Back So Soon: Estimating dengue re-emergence probabilities in Rio de Janeiro, Brazil via iterated filtering

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Introduction:

- Predicting times of disease re-emergence has public health relevance and it is a fundamental question on nonlinear SIR dynamics.
- Current models of Zika re-emergence assume that susceptible depletion is main driver, ignoring other factors like spatial or inter-annual climate variation.
- Previous studies have predicted the number of "skips" (small epidemics in which both infected and susceptible populations experience net increases) that will occur following an outbreak for measles-like diseases with high reproductive numbers (R_0). (Stone et al, Nature 2007).
- This question has not been examined for diseases with low R_0 values such as in regions where seasonal climate conditions strongly limit mosquito transmission, such as in southeastern Brazil.
- We examine dengue re-emergence dynamics in Rio de Janeiro, Brazil, where DENV1 first invaded in 1986-1987 and re-emerged in 1990.

Objectives of the Study:

- Extend deterministic "skip" calculation for measles to dengue-like diseases to calculate predicted time to re-emergence in Rio as a function of R_0 and reporting rate.
- Estimate reporting rate R_0 of the DENV1 invasion by fitting a stochastic model to monthly case counts.
- Examine how predicted re-emergence times from a fitted stochastic model compare with deterministic skip calculations.

Methods: Models

Transmission Model:

The seasonal transmission rate $\beta(t)$ is represented non-parametrically using a series of three periodic splines : s_i with coefficients b_i :

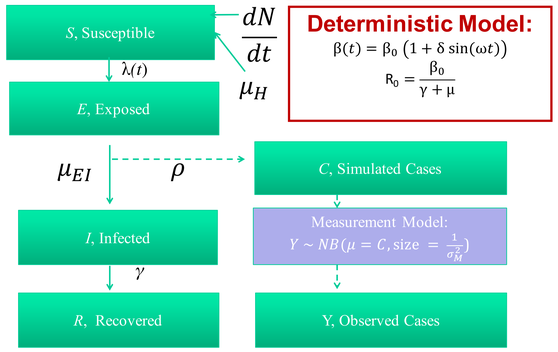
$$\beta(t) = e^{\sum_{i=1}^{3} b_i s_i}$$

The force of infection $\lambda(t)$ includes immigration (ϵ):

$$\lambda(t) = \beta(t)\left(\frac{I+\epsilon}{N}\right)$$

Governing Equations:

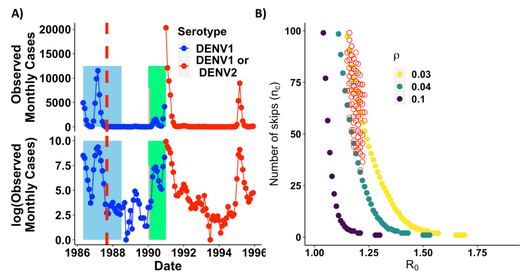
$$\frac{dS}{dt} = \mu_H N + \frac{dN}{dt} - \lambda(t)S - \mu_H S$$
$$\frac{dE}{dt} = \lambda(t)S - \mu_{EI}E - \mu_H E$$
$$\frac{dI}{dt} = \mu_{EI}E - \gamma I - \mu_H$$
$$\frac{dR}{dt} = \gamma I - \mu_H R$$
$$\frac{dC}{dt} = \rho\mu_{EI}E$$



Deterministic Model:

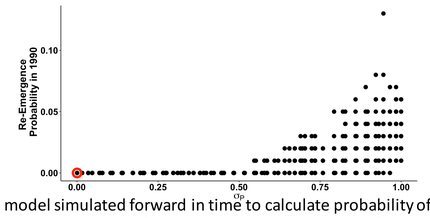
$$\beta(t) = \beta_0\left(1 + \delta\sin(\omega t)\right)$$
$$R_0 = \frac{\beta_0}{\gamma + \mu}$$

Result 2: Expected skips in Rio de Janeiro following 1987 invasion from fitted model parameters



