



Cairo University

CONSTRUCTING GENE REGULATORY NETWORK USING TIME SERIES GENE EXPRESSION

By

Shaimaa Mohammed Elembaby Hassan Sharaf Eldien

A Thesis Submitted to the
Faculty of Engineering at Cairo University
in Partial Fulfillment of the
Requirements for the Degree of
DOCTOR OF PHILOSOPHY
in
Biomedical Engineering and Systems

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Title of Thesis:

Constructing Gene Regulatory Network Using Time Series Gene Expression
Microarrays

Key Words:

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Summary:

Inferring Gene Regulatory Network (GRN) is important to understand genetic changes occurring in cells. GRNs help in designing drugs and vaccines. As changes occurred in cell are dynamic, time series gene expression is very important to understand how genes regulates each other. There are many competitions to infer GRN, here we used DREAM4 in-silico 10 genes, DREAM 4 insilico-100 genes and DREAM 5. As H1N1 is the most endemic disease recently and still does not have a known medication. To comprehend alterations in genes due to H1N1 infection, we attempted to build GRN based on gene expressions of H1N1 infected cells. We improved two algorithms to infer GRN GENIE 3 and PLSNET by one-way ANOVA and produce two new hybrids Algorithms ANOVAPLSN and ANOVAG3 which record best results to infer large scale GRN from time series gene Expression. we used other methods to infer GRN as sparse linear Equation, Distance matrices and Artificial neural network to infer GRN.

Disclaimer

I hereby declare that this thesis is my own original work and that no part of it has been submitted for a degree qualification at any other university or institute.

I further declare that I have appropriately acknowledged all sources used and have cited them in the references section.

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Nomenclature

Gene a unit of inheritance is transferred from parents to its Childs and consist of long strand of DNA sequence.

DNA Deoxyribonucleic acid chains of nucleic acids contains genetic instructions used in the development and functioning of all known living organisms.

RNA Ribonucleic Acid formed by DNA and found in the cytoplasm.

Gene Expression a gene inheritable information is gained from synthesis of a functional gene products (functional RNA) as proteins, small nuclear RNA (snRNA) genes or transfer RNA (tRNA) in non-protein coding genes .

Transcription synthesis of RNA under direction of DNA this process is before translation.

Translation mature mRNA is translated into polypeptide chain of amino acids then to protein according genetic codes.

Transcription factor (TF) DNA-binding protein (promoter) to initiate the biological process in the cell.

A gene regulatory network (GRN) directed graph represents a collection of molecular regulators .The regulator can be DNA, RNA, protein and complexes of these that interact with each other and with other substances in the cell. The interaction can be direct or indirect (through transcribed RNA or translated protein).

An adjacency matrix is a square zero diagonal matrix used to represent GRN or any finite graph between some nodes .

ACO	Ant Colony Optimization
ALO	Ant Lion Optimizer
AUPR	Area Under Precision Recall Curve
AUROC	Area Under Receive Operating Characteristic Curve.
DBN	Dynamic Bayesian Network
DE	Differential Evolution
EA	Evolutionary Algorithm
GA	Genetic Algorithm

GWO	Grey Wolf Optimizer
GRN	Gene Regulatory Network
mRNA	Messenger RNA
MI	Mutual Information
PDE	Partial Differential Equation
PLDE	Piecewise-Linear Differential Equation
PSO	Particle Swarm Optimization
QDE	Qualitative Differential Equation
RNN	Recurrent Neural Network
SI	Swarm Intelligence
SsDNA	Single-Stranded DNA