cases} x'(t) = \mathcal{F}(x(t), x(t-\tau)) = f(x(t)) + W(x(t-\tau)), \\ x_0 = \varphi, \end{cases}$$

where $t \in \mathbb{R}$, $t \geq 0$, $x : \mathbb{R} \to \mathbb{R}^{20}$, $f, W : \mathbb{R}^{20} \to \mathbb{R}^{20}$

- Not a common DDE system: the delay terms require the solution of another differential equation system

$$\begin{cases} y'(s) = g(y(s)), \\ y(0) = y_*, \end{cases}$$

where $s \in \mathbb{R}$, $s \geq 0$, $y : \mathbb{R} \to \mathbb{R}^{20}$, $g : \mathbb{R}^{20} \to \mathbb{R}^{20}$ and

$$W(z) := y(\tau, 0; h(z)),$$

where $z \in \mathbb{R}^{20}$ and $h : \mathbb{R}^{20} \to \mathbb{R}^{20}$

Fundamental properties of system (1)

1. Existence and uniqueness of solution
2. Boundedness and nonnegativity of solution

Reproduction number: average number of new infections generated by 1 exposed individual introduced into a wholly susceptible population

3. The unique DFE is asymp. stable (unstable) if $R_0<1$ ($R_0>1$)
4. In the disease free subspace the DFE is GAS

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Reproduction number

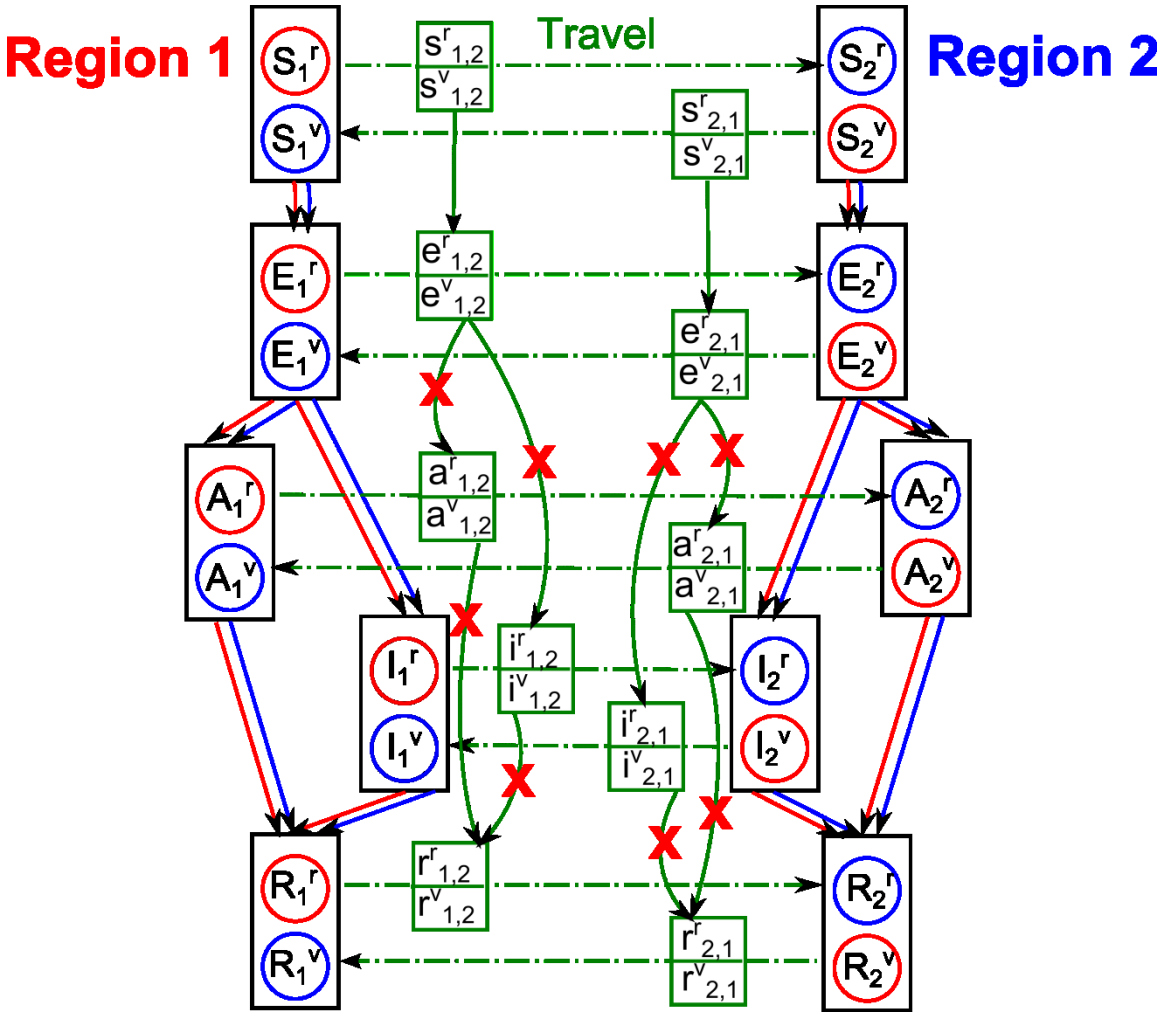
- Average number of new infections generated by 1 exposed individual introduced into a wholly susceptible population
- In absence of travel: local reproduction numbers are easy to obtain

