Leveraging Existing Biological Data and Making Sense of it

Finding, Accessing, Integrating and Reusing

Alberto Santos - Multi-omics Network Analytics

17 June 2025

Introduction

Multi-omics Network Analytics

Multimodal Data

Implementing tools to process, integrate, and analyse multimodal data. Diving into the benefits of harmonising multimodal data that converge to provide a comprehensive view of complex biological systems. Specifically we are interested in high-throughput multi-omics data generated using Mass spectrometry technology (proteomics and metabolomics) and metaomics data (metagenomics and metaproteomics).

Knowledge Graphs

Building High-quality Knowledge Graphs. Using and developing Knowledge Graph technologies and methods to structured data and to connect them to existing biological knowledge. These structures facilitate analysis and interpretation of complex data. We are contributing to a groundbreaking field by developing tools and methods to build, assess and investigate Knowledge Graphs and applying them to solve challenges in biology and health.

Graph Machine Learning

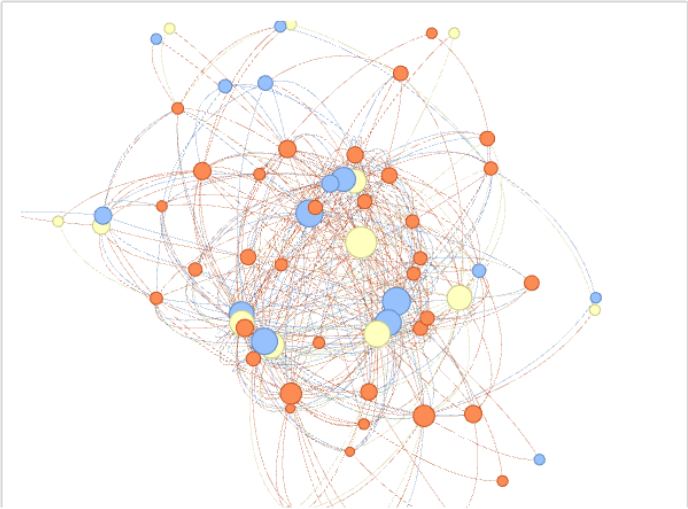
Developing and Applying Novel Methods on Graphs. Unleashing the power of Machine Learning on Graphs, a cutting-edge approach to extracting valuable insights from network data. We explore how this fusion of machine learning and graph theory helps to recognize patterns, generate predictions, and discovering new knowledge across a multitude of applications, including biological and medical networks.

Open Science

Data Science Democratisation. Focusing on data literacy training as a means to reduce inequality, and promoting open science by making all research, data content, and software open and accessible.

Microbial Communities

Exploring Microbial Communities and their Environments. Integrating multiple biological resources to unravel the assembly, interaction and adaptation mechanisms of microbial networks, offering insights into their functions and inpact on ecosystems, and how changes affect those communities.

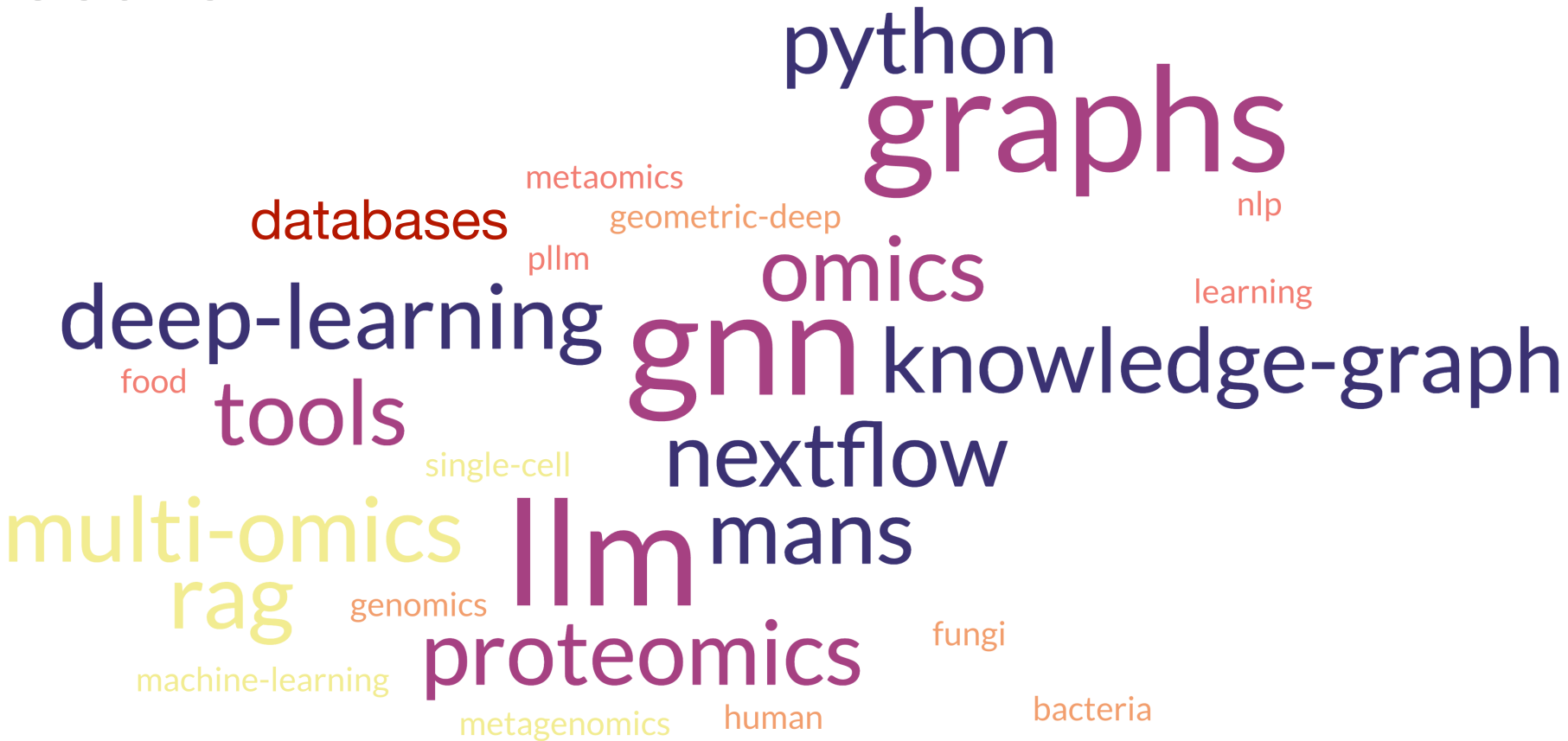


Clinical Computational Omics

Providing tools for the analysis and interpretation of clinical omics data. Integration of high-throughput omics data with computational and bioinformatics approaches to advance precision medicine and disease research. These projects aim to identify biomarkers, uncover disease mechanisms, and tailor treatments based on individual molecular profiles.

https://multiomics-analytics-group.github.io/

Research


python
graphs
metaomics
databases
geometric-deep
nlp
pllm
omics
learning
deep-learning
gnn
knowledge-graph
food
tools
nextflow
single-cell
multi-omics
llm
mans
rag
genomics
proteomics
fungi
machine-learning
metagenomics
human
bacteria

Objectives

- Show
  - The **value** of **Open** and **standardised data**
  - How to **generate** and **find** these data
  - How to **access** and **use** them
  - Some **examples**

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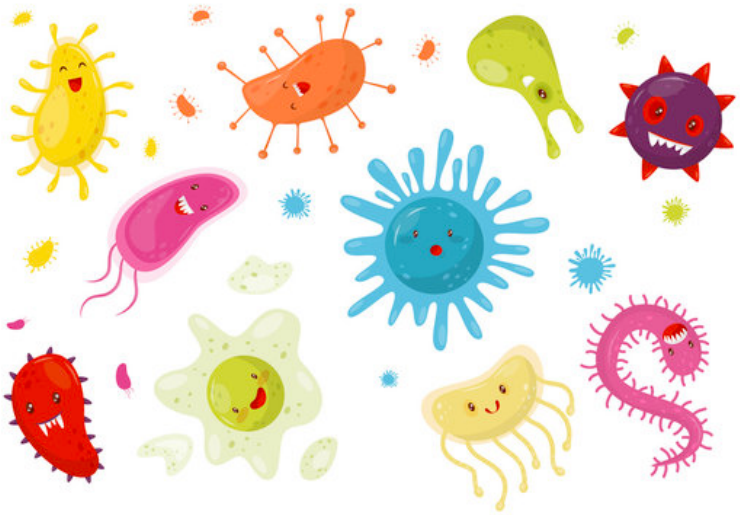
How to become a data parasite



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6258825/

Course website

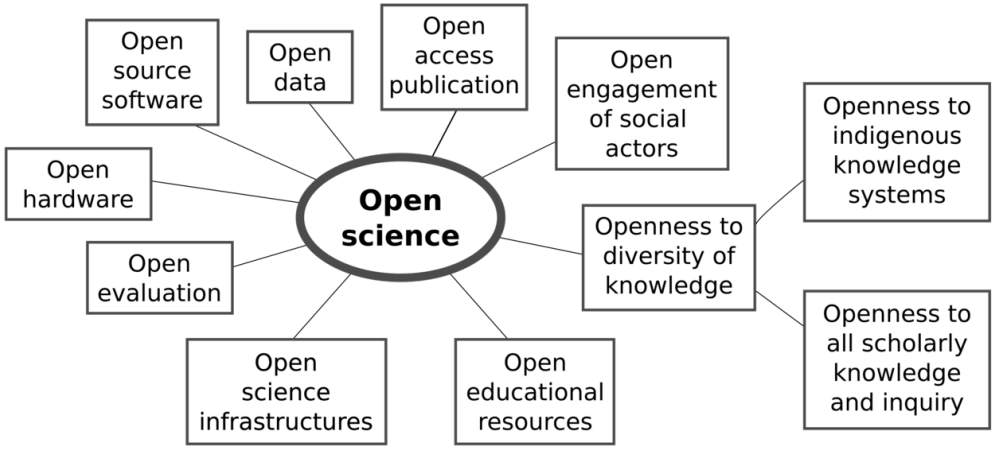
https://github.com/Multiomics-Analytics-Group/course_synthetic_biology_data

Open Science

What is Open Science

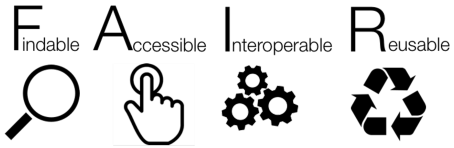
Impact, Contribution, Trust

- Make scientific research **accessible** to all levels of society:
  - Publications
  - Samples
  - **Methods**
  - **Software**
  - **Data**
- Advantages:
  - **Reproducibility** and **replicability**
  - Societal **responsibility** — publicly funded, publicly available
  - **Multi-purpose** of research outputs
- Disadvantages: concerns of data **misuse**



https://en.wikipedia.org/wiki/Open_science

FAIR Data and Software



- **F**indable and **A**ccessible
  - Add enough **metadata** — data about your data
  - Deposit your data in **public repositories** or make them available in **databases**
- **I**nteroperable:
  - Use **standard** and **open formats**
  - Provide **all data needed** to reproduce your analysis
- **R**eusable:
  - **Describe** your data well, e.g., good metadata but also
  - Attach a **license**

Minimum Information for Biological and Biomedical Investigations

Zenodo
Figshare
Pride
Metabolights
GEO
GitHub

Provide README files describing the data
Use descriptive column headers for the data tables

Challenges Sharing and Reusing

The marshmallow test — delayed gratification

- **Open does not mean FAIR**
- Requires an **effort**
- **Metadata** becomes **the most important data**
- In many cases there are **no standards or multiple ones**
- **Most** of the **data** out there **not FAIR**

https://imgflip.com/memegenerator

https://en.wikipedia.org/wiki/Stanford_marshmallow_experiment

Standardisation and Ontologies

- Data **standardisation** requires defining **terminologies** and **vocabularies** that:
  - Assign **unique identifiers** to entities/concepts such as proteins, genes, diseases
  - **Describe** those entities/concepts and **provide meaning**
  - **Relate** those concepts to other terms
  - Classify those entities/concepts into **categories**
- **Solution** —> **Ontologies**
- **Ontology**:

formal way of representing knowledge in which concepts are described both by their meaning and their relationship to each other

