# Integrative Network Analysis: Unveiling Symptom-Disease Interactions and Enhancing Predictive Models

Andreoli C. • Ligari D. • Alberti A. • Scardovi M. [1]

[1] *Department of Computer Engineering, Data ScienSickness predictionce, University of Pavia, Italy*
*Course of Financial Data Science*

*Github repository: https://github.com/AndreaAlberti07/enhancing-disease-prediction*

## Abstract

We will write it once we have the results.

***Keywords—*** *Graph theory • Features Engineering • Community detection • Null models • Random forest • MLP*

## Contents

# 1 Introduction

In the dynamic landscape of healthcare, understanding the intricate interplay between symptoms and diseases is paramount for effective diagnosis and prediction. This report embarks on a comprehensive journey through the realms of network analysis, leveraging both theoretical foundations and empirical data to unravel the complexities of symptom-disease interactions. Our dual-fold objective is to provide a nuanced descriptive analysis of these interactions while identifying key features to bolster predictive models.

The foundation of this endeavor lies in an extensive review of existing literature, drawing insights from seminal works on network theory and disease prediction. By establishing a baseline through prior research, we pave the way for a deeper understanding of the subject matter and ensure the relevance of our findings in the broader context of scientific inquiry.

Guided by insights gleaned from the literature, our exploration extends to the realm of data, where we meticulously curate and analyze datasets of varying sizes. Through a systematic process of exploratory data analysis and cleaning, we prepare the groundwork for constructing meaningful networks that encapsulate the relationships between symptoms and diseases.

The heart of our analysis lies in the creation of intricate network structures, employing bipartite models and non-weighted links to distill meaningful patterns. We delve into a spectrum of network metrics, from fundamental measures like degree distribution and clustering coefficients to more nuanced assessments of node importance and betweenness centrality. Statistical significance is rigorously assessed through the lens of a null model, ensuring that our observations transcend mere chance.

Community detection algorithms further dissect the network, revealing hidden structures and relationships between diseases. This not only enriches our understanding but also lays the groundwork for subsequent analyses. As we traverse the terrain of network analysis, we introduce novel metrics inspired by the Hidalgo-Hausmann framework, stratifying symptoms and diseases based on their predictive importance. These metrics, coupled with traditional measures like betweenness centrality, contribute to the definition of features that fuel our predictive models.

With a robust foundation established, we transition to the realm of predictive modeling, where our feature-rich approach promises to enhance the performance of established models. Logistic regression, random forest, and multi-layer perceptron models are trained, tested, and validated, with a keen eye on feature importance and model improvement strategies.

This report unfolds as a holistic exploration, weaving together theoretical frameworks, empirical analyses, and predictive modeling into a cohesive narrative. As we traverse the intricate web of symptom-disease interactions, our aim is not only to elucidate the underlying dynamics but also to pave the way for more accurate and insightful predictive models in the realm of healthcare.

## 1.1 Network Creation (Not Weighted - Bipartite)

## 1.2 L1 and L2 measures

## 1.3 Betweenness Centrality

The betweenness centrality of a node $v$, according to Brandes [2], is defined as the sum of the fraction of all-pairs shortest paths that pass through $v$:

$$c_B(v) = \sum_{s,t \in V} \frac{\sigma(s,t|v)}{\sigma(s,t)} \tag{1}$$

where:

- $V$: The set of nodes.
- $\sigma(s,t)$: The number of shortest paths from node $s$ to node $t$.
- $\sigma(s,t|v)$: The number of those shortest paths from node $s$ to node $t$ that pass through some node $v$ other than $s$ and $t$.
- If $s = t$, then $\sigma(s,t) = 1$.
- If $v \in \{s,t\}$, then $\sigma(s,t|v) = 0$.

To compute the betweenness centrality we used the NetworkX function `nx.bipartite.betweenness_centrality` which implements the algorithm proposed by Brandes [1] and uses a proper normalization for bipartite graphs.

## 1.4 Communities Detection

Prior to apply any community detection algorithm, we need to perform two steps:

- **Graph Projections**: We need to project the bipartite graph into two graphs, one for each set of nodes. In our case the two sets are represented by symptoms and

diseases. At this scope is available the NetworkX function `nx.bipartite.projected_graph` which returns the projection of the bipartite graph onto the specified nodes.

- **Compute Similarity**: We need to compute the similarity between nodes. For our purposes, it is possible to create a co-occurrence matrix, for each set of nodes. Taking as example the co-occurrence matrix of symptoms, each entry $s_{ij}$ represents the number of times the symptom $i$ and the symptom $j$ co-occur in the same disease.

