Computational framework for modelling multiple non-cooperative transcription factor binding and its application to the analysis of NF-κB oscillatory response

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Abstract

Recent studies have shown that regulation of many important genes is achieved with multiple transcription factor binding sites with low or no cooperativity. Additionally, non-cooperative binding sites are gaining more and more importance in the field of synthetic biology. Herein we introduce a computational framework that can be applied to dynamical modelling and analysis of gene regulatory networks with multiple non-cooperative transcription factor binding sites. We propose two computational methods to be used within the framework, i.e. average promoter state approximation and expression profiles based modelling. We demonstrate the application of the proposed framework on the analysis of NF-κB oscillatory response analysis. We show that different promoter expression hypotheses in a combination with the number of transcription factor binding sites drastically affect the dynamics of the observed system and should not be ignored in the process of quantitative dynamical modelling, as is usually the case in existent state-of-the-art computational analyses.

Key words: gene regulatory networks, non-cooperative transcription factor binding, quantitative modelling, computational analysis, transcription factor NF-κB.

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