A computational model to study the effects of different vaccine policies on Pertussis epidemiology.

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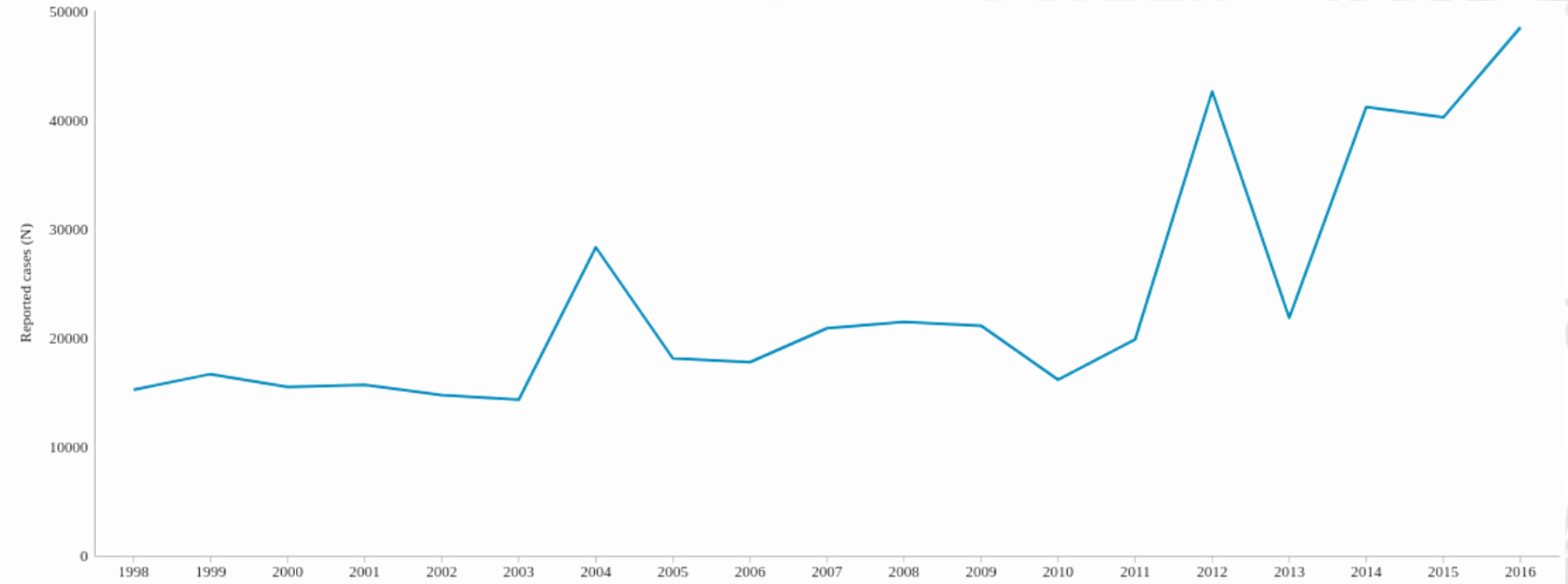
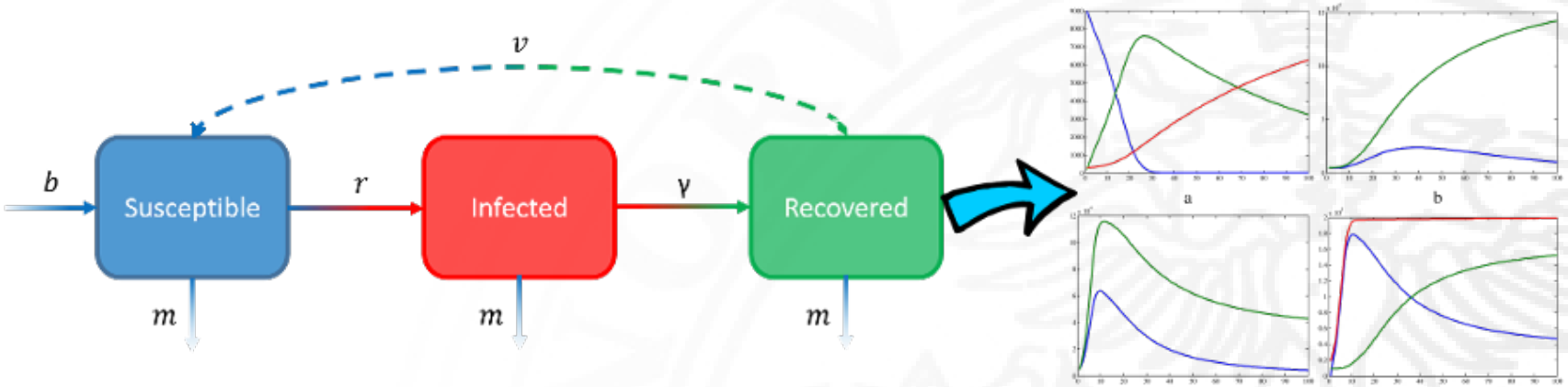
Introduction to computational models for Pertussis

