Genetic Regulatory Network Inference using Recurrent Neural Networks trained by a Multi Agent System

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Abstract — **We propose a novel algorithm for gene regulatory network inference. Gene Regulatory Network (GRN) inference is approximating the combined effect of different genes in a specific genome data. GRNs are nonlinear, dynamic and noisy. Time-series data has been frequently used for GRN modeling. Due to the function approximation and feedback nature of GRN, a Recurrent Neural Network (RNN) model is used. RNN training is a complicated task. We propose a multi agent system for RNN training. The agents of the proposed multi agent system trainer are separate swarms of particles building up a multi population Particle Swarm Optimization (PSO) algorithm. We compare the proposed algorithm with a similar algorithm that uses RNN with standard PSO for training. The results show improvements using the E. coli SOS dataset.**

Keywords- Gene Regulatory Network Inference, Particle Swarm Optimization, Multi Population PSO, Recurrent Neural Networks, Multi Agent Systems

I. INTRODUCTION

The genomic revolution is seeking its path to understand the complex genetic relations inside living organisms. One of the substantial obstacles of this path is the interaction among genes and proteins as the two main components present in any living organism. The first step in understanding the interaction among genes and proteins is determining the interaction among each component individually. In this research we are focusing on the relations between genes known as Genetic Regulatory Network (GRN).

GRNs could be inferred by different approaches. One scheme is experimental techniques. Experimental techniques are usually difficult and limited. One other approach for GRN inference is incorporating mathematical models. In this research we are concentrating on computational approaches which use mathematical models to infer GRNs.

Computational approaches for GRN inference rely on data gathered from GRN experiments. The main form of data for GRN inference is Microarrays [1].

Much research has been done on GRN learning. One of the first methods used for GRN learning was neural networks. Mjolsness et. al. [2,3] used differential equations to model GRNs and used Recurrent Neural Networks (RNN) to learn the GRN. In this method gene regulation was represented as a combination of (i) cis-acting regulation by the promoter, and (ii) trans-acting regulation by the TF products of other genes. Later on, Vohradsky used RNN [4] but he assumed that GRN's have Multi-genic regulation, including positive and/or negative feedback.

Another paradigm used to model GRN is Fuzzy sets. Woolf & Wang [5], used Fuzzy rules to transform the gene expression values into qualitative descriptors. Sokhansanj et. al. [6], used a scalable linear variant of fuzzy logic to learn GRN. Du et al [7] used multi scale fuzzy c-means clustering. In this method domain knowledge from different sources was used.

Besides this Evolutionary computation was used for GRN learning too. S. Kikuchi et al. [8] used GA to learn the best GRN that fits the data. Qian et al. [9] modeled GRN with a nonlinear differential equations and used GP with kalman filter to learn this model. Another group of methods are hybrids which usually combine two or more of the above paradigms. Ritchie et al. [10] used multi layer perceptron with GP to learn GRN from microarray time series data. Xu et al. [11] modeled GRN using RNN and then used particle swarm optimization to train the network. In this method the training is done for structures as well as parameters.

Since GRNs have a nonlinear and feedback nature we use a RNN model. RNN training is a complicated task. We propose a Multi Agent System (MAS) for RNN training. In the proposed MAS the agents are particle swarms. We aim to enhance the results of GRN inference by training the RNN more precisely.

The paper is organized as follows. Section II discusses some preliminary paradigms used in the main algorithm. Section III describes our proposed algorithm for inferring network interactions. Section IV presents the experimental results, and Section V concludes the paper.