Modeling environmental impacts of plankton reservoirs on cholera population dynamics

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Epidemiological and ecological backgrounds

Epidemiology

Acute intestinal infection caused by the bacteria *V. cholerae* O1 and O139.
Short incubation period, from less than one day to five days

Epidemiological and ecological backgrounds

Ecology of *V. cholerae*

Environmental and climatic drivers, such as water temperature

- direct influence on the abundance and/or toxicity of *V. cholerae*
- indirect influence on other aquatic organisms such as zooplankton, phytoplankton and macrophytes to which the pathogen is found to be attached.

Commonly, phytoplankton blooms are strongly associated with the development of zooplankton blooms, which both have an impact upon the *V. cholerae* life-cycle.

Review of mathematical models (differential equations)

1. Capasso and Paveri-Fontana in 1979. Two variables: the mean concentration of *V. cholerae* (measured in bacteria/cm^3) and the number of infected people.
2. Codeço in 2001. Three variables: the number of susceptible individuals, the number of infected and the concentration of toxigenic *V. cholerae* in water (measured in cells/ml).
3. Pascual et al. in 2002. Four variables: the number of susceptible individuals, the number of infected, the number of fomites (or bacterial abundance) and the water volume.

Capasso and Paveri-Fontana, 1979

$$\begin{cases} \dfrac{dx_1}{dt} &= -a_{11}x_1 + a_{12}x_2 \\ \dfrac{dx_2}{dt} &= g(x_1) - a_{22}x_2 \end{cases} \tag{1}$$

1. x_1 is the mean concentration of *V. cholerae* in the sea water surrounding the city of Bari
2. x_2 is the mean number of infective people in the community.

Codeço's model, 2001

$$\begin{cases} \dfrac{dS}{dt} = n(H-S) - a\dfrac{B}{K+B}S \\ \dfrac{dI}{dt} = a\dfrac{B}{K+B}S - rI \\ \dfrac{dB}{dt} = B(n_b - m_b) + eI \end{cases} \qquad (2)$$

S	number of susceptible individuals (ind.)
I	number of infected individuals (ind.)
B	concentration of toxigenic *V. cholerae* in water (cells/m

Codeço's model, 2001

$$\frac{dS}{dt} = \overbrace{n(H-S)}^{S(t)-H=e^{-nt}(S(0)-H)} - \overbrace{a}^{exposure\ rate} \underbrace{\lambda(B)}_{probability} S$$

$$\frac{dI}{dt} = a\lambda(B)S - \overbrace{r}^{recovery/death\ rate} I$$

$$\frac{dB}{dt} = B \overbrace{(n_b - m_b)}^{V.\ cholerae\ growth-loss\ rate} + \overbrace{eI}^{contaminated\ sewage}$$

$$\lambda(B) = \underbrace{\frac{B}{K+B}}_{logistic\ dose\ response}$$

Parameters

H	total human population (ind.)
n	human birth and death rates (day^{-1})
a	rate of exposure to contaminated water (day^{-1})
K	concentration of *V. cholerae* in water that yields 50% chance of catching cholera (cells/ml)
r	rate at which people recover from cholera (day^{-1})
$n_b - m_b$	difference between the growth and loss rates of *Vibrio cholerae* in the aquatic environment (c
e	contribution of each infected people to the population of *V. cholerae* in the aquatic environment (cells/ml day^{-1} person^{-1})