- Pertussis, also called whooping cough, is a highly contagious respiratory disease;
- From the second half of 20th century Vaccination programs decreased its diffusion and mortality, but its hospital admissions and fatalities are still elevated;
- *European Centre for Disease Prevention and Control* reports an increasing trend of pertussis cases in EU from 2014.



Introduction to computational models for Pertussis

Computational-mathematical models can be exploited to help scientists in the study of Pertussis epidemiology.



For instance, they can be used:

- to provide new insights into drivers of pertussis epidemiology;
- to investigate different explanations of the observed resurgence;
- to predict potential effects of different vaccination strategies.

Introduction to computational models for Pertussis

- Some Pertussis models were proposed in the literature:

Model	Pop. Age	Vac. doses	Booster doses	Imm. levels	Pertussis sesonality	Sol. technique
Rohani 2016	1 class	1 dose	No	1 level	YES	SSA
Lavine 2011	50 classes	No	No	1 level	NO	PDE
Hethcote 2004	9 classes	4 doses	1 dose	4 levels	NO	ODE

- Starting from these models our goal was to develop a *new model for studying Italian Pertussis epidemiology*;
- To achieve this we decide to exploit a *high level formalism* to make easier the model creation.

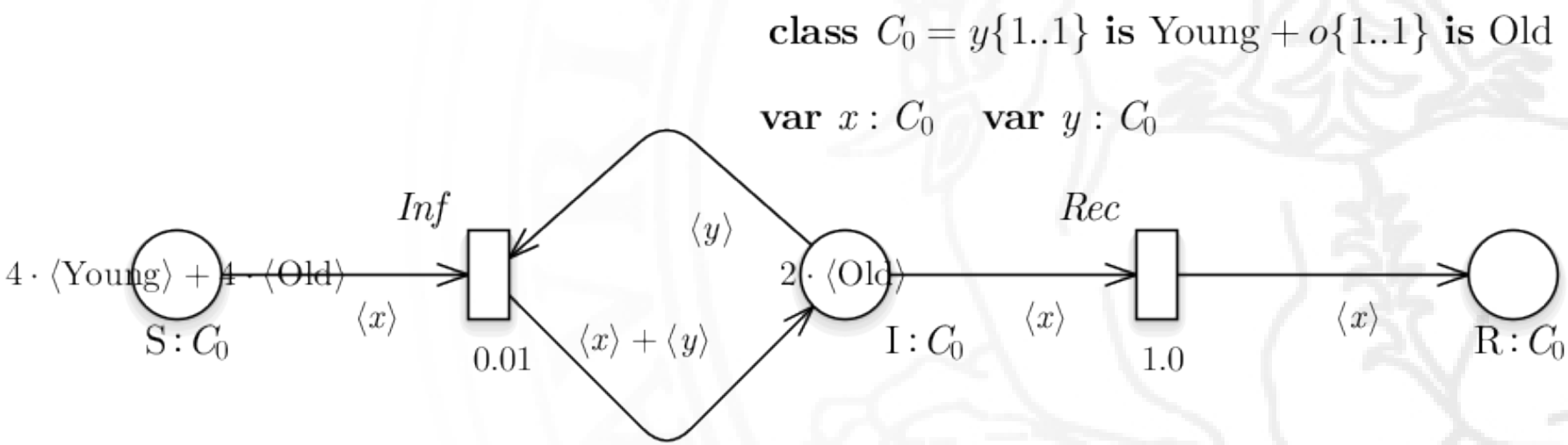
[1] *F.M.G. Magpantay, M.D. De Celles, P. Rohani, A.A. king.* **Pertussis immunity and epidemiology: mode and duration of vaccine-induced immunity**, Journal of Parasitology, 143(7), 835-849,2016.

