THE ROLE OF NEGATIVE LINKS IN BRAIN NETWORKS

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Functional connectivity studies focused more on positive than negative correlations, caused by the not well-defined nature of negative correlations. However, several authors pointed out the persistence of significant negative correlations and a possible physiological role for them [1-2-3]. A clear mechanism about how negative interactions are related to the positive one has not been proposed as yet and in such a context the Network Theory [4] is useful in providing general quantifiers of network topology and the Balance Theory helps in defining the conditions for the signed networks' functional stability [5]. Here we report about: 1) characterizing negative correlations in fMRI acquisitions of healthy people; 2) reproducing an equilibrium between different brain areas implementing a negative feedback mechanism in a Multi Agent System (MAS) for a small network model.

For the first issue, images from the 1000 Functional Connectomes Classic collection (180 healthy controls in resting state conditions, http://fcon 1000.projects.nitrc.org/indi/retro/BeijingEnhanced.html) was taken [6]. The images of each subject were divided into 90 Regions Of Interest (ROIs) and the correlation matrices were calculated (Figure 1). Finally, a number of topological indexes were calculated for the positive and negative matrices separately: Efficiency (segregation-integration index), Assortativity and Rich-club coefficient [4]. The Assortativity calculates the probability of interaction among nodes in the entire network, while the Rich-Club coefficient [10] indicates the node interactions in a particular range of the node degree. Our results show that negative networks are characterized by a lower segregated structure as compared to positive networks, while the Assortativity assumed a negative value (nodes tend to be connected to other nodes with different node degree). The Rich-Club analysis demonstrates that this average trend of node degree interaction is kept only by the most connected nodes (Figure 2). The architecture emerging from our analysis describes a small number of central nodes less connected between each other but interacting with nodes of lower degree.

As for the second issue we describe a minimalistic computational model simulating the homeostatic regulation between regions having positive and negative correlations, and using the Balance Theory to define the conditions for the networks' functional stability [5]. The concept of balance refers to a triadic model in which agents can have positive or negative relation among them, thus the triangular graph is balanced (or stable) if cycling through it (by multiplying the links) produces a positive result (Figure 3). In this regard, a simple 9-node network representing a crude model of 9 interacting brain regions was made in a Multi Agents System (Figure 4), and reproduced in the NetLogo[TM] MAS programming environment (https://ccl.northwestern.edu/netlogo/): the scheme of a 9-node graph including three stable modules (A,B,C) connected among each other by negative connections. The stability in the scheme on the left can be reproduced, as testified by the finite value (= 2) of the <ShortestPathLength> (APL) if and only if the clockwise and anticlockwise direction of each links on the right model correspond to the positive and negative sign of the corresponding link on the left. Worthless to say that also the specular correspondence between sign and direction holds. By this strategy we obtained different activity levels among sub-networks by reversing the sign of some links or adding new links of reversed sign. We also represented the dynamics of the system by the energy flow through the links, up to the reaching of a stable state, as predicted by the Balance Theory.

In conclusion, we showed how a combined approach of experimental and MAS-based simulation techniques may clarify complex brain functions and, in principle, even explain some stability alterations of pathological significance.

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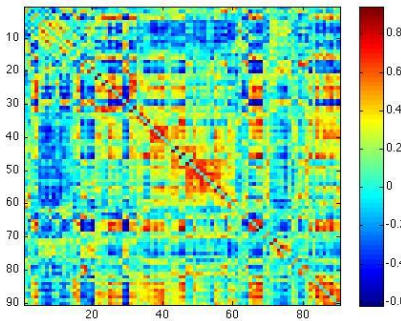[5] F. Heider, Journal of Psychology, 21 (1946) 107-112.

Figure 1. Correlation Matrix with positive and negative values between ROIs of a single subject from fMRI data. The raw data are plotted in a normalized, false color scale.
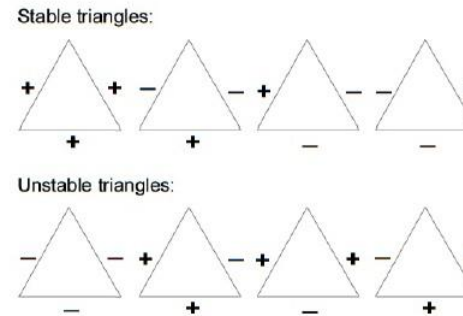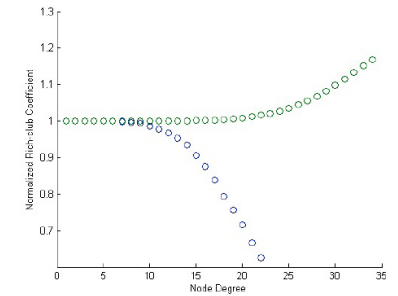

Figure 2. Rich-Club coefficient: blue dots negative networks, green dots positive networks. A node degree interval having a Rich-Club coefficient greater than 1 indicates a set of particular nodes more connected among each other; a Rich-Club coefficient lower that 1 refers to nodes avoiding reciprocal links.

Figure 3. The sign multiplication of all stable configurations results in a positive value, and in a negative value for the unstable ones.
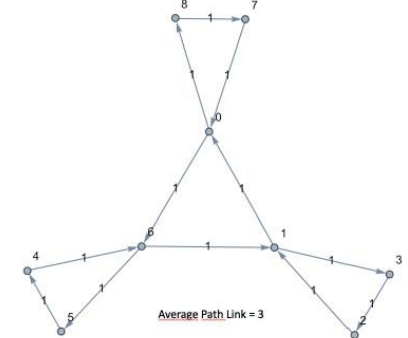

Figure 4. Simple 9-nodes network implemented in MAS. Notice the clockwise and anticlockwise direction of links within and between modules. The nodes are indicated by numbers (0 ... 8) and the links by weigths which, in the case of binary networks, = 1.