Title: Discover minimal sets of elements in biological networks responsible of reverting the system's dynamics
Subject: Formal methods, Constraint programming, Logic programming, Systems Biology

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General overview of the domain
A biological network can be seen as a graph which nodes represent proteins or genes, and edges represent the interactions or influences that the molecules hold among themselves. If these networks are modeled as binary Boolean networks: nodes represent discrete concentration values (0, 1), and the state of a node in the graph is given by a Boolean function of the state of its predecessors, then we can study the dynamics of large-scale (over tens of components) networks with the Process Hitting framework [1,2]. We are interested in applying this framework to a real case study, which is skin wound healing. For this, we have compiled a discrete and qualitative model of keratinocytes human cells [3], in which the signal is perceived by nodes that represent cellular receptors, the signaling cascades are represented by signed-oriented edges and the transcription factors with the transcribed genes are identified. The response of stimulating this network leads to a cellular response that can be either "proliferation", "migration" or "differentiation". In order to understand this complex process we dispose with gene expression time series data [4], related to the gene expression on account of the stimuli of the cellular receptors across time.

Internship objectives
The aim of this internship will be first to validate the proposed network structure with respect to real experimental gene observations of the system's dynamics. Second, we would like to predict the behavior of important unobserved elements in the network, related to main cellular states. Finally, we would like to propose a method that automatically extracts the subset of key molecules in the network which is responsible of an observed system behavior, and check if by altering them *in-silico* we can alter the system dynamics.

Team description
The MeForBio team at the IRCCyN participates in the French projects CirClock (CNRS) and BioTempo (ANR). It collaborates with the French research teams Bio-Info of I3S at Sophia Antipolis and Dyliss at INRIA Rennes. Also it collaborates with international research teams as Systems Biomedicine at the European Bioinformatic Institute (EBI), UK; the Universities of Potsdam and Heidelberg, Germany; and the University of Chile, Chile.

References
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