
Clinical Knowledge Graph Documentation

Release 1.0.0

Alberto Santos, Ana Rita Colaço, Annelaura B. Nielsen

May 09, 2020

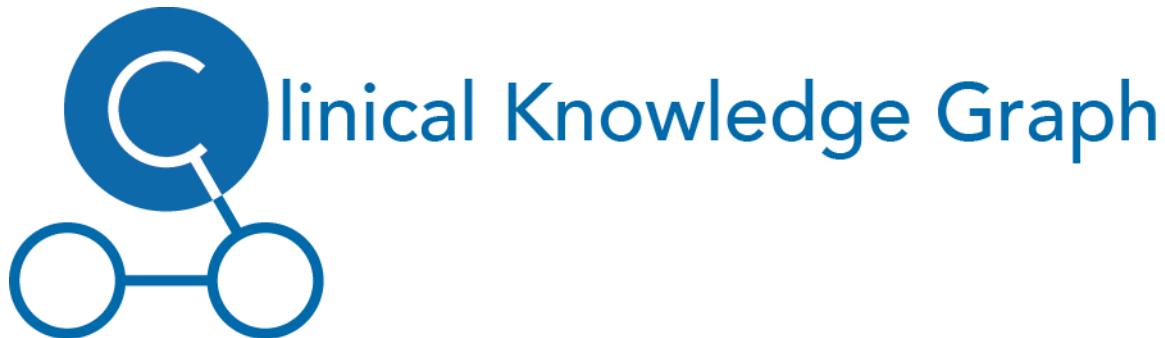
CONTENTS

This web page contains the documentation for the Python code using **Sphinx**.

CLINICAL KNOWLEDGE GRAPH

A Python project that allows you to analyse proteomics and clinical data, and integrate and mine knowledge from multiple biomedical databases widely used nowadays.

- Documentation: <https://CKG.readthedocs.io>
- GitHub: <https://github.com/MannLabs/CKG>
- Free and open source software: MIT license



1.1 Abstract



Several omics data types are already used as diagnostic markers, beacons of possible treatment or prognosis. Advances in technology have paved the way for omics to move into the clinic by generating increasingly larger amounts of high-quality quantitative and qualitative data. Additionally, knowledge around these data has been collected in diverse

public resources, which has facilitated the understanding of these data to some extent. However, there are several challenges that hinder the translation of high-throughput omics data into identifiable, interpretable and actionable clinical markers. One of the main challenges is the interpretation of the multiple hits identified in these experiments. Furthermore, a single omics dimension is often not sufficient to capture the full complexity of disease, which would be aided by integration of several of them. To overcome these challenges, we propose a system that integrates multi-omics data and information spread across a myriad of biomedical databases into a Clinical Knowledge Graph (CKG). This graph focuses on the data points or entities not as silos but as related components of a graph. To illustrate, in our system an identified protein in a proteomics experiment encompasses also all its related components (other proteins, diseases, drugs, etc.) and their relationships. Thus, our CKG facilitates the interpretation of data and the inference of meaning by providing relevant biological context. Further, ~. Here we describe the current state of the system and depict its use by applying it to use cases such as treatment decisions using cancer genomics and proteomics.

1.2 Cloning and installing

The setting up of the CKG includes several steps and might take a few hours (if you are building the database from scratch). However, we have prepared documentation and manuals that will guide through every step. To get a copy of the GitHub repository on your local machine, please open a terminal window and run:

```
$ git clone https://github.com/MannLabs/CKG.git
```

This will create a new folder named “CKG” on your current location. To access the documentation, use the ReadTheDocs link above, or open the html version stored in the *CKG* folder *CKG/docs/build/html/index.html*. After this, follow the instructions in “First Steps” and “Getting Started”.

1.3 Features

- Cross-platform: Mac, and Linux are officially supported.
- Docker container runs all neccessary steps to setup the CKG.

1.4 Disclaimer

This resource is intended for research purposes and must not substitute a doctor’s medical judgement or healthcare professional advice.

FIRST STEPS

Are you new to the Clinical Knowledge Graph? Learn about how to use it and all the possibilities.

- **Getting started:** *With Requirements | With Neo4j | With Clinical Knowledge Graph | With Windows*

2.1 Getting Started with some Requirements

The following instructions on installation of software requirements and setting up the Clinical Knowledge graph, are optimized for operating systems MacOS and Linux. For more detailed instructions on how to set up the CKG in Windows, please go to *Getting started with Windows*.

2.1.1 Java

Before starting setting up Neo4j and, later on, the Clinical Knowledge Graph, it is very important that you have *Java* installed in your machine.

Different versions of a Neo4j database can have different requirements. For example, Neo4j 3.5 versions require Oracle Java 8, while Neo4j 4.0 versions already require Oracle Java 11. When using a new version of Neo4j, always remember to read the respective Operations Manual, and check for the software requirements.

To check if you already have **Java SE Development Kit** installed, run `java -version` in your terminal window. This should print out three lines similar to the following, with possible variation in the version:

```
java version "1.8.0_171"
Java(TM) SE Runtime Environment (build 1.8.0_171-b11)
Java HotSpot(TM) 64-Bit Server VM (build 25.171-b11, mixed mode)
```

Running `/usr/libexec/java_home` in the terminal should print out a path like `/Library/Java/JavaVirtualMachines/jdk1.8.0_171.jdk/Contents/Home`. Otherwise, please follow the steps below:

1. Go to <https://www.oracle.com/java/technologies/javase-downloads.html> and download the version that fits your Neo4j version and OS requirements.
2. Install the package.
3. Run `/usr/libexec/java_home` in the terminal to make sure the *Java* package has been installed in `/Library/Java/JavaVirtualMachines/`.

2.1.2 R

Another essential package for the functioning of the Clinical Knowledge Graph is R.

Make sure you have installed **R version >= 3.5.2**:

```
$ R --version
```

And that R is installed in /usr/local/bin/R:

```
$ which R
```

To install the neccessary R packages, simply initiate R (terminal or shell) and run:

```
install.packages('BiocManager')
BiocManager::install()
BiocManager::install(c('AnnotationDbi', 'GO.db', 'preprocessCore', 'impute'))
install.packages(c('flashClust','WGCNA', 'samr'), dependencies=TRUE, repos='http://
˓→cran.rstudio.com/')
```

Note: If you need to install R, follow [these](#) tutorial.

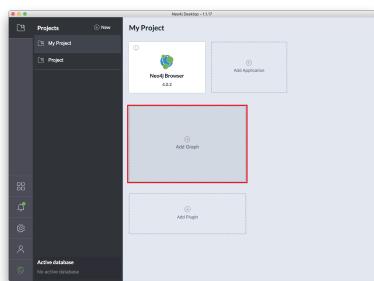
Warning: In Mac OS, make sure you have **XQuartz** installed.

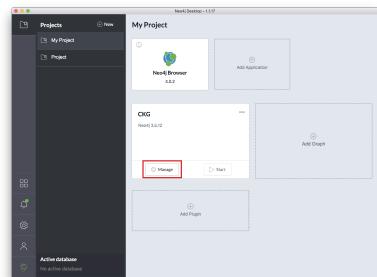
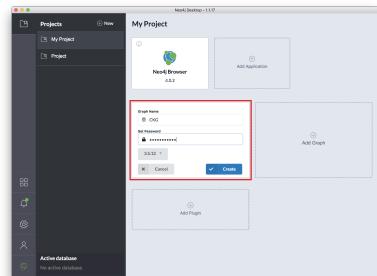
Now that you are all set, you can move on and start with Neo4j.

2.2 Getting Started with Neo4j

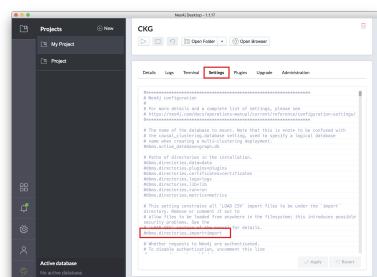
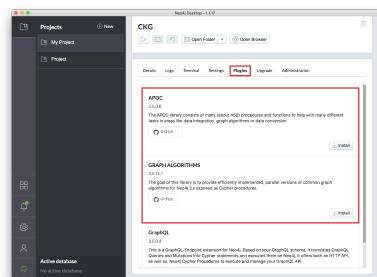
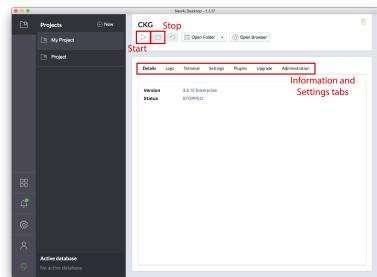
Getting started with Neo4j is easy.

First download a copy of the Neo4j desktop version from the [Neo4j download page](#). The Community Edition of the software is free but a sign up is required. Once the file has downloaded, you can install Neo4j by following the instructions automatically opened in the browser.





