upro EU
PROMOTIONAL PARTNERSHIP

Graph-Based Diagnosis and Treatment of Neuronal Communication Disorders

Mladen Veletić
University of Banja Luka (UNIBL), Faculty of Electrical Engineering, Dept. of Telecommunications
Norwegian University of Science and Technology (NTNU), Dept. of Electronics and Telecommunications
E-mail: mladen.veletic@etfbl.net; mladen.veletic@iet.ntnu.no

Introduction

- **Research topic**: Intra-body Molecular Communication Nano-Networks
- **Paper topic**: Strategy for affecting the performance of a network
- "*The report issued by Alzheimer's Disease International in 2009 estimated that 35.6 million people worldwide would be suffering from the disease in 2010, and the number was estimated to 115.4 million in 2050*."
- The paper does not delve with any specific treatment fashion in terms of technique being deployed, but discusses one possible strategy formation of controlling the neuronal communication
- **Tool**: Graph theory concepts deployed and integrated from a theoretical neuroscience perspective
- **Goal**: altering the performance of neuronal communication in order to slow down, halt or reverse mental disorders

Motivation and Justification

- **Hot topic:** Development of either non-invasive or invasive methods that can control neuronal communication
- Non-invasive methods
  - Recent studies performed showed that EMR exposure and MF can improve the cognitive abilities of the brain eliminating the possibility that the positive effects were caused by increased temperature
- Invasive methods
  - “Current clamp” technique (micro-pipetts)
  - Optogenetics
  - Via nano-machines based on graphene or carbon nanotubes
- Graph-based strategy of driving the neuronal communication through controlled membrane voltage (concentration of calcium ions)
- **How to recruit the neurons whose $[Ca^{2+}]_i$ is to be controlled when large-scale malfunctioning network is to be treated?**

Graph-Theoretical Modeling of Neuronal Connectivity

- Quantitative characterization of anatomical patterns within neuronal nano-network can be mathematically described through matrices - adjacency matrix (AM), also called the connection matrix
- An AM is with non-zero entries a_{ij} if the connection, i.e. synapse, is present between neurons *i* and *j*; otherwise, a_{ij} is zero
- Two types of synapses: excitatory and inhibitory
  - Correspond to positive and negative a_{ij} values in AM
- One-way axonal transmission
- Graph being analyzed is **directed**, **weighted**, and **signed**

Strategy of Diagnosis and Treatment of Neuronal Disorders – Network Analyzed

- Mental disorders struck hippocampal neurons (mostly)
- **Two-dimensional spatial representations of a local sub-network of 131 neurons with 764 unidirectional connections within *Caenorhabditis elegans* rostral ganglia [Ref.]**

[Ref.] (2013) Resources. [Online]. Available: http://www.biological-networks.org/?page id=25

Strategy of Diagnosis and Treatment of Neuronal Disorders - Visualization

- Visualization of nano-network (Inhibitory and Excitatory cells)
- Distribution of inhibitory and excitatory cells is not temporal, unlike the time-variable synaptic weight values
- Different patterns formed by the synaptic weights are beyond the long terms potentiation (LTP) and long term depression (LTD) processes.
- Synchronized and nonsynchronized neuronal activity (LTP and LTD) in the hippocampus is crucial for memory formation and learning
- **Visualization tool presented might provide a clinically useful diagnostic marker indicating a disease**

