

Network Science applied to Epilepsy

BioBytes Group

MO413 · 1º semester of 2024 · Institute of Computing · UNICAMP

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23/05/2024

Introduction

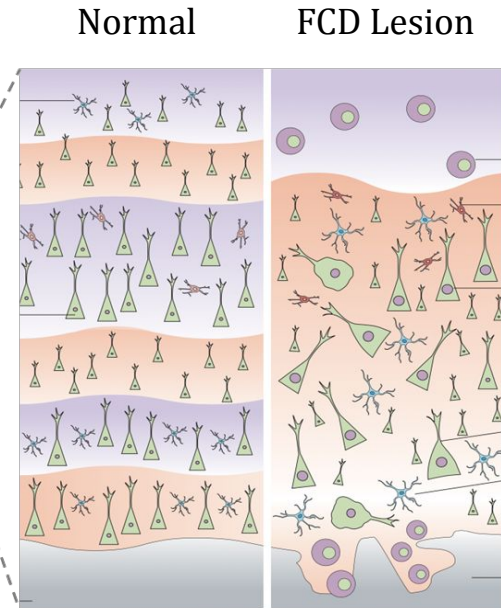


Epilepsy

- Epilepsy is a disease caused by the **synchronous**, **excessive** or **abnormal** activity of neuronal cells in the brain.

Focal Cortical Dysplasia

- Pediatric epilepsy
- Malformation of cortical development
- Cortical and cellular abnormalities



Sisodiya et al., Lancet Neur., 2009

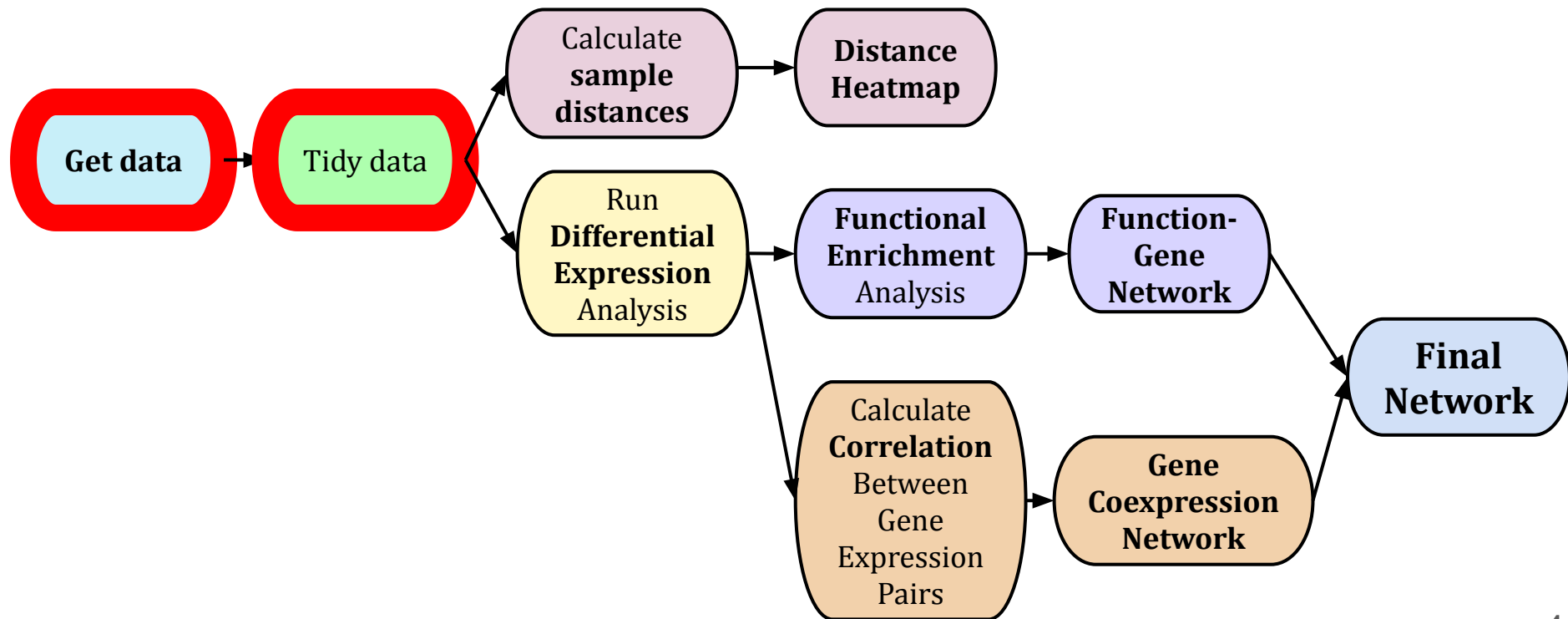
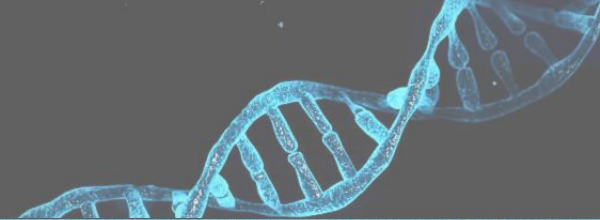
Proposal and Research Questions



Analyze the correlation between **genes** and **biological functions** in the analysis of differentially expressed genes in patients diagnosed with **epilepsy** caused by Focal Cortical Dysplasia type 2b (FCD 2b)

- What are the differentially expressed genes between **disease** and **control group**?
- Which **biological functions** are most represented in the disease? → **functional networks**
- How are these genes being regulated? → **regulation networks**