Open the Neo4j Desktop App and create a database by clicking *Add graph*, followed by *Create a Local Graph*, using the password “bioinfo1112”. Now that your database is created:



1. Click *Manage* and then *Plugins*. Install “APOC” and “GRAPH ALGORITHMS”.

2.2. Getting Started with Neo4j

2. Click the tab *Settings*, and comment the option `dbms.directories.import=import` by adding `#` at the beginning of the line.
3. Click *Apply* at the bottom of the window.
4. Start the Graph by clicking the play sign, at the top of the window.

If the database starts and no errors are reported in the tab *Logs*, you are ready go to!

2.2.1 Add Neo4j graph database to `.bashrc`

In order to run the graph database, add the path to the database to your `.bashrc` (or `.bash_profile`) file.

To find out which of the files your machine uses, go to the terminal and type `more ~/.bash` and double press the tab key on your keyboard for auto-complete. Immediately below, multiple filenames will be printed, check if among those, is `.bashrc` or `.bash_profile`.

Note: The bash file can be named `.bashrc` or `.bash_profile`. If your system does not have either, create one of them (e.g. `vi ~/.bash_profile`).

1. Open the `.bash_profile` (or `.bashrc`) with your favourite text editor. In this case, we use the `vi` editor:

```
$ vi ~/.bash_profile
```

Note: To edit with `vi` press `i` on your keyboard.

1. Add the path to the previously created Neo4j database to the file:

```
NEO4J_HOME="/Users/username/Library/Application Support/Neo4j Desktop/Application/  
↳ neo4jDatabases/database-identifier/installation-3.X.X/"  
export NEO4J_HOME
```

Note: To save and close a file with `vi` editor, press `Esc` followed by `:wq`.

Warning: Depending on your system, the path may vary. To check the path to the database go to *Logs* in the Neo4j Desktop interface.

1. Reload the `.bashrc` (or `.bash_profile`) file:

```
$ source ~/.bashrc
```

or

```
$ source ~/_.bash_profile
```

2.3 Getting Started with the CKG Build

Setting up the Clinical Knowledge Graph is straightforward. Assuming you have **Python 3.6** already installed and added to `PATH`, you can choose to create a virtual environment where all the packages with the specific versions will be installed. To do so, use `Virtualenv`.

To check which Python version is currently installed:

```
$ python3.6 --version
```

And where this Python version is:

```
$ which python3.6
```

If this does not correspond to the correct Python version you want to run, you can create a shell alias in the bash file:

1. Open the bash file:

```
$ vi ~/.bash_profile
```

1. Add at the end of the file:

```
alias python3.6="/path/to/correct/python3.6"
```

1. Save and close the bash file
2. Make the alias available in the current session:

```
$ source ~/.bash_profile
```

Note: If you don't have **Python 3.6** installed, [download](#) the Python 3.6 version appropriate for your machine, and run the installer package. Python should be installed in `/Library/Frameworks/Python.framework/Versions/3.6/bin/python3.6` and also found in `/usr/local/bin/python3.6`.

2.3.1 Create a virtual environment

`Virtualenv` is not installed by default on Macbook machines. To install it, run:

```
$ python3 -m pip install virtualenv
```

To create a new virtual environment using a costum version of Python, follow the steps:

1. Take note of the full path to the Python version you would like to use inside the virtual environment.
2. Navigate to the directory where you would like your virtual environment to be (e.g. user's root).
3. Create the virtual environment at the same time you specify the version of Python you wish to use. `env_name` is the name of the virtual environment and can be set to anything you like.

```
$ virtualenv -p /path/to/python env_name
```

1. Activate the virtual environment by running:

```
$ source path/to/env_name/bin/activate
```

After this, the name of the virtual environment will now appear on the left of the prompt:

```
(env_name) username$
```

If you are finished working in the virtual environment for the moment, you can deactivate it by running:

```
$ deactivate
```

2.3.2 Setting up the Clinical Knowledge Graph

The first step in setting up the CKG, is to obtain the complete code by clone the GitHub repository:

```
$ git clone https://github.com/MannLabs/CKG.git
```

Once this is finished, you can find all the Python modules necessary to run the Clinical Knowledge Graph in `requirements.txt`. To install all the packages required, simply run:

```
$ cd CKG/
$ pip install -r requirements.txt
```

Warning: Make sure the virtual environment previously created is active before installing `requirements.txt`.

Now that all the packages are correctly installed, you will have to create the appropriate directory architecture within the local copy of the cloned repository:

```
$ python setup_CKG.py
$ python setup_config_files.py
```

This will automatically create the `data` folder and all subfolders, as well as setup the configuration for the log files where all errors and warnings related to the code will be written to.

2.3.3 Add CKG to `.bashrc`

In order run the the Clinical Knowledge Graph, add the path to the code to your `.bashrc` (or `.bash_profile`):

1. Open the `.bashrc` file.
2. Add the following lines to the file and save it:

```
PYTHONPATH="${PYTHONPATH}:/path/to/folder/CKG/src/"
export PYTHONPATH
```

Notice that the path should always finish with “`/CKG/src/`”.

1. To reload the bash file, first deactivate the virtual environment, reload `~/.bashrc`, and activate the virtual environment again:

```
$ deactivate
$ source ~/.bashrc
$ source /path/to/env_name/bin/activate
```

2.3.4 Build Neo4j graph database

The building of the CKG database is thoroughly automated. Most of the biomedical databases and ontology files will automatically be downloaded during building of the database. However, the following licensed databases have to be downloaded manually.

- [PhosphoSitePlus](#): *Acetylation_site_dataset.gz*, *Disease-associated_sites.gz*, *Kinase_Substrate_Dataset.gz*, *Methylation_site_dataset.gz*, *O-GalNAc_site_dataset.gz*, *O-GlcNAc_site_dataset.gz*, *Phosphorylation_site_dataset.gz*, *Regulatory_sites.gz*, *Sumoylation_site_dataset.gz* and *Ubiquitination_site_dataset.gz*.
- [DrugBank](#): All drugs (under *COMPLETE DATABASE*) and *DrugBank Vocabulary* (under *OPEN DATA*).

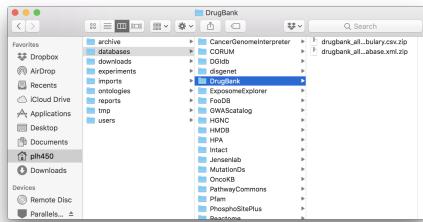


Fig. 2: DrugBank database folder.

- [SNOMED-CT](#): *Download RF2 Files Now!*.

After download, move the files to their respective folders:

- PhosphoSitePlus: CKG/data/databases/
PhosphoSitePlus
- DrugBank: CKG/data/databases/DrugBank
- SNOMED-CT: CKG/data/ontologies/SNOMED-CT

In the case of SNOMED-CT, unzip the downloaded file and copy all the subfolders and files to the SNOMED-CT folder.

Warning: These three databases require login and authentication. To sign up go to [PSP Sign up](#), [DrugBank Sign up](#) and [SNOMED-CT Sign up](#). In the case of SNOMED-CT, the UMLS license can take several business days.

Note: If the respective database folder is not created, please do it manually.

The last step is to build the database, which can be done using the `builder.py` module or a `dump` file.

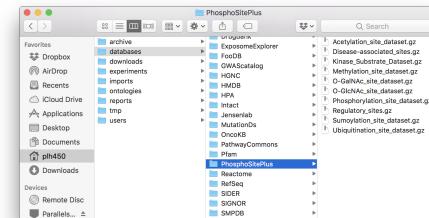


Fig. 3: PhosphoSitePlus database folder.

From builder.py

To build the graph database, run `builder.py`:

```
$ cd src/graphdb_builder/builder  
$ python builder.py -b full -u neo4j
```

Warning: Before running `builder.py`, please make sure your Neo4j graph is running. The builder will fail otherwise.

This action will take approximately 6 hours but depending on a multitude of factors, it can take up to 10 hours.

From a backup dump file

A dump file of the database is also made available in *add link to the dump file!!* and alternatively, you can use it to load the graph database contained in it:

```
$ cd /path/to/neo4jDatabases/database-identifier/installation-x.x.x/  
$ mkdir backups  
$ mkdir backups/graph.db  
$ cp 2019-11-04.dump backups/graph.db/.
```

After copying the dump file to `backups/graph.db/`, make sure the graph database is shutdown and run:

```
$ bin/neo4j-admin load --from=backups/graph.db/2019-11-04.dump --database=graph.db --  
  ↪force
```

Warning: Make sure the dump file naming in the command above, matches the one provided to you.

In some systems you might have to run this as root:

```
$ sudo bin/neo4j-admin load --from=backups/graph.db/2019-11-04.dump --database=graph.  
  ↪db --force  
$ sudo chown -R username data/databases/graph.db/
```

Once you are done, start the database and you will have a functional graph database.

However, be aware the database contained in the dump file **does NOT** include the licensed databases (**PhosphoSitePlus**, **DrugBank** and **SNOMED-CT**).