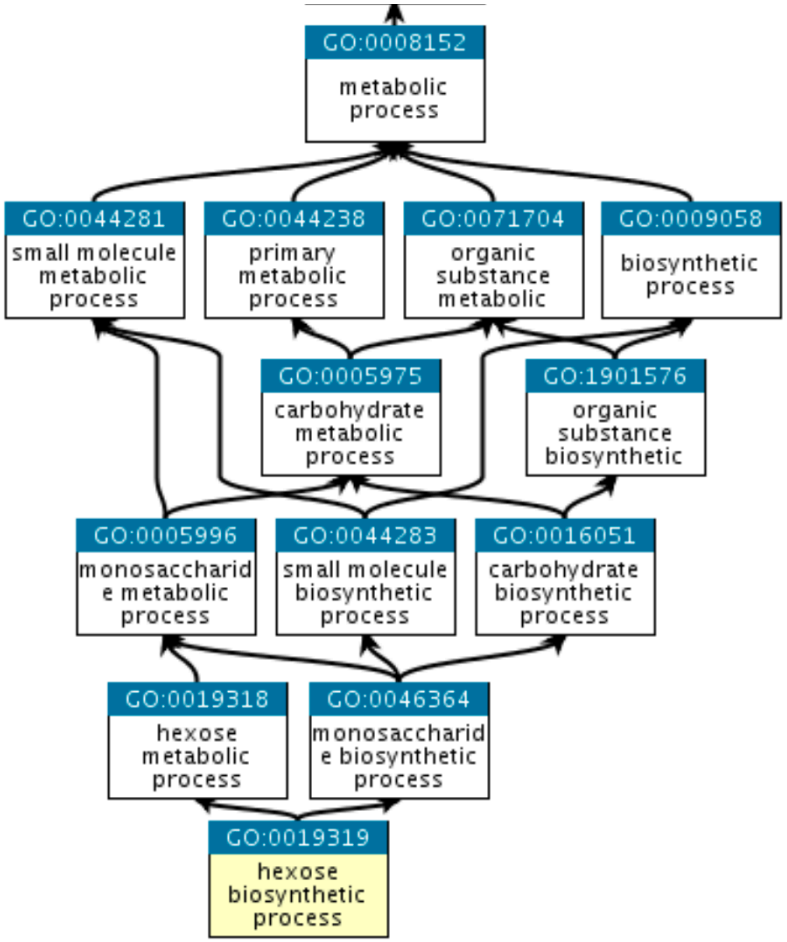
A collection of terms and their definitions for a specific domain

https://www.ebi.ac.uk/ols/index

https://www.nature.com/articles/nrg1295

Ontologies

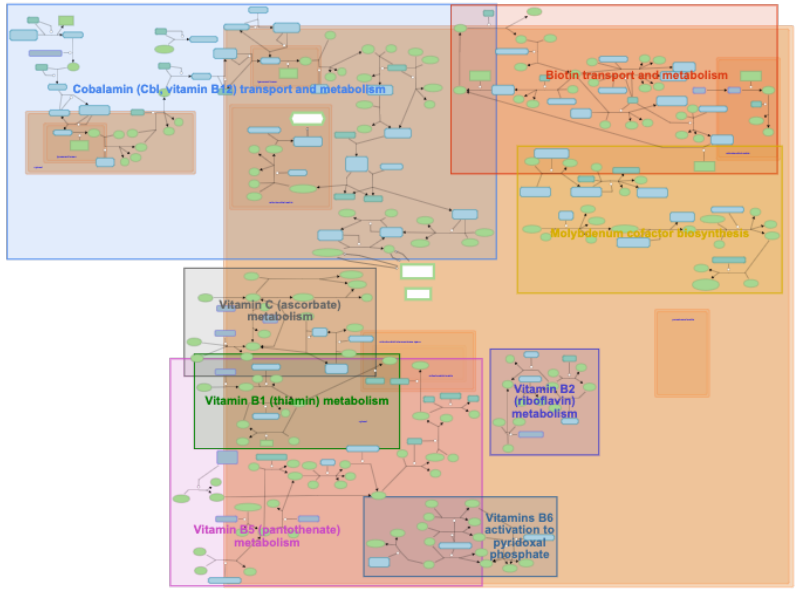
Gene Ontology



Disease Ontology

- disease
  - disease by infectious agent
    - bacterial infectious disease
    - fungal infectious disease
    - infective endocarditis
    - ornithine translocase deficiency
    - osteomyelitis
    - parasitic infectious disease
    - pelvic inflammatory disease
    - viral infectious disease
  - disease of anatomical entity
    - cardiovascular system disease
    - endocrine system disease
    - gastrointestinal system disease
    - hematopoietic system disease
    - immune system disease
    - integumentary system disease
    - musculoskeletal system disease
    - nervous system disease
    - reproductive system disease
    - respiratory system disease
    - thoracic disease
    - urinary system disease
  - disease of cellular proliferation
  - disease of mental health
  - disease of metabolism
  - genetic disease
  - physical disorder
  - syndrome

REACTOME Pathways

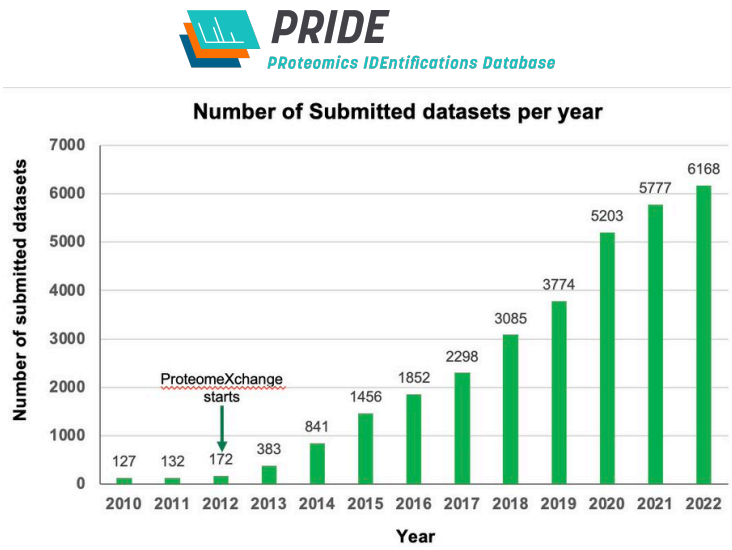


https://www.ebi.ac.uk/ols/ontologies

https://reactome.org/

http://geneontology.org/

Publicly Available Resources



- **Do not reinvent the wheel**
- **Extend** the **life** and **purpose** of publicly available **data**
- Build **in-silico hypotheses** before jumping into experiments (cheaper, higher success rate)
- **Download — Use — Test — Transform — Upload**
- **Growing number** of **resources** and **datasets** available

https://www.ebi.ac.uk/pride/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6258825/

Data Sources

NCBI

Organisms Database

- The **NCBI Taxonomy** database allows **browsing** of the **taxonomy** tree, which contains a classification of organisms
- Provides information about:
  - **Taxonomic identifier** for organisms
  - **Genomic overview**
  - Link-outs to **domain-specific databases**

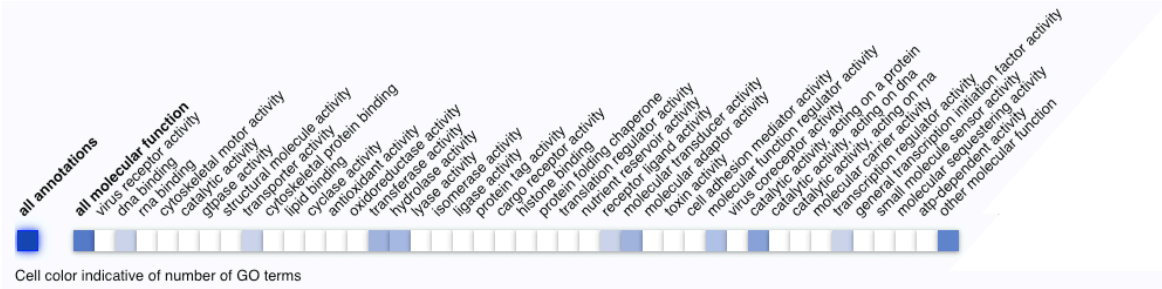
Entrez records			
Database name	Subtree links	Direct links	Links from type
Nucleotide	2,721,504	2,578,488	7,410
Protein	22,445,169	20,989,652	-
Structure	2,632	1,230	-
Genome	1	1	-
Popset	1,043	1,043	-
Conserved Domains	10	8	-
GEO Datasets	6,794	4,153	-
PubMed Central	111,167	111,167	-
Gene	128,094	3,304	-
SRA Experiments	41,306	33,055	-
GEO Profiles	141,600	141,600	-
Protein Clusters	7,547	7,547	-
Identical Protein Groups	3,556,802	3,524,631	-
BioProject	2,696	2,004	-
BioSample	56,942	49,071	15
Assembly	21,782	21,326	9
PubChem BioAssay	12,338	10,607	-
Taxonomy	383	1	-

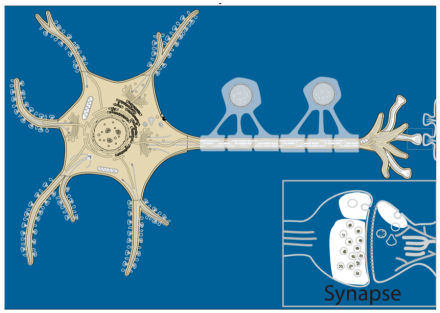
https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi

UniProt

Protein Database

- Comprehensive view on **proteins**
- Aggregates information about:
  - **Function**
  - **Sequence features**
  - **Subcellular localisation**
  - **Tissue expression**
  - **Disease association**
  - **Variants and PTMs**
  - **Interactions**
  - **Structure**



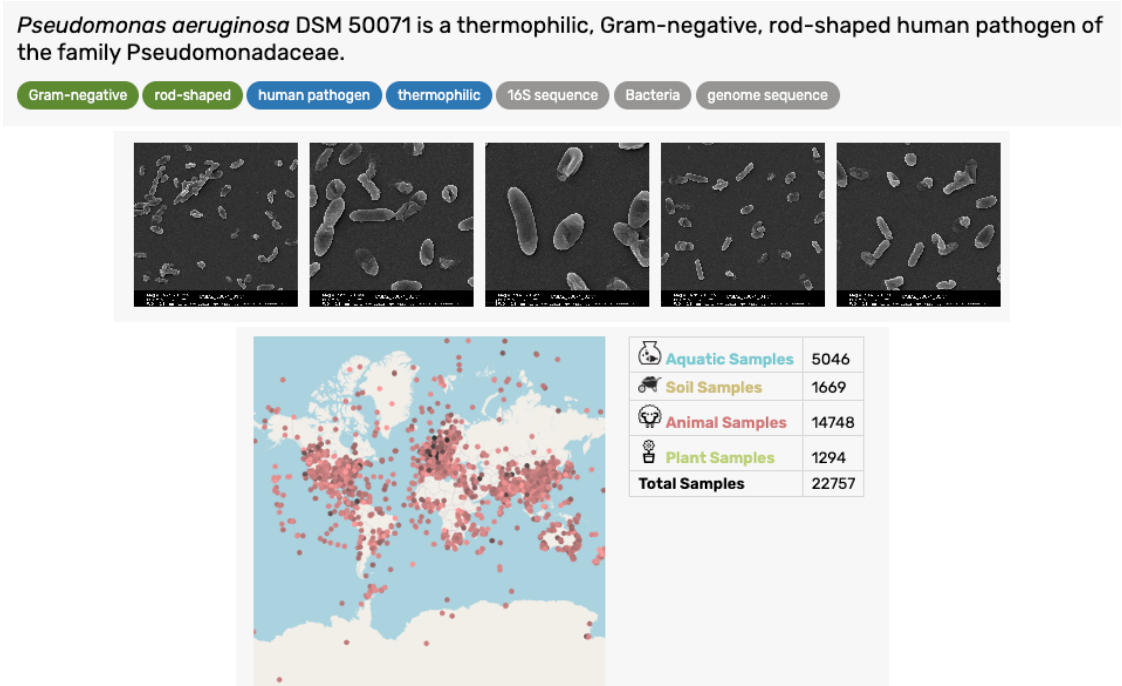


https://www.uniprot.org/

BacDive

Bacterial Database

- Largest database for **standardised bacterial phenotypic information**
- Collects information about:
  - **Bacterial classification**
  - **Morphology**
  - **Culture** and **growth** conditions
  - **Physiology** and **metabolism**
  - **Environment**
  - **Genome-based predictions**



https://bacdive.dsmz.de/

The Microbial Metabolites Database

MiMeDB

- The **human microbiome** is believed to produce or process **>55,000 different compounds –** many of which **affect** human **health**, **behavior** and **disease**
- **Microbes synthesise primary metabolites** required for their own survival, but they also **produce** other **compounds** arising **from substrates or host-derived food sources**

  E.g., microbes transform xenobiotics from food constituents, food additives, phytochemicals, drugs, cosmetics and other exogenous or man-made chemicals

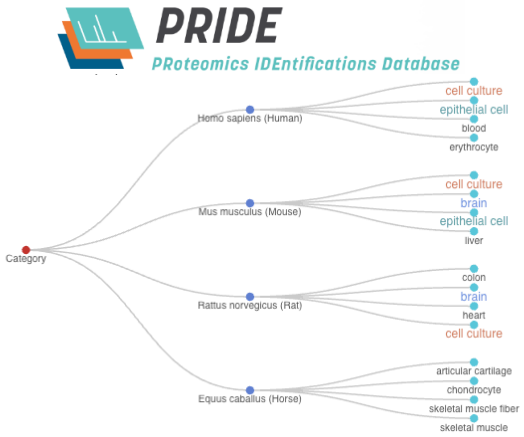
- **MiMeDB** is a **database** of **small molecule metabolites found** in the **human microbiome**
- Provides links between **metabolites**, **microbes**, **hosts**, **health** and **exposure** data