Codeço's 3 hypothetical human communities

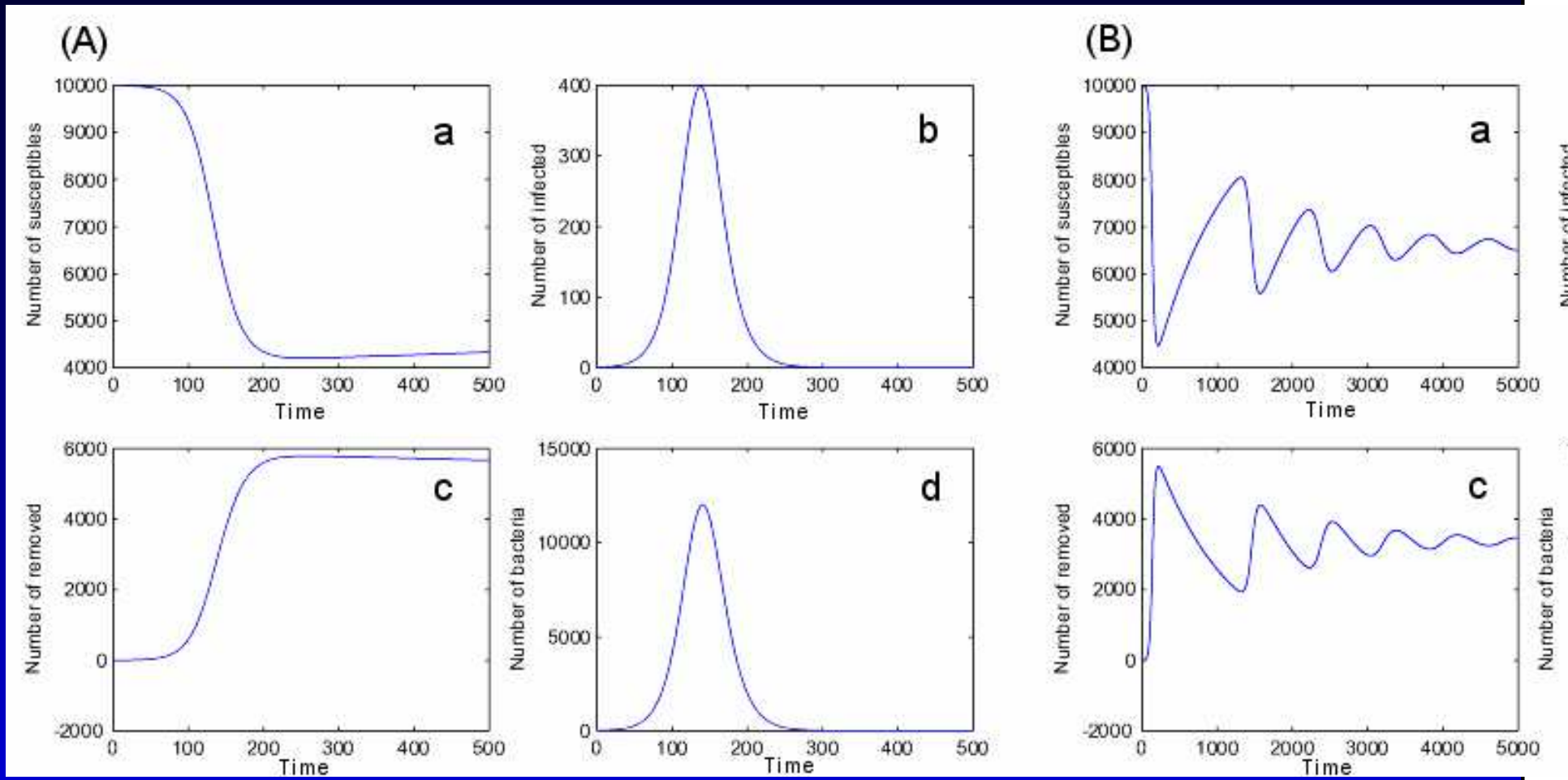
	Community 1	Community 2	Community 3
	cholera-free	epidemic	endemic
H	$10,000$ ind.	$10,000$ ind.	$10,000$ ind.
n	0.0001	0.0001	0.001
a	0.5	1	1
K	10^6 cells/ml	10^6 cells/ml	10^6 cells/ml
r	0.2	0.2	0.2
$n_b - m_b$	-0.33	-0.33	-0.33
e	10 cells/ml	10 cells/ml	10 cells/ml
critical threshold	$13,200$ ind.	$6,600$ ind.	$6,600$ ind.

Codeço's model predictions

"Stability analysis [...] indicates that if the number of susceptibles in this population is greater than a critical number S_C, an outbreak will occur".

"In the limit, [...] endemism in sanitized communities requires a permanent reservoir while endemism in poor communities requires just transient reservoirs (and a sufficiently high turnover of susceptible)".

"This result suggests that cholera endemism in the US Golf Coast, for example, may be due to a permanent reservoir of *V. cholerae*".