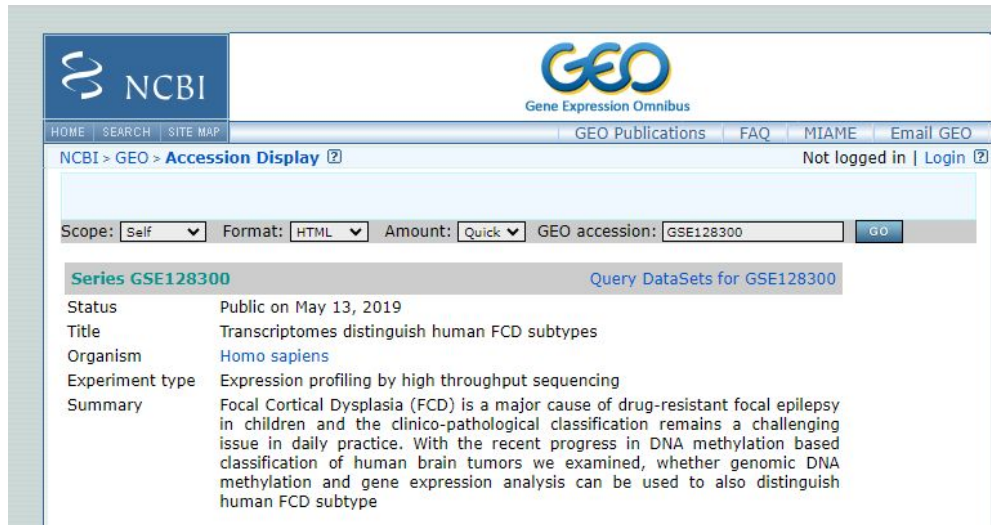
Workflow



Get Data

GSE128300

- RNA-seq data
- Expression matrix
- n = 5 FCD IIb
- n = 8 control
- Metadata obtained from the authors (.xlsx)

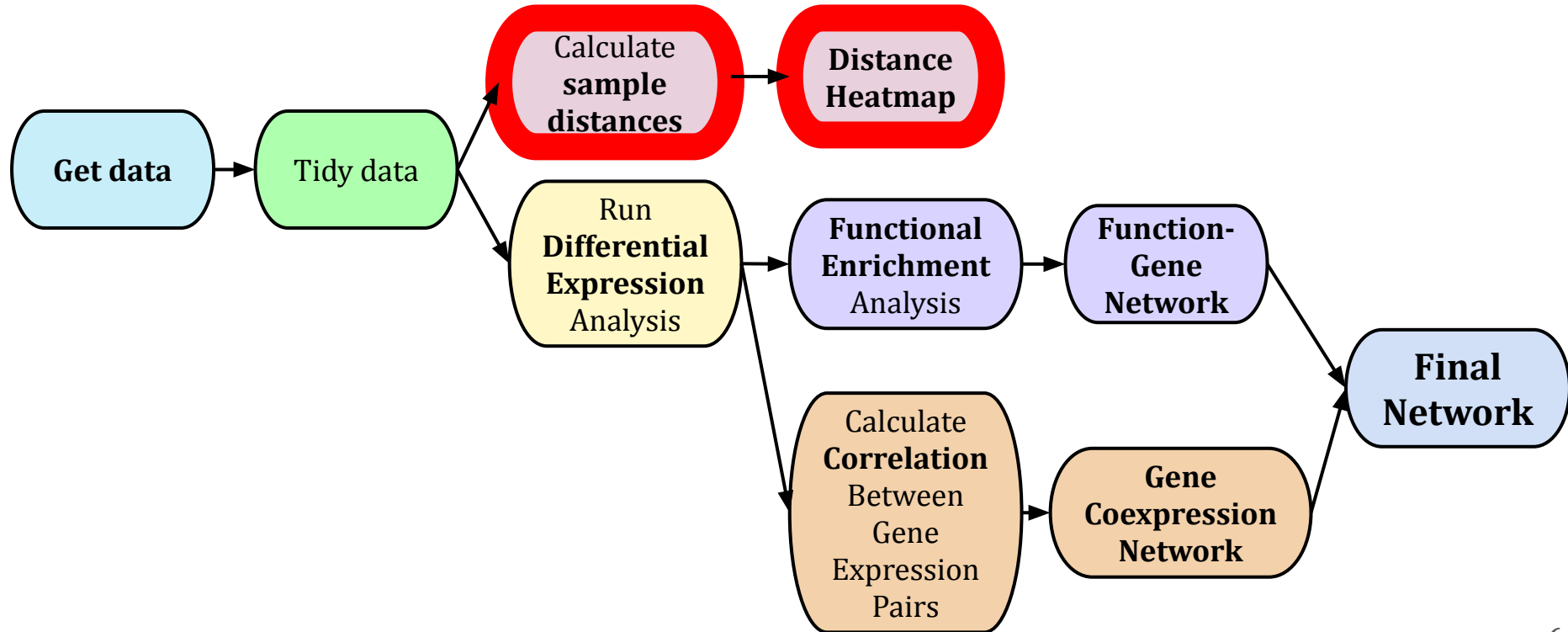
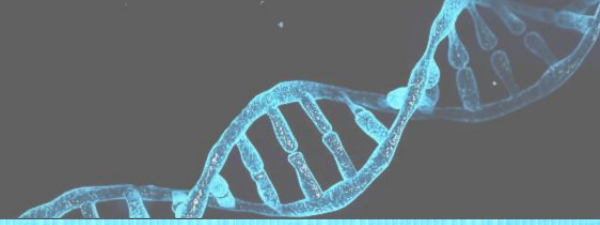


The screenshot shows the NCBI GEO Accession Display page for GSE128300. The page header includes the NCBI logo and the GEO Gene Expression Omnibus logo. Navigation links for HOME, SEARCH, and SITE MAP are present. The main content area displays the accession number GSE128300 and provides a link to query the data sets. The summary section includes the following information:

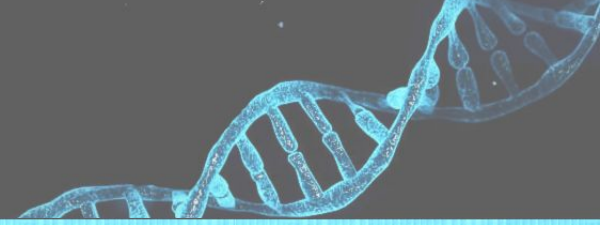
Status	Public on May 13, 2019
Title	Transcriptomes distinguish human FCD subtypes
Organism	Homo sapiens
Experiment type	Expression profiling by high throughput sequencing
Summary	Focal Cortical Dysplasia (FCD) is a major cause of drug-resistant focal epilepsy in children and the clinico-pathological classification remains a challenging issue in daily practice. With the recent progress in DNA methylation based classification of human brain tumors we examined, whether genomic DNA methylation and gene expression analysis can be used to also distinguish human FCD subtype

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE128300>

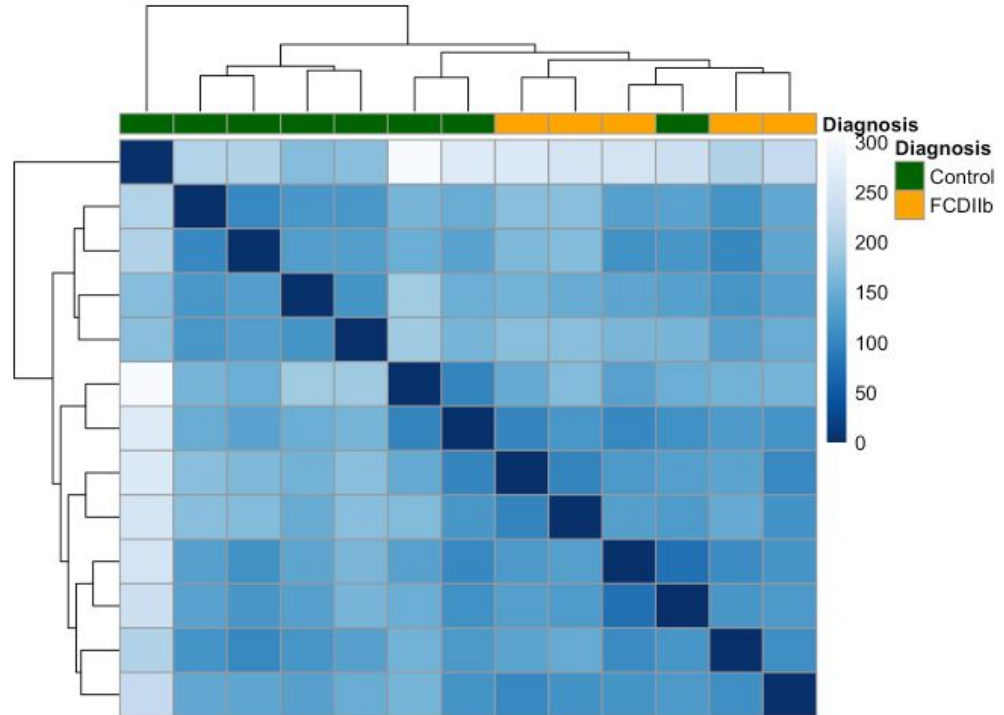
Workflow



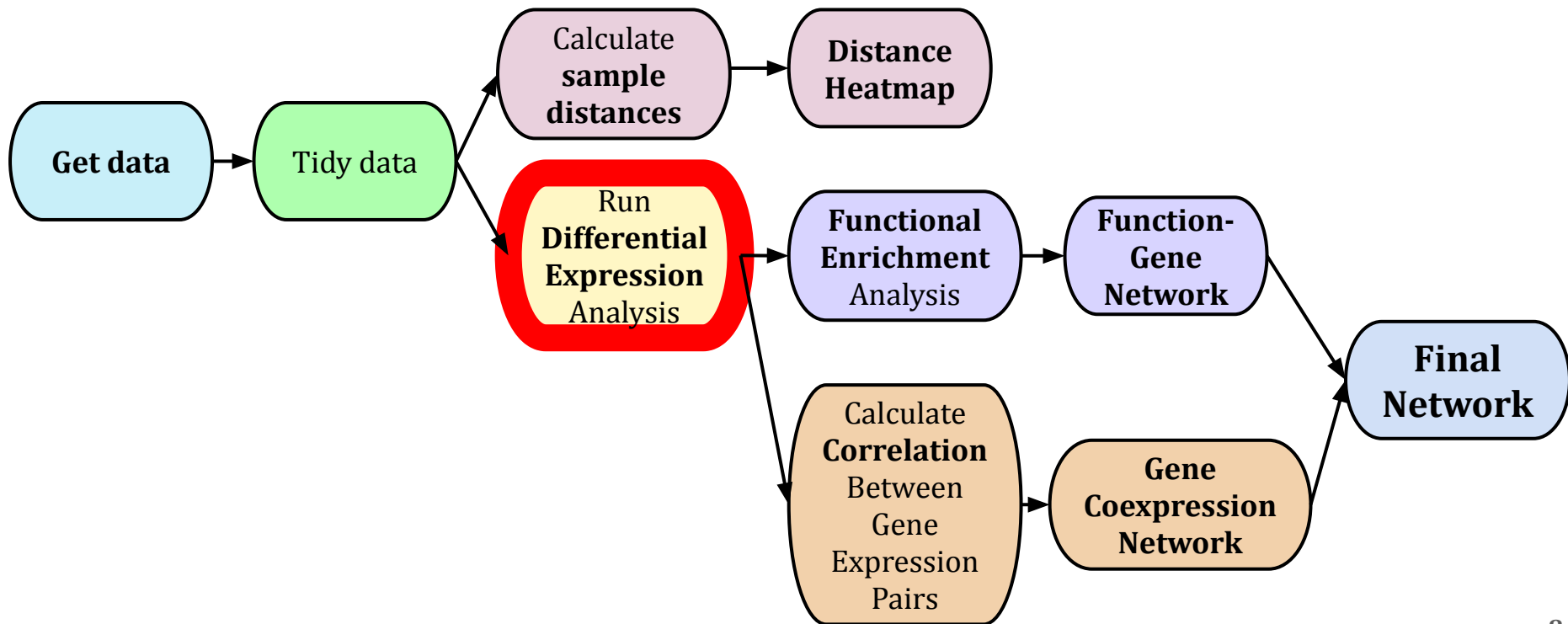
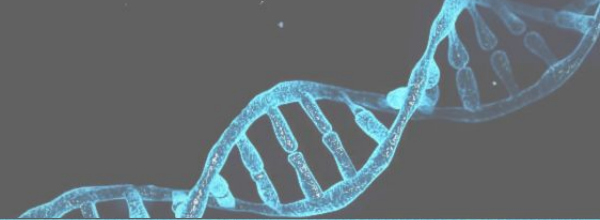
Sample Distances