[2] *J. S. Lavine, A. A. King, O. N. BjÃ¸rnstad* **Natural immune boosting in pertussis dynamics and the potential for long-term vaccine failure**, Proceedings of the National Academy of Sciences of the United States of America, 108(17), 7259-7264, 2011.

[3] *H. W. Hethcote, P. Horby, P. McIntyre.* **Using computer simulations to compare pertussis vaccination strategies in Australia**, , Vaccine 22 (17) 2004.

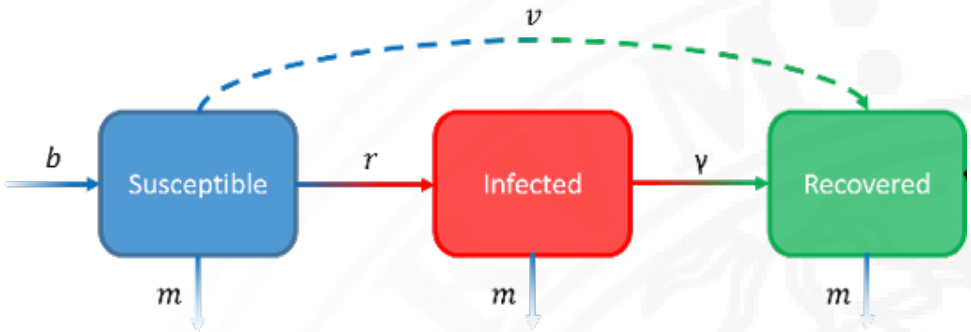
Stochastic Symmetric Net (SSN) in a nutshell

- SSN is a high level Petri Net (PN) formalism;
- SSN extends Stochastic PN (SPN) with colores so that token carries some kind of information;
- It provides a more parametric description of the system;
- It is always possible from an SSN model derived a corresponding SPN through unfolding procedure.
- A deterministic process approximating the stochastic behavior of SSN model can be derived exploiting Kurtz's results.