(A)
a
Number of susceptibles
Time
b
Number of infected
Time
c
Number of removed
Time
d
Number of bacteria
Time
(B)
a
Number of susceptibles
Time
c
Number of removed
Time
Number of bacteria

Pascual et al., 2002

$$\begin{cases} \dfrac{dS}{dt} = (b-d)(H-S-I) + \rho I - \beta \dfrac{SF}{kW+F} \\ \dfrac{dI}{dt} = \beta \dfrac{SF}{kW+F} - (d+\rho+\alpha)I \\ \dfrac{dF}{dt} = (r-\mu)F + \lambda I \\ \dfrac{dW}{dt} = p + s - DW \end{cases}$$

F	number of fomites (or bacterial abundance)
W	water volume

Codeço *versus* Pascual et al., 2002

$$\frac{dS}{dt} = (b-d)(H-S-I) + \overbrace{\rho I}^{recovery} - \beta\frac{SF}{kW+F}$$

$$\frac{dI}{dt} = \beta\frac{SF}{kW+F} - (d+\rho+\alpha)I$$

$$\frac{dF}{dt} = (r-\mu)F + \lambda I$$

$$\frac{dW}{dt} = \underbrace{p}_{precipitation\ rate} + \underbrace{s}_{river\ flow\ rate} - \overbrace{D}^{drainage\ rate} W$$

Parameters

H	total human population (not specified in the paper)
b	host per capita birth rate
d	host per capita death rate
β	infection rate at which fomites cause infection in susceptible hosts
ρ	recovery rate of infected individuals
k	scaling constant that modifies water volume to determine number of fomites required to induce infection in a susceptible
α	increased mortality rate of infected hosts

Parameters

r	reproductive rate of free-living fomites (may be a function of temperature)
μ	death rate of free-living infective stages
λ	rate at which infected produce infective stages
p	precipitation rate (may vary on an annual cycle)
s	river flow rate (may vary on an annual cycle)
D	drainage rate of water downstream from site of infection per volume of water

A mathematical model with temporary immunity including environmental impact

Distinguish between dead individuals (D) and recovered individuals (R), in contrast with the previous mathematical models by Pascual *et al.* where they are considered as belonging to the same group of removed individuals

No dunamic model for the reservoir, but concentration of chlorophyll a is the data feeding the model (input).

State and input variables

Symbol	Description
S	number of susceptible individuals
I	number of infected individuals
D	number of dead individuals
R	number of recovered individuals
C	concentration of chlorophyll a (mg/m^3)

$$
\begin{cases}
\dfrac{dS_t}{dt} = (b-d)S_t - \overbrace{\beta S_t I_t}^{transmission} - \dfrac{\gamma S_t C_{t-\delta}}{k + C_{t-\delta}} + \rho' R_t \\
\dfrac{dI_t}{dt} = \beta S_t I_t + \dfrac{\gamma S_t C_{t-\delta}}{k + C_{t-\delta}} - \tau I_t \\
\dfrac{dD_t}{dt} = \lambda \tau I_t + d(S_t + R_t) \\
\dfrac{dR_t}{dt} = (1-\lambda)\tau I_t + (b-d)R_t - \rho' R_t
\end{cases}
$$

Time is measured in months: epidemiological data are recorded more or less monthly.

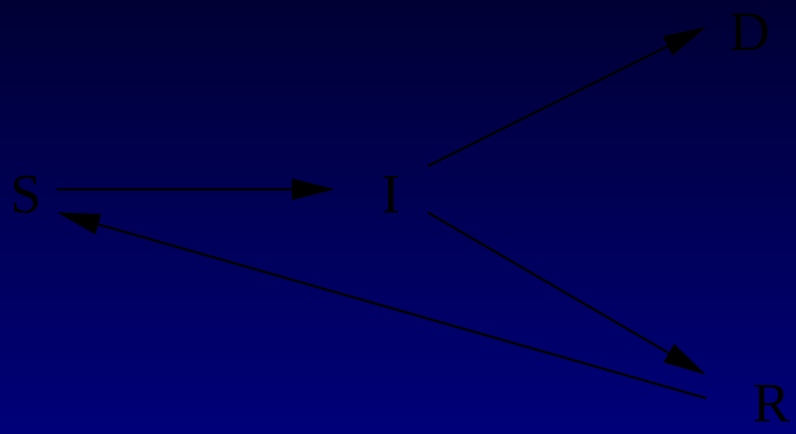


Figure 1: SIDR model with transitions between the different possible states.

