Identification of Driver Nodes in Genetic Networks Regulating Macrophage Activation

Giulia Bassignana1,2, Jennifer Fransson2, Olivier Colliot1,2, Violetta Zujovic2, Fabrizio De Vico Fallani1,2

Introduction

Macrophage cells play an important role in the multiple sclerosis disease. They participate in:
- the degenerative process, myelin destruction
- the regenerative one, coordinating remyelination [1].

Methods & Materials

HP: Linear Time Invariant dynamics

\[ x(k+1) = Ax(k) + Bu(k) \]

- A adjacency matrix of the network
- B input matrix
- \( x(k) \) state of the system at time step \( k \)
- \( u(k) \) input signal

Algebraic condition

Kalman criterion

Structural controllability

Maximum cardinality matching

Results

Different configuration of driver nodes are in general possible.

We repeated the analysis \( R=60000 \) times and shuffled the order of the nodes in the adjacency matrix in order to explore different configurations. We defined the node drivelessness as the frequency of times a node is selected as driver over \( R \) iterations.

\[ \text{Drivelessness}_i = \frac{1}{R} \sum_{j=1}^{R} \delta_{ij} \in [0,1] \]

where \( \delta_{ij} = 1 \) if node \( i \) was classified as driver in the repetition \( j \) and 0 otherwise.

Drivelessness

In accordance with [3], driver nodes tend to avoid hubs. This may be due to the fact that one node cannot propagate independent signals.

Concentration

Our work is a preliminary step towards the identification of the genes influencing the inflammatory process of macrophages, a crucial mechanism in multiple sclerosis’ disease. Further studies could involve the dedicated input case, a more complete exploration of the configurations of the maximum cardinality matching and the biological test of the chosen genes.

References


Contact

giulia.bassignana@gmail.com