$$\mathcal{R}_{L,1} = \beta_1^{rr}\left(\frac{p}{\mu_I} + (1-p)\frac{\rho}{\mu_A}\right), \mathcal{R}_{L,2} = \beta_2^{rr}\left(\frac{p}{\mu_I} + (1-p)\frac{\rho}{\mu_A}\right)$$

$$\mathcal{R}_0 = \max\{\mathcal{R}_{L,1}, \mathcal{R}_{L,2}\}$$

- With travel dynamics, unlimited # of travels: very complicated

- The period of travel is relatively short (~12 hours).
- ASSUMPTION: no movement from E to I, A (1.4 days), from I, A to R (3 days / 4.1 days)



Next generation matrix

- 4 types of individuals:
  resident / visitor in region 1 / 2
- 4x4 next generation matrix
- R_0: dominant eigenvalue of NGM

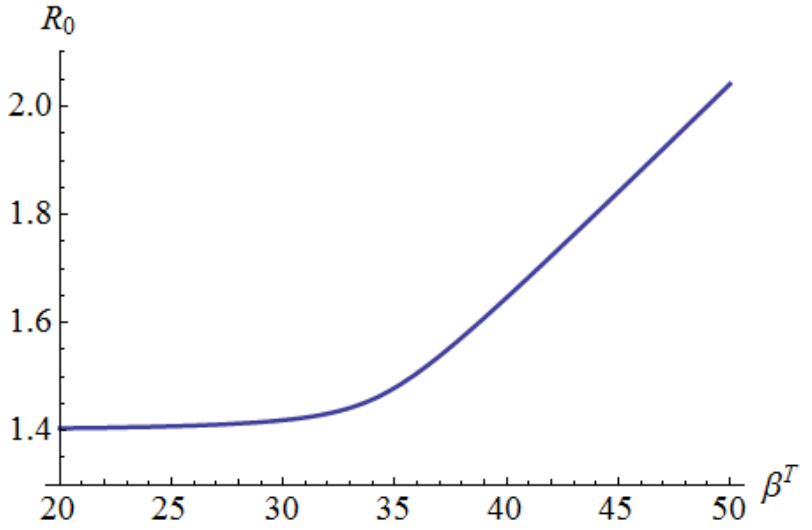
$$\mathcal{NGM} = \begin{pmatrix} R_{11}^{rr} & R_{11}^{vr} & R_{21}^{rr} & R_{21}^{vr} \\ R_{11}^{rv} & R_{11}^{vv} & R_{21}^{rv} & R_{21}^{vv} \\ R_{12}^{rr} & R_{12}^{vr} & R_{22}^{rr} & R_{22}^{vr} \\ R_{12}^{rv} & R_{12}^{vv} & R_{22}^{rv} & R_{22}^{vv} \end{pmatrix}$$

Each element of this NGM is complicated to find.