Once we have the two graphs, whose links are weighted by the similarity between nodes, we can apply the community detection algorithm. We used the Clauset-Newman-Moore greedy modularity maximization algorithm [3], implemented in the NetworkX function `nx.algorithms.community.greedy_modularity_communities`. This algorithm aims at finding the partition of the graph that maximizes the modularity, which is defined by Newman [6] as:

$$Q = \frac{1}{2m} \sum_{ij} \left[ A_{ij} - \frac{k_i k_j}{2m} \right] \delta(c_i, c_j) \tag{2}$$

where:

- $Q$: Modularity of the network.
- $A_{ij}$: Element of the adjacency matrix representing the connection between nodes $i$ and $j$.
- $k_i$ and $k_j$: Degrees of nodes $i$ and $j$, respectively.
- $m$: Total number of edges in the network.
- $\delta(c_i, c_j)$: Kronecker delta function, which is 1 if $c_i$ is equal to $c_j$ (i.e., nodes $i$ and $j$ belong to the same community) and 0 otherwise.
- The sum is taken over all pairs of nodes $i$ and $j$.

## 1.5 Degree Distribution and Power Law

## 1.6 Most Important Symptoms/Diseases (4 Classes)

## 1.7 Betweenness Centrality

As shown in Figure 1, the betweenness centrality of the nodes in the network follows a Power Law Distribution. This suggests a scale-free structure of the network, with a few central nodes working as connecting actors, while the majority of the nodes have a low betweenness centrality. Dividing the centrality values into the two classes of symptoms and diseases (Figures 2 and 3), we can see that the symptoms have a higher betweenness centrality than the diseases. To understand the meaning of this result we have to delve into the interpretation of the betweenness centrality. In general, a symptom is more likely to have a high betweenness centrality if it is connected to many diseases and these latter are connected to few symptoms. Conversely a disease is more likely to have a high betweenness centrality if it is connected to many symptoms and these latter are connected to few diseases. Looking at the results of L1 and L2, we can see that in our case the justification of the higher symptoms betweenness centrality is due to the fact that the symptoms are connected to many diseases, while the diseases are connected to few symptoms. From a predictive point of view, this is not a good result, since each symptom is not very specific contributing to many different classes.

Figure 5 shows the top 10 nodes with the highest betweenness centrality. As expected, they are all symptoms and seems reasonable that they are the most generic symptoms.