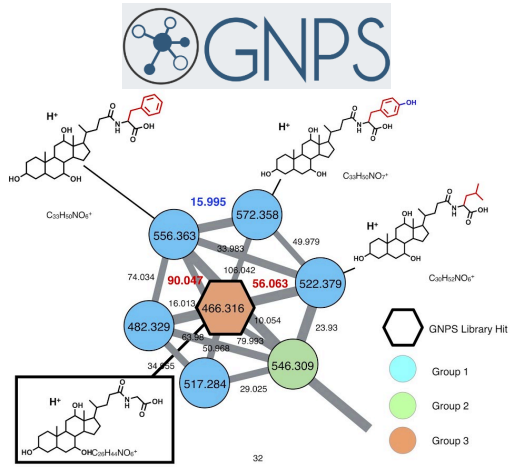
https://mimedb.org/

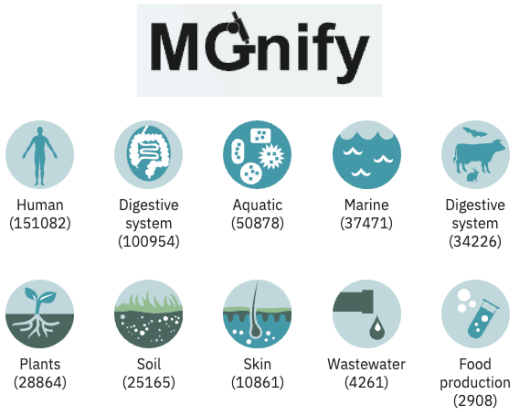
Meta-databases

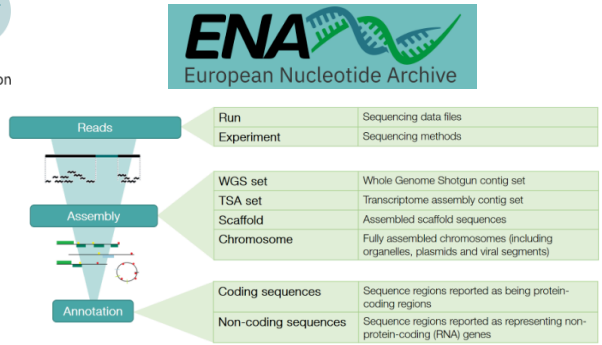
Data Repositories

- **PRIDE**: Mass Spectrometry-based (MS-based) Proteomics
- **GNPS:** MS-based Metabolomics
- **MGnify**: Microbiome data
- **ENA:** sequencing information, covering raw sequencing data, sequence assembly information and functional annotation





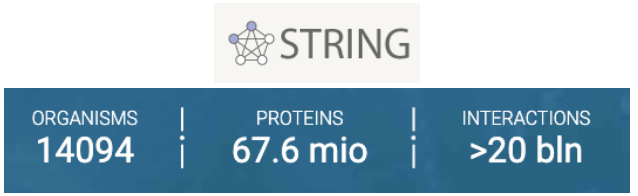




Protein-Protein Interactions

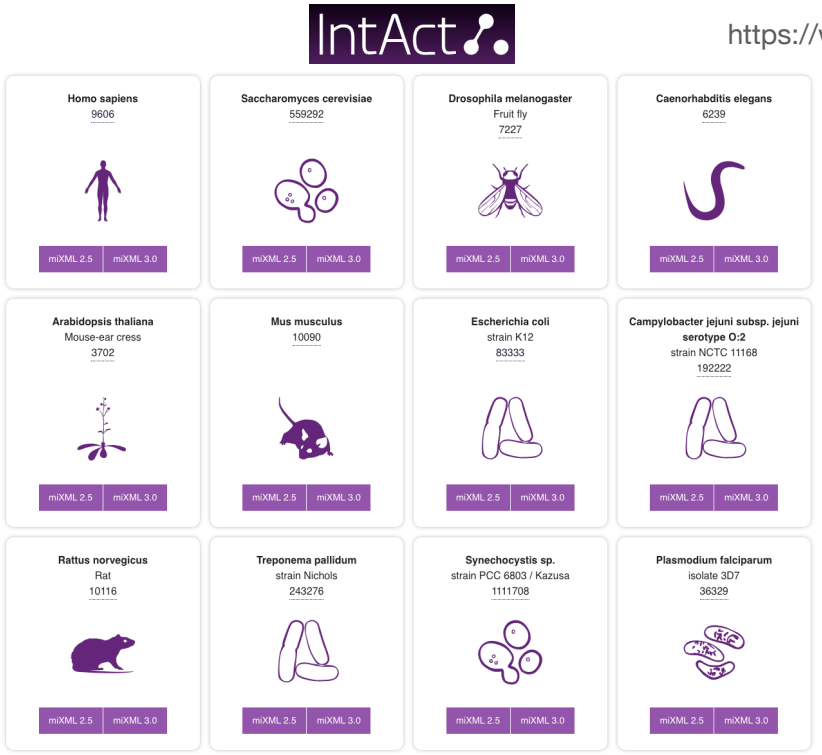
Interactions

- **STRING**: PPIs and functional enrichment



https://string-db.org/

- **Intact:** intra- and inter-species PPIs



https://www.ebi.ac.uk/intact

Other Resources

ALEdb 1.0: a database of mutations from adaptive laboratory evolution experimentation https://aledb.org/

Web of microbes (WoM): a curated microbial exometabolomics database for linking chemistry and microbes https://metatlas.nersc.gov/wom/project-begin.view

MicroPhenoDB Associates Metagenomic Data with Pathogenic Microbes, Microbial Core Genes, and Human Disease Phenotypes http://www.liwzlab.cn/microphenodb

MASI: microbiota—active substance interactions database http://www.aiddlab.com/MASI/

iModulonDB: a knowledgebase of microbial transcriptional regulation derived from machine learning https://imodulondb.org/index.html

MIBiG 3.0: a community-driven effort to annotate experimentally validated biosynthetic gene clusters https://mibig.secondarymetabolites.org/

FooDB: most comprehensive resource on food constituents, chemistry and biology https://foodb.ca/

Accessing Data

GUI vs API

Graphical **U**ser **I**nterface

- **View** the data
- **Facilitates** initial work
- Limited to the **interface**

Application **P**rogramming **I**nterface

- **Access** the data
- **Free** to do whatever you want
- Limited to **provided data**

Jupyter Notebooks

https://jupyter.org/

- **Web-based development environment** for **creating**, **running** and **sharing Python** (and other languages) code
- A **notebook** is an interactive document that combines **live code**, **equations**, **text or markdown**, and **visualisations** (output of your code)
- Notebooks are divided into **cells** that **run sequentially**! (Need to pay attention)
- It **requires** having **Python installed** on your local machine

Colab Notebooks

https://research.google.com/colaboratory/faq.html

- Google Colab is based on **Jupyter Notebook** open source project **hosted on Google's servers**
- Advantages:
  - Requires **no setup** to use (no python installation)
  - Provides **free** access to **computing resources** on Google's servers including GPUs
  - **Notebooks** can be **shared** just as you would with Google Docs or Sheets.
  - You can **import** existing **Jupyter notebooks**
- **Own data and notebooks** need to be accessed through **Google Drive** — Need Google account

Example: https://colab.research.google.com/github/biosustain/data_club/blob/main/notebooks/data_annotation/uniprot_api-solved.ipynb

Sharing Data

Community Repositories

Working with Data

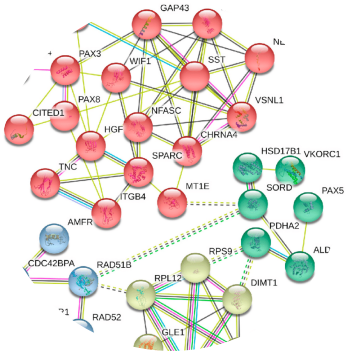
Graphs

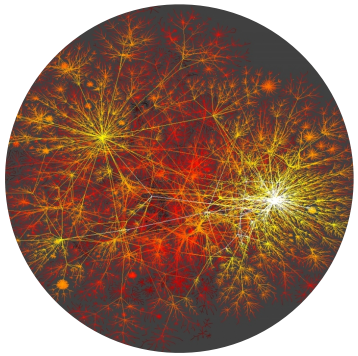
What is a Graph/Network?

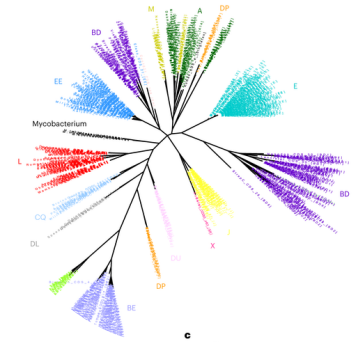
- Data structures of **components (nodes)** connected by **relationships (edges)**

Social networks

Biological networks



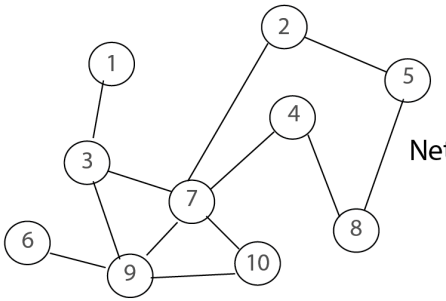




Graphs

Node

Edge



Network

$$\begin{bmatrix}
0&0&1&0&0&0&0&0&0&0\\
0&0&0&0&1&0&1&0&0&0\\
1&0&0&0&0&0&1&0&1&0\\
0&0&0&0&0&0&1&1&0&0\\
0&1&0&0&0&0&0&1&0&0\\
0&0&0&0&0&0&0&0&1&0\\
0&1&1&1&0&0&0&0&1&1\\
0&0&0&1&1&0&0&0&0&0\\
0&0&1&0&0&1&1&0&0&1\\
0&0&0&0&0&0&1&0&1&0
\end{bmatrix}$$

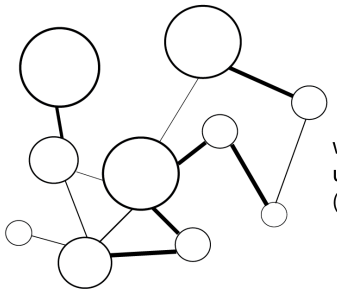
Adjacency matrix

weighted nodes (size)

weighted edges (thickness)

undirected edge

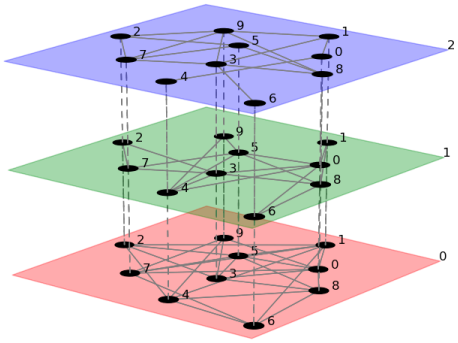
directed edge

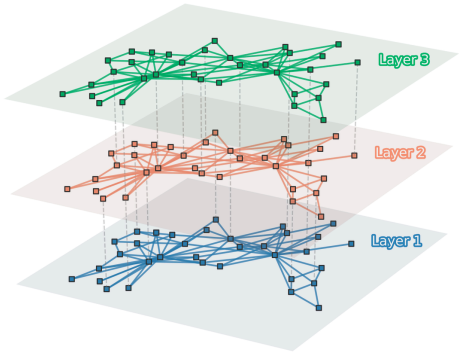


weighted
undirected network
(thickness)

$$\begin{bmatrix}
0&0&w_{1,3}&0&0&0&0&0&0&0\\
0&0&0&0&0&w_{5,7}&0&0&0&0\\
w_{1,3}&0&0&0&0&0&w_{7,8}&0&0&0\\
0&0&0&0&0&0&w_{7,9}&w_{7,10}&0&0\\
0&w_{2,5}&0&0&0&0&0&w_{8,10}&0&0\\
0&0&0&0&0&0&0&0&w_{9,10}&0\\
0&0&w_{3,7}&w_{3,9}&0&0&0&0&w_{9,10}&w_{9,10}\\
0&0&0&w_{4,7}&w_{4,9}&0&0&0&0&0\\
0&0&w_{6,9}&0&0&w_{6,9}&w_{7,9}&0&0&w_{9,10}\\
0&0&0&0&0&0&w_{7,10}&0&w_{9,10}&0
\end{bmatrix}$$

Weighted
adjacency matrix





Why Graphs?

