

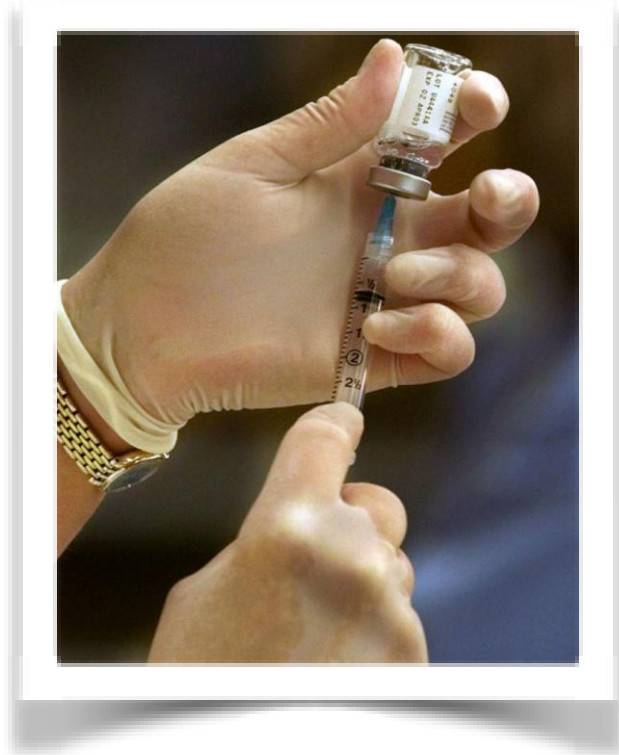
Uncertainty quantification for meningococcus B carriers prediction

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Introduction

Meningitis is an infection of the brain and spinal cord which is caused by the bacterium *Neisseria meningitidis*. This disease is transmitted exclusively among humans, mainly during the adolescence.

In Spain the major cause of meningitis in the last decades has been genogroup C (MenC), with most of other cases corresponding to meningococci genogroup B (MenB).



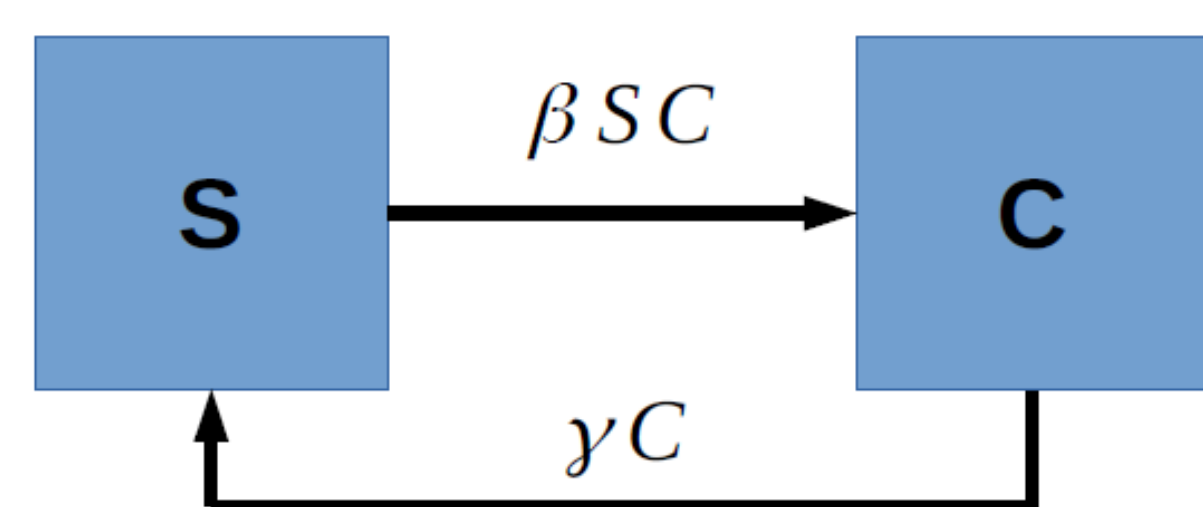
Nowadays the 12-year children are vaccinated against Men C, but it would be interesting to know the risk of a MenB outbreak in the next few years in the case no vaccination program is implemented.

We have proposed a study combining two different models:

- Susceptible- Carrier Model: We will be able to predict the proportion of carriers without specifying the genogroup.
- Lotka-Volterra competition Model: We will know the proportion of carriers of MenB among the carriers specified in the last model.