- FCD IIb and controls are transcriptomically distinct



Workflow

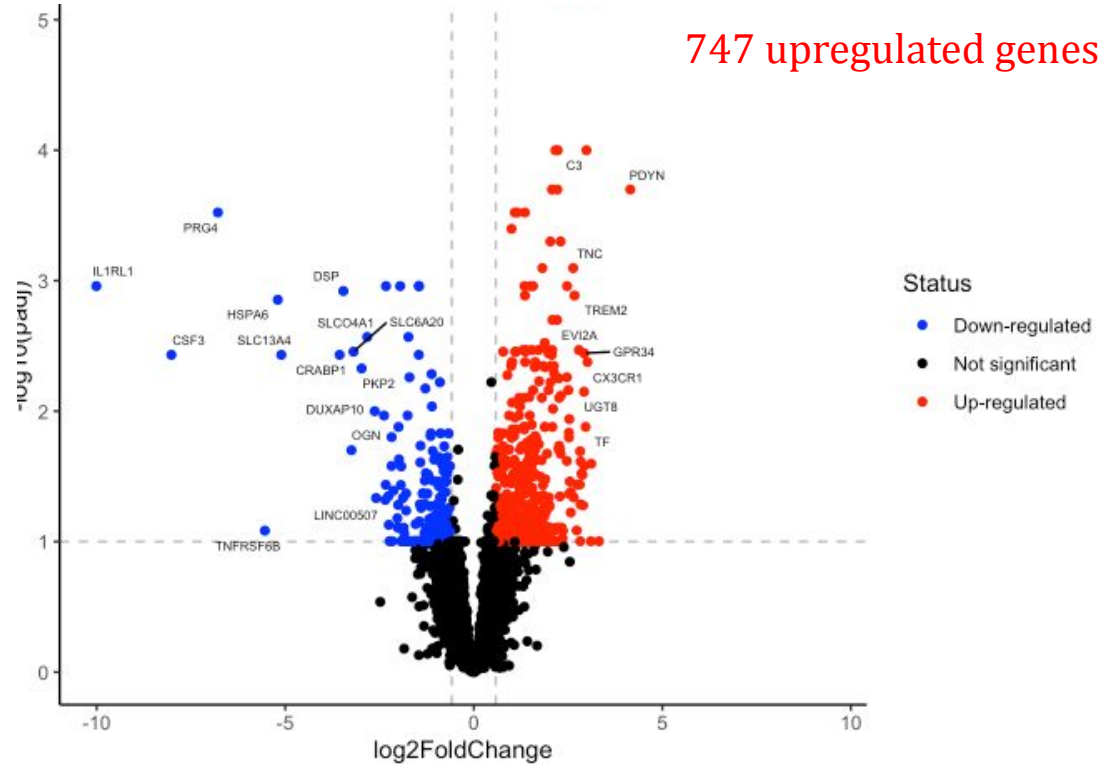


Differential Expression Analysis

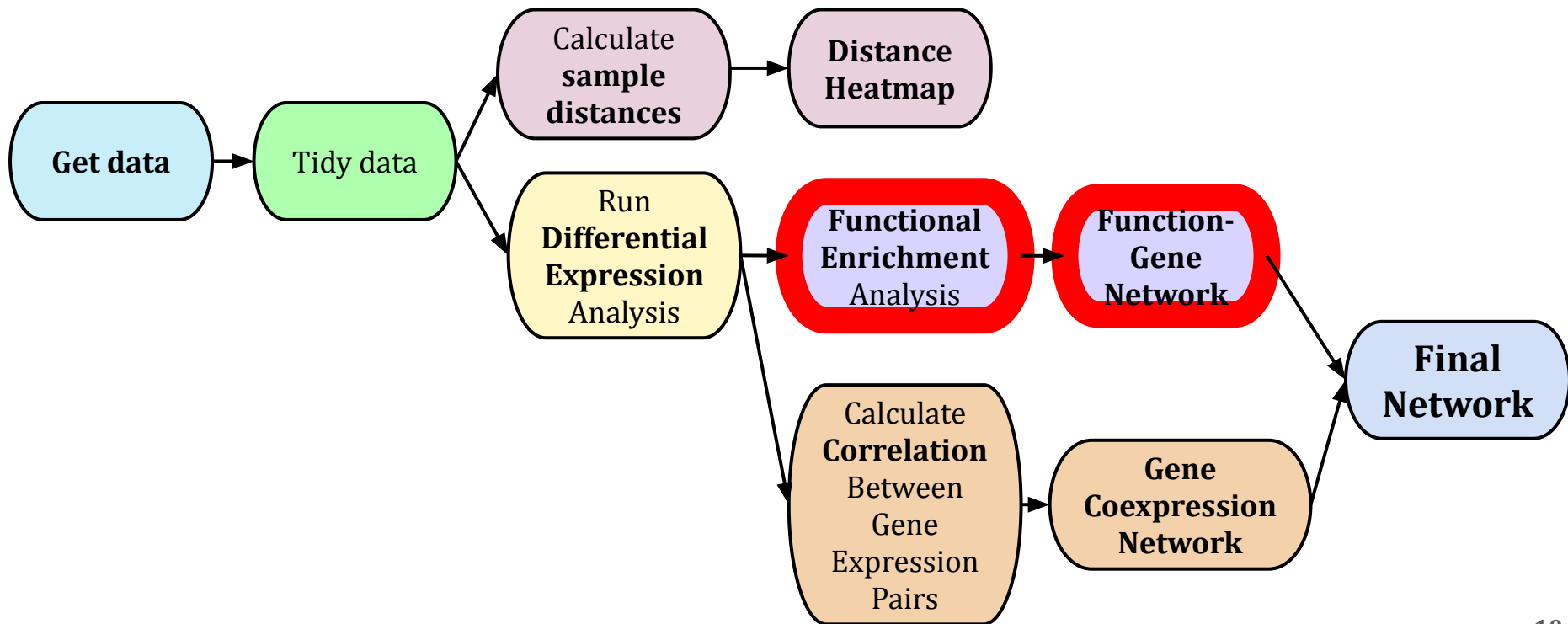
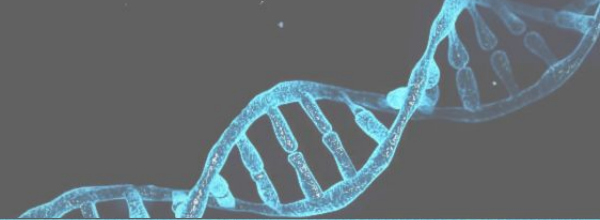


Criteria:

- $FC > 1.5$
- $padj < 0.1$



Workflow



Functional Enrichment Analysis

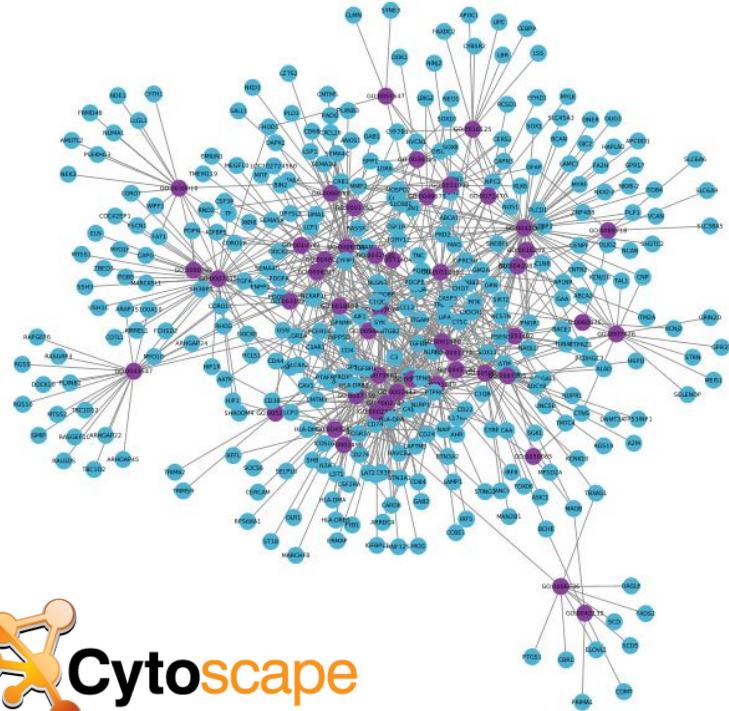


Bioconductor
OPEN SOURCE SOFTWARE FOR BIOINFORMATICS

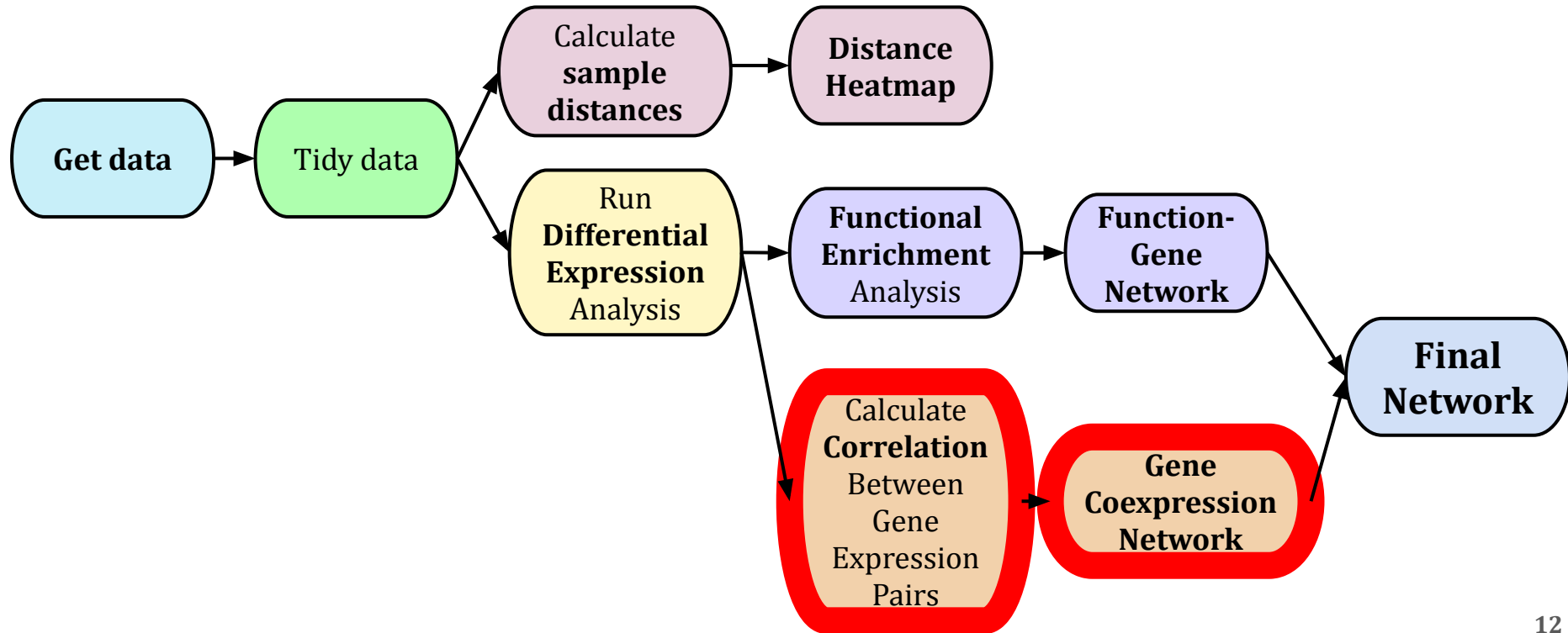
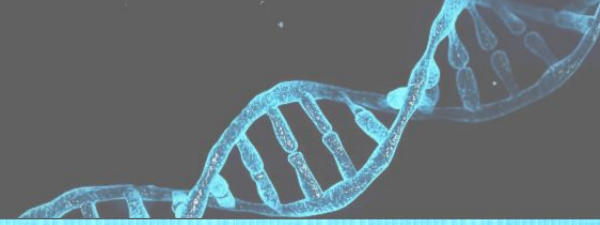


