Stochastic modeling of the transmission of respiratory syncytial virus (RSV) in the region of Valencia, Spain

...

Abraham J. Arenas, Gilberto González-Parra, Jose-A. Morano˜c

Nicola Perotti, Chiara Rosati, Thomas Sirchi

INTRODUCTION 1/2

Respiratory Syncytial Virus (RSV) → spread through respiratory secretions

Two vaccines available

Syncytia are created thanks to the virus envelope proteins

↓

RhoA has a role in syncytia formation

Covid-19 → putative role in RSV diffusion

→ Off-season cases

→ Increased age at infection

→ Downregulation of CD19

INTRODUCTION 2/2

15,000-20,000 cases in Spain

High costs for the Spanish public health system

THUS

Crucial role of mathematical models in studying diseases

Role of environmental factors and other diseases

Assess the role of external factors in RSV dynamics

Deterministic (Weber et al., 2001) and stochastic strategies

MODELS

Deterministic strategy

- Balance between simplicity and power
- Noise in real data

Stochastic strategy

- Better to handle noisy data and complex system unpredictability
- Demographic data show inherited variability

- DETERMINISTIC MODEL
- STOCHASTIC MODEL: perturbations on birth rate and transmission rate

Deterministic Model 1/3

SIRS model:

Susceptibles
Infected
Recovered

Assumptions:

- Temporary immunity
- Birth and death rates are equal $\rightarrow$ constant population
- $\nu \rightarrow$ recovery rate, $\gamma \rightarrow$ immunization rate
- Function $\beta(t)$ models the transmission rate

Deterministic Model 2/3

$$\beta(t) = b_0(1 + b_1 * cos(2\pi * t + \Phi))$$

$$\dot{S}(t) = \mu - \mu S(t) - \beta(t)S(t)I(t) + \gamma R(t), \ \ S(0) = S_0 > 0$$
$$\dot{I}(t) = \beta(t)S(t)I(t) - \nu I(t) - \mu I(t), \ \ I(0) = I_0 > 0$$
$$\dot{R}(t) = \nu I(t) - \mu R(t) - \gamma R(t), \ \ R(0) = R_0 > 0$$

Model fitted to hospitalization data of children (<4 yo) of Valencia

Deterministic Model 3/3 - Parameters and Initial values

$b_0 = 36.4$

$b_1 = 0.38$

$\Phi = 1.07$

s = 0.38

Paper

$\mu = 0.009$

$\nu = 36$

$\gamma = 1.8$

Literature

$S(0) = 0.9988$

$I(0) = 0.0012$

$R(0) = 0$

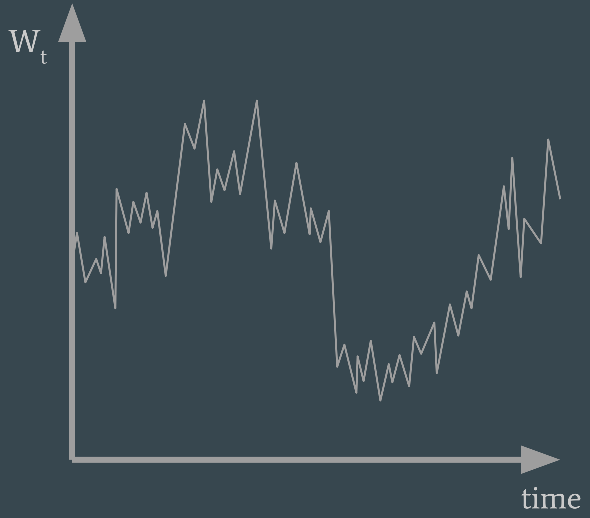
Paper/Inferred by us

Stochastic models

Itô system

$$\dot{X}(t) = f(t, X(t))dt + g(t, X(t))dW(t)$$
$$X(t_0) = t_0, \; t \in [0, t_f]$$

Wiener process



It’s a continuous time process where each increment is independent of the past values and follows a normal distribution N(0,dt)