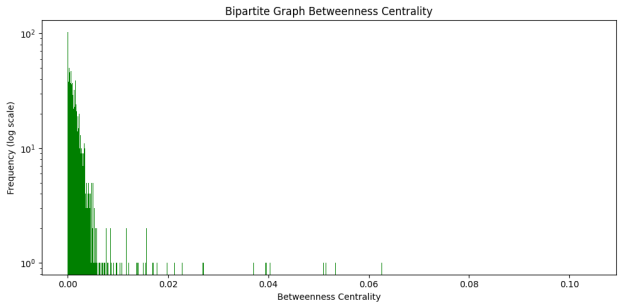


**Figure 1.** Betweenness Centrality of the entire network

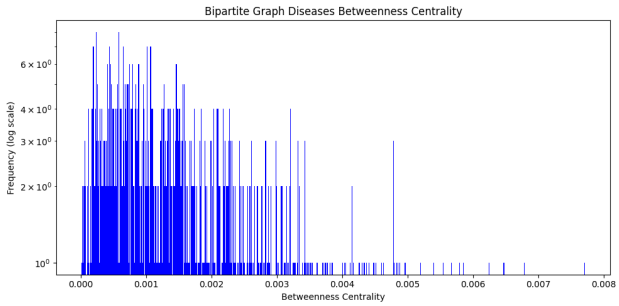


**Figure 2.** Betweenness Centrality of the diseases

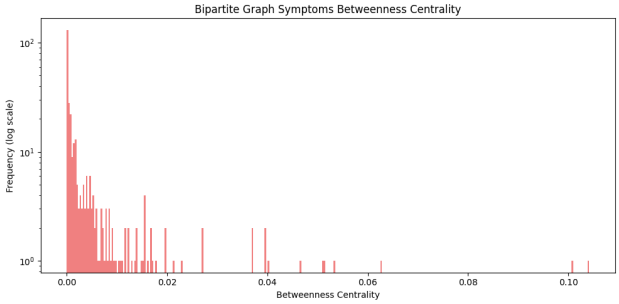


**Figure 3.** Betweenness Centrality of the symptoms

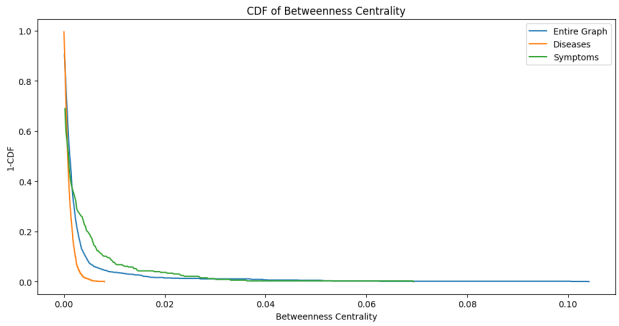


**Figure 4.** Betweenness Centrality CDFs

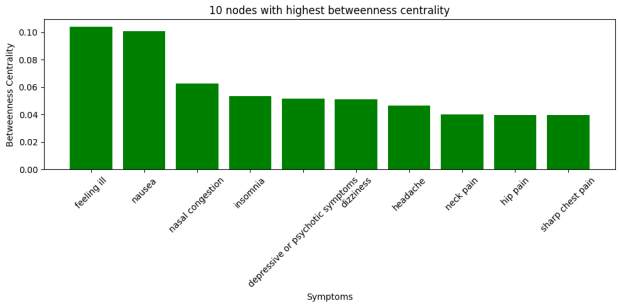


**Figure 5.** Top 10 nodes with the highest betweenness centrality

## 1.8 Communities

The detection of communities in a network can be useful both for the interpretation of the network itself and for the ML model prediction Enhancing. As regard the network interpretation it is worth to underline that a community of symptoms identifies a set of symptoms that are often co-occurring within the same diseases, while a community of diseases identifies a set of diseases that are often co-occurring within the same symptoms. The size of the different communities is reported in Figure 6.

Given a symptoms community could be of clinical interest to understand which are the diseases that are most often associated with the symptoms of the community. This information is depicted in (Figures 7, 8 and 9). As an interpretation example we can look at the community 1 of symptoms (Figure 7). In this case we can say that 'herniated disk' is the third most pointed disease by the symptoms of the community. It is pointed by 12 symptoms each one pointing on average 3 diseases.

The same kind of study can be done for the communities of diseases. In this case the results are shown in Figures 10, 11 and 12. This kind of information could be useful to profile the diseases and understanding the significance of each symptom. For example, looking at community 1 of diseases (Figure 10), the 'sharp abdominal pain' symptom is present in almost half of the diseases of the community. This means that this symptom is very generic and it is not very useful to discriminate between the diseases of the community.

Switching now the the creation of features for the Ml model, we created two kinds of features:

- **Community Count**: taking a symptoms one hot vector, we count how many symptoms of the vector are in each community. The new features vector has a length equal to the number of communities and a value equal to the number of symptoms of the original vector that are in the community.
- **Community Size**: taking a symptoms one hot vector, we replace each symptom with the size of the community of the symptom.

