# Generation of oscillating gene regulatory network modules [1]

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*Short Abstract* — **Using an improved version of an evolutionary algorithm originally proposed by François and Hakim [2], we generated small gene regulatory networks in which the concentration of a target protein oscillates in time. These networks may serve as candidates for oscillatory modules to be found in larger regulatory networks and protein interaction networks. Here we present the smallest modules found. We also evaluate and compare their robustness against variations in the kinetic rates.**

***Keywords* — Gene regulatory networks, module generation, oscillatory, evolutionary algorithm.**

## I. Introduction

GENE regulatory networks (GRN) are composed of a large number of genes (typically ~$10^4$) and their products (mRNA and proteins) interacting through complex feedback mechanisms [3]. Understanding the behavior of such large systems is a very challenging task. Therefore in the past decade a lot of effort was devoted in studying the dynamics of smaller modules comprising a few genes, their mRNAs and proteins, as a first step towards complexity [4].

Here we focus on modules in which a target protein oscillates in time. Oscillatory behavior is found in many processes in the cell. For instance the circadian rhythms which keep control over the daily processes of the cell are driven by genetic modules [4]. But there are also oscillations which are sub circadian like those in NF-kB, p53, Wnt … [6-7]

## II. Method

For the production of these modules we used an improved version of the evolutionary algorithm proposed by François and Hakim [2]. This algorithm is inspired by the dynamics of an evolving population. The most crucial part of this algorithm is the design of a score function used to define which elements are considered the fittest. For this purpose we designed two score functions: one to score oscillatory behavior and one to score small GRN modules.

## III. Results

We found three basic oscillating modules in which the number of components and the non-linearity's are minimal. One of these is the Mixed Feedback Loop [8] already discussed in the literature, the two other modules are new. One is base on a self-repressed gene coupled to a protein heterodimer and the other is a single gene module which is competitively regulated by a monomer and a dimer.

Running the algorithm a large number of times (~$10^5$) we produced a library of small oscillating modules. Some being extensions of the three smallest fundamental modules mentioned above, whereas others are based on different mechanisms. The produced networks contain "classical" genetic oscillators based on negative feedback induced by transcription factors repressing gene synthesis like in [9], as well as many purely post-transcriptional oscillators. Post-transcriptional oscillators have attracted quite some interest in the recent biological literature, as several cases of circadian rhythms were shown to persist even in absence of transcription [10-11].

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