System with perturbation on the birth rate

$$\widetilde{\mu} = \mu + \alpha \dot{W}(t)$$

$$\dot{S}(t) = [\mu - \mu S(t) - \beta(t)S(t)I(t) + \gamma R(t)]\ dt + \alpha(1 - S(t))\ dW(t)$$

$$\dot{I}(t) = [\beta(t)S(t)I(t) - \nu I(t) - \mu I(t)]\ dt - \alpha I(t)\ dW(t)$$

$$\dot{R}(t) = [\nu I(t) - \mu R(t) - \gamma R(t)]\ dt - \alpha R(t)\ dW(t)$$

System with perturbation on the transmission rate (b_0)

$$\widetilde{b_0} = b_0 + \alpha \dot{W}(t)$$

$$\dot{S}(t) = [\mu - \mu S(t) - \beta(t)S(t)I(t) + \gamma R(t)]\ dt - \frac{\alpha\beta(t)}{b_0}S(t)I(t)\ dW(t)$$

$$\dot{I}(t) = [\beta(t)S(t)I(t) - \nu I(t) - \mu I(t)]\ dt - \frac{\alpha\beta(t)}{b_0}S(t)I(t)\ dW(t)$$

$$\dot{R}(t) = [\nu I(t) - \mu R(t) - \gamma R(t)]\ dt$$

Solve_ivp (ODE simulation)

- Function within the scipy.integrate module;
- Takes in input a function describing the ODE system, the time span, the initial values and a specified method of integration (RK45);
  - Runge-Kutta 45 is a method of fifth order in which the error is estimated using a fourth order method (looks like this function works in the opposite way with respect to the standard RK45);
    - Allows for an adaptive stepsize.

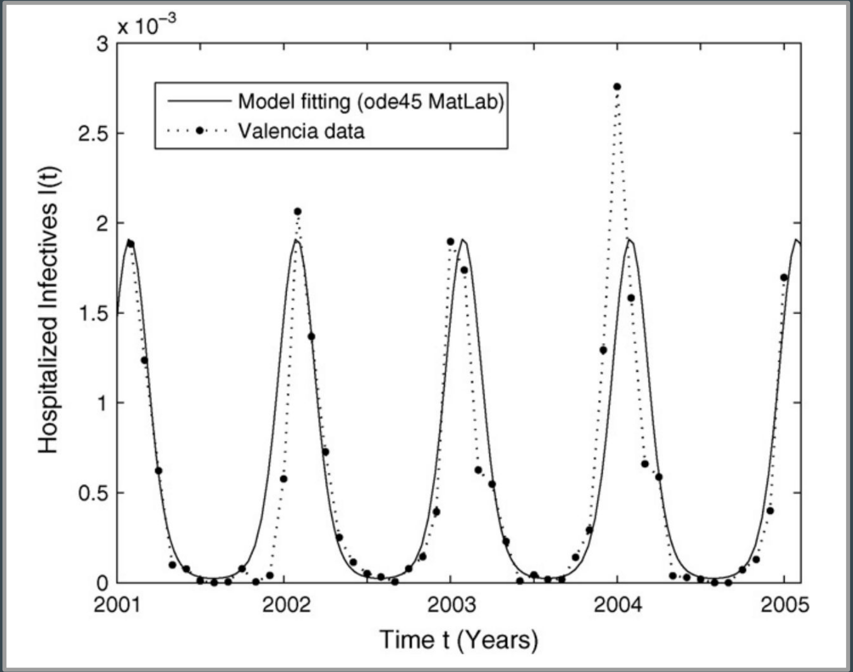
Euler Maruyama method (stochastic simulations)

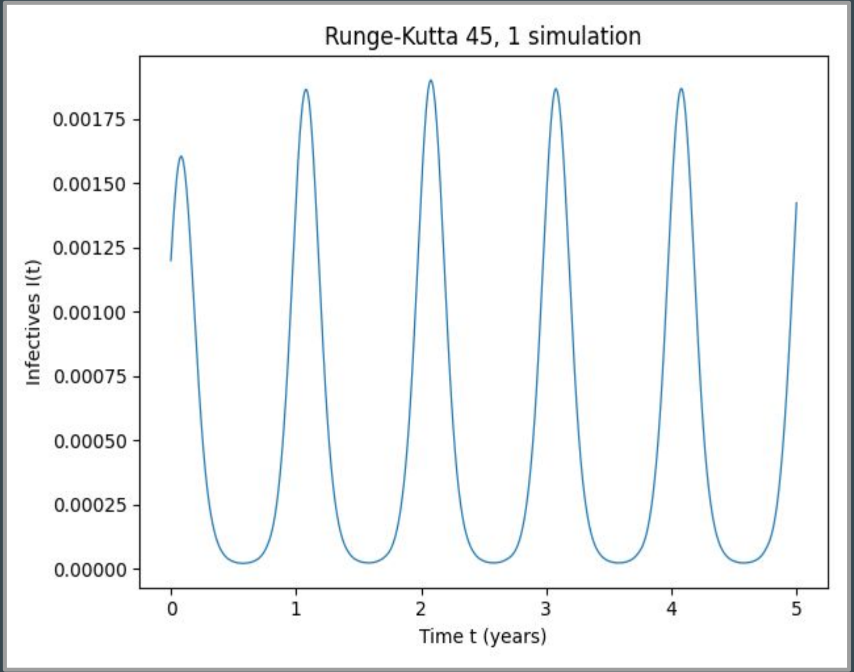
- Returns approximate solutions for a system of SDEs;
- Lower order method than Milstein, but comparable results;
- We decided to perform 10 simulations rounds for each SDE system.