GENEONTOLOGY
Unifying Biology

- ClusterProfiler
 - EnrichGO
 - ont = "BP"



Workflow



Functional Enrichment Analysis

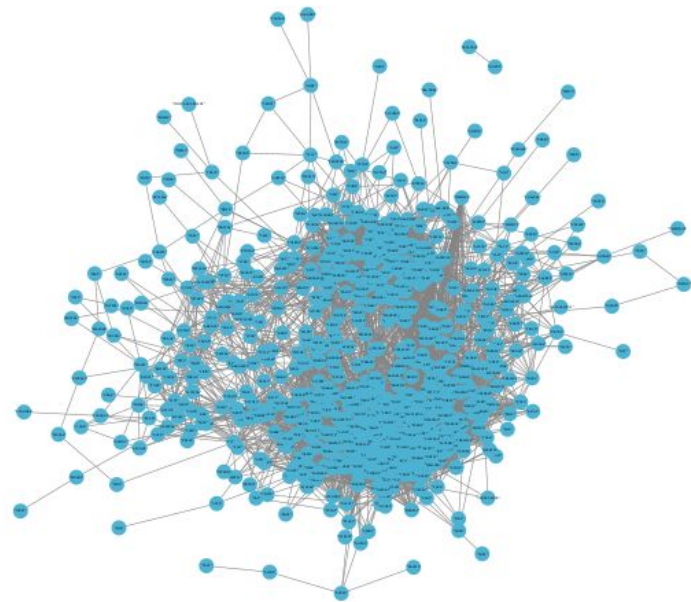


SciPy



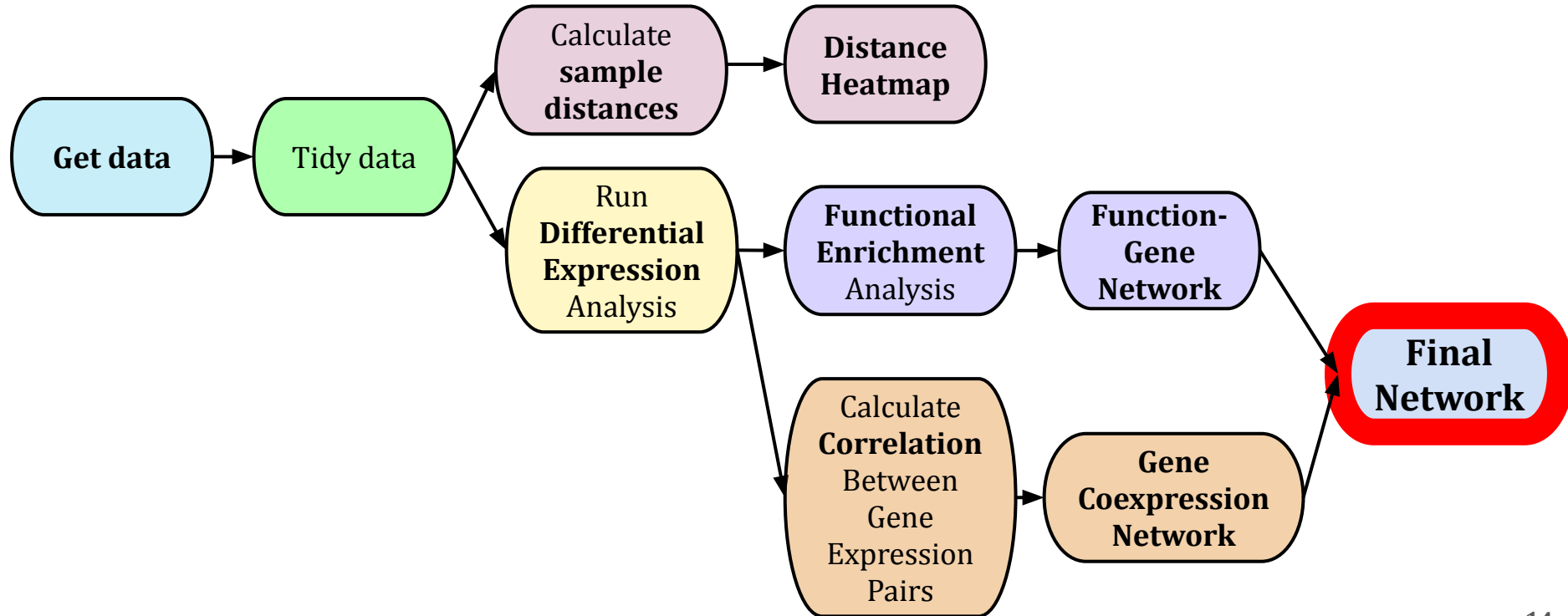
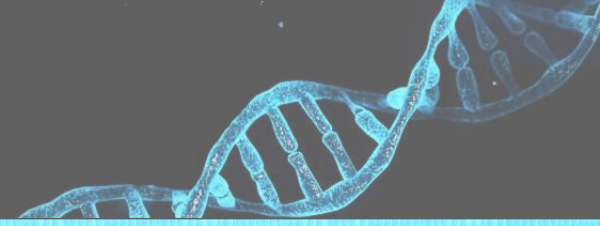
pandas