Modelling and Data

Susceptible –Carrier-Susceptible Model



S_t % of susceptible in month t
 C_t % of carriers in month t
 $\beta > 0$ is the transmission rate
 $\gamma > 0$ is the rate of recovery

$$S_{t+1} = S_t - \beta S_t C_t + \gamma C_t$$

$$C_{t+1} = C_t + \beta S_t C_t - \gamma C_t$$

Our data is given in probabilities, so is necessary scale the model. Moreover taking into account that we assume constant population, $S_t + C_t = 1$ the above equations can be transformed into:

$$C_{t+1} = (1 + \beta - \gamma)C_t - \beta C_t^2$$

Lotka-Volterra competition Model

$$X_1'(t) = r_1 X_1(t)(K_1 - X_1(t)) - \alpha_{1,2} X_1(t) X_2(t)$$

$$X_2'(t) = r_2 X_2(t)(K_2 - X_2(t)) - \alpha_{2,1} X_2(t) X_1(t)$$

where $i = 1$ corresponds to Men B genogroup, $i = 2$ corresponds to non-Men B genogroup, and

$X_i(t)$, $1 \leq i \leq 2$ denotes the total amount of the genotype i meningococcus at the month t ,

$r_i > 0$ is the growth rate of the genotype i .

$K_i > 0$ is the carrying capacity of the genotype i .

$\alpha_{i,j}$, $i \neq j$ is the effect of the genotype j bacteria on the growth of the genotype i

On the one hand as our data is also given in probabilities, we rescale the model. On the other hand taking into account that memory effects arising from DNA recombination with other genogroups that coexist and compete with this one, we replace the classical derivative by the fractional Caputo derivative and we discretize the model, obtaining the following equation,

$$x_t = x_0 + \frac{N_1}{\Gamma(\alpha)} \sum_{k=1}^t \frac{\Gamma(t-k+\alpha)}{\Gamma(t-k+1)} x_{k-1} (1 - x_{k-1})$$

where x_t represents the percentage of carrier people of MenB up to all the carrier people.

Data

In order to study an outbreak of Meningitis, we will take account the data provided by Reference Laboratory for Meningococcus. Moreover, assuming that the data follows a Beta-Binomial distribution, we can establish a confidence interval of each data, obtaining:

Dates	Carriers (X_1^j)	Susceptible (X_2^j)
$t_1 = 2011 (j = 1)$	[0.1137%, 0.1370%]	[0.8630%, 0.8663%]
$t_2 = 2012 (j = 2)$	[0.1480%, 0.2140%]	[0.7860%, 0.8520%]

Dates	Genotype Men B (Y_1^j)	Genotype non-Men B (Y_2^j)
$t_1 = 2011 (j = 1)$	[0.4343%, 0.4698%]	[0.5302%, 0.5657%]
$t_2 = 2012 (j = 2)$	[0.2640%, 0.3440%]	[0.6560%, 0.7360%]

With this data and with the above model we will use the technique called *probabilistic fitting* [1] in order to obtain the parameters that best fit both models to their corresponding 95% confidence intervals.

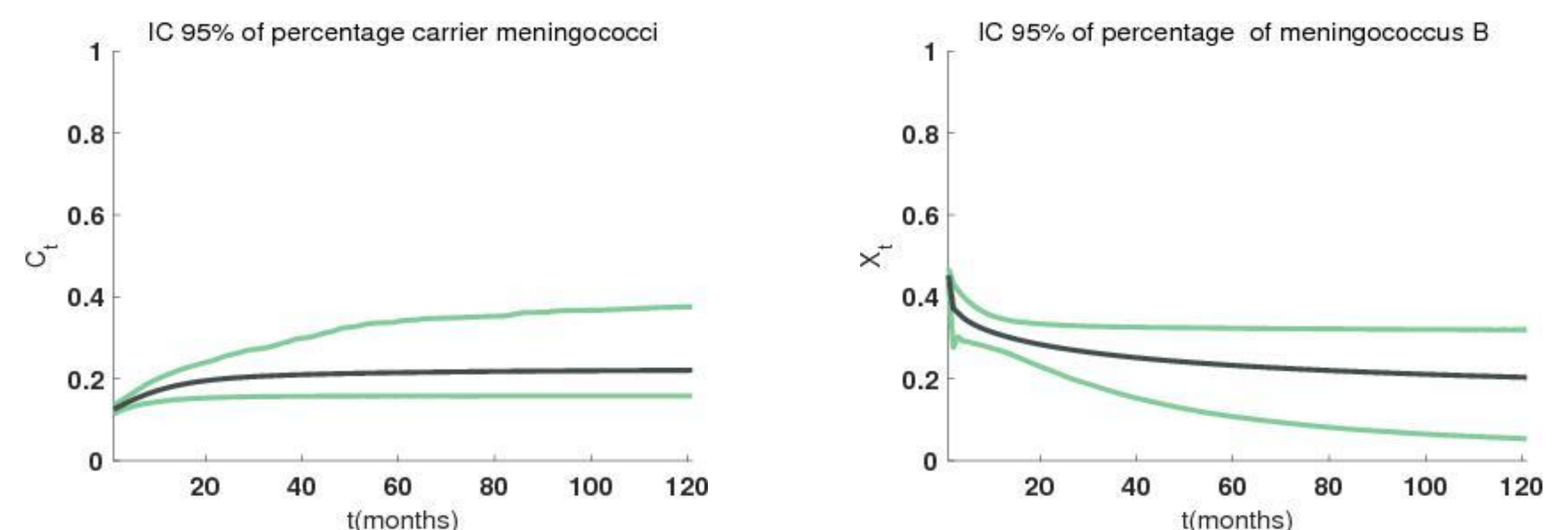
Probabilistic Fitting

This approach among many other things allow us to obtain predictions of the model. These predictions are given by confidence intervals in order to capture the uncertainty of the data.