Define N subintervals of length dt → Define the Wiener process dW → Update the system state (forward method) and time

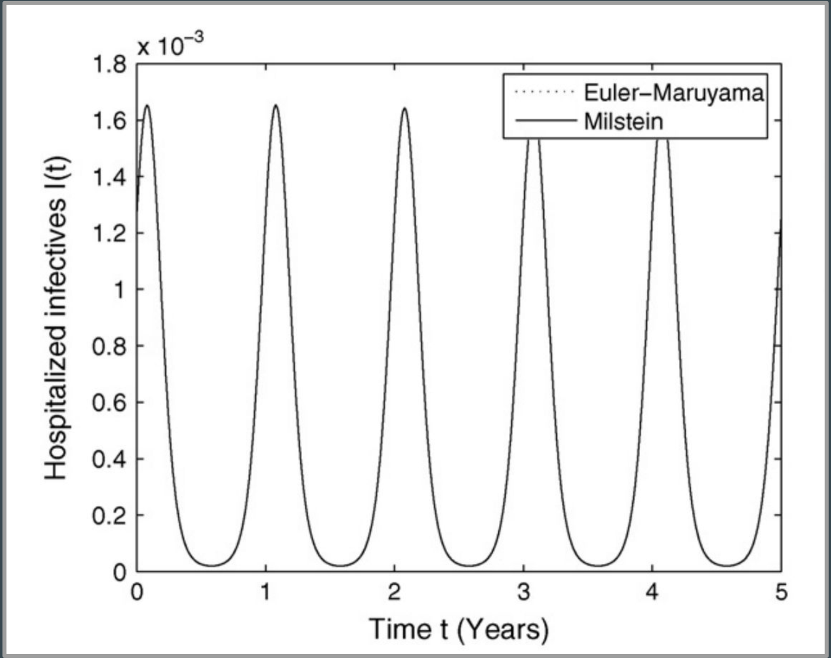
