

Moment closure approximation and distribution reconstruction for Markov Population Models

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Markov Population Models are a popular stochastic modeling framework in application fields such as systems biology and performance evaluation of computer systems. For their analysis computationally extensive numerical methods are necessary due to the largeness problem of the discrete state space. Instead of a direct integration of the underlying probability distribution it is often much faster to approximate only the corresponding moments over time based on a moment closure approach. However, when probabilities of certain events are of interest one has to reconstruct the probability distribution from its moments. Here, we address this problem in the context of a maximum entropy approach and assess the efficiency and accuracy of a combination of moment closure approximation and maximum entropy reconstruction.

1 Introduction

Markov Population Models (MPMs) are used to describe the dynamics of many different real-world networks such as biochemical networks, pharmacokinetic networks, social networks, ecological networks or communication networks [5]. The probability distribution over the states of an MPM can be obtained by solving the corresponding Kolmogorov Differential Equations (KDE). The analytical solution is available only for very simple networks and therefore an approximation has to be computed using numerical methods. Since each dimension in the state structure of the MPM corresponds to a certain population variable involved in the network, the numerical procedures to integrate the KDE directly suffer from the so-called curse of dimensionality or state space explosion problem. It is infeasible to efficiently solve the KDE for systems that involve a large number of different populations having large sizes. Another difficulty comes from the fact that in some application areas bounds for the population sizes are not known a priori therefore the size of the state space is infinite. In order to overcome these hurdles sophisticated truncation approaches have been developed [7], where only a subset of the state space is considered. This subset contains the significant part of the probability mass and thus the truncated part describes only rare behavior of the system.

Truncation approaches perform well as soon as the average population counts are relatively small. If (some of) the population counts are large it is possible to change the representation of the distribution and integrate a finite number of its moments instead [4, 2]. Such moment closure methods allow to construct a system of ODEs where each equation corresponds to a certain moment of the distribution of the MPM. Typically, central moments of an order higher than a certain bound are assumed to be zero which gives a finite system of ODEs. The solution at a particular time instant approximates the values of moments that can be used to reconstruct the full distribution of the MPM.

The problem of distribution reconstruction from a number of moments is referred to as the classical moment problem. Under a finite number of constraints (given by the values of the moments) the solution

reveals to be not unique. One way of finding a unique solution is based on a maximum entropy approach which has its roots in statistical mechanics and information theory. The maximum entropy reconstruction is the least biased estimate possible given the constraints, and it makes no assumptions about the missing information. Recently there was a large amount of attempts to overcome the numerical difficulties arising in the solution of the corresponding optimization problem [1, 3]. In addition, distributions with multiple dimensions have been considered. Here we propose a combination of moment closure technique and the maximum entropy reconstruction to approximate the solution of KDE. We compute the moment values at certain times and use them as constraints for the maximum entropy reconstruction. Previous work in this direction considers only small and finite models and rely on Monte-Carlo simulations to assess the accuracy of the reconstruction [8]. Here, we discuss the applicability of the approach in an infinite setting and compare to a direct numerical solution based on a truncation technique. We present two case studies where the state space of the associated MPM is infinite and the distribution is multi-modal which renders the reconstruction to be numerically more difficult. The running times and accuracy is then compared to a very precise approximation of solution for KDE obtained via numerical integration.

2 Kolmogorov Differential Equations

An MPM $\{X(t), t \geq 0\}$ is a continuous-time Markov chain with state space $S = \mathbb{Z}_+^n$. Here, $X(t) = (X_1(t), \dots, X_n(t))$ and X_i corresponds to i -th population variable. We assume that the transitions of the MPM are specified as a set of m transition classes τ_1, \dots, τ_m . For $1 \leq j \leq m$, let $\tau_j = (G_j, v_j, \alpha_j)$, where G_j is the guard set (the subset of S where τ_j is possible), $v_j \in \mathbb{Z}^n$ is the population change vector and $\alpha_j : S \rightarrow \mathbb{R}_{\geq 0}$ is the (continuous) transition rate function. Thus, if state $x \in G_j$, then a transition to state $x + v_j$ is possible at rate $\alpha_j(x)$. For each state $x \in S$ the time-evolution of the probability $p^{(t)}(x) = P(X(t) = x)$ is governed by KDE

$$\frac{\partial p^{(t)}(x)}{\partial t} = \sum_{j=1}^m (\alpha_j(x - v_j) p^{(t)}(x - v_j) - \alpha_j(x) p^{(t)}(x)),$$

If the underlying Markov chain is regular, the KDE has a unique solution given an initial distribution $p^{(t_0)}$. Note that a direct integration of the KDE is only possible if large or infinite state spaces are truncated appropriately.

3 Moment closure method

Instead of a direct integration of the KDE, it is possible to change the representation of the distribution $p^{(t)}$ and apply the moment closure method. It allows to construct a system $\{F_1, F_2, \dots\}$ of ODEs that directly describes time evolution of first K moments $E(X^k)$ of the distribution $p^{(t)}$, $1 \leq k \leq K$ (the notion of time is further omitted for the sake of readability).

$$\frac{d}{dt} E \begin{pmatrix} E(X^k) \\ E(X - E(X))^k \end{pmatrix} = F_k \begin{pmatrix} E(X^1), E(X^2), E(X^3), \dots \\ E(X - E(X))^2, E(X - E(X))^3, \dots \end{pmatrix}, \quad k = 1, 2, \dots, K. \quad (1)$$

In general, the system $\{F_1, F_2, \dots\}$ is infinite and it is typically truncated at a certain order of moments. For instance, if we truncate it at order 2, then only the mean population values $E(X)$ and the covariances are integrated over time, while we assume that all central moments $E(X - E(X))^k$ of higher order are zero. However, for systems that exhibit oscillations or multi-stability a higher truncation order K is often needed. The integration of the truncated system is usually faster than the direct numerical solution of the KDE or an approximation of the distribution using Monte-Carlo simulation.