- These structures allow:
  - Quick **integration** of **heterogeneous data** based on relationships
  - **Graph theory** methods can be used to **analyse** and **interpret** data, e.g., topological properties can be used to explain:
    - The possible **role** of specific components
    - The **flow** of information
    - The **robustness** of the system
- **Visualize** data

How to Analyse Graph Structures

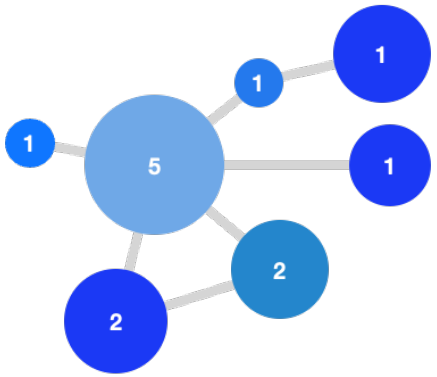
Using and Analysing Relationships

- **Graph Theory**: algorithms that allow you to extract relevant information from the topology of the graph.
  - **Topological Features:** Centrality, degree, clustering, etc.
- **Graph Machine Learning**:
  - Embeddings
  - Graph Neural Networks

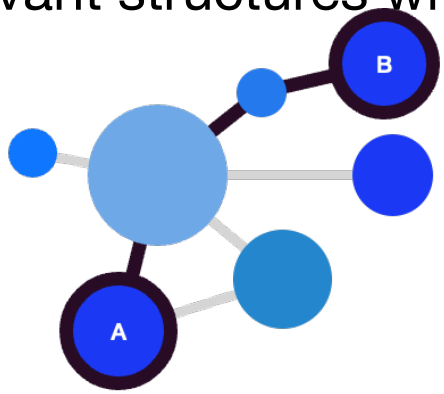
https://huggingface.co/blog/intro-graphml

Graph Theory — Some Topological Properties

Topological properties can help extract meaningful information and identify relevant structures within the network

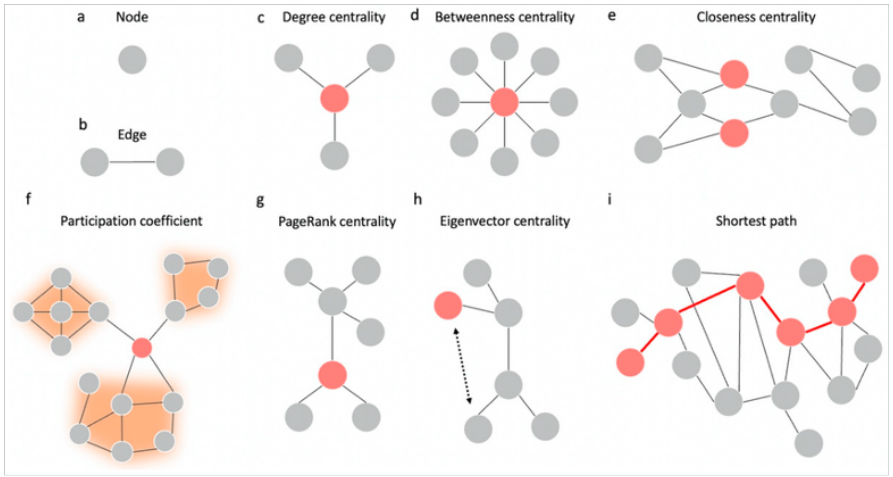


Degree

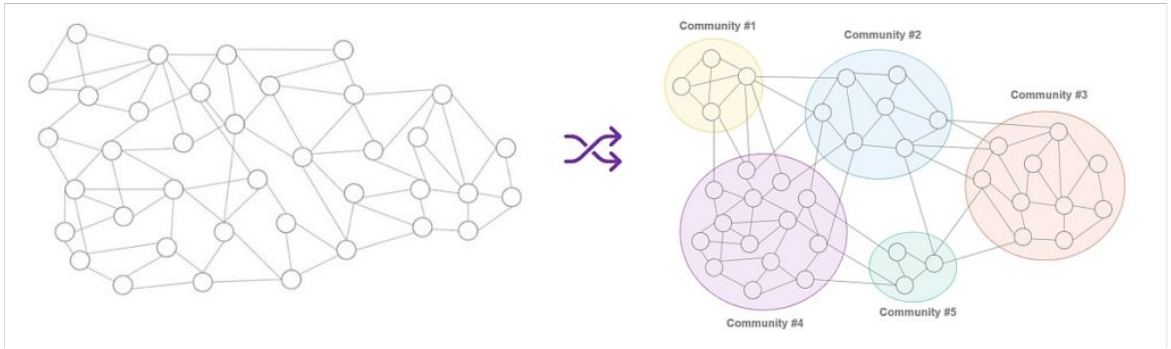


Shortest path

Centrality



Clustering



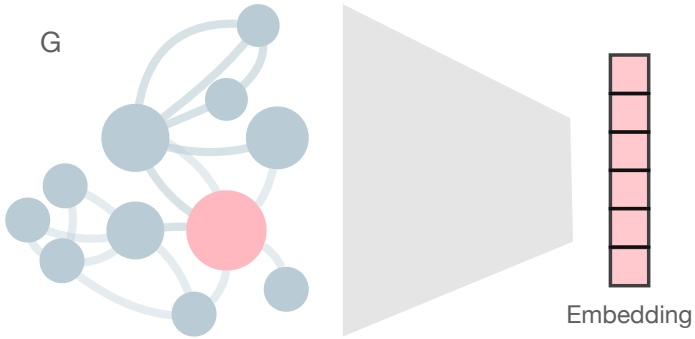
https://timbr.ai/community-detection-algorithm/

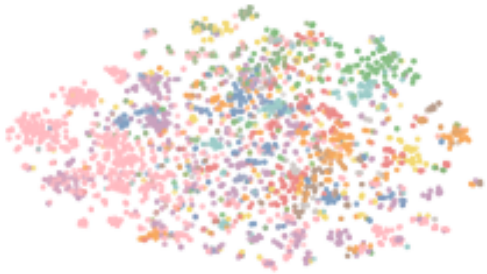
Graph Theory Measures and Their Application to Neurosurgical Eloquence. Cancers 2023

Embeddings

Representing graph structures

- **Large biomedical networks** require **high computation and space** —> **dimensionality reduction** techniques to represent nodes and edges
- **Graph Embedding**: **graphs**, **nodes** and **edges** represented as **numerical features** in a low dimensional space
- Use for:
  Node classification
  Node recommendation
  Link prediction
- Methods:
  - Shallow/Walk-based approaches: Node2Vec, Path2Vec, etc.
  - Graph Neural Networks
- **Python libraries:** NetworkX, DGL, StellarGraph, PyTorch Geometric



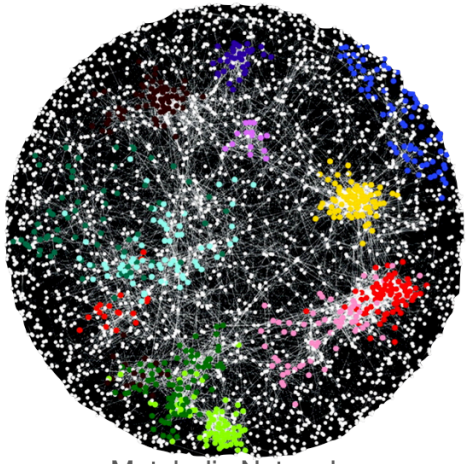


https://www.nature.com/articles/s41467-022-33026-0

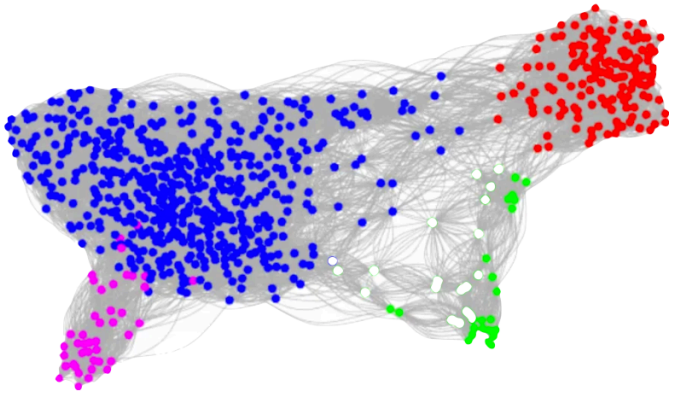
Graphs in Biology

https://towardsdatascience.com/umap-for-data-integration-50b5cfa4cdcd
http://snap.stanford.edu/deepnetbio-ismb/ipynb/Human+Disease+Network.html
https://cytoscape.org/cytoscape-tutorials/presentations/ppi-tools1-2017-mpi.html#/
https://en.wikipedia.org/wiki/Metabolic_network
https://www.scienceandfood.org/the-flavor-network/