Parameters

- b human birth rate (only for susceptible and recovered individuals)
- d human death rate (idem)
- δ delay parameter (month^{-1})
- β contact infection rate from infected individuals to susceptible individuals (month^{-1})
- k quantity of phytoplankton yielding 50% chance of catching cholera (mg/m^3)
- τ removed rate (month^{-1})
- λ case-fatality rate (%)
- ρ' loss of immunity rate (month^{-1})
- γ contact infection rate from contaminated water to susceptible individuals (month^{-1})

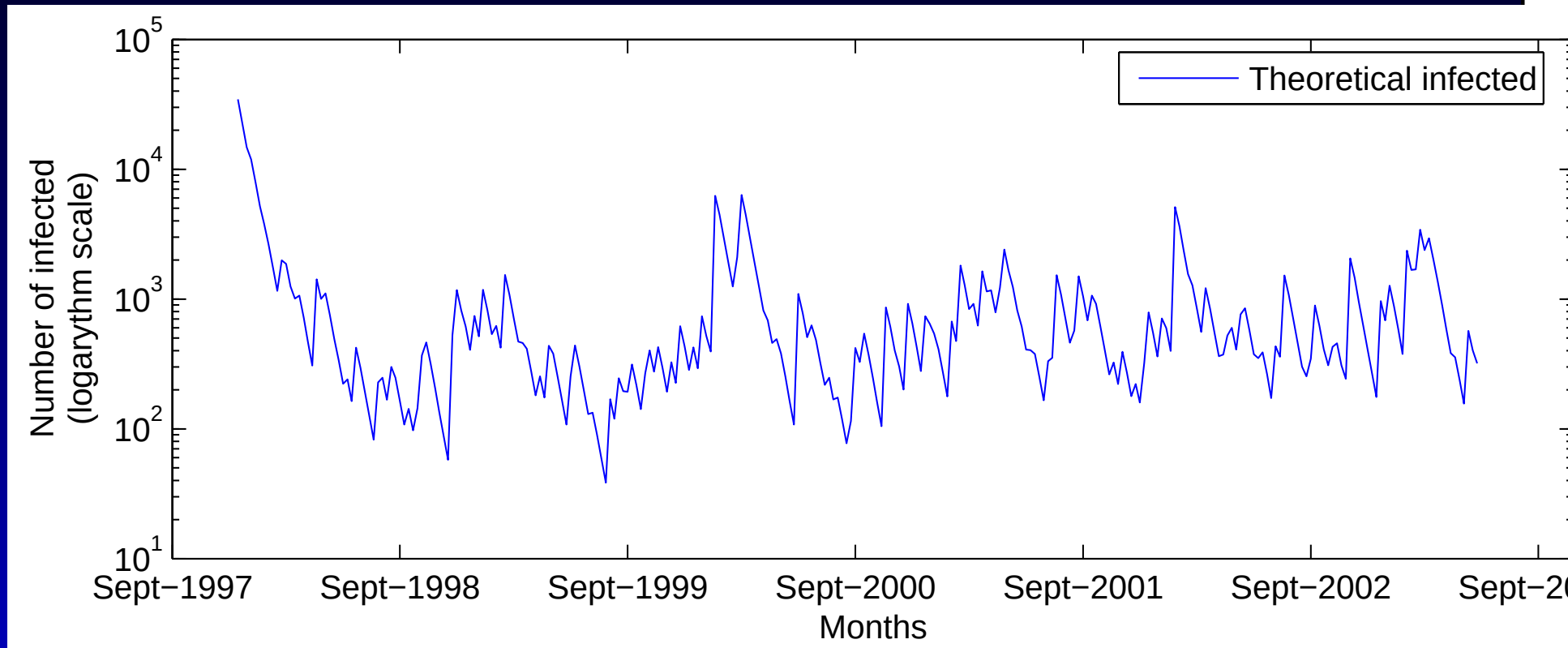
Parameters estimation

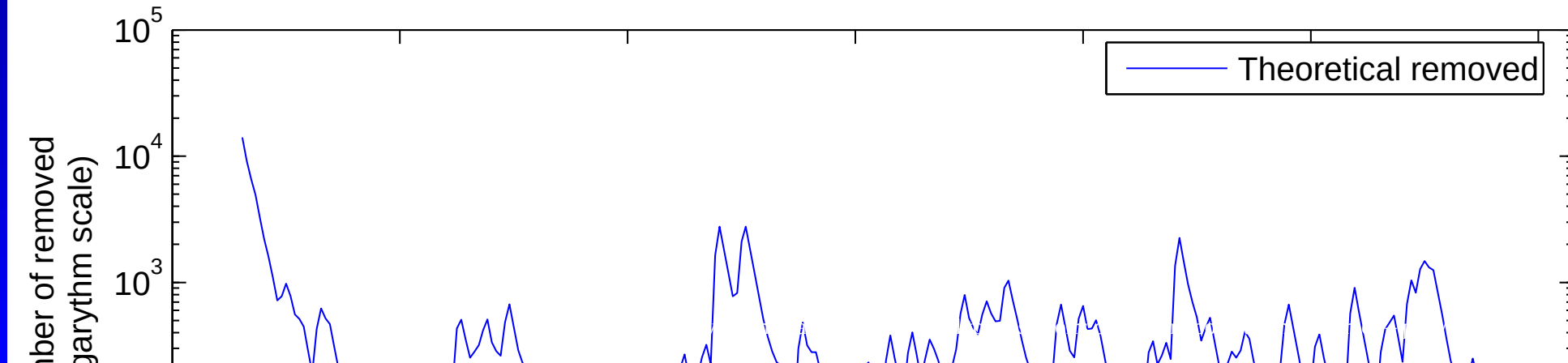
Observed number of hospitalization and death ΔY_k in the time interval $[(k-1)\Delta t, k\Delta t]$ is

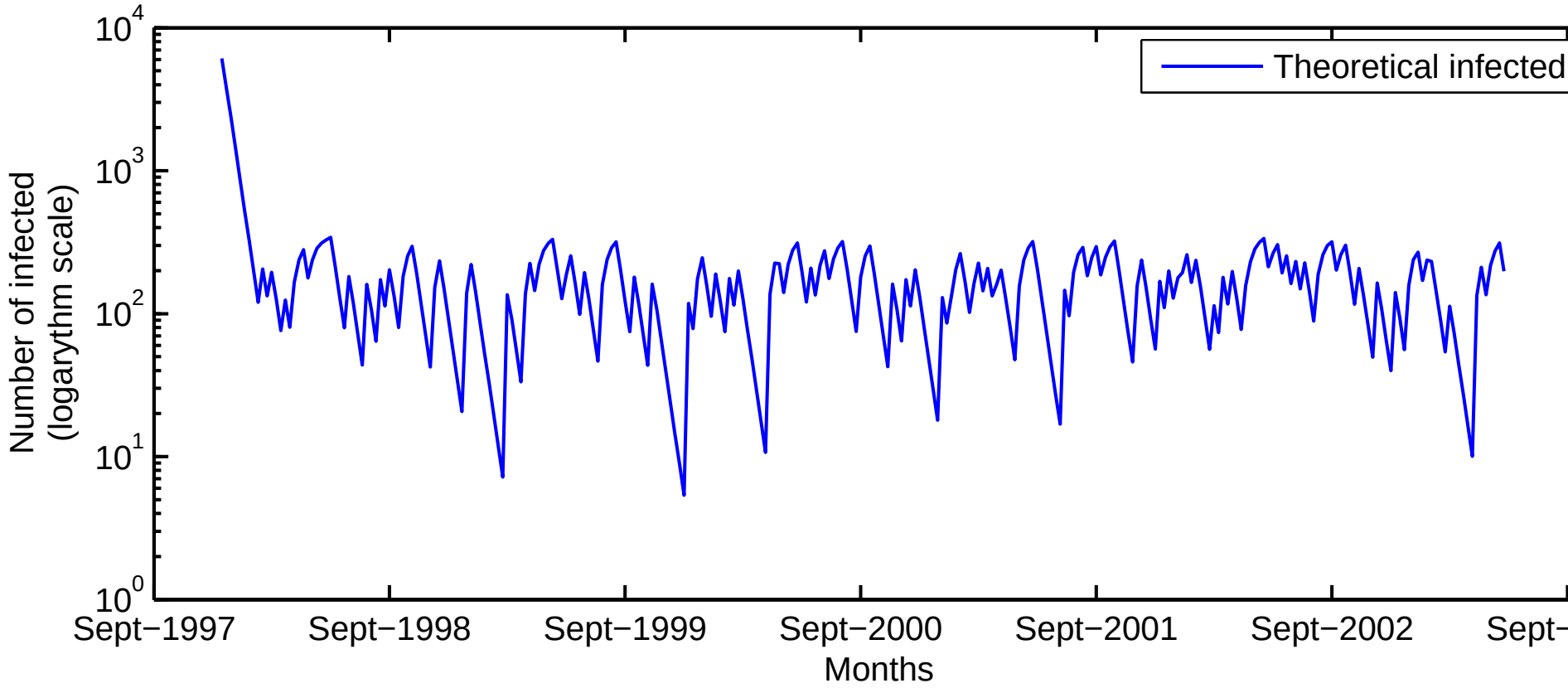
$$\Delta Y_k = \int_{(k-1)\Delta t}^{k\Delta t} \tau I_s \, ds \ . \tag{3}$$

