Multi-level modeling, simulation for optimizing vaccination policies

Phd: TRAN Thi Cam Giang

Directors : Yann CHEVALEYRE, Marc CHOISY

VU Dinh Thiem, Jean-Daniel ZUCKER

Doctoral School : EDITE 130,Université Pierre et Marie CURIE

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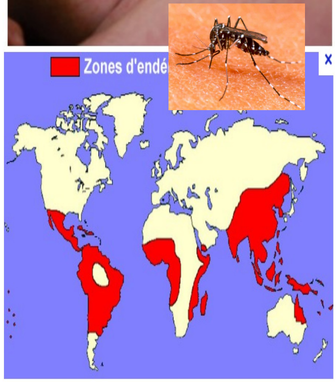
Context et Objective

- Many infectious diseases such as measles, dengue in Asia and most countries of southeast Asia. (REF)

- Vaccination: Mass policy, the oldest and still most widely used in the world, is to vaccinate a maximal number of children before a certain age. It is already getting a significant decrease about the incidence in many countries,

- Problem : is too expensive, ineffective and absolutely impossible to implement in many poor countries, in particular in Africa, Southest Asia..as at the same time financial and logistical problems. (ex. the projet of the WHO about extinction of measles in Vietnam before 2012 is failed).

OPTIMIZING vaccination policies that would be more effective, less expensive than the mass policies.



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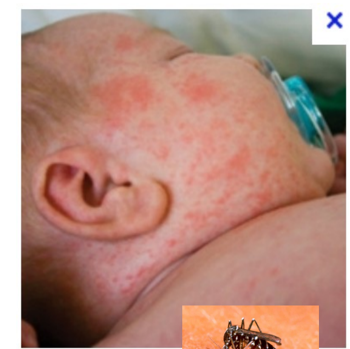
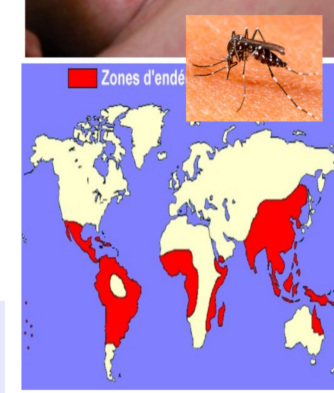




OPTIMIZING vaccination policies that would be more effective, less expensive than the mass policies.

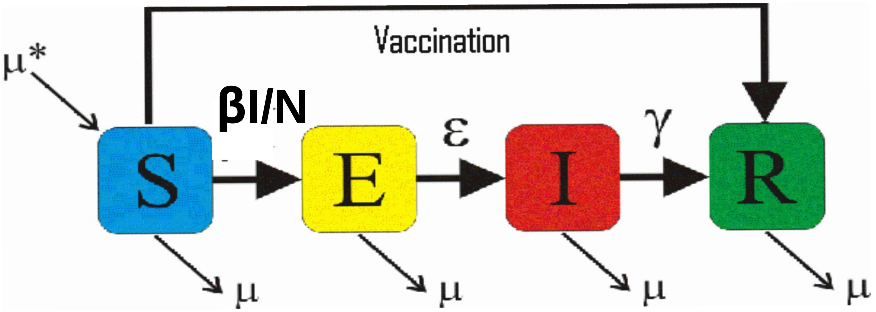
Tool?

- There exists the R package : very slow !
- Using C++ to do stochastic simulation with N = 10M → excellent !
- Developping a package integrating R/C++.

Method

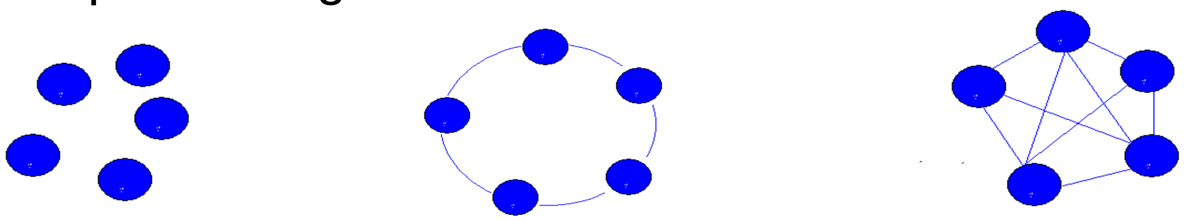
(1) **Stochastic Epidemiological model**

- SEIR Model of population :



- Gillespie's Stochastic Algorithm (1977)
  - Motivation : no extinction in deterministic model
  - Approach: population-based time-to-event model, 2 steps:
    - Searching the time of next event
    - Searching the nature of next event

(2) Spacial Epidemiological Modeling



Method

(3) **Optimizing vaccinations policies : reinforcement learning**

For a structure ò population given, where and when we must vaccinate to vacciner afin de decrease at most the global incidence or crease at most the probability of global eradication.