To add the missing ontology and databases, as well as their dependencies (relationships to other nodes), please manually download the files as explained in *Build Neo4j graph database*, and run the following commands:

```
$ cd CKG/src/graphdb_builder/builder  
$ python builder.py -b import -i ontologies -d Clinical_variable -w False -u username  
$ python builder.py -b import -i databases -d phosphositeplus drugbank -n 2 -w False -  
  ↪u username  
$ python builder.py -b load -l ontologies -s SNOMED_CT -u username  
$ python builder.py -b load -l modified_proteins drugs mentions side_effects pathway_  
  ↪project experiment -u username
```

Note: Remember of replace the `username` in each command, with your own neo4j username.

More on the dump file

Another great use for the dump file, is to generate backups of the database (e.g. different versions of the imported biomedical databases). To generate a dump file of a specific Neo4j database, simply run:

```
$ cd /path/to/neo4jDatabases/database-identifier/installation-x.x.x/
$ bin/neo4j-admin dump --database=neo4j --to=backups/graph.db/name_of_the_file.dump
```

Warning: Remember to replace `name_of_the_file` with the name of the dump file you want to create.

2.4 Getting started with Windows

In this section we describe how to install all the neccessary requirements and set up the Clinical Knowledge Graph on a Windows operating system.

2.4.1 Java

Similarly to MacOS and Linux, Windows will also need a **Java** installation. Be aware that different versions of a Neo4j database can have different requirements. For example, Neo4j 3.5 versions require Oracle Java 8, while Neo4j 4.0 versions already require Oracle Java 11. When using a new version of Neo4j, always remember to read the respective Operations Manual, and check for the software requirements.

To check if you already have **Java SE Development Kit** installed, run `java -version` in your terminal window. This should print out three lines similar to the following, with possible variation in the version:

```
java version "1.8.0_171"
Java(TM) SE Runtime Environment (build 1.8.0_171-b11)
Java HotSpot(TM) 64-Bit Server VM (build 25.171-b11, mixed mode)
```

Running `/usr/libexec/java_home` in the terminal should print out a path like `/Library/Java/JavaVirtualMachines/jdk1.8.0_171.jdk/Contents/Home`. Otherwise, please follow the steps below:

1. Go to <https://www.oracle.com/java/technologies/javase-downloads.html> and download the version that fits your Neo4j version and OS requirements.
2. Install the package.
3. Run `/usr/libexec/java_home` in the terminal to make sure the *Java* package has been installed in `/Library/Java/JavaVirtualMachines/`.

2.4.2 R

Another essential package for the functioning of the Clinical Knowledge Graph is R.

You can check if an **R version >= 3.5.2** is already installed by running:

```
> where R
```

And all R packages can be installed by simply initiating R (command prompt or R shell) and running:

```
install.packages('BiocManager')
BiocManager::install()
BiocManager::install(c('AnnotationDbi', 'GO.db', 'preprocessCore', 'impute'))
install.packages(c('flashClust', 'WGCNA', 'samr'), dependencies=TRUE, repos='http://
→cran.rstudio.com/')
```

If R is not installed in your machine, please follow [these tutorial](#).

2.4.3 Neo4j

The installation of Neo4j on Windows follows the same steps as *Getting Started with Neo4j*:

1. Download a copy of the Neo4j desktop version from the [Neo4j download page](#).
2. Install Neo4j by following the instructions automatically opened in the browser.
3. Open the Neo4j Desktop App and create a database by clicking *Add graph*, followed by *Create a Local Graph*, using the password “bioinfo1112”.
4. Click *Manage* and then *Plugins*. Install “**APOC**” and “**GRAPH ALGORITHMS**”.
5. Click the tab *Settings*, and comment the option `dbms.directories.import=import` by adding # at the beginning of the line.
6. Click *Apply* at the bottom of the window.
7. Start the Graph by clicking the play sign, at the top of the window.

To check for errors, please go to tab *Logs*.

Add Neo4j graph database to environmental variables

To add the Neo4j database you just created to your Windows environment variables:

1. Go to the Windows menu, right-click on *Computer* and click on *Properties*.
2. From the computer properties dialog, select Advanced system settings on the left panel. And from there, click on *Environment variables* button.
3. In the Environment variables dialog, click the *New* button in the top half of the dialog, to make a new user variable
4. Give the variable name as `NEO4J_HOME` and the value is the path to the previously created Neo4j database to the file, for example `C:\Neo4J\neo4jDatabases\database-bab515f2-ffe7-4282-9bb5-648a53b8b566\installation-3.5.2\`
5. Click *OK* and *OK* again to save this variable.

To confirm that the environment variable is correctly set in command line type:

```
> echo %NEO4J_HOME%
```

This will print the path you used as value (e.g. C:\Neo4J\neo4jDatabases\database-bab515f2-ffe7-4282-9bb5-648a53b8b566\installation-3.5.2\).

Warning: Depending on your system, the path may vary. To check the path to the database go to Logs in the Neo4j Desktop interface.

2.4.4 Getting Started with the CKG Build

Setting up the Clinical Knowledge Graph is thoroughly described here. Assuming you have **Python 3.6** already installed, you can choose to create a virtual environment where all the packages with the specific versions will be installed.

To check which Python version is currently installed, run in the command prompt (cmd.exe):

```
> python --version
```

And to find your this Python version is installed:

```
> where python
```

If you don't have **Python 3.6** installed in Windows, we recommend installing and using the Anaconda distribution of Python. Download at <https://www.anaconda.com/products/individual#Downloads>, and follow the instructions from <https://docs.anaconda.com/anaconda/install/windows/#>.

Create a virtual environment

To create a new Python virtual environment, please use Anaconda conda installation.

1. In the command prompt (cmd.exe) type:

```
> conda create -n env_name python=3.6
```

The key word `python` specifies which version of Python the virtual environment is requested to use, while `env_name` is the name of the virtual environment and can be set to anything you like.

2. Activate the virtual environment by running:

```
> conda activate env_name
```

3. After this, the name of the virtual environment will now appear on the left of the prompt:

```
(env_name) C:>
```

4. If you are finished working in the virtual environment for the moment, you can deactivate it by running:

```
> conda deactivate
```

Warning: Remember, everytime you are working with the CKG, the virtual environment needs to be activated first.

Setting up the CKG

Once you have cloned the master branch of the CKG GitHub repository, all the Python packages necessary to run the Clinical Knowledge Graph can be found in `requirements.txt`.

Unfortunately, due to incompatibilities of the current Anaconda version of the `rpy2` package, this package needs to be removed from `requirements.txt` before installing all other packages.

To do so, open the mentioned file in your preferred text editor tool (e.g. Notepad) and remove the line `rpy2==3.0.5`. Save and close the file, making sure it is saved as a plain text file.

Warning: Part of the CKG functionality includes interfacing Python and R, and seemingly use R functions for data analysis. The python package `rpy2` is used as this interface and unfortunately, the current release of this package for Windows is not compatible with CKG. Installation of the CKG on Windows machines, will therefore **not** allow the usage of R packages (SAMR and WGCNA) within the CKG.

To install all the required packages, simply run:

```
> cd CKG/  
> conda install --file requirements.txt
```

Warning: Make sure the virtual environment previously created is active before installing `requirements.txt`.

Now that all the packages are correctly installed, you will have to create the appropriate directory architecture within the local copy of the cloned repository:

```
> python setup_CKG.py  
> python setup_config_files.py
```

This will automatically create the `data` folder and all subfolders, as well as setup the configuration for the log files where all errors and warnings related to the code will be written to.

Add CKG to environmental variables

Similarly to *Add Neo4j graph database to environmental variables*, CKG also needs to be added to the environmental variables.

1. Go to the Windows menu, right-click on *Computer* and click on *Properties*.
2. From the computer properties dialog, select *Advanced system settings* on the left panel. And from there, click on *Environment variables*.
3. In the Environment variables dialog, click *New* in the top half of the dialog, to make a new user variable
4. Give the variable name as `PYTHONPATH` and the value is the path to the CKG code directory, for example `C:\CKG\src`. Notice that the path should always finish with `\CKG\src`.
5. Click *OK* and *OK* again to save this variable.

To confirm that the environment variable is correctly set in command line type:

```
> echo %PYTHONPATH%
```

This will print the path you used as value (e.g. `C:\CKG\src`).

Build Neo4j graph database (Windows)

Building the CKG database in Windows follows the same steps as in MacOS and Linux so, from here on, please follow the tutorial *Build Neo4j graph database*.

GETTING STARTED

- **Connecting to the CKG:** *Connect to DB*
- **Create a new user in the graph database:** *Create new user*
- **Create a project in the database:** *Project Creation*
- **Upload experimental data:** *Data Upload*
- **Define data analysis settings:** *Configuration*
- **Access the analysis report:** *Access report*
- **Report notification:** *Notifications*

3.1 Connecting to the Clinical Knowledge Graph database

In order to make use of the CKG database you just built, we need to connect to it and be able to query for data. This connection is established via one of Neo4j's Python drivers Py2neo, a library and comprehensive toolkit developed to enable working with Neo4j from within Python applications, and should already be installed in your virtual environment.

Another essential tool when working with Neo4j databases, is the [Cypher query language](#). We recommend becoming familiar with it, to understand the queries used in the different analyses.