Our SSN Pertussis model

It is inspired by SIR model with vaccination,



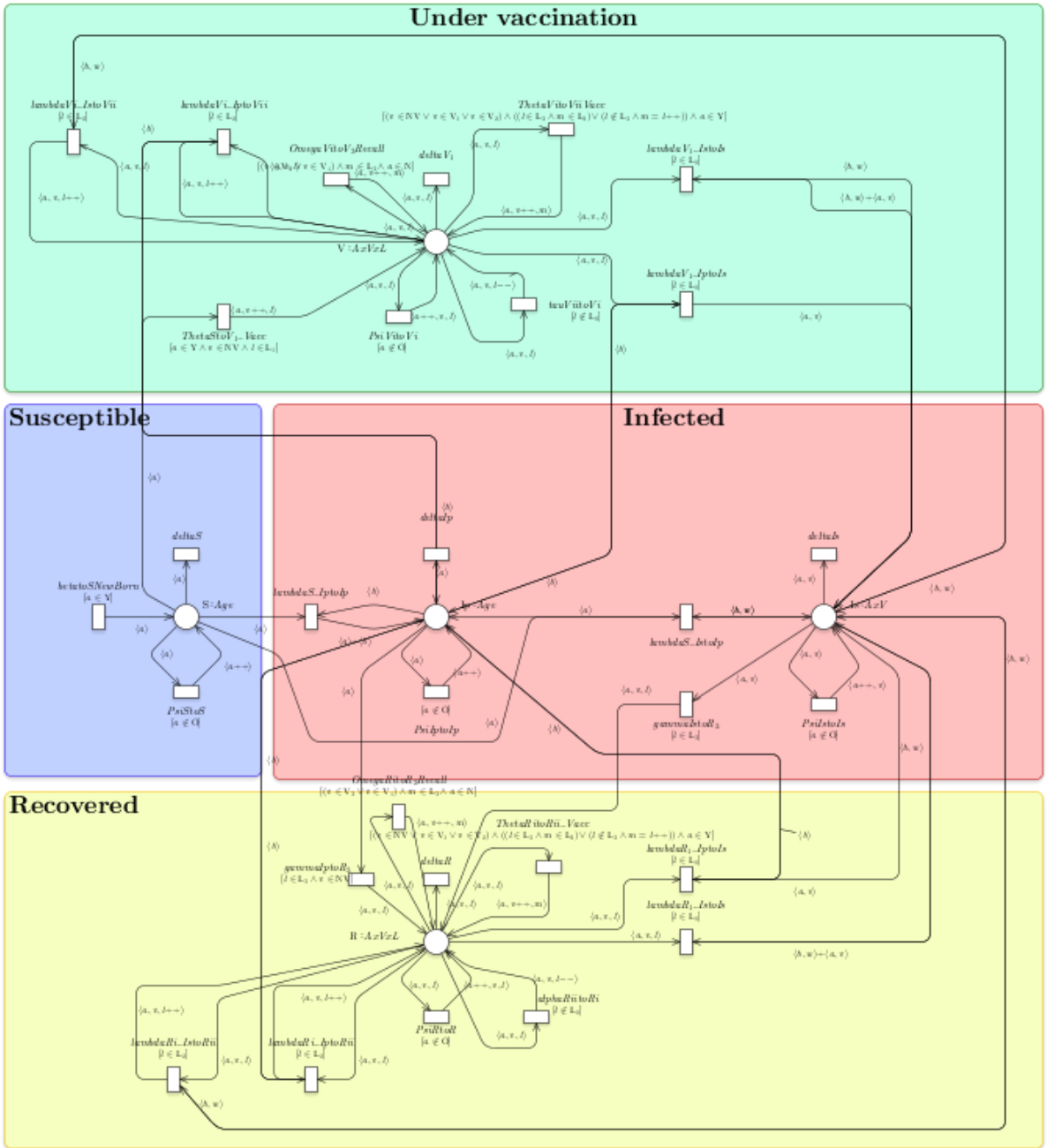
we consider the following health states (as places):

- Susceptible;
- Primary infected;
- Secondary infected;
- Under vaccination;
- Recovered;