- SARSA : State - Action - Reward – State – Action
  - A state at time t : (Є N4)

$$S = \left(\left(s_1, e_1, i_1, r_1\right), \left(s_2, e_2, i_2, r_2\right), \ldots, \left(s_n, e_n, i_n, r_n\right)\right)$$

- Set of states : $N^{4*nbVilles}$
- Action at time t, vaccination ou non vaccination

- Sum of rewards for a policy : ∏ : S → A

$$\sum_{t=0}^{\infty} \gamma^t r_t = r_0 + \gamma r_1 + \gamma^2 r_2 + \gamma^3 r_3 + \ldots$$

Expected Results

- The results of this thesis are: an efficient **algorithm** for optimizing vaccination policies evaluated by **spacial and stochastic simulation.**

- An informatic tool supporting decision of vaccination policies used by health professionals available in the form of an R package (R/C++)

Results 1

- Finding the formula of the force of infection in spatial structure.

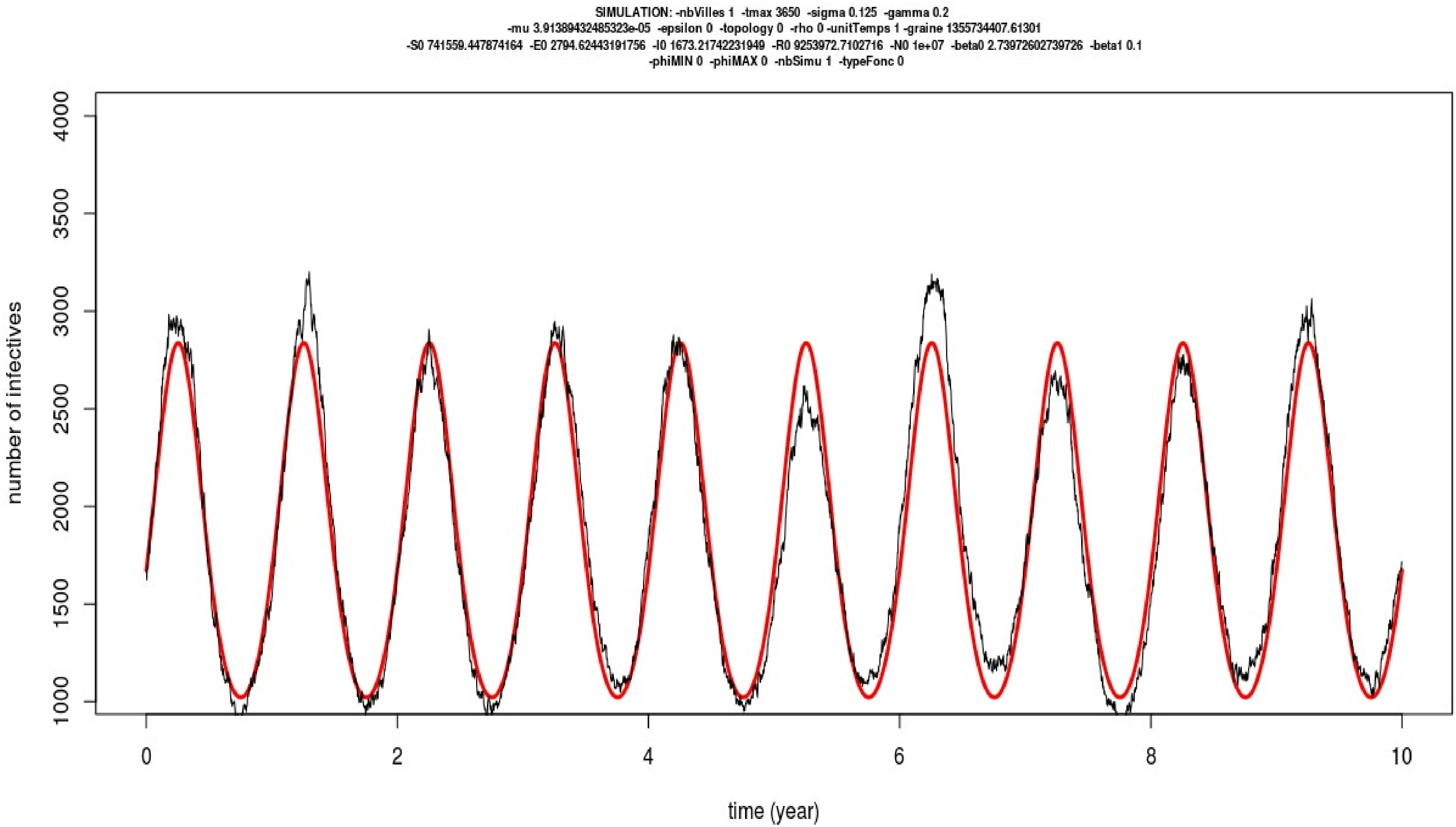
$$\lambda_i = \left(1 - \sum_{\substack{k=1 \\ k\neq i}}^{n} \rho_{ik}\right) \beta_i \frac{I_i}{N_i} + \sum_{\substack{k=1 \\ k\neq i}}^{n} \rho_{ik} \frac{(1-\varepsilon_{ik})\beta_i N_k + \varepsilon_{ik}\beta_k N_i}{N_i N_k} I_k$$

