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Retroactivity effects dependency on the transcription factors binding mechanisms

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Abstract

Downstream connection effects on transcription are caused by retroactivity. When biomolecular dynamical systems interconnect retroactivity is a property that becomes important. The biological functional meaning of these effects is increasingly becoming an area of interest. Downstream targets, which are operator binding sites in transcriptional networks, may induce behaviors such as ultrasensitive responses or even represent an undesired issue in regulation. To the best of our knowledge, the role of the binding mechanisms of transcription factors in relation to minimizing –or enhancing– retroactivity effects has not been previously addressed.

Our aim is to evaluate retroactivity effects considering how the binding mechanism impacts the number of free functional transcription factor (FFTF) molecules using a simple model via deterministic and stochastic simulations. We study four transcription factor binding mechanisms (BM): simple monomer binding (SMB), dimer binding (DB), cooperative sequential binding (CSB) and cooperative sequential binding with dimerization (CSBD). We consider weak and strong binding regimes for each mechanism, where we contrast the cases when the FFTF is bound or unbound to the downstream loads. Upon interconnection, the number of FFTF molecules changed less for the SMB mechanism while for DB they changed the most.

Our results show that for the chosen mechanisms (in terms of the corresponding described dynamics), retroactivity effects depend on transcription binding mechanisms. This contributes to the understanding of how the transcription

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