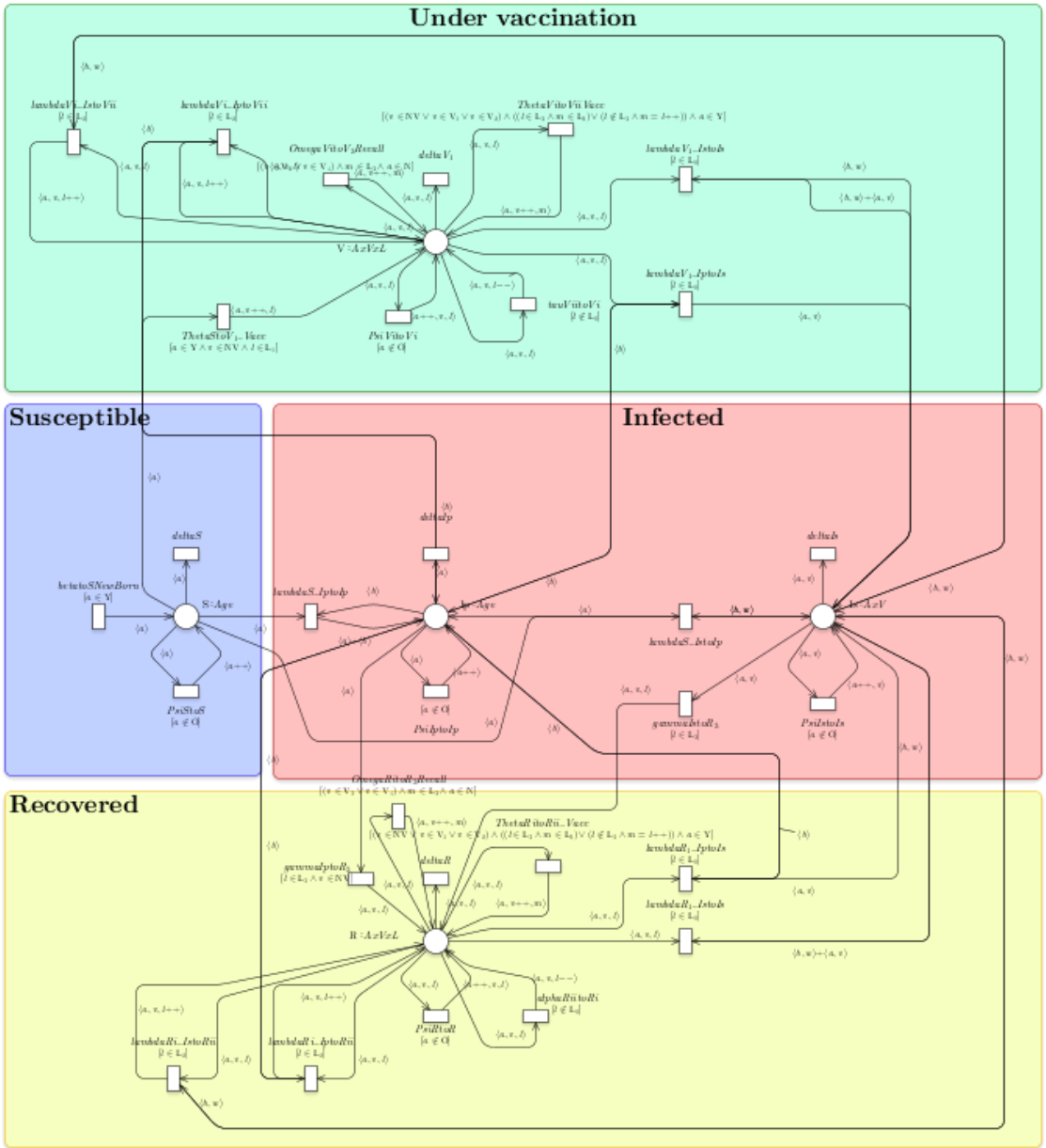
then the tokens in each place are characterized by:

- Age divided into three classes:
  $Young = [0, 1]$, $Adult = (1, 18]$ and $Old = (18, 99+)$;
- Immunization levels divided into four levels;
- Vaccination levels divided into No vaccination, three vaccination doses, and two booster vaccination doses.

