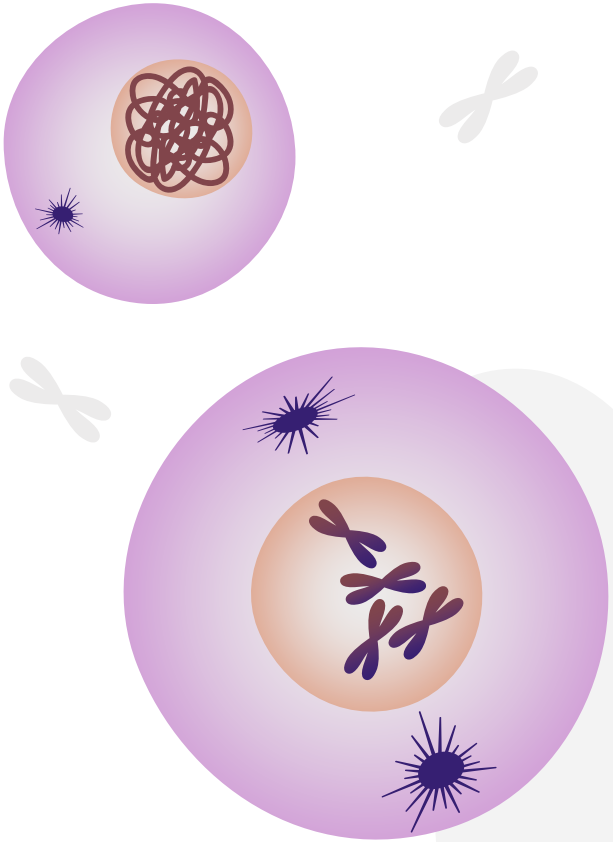
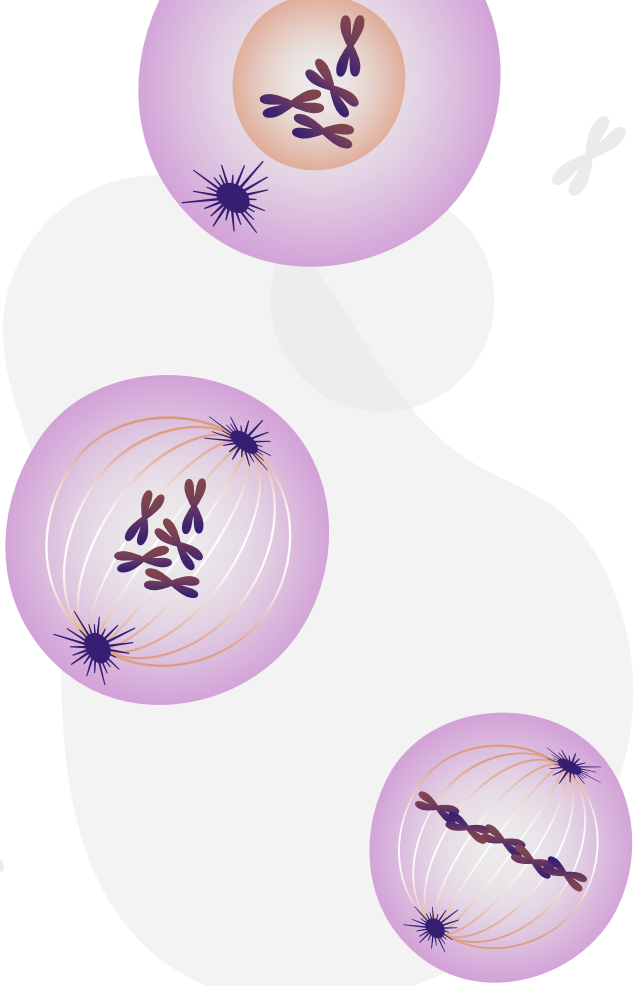
Metabolic Diseases: Pathway Analysis

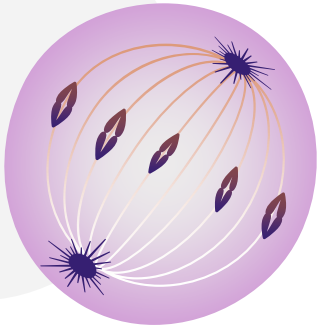
Computation Health Laboratory Final Project