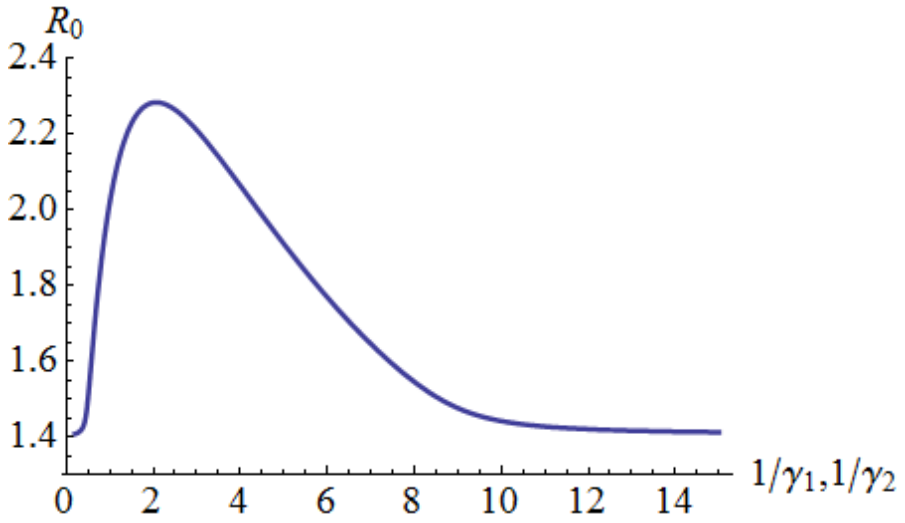
$$
\begin{aligned}
R_{12}^{rv} =& p\left(\frac{\mu_E\alpha_1}{(\alpha_1+\mu_E+d_1^r)(\gamma_2+\mu_E+d_2^v)-\alpha_1\gamma_2}\cdot\right.\\
&\frac{(\gamma_2+\mu_E+d_2^v)(\gamma_2+\mu_I+\delta+d_2^v)+\alpha_1\gamma_2}{(\alpha_1+\mu_I+\delta+d_1^r)(\gamma_2+\mu_I+\delta+d_2^v)-\alpha_1\gamma_2}\tau\beta^T\frac{\alpha_1\hat{N}_1^r}{\gamma_1\hat{N}_1^v+\alpha_1\hat{N}_1^r}\\
&+\frac{\mu_E\alpha_1}{(\alpha_1+\mu_E+d_1^r)(\gamma_2+\mu_E+d_2^v)-\alpha_1\gamma_2}\cdot\\
&\left.\frac{\gamma_2+\mu_E+d_2^v+\alpha_1+\mu_I+\delta+d_1^r}{(\alpha_1+\mu_I+\delta+d_1^r)(\gamma_2+\mu_I+\delta+d_2^v)-\alpha_1\gamma_2}\beta_2^{vv}\frac{\hat{N}_2^v}{\hat{N}_2^r+\hat{N}_2^v}\right)\\
&+(1-p)\left(\frac{\mu_E\alpha_1}{(\alpha_1+\mu_E+d_1^r)(\gamma_2+\mu_E+d_2^v)-\alpha_1\gamma_2}\cdot\right.\\
&\frac{(\gamma_2+\mu_E+d_2^v)(\gamma_2+\mu_A+d_2^v)+\alpha_1\gamma_2}{(\alpha_1+\mu_A+d_1^r)(\gamma_2+\mu_A+d_2^v)-\alpha_1\gamma_2}\tau\rho\beta^T\frac{\alpha_1\hat{N}_1^r}{\alpha_1\hat{N}_1^r+\gamma_1\hat{N}_1^v}\\
&+\frac{\mu_E\alpha_1}{(\alpha_1+\mu_E+d_1^r)(\gamma_2+\mu_E+d_2^v)-\alpha_1\gamma_2}\cdot\\
&\left.\frac{\gamma_2+\mu_E+d_2^v+\alpha_1+\mu_A+d_1^r}{(\alpha_1+\mu_A+d_1^r)(\gamma_2+\mu_A+d_2^v)-\alpha_1\gamma_2}\rho\beta_2^{vv}\frac{\hat{N}_2^v}{\hat{N}_2^r+\hat{N}_2^v}\right).
\end{aligned}
$$

Dependence of R0 on key model parameters

- Increasing in terms of the transmission rates, infectious periods



- Non-monotonic behaviour in the duration of visitors' stay



Exposed period: 1.4 days
Infectious period: 3 - 4.1 days

Pandemic preparation – imported cases

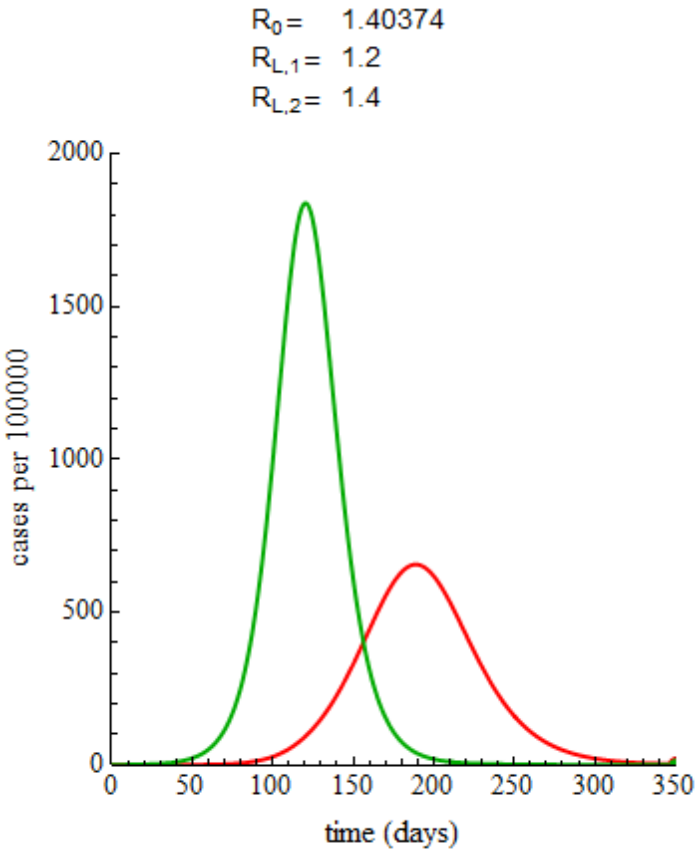
- Regions symmetric in ep. parameters, population size etc.
- Except reproduciton numbers:

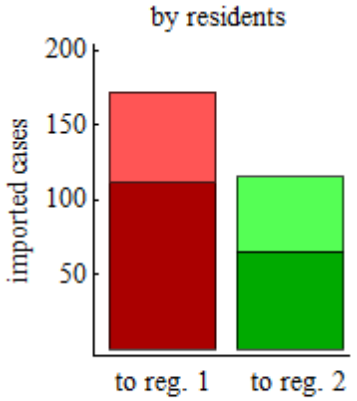
R1=1.2 (DF at Day 0)

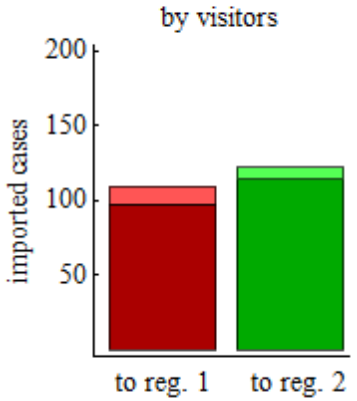
R2=1.4 (source)

α1=5*10^-5 (~55 yrs)

α2=5*10^-5







Pandemic preparation – imported cases

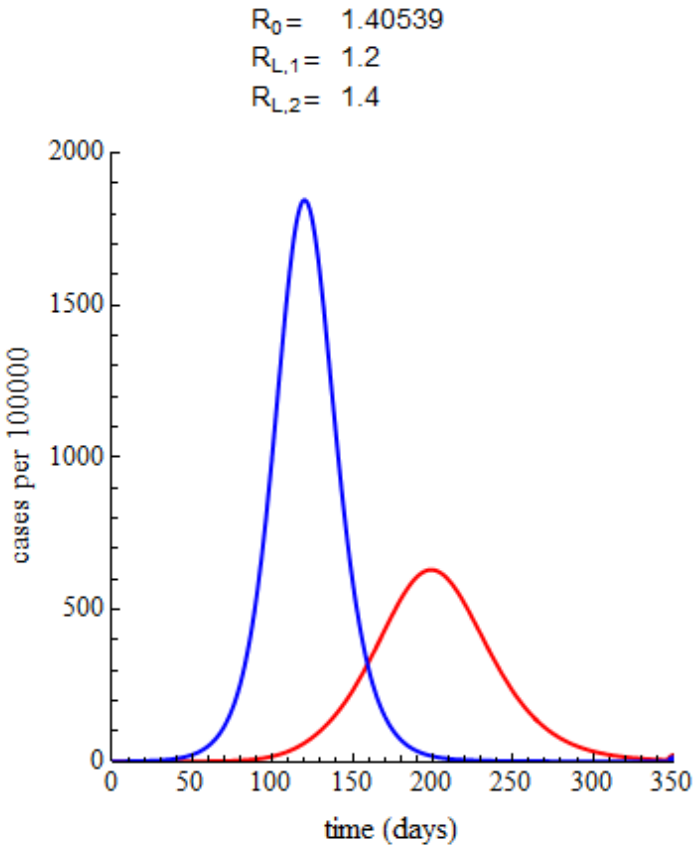
- Regions symmetric in ep. parameters, population size etc.
- Except reproduciton numbers & travel rates

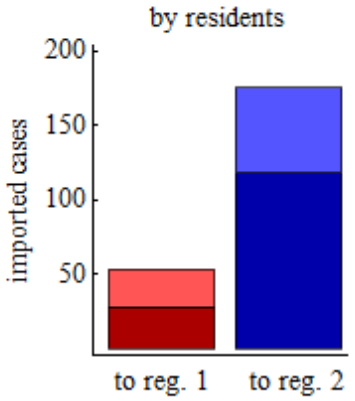
R1=1.2 (DF at Day 0)

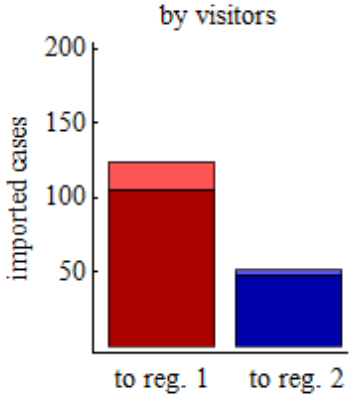
R2=1.4 (source)

α1=2*10^-5 (~137 yrs)

α2=8*10^-5 (~34 yrs)