Our SSN Pertussis model



Our SSN Pertussis model

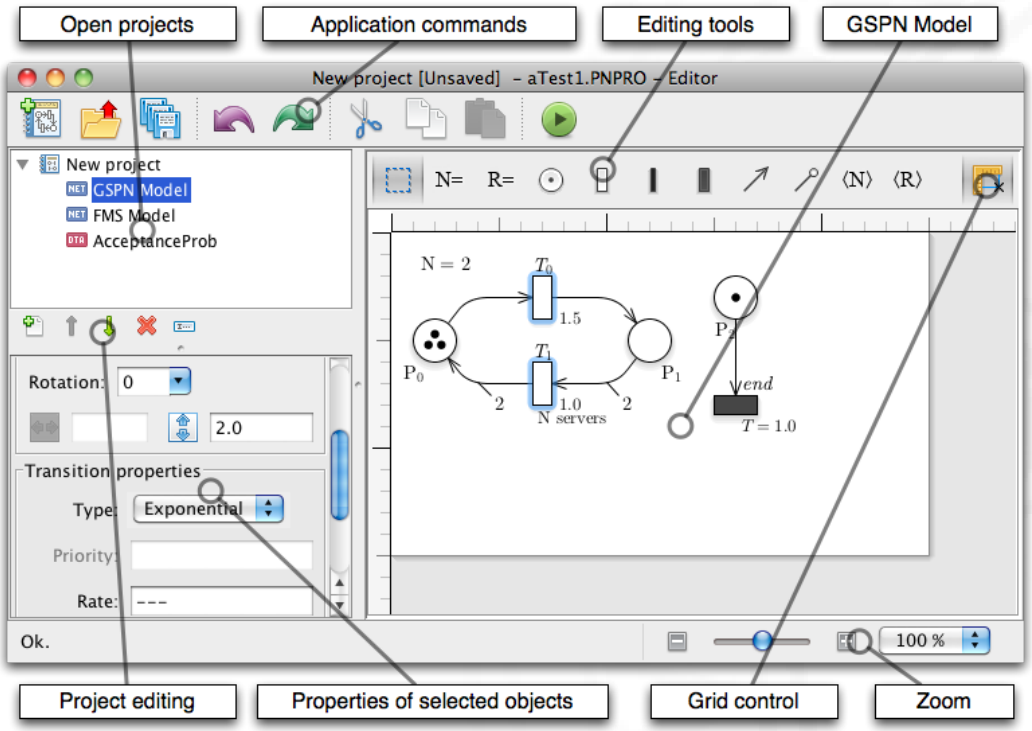


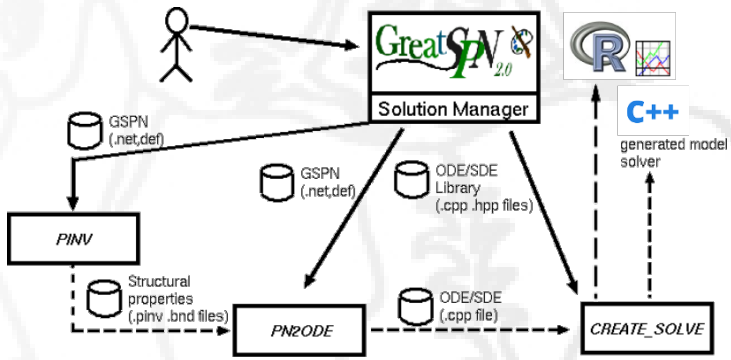
From this model we derive an ODE system with

- 168 equations

Our tool for modeling complex systems

GreatSPN 2.0





Model calibration

Most of the model parameters were derived by:

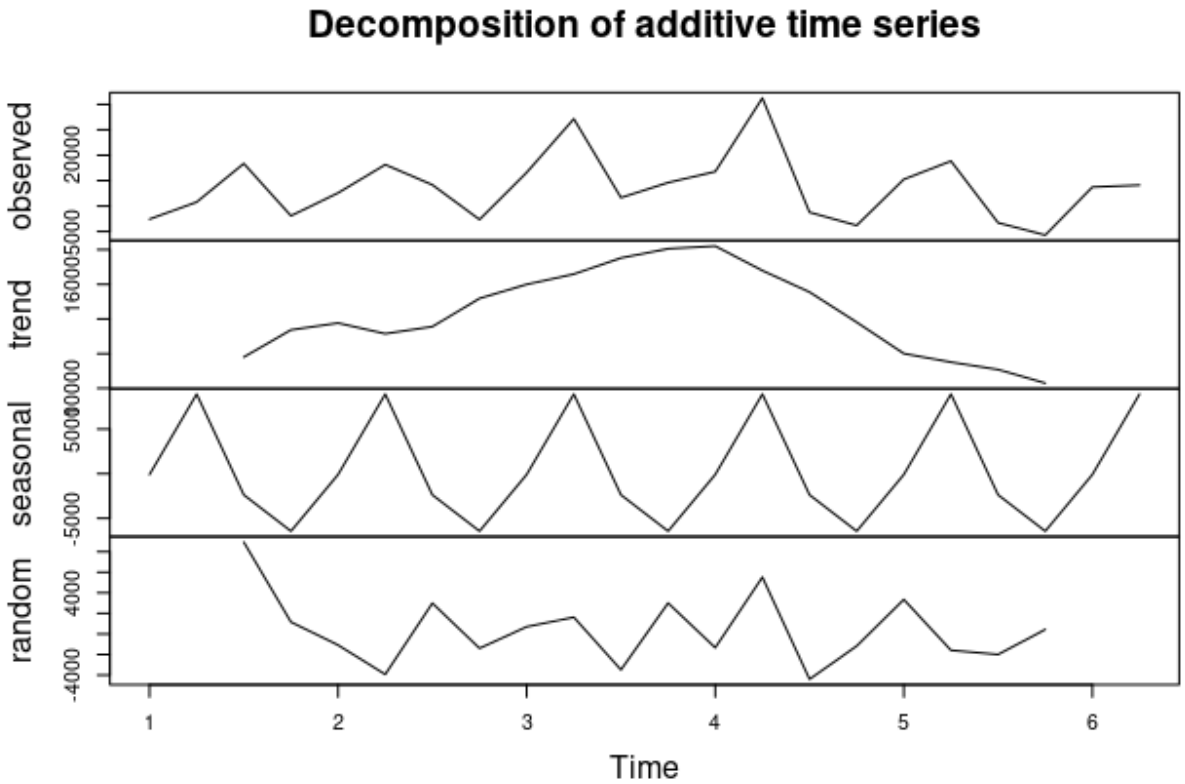
- annual reports of Italian Ministry of Health (e.g. pertussis cases, vaccination coverage, ...);
- annual reports of Istat (e.g. births, deaths, ...);
- previous works (contact rates, immunity reduction rate, ...)

However some parameters have to be estimated:

- *ProbInfect* probability to be infected when a susceptible comes in contact with an infected;
- *ProbResist* probability to resist to the infection when a susceptible is infected;
- *Initial marking* for system quantities.

Model calibration

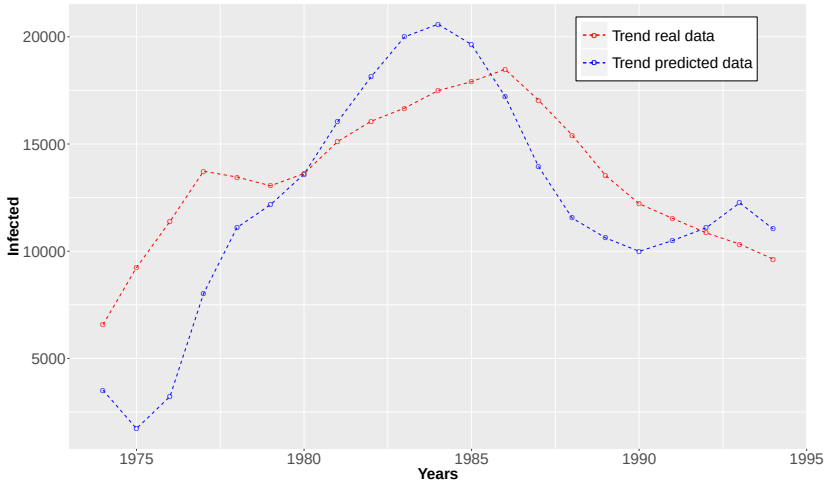
- We use *pre-vaccine-era* (from '74 to '95);
- *Fourier Transform* is used to detect the data seasonality;
- *Additive decomposition* based on LOESS regression is exploited to obtain:
  - seasonal component;
  - trend component;
  - ramdom component.