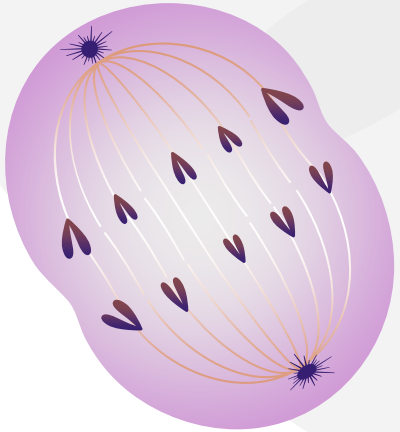
Marzeddu Simone
Raffi Jacopo





01
Project Introduction



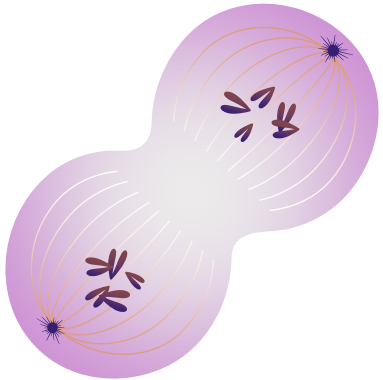


02

Metabolic Diseases: Background

Background

Metabolic Diseases



What is Metabolism?

The process of converting food to energy on a cellular level.

Metabolic Diseases Effects

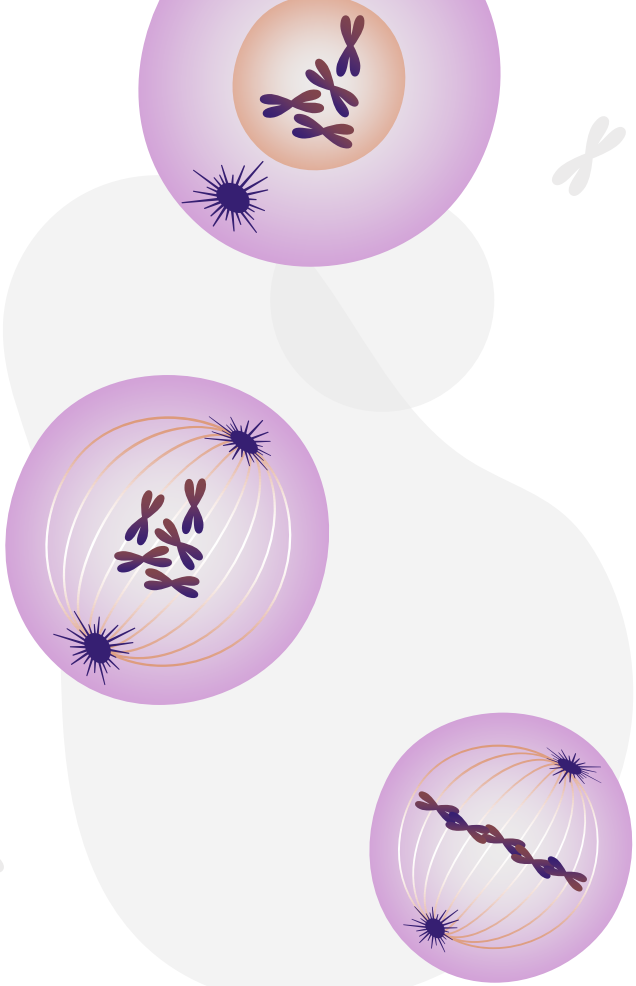
These diseases affect the ability of the cell to perform biochemical reactions that involve the processing or transport of proteins, carbohydrates, or lipids.

Contraction of Diseases

Metabolic diseases are typically hereditary, yet most persons affected by them may appear healthy for days, months, or even years.

Diseases Consequences

Consequences may be severe: intellectual disability, seizures, decreased muscle tone, organ failure, blindness, or even deafness depending on which enzyme is dysfunctional.