3.1.1 Py2neo connector

Within the CKG package, the `graph_connector` module was created to connect the different parts of the Python code, to the Neo4j database and allow their interaction.

In this module, the `Graph` class from `py2neo` is used to represent the graph data storage space within the Neo4j database, and a YAML configuration file is parsed to retrieve the connection details. The configuration file `connector_config.yml` contains the database server host name, server port, user to authenticate as, and password to use for authentication.

```
from graphdb_connector import connector
driver = connector.getGraphDatabaseConnectionConfiguration()
```

Once the connection is established, we can start querying the database. For example:

```
example_query = 'MATCH (p:Project)-[:HAS_ENROLLED]-(s:Subject) RETURN p.id as project_id, COUNT(s) as n_subjects'
results = connector.getCursorData(driver=driver, query=example_query, parameters={})
```

This query searches the database for all the available projects and counts how many subjects have been enrolled in each one, returning a pandas DataFrame with “project_id” and “n_subjects” as columns.

3.2 Create a new user in the graph database

The creation of a new user includes two steps:

1. The user who is currently logged-in in the database and invoking the commands, has to add the new user to the system and attribute it a role, by default reader.
2. Each user is added in the graph database as a new User node, with attributes: id, username, name, acronym, email, secondary email, phone number, affiliation, rolename and expiration date.

There are multiple ways to create a new user:

From the command line: (*one user at a time*)

```
$ cd src/graphdb_builder/builder  
$ python create_user.py -u username -d password -n name -e email -s second_email -p  
->phone_number -a affiliation
```

From an excel file: (*multiple users*)

```
$ cd src/graphdb_builder/builder  
$ python create_user.py -f path/to/excel/file
```

For help on how to use `create_user.py`, run:

```
$ python create_user.py -h
```

For each new user, an access password is set be the same the the `username`. All users are advised to modify the default password as soon as they are granted access.

3.3 Create a new project in the database

The project creation app in the Clinical Knowledge Graph was designed to make the process straightforward and user-friendly. To create a project, please follow the steps below.

Neo4j

1. Open neo4j desktop
2. Start the database

Terminal

1. In one terminal window:
 - Activate the virtual environment (if created beforehand)

```
$ source /path/to/virtualenvironment/bin/activate;
```

- Start a redis-server:

```
$ redis-server
```

Warning: If redis-server is not found, install with brew install redis (Mac) or sudo apt-get install redis-server (Linux).

Warning: On Windows, redis-server should be installed by default (to check, go to start menu > services.msc > Redis). If that is not the case, go to <https://github.com/microsoftarchive/redis/releases>, download the latest release installer (.msi file), and follow the installation instructions. Let all options as default but remember to select **Add the Redis installation folder to the PATH environment variable.**. To start a redis-server, make sure it is **not running in ``services.msc``**, and run in the command prompt: C:"Program Files"Redisredis-server

Note: C:\Program Files" can be replaced with the correct path where you installed Redis from the installer (.msi file).

2. In two separate terminal windows:

- Navigate to report_manager in both of them

```
$ cd CKG/src/report_manager
```

- Start a celery queue from the report_manager directory, in each window:

Default queue

```
$ celery -A worker worker -l debug
```

Compute queue - Report generation

```
$ celery -A worker worker --loglevel=DEBUG --concurrency=3 -E -Q compute
```

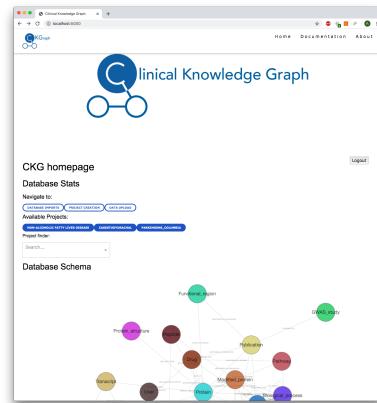
3. In a fourth terminal window:

- Run the report manager index app:

```
$ cd CKG/src/report_manager
$ python index.py
```

This will print some warnings, which should be okay.

Warning: Make sure that your virtual environment is always activated in each terminal window, before running any other command.



Browser

1. Copy the url `http://localhost:5000/` into a web browser and you will be directed to a login page.
2. Enter your username and password

This action will redirect you to the CKG home page app. From here, you can navigate to different applications, including the “Project Creation” app.

Note: Username and password will be authenticated in the CKG database. For this reason, you should have been created as a new user in the database before this step.

3.3.1 Project creation

From the CKG app home page, you can navigate to the project creation app by clicking PROJECT CREATION or pasting the url `http://localhost:5000/apps/projectCreationApp` in the browser.

Once you have been redirected, please fill in all the information needed to create a project. This includes all the fields marked with * (mandatory). **(1)** After all fields are filled in, please revise all the information and press Create Project. **(2)** The page will refresh and once finished, the project identifier will be depicted in front of the Project information header. **(3)** Use this identifier to search for data related to your project.

At this stage, and if your project has been successfully created in the database, a new button will appear and the message will instruct you to download a compressed file with the experimental design and clinical data template files. To do so, please press the button “Download Clinical Data template”. **(4)**

Note: Each field, with the exception of Project name, Project Acronym, Number of subjects, Project Description, Starting Date and Ending Date, can take multiple values. Select the most appropriate ones for your specific project.

Fill in the `ExperimentalDesign_Pxxxxxxxx.xlsx` file with your subject, biological sample and analytical sample identifiers.

Fig. 1: Project Creation App

Please double-check they are correct, this information is essential to map the results correctly in the database.

The `ClinicalData_Pxxxxxxxx.xlsx` file needs to be filled in with all the relevant clinical data and sample information. For more instructions on how to fill in the file, please see *Upload project experimental data*.

To check your project in the neo4j database interface:

- Open the Neo4j desktop app
- Find the graph database in use and click *Manage*, followed by *Open Browser* (opens a new window).
- In the new Neo4j window, click on the database symbol (top left corner) and, under *Node Labels*, click *Project*

At this point, you should be able to see all the nodes corresponding to projects loaded in the database. To expand your project information, click on your project node and in the bottom of the window press the < symbol. Here you will find all the attributes of the project, including the project identifier (typically “P000000xx”).

3.4 Upload project experimental data

3.4.1 Prepare data for upload

Experimental Design

Open the Experimental Design excel file, automatically downloaded when the project was created, and fill in the columns for *subject external_id*, *biological_sample external_id* and *analytical_sample external_id*. The identifiers provided in this file **must** correspond to the identifiers used in the *Clinical Data* file, and to the column names in the *Proteomics* files (see below).

Warning: Make sure, within each column, the identifiers are unique. This means, if you have a subject “KO1”, no other subject can have the same identifier, but you can have a biological sample and/or analytical sample “KO1”.

Clinical Data

Open the Clinical Data excel file, automatically downloaded when the project was created, and fill in as much information as you can. Be aware that the following columns are mandatory to fill in:

- **subject external_id:** This is the identifier your subject has in your study so far (same identifiers as used in *Experimental Design*, *subject external_id*).
- **tissue:** This is the name of the tissue each sample came from. Make sure it is also one of the tissues selected during Project creation.
- **disease:** This should match the disease(s) you selected from the drop-down menu in the *Project creation*.

Subject external_id	Biological sample external_id	Analytical sample external_id
1	1	sample_1
1	2	sample_2
1	3	sample_3
2	1	sample_4
2	2	sample_5
2	3	sample_6

Fig. 2: Experimental Design file example

Clinical Knowledge Graph Documentation, Release 1.0.0

ExperimentalDesign_...

E21

	A	B	C	D	E	F
1	subject external_id	biological_sample external_id	analytical_sample external_id			
2	1	1_1	sample_1			
3	1	1_2	sample_2			
4	1	1_3	sample_3			
5	2	2_1	sample_4			
6	2	2_2	sample_5			
7	2	2_3	sample_6			
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						
21						
22						
23						
24						
25						
26						
27						

Fig. 3: Experimental Design file example

Fig. 4: Clinical Data file example

- **biological_sample external_id:** This is the identifier of the sample taken from your subject, if you have both blood and urine for every subject, you should correspondingly have two biological sample identifiers for each subject identifier (same identifiers as used in *Experimental Design*, **biological_sample external_id**).
- **biological_sample quantity:** Amount of biological sample.
- **biological_sample quantity_units:** Unit.
- **analytical_sample external_id:** If multiple analyses were performed on the same biological sample, eg. proteomics and transcriptomics, there should be multiple analytical sample identifiers for every biological sample (same identifiers as used in *Experimental Design*, **analytical_sample external_id**).
- **analytical_sample quantity:** Amount of sample used in the experiment.
- **analytical_sample quantity_units:** Unit.
- **grouping1:** Annotated grouping of each sample.
- **grouping2:** If there are more than one grouping (two independent variables) use this column to add a second level.

Additional clinical information about your study subjects can be added in the subsequent columns (i.e. columns after “grouping2”). Please use SNOWMED terms as headers for every new column you add. This will be used to gather existing information about the type of data you have. To find an adequate SNOMED term for your clinical variables, please visit the [SNOMED browser](#).

