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Type	Oral communication
Session	Systems Biology and Interaction Networks
Title	A computational model for studying the effects of different vaccine policies on pertussis epidemiology
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Motivation

Pertussis is an infectious bacterial disease that causes uncontrollable coughing which often makes hard the breathing.
Despite several recent studies provided an its better characterization, it remains a challenging public health problem because many aspects of its infection, disease and immunity are still poorly understood.

In particular, even if the implementation of vaccination programs in many countries has decreased substantially its diffusion and mortality, the pertussis-related hospital admissions and fatalities are still evident, particularly in young infants.
Moreover, the European Centre for Disease Prevention and Control (ECDC) in its annual 2017 report highlighted an increasing trend of pertussis cases in EU, probably due to the decrease in vaccine effectiveness over time and pathogen adaptation.

In this context, computational-mathematical models can be efficiently used (a) to provide new insights into drivers of pertussis epidemiology, (b) to investigate different explanations of this observed resurgence, and (c) to predict potential effects of different vaccination strategies as well as prenatal vaccination and booster vaccinations.

Methods

In this work we propose a new methodology for studying pertussis infection and the relative vaccination cycle.
This methodology exploits:
(a) an extended Colored Petri Net formalism to provide a compact graphical description of the system and to automatically derive the model dynamics as a stochastic or deterministic process; (b) the Latin Hypercube Sampling (LHS) and mathematical programming to calibrate model parameters for reproducing the real behaviours;
(c)the Mean Squared Error (MSE) and Akaike Information Criterion (AIC) estimators to identify the optimal parameter ranges whose better approximate the real data.

Then, a model has been constructed following this proposed methodology.
It extends the classical SIRS infection model to include the peculiarities of the pertussis infection and the relative vaccination cycle.
In particular the developed model considers a population in which any member is described by her/his age (e.g. baby, child, adult), level of immunization, vaccination status (i.e. how many doses were administered) and health state (i.e. susceptible, infected and recovered). The main system events are: the infection of a susceptible due to a contact with an infect, the vaccination of a population member involving the administration of some vaccine doses at different times, and the recovering of an infect.

The model parameters were instead estimated in two steps:
(1) The deterministic process automatically derived by the model was fitted to the data using mean squared error estimator via trajectory matching. LHS method was initially exploited to reduce the search parameter space for the optimization algorithm. Then, the simulated annealing algorithm was applied on the reduced solution space to identify best parameter set minimizing the mean squared error with respect to the real observed data.
(2)The stochastic process derived by the model was fitted to the data using Akaike Information Criterion (AIC) via trajectory matching. LHS method was exploited again to generate 250 starting points over the parameter ranges obtained considering 95% confidence intervals for parameters estimated by the

deterministic process. Then, for each starting point the corresponding trajectory was generated using Gillespie Stochastic Simulation Algorithm, and the most promising parameter set is selected by comparing its trajectory with real data through AIC estimator.

Results

We propose a new computational methodology to study Pertussis disease. Moreover, we show that model generated and calibrated according to this methodology is able to reproduce the real observed pertussis spread considering the time period from 1974 to 2016.
Finally, this model can be suitably exploited to investigate different explanations of the recent pertussis resurgence and predict effects of several vaccination strategies.

Info

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Figure

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Availability	-

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