RESULTS

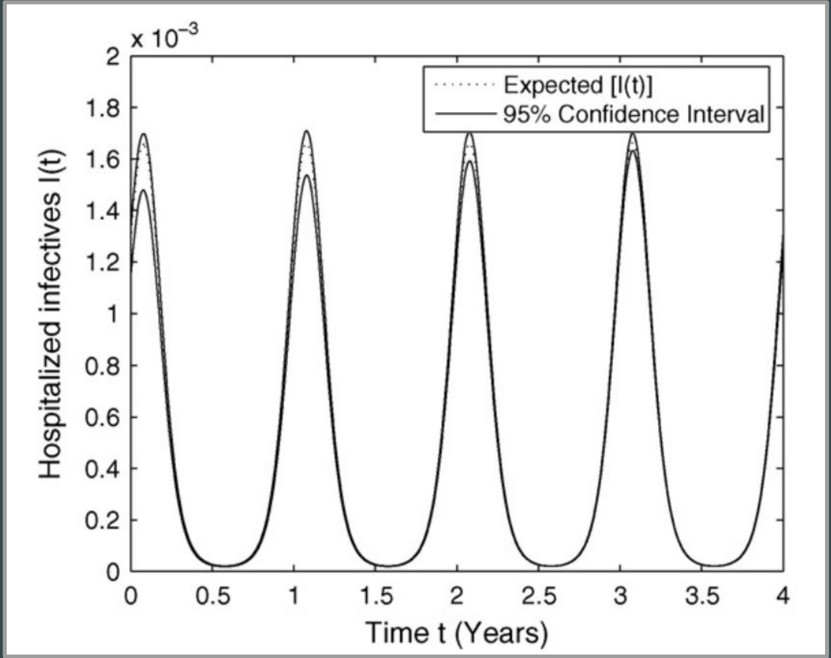
Deterministic Model



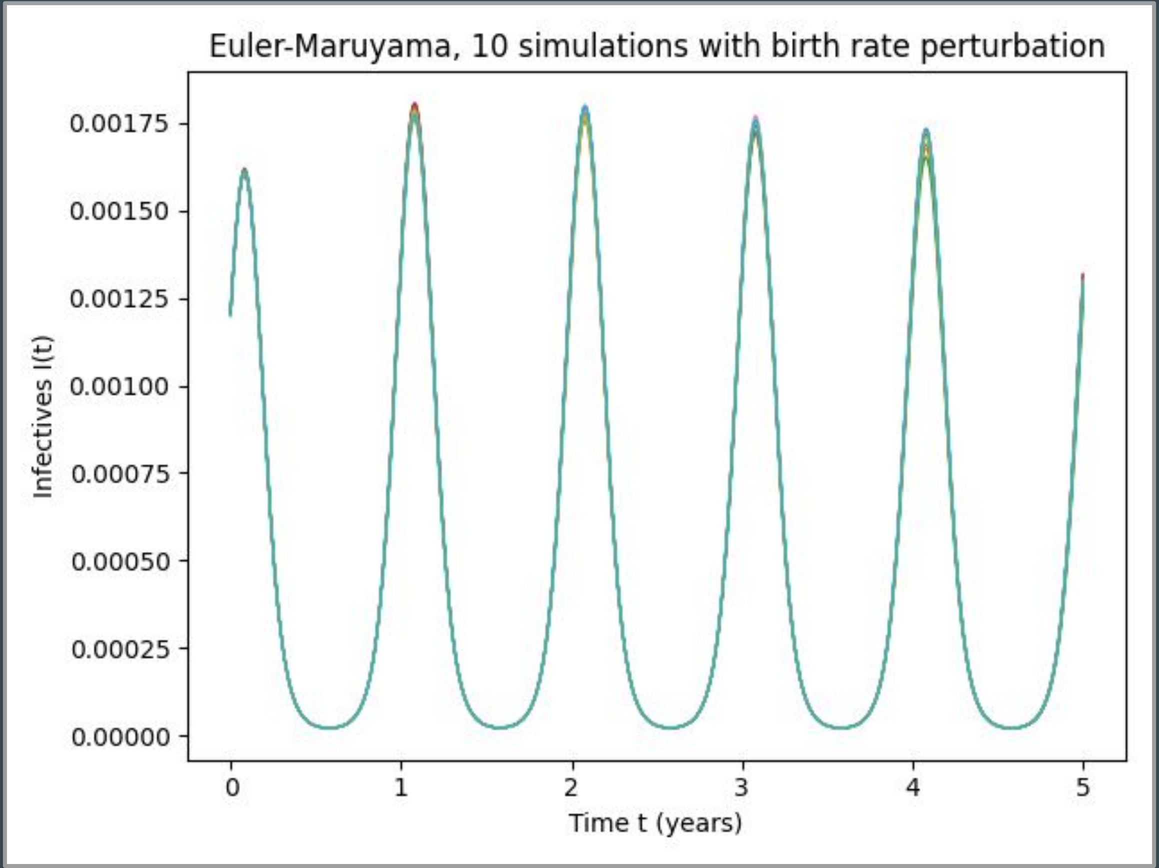


Stochastic Model with perturbation on the birth rate

