

Bayesian Parameter Inference for Continuous Time Markov Chains with Intractable Likelihood

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Abstract : Systems biology is an important field in science which focuses on studying behaviour of biological systems. Modelling is required to produce detailed description of the elements of a biological system, their function, and their interactions. A well-designed model requires selecting a suitable mechanism which can capture the main features of the system, define the essential components of the system and represent an appropriate law that can define the interactions between its components. Complex biological systems exhibit stochastic behaviour. Thus, using probabilistic models are suitable to describe and analyse biological systems. Continuous-Time Markov Chain (CTMC) is one of the probabilistic models that describe the system as a set of discrete states with continuous time transitions between them. The system is then characterised by a set of probability distributions that describe the transition from one state to another at a given time. The evolution of these probabilities through time can be obtained by chemical master equation which is analytically intractable but it can be simulated. Uncertain parameters of such a model can be inferred using methods of Bayesian inference. Yet, inference in such a complex system is challenging as it requires the evaluation of the likelihood which is intractable in most cases. There are different statistical methods that allow simulating from the model despite intractability of the likelihood. Approximate Bayesian computation is a common approach for tackling inference which relies on simulation of the model to approximate the intractable likelihood. Particle Markov chain Monte Carlo (PMCMC) is another approach which is based on using sequential Monte Carlo to estimate intractable likelihood. However, both methods are computationally expensive. In this paper we discuss the efficiency and possible practical issues for each method, taking into account the computational time for these methods. We demonstrate likelihood-free inference by performing analysing a model of the Repressilator using both methods. Detailed investigation is performed to quantify the difference between these methods in terms of efficiency and computational cost.

Keywords : Approximate Bayesian computation(ABC), Continuous-Time Markov Chains, Sequential Monte Carlo, Particle Markov chain Monte Carlo (PMCMC)

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