4 Maximum entropy reconstruction

The moment closure technique allows to approximate the moments of the distribution $p^{(t)}$ at certain time instant. We use them further to obtain the symbolic representation of the one-dimensional marginal probability distributions $p_i^{(t)} = P(X_i(t))$ of the i -th population. Given a finite amount of moments μ_1, \dots, μ_K such that $\mu_k := E(X_i^k)$, there is a set of distributions \mathcal{G} having these moments. Thus we are applying the maximum entropy technique to select the distribution $q(x)$ with the highest entropy $H(q)$, i.e. $q(x)$ is a solution of the optimization problem

$$q = \arg \max_{g \in \mathcal{G}} H(g) = \arg \max_{g \in \mathcal{G}} (-\sum_x g(x) \ln g(x)), \quad (2)$$

where $H(g)$ is the entropy functional. In our case the class of possible distributions \mathcal{G} includes all distributions that are subject to the constraints given by the finite amount of approximated moment values

$$\sum_x x^k g(x) = \mu_k, \quad k = 0, 1, \dots, K. \quad (3)$$

We also include the constraint $\mu_0 = 1$ to guarantee that the reconstruction $q(x)$ is a valid probability distribution. The problem in Eq. (2) can be addressed by the method of Lagrange. The general form of the solution is then given by $g(x) = \exp\left(-1 - \sum_{i=0}^K \lambda_i x^i\right)$ where the coefficients $\lambda_0, \dots, \lambda_K$ are to be determined. To cope with the latter problem, we use the approach proposed by Abramov [1] and the corresponding software ¹ that computes an approximation λ^* of the optimal vector of coefficients. The maximum entropy distribution is then given by $q(x) = \exp\left(-1 - \sum_{i=0}^K \lambda_i^* x^i\right)$. Please note that the support of $q(x)$ is \mathbb{R} , though it is possible to approximate the discrete probability distribution $p_i^{(t)}$ defined on \mathbb{Z}^+ by truncating the negative part of the original support and rescaling. The discrete probabilities $P(X_i = x_i)$ are then approximated as $\hat{p}_i(x) = \int_{x_i - \frac{1}{2}}^{x_i + \frac{1}{2}} q_i(x) dx$. Here, we concentrate on a comparison of the distribution that is obtained using direct numerical integration of KDE with the reconstructed distribution q . In Figure 1 we plot the results obtained for a biochemical reaction system known as the exclusive switch [6], that describes the dynamics of two proteins P_1 and P_2 and the corresponding genes. The solution obtained by direct integration of the KDE is shown in red and the maximum entropy reconstruction is shown by blue triangles. For the latter we use the moment closure method to approximate the moment values μ_1, \dots, μ_K , where the truncation order for ODE system in Eq. (1) is chosen as $K = 5$.

5 Conclusions

We investigate the accuracy and efficiency of the combination of two methods, namely the moment closure method and the maximum entropy method, which can be used to analyze Markov Population Models. With the Kolmogorov differential equation as a starting point we described how the moments of the corresponding probability distributions can be integrated efficiently over time and how a distribution can be reconstructed based on the moments. Our experimental results show that the proposed combination of methods has many advantages. It is a fast and surprisingly accurate way of obtaining the distribution of the system at specific points in time and therefore well suited for computationally expensive tasks such as the approximation of likelihoods or event probabilities.

¹The software is available at <http://homepages.math.uic.edu/~abramov/>

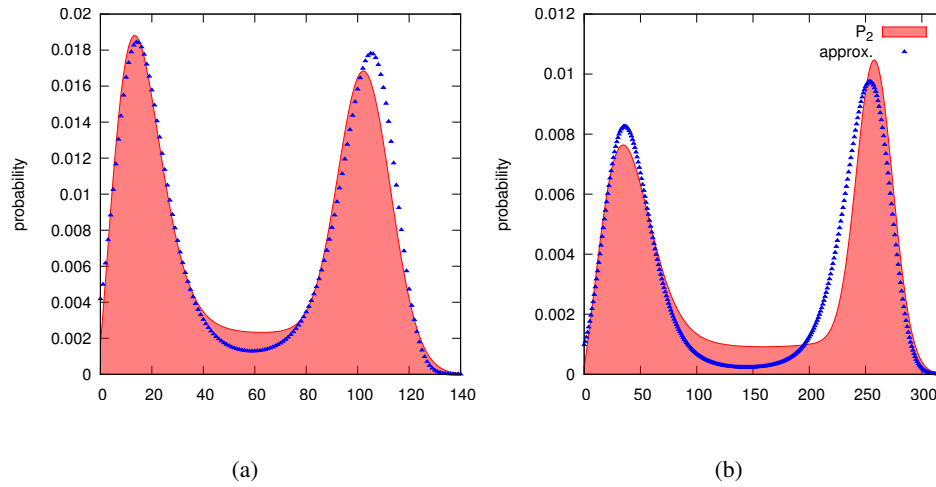


Figure 1: Maximum entropy reconstruction of marginal probability distributions of the protein counts (a) P_1 and (b) P_2 for exclusive switch system.

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