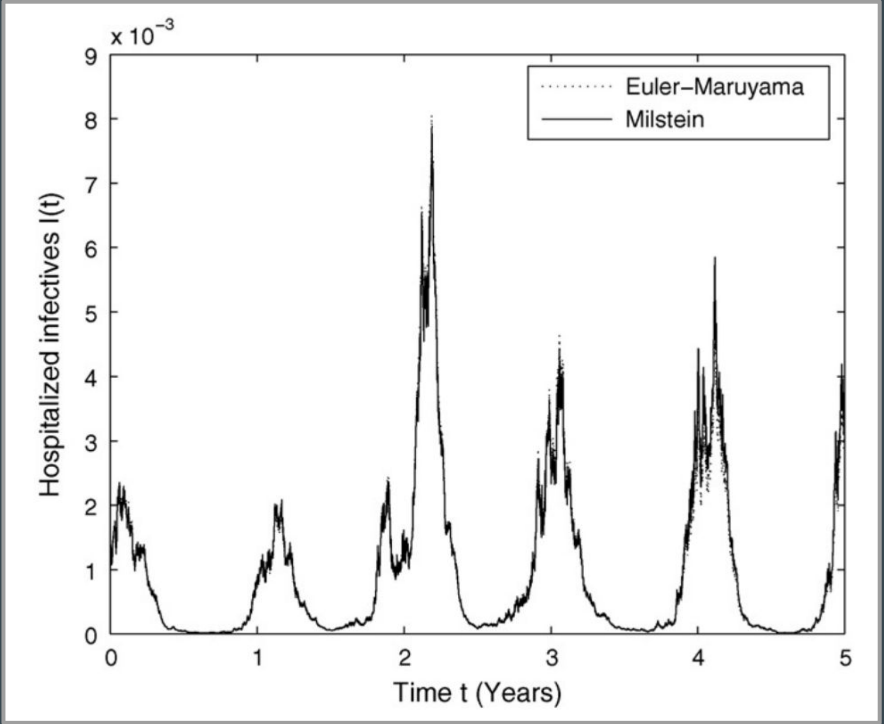


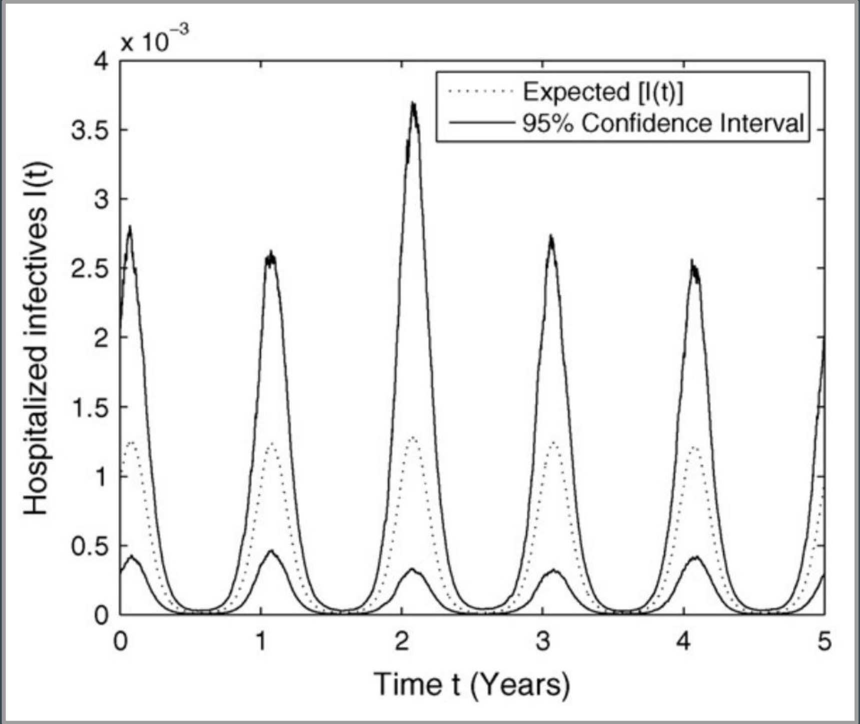


Our stochastic implementation for Infected I(t)