- Modeling and simulation of deterministic and stochastic SEIR model in programming languages.

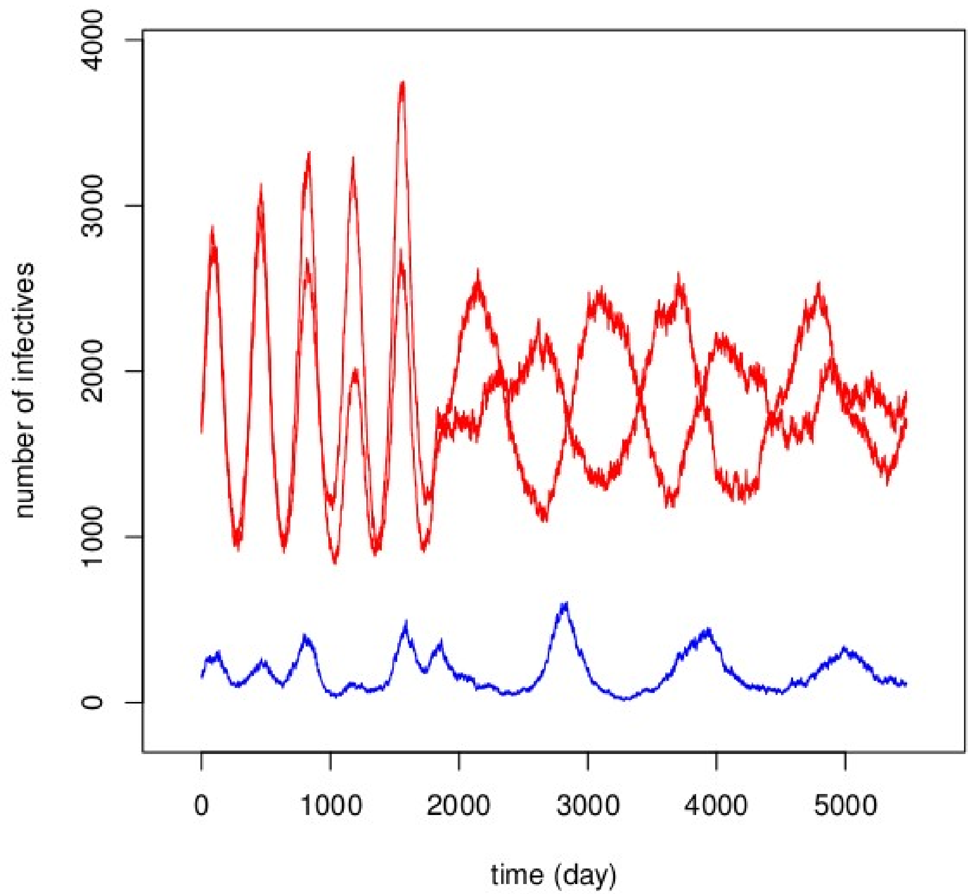
Result 1: package **dizzys**

- The package **dizzys** simulating temp-spatial epidemic models.
  - Allow to integrate C ++ in R.
  - Make deterministic / stochastic simulations for SIR and SEIR epidemic models by using deterministic equations, stochastic algorithms and adaptivetau Gillespie algorithm.
  - Make simulations for n sub-populations in a meta-population.
