Mathematics and Medicine

BAYESIAN INFERENCE FOR COMPLEX NETWORK: APPLICATION TO DIFFERENT STAGES OF GLIOBLASTOMA EVOLUTION

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Abstract

Biological systems are characterised by huge complexity giving rise to mathematical models highly non-linear and multiparametric. The determination of the model- parameters' values becomes a challenge as they are often difficult to measure experimentally and so, usually fitted for specif conditions, making the conclusions drawn difficult to generalise. The main objective of this project is to present the application of an algorithm for parameter estimation of dynamical systems, concretely to a model for the evolution of a Glioblastoma Multiforme. This algorithm belongs to the Approximate Bayesian Computation (ABC) family, which comprises methods that evaluate posterior distributions without calculating the likelihoods, and follows a sequential Monte Carlo (SMC) approach. The algorithm is applied first to two deterministic biological systems: prey-predator Lotka Volterra and Succeptible-Infected-Recovered (SIR). Finally we apply it to the evolution of a Glioblastoma Multiforme , which considers the interaction of tumour cells with oxygen concentration (pseudopalisade and necrotic core formation).

Introduction

Mathematical biology intends to predict the course or outcome of a biological event through the use of dynamical systems derived from biological data. Most of them are modelled by ordinary, delay or stochastic differential equations which are characterised by the large number of species as well as the complexity of interactions between the components of the system what makes their analysis difficult. Indeed, for the vast majority there is a lack of reliable information about parameter values and frequently have several competing models for the structure of the underlying equations.

One of the main issues when modelling biological networks is to move from the theoretical biological knowledge of the system to the equations that describe its temporal behavior due to the incompleteness and sparsity of the biological experimental data, moreover the likelihood surfaces of large models are complex. The analysis of such dynamical systems therefore requires new, more realistic quantitative and predictive models (Sunnåker et al. 2013). The statistical analysis of the information generated by medical follow-up is a very important challenge as the evolutionary course of a disease generates information that should be processed in order to review and update its prognosis and treatment (Alvares et al. 2017).

In this project we present a parameter estimation algorithm for dynamical systems using Approximate Bayesian Computation through Sequential Monte Carlo (ABC-SMC) as in Toni et al. 2009. This algorithm is an ABC approach (evaluation of posterior distributions without calculating likelihoods) where a sequence of distributions is eventually obtained by gradually decreasing a prespecified tolerance. From a Bayesian perspective, the unknown set of parameters is considered random and assigned suitable prior distributions. The posterior density, is approximated by using a set of simulated samples (particles) and their respective weights. Through a sequential procedure, the distribution is updated by incorporating the information provided by new data. (Andrieu, Doucet, and Holenstein 2010).

The algorithm is applied to two deterministic biological systems (Predator-prey Lotka Volterra and Susceptible-Infected-Recovered, or SIR model for infectious diseases) in order to obtain posterior parameter distributions and draw inferences from different data frameworks. After proving its efficiency, it is used to infer the parameters governing the equations of a deterministic glioblastoma evolution multi-scale model (Cruz et al. 2017) that intends to describe the growth of cellular populations in a spatially heterogeneous environment under the restriction of finite amount of available resources, in this case, oxygen. The results are compared to the real data offered by the Manuel Doblare's laboratory in Zaragoza.

References

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