

CELL'S FUNCTIONAL ORGANIZATION IN A BIOLOGICAL NETWORK

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Abstract— Aim of this paper is to catalogue all molecules and interactions in living cell. We show that the tools of network theory offer unseen possibilities to understand the cell's internal organization and evolution, altering our view of cell biology. The generic principles of cellular networks is fundamental to our understanding of the cell as a system, it also needs to develop relevant system for the experimental biologist, helping to explain the role of individual molecules in various cellular processes.

Index Terms— Back propagation network , Cell Signalling network , Feed forward network ,Gene Regulatory networks, Metabolic networks, Multi scale clustering, Neurl network, Perceptron network ,Recurrent network.

1 INTRODUCTION

All living things are made of cells. Cells are the smallest units of life. These are come only from other cells. The molecules are Carbohydrates and Proteins. Glucose and Sucrose are the main carbohydrates in cell biology. Proteins are long chain of components called amino acids.

Structure-

Most cells have appropriate shapes, which are commonly held against each other by proteins that connect to the outer membrane and often to each other. Cells are held together often with many protein-based structures.

Movement-

A single cell moves, or swims, using a protein-based movement system.

Communication-

Signals are sent between cells to one another using varieties of proteins. Many hormones are proteins which may once again be pheromones (signals by scent) and alarmones (signal that alert other individual).

II. BIOLOGICAL NETWORK MODEL

Network-

It is a linked list of interconnected nodes.

Node-

It is a protein, peptide, or non-protein biomolecules.

Edges-

These are different levels of a biological relationship:-

Interactions, regulations, reactions, activation, Transformations, inhibitions.

Types of biological network models:

- 1) Gene regulatory networks
- 2) Metabolic networks
- 3) Cell signalling networks
- 4) Neuronal networks

Approaches of this network models are used to understand the mechanisms behind the evolution of molecular networks.

1) Gene Regulatory networks

In this network model Genes act as a nodes and the edges are directed. A gene act or serves as a source of a direct regulatory edge to a target gene by producing a protein molecule that functions as an inhibitor of the target gene. If the gene found as an activator, then it is the source of a +ve regulatory connection. If the gene an inhibitor, then it is the source of a -ve regulatory connection. To check the relationships between the genes, that is, to define the influence of each gene on the others, People typically attempts to reconstruct the Gene regulatory network.

Gene regulatory network representation:

We use a weighted directed graph $G(V, E)$ with feedback to represent a gene regulatory network. The vertices of the graph represent genes, and the weight w_{ij} of the edge between vertices represents regulatory relationship of the corresponding two genes g_i and g_j . Consequently, we get a vertex set $V = \{g_i | g_i \in D\}$ of the graph and an edge set $\{(,) , , \}$

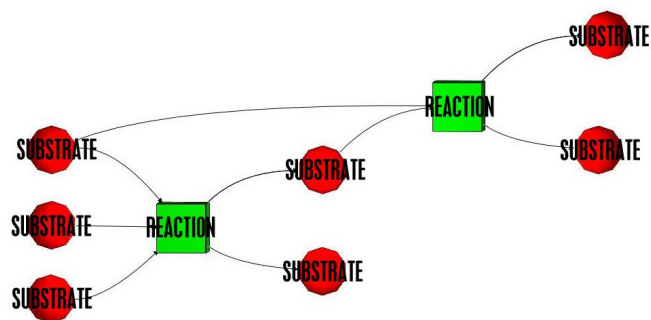
There are three types of regulatory relationship:

- 1) $w_{ij} > 0$ indicates positive direct regulatory influence between g_i and g_j , which means that the increase (decrease) in the value of g_i leads to the increase (decrease) on the value of g_j .
- 2) $w_{ij} < 0$ indicates inverse (negative) causality between g_i and g_j , which means that the increase (decrease) in the value of g_i leads to the decrease (increase) on the value of g_j .
- 3) $w_{ij} = 0$ indicates no correlation between g_i and g_j .

The regulatory network of n genes can be represented by an $n \times n$ adjacency matrix.

2) Metabolic Network

A metabolic network is a set of interconnected sub networks. So basically the metabolism corresponds to the energy transfers or transformations of molecules in the cell or in living organisms. To study metabolism consists in focusing on small subsets of biochemical reactions which are called metabolic pathways. These are considered to be disjoint processes. The advantage of this metabolic pathway is that information is presented but its major drawback is that they have drawn manually so that it is not easy to update. These reaction converts one or more compounds into one or more other compounds. The nodes of the network are reactions and compounds. Thus the network is modeled as graph $G = (V, E)$ such that $V = (R, S)$ where $V = R \text{ xor } S$ and $E = (u, v)$.

