

# Retroactivity analysis of a memory synthetic system

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**Short Abstract** —In biological systems, modules are expected to transfer information signals each other in a reliable way. However, when new connections are added downstream a signal arouses: retroactivity. Recently, the role of retroactivity in biological systems has been approached by computational methods and in vitro assays. In this work we aim to test the role of retroactivity in the behavior and properties of a well known memory synthetic system by a reliable and realistic theoretical model, as well as to propose an insulation device which may reduce the retroactivity effects.

**Keywords** —Retroactivity, Synthetic Biology, Rule based models.

## I. INTRODUCTION

THE retroactivity signal emerges when a module with an input and an output is connected to another one by its output (or downstream). This signal has been proposed to be potentially parasitic for synthetic systems [1]. In transcriptional modules this is simple to observe as a transcription factor (TF) produced by a module can be depleted when there are many elements to regulate [2,3] as well as when the regulatory sequences to be regulated have a very strong affinity for the TF [2].

In this work, we chose the synthetic system developed by Ajo-Franklin and Cols. [4] because of its extensive characterization and careful design. To proceed for the evaluation of the impact of the retroactivity in the systems performance the association rate ( $k_{on}$ ) and the dissociation rate ( $k_{off}$ ) of the TF to the regulatory region should be considered [2,5].

## II. RESULTS

In order to approach retroactivity in the Ajo-Franklin's memory device. Three alternatives are being explored: ODE's, Rule based, and Hybrid modeling strategies. At this time we are presenting some ODE's and Rule based results in the basis of which we realized that a hybrid approach was needed to achieve a better approximation to the observed behavior.

### A. ODE's modelling

The ODE's based modeling served as a good tool to test

previously observed steady states by Ajo-Franklin and Cols. However, the modeling from a rate equations perspective, where the  $k_{on}$  and  $k_{off}$  of the transcription factors for its regulatory region is contemplated, is far from simple to asses by this method.

### B. Rule based modeling

A rule based model was proposed in RuleBender [6] including whole tentative systems in three versions: original systems, retroactivity induced system and system with an isolation device. Here, the problem consisted in the lack of an ultrasensitive switch like response as the observed in the original work. This is being tackled by the implementation of the ideas in [7], where nucleosomes modifications and their relation with TF's are included. In fact, this work considered the system by Ajo-Franklin and Cols. as an example to compare their results with experimental data.

### C. Hybrid model

At this time the hybrid model is still under construction in NFsim [8] to test ultrasensitive response in a model that includes rules as well as probability functions.

## III. CONCLUSION

The combinations needed to explain the ultrasensitivity response that arises from the interaction between TF's, regulatory regions and nucleosomes is not trivial to depict by an ODE's or a Rule based approach. Further efforts are needed to construct more inclusive tools for realistic models.

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