Abstract

Elementary flux modes are minimal metabolic pathways in metabolic networks. Several methods exist to compute elementary flux modes. Some of methods compute the complete set of EFMs of the network. The number of EFMs increase sharply with the size of the network. The calculation of the whole set of EFMs require large computational and memory resources, and computations is limited to small networks. To solve these problems, several methods have been proposed to sample EFMs. These methods compute a subset of the whole set of EFMs. The quality of these methods is determined by the quality of the generated samples and the similarity of the samples and the complete set of EFMs. The computational time is another important challenge in EFM sampling methods.

The aim of this study is to develop a method for sampling EFMs. In this work was tried to provide solutions to speed up the computation of EFMs and to produce representative subsets of elementary modes. The proposed procedure for computing a single EFM consists of step by step elimination of reactions from the network and checking the impact of the eliminations on the network behavior. We tried to speed up the computations by optimum utilization of flux coupling relations. Then, we generated samples by repeating this procedure. To avoid the production of previously produced EFMs we used a tree structure.

Finally, the proposed method was compared with other sampling methods, ShortestEFMs, EMSampler, RandomEFM and TreeEFM. The generated samples in proposed method are more similar to the complete set of EFMs. The computation time of proposed method grows linearly and its complexity doesn't change. The proposed method can be used to compute EFMs in networks with different sizes.

Keywords: Metabolic Networks, Stoichiometric modeling, Constraint based modeling, Elementary flux modes, Flux coupling Analysis, Flux balance Analysis, Tree search