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A simple SIR-vaccination model: Estimating Parameters.

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Introduction

We model childhood diseases such as measles. Vaccination is key in controlling such diseases. The aim here is to identify which vaccination strategies are optimal given constraint on resources. Pulse vaccination (e.g., Agur, 1993) has been shown to yield better results than constant vaccination, with success stories in Argentina, Brazil, Israel, among others(Chavez and Feng, 1998).

Fairly good parameters are needed to validate any model assumptions or conclusions made, to ensure the model analysis and reporting makes much sense.

Parameters:

$$\theta=\{b,\mu,\psi(t),\beta(t),\alpha,S_0,I_0,R_0\}$$

$$\psi(t)=p\sin(\varpi t)$$

$$\beta(t)=q\sin(\varpi t)$$

Parameters: at least 6.
Birth rate(b)
Death rate(mu)
Vaccination rate(psi)
Contact rate(beta)
Recovery rate(alpha)

Model

$$(1a)\quad \begin{aligned} \frac{dS}{dt} &= b-\mu S-\psi(t)S-\beta(t)SI, & S(t_0)&=S_0>0\\ \frac{dI}{dt} &= -\mu I+\beta(t)SI-\alpha I, & I(t_0)&=I_0>0\\ \frac{dR}{dt} &= -\mu R+\psi(t)S+\alpha I, & R(t_0)&=R_0>0 \end{aligned}$$

$$(1b)\quad \begin{aligned} \frac{dS}{dt} &= b-\mu S-\psi(q)S-\frac{1}{\varepsilon}\beta(q)SI, & S(t_0)&=S[\psi](t_0)\\ \frac{dI}{dt} &= -\mu I+\frac{1}{\varepsilon}\beta(q)SI-\frac{1}{\varepsilon}\alpha I, & I(t_0)&=\varepsilon\hat{I}_0\\ \frac{dR}{dt} &= -\mu R+\psi(q)S+\frac{1}{\varepsilon}\alpha I, & R(t_0)&=\frac{b}{\mu}-S[\psi](t_0)\\ \frac{dq}{dt} &= 1, & q(t_0)&=t_0 \end{aligned}$$

Mathematical Analysis

<u>FLOQUET THEORY:</u>

Three independent solutions of the linearization of (1a), with initial conditions (1,0,0)´, (0,1,0)´, and (0,0,1)´ are obtained. The vectors form the columns of the Monodromy matrix below, (*) entries assumed to be equal to zero.

$$M(t)=\begin{pmatrix} \exp\left(-\int_0^T \mu+\psi(t)dt\right) & * & 0\\ 0 & \exp\left(-\int_0^T \mu+\alpha dt+\int_0^T \beta(t)S[\psi](t)dt\right) & 0\\ * & * & \exp\left(-\int_0^T \mu dt\right) \end{pmatrix}$$

The main diagonal defines the spectrum of the matrix, and stability of the disease free periodic orbit is defined if

$$\tilde{F}=\int_0^T \beta(t)S[\psi](t)dt<T(\mu+\alpha)$$

<u>SINGULAR PERTUBATION THEORY:</u>

Both t-Time and I(t)-the Infective Population, are rescaled to obtain the <u>fast system</u>. Then with infinite separation of time, one obtains the limiting fast and slow systems. Below is the slow system, and the slow manifold- h(s).

$$\frac{dX}{dt}=-b-\mu X-g(S,q)-\frac{\alpha\beta'(q)q'\ln S}{[\beta(q)]^2}$$

$$\varepsilon\frac{dS}{dt}=\varepsilon\{b-\mu S-\psi(q)S\}-\beta(q)S\left\{-S+\frac{\alpha}{\beta(q)}\ln S-X\right\}$$

$$\frac{dq}{dt}=1,$$

$$h(S)=-\beta(q)S[-S+\frac{\alpha}{\beta(q)}\ln S-X]$$

$$\frac{dh(S)}{dS}=-\beta(q)[-S+\frac{\alpha}{\beta(q)}\ln S-X]-\beta(q)S[-1+\frac{\alpha}{\beta(q)S}]$$

$$\frac{dh(S)}{dS}<0\quad\Rightarrow\text{Stability}$$

We say the uninfected periodic orbit is instantaneously stable if

$$\|R_v[\psi]\|_{L^\infty}<1,\quad where\quad R_v[\psi]=\frac{\beta(t)S[\psi](t)}{\alpha}$$