  - Interface displayed by R in 2D, in 3D.

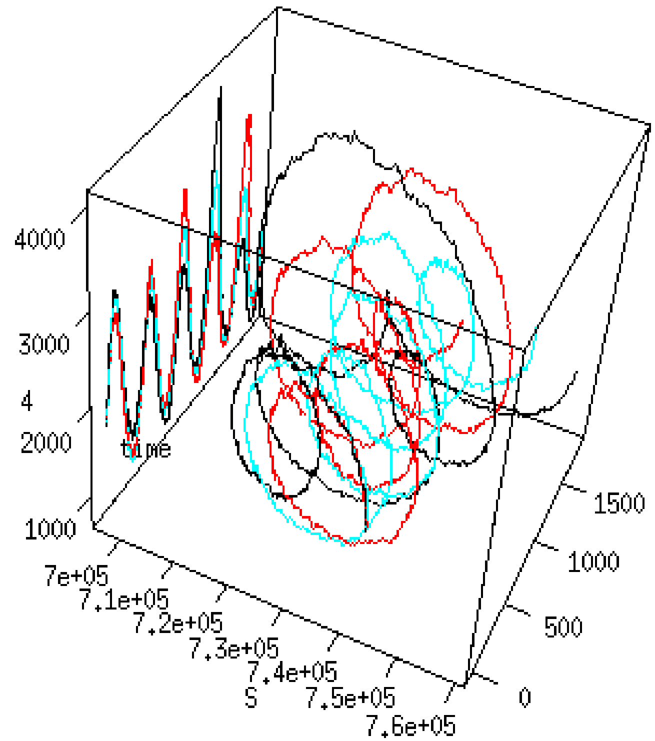
Result 1: Prototype developed under C++ : Example Number of infected for 1 city of 10M individuals



Result 1: : package **dizzys**
simulation in 2D and 3D



Metapopulation of three cities,
N={10^6,10^6,10^5}, φ_{Max}={0,π}



Metapopulation of three cities,
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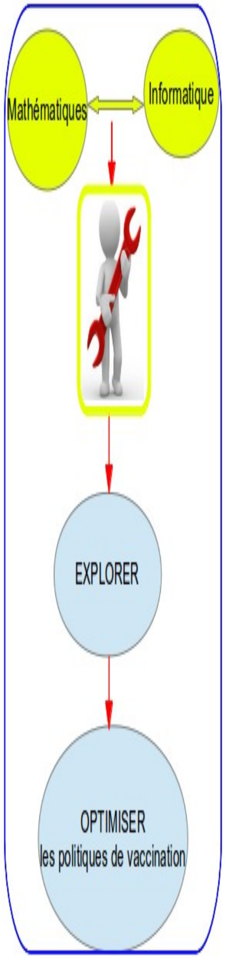
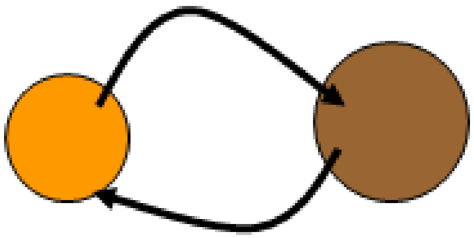