- Pearson Correlation
 - $P < 0.05$ and statistic > 0.85

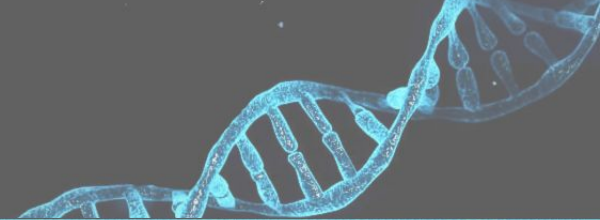


Cytoscape

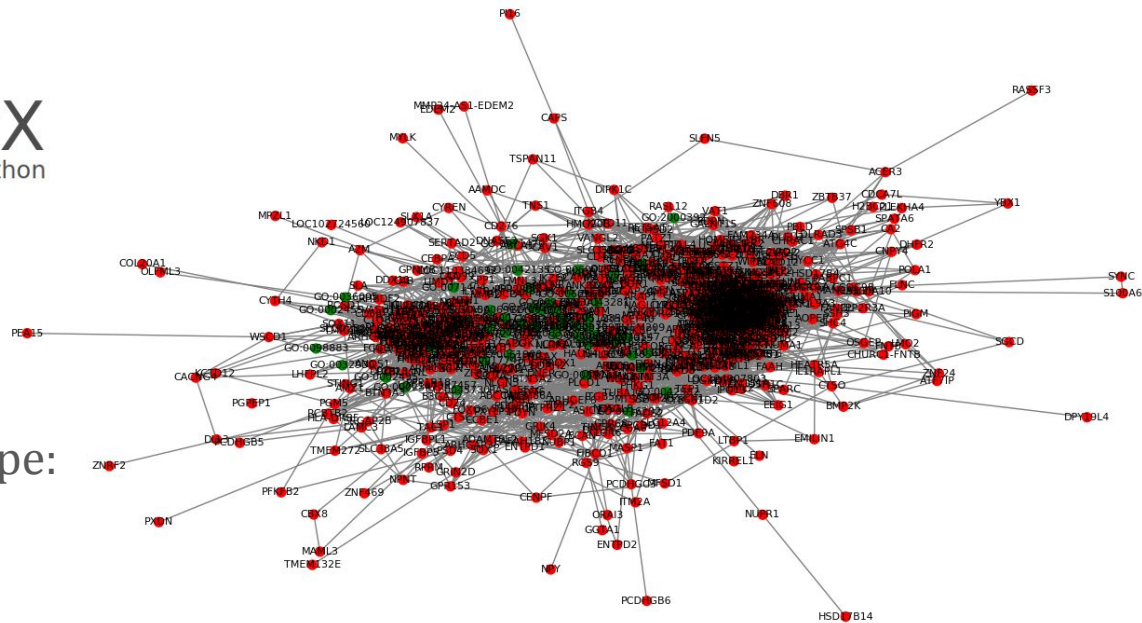
Workflow



Final Network

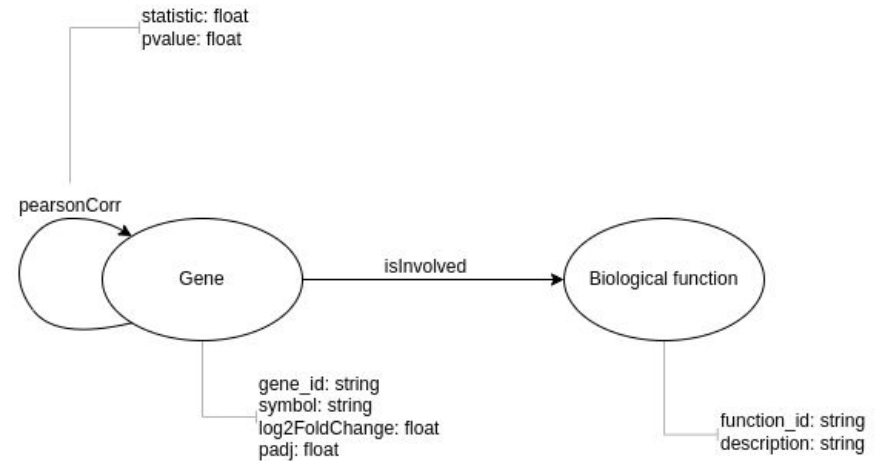


NetworkX
Network Analysis in Python



- NetworkX instead Cytoscape:
 - Need to use heterogeneous edges and nodes to perform analyzes