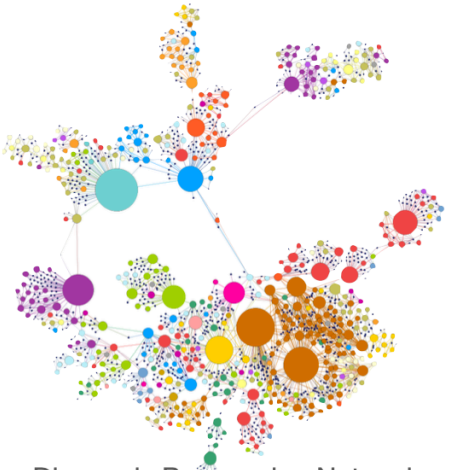
Protein-protein Interaction Networks



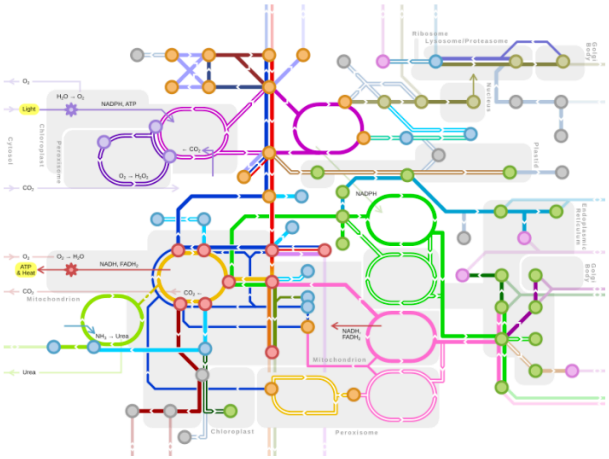
Single cell Networks



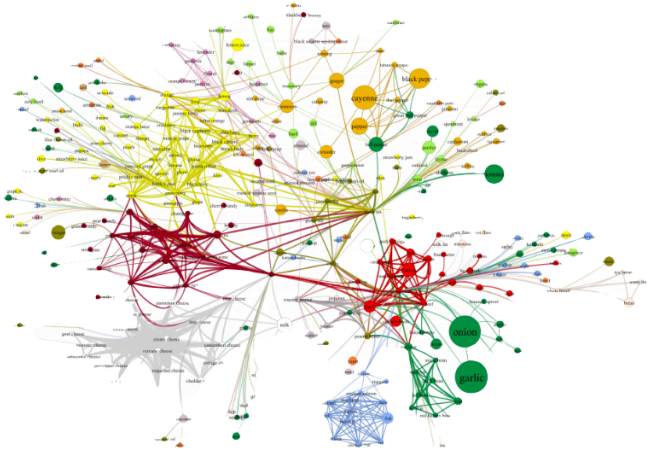
Disease Networks



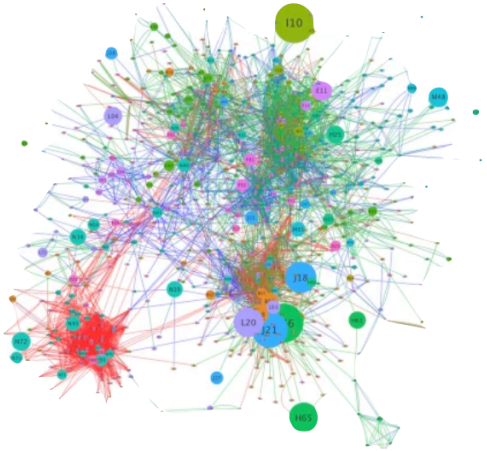
Metabolic Networks



Food Networks

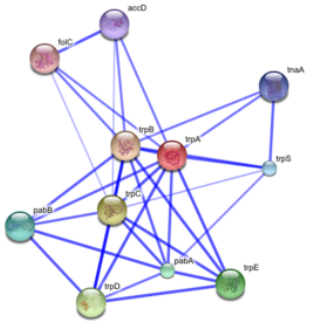


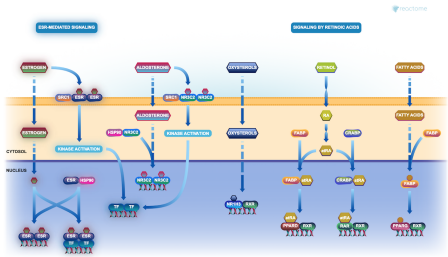
Diagnosis Progression Networks

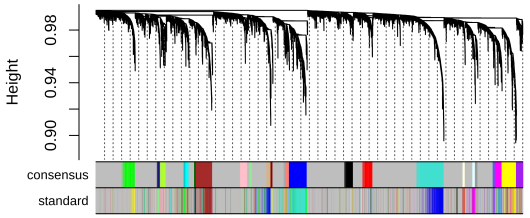


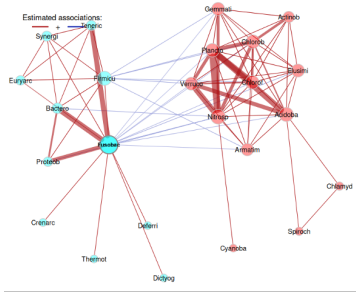
How to Build a Graph

Data to Graph





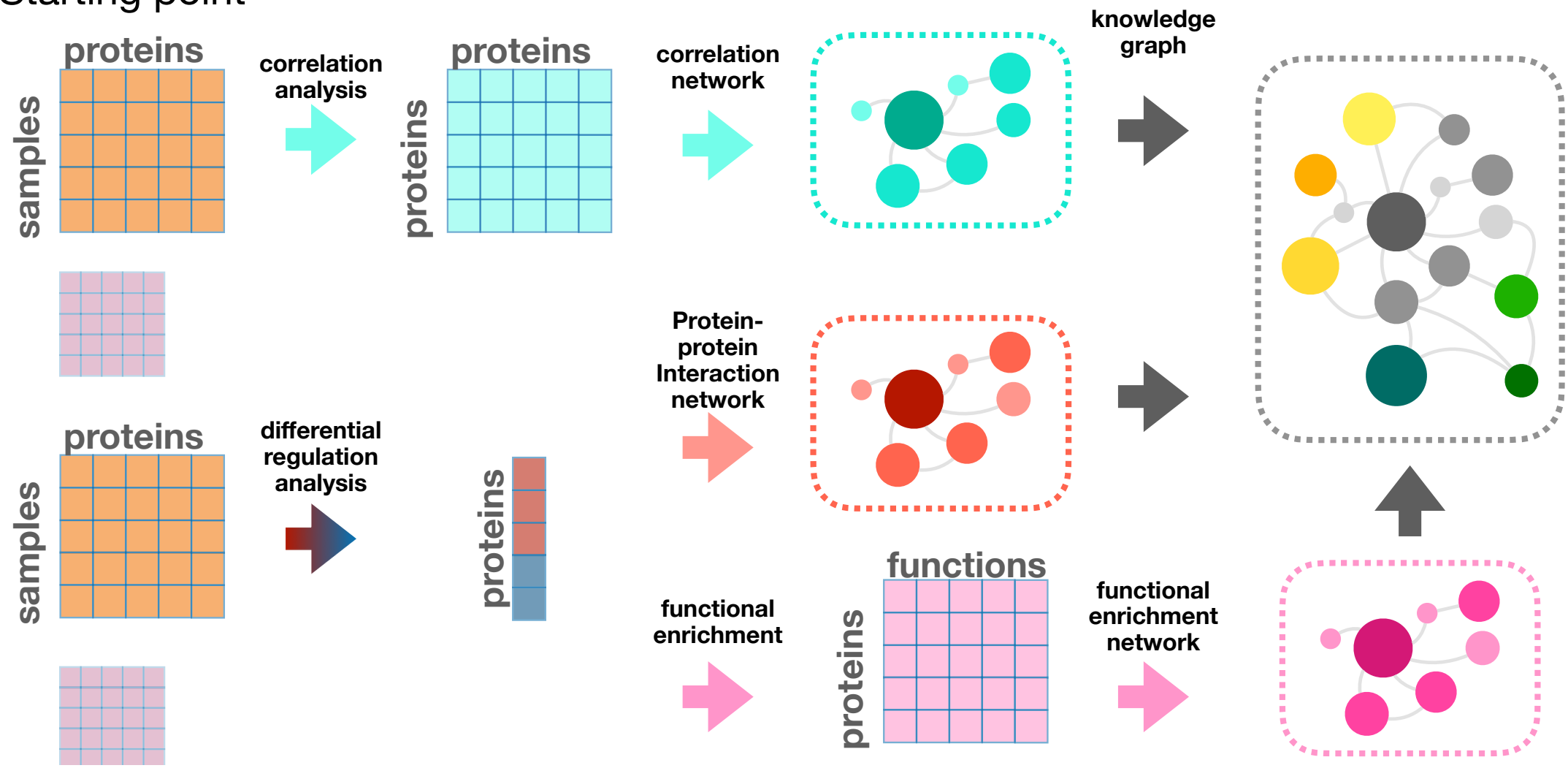




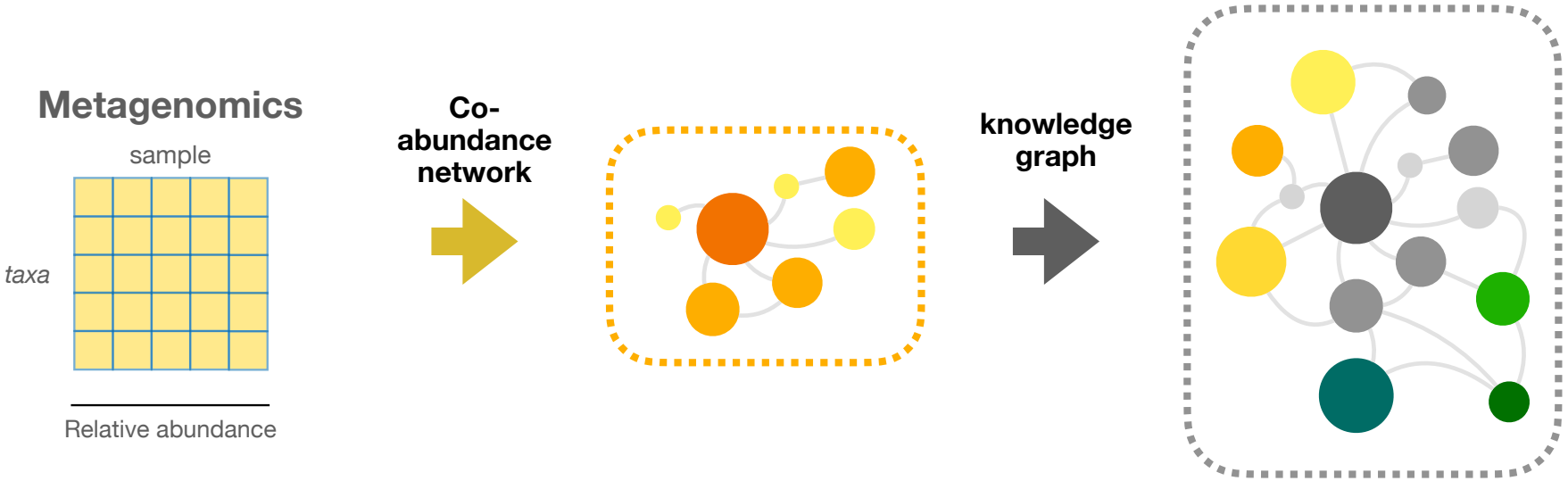
- **Data sources**
  - STRING — https://string-db.org/
  - BioGRID — https://thebiogrid.org/
  - IntAct — https://www.ebi.ac.uk/intact
  - REACTOME — https://reactome.org/
  - KEGG — https://www.genome.jp/kegg/
  - MINT — https://mint.bio.uniroma2.it/
- **Correlation-based networks —** constructed by calculating pairwise correlations between entities based on their expression profiles across multiple conditions, time points, or samples (Weighted gene co-expression network analysis (WGCNA), co-abundance networks)
- **Knowledge-base approaches** — also called knowledge graphs and built by integrating heterogeneous data from multiple sources —> **Knowledge Graphs**

Omics Graphs

Starting point



Microbial Association Networks — MANs

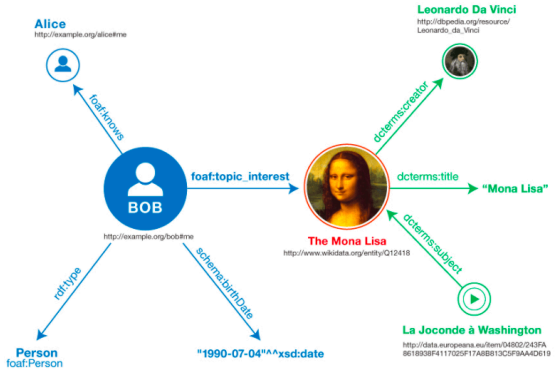


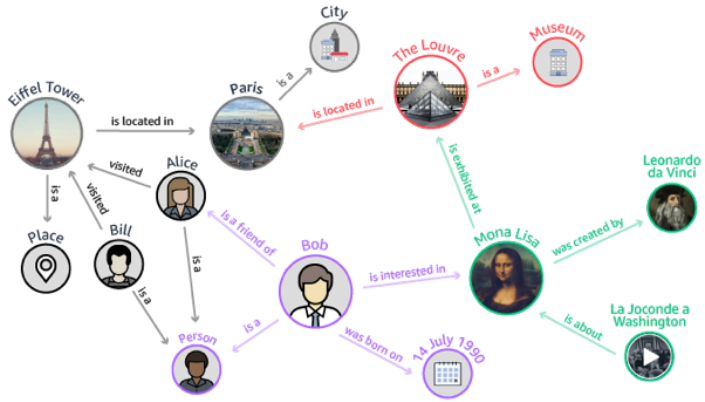
Knowledge Graphs

What is a Knowledge Graph (KG)

Relationships firsts everything else second

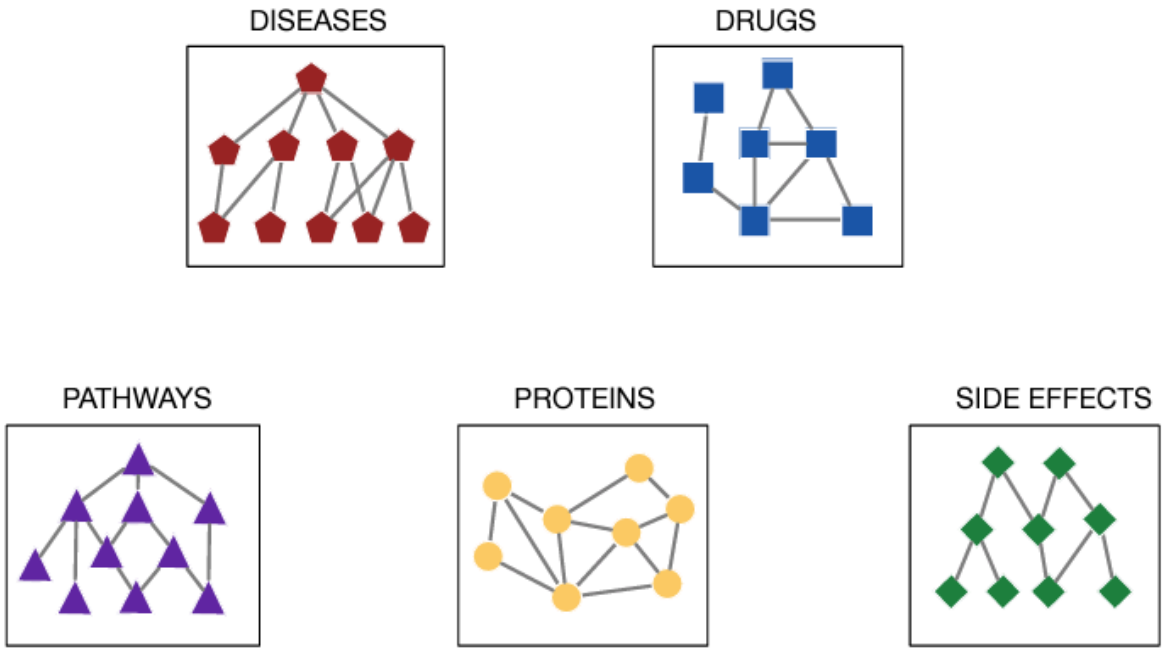
- A way to organise **knowledge**/information by defining **associations** or **relationships**
- These relationships facilitate the **integration**, **management** and **enrichment** of data
- The **objectives** when setting up a KG:
  - Standardisation
  - Quality
  - Reusability
  - Interpretability
  - Automation
  - Representation/Visualisation