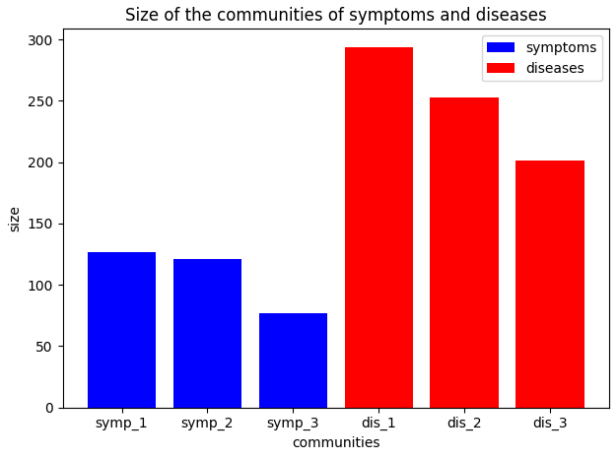


**Figure 6.** Sizes of the communities of symptoms and diseases

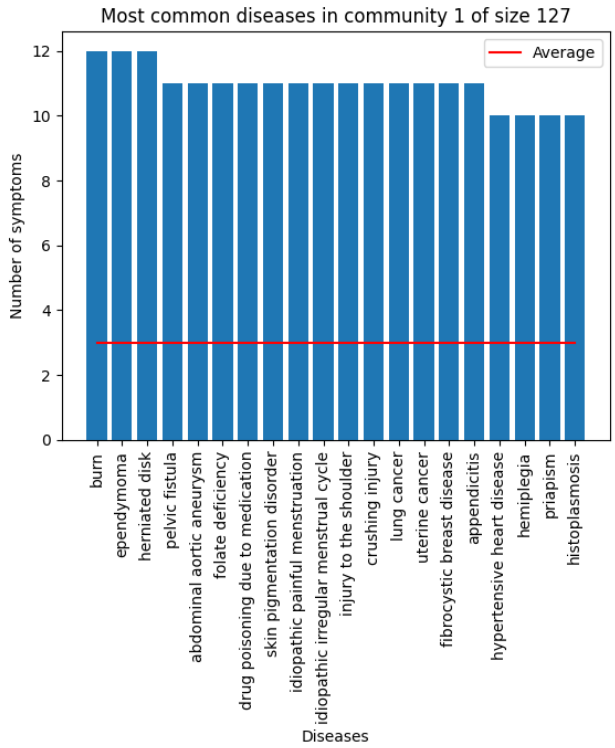


**Figure 7.** Community 1 of symptoms

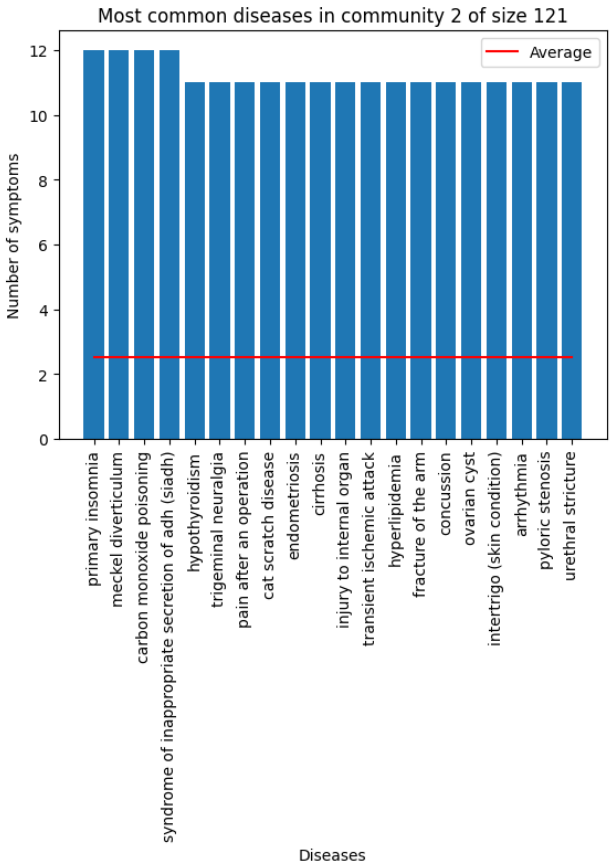


**Figure 8.** Community 2 of symptoms

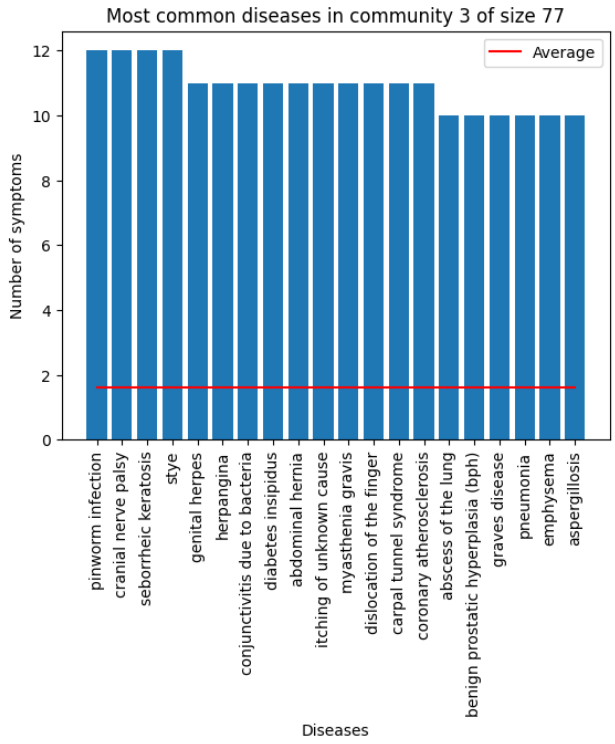