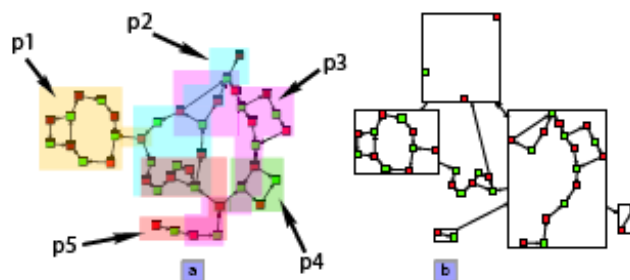


Metabolic Network Drawing Algorithm:

The algorithm we use has two main phases : initially, we perform a multi-scale clustering creating a quotient graph, and second, clusters and quotient graph are drawn.

Multi-scale clustering

One of the main problem is that metabolic pathways often share nodes. For instance in the below diagram where the yellow colour, the blue and the green region respectively represent pathways p_1, p_2 and p_3 one can see an overlap between p_1 and p_2 (one node) and between p_2 and p_3 (four nodes). Since we chose not to duplicate nodes and since vertices of a pathway have to be drawn next to each other, our algorithm will have to decide whether a node will be embedded next to a pathway or next to another. For example, the shared node between p_1 and p_2 could be drawn near p_1 or near p_2 . This will be achieved by a two-step process.



(a) A colour is used to individually represent every other pathway, (b) clustering according to metabolic pathways overlapping.

The first step consists in computing independent set and second in detecting cycles and paths.

First pass: Computation of independent set:

Initially this algorithm searches for the subset $P_{ind} = \{p_1, \dots, p_{ind}\}$, $ind \geq 1$ P_{ind} subset to P_G such that:

1 Pathways of P_{ind} are independent 2. $|p_i|$ is maximized. Thus we find the longest independent cycles and these are clustered into metanodes yielding a multi-scale graph.

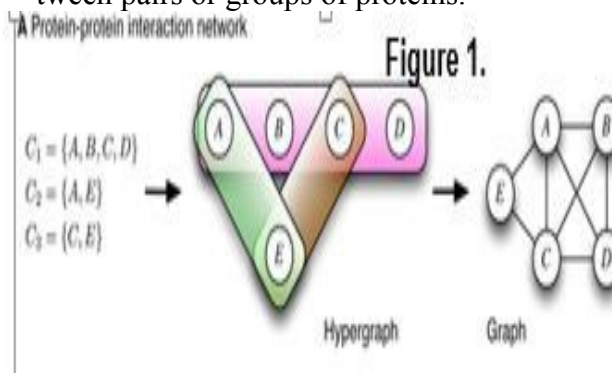
Second pass: To detect cycles and paths

The next step of the algorithm consists in computing the longest independent cycles in G , excluding metanodes. At each iteration, we clusterize the longest cycle into a metanode and exclude it for the next search. We then compute the longest paths of nodes of degree less than or equal to two.

3) Cell Signalling Network:

Cell signalling is part of a system of communication that controls basic cellular activities and coordinates cell actions. Cells receive information from their neighbours through a class of proteins known as receptors. In general, Physical interactions are shown as solid lines. Functional interactions are shown as dashed arrows. The functional interactions represent enzymatic reactions, conformational changes or non-protein intermediates.

- 1) Cell signaling finds its applications in studying the behavior and functioning between pairs or groups of proteins.



For example, In the above figure C_1 , C_2 , C_3 represents different groups of combination of proteins. In order to study the functioning between these groups linkage structure should be known. This structure can be developed using cell signaling network.

The individual proteins in the groups are assumed as nodes. If the proteins belongs to same group represent their linkage through an edge. Likewise the resulting graph is shown for the example group of proteins.

Based on these protein-protein interaction structure, the functioning of these proteins can be studied.

- 2) For a given set of reactions between elementary units a substrate graph can be developed to study the nature of reactions.

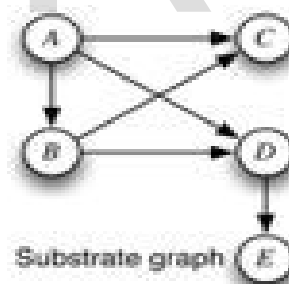
R1: $A \rightarrow B$

R2: $A+B \rightarrow C+D$

R3: $D \rightarrow E$

To develop a substrate graph, identifying nodes and edges is important. The elementary units represents the nodes and the edges represents the reaction between the reactants for forming the product. For example in reaction R1, A and B represents the nodes and an edge is drawn from A to B

To represent the reaction. Similarly, we draw the edges to represent R2 and R3. The substrate graph looks like the below figure.