Pandemic preparation – imported cases

- Regions symmetric in ep. parameters, population size etc.
- Except reproduciton numbers:
  R1=1.2 (DF at Day 0)
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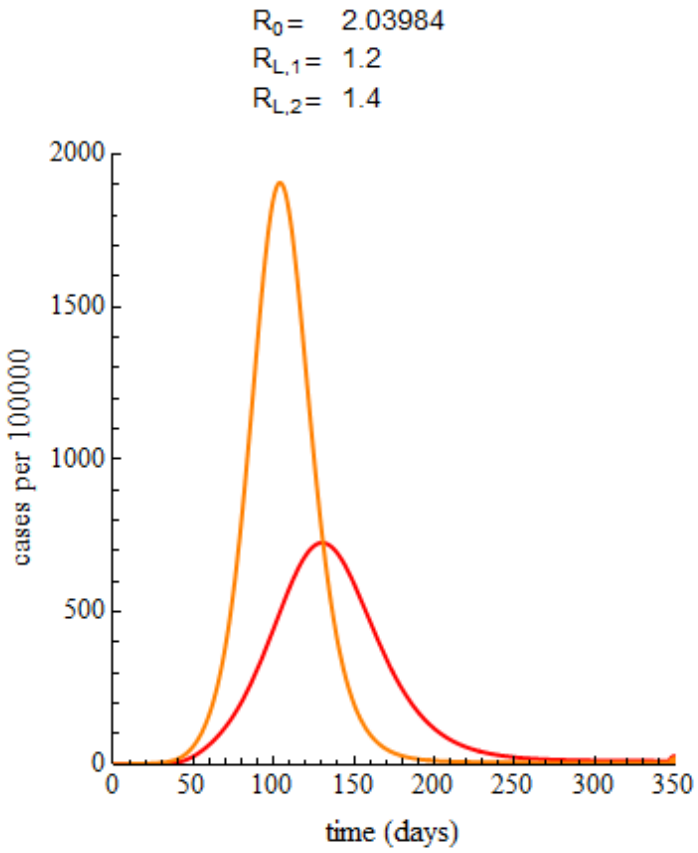
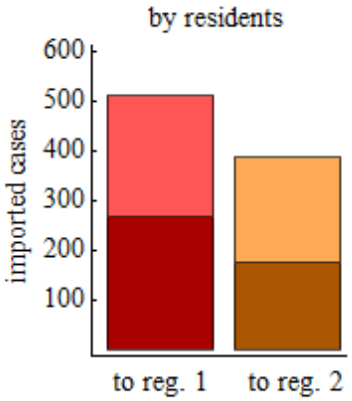
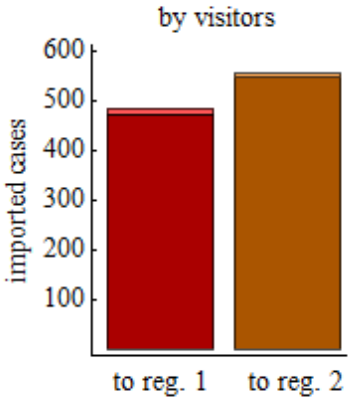
  α1=5*10^-5 (~55 yrs)
  α2=5*10^-5
- Elevated transm. rate during travel







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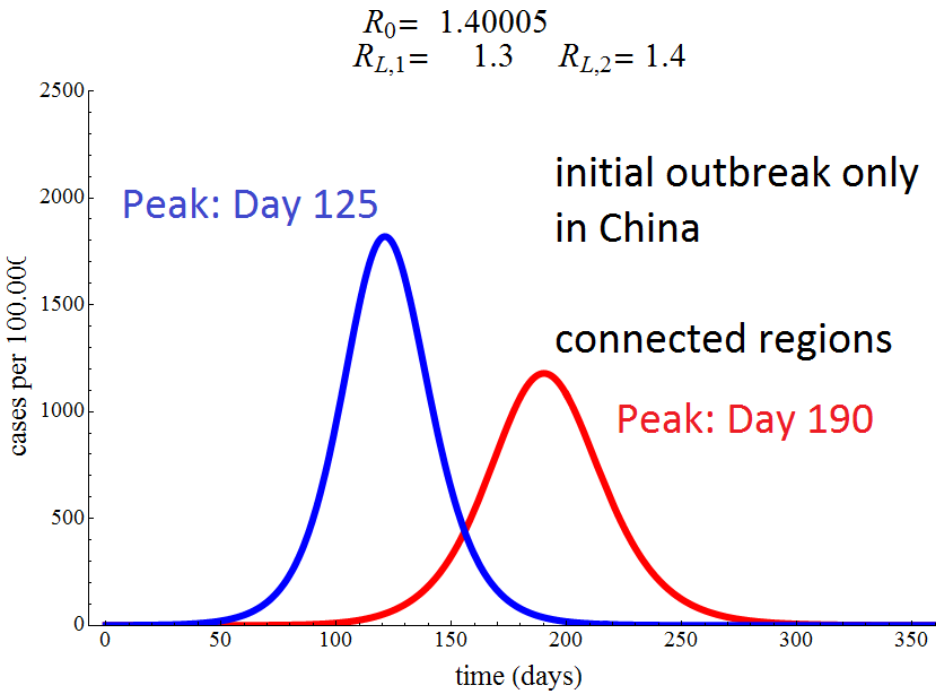
Simulations