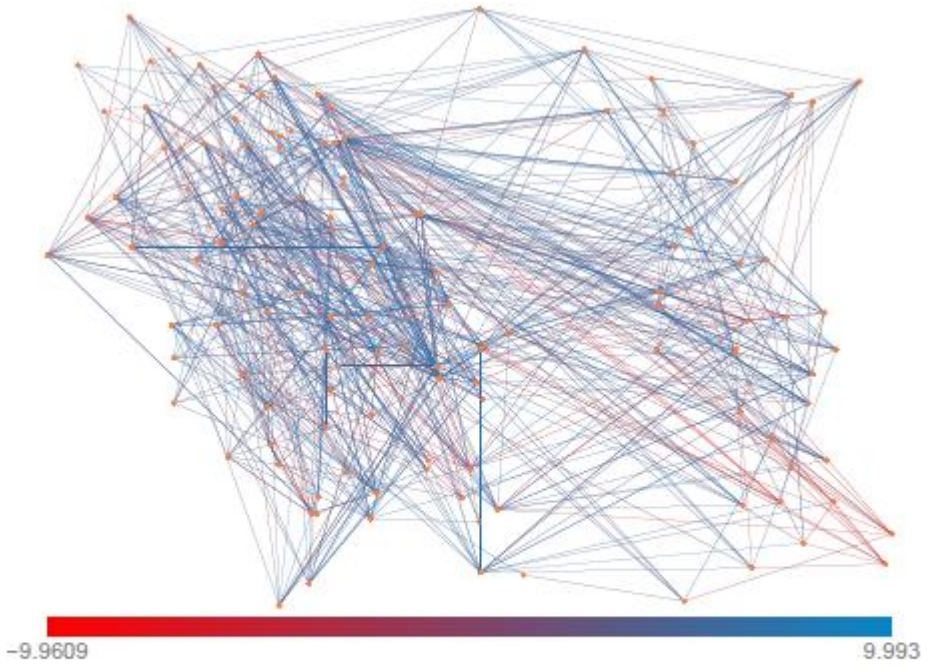


Fig. 1. Two-dimensional spatio-temporal pattern of weighted excitatory and inhibitory synapses. Red lines denote the inhibitory connections, whereas blue lines denote excitatory ones.

Strategy of Diagnosis and Treatment of Neuronal Disorders – Centrality Criterion (1)

- To produce large-scale effects, avoid small-scale alterations and effectively cure a brain region of interest, 'important' target neurons should be determined
- Centrality of a vertex measures its importance within a graph
- In this study, centrality is applied to examine how involved a cell is in neuronal communication system in order to identify those to be monitored, "guided", and controlled
- Variety of centrality concepts: **degree**, **betweenness**, closeness, and eigenvector

Strategy of Diagnosis and Treatment of Neuronal Disorders – Centrality Criterion (2)

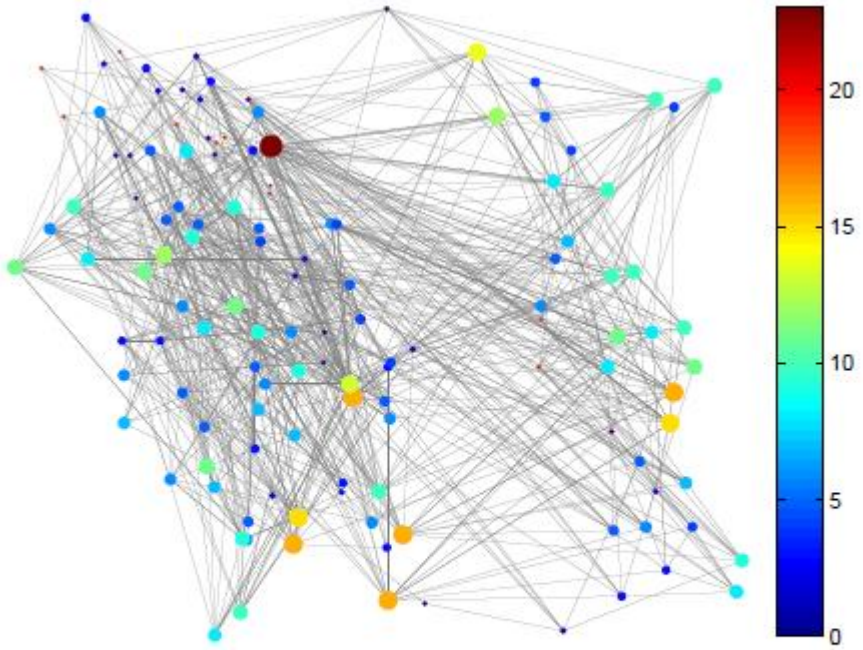


Fig. 2. Representation of neurons according to the outdegree criterion. Blue color indicates cells with no importance communication-wise. Important and potentially treated neurons are orange and red colored.