03
Project Roadmap

Project Roadmap

Selection of the subclass of Metabolic Diseases

Disorders of **Aminoacid Metabolism**

Pathways download and combination

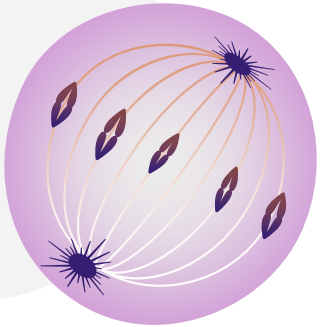
- **Reactome**
- **Drugbank**
- **rBiopaxParser**
- **igraph**

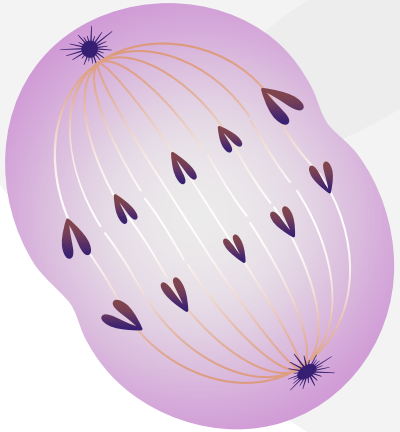
Network Extension and Completion

- **Biogrid:** biologic interactions download and integration.
- **General human organism interactions**
- **biogridr**