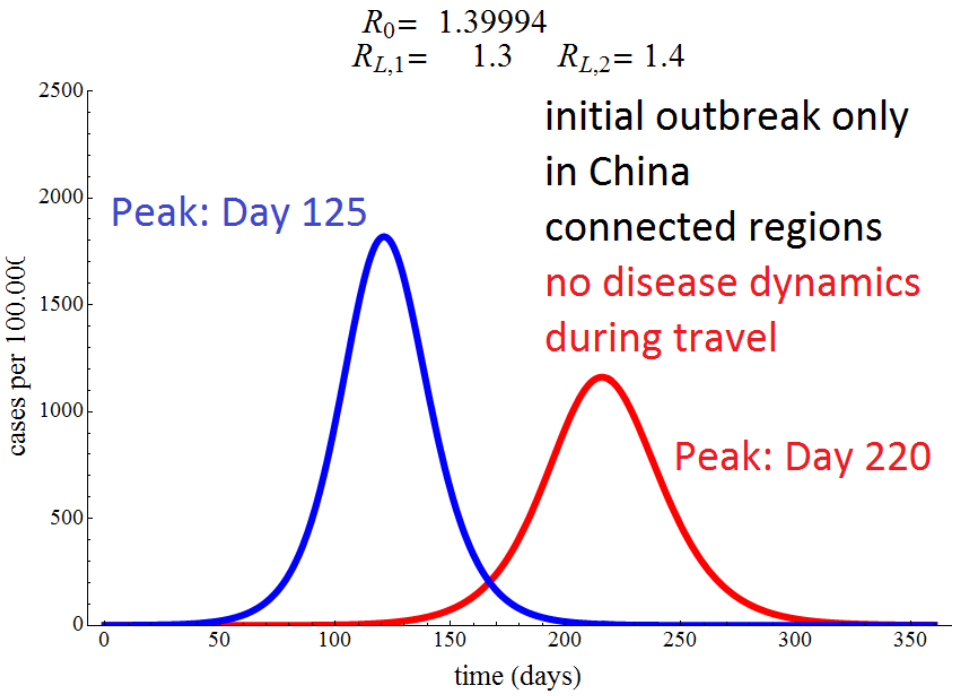
- Reasonable values for epidemiological parameters
- Real demographic and air traffic data (Bio.Diaspora project, Arino *et al*)

- Three distinct scenarios for the regions:
  - Canada-UK („symmetric”)
  - Canada-China („asymmetric population”)
  - Canada-Mexico („asymmetric travel”)
- Questions of interest
  - effect of travel restrictions
  - effect of elevated transmission potential during travel
  - impact of visit durations
  - fitting the model to real morbidity data

Canada – China

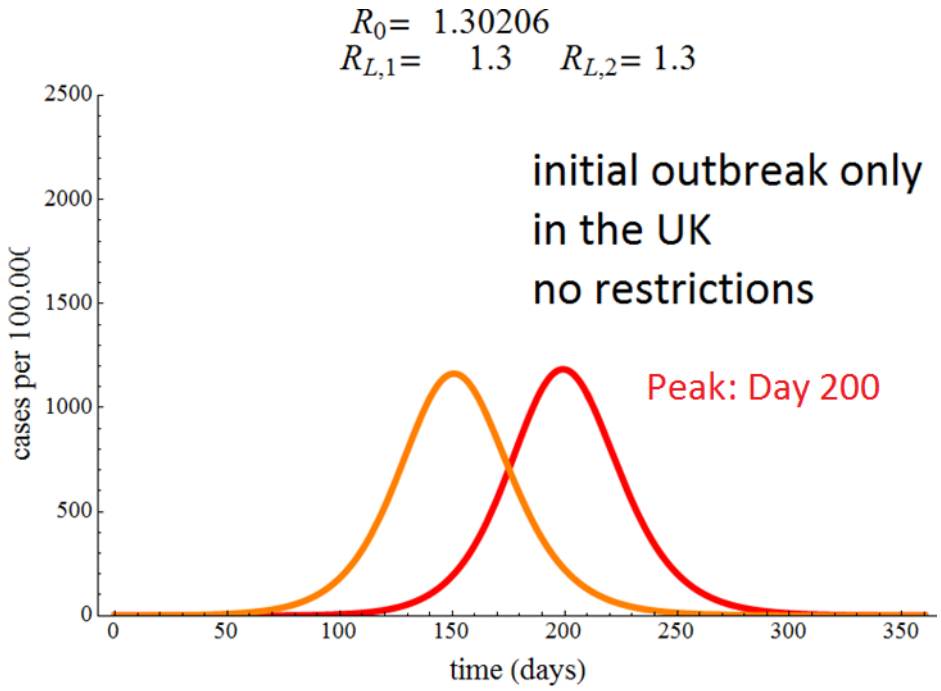
- Impact of disease transmission during travel
- Ignoring the possibility of on-board transmission overestimates the time for preparation before the outbreak