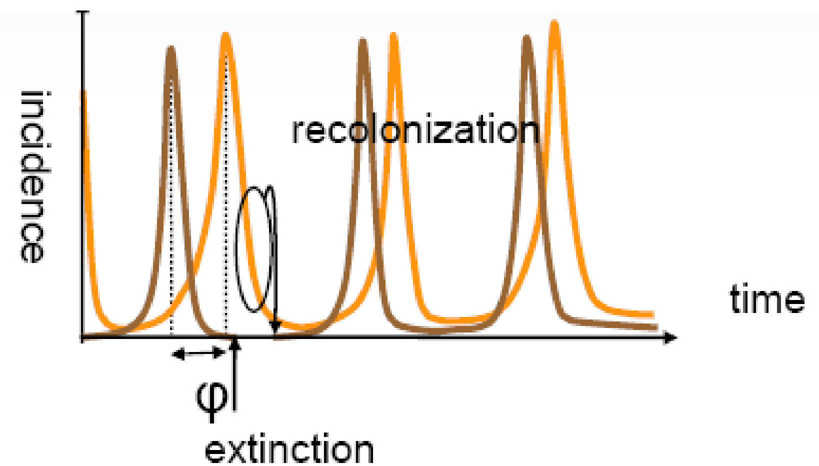
\mu=1/(70*365) par jour, \beta_0=1250/365 jour, \beta_1=0.1jour, 1/\sigma=8 jours, 1/\gamma=5 jours, \varphi=0, temps de simulation = 10 ans.

Question 1: persistence in the simulated model



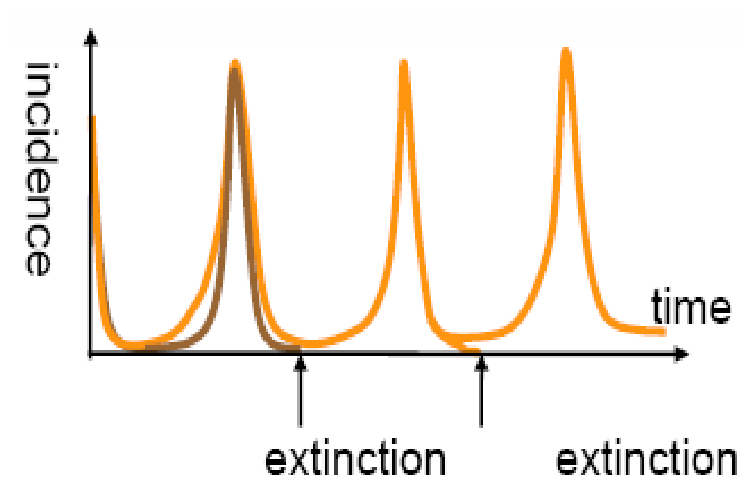
Spatial Asynchrony

no extinction at larger scale



Spatial synchrony

Extinction at larger scale



Solution of Q1 : EXPLOITING **dizzys**

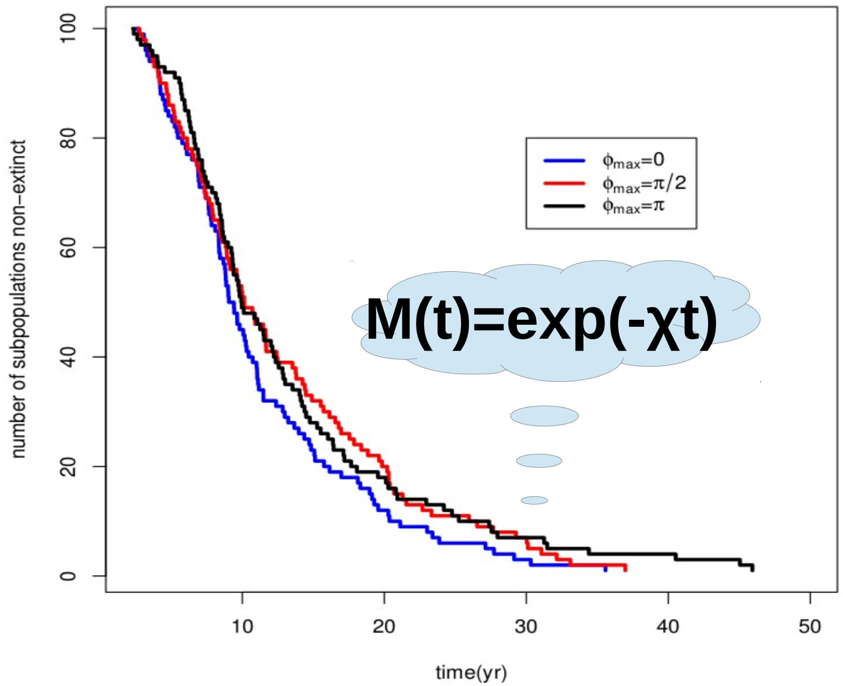
- EXPLOITING the tool dizzys for the persistence in the model simulated.