Note: Be aware, the two-independent-variable statistics is not yet implemented in the default analysis pipeline.

Note: To add a column with “Age” search for “age” in the SNOMED browser. This gives multiple matches, with the first one being: “Age (qualifier value), SCTID:397669002”. Please enter this information as your clinical variable column header with the SCTID in brackets: Age (qualifier value) (397669002)

Warning: If an adequate SNOMED term is not available, please write an e-mail to annelaura.bach@cpr.ku.dk with the subject “Header Creation, CKG”. In the email please provide your “missing” header and a description of what it is. Do this before uploading the Clinical Data.

Additional columns:

- **timpeoint:** To be used in the case of a longitudinal study. This is a relative measure within your samples timepoints. For example, if your timepoints are years 2015, 2016, 2017, 2018 and 2019, you would use “0”, “1”, “2”, “3” and “4” as values in this column.
- **timepoint units:** Unit in which your **timepoint** is measured (e.g. “hours”, “days”, “years”).
- **had_intervention:** If a subject has been subjected to a determined medical intervention. For now, select only drugs that have been given to the subject (e.g. “327032007”). Use an appropriate SNOMED SCTID value.
- **had_intervention_type:** This is the type of intervention applied to a subject. “drug treatment” is the only value available for now.
- **had_intervention_in_combination:** Boolean. If True, requires more than one value in **had_intervention**.
- **had_intervention_response:** “positive” or “negative”.
- **studies_intervention:** A medical intervention under study in the project. For example, study subjects before and after stomach bypass (SCTID:442338001). Use an appropriate SNOMED SCTID value.

Proteomics data

- **MaxQuant:** Use “proteinGroups.txt”, “peptides.txt” and “Oxidation (M)Sites.txt” files, and any other relevant MaxQuant output files.
- **Spectronaut:** Use “proteinGroupsReport.xlsx”. When exporting the results table from Spectronaut, please select “PG.ProteinAccessions” and “PG.Qvalue” under *Row Labels*, and under *Cell Values* select “PG.Quantity”, “PG.NrOfStrippedSequencesMeasured”, “PG.NrOfStrippedSequencesIdentified”, “PG.NrOfPrecursorsIdentified”, “PG.IsSingleHit”, “PG.NrOfStrippedSequencesUsedForQuantification”, “PG.NrOfModifiedSequencesUsedForQuantification”, “PG.NrOfPrecursorsUsedForQuantification”, “PG.MS1Quantity” and “PG.MS2Quantity”.

It is very important that all your column names have the following format: “LFQ intensity TechnicalReplicateNumber_AnalyticalSampleIdentifier” or “TechnicalReplicateNumber_AnalyticalSampleIdentifier.PG.Quantity”. Where “TechnicalReplicateNumber_AnalyticalSampleIdentifier” should be replaced as shown in the example table below:

Technical replicate	Analytical sample id	Timepoint	Result
1	KO_plate1		1_KO_plate1
1	KO2_plate1	0	1_KO_plate1_0
1	KO3_plate1	30	1_KO_plate1_30
1	KO4_plate2		1_KO4_plate2
2	KO4_plate2		2_KO4_plate2

As shown in the example table, if your experimental design is a timecourse experiment, you should add “_” followed by the timepoint, right after the analytical sample identifier. Otherwise, you can omit it.

Do not perform any post-processing filtering, imputations or similar on your data before uploading it. This will be carried out by the CKG. In the case of Spectronaut outputs, the missing values are automatically replaced by the keyword “Filtered”.

You can proceed to *Upload Data* when you have prepared your experimental design file, clinical and proteomics data.

3.4.2 Upload Data

In order to make data uploading simple, we created an app that takes care of this in only a few steps:

Go to [dataUploadApp](#) or use the **Data Upload** button in the [homepage](#) app, and follow the steps.

1. Fill in **Project identifier** with your project external identifier from *Project creation* and press *Enter*.
 (1) If the project identifier does not exist in the database, you will get an error. Otherwise, the menus below will unlock.
2. Select the type of data you will upload first. (2)
 - If **proteomics** or **longitudinal_proteomics** is selected, please also select the processing tool used (MaxQuant or Spectronaut). (2a)
3. Drag and drop or select the files to upload to the selected data type. (3)
 - Multiple files can be selected at once. This is specially important in the case of proteomics files, please make sure you select all of the relevant MS files at once.
4. Select another data type to upload (2), and drag and drop or select the files to upload (3).
5. When you have uploaded all the relevant files, click **UPLOAD DATA TO CKG**. After this button is clicked, it will deactivate all the menus. To restore its function, insert the project identifier and go through the previous steps again. (4)

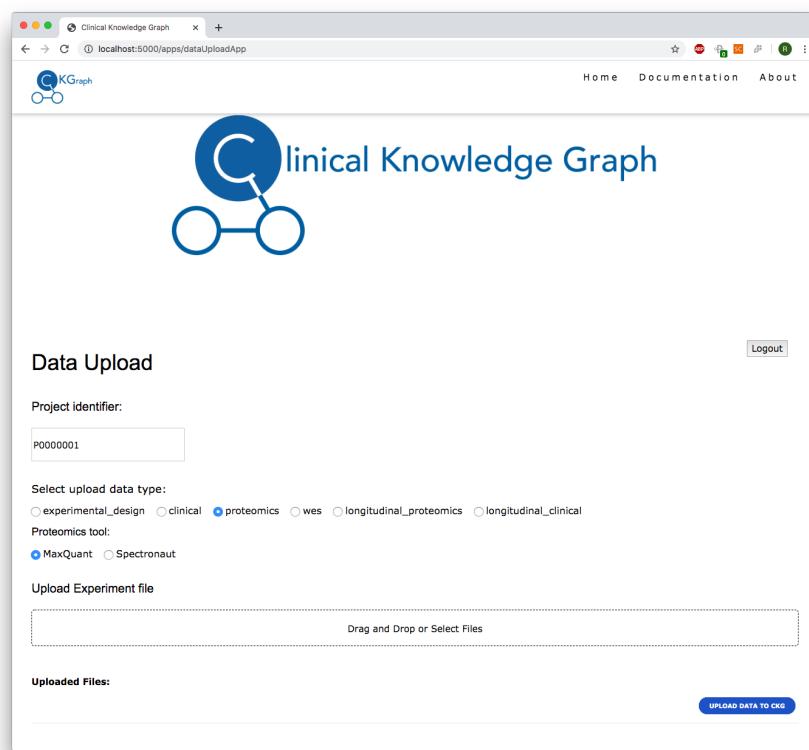


Fig. 5: Data Upload App

6. Once the data is uploaded, click **Download Uploaded Files (.zip)** to download all the upload files in a compressed format. (5)

Note: When the files are uploaded, the filenames are shown under **Uploaded Files**: To replace the files uploaded, just select the correct data type and processing tool, and reselect the files again.

Warning: It is very important that you select **all** the files that should be uploaded to a certain data type **at once**.

3.5 Define data analysis parameters

A multitude of different analysis methods and visualization plots have been implemented within the `analytics` core of the Clinical Knowledge Graph. The default workflow makes use of these resources and runs, for each data type, the analysis pipeline defined in a configuration file. In the CKG, we have default analysis defined for Clinical data, Proteomics, and Multiomics. All the analysis configuration files can be modified to fit your project or data.

To check how each configuration file looks like and how to modify them, please follow the links below.

3.5.1 Clinical data analysis parameters

The Clinical data configuration file contains two sections: `args` and `overview`. The first section contains the parameters used for the processing of the raw clinical data. To obtain the raw clinical data, we query the CKG database for all the clinical variables connected to biological samples in a specific project. This results in a Pandas dataframe with all the relevant information. To process the raw data, a number of parameters are defined in the `args` section of the configuration file:

- **subject_id**: column label containing subject identifiers.
 - **sample_id**: column label containing biological sample identifiers.
 - **group_id**: column label containing group identifiers.
 - **imputation_method**: method for missing values imputation (“KNN”, “distribution”, or “mixed”).
 - **columns**: list of column names whose unique values will become the new column names
 - **values**: column label containing clinical variable values.



Fig. 6: Clinical Data configuration file

- **extra**: additional column labels to be kept as columns

The result is another Pandas dataframe, stored as “processed”, where columns are the clinical variables and biological samples are rows, group and subject identifier are kept as columns as well.

Note: We advise to change only **imputation_method**, if needed.

The second section (`overview`) depicts the analysis performed for the clinical data, and the parameters used to do it. Among the analysis is:

- Summary table (**clinical variables**)
- Stratification plot (**stratification**)
- Clinical variables per group (**measurement matrix**)
- Hypothesis test (**regulation**)
- Correlation network (**correlation**)

Within each analysis, specific parameters are defined:

- **description**: Definition of the analysis used.
- **data**: defines on which dataset dataframe the analysis will be ran (e.g. “clinical variables”, “original”, “processed”).
- **analyses**: which statistical analysis to run on the `data`. These functions are called from the module `analytics_factory.py`.
- **plots**: which plot to use to show the results of **analyses**. Functions also called from the module `analytics_factory.py`.
- **store_analysis**: boolean. True if the dataframe resulting from **analyses** is to be stored.
- **args**: all arguments necessary for **analyses** and **plots**.