**Figure 9.** Community 3 of symptoms

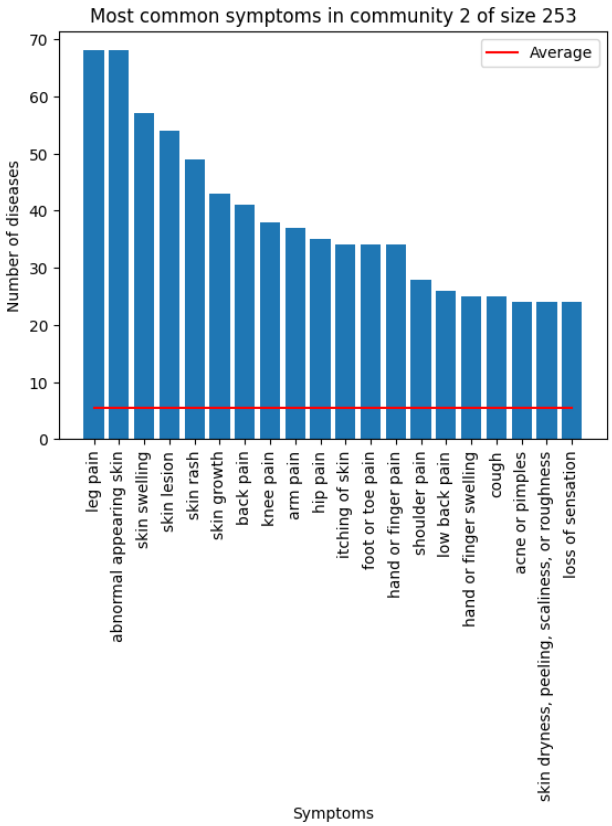


**Figure 11.** Community 2 of diseases

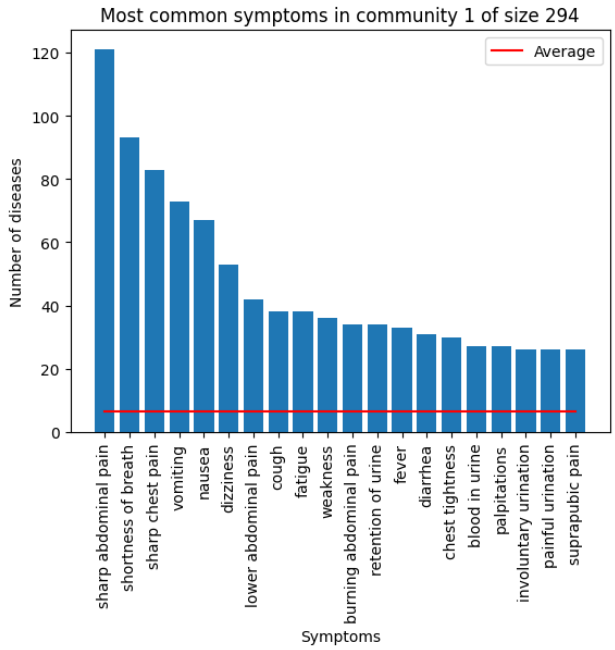


**Figure 10.** Community 1 of diseases

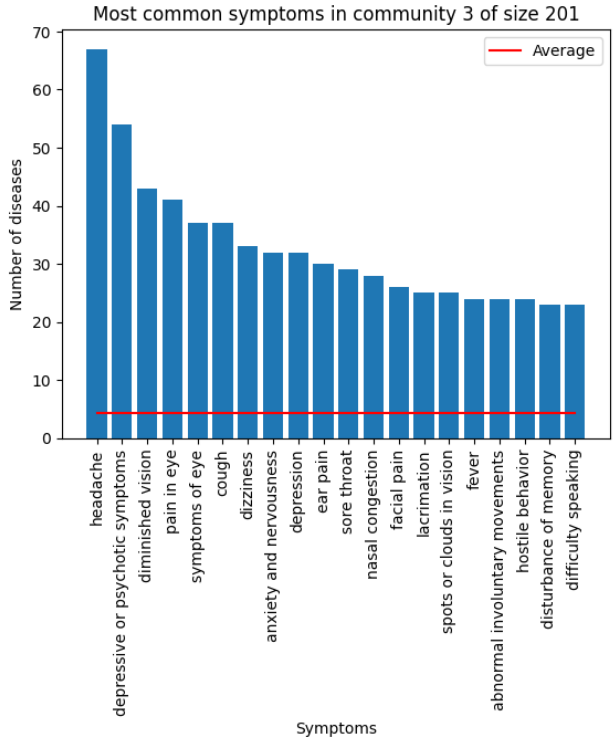


**Figure 12.** Community 3 of diseases

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