The Knowledge Graph Cookbook. Andreas Blumauer and Helmut Nagy. 2020

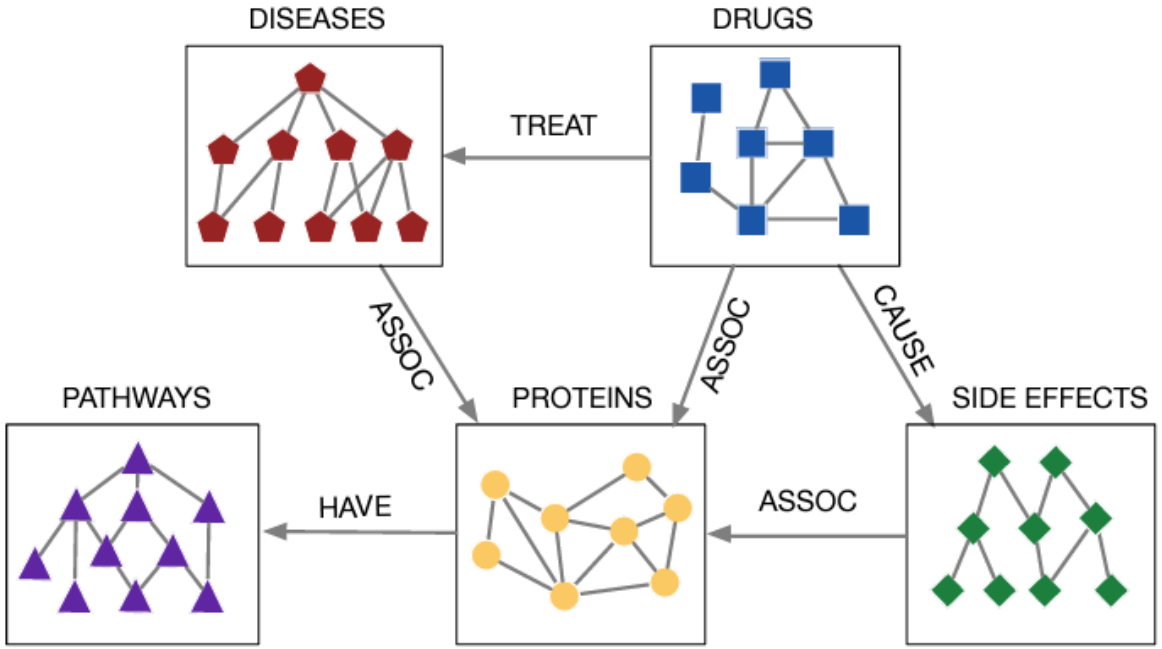
Knowledge Graph vs Graph Database

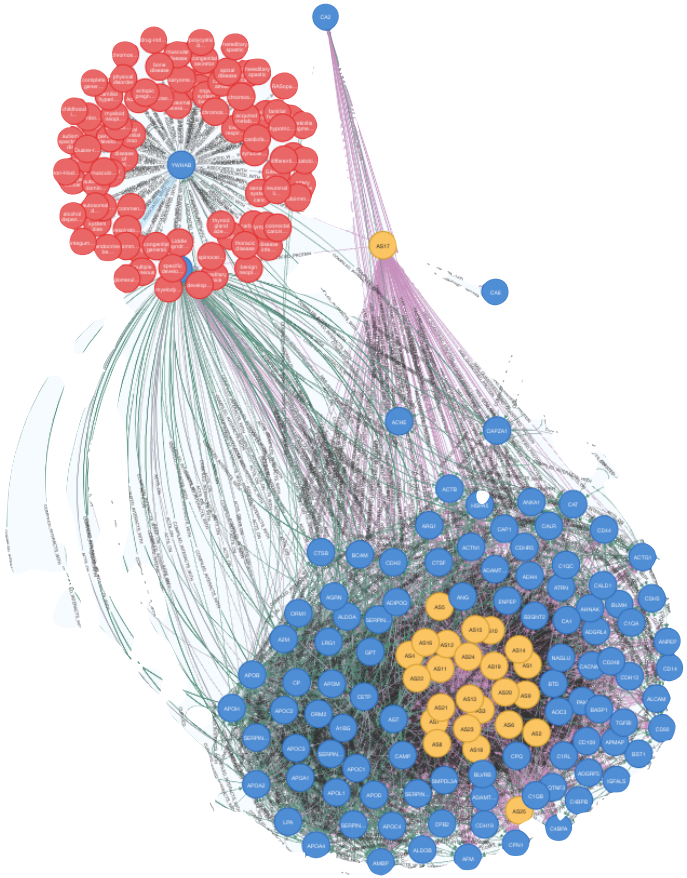


https://snap.stanford.edu/graphlearning-workshop/slides/stanford_graph_learning_Biomedicine.pdf

Knowledge Graph vs Graph Database

Focus on **data integration** to **represent complex biological systems** and be able **to reason over them**





https://snap.stanford.edu/graphlearning-workshop/slides/stanford_graph_learning_Biomedicine.pdf

Building a Knowledge Graph

1. Define the **questions** you want to answer
2. Define **what data** can be used to answer these questions and **how it is linked** — Data model
3. Find **where to get these data**
4. Get the data, **standardise** it and **format** it
5. Generate the **graph**
6. **Query the graph** to answer the questions

Building a Knowledge Graph

Building a Knowledge Graph

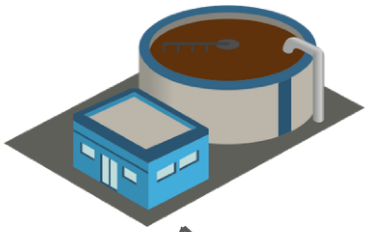
Exercise

Create a data model that allows us to answer the question:

What drugs related to our disease of interest target some of the proteins identified in our experiment or relevant protein complexes and pathways?

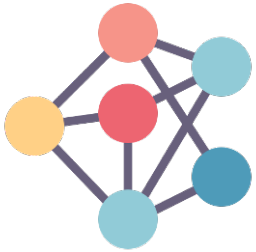
Knowledge Graph Use Case
Wastewater Microbial Communities

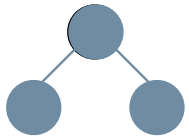
Sebastian Ayala Ruano



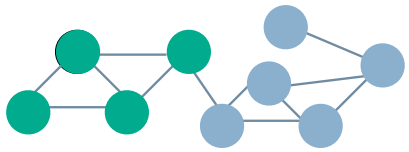
Harmonising data from multiple studies

Building Microbial Association Networks





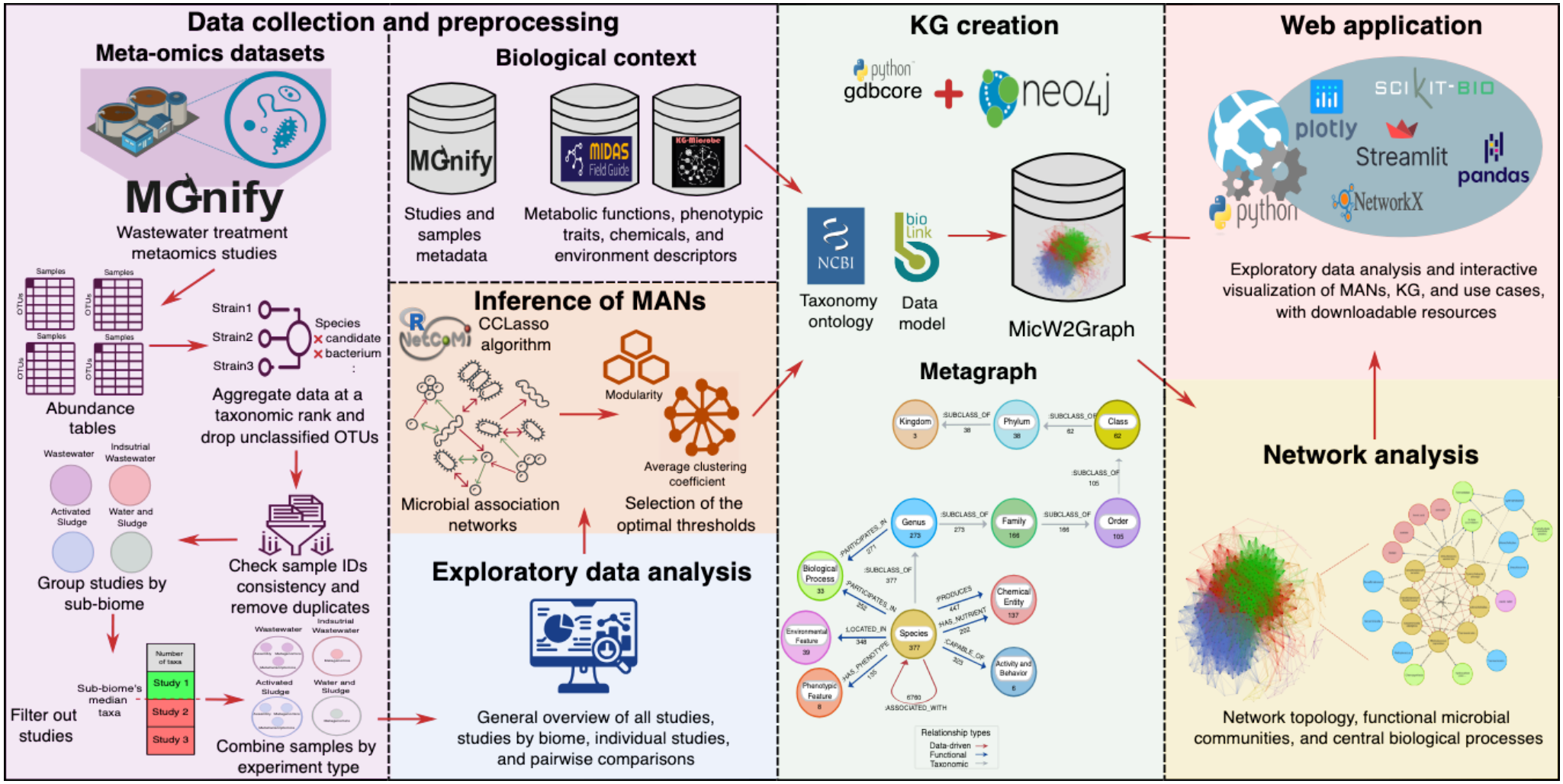
Pattern discovery



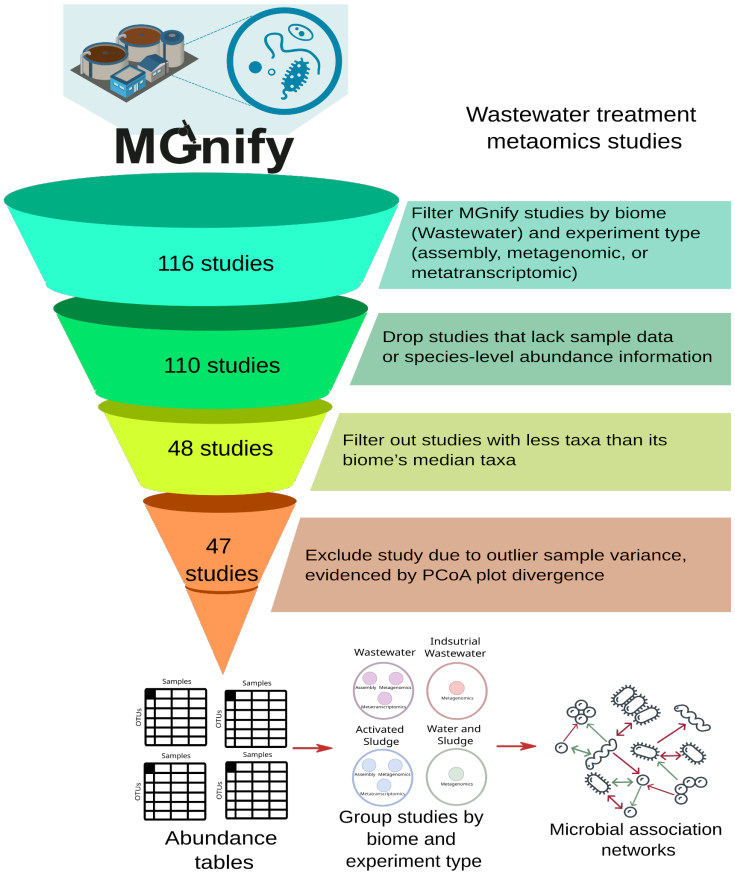
Community detection

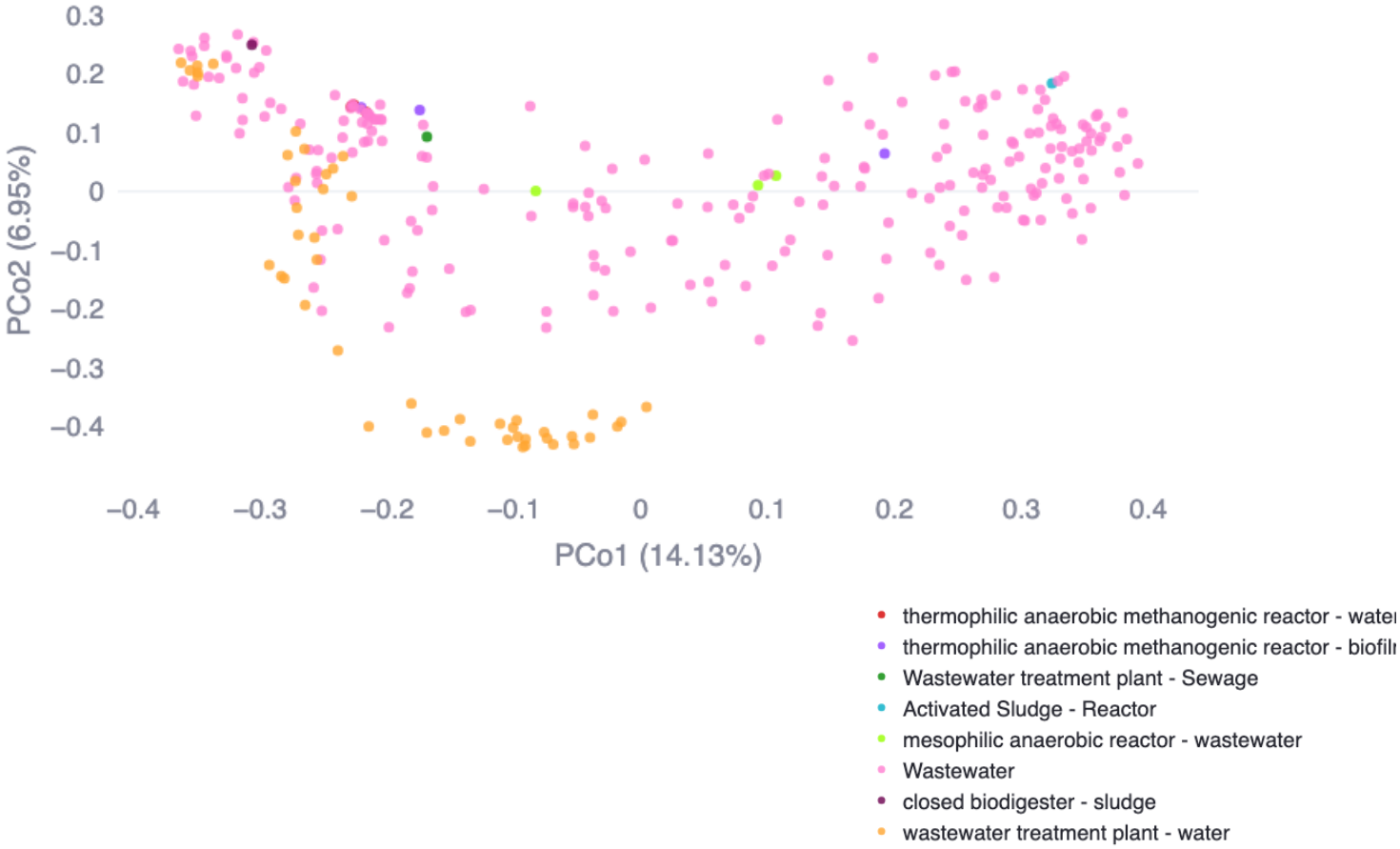
Analyses	Identify microbial communities that relate to environmental conditions or perturbations	Detection of synergistic clusters based on graph structure and interpretation by using connective biological context