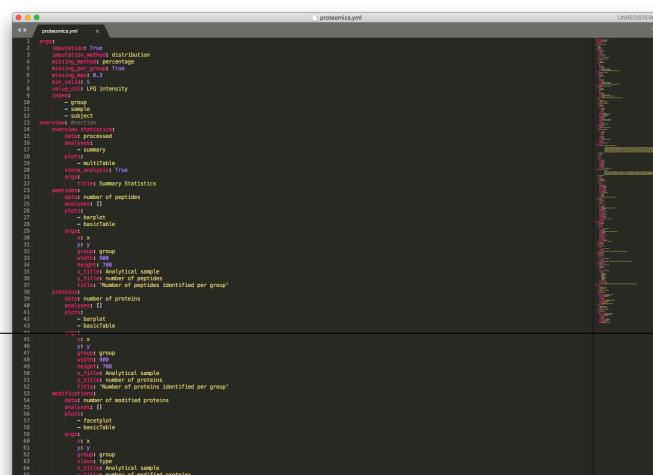
You can modify the analysis parameters just by changing the respective parameters within the configuration file. Remember to consult the modules `analytics.py` and `viz.py`, to learn more about the arguments of each function. If you would like to add a specific analysis step to the default pipeline, remember to add a call to the function in `analytics_factory.py`.

3.5.2 Proteomics data analysis parameters

Similarly to the *Clinical data analysis parameters*, the Proteomics configuration file is divided into sections: `args`, `overview`, `data exploration`, `data associations` and `enrichment`.

The `args` section contains the parameters used to process the proteomics data extracted from the CKG database, which includes the filtering of proteins according to the determined threshold, as well as the imputation of all missing values. These parameters include:

- **imputation**: boolean. Set to *True* if missing values shall be imputed.



- **imputation_method:** method for missing values imputation (“KNN”, “distribution”, or “mixed”).
- **missing_method:**
- **missing_per_group:** boolean. If *True*, proteins are filtered based on valid values per group; if *False* filter across all samples.
- **missing_max:** maximum ratio of missing/valid values to be filtered. (e.g. **0.3** filters all proteins with more than 30% missing values).
- **min_valid:** minimum number of required valid values to keep a protein.
- **value_col:** column label containing expression values.
- **index:** column labels to be kept as index identifiers.

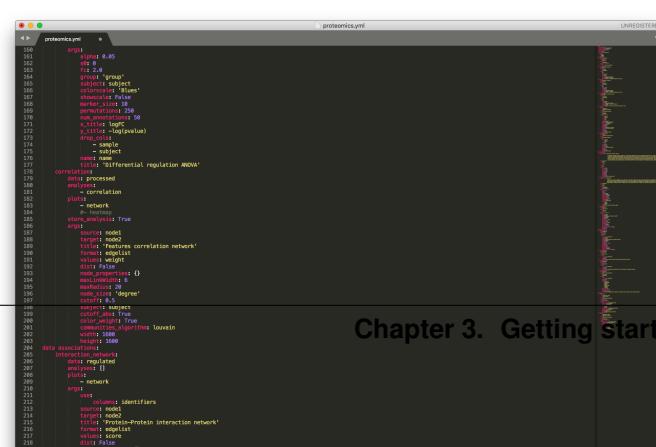
The result is a Pandas dataframe, stored as “processed”, where columns are protein identifiers (UniprotID~GeneName) and analytical samples are rows, group and subject identifier are kept as columns as well.

Note: We advise to change only **imputation**, **imputation_method**, **missing_method**, **missing_per_group**, and **missing_max** or **min_valid**.

The second section (`overview`) corresponds to basic statistics and includes:

- Data summary statistics (**overview statistics**)
- Number of peptides per sample (**peptides**)
- Number of proteins per sample (**proteins**)
- Number of modifications per sample (**modifications**)
- Dynamic range per group (**ranking**)
- Coefficient of variation per group (**coefficient_variation**)

In the data exploration section, we look at the sample stratification (**stratification**), differentially expressed proteins (**regulation**), and protein-protein correlation network (**correlation**). In this section, you can choose to modify parameters like alpha (FDR value), s0 (artificial within groups variance) or fc (fold-change), to better fit your data and experimental design. Likewise, the correlation network is,



by default, set to show correlations above 50% (cutoff: 0.5), this too can be changed.

The data associations section includes analyses that correlated differentially expressed proteins to proteins (**interaction_network**), drugs (**drug_associations**), diseases (**disease_associations**) and publications (**literature_associations**). All these associations are directly queried from the CKG database.

The last section in the default analysis pipeline corresponds to the enrichment analysis, and includes both Gene Ontology (**go_enrichment**) and Pathway (**pathway_enrichment**) enrichment analyses, using Fisher's exact test (method: `fisher`)

Likewise in the *Clinical data analysis parameters*, within each analysis, specific parameters are defined:

- **description:** Definition of the analysis used.
- **data:** defines on which dataset dataframe the analysis will be ran (e.g. “clinical variables”, “original”, “processed”).
- **analyses:** which statistical analysis to run on the data. These functions are called from the module `analytics_factory.py`.
- **plots:** which plot to use to show the results of **analyses**. Functions also called from the module `analytics_factory.py`.
- **store_analysis:** boolean. True if the dataframe resulting from **analyses** is to be stored.
- **args:** all arguments necessary for **analyses** and **plots**.

You can modify the analysis parameters just by changing the respective parameters within the configuration file. Remember to consult the modules `analytics.py` and `viz.py`, to learn more about the arguments of each function. If you would like to add a specific analysis step to the default pipeline, remember to add a call to the function in `analytics_factory.py`.

3.5.3 Multiomics data analysis parameters

The Multiomics configuration file allows you to integrate different data types and, as a default we integrate clinical and proteomics data. In this context, the configuration file includes a multi-correlation section where all clinical and proteomics data are correlated and depicted as a network, and a Weighted Gene Co-expression Network Analysis (WGCNA) section, where features (proteins) are clustered in co-expression modules and further correlated to the clinical variables.

3.6 Accessing the analysis report

The standard report provides initial evaluation of the quality of the generated data, highlight relevant hits, and contextualize these hits in relation to different biomedical components in the graph.

There are two ways to acces the report, on the browser using a Dash App, or in a Jupyter notebook. For more information on each, please follow the links below.