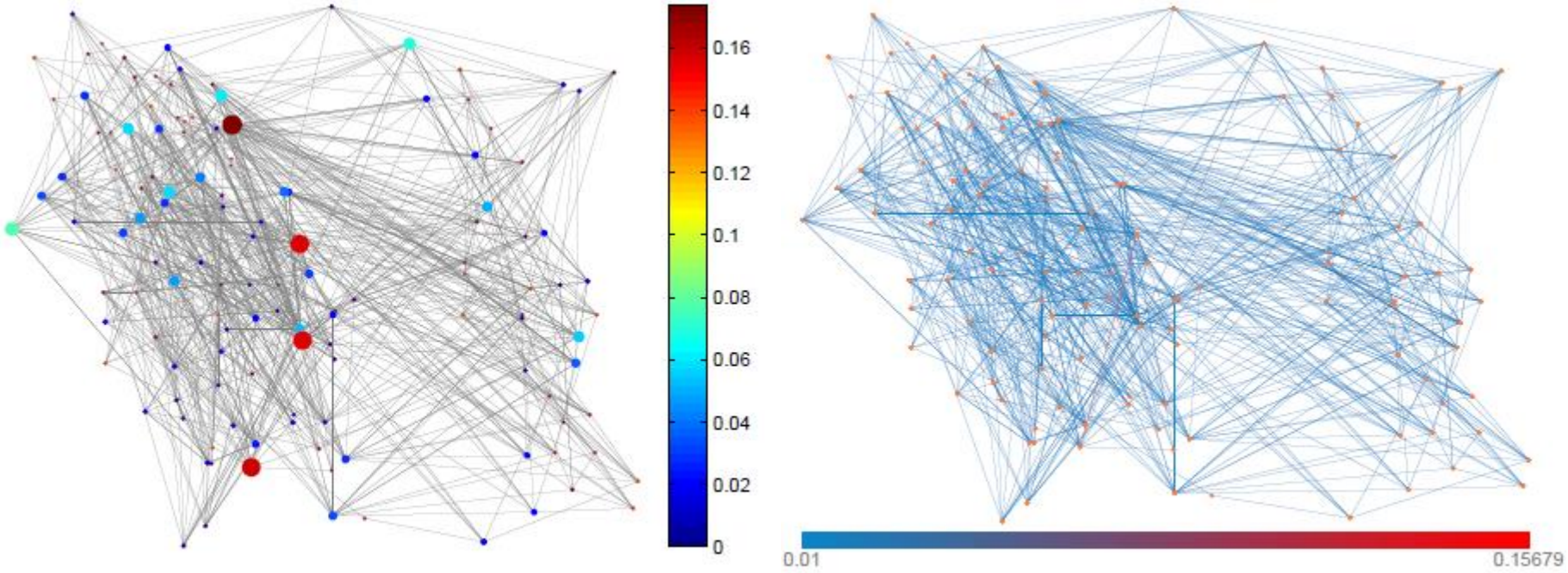
Obvious functional interpretation

- High outdegree of analyzed neuron indicates a large number of its potential functional targets, i.e. receivers

Strategy of Diagnosis and Treatment of Neuronal Disorders – Centrality Criterion (3)