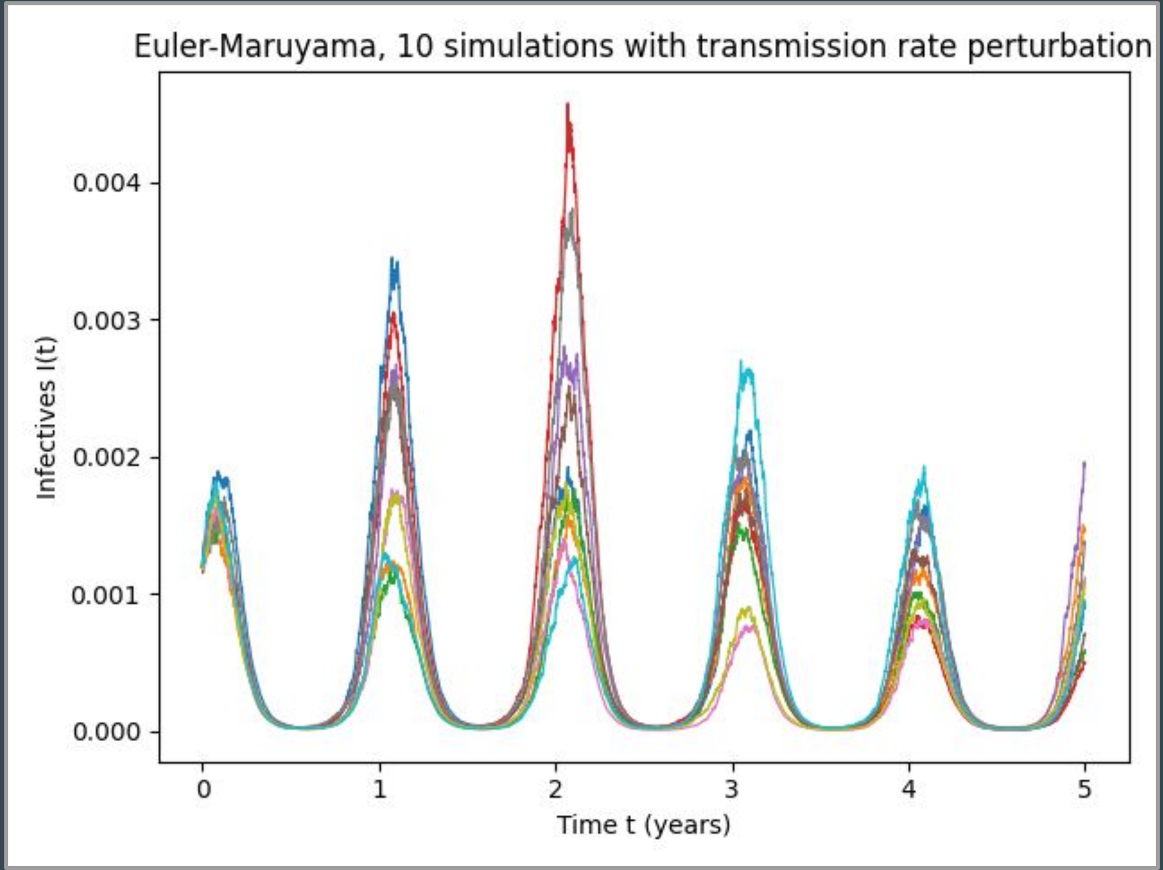


Stochastic Model with perturbation on the transmission rate

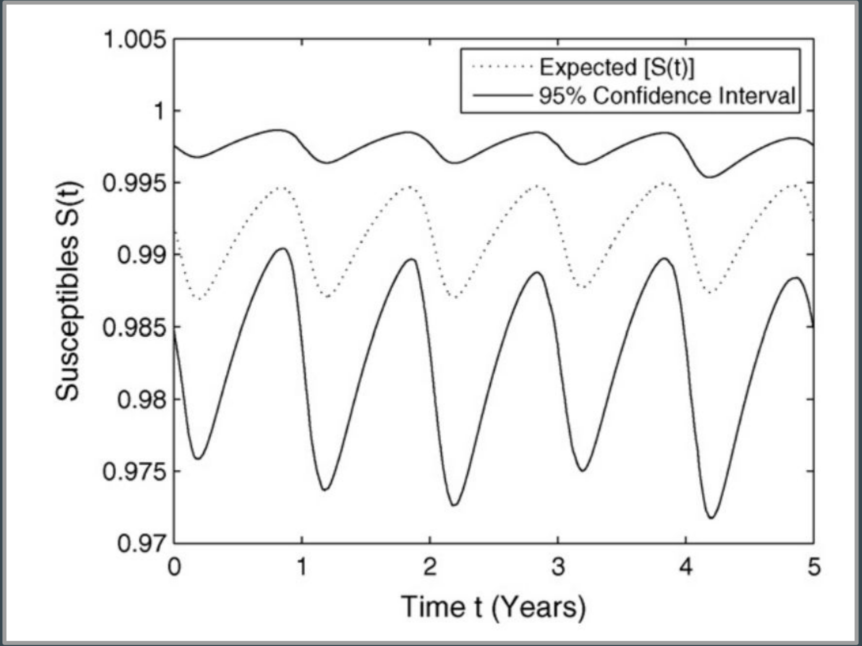


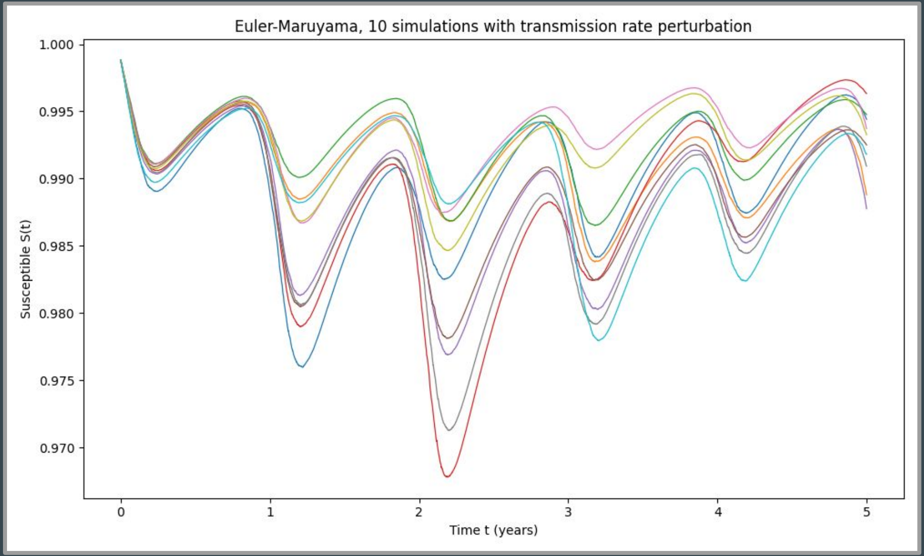