Data Analysis and Results

- **Ranking Algorithm**
- **Qualitative** Validation



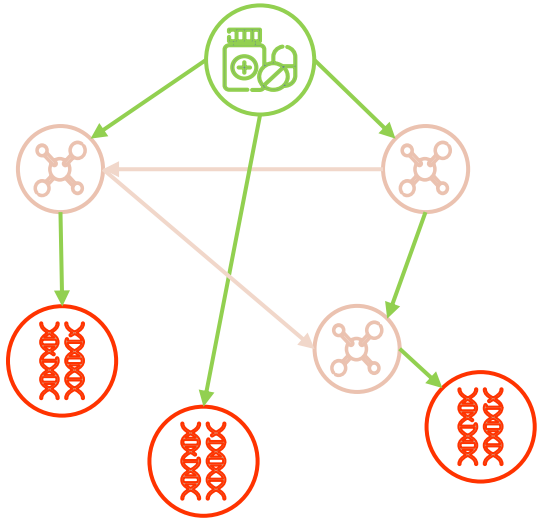


04

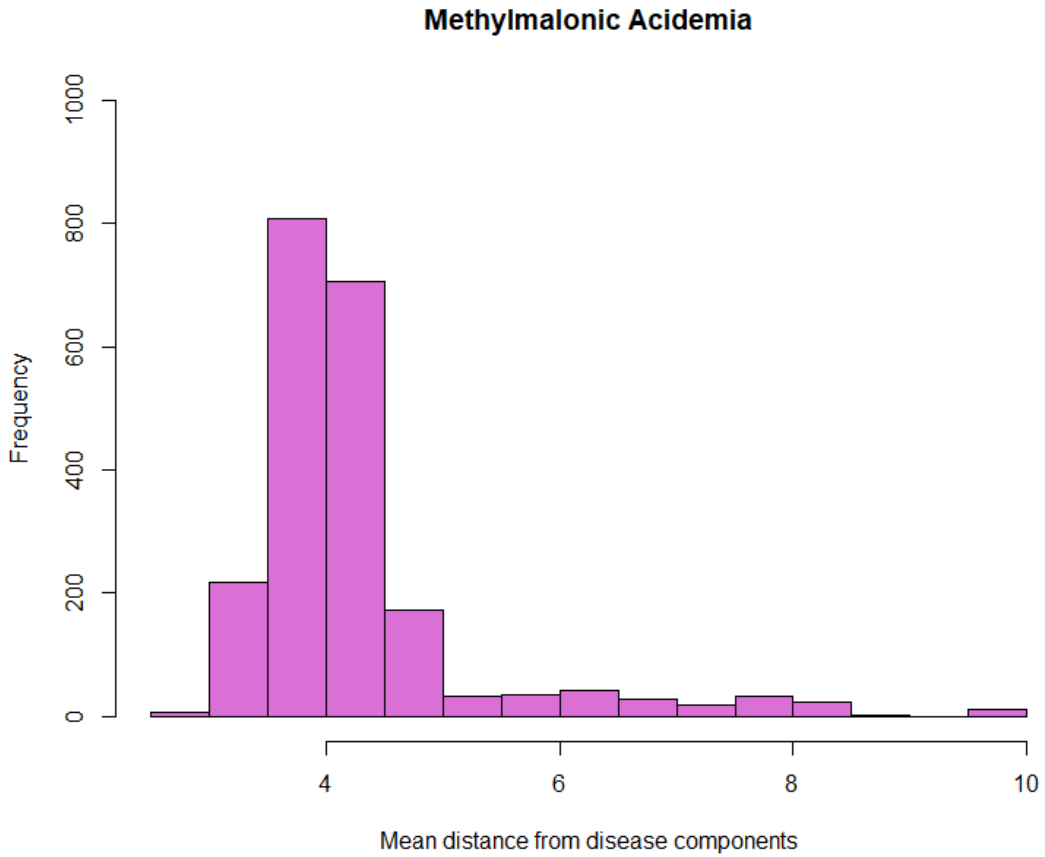
Drug Ranking

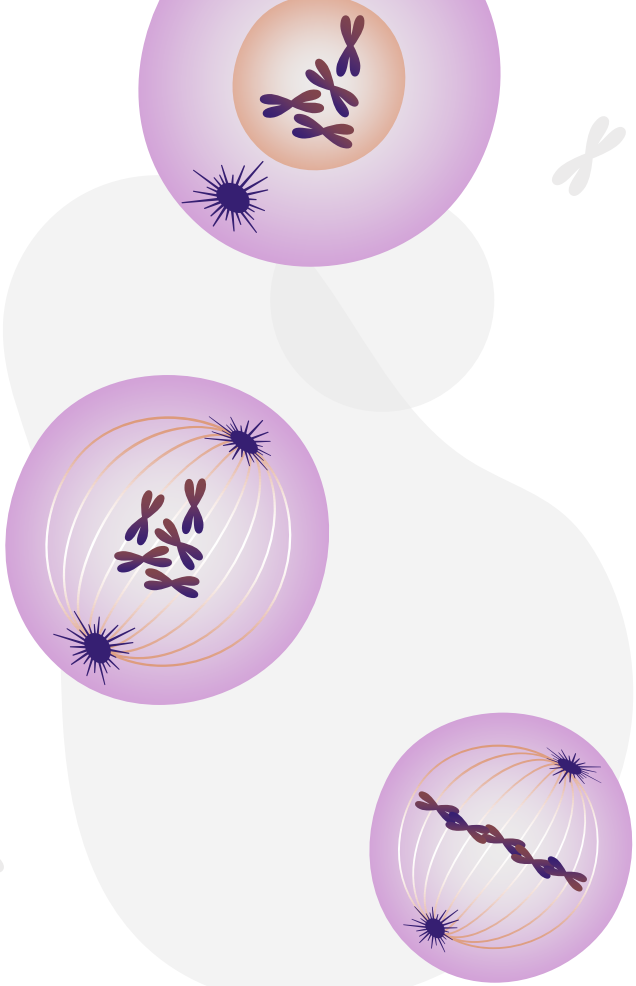
Mean Distance Algorithm

```r
ranking <- function(ig, drugs, genes, directed){

  # ig -> igraph representation of the global network
  # drugs -> vector containing all drugs
  # genes -> vector containing all the genes of the studied disease
  # directed -> boolean: TRUE: consider edges directions, FALSE: elsewise

  m = "all"
  if(directed)
    m = "out"

  # igraph library function that calculate the shortest path lenghts between two sets of nodes
  dist = distances(ig, v = drugs, to = genes, mode = m)

  # generation of a matrix containing association between drugs and mean distances from the genes of the disease
  # columns: 1 -> drug_id ; 2 -> mean_distance; 3 -> rank; 4 -> percentage of drugs falling under this rank
  means = matrix(nrow = length(drugs), ncol = 4)
  for(i in 1:nrow(dist)){
    means[i,1] = drugs[i]
    means[i,2] = mean(dist[i,])
  }

  # sorting of the matrix based on the mean distances: -> the drugs column represent the ranking
  means = means[order(as.numeric(means[,2]), decreasing = FALSE),]

  return(means)
}
```



Ranking Results Example



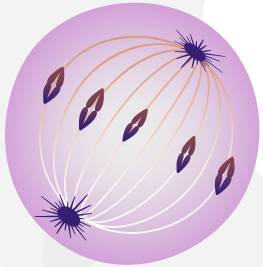


05
Validation and Results

Validation

First Qualitative Validation

79.17% of drugs known for the analysed diseases qualify in **high rankings** for those diseases



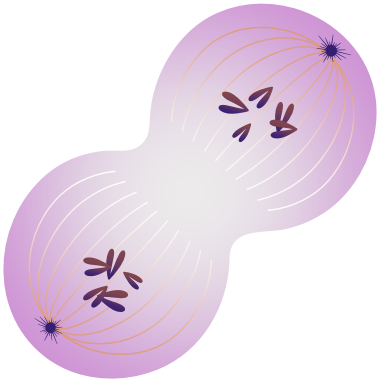
Mean Rank Analysis

Comparison between the mean rank achieved by **drugs** in **target diseases**'rankings and in **non target diseases**'rankings

3 out of **14** drugs **failed** this test

Interesting Insights

Among the **“new” drugs** that emerged from our analysis, we identified **interesting** factors



Drugs used for Cancer treatment

Such as ***Entinostat***, ***Vorinostat***, ***Belinostat*** in the top ranking for Propionic Acidemia.