- FINDING the characteristics of the global persistence. This is the survival curve which is shaped

$$M(t) = \exp(-\chi t)$$

where M (t) is the number of meta-populations that are not extinct at time t.

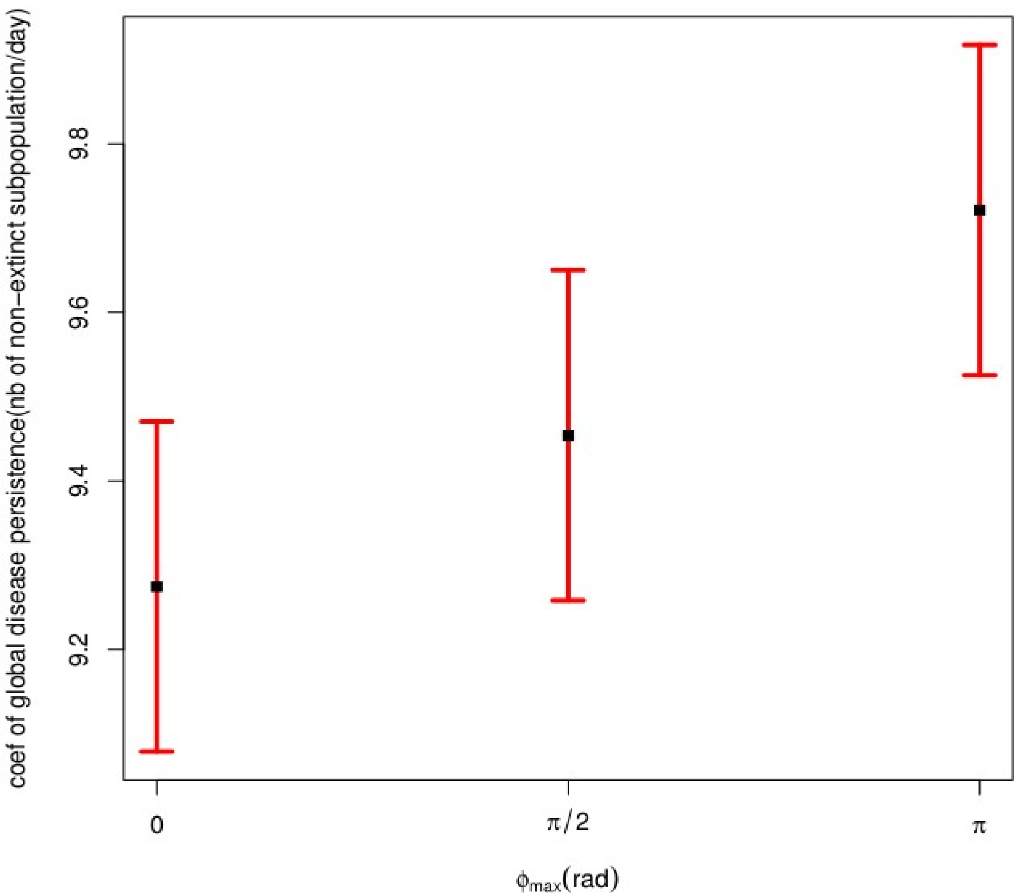
Survival curve Kaplan-Meier



NbVilles=02, N=3*10^5 tmax=50 ans, ρ=0.001

Result 2 : Persistence 1

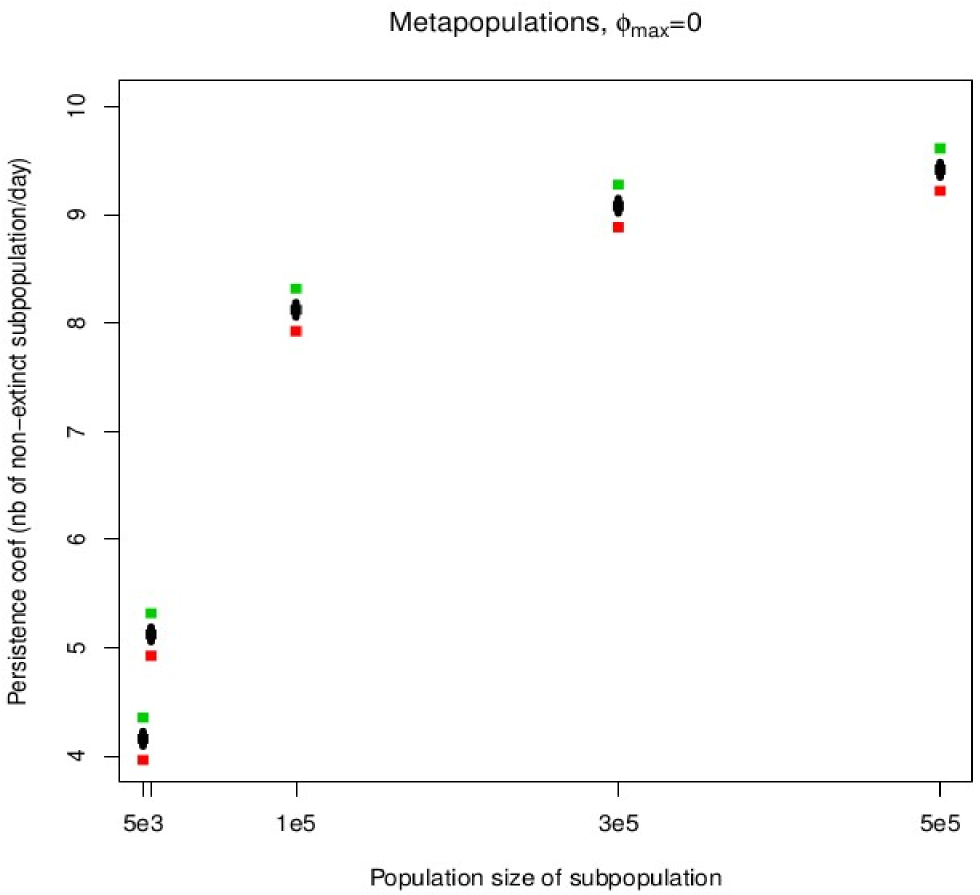
ESTIMATING the global persistence of an infectious disease and φ_{Max}