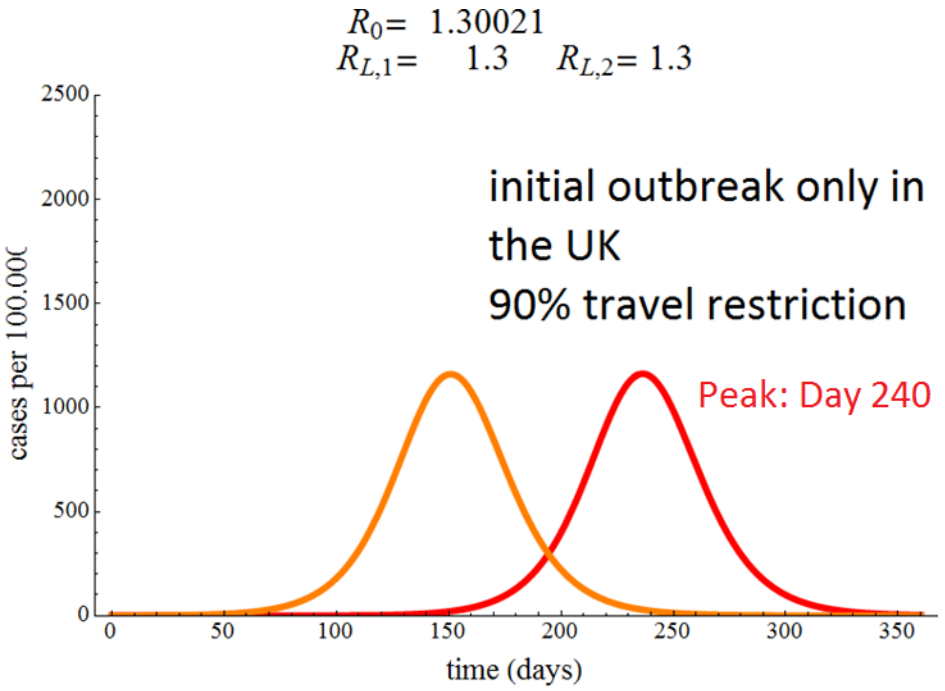




Canada – United Kingdom

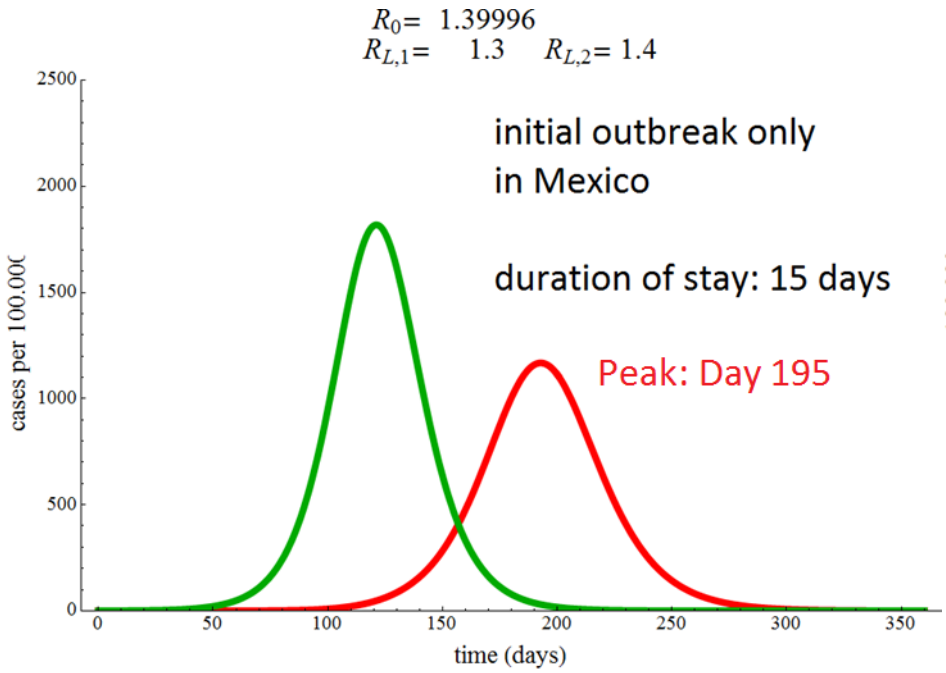
- UK produces ~7% of all air traffic to Canada
- Effect of reduction of traveling by 90%