Drugs linked to Alzheimer treatment

Such as **Gantenerumab**, found now linked to Methylmalonic Acidemia.

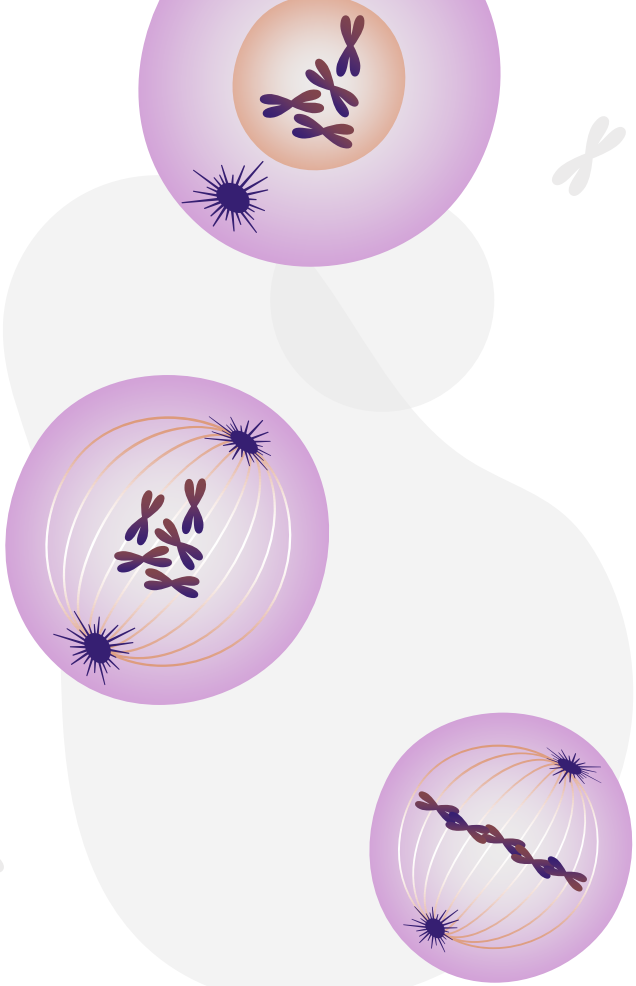
Drugs found in Rabies’Pathway

Rabies Immune Globuline, in the top ranking for Homocystinuria.

Drugs/Disease links mentioned in Scientific Literature

Vitamine **B12** and **Hydroxocobalamin**, found as the best drugs against Methylmalonic Acidemia.

source: PubMed



06

Future Plans

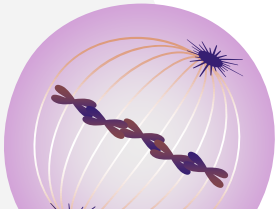
Future plans

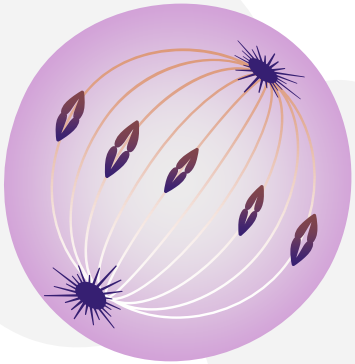
Test the method with different and more drugs

Update the project with less naive approaches

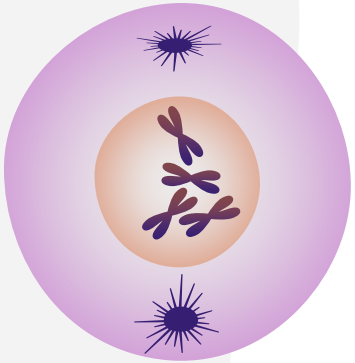
Biological study to confirm or reject the implications of rankings

- Hyperglicinemia
- Methylmalonic Acidemia





Thank you for your attention



Marzeddu Simone – Raffi Jacopo


slidesgo