Our stochastic implementation for Infected I(t)

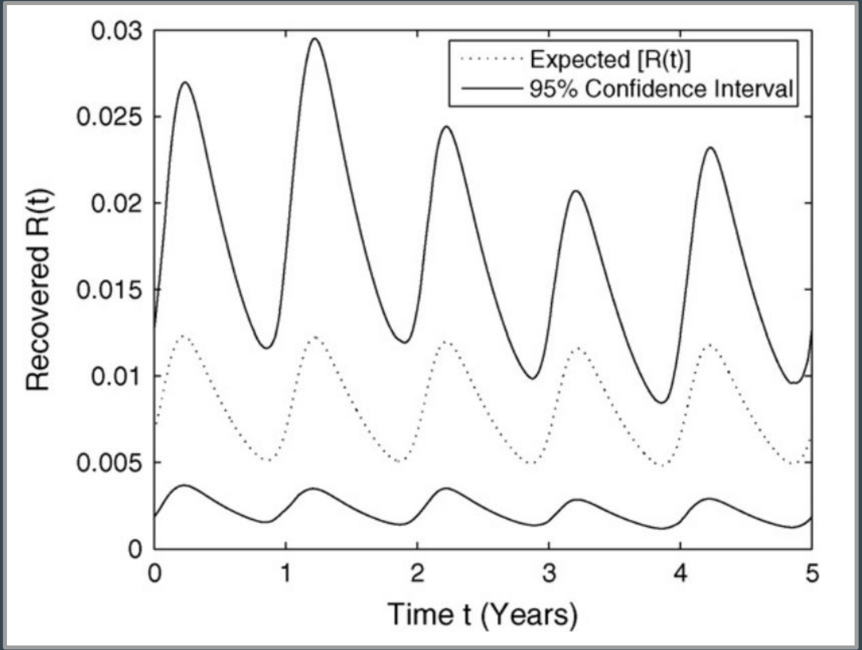


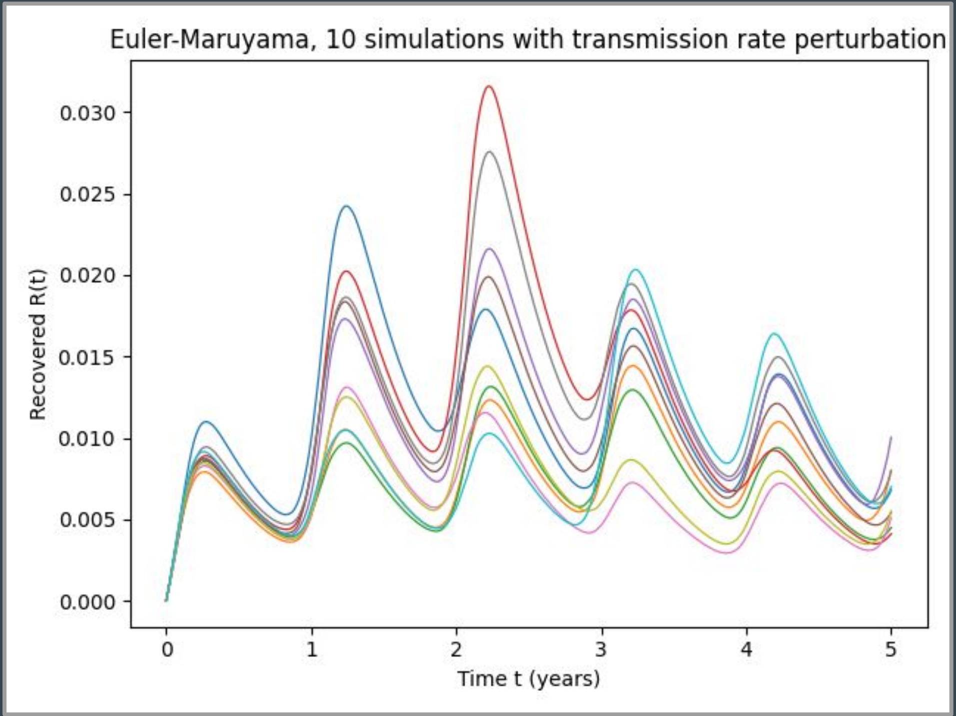
About the Susceptible S(t)