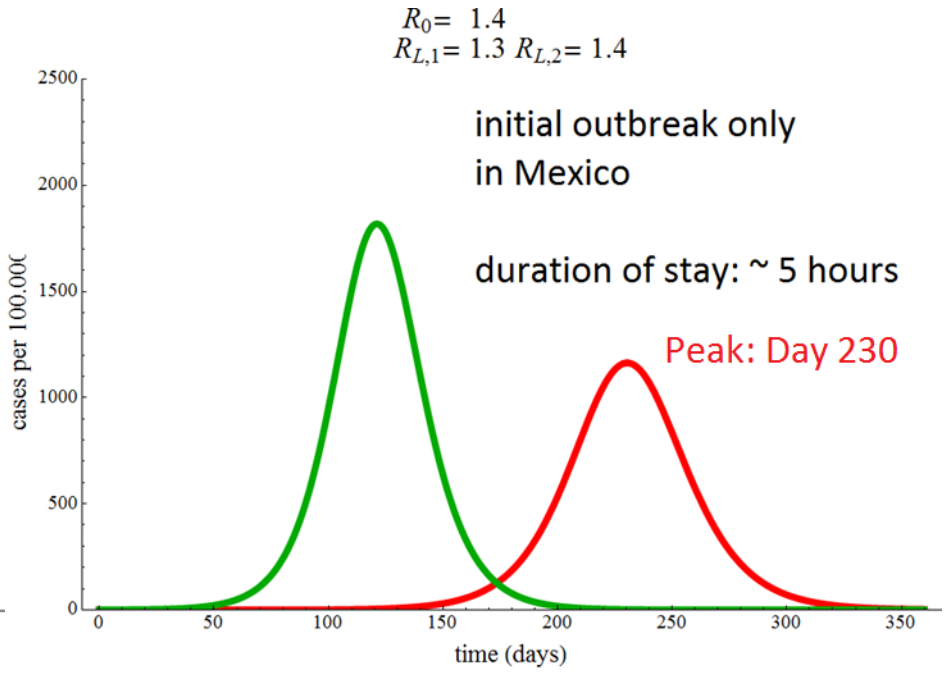




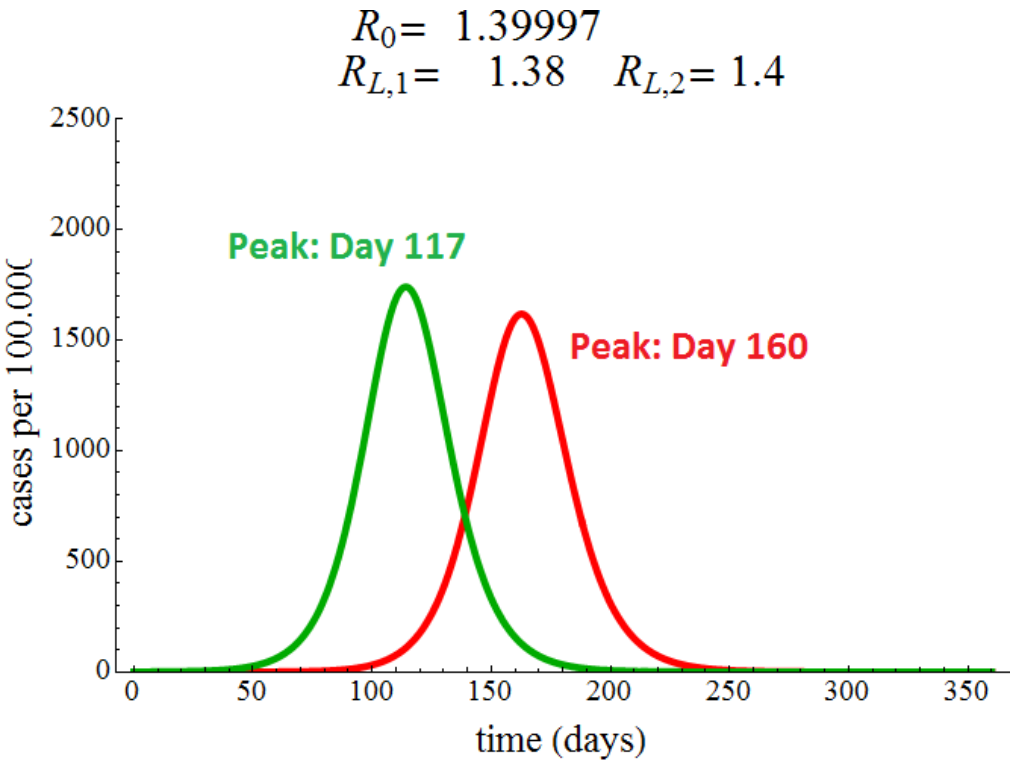
Canada – Mexico

- Visitors stay for 7 days on average
- Impact of lengthening vs. shortening this time





Fitting the model to the 1st wave of the H1N1 2009



Local R in **Mexico**: 1.4
Local R in **Canada**: 1.38

Peak time in **Mexico**:
Day 117-123
Peak time in **Canada**:
Day 155-162

(Day 0: Decemeber 31, 2008)

Thank you for your attention!

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