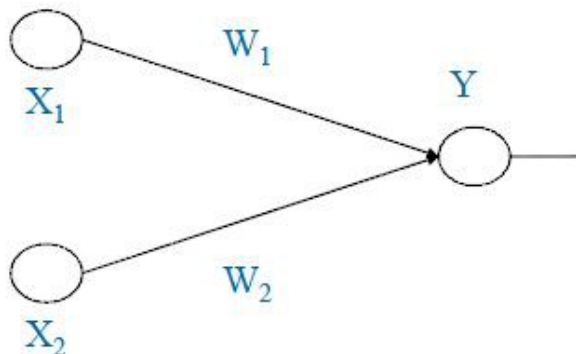
Errors in signaling causes serious diseases like cancer, autoimmunity, diabetes etc.

4) Neural Network

A neural network is a powerful data modelling tool that is able to capture and represent complex input/output relationships. Neural networks resemble the human brain in the following two ways:

1. A neural network acquires knowledge through learning.

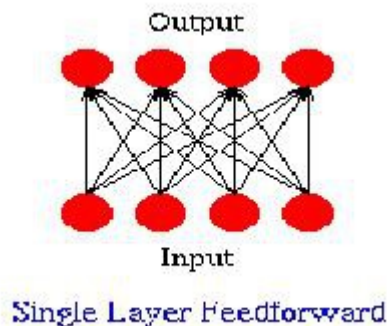
- A neural network's knowledge is stored within inter-neuron connection strengths known as synaptic weights.



There are many different types of neural networks.

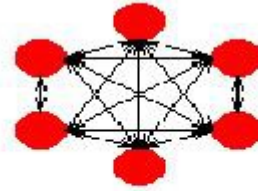
Feed Forward Network: This is the most simple type of neural network. From the input nodes data goes through the hidden nodes (if any) and to the output nodes. Cycles or loops doesn't exist.

McCulloch-Pitts Neural Network, Perceptron are the main examples of feed forward network.



Single Layer Feedforward

Recurrent Network: In recurrent network connections between units form a cycle. Unlike feed forward neural networks, RNNs can use their internal memory to process arbitrary sequences of inputs. This type of Recurrent networks helps in handwriting recognition.

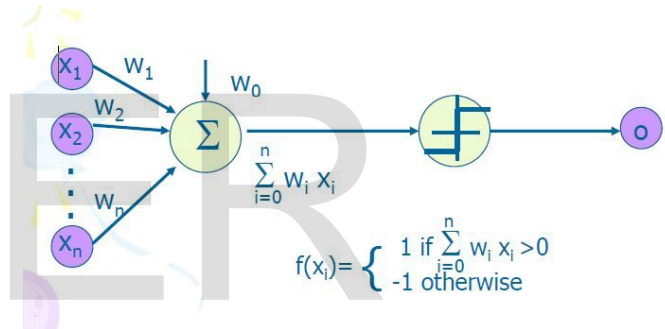


Fully Recurrent Network

Training Algorithms:

Perceptron networks:

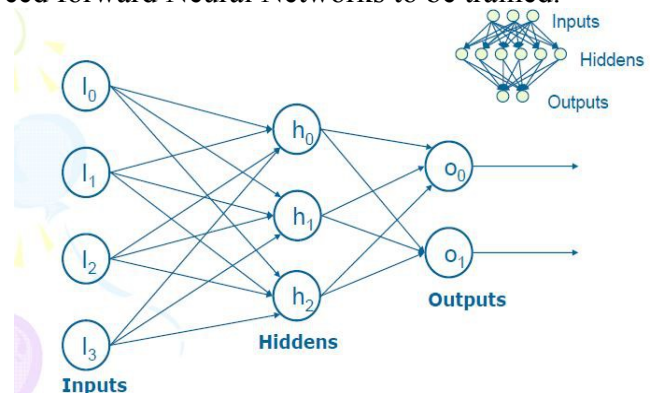
A perceptron computes a sum of weighted combination of its inputs, if the sum greater than a threshold (bias), then it outputs a "1", else a "-1".



$w_i = w_i + \Delta w_i$
 $\Delta w_i = \eta (t - o) x_i$
 where
 $t = c(x)$ is the target value,
 o is the perceptron output,
 η is a small constant (e.g., 0.1) called learning rate.

Backpropagation network:

A training procedure which allows multilayer Feed forward Neural Networks to be trained.



Conclusion:

We have studied about different concepts of cell organization and biological sciences. These concepts helps us in studying various functions of networks which find their applications in various fields. It is important that network biology concepts are studied briefly for developing applications for critical mathematical and real time problems.

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