- Betweenness centrality also measures a vertex's or edge's importance in a network
- Vertices and edges with high centrality values are assumed to be crucial for the graph connectivity and, thereby, shall be monitored in potentially malfunctioning brains
- For finding shortest paths of a binary directed graph with positive edge (but with no cycles), Floyd-Warshall algorithm is deployed
- High values indicate cells that are either to be monitored in order to prevent disorders producing malfunctioning network, or whose behavior is to be regulated in case disorder has already took place

Strategy of Diagnosis and Treatment of Neuronal Disorders – Centrality Criterion (4)



(a) (b)

Fig. 3. (a) Representation of neurons according to the node betweenness centrality criterion. Red markers identify the most influential cells in the region. Death of these cells would produce two weakly connected- or even disconnected clusters which is further ruinous in terms of both anatomical and functional connectivity. (b) Representation of neurons according to the edge betweenness centrality criterion. Similarly, red lines denote crucial synaptic junctions which disunity produce harmful effects.

Strategy of Diagnosis and Treatment of Neuronal Disorders – Clustering Criterion

- Clustering coefficient indicates how many connections are maintained between a vertex's neighbours
- Defined as the ratio of actually existing connections between the neighboring neurons and the maximal number of such connections possible
- High coefficient points to a neuronal region consisting of groups of units that mutually share structural connections and function in a closely related manner

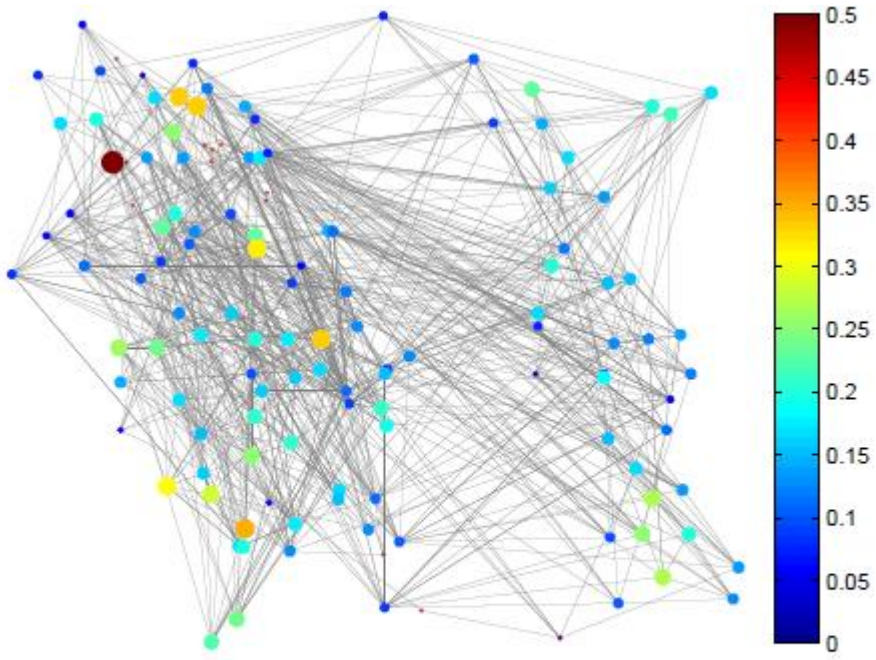


Fig. 4. Representation of neurons according to the clustering coefficient criterion. Red colored cell points to a region consisting of neurons that mutually share structural connections and function in a closely related manner.

Conclusion

- This paper helps in development of an effective graph-based strategy of neurons selection whose electrical properties should be altered in order to evoke certain changes in communication abilities
- A set of graph theory measures that might have certain relevance for neuroscience engineering applications is stated and deployed in this study to create a visualization tool that helps in selection of targeted neurons
- Computationally demanding handling of huge AM describing large-scale networks, that are more likely to be recorded with functional magnetic resonance imaging, electroencephalography and magnetoencephalography, is not analyzed in this paper

Thank you for your attention!

Questions?

Contact:

mladen.veletic@etfbl.net or mladen.veletic@iet.ntnu.no