Estimated rate of global disease persistence in the metapopulation of 08 subpopulations after 100 different simulations N=3e5, coupling rate $\rho=0.1.

Result 2 : Persistence 2

Influence of the population size on the global persistence of disease

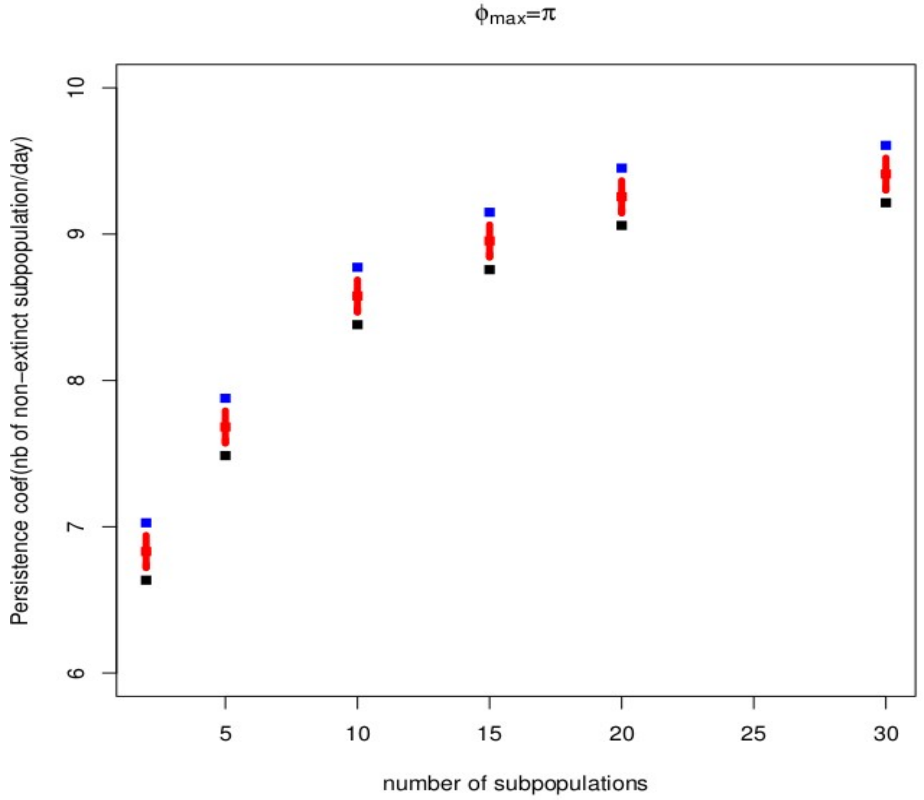


Estimated persistence rate in the metapopulation of 06 subpopulations after 100 different simulations.