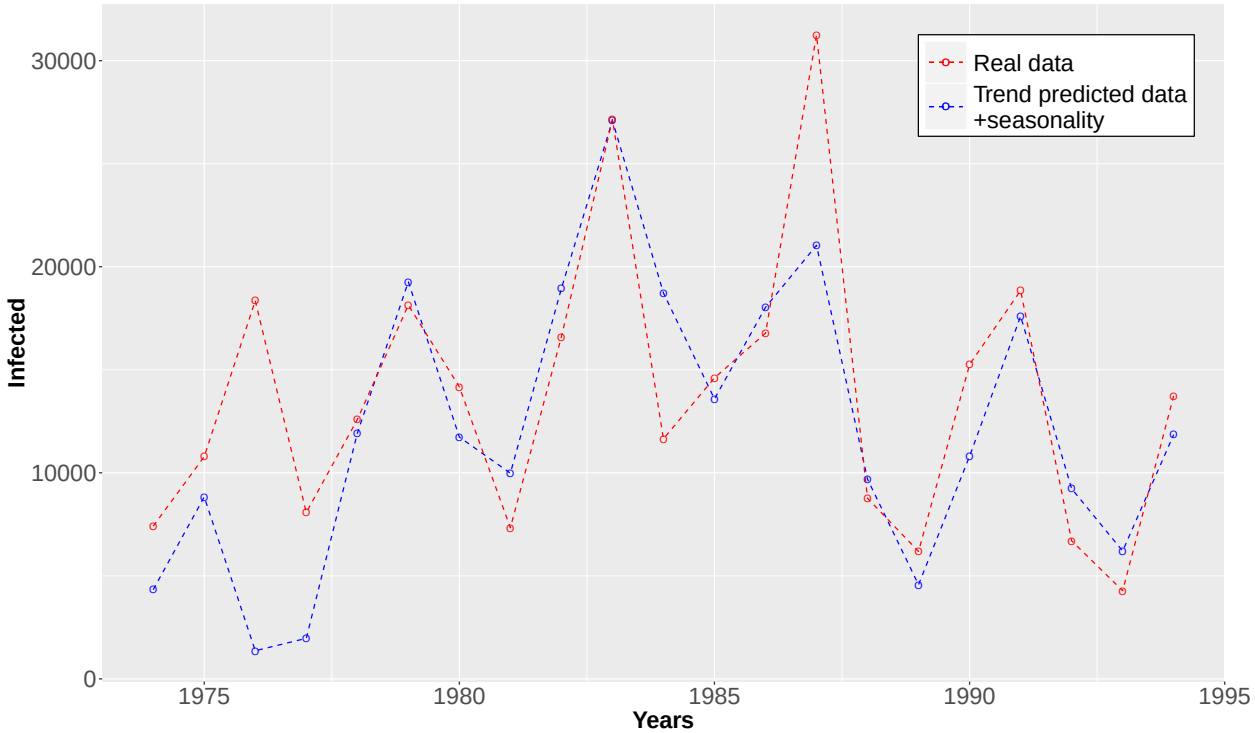
Model calibration

- Missing parameters are estimated *minimizing mean square error* between the real trend component and the one obtained by the model;
- *Latin Hypercube Sampling* technique is used to reduce the solution space;
- *Parallel Generalized Simulated Annealing* algorithm is exploited to solve the optimization problem.

Model calibration



- Adding real seasonal component to the model trend;



Conclusion

- In this presentation we described an ongoing work for studying Pertussis epidemiology;
- We showed how Petri Net formalism and its colored extension can make easier and parametric the modeling creation;
- We discussed how model calibration can be carried out by combining LHS and Optimization techniques.

Future works

- To validate the model when a vaccination program is considered;
- To extend the system considering the infection as a stochastic event.


Thanks!


Any
Questions