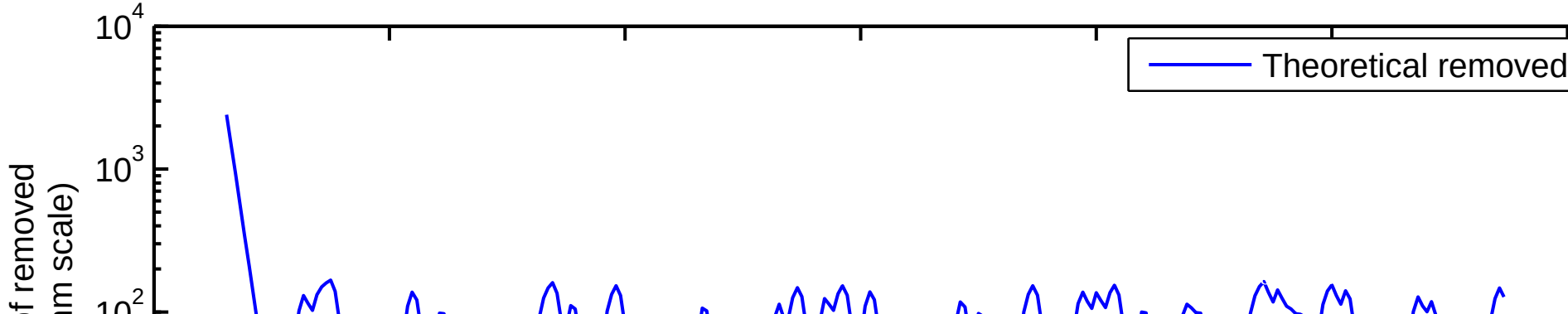
Least square minimization

$$\inf_{I_0, R_0, \delta, \beta, \gamma, k} \sum_{k=0}^{N} \left| \Delta Y_k - \int_{(k-1)\Delta t}^{k\Delta t} \tau I_s \, ds \right|^2 . \tag{4}$$


Theoretical infected
Number of infected
(logarythm scale)
10^5
10^4
10^3
10^2
10^1
Sept−1997
Sept−1998
Sept−1999
Sept−2000
Sept−2001
Sept−2002
Months


Theoretical removed
10^5
10^4
10^3


Theoretical infected
Number of infected
(logarythm scale)
10^4
10^3
10^2
10^1
10^0
Sept−1997
Sept−1998
Sept−1999
Sept−2000
Sept−2001
Sept−2002
Sept−
Months


Theoretical removed
10^4
10^3
10^2

Discussion and conclusion

- Elaborating a discrete time model, with months as time unit . Taking stochasticity into account in the dynamics is rather straightforward in discrete time models. This allows to let aside mathematical technicalities of continuous time modelling which are not central.
- Threshold relationship for the impact of Chlorophyll a concentration.

Discussion and conclusion

- Model with asymptomatics: above only 33% of infected show the symptoms and thus can die because of cholera. Indeed, the other fraction of infected individuals do not develop symptoms (asymptomatics), but they could play a role in the spread of the disease: first, they constitute a human reservoir of bacteria and can infect susceptibles, and second their offspring are immune.

Discussion and conclusion

- Multi-level of immunity age-dependent model: we can distinguish three classes of ages: less than 2 years old , between 2 and 18 years old and more than 18 years old. Individuals less than 2 years old are the more resistant face to cholera (immunity from the mother); individuals more than 18 years old are a little less resistant; and the class of individuals between 2 and 18 years old is the least resistance class.

Discussion and conclusion

- Time-dependent rates: one can imagine that contact rates (i.e. the parameters β and γ) decrease quickly after the start of an epidemic, due to the sensitization of the population by the authorities.
- Modelling different stochastic components, at the epidemiological level (the epidemiological processes) and at the observational level (the data acquisition process). Together with the natural monthly time unit, this is another argument in favor of developing a discrete time model.