Knowledge Graph Use Case
Wastewater Microbial Communities

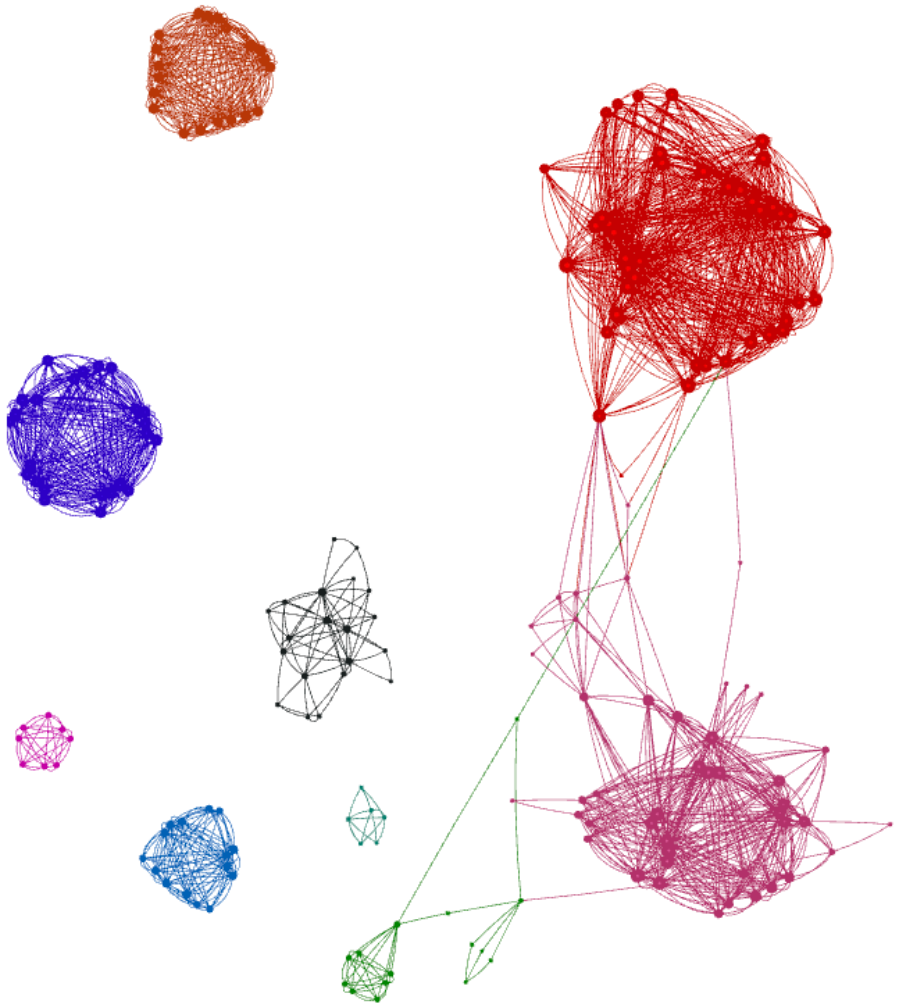


Knowledge Graph Use Case
Wastewater Microbial Communities





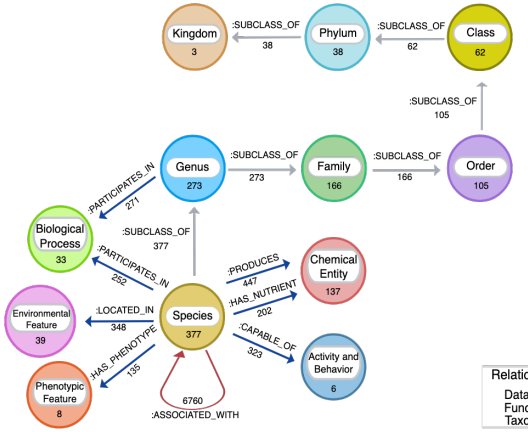
Microbial Association Networks

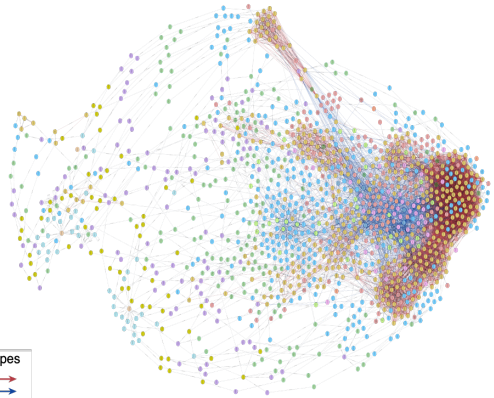


Microbial Association Network built using CCLASSO method — co-abundance.

Colors indicate microbial communities identified using Louvain clustering.

Functional Annotation:
Using MIDAS and KG Microbe





NetCoMi: network construction and comparison for microbiome data in R

Stefanie Peschel, Christian L Müller, Erika von Mutius, Anne-Laure Boulesteix, Martin Depner

MIDAS Field Guide

KG-Microbe

Home | Exploratory data analysis | **Microbial association networks** | Knowledge graph | Case studies

MicW2Graph

Building a knowledge graph of the wastewater treatment microbiome and its biological context

---

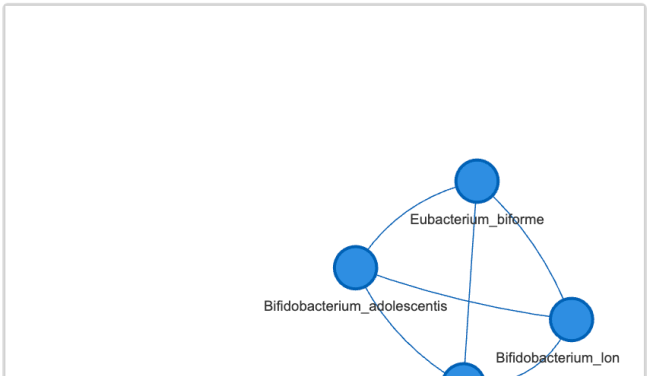
Microbial association networks by wastewater treatment sub-biome and experiment types

Water and sludge | Metagenomics

Number of nodes: 9

Number of relationships: 14

Add panel to control layout



https://micw2graph.streamlit.app/

Tools

Cytoscape

https://cytoscape.org/

- An open source **software platform** for **visualising** and **analysing** complex **networks**
- Used for any kind of networks but **specialised** on **biological domains**:

  e.g, Molecular interaction networks and biological pathways and integrating these networks with annotations, gene expression profiles and other state data.
- **Additional features** are available as freely available **Apps** (https://apps.cytoscape.org/)

Getting Started

Gephi

https://gephi.org/

- Open source **platform** for **graph visualisation** and **analysis**
- Used across **many domains** and by **many industries**
- **Performs well** for large graphs
- **Connects to Graph databases** such as Neo4j
- Some of the **visualisations and analysis** require **plugins**

Getting Started

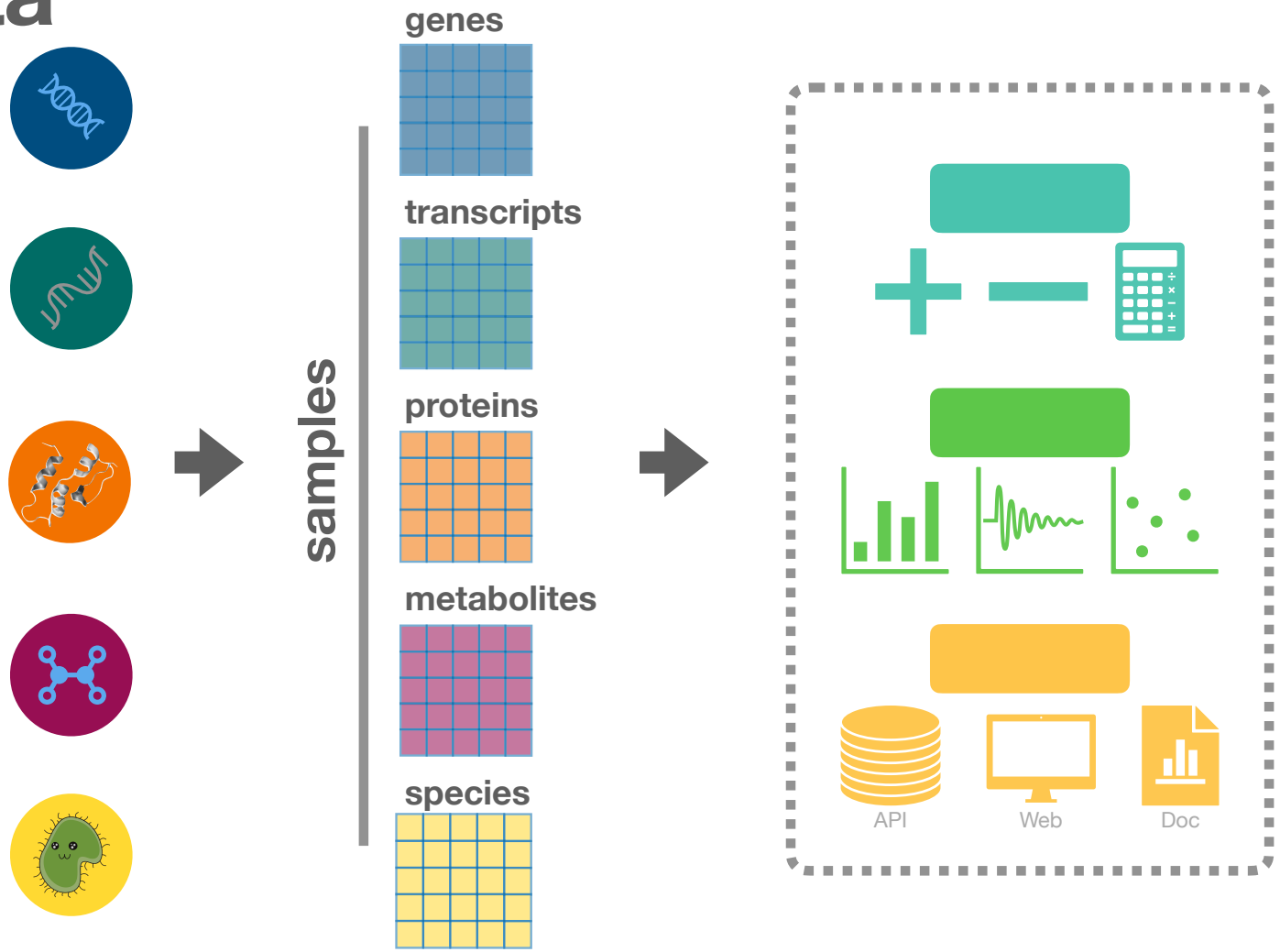
Code

https://networkx.org/

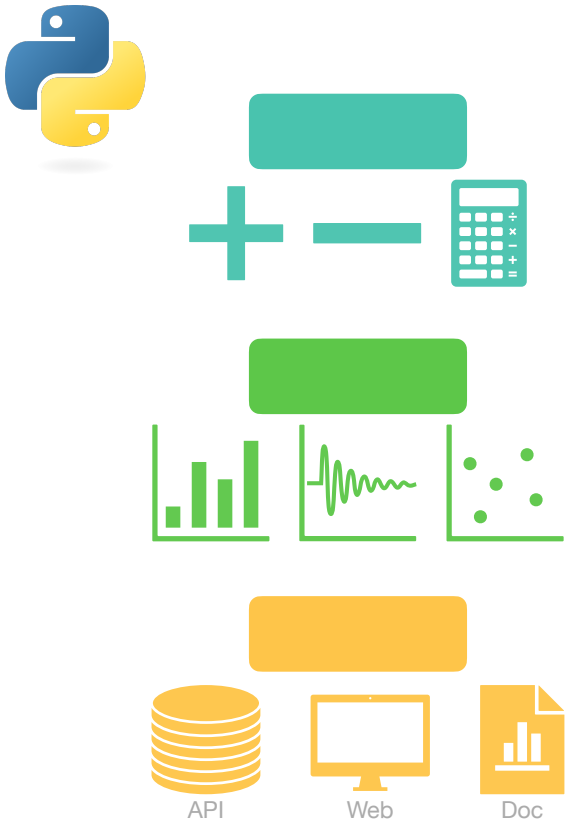
https://r.igraph.org/

Open Source Libraries

Omics Data


genes
transcripts
proteins
metabolites
species
samples
API
Web
Doc

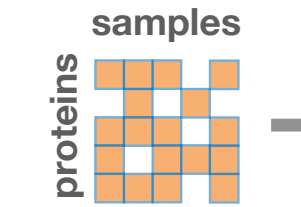
Open Source Libraries



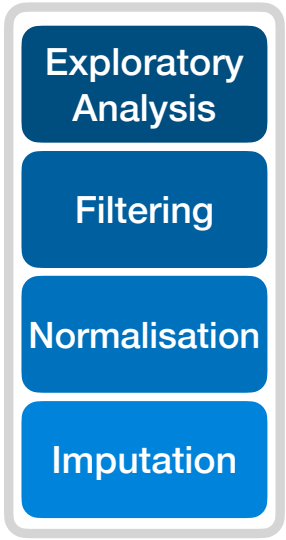
Analytics core library https://analytics-core.readthedocs.io/