3.6.1 Report: Dash web app

3.6.2 Report: Jupyter-notebook

- Easy access to all the experimental data generated in the lab
- All the results from statistical analysis
- Visualization of reports
- All the python functionality at hand
- Additional analysis of project (e.g. treatment candidate selection, PTMs, predictions)

```

multiomics.yml
1 data_exploration:
2   class: Correlations
3   data:
4     - protomomics: processed
5     - clinical: processed
6   analyses:
7     - multi_correlation
8     - network
9   store_analysis: True
10  args:
11    - on_corr:
12      - subject
13      - group
14      - source
15      - target: nodes
16      - title: 'Clinical-Proteomics correlation network'
17      - form: edge_list
18      - method: spearman
19      - cutoff: 0.5
20      - dist: False
21      - node_properties: {}
22      - maxRedist: 20
23      - root: 'Protein' degree'
24      - cutoff: 0.5
25      - subject: subject
26      - color_weight: True
27      - algorithm: louvain
28      - height: 1000
29
30  wgcna:
31   data:
32     - protomomics: processed
33     - clinical: processed
34   analyses:
35     - wgcna
36     - wgnaplot
37   plots:
38     - wgnaplot:
39       store_analysis: True
40       args:
41         - drop_cols_ex:
42           - subject
43           - sample
44           - group
45           - biological_sample
46           - index
47           - subject
48           - group
49           - biological_sample
50           - RscriptPath: 'R'
51           - networkXpath: 'unsigned'
52           - minModuleSize: 50
53           - depthSplit: 2
54           - parRespectsDensity: False
55           - minModSize: 100
56           - MEDissThresh: 0.3
57           - verbose: 0
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
259
260
261
262
263
264
265
266
267
268
269
269
270
271
272
273
274
275
276
277
278
279
279
280
281
282
283
284
285
286
287
287
288
289
289
290
291
292
293
294
295
296
297
297
298
299
299
300
301
302
303
304
305
305
306
307
307
308
309
309
310
311
311
312
312
313
313
314
314
315
315
316
316
317
317
318
318
319
319
320
320
321
321
322
322
323
323
324
324
325
325
326
326
327
327
328
328
329
329
330
330
331
331
332
332
333
333
334
334
335
335
336
336
337
337
338
338
339
339
340
340
341
341
342
342
343
343
344
344
345
345
346
346
347
347
348
348
349
349
350
350
351
351
352
352
353
353
354
354
355
355
356
356
357
357
358
358
359
359
360
360
361
361
362
362
363
363
364
364
365
365
366
366
367
367
368
368
369
369
370
370
371
371
372
372
373
373
374
374
375
375
376
376
377
377
378
378
379
379
380
380
381
381
382
382
383
383
384
384
385
385
386
386
387
387
388
388
389
389
390
390
391
391
392
392
393
393
394
394
395
395
396
396
397
397
398
398
399
399
400
400
401
401
402
402
403
403
404
404
405
405
406
406
407
407
408
408
409
409
410
410
411
411
412
412
413
413
414
414
415
415
416
416
417
417
418
418
419
419
420
420
421
421
422
422
423
423
424
424
425
425
426
426
427
427
428
428
429
429
430
430
431
431
432
432
433
433
434
434
435
435
436
436
437
437
438
438
439
439
440
440
441
441
442
442
443
443
444
444
445
445
446
446
447
447
448
448
449
449
450
450
451
451
452
452
453
453
454
454
455
455
456
456
457
457
458
458
459
459
460
460
461
461
462
462
463
463
464
464
465
465
466
466
467
467
468
468
469
469
470
470
471
471
472
472
473
473
474
474
475
475
476
476
477
477
478
478
479
479
480
480
481
481
482
482
483
483
484
484
485
485
486
486
487
487
488
488
489
489
490
490
491
491
492
492
493
493
494
494
495
495
496
496
497
497
498
498
499
499
500
500
501
501
502
502
503
503
504
504
505
505
506
506
507
507
508
508
509
509
510
510
511
511
512
512
513
513
514
514
515
515
516
516
517
517
518
518
519
519
520
520
521
521
522
522
523
523
524
524
525
525
526
526
527
527
528
528
529
529
530
530
531
531
532
532
533
533
534
534
535
535
536
536
537
537
538
538
539
539
540
540
541
541
542
542
543
543
544
544
545
545
546
546
547
547
548
548
549
549
550
550
551
551
552
552
553
553
554
554
555
555
556
556
557
557
558
558
559
559
560
560
561
561
562
562
563
563
564
564
565
565
566
566
567
567
568
568
569
569
570
570
571
571
572
572
573
573
574
574
575
575
576
576
577
577
578
578
579
579
580
580
581
581
582
582
583
583
584
584
585
585
586
586
587
587
588
588
589
589
590
590
591
591
592
592
593
593
594
594
595
595
596
596
597
597
598
598
599
599
600
600
601
601
602
602
603
603
604
604
605
605
606
606
607
607
608
608
609
609
610
610
611
611
612
612
613
613
614
614
615
615
616
616
617
617
618
618
619
619
620
620
621
621
622
622
623
623
624
624
625
625
626
626
627
627
628
628
629
629
630
630
631
631
632
632
633
633
634
634
635
635
636
636
637
637
638
638
639
639
640
640
641
641
642
642
643
643
644
644
645
645
646
646
647
647
648
648
649
649
650
650
651
651
652
652
653
653
654
654
655
655
656
656
657
657
658
658
659
659
660
660
661
661
662
662
663
663
664
664
665
665
666
666
667
667
668
668
669
669
670
670
671
671
672
672
673
673
674
674
675
675
676
676
677
677
678
678
679
679
680
680
681
681
682
682
683
683
684
684
685
685
686
686
687
687
688
688
689
689
690
690
691
691
692
692
693
693
694
694
695
695
696
696
697
697
698
698
699
699
700
700
701
701
702
702
703
703
704
704
705
705
706
706
707
707
708
708
709
709
710
710
711
711
712
712
713
713
714
714
715
715
716
716
717
717
718
718
719
719
720
720
721
721
722
722
723
723
724
724
725
725
726
726
727
727
728
728
729
729
730
730
731
731
732
732
733
733
734
734
735
735
736
736
737
737
738
738
739
739
740
740
741
741
742
742
743
743
744
744
745
745
746
746
747
747
748
748
749
749
750
750
751
751
752
752
753
753
754
754
755
755
756
756
757
757
758
758
759
759
760
760
761
761
762
762
763
763
764
764
765
765
766
766
767
767
768
768
769
769
770
770
771
771
772
772
773
773
774
774
775
775
776
776
777
777
778
778
779
779
780
780
781
781
782
782
783
783
784
784
785
785
786
786
787
787
788
788
789
789
790
790
791
791
792
792
793
793
794
794
795
795
796
796
797
797
798
798
799
799
800
800
801
801
802
802
803
803
804
804
805
805
806
806
807
807
808
808
809
809
810
810
811
811
812
812
813
813
814
814
815
815
816
816
817
817
818
818
819
819
820
820
821
821
822
822
823
823
824
824
825
825
826
826
827
827
828
828
829
829
830
830
831
831
832
832
833
833
834
834
835
835
836
836
837
837
838
838
839
839
840
840
841
841
842
842
843
843
844
844
845
845
846
846
847
847
848
848
849
849
850
850
851
851
852
852
853
853
854
854
855
855
856
856
857
857
858
858
859
859
860
860
861
861
862
862
863
863
864
864
865
865
866
866
867
867
868
868
869
869
870
870
871
871
872
872
873
873
874
874
875
875
876
876
877
877
878
878
879
879
880
880
881
881
882
882
883
883
884
884
885
885
886
886
887
887
888
888
889
889
890
890
891
891
892
892
893
893
894
894
895
895
896
896
897
897
898
898
899
899
900
900
901
901
902
902
903
903
904
904
905
905
906
906
907
907
908
908
909
909
910
910
911
911
912
912
913
913
914
914
915
915
916
916
917
917
918
918
919
919
920
920
921
921
922
922
923
923
924
924
925
925
926
926
927
927
928
928
929
929
930
930
931
931
932
932
933
933
934
934
935
935
936
936
937
937
938
938
939
939
940
940
941
941
942
942
943
943
944
944
945
945
946
946
947
947
948
948
949
949
950
950
951
951
952
952
953
953
954
954
955
955
956
956
957
957
958
958
959
959
960
960
961
961
962
962
963
963
964
964
965
965
966
966
967
967
968
968
969
969
970
970
971
971
972
972
973
973
974
974
975
975
976
976
977
977
978
978
979
979
980
980
981
981
982
982
983
983
984
984
985
985
986
986
987
987
988
988
989
989
990
990
991
991
992
992
993
993
994
994
995
995
996
996
997
997
998
998
999
999
1000
1000
1001
1001
1002
1002
1003
1003
1004
1004
1005
1005
1006
1006
1007
1007
1008
1008
1009
1009
1010
1010
1011
1011
1012
1012
1013
1013
1014
1014
1015
1015
1016
1016
1017
1017
1018
1018
1019
1019
1020
1020
1021
1021
1022
1022
1023
1023
1024
1024
1025
1025
1026
1026
1027
1027
1028
1028
1029
1029
1030
1030
1031
1031
1032
1032
1033
1033
1034
1034
1035
1035
1036
1036
1037
1037
1038
1038
1039
1039
1040
1040
1041
1041
1042
1042
1043
1043
1044
1044
1045
1045
1046
1046
1047
1047
1048
1048
1049
1049
1050
1050
1051
1051
1052
1052
1053
1053
1054
1054
1055
1055
1056
1056
1057
1057
1058
1058
1059
1059
1060
1060
1061
1061
1062
1062
1063
1063
1064
1064
1065
1065
1066
1066
1067
1067
1068
1068
1069
1069
1070
1070
1071
1071
1072
1072
1073
1073
1074
1074
1075
1075
1076
1076
1077
1077
1078
1078
1079
1079
1080
1080
1081
1081
1082
1082
1083
1083
1084
1084
1085
1085
1086
1086
1087
1087
1088
1088
1089
1089
1090
1090
1091
1091
1092
1092
1093
1093
1094
1094
1095
1095
1096
1096
1097
1097
1098
1098
1099
1099
1100
1100
1101
1101
1102
1102
1103
1103
1104
1104
1105
1105
1106
1106
1107
1107
1108
1108
1109
1109
1110
1110
1111
1111
1112
1112
1113
1113
1114
1114
1115
1115
1116
1116
1117
1117
1118
1118
1119
1119
1120
1120
1121
1121
1122
1122
1123
1123
1124
1124
1125
1125
1126
1126
1127
1127
1128
1128
1129
1129
1130
1130
1131
1131
1132
1132
1133
1133
1134
1134
1135
1135
1136
1136
1137
1137
1138
1138
1139
1139
1140
1140
1141
1141
1142
1142
1143
1143
1144
1144
1145
1145
1146
1146
1147
1147
1148
1148
1149
1149
1150
1150
1151
1151
1152
1152
1153
1153
1154
1154
1155
1155
1156
1156
1157
1157
1158
1158
1159
1159
1160
1160
1161
1161
1162
1162
1163
1163
1164
1164
1165
1165
1166
1166
1167
1167
1168
1168
1169
1169
1170
1170
1171
1171
1172
1172
1173
1173
1174
1174
1175
1175
1176
1176
1177
1177
1178
1178
1179
1179
1180
1180
1181
1181
1182
1182
1183
1183
1184
1184
1185
1185
1186
1186
1187
1187
1188
1188
1189
1189
1190
1190
1191
1191
1192
1192
1193
1193
1194
1194
1195
1195
1196
1196
1197
1197
1198
1198
1199
1199
1200
1200
1201
1201
1202
1202
1203
1203
1204
1204
1205
1205
1206
1206
1207
1207
1208
1208
1209
1209
1210
1210
1211
1211
1212
1212
1213
1213
1214
1214
1215
1215
1216
1216
1217
1217
1218
1218
1219
1219
1220
1220
1221
1221
1222
1222
1223
1223
1224
1224
1225
1225
1226
1226
1227
1227
1228
1228
1229
1229
1230
1230
1231
1231
1232
1232
1233
1233
1234
1234
1235
1235
1236
1236
1237
1237
1238
1238
1239
1239
1240
1240
1241
1241
1242
1242
1243
1243
1244
1244
1245
1245
1246
1246
1247
1247
1248
1248
1249
1249
1250
1250
1251
1251
1252
1252
1253
1253
1254
1254
1255
1255
1256
1256
1257
1257
1258
1258
1259
1259
1260
1260
1261
1261
1262
1262
1263
1263
1264
1264
1265
1265
1266
1266
1267
1267
1268
1268
1269
1269
1270
1270
1271
1271
1272
1272
1273
1273
1274
1274
1275
1275
1276
1276
1277
1277
1278
1278
1279
1279
1280
1280
1281
1281
1282
1282
1283
1283
1284
1284
1285
1285
1286
1286
1287
1287
1288
1288
1289
1289
1290
1290
1291
1291
1292
1292
1293
1293
1294
1294
1295
1295
1296
1296
1297
1297
1298
1298
1299
1299
1300
1300
1301
1301
1302
1302
1303
1303
1304
1304
1305
1305
1306
1306
1307
1307
1308
1308
1309
1309
1310
1310
1311
1311
1312
1312
1313
1313
1314
1314
1315
1315
1316
1316
1317
1317
1318
1318
1319
1319
1320
1320
1321
1321
1322
1322
1323
1323
1324
1324
1325
1325
1326
1326
1327
1327
1328
1328
1329
1329
1330
1330
1331
1331
1332
1332
1333
1333
1334
1334
1335
1335
1336
1336
1337
1337
1338
1338
1339
1339
1340
1340
1341
1341
1342
1342
1343
1343
1344
1344
1345
1345
1346
1346
1347
1347
1348
1348
1349
1349
1350
1350
1351
1351
1352
1352
1353
1353
1354
1354
1355
1355
1356
1356
1357
1357
1358
1358
1359
1359
1360
1360
1361
1361
1362
1362
1363
1363
1364
1364
1365
1365
1366
1366
1367
136
```

3.7.1 Slack notifications

3.7.2 E-mail notifications

CHAPTER
FOUR

THE PROJECT REPORT

- Generate a project: *Project*
- The Tabs: *Project tabs*

4.1 Generating a project report

4.2 Project report tabs

CKG BUILDER

- **Ontology sources and parsers:** *Ontologies*
- **Biomedical databases and resources:** *Databases*
- **Parsing experimental data:** *Experiments*
- **Building the graph database from one module:** *Builder*

5.1 Ontology sources and raw file parsers

5.2 Biomedical databases and resources

5.3 Parsing experimental data

5.3.1 Clinical data

5.3.2 Proteomics

- MaxQuant
- Biognosys

5.3.3 Phosphoproteomics

5.3.4 WES

5.4 Building the graph database from one Python module

ADVANCED FEATURES

- **CKG Statistics:** *Imports stats | Graph database stats*
- **Jupyter notebooks:** *Notebooks*
- **Retrieving data from the CKG:** *DB Querying >>>> query_utils.find_queries_involving_nodes + query_utils.read_knowledge_queries()*
- **Data Analysis:** *Analysis*
- **Visualization:** *Plots*
- **R interface:** *R wrapper*

6.1 Clinical Knowledge Graph Statistics: Imports

6.2 Clinical Knowledge Graph Statistics: Database

6.3 Using Jupyter Notebooks with the Clinical Knowledge Graph

The Jupyter Notebook is used to interact with the notebooks provided in the Clinical Knowledge Graph. This open-source application allows you to create and share code, visualize outputs and integrated multiple big data tools.

In order to get started, make sure you have Python installed (3.3 or greater) as well as Jupyter Notebook. The latter can be installed using pip (see below). For more detailed instructions, visit the [official guide](#).

```
$ python3 -m pip install --upgrade pip
$ python3 -m pip install jupyter
```

Congratulations! Now you can run the notebook, by typing the following command in the Terminal (Mac/Linux):

```
$ jupyter notebook
```

Or,

```
$ jupyter-notebook
```

As part of the Clinical Knowledge Graph package, we provide a series of Jupyter notebooks to facilitate the analysis of data, database querying and the use of multiple visualization tools. These notebooks can be found in `src/notebooks`, under `reporting` or `development`.

Note: If you would like to use two instances of the same notebook, just duplicate in place and modify the name accordingly.

Warning: If the Clinical Knowledge Graph is deployed in a server, please set up a Jupyter Hub in order to allow access to the Jupyter Notebook.

6.3.1 Reporting notebooks

Reporting notebooks refer to Jupyter notebooks that have been finished and properly tested by the developers, and are ready to be used by the community.

- **project_reporting.ipynb**

Easy access to all the projects in the graph database. Loads all the data from a specific project (e.g. “P0000001”) and shows the report in the notebook. This notebook enables the visualization of all the plots and tables that constitute a report, as well as all the dataframes used and produced during its generation. By accessing the data directly, you can use the python functionality to further the analysis or visualization.

- **working_with_R.ipynb**

Notebook entirely written in R. One of the many advantages of using Jupyter notebooks is the possibility of writing in different programming languages. In this notebook, we demonstrate how R can be used to, similarly to *project_reporting.ipynb*, load a project and explore the analysis and plots.

In the beginning of the notebook, we create custom functions to load a project, read the report, read a dataset, and plot and network from a json file. Other R functions like these can be developed by the users according to their needs.

- **Parallel plots.ipynb**

An example of a new interactive visualization method, not currently implemented in the Clinical Knowledge Graph, but using data from a stored project. We start by loading all the data and the report of a specific project (e.g. “P0000001”), and accessing different dataframes within the proteomics dataset, as well as, the correlation network. This plot is then converted into a Pandas DataFrame and used as input for the interactive Parallel plot.

The function is created and made interactive with Jupyter Widgets `interact` function (`ipywidgets.interact`), which automatically creates user interface (UI) controls within the notebook. In this case, the user can select different clusters of proteins (from the correlation network) and observe their variation across groups.

- **Urachal Carcinoma Case Study.ipynb**

Jupyter notebook depicting the use of the Clinical Knowledge Graph database and the analytics core as a decision support tool, proposing a drug candidate in a specific subject case.

The project is analysed with the standard analytics workflow and a list of significantly differentially expressed proteins is returned. To further this analysis we first filter for regulated proteins that have been associated to the disease in study (lung cancer); we then search the database for known inhibitory drugs for these proteins; and to narrow down the list, we can query the database for each drug’s side effects. The treatment regimens are also available in the database and their side effects can be used to rank the proposed drugs. We can prioritize drugs with side effects dissimilar to the ones that caused an adverse reaction in the patient, and identify papers where these drugs have already been associated to the studied disease, further reducing the list of potential drugs candidates.

6.3.2 Development notebooks

In `src/report_manager/development` we gathered Jupyter notebooks with analysis and workflows we believe are of interest for the users but are still under development.

When a notebook in this folder is functional and successfully benchmarked, the notebook is moved to the reporting directory.

6.4 Retrieving data from the Clinical Knowledge Graph database

6.5 Standardizing the data analysis

6.6 Visualization plots

6.7 Python - R interface

SYSTEM REQUIREMENTS

7.1 System Requirements

The Clinical Knowledge Graph was conceived as a multi-user platform and therefore requires installation in a server-like setup and data systems administration knowledge. However, individual users can have local instances of the CKG, making sure data, software and hardware requirements are fulfilled.

7.1.1 Data

Licensed databases used by the CKG package require login and authentication in order to download their data. This is the case of **SNOMED-CT**, **DrugBank** and **PhosphoSitePlus**. Make sure you sign up to these three databases well in advance as the licensing process can take several days to conclude.

To sign up go to [PSP Sign up](#), [DrugBank Sign up](#) and [SNOMED-CT Sign up](#), and follow the instructions.

Once you have been given authorization to access the data, please download the files as follows:

- **PhosphoSitePlus**: *Acetylation_site_dataset.gz*, *Disease-associated_sites.gz*, *Kinase_Substrate_Dataset.gz*, *Methylation_site_dataset.gz*, *O-GalNAc_site_dataset.gz*, *O-GlcNAc_site_dataset.gz*, *Phosphorylation_site_dataset.gz*, *Regulatory_sites.gz*, *Sumoylation_site_dataset.gz* and *Ubiquitination_site_dataset.gz*.