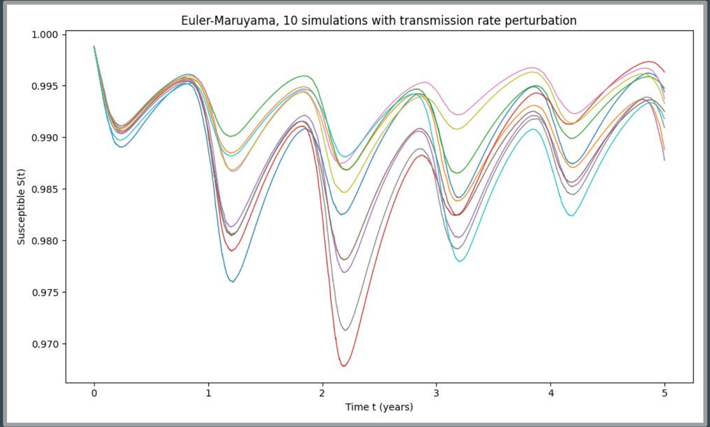


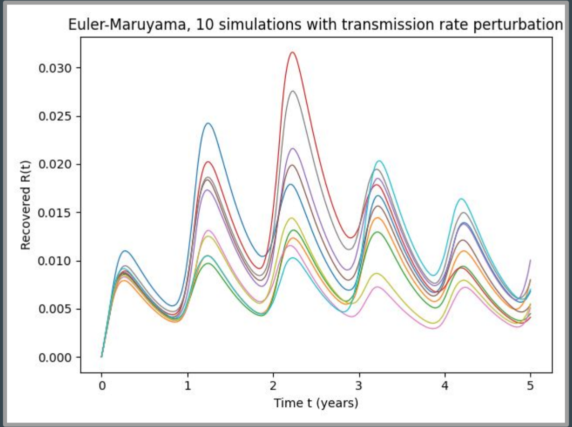
About the Recovered R(t)





About the Recovered R(t) and Susceptible S(t)





- The variation in the R(t) and S(t) subpopulations increases with higher transmission rate perturbations.
- This increase in variation occurs despite the **absence of explicitly included noisy seasonally forced co-sinusoidal functions in the SDEs** governing the variables.
- Introducing a noise term in the equations **reveals the fundamental oscillatory nature of these subpopulations**.

CONCLUSIONS

Deterministic vs. Stochastic Approaches

- Serve different purposes in understanding biological systems through mathematical models.
- Stochastic models better capture intrinsic variability and environmental factors
- Deterministic models may be suitable when the environment has minimal impact on simulations.

Parameters in Stochastic Simulation

- Value of α provided only for perturbation on the birth rate, missing for perturbation on the transmission rate.
- Hypothesizes that **α represents a fraction defining fluctuations above and below the reference parameter value**.
- Other parameters had to be **implemented from literature**

Perturbation Ranges

- Authors experimented with perturbation ranges without explaining the rationale behind these values.
- Small **perturbations of transmission** led to a significant change in the populations
- **Recommends a sensitivity analysis** to better understand the role of perturbations for effective healthcare policy decisions.

Importance of Transmission Rate Perturbations in SIR

- Transmission rate **highly sensitive to perturbations**.
- Notes the **influence of global movement and changing meteorological conditions on diseases** spread, emphasizing the significance of modeling studies.

Thank you for your attention!