Matrix Equations and Tensor Techniques
IX
Perugia, September 9-10, 2021

Low-rank tensor uniformization for tumor progression modeling

Peter Georg Lars Grasedyck *Maren Klever* Rudolf Schill
Rainer Spang Tilo Wettig

Institut für Geometrie und Praktische Mathemaik, RWTH Aachen University

Inspired by current research in tumor progression modeling, we consider continuous-time Markov chains that describe interacting processes. In general a Markov chain is defined by its state space S, its initial probability distribution $\mathbf{p}(0) \in \mathbb{R}^S$ and its transition rate matrix $\mathbf{Q} \in \mathbb{R}^{S\times S}$. In tumor progression models, a tumor is identified by its genotype where d mutations may have occurred or not. The Markov chain starts with the absence of all mutations and then gradually accumulates mutations. Its state space S describes the set of possible tumors and thus, grows exponentially in the number of mutations d with $|S| = 2^d$. Modeling the transition rate matrix $\mathbf{Q}$ leads to an optimization problem based on given tumor data. Since the age of a tumor at its diagnosis is typically unknown, this optimization requires the so-called *time-marginal distribution* $\mathbf{p} \in \mathbb{R}^S$ which is defined as

$$\mathbf{p} := \int_0^\infty \exp(-t) \cdot \exp\left(\mathbf{Q}t\right) \mathbf{p}(0)\ \mathrm{d}t \qquad \text{where} \quad t \sim \mathrm{Exp}[1].$$

The time-marginal distribution is obtained as the solution of the linear system

$$(\mathbf{Id} - \mathbf{Q})\mathbf{p} = \mathbf{p}(0). \tag{1}$$

However, the size of this system renders classical solvers infeasible.

In this talk, we introduce the concept of *Mutual Hazard Networks* [3] which allows for a low-rank tensor representation of the transition rate matrix $\mathbf{Q}$. Using low-rank tensor techniques reduces the computational complexity from exponential to linear provided the distribution $\mathbf{p}$ exhibits a low-rank structure. Previously known iterative methods also allow for low-rank approximations of the solution for (1) but are unable to guarantee that its entries sum up to one, i.e,

$$\sum_{x\in S} \mathbf{p}_x = 1, \tag{2}$$

as required for a probability distribution. We present a convergent iterative method based on the concept of uniformization [2]. This strategy allows us to use low-rank tensor formats and, at the same time, to satisfy condition (2). Numerical experiments illustrate that the time-marginal distribution is well approximated with low rank.

References

[1] P. Georg, L. Grasedyck, M. Klever, R. Schill, R. Spang, T. Wettig, *Low-rank tensor methods for Markov chains with applications to tumor progression models*, arXiv:2006.08135, (2020).

[2] W. K. Grassmann, *Transient solutions in markovian queueing systems*, Computers & Operations Research, (1977), pp. 47-53.

[3] R. Schill, S. Solbrig, T. Wettig, R. Spang, *Modelling cancer progression using Mutual Hazard Networks*, Bioinformatics, (2019), pp. 241-249.