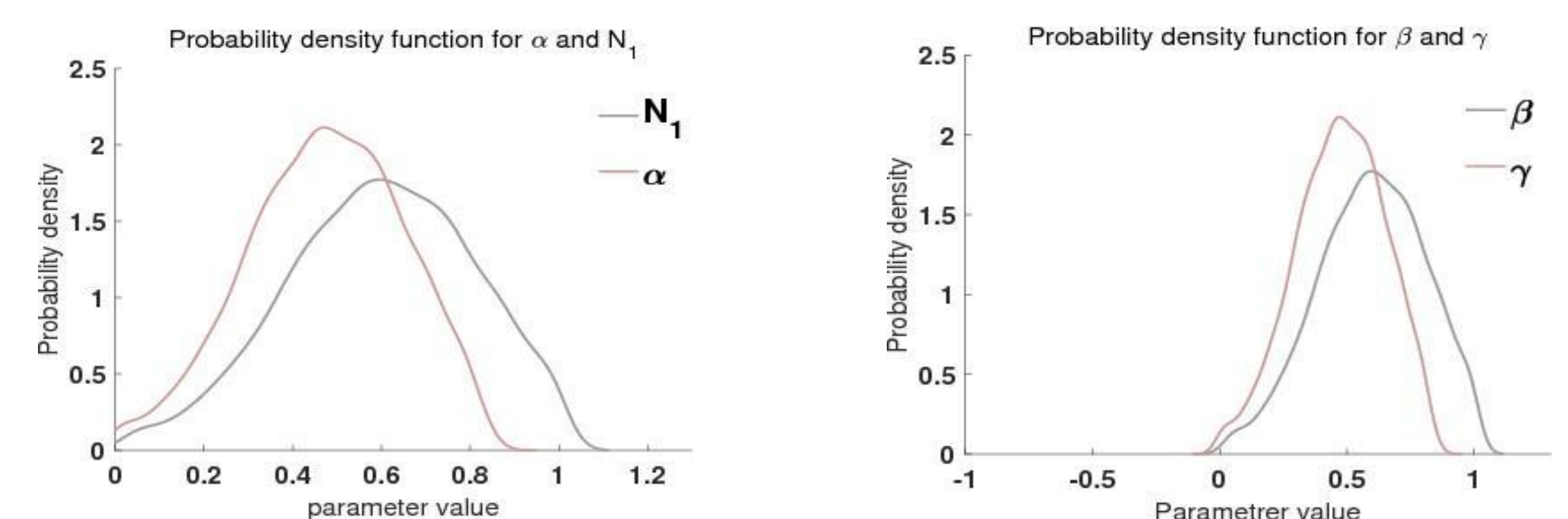
Furthermore, this technique permits to approximate the probability density functions for the model parameters β and γ of the Susceptible- Carrier-Susceptible model and α and N_1 of the Lotka- Volterra Model.

Results

The probabilistic fitting applied to the epidemiological model and the fractional Lotka-Volterra model allows to obtain the following probabilistic predictions until Dec 2021.



The probability density functions (PDF) of the parameters has been built using parameters that best fit the data using the probabilistic fitting technique and a numerical kernel distribution function. Their graphs can be seen above.



Outbreaks in the near Future

Mixing both models we can obtain the percentage of Men B carriers among all the population. Dr. Julio Vázquez told us that a percentage of 20% – 25% or greater of carriers of Men B in Spain would begin to be concerning. In the following table we can see the percentage of carriers of MenB. So according with Julio Vazquez speech , the probability of having worrying percentages of carriers of Men B is very low, therefore, an outbreak is not expected.

Date	Probability B $\geq 20\%$
December 2017	0.0029
December 2018	0.0036
December 2019	0.0047
December 2020	0.0062

Conclusion

In this work we have used data corresponding to the prevalence of genogroup B to perform a probabilistic prediction for the next few years and an outbreak of Meningitis B. Our model consists of two coupled systems: First, the transmission of the disease among the human population. Second, a competition Lotka-Volterra discrete equation with fractional dynamics.

Experts consider that a percentage of carriers of MenB larger than 20% could unleash a pandemic but we have found that, according to our data, the probability for this event is below 1% and, consequently, there is little chance for the emergence of MenB as a major threat in the next five years.

[1] Juan-Carlos Cortés, Francisco-J. Santonja, Ana-C. Tarazona, Rafael-J. Villanueva, Javier Villanueva-Oller, A probabilistic estimation and prediction technique for dynamic continuous social science models: The evolution of the attitude of the Basque Country population towards ETA as a case study, Applied Mathematics and Computation, Volume 264, 1 August 2015, Pages 13-20, ISSN 0096-3003, <http://dx.doi.org/10.1016/j.amc.2015.03.128>

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