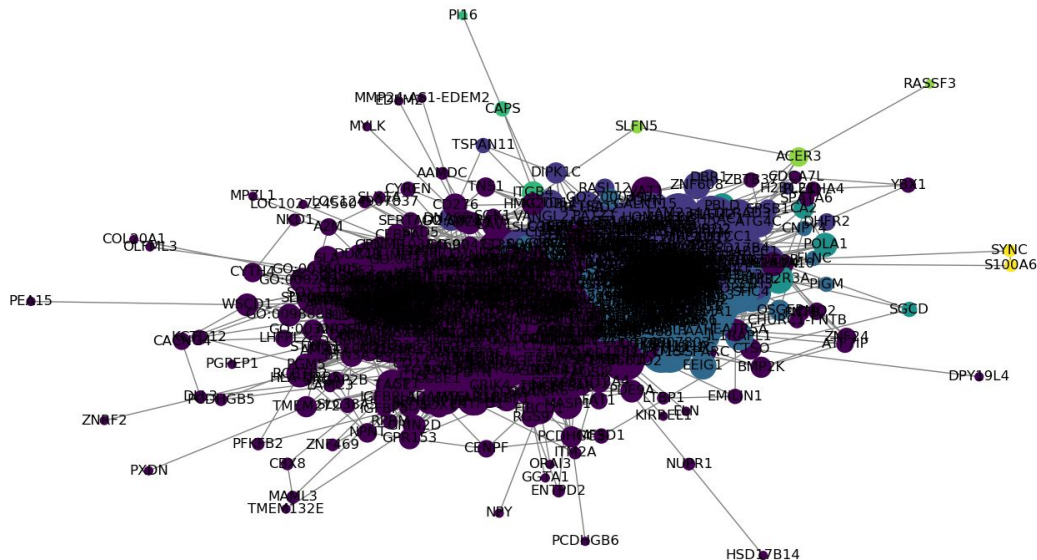
Logic Model



Preliminary analysis



- Community detection through the **greedy modularity communities** algorithm:
 - 6 communities

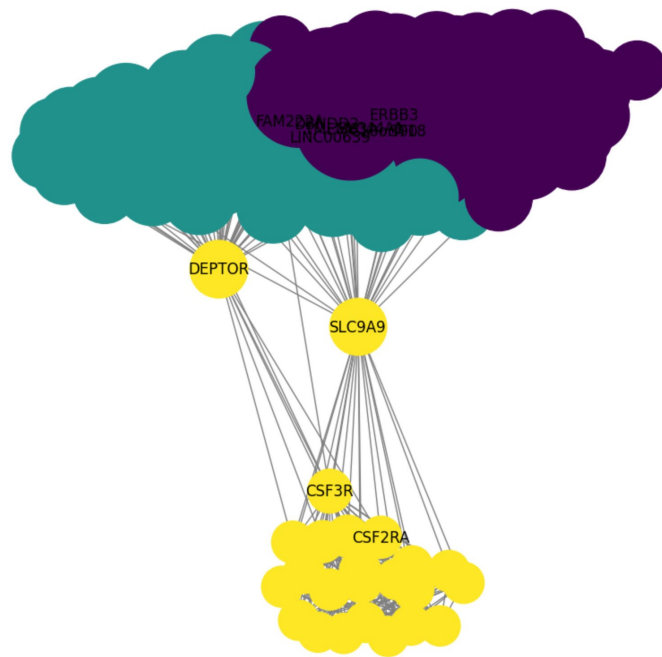


Preliminary analysis



- Node filter with **degree** greater than 70 applied:
 - 3 largest communities
 - Highest degree genes in each community:

Gene	Degree	Community
ERBB3	181	blue
DBNDD2	190	purple
DEPTOR	43	yellow



Future analysis and Problems



Future analysis:

- Use other algorithms to detect **communities**
- Identify which **biological functions** are most relevant
- Find most relevant genes/functions using **betweenness centrality**
- **Perturbation and robustness analysis**: assess how the removal or perturbation of specific genes affects network structure and function
- Improve visualization of analyzes by exporting graphs to **Cytoscape**

Problems:

- Difficulty using node and edge properties in Cytoscape and Neo4j
- Difficulty in visualizing the most important genes/functions, due to the large graph



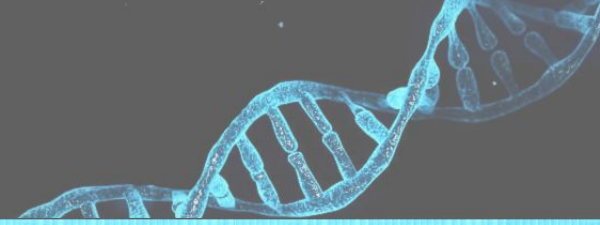
Thank You!
Questions?

References



- [1] - Patel P, Moshé SL. The evolution of the concepts of seizures and epilepsy: What's in a name? *Epilepsia Open*. 2020 Jan 10;5(1):22-35. doi: 10.1002/epi4.12375. PMID: 32140641; PMCID: PMC7049807.
- [3] - Drugs.com: <https://www.drugs.com/health-guide/seizure.html>
- [4] - Associations of B-Type Natriuretic Peptide and Its Coding Gene Promoter Methylation With Functional Outcome of Acute Ischemic Stroke: A Mediation Analysis - DOI:10.1161/JAHA.120.017499
- [5] - DESeq2 (Bioconductor Software Package):
<https://bioconductor.org/packages/release/bioc/html/DESeq2.html>

References



- [6] - Gene Ontology: <https://geneontology.org/>
- [7] - Cytoscape: <https://cytoscape.org/>
- [8] - Transcriptomes distinguish human FCD subtypes:
<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE128300>
- [9] - Brain image theme: Getty Images (Yuichiro Chino)
- [10] - DNA image theme: iStock (Shutter2U)