Comments

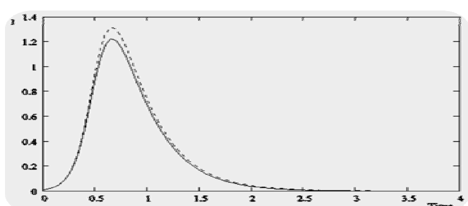


Fig 1: A simulation of the epidemic. time independent contact rate (dashed curve), varying periodic contact rate (solid curve), constant case, β=1.4 , varying case, β=0.9+cos(t)0.5.

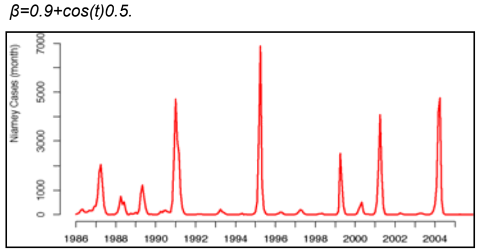


Fig 2: Local Measles Dynamics: Niamey-Niger (Ferrari et al, 2008). Measles spreads is characterized by outbreaks that last a short time, and die off. Orbital stability assessed over say 5 year period means that such outbreaks my go undetected.

<u>Comment 1:</u>

➢Does orbital stability in the sense of Floque't offer a true picture?Figure 1 shows that despite an argument for orbital stability, instantanious stability may be violated(see sharp spikes in fig 2).
➢Fig 2 is true data for measles showing periodic outbreaks that go extict in short time spans

<u>Comment 2:</u>

➢Classical methods used to estimate parameters,
➢Lack of data (Simulations used) and step changes in inputs, vaccination and contact rates make parameter estimation challanging. Surface plots do not potray clear minimums.

<u>Comment 3:</u>

➢Lack of data (Simulations used) and step changes in inputs, vaccination and contact rates. The parameter estimates here are not yet so good, eg, see surface curves or even fig. 3.

Parameter Estimation.

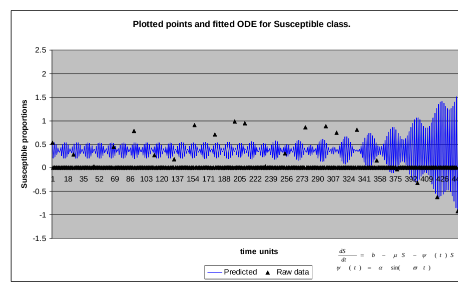
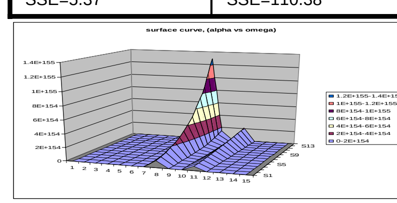
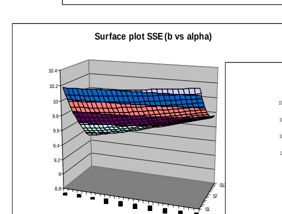
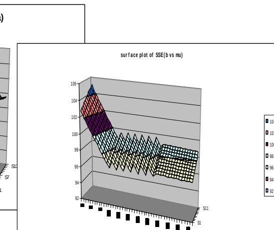


Fig 3: Original data obtained from simulations in XPPAUT. Numerical solutions of the ODE obtained by a Euler method. Data and ODE model syncronized to obtain minimum Error Sums of Squares(SSE) and new parameter estimates. No constraints on susceptible group.

Parameter Estimates (S(0)=0.53)	Original Parameters
b=0.74	b=0.78
mu=2.02	mu=0.32
alpha=0.11	alpha=0.01
omega=2.90	omega=3.00
SSE=5.37	SSE=110.38







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