The population size of subpopulation is in the set {5000, 10000, 1e5, 3e5, 5e5}

Result 2 : Persistence 3

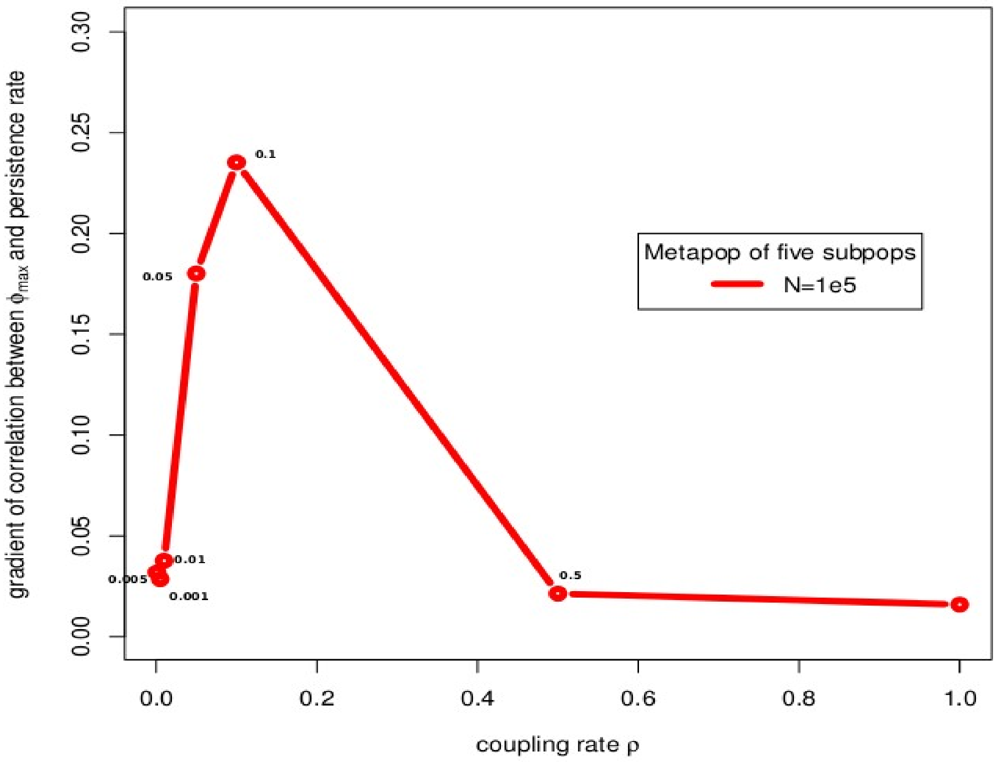
Influence of the number of subpopulation in one metapopulation On the global persistence of disease.



Estimated persistence rate in the metapopulation of multi-subpopulations after 100 different simulations.
The number of subpopulations alters in the set {2, 5, 10, 15, 20, 25, 30}

Result 2 : Persistence 4

Influence of the coupling rate among subpopulations in a metapopulatio on the slope of the coef. of global persistence to φ_{Max}



Coupling rate \rho = {0.001, 0.005, 0.01, 0.05,0.1, 0.5, 1}, phiMAX={0,pi/2,pi} and the population size N=1e5.
NbVilles = 05

Conclusion

- In summary, the degree of asynchrony increases the global persistence time of an infectious disease.
- NOW :
  - GIVING an efficient **algorithm** for optimizing vaccination policies evaluated by **spacial and stochastic simulation.**
  - **Evaluating this algorithm.**

Manuscript in preparation:

T.C.G. Tran, J.D. Zucker, M.Choisy, Quantifying the effect of synchrony on the persistence of infectious diseases in a metapopulation.

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