- We fit the stochastic model to the DENV1 invasion from 1986-1988(blue region in (A))
- Parameters from fitted model used to calculate expected number of skips (B)
  - Number of skips >> 2 (re-mergence occurred too soon)

Result 4: Re-Emergence Probability (Forward Simulation from Stochastic Model)

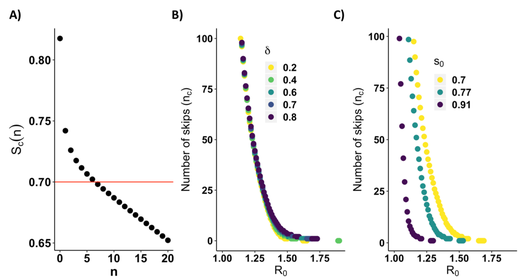


- Fitted model simulated forward in time to calculate probability of re-emergence in 1990-1991 (green region in Result 3 Panel A) assuming sparks of infected people arriving during that time.
- Low probability of obtaining a re-emergent outbreak in 1990 from forward simulation of fitted model unless extremely large spark size used.

Methods: Stochastic Model Fitting and Parallelization Strategies:

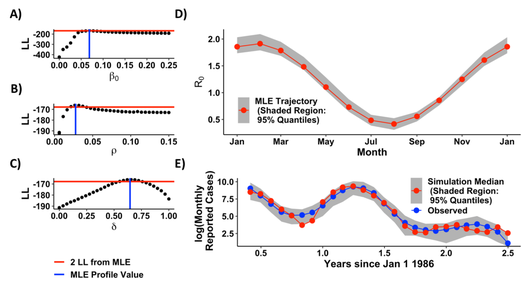
- We use the particle filtering algorithms from the R package POMP to estimate likelihood and parameters.
  - Likelihood Estimation: Sequential Monte Carlo (pfitler)
  - Parameter Estimation: Iterated Filtering (mif)
- Construction of Monte Carlo Profiles (10 parameters)
  - For parameter being profiled, fix parameter at 30 equally spaced values. For each value, create 40 different initial sampling points drawing from box given by boundaries of original parameter range for other parameters. (1200 starting points)
  - Allow MIF to vary all other fitted parameters during search except process noise size, run for 100 iterations with 10,000 particles, repeat 5 times.
  - Total # of simulations: 10*1200*100*5*1000 = 6*10^9
- Midway parallelization scheme:
  - For each profile, split 1200 starting points into 50 array jobs.
  - Within each array job, parallelize output over 28 cores via doParallel R library
  - Profiles can be run/submitted concurrently.

Result 1: Expected Number of Skips as a Function of Fraction of Susceptible Population and R_0 (Analytical Derivation)



- We analytically derive an expression for the time to re-emergence (n_c)of dengue-like diseases with seasonality, population growth and low R_0 as a function of both R_0 and the reporting rate.
- The number of skips is shown to be very sensitive to the initial fraction of susceptible individuals (s_0) and R_0, but less sensitive to seasonality amplitude δ.

Result 3: R_0 of 1st Dengue Invasion (1986-1989)



- Panels A-C: Monte Carlo transmission parameter profiles
- Panel D: Estimated R_0: 0.5-0.6 (off-season) to 2.0-2.25 (on-season).
- Panel E: Model captures two-peak invasion dynamics and low-level persistence during next two years (1988-1989).

Conclusion:

- **Re-emergent dynamics for low R_0 look very different from those of measles:** Threshold effect: Small changes in R_0 can result in large increases in the number of expected skips.
- **Susceptible depletion and replenishment cannot explain past arbovirus re-emergence**
  - Very low probability of re-emergence of DENV1 in 1990.
  - Given that re-emergence occurred, either DENV1 had sufficiently changed antigenically or a temporal model at the whole-city scale is not applicable to predict the replenishment of the susceptible population.
  - Future arbovirus re-emergence (like Zika) may re-emerge faster than expected if other potential drivers not included in current forecasting models are very important.

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