Visualization core library https://github.com/Multiomics-Analytics-Group/vuecore

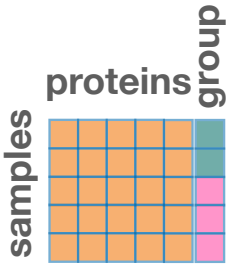
Analytical Workflow

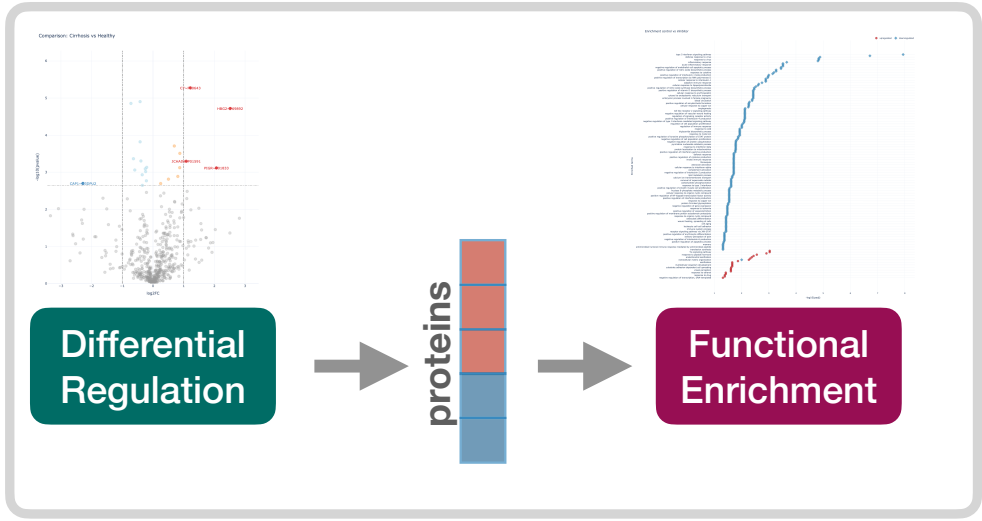


Protein Table

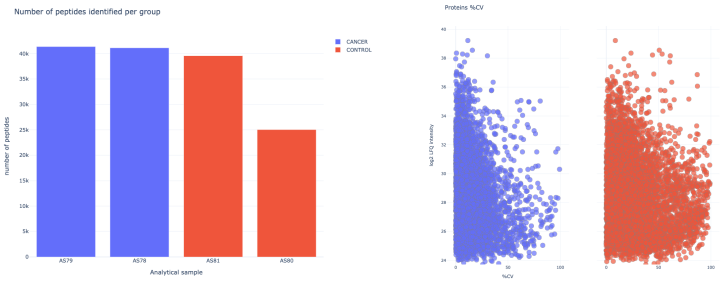


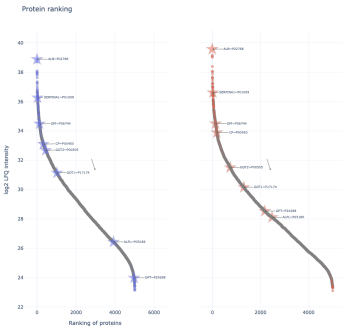
Data Preparation

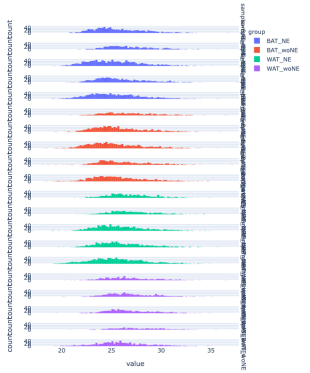


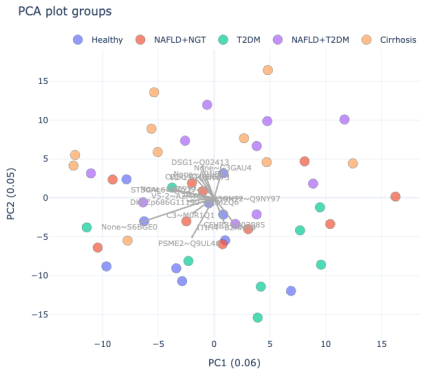


Data Analysis









Open Source Libraries

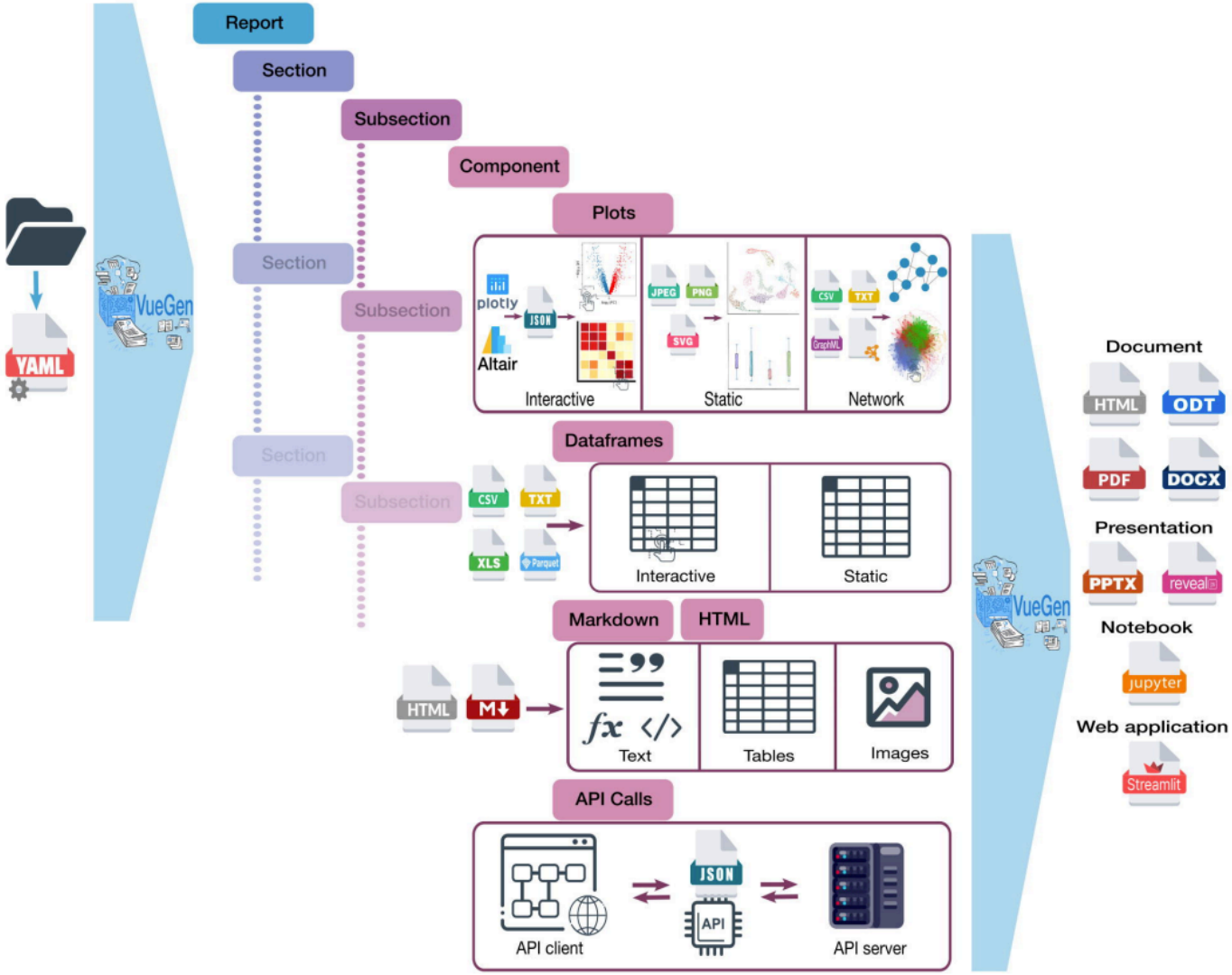
Analytics core library

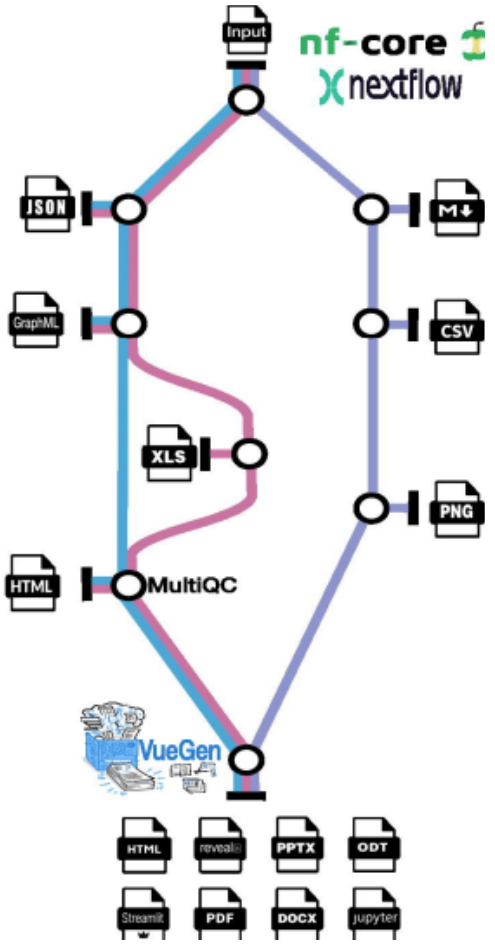
https://analytics-core.readthedocs.io/

Visualization core library

https://github.com/Multiomics-Analytics-Group/vuecore

VueGen





VueGen: Automating the generation of scientific reports

Sebastian Ayala-Ruano, Henry Webel, Alberto Santos

doi: https://doi.org/10.1101/2025.03.05.641152

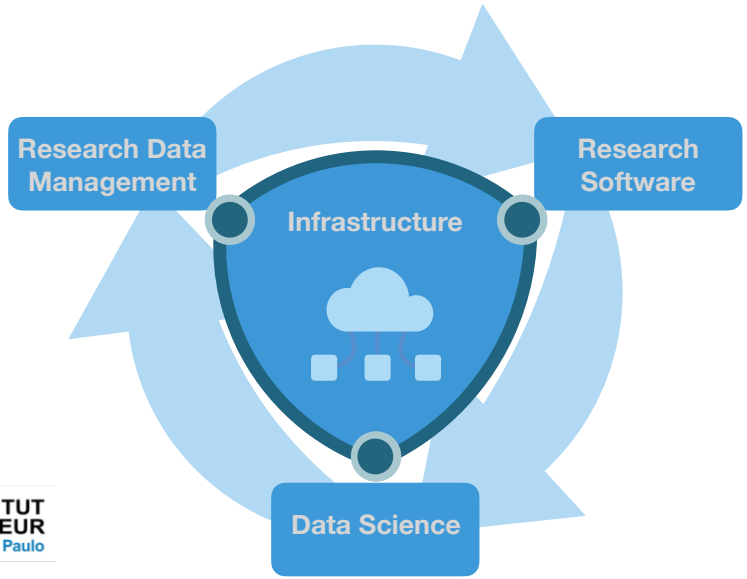
https://www.biorxiv.org/content/10.1101/2025.03.05.641152v1

QA

Acknowledgements

Multi-omics Network Analytics

Informatics Platform



Thank you

The Novo Nordisk Foundation Center for Biosustainability

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https://github.com/Multiomics-Analytics-Group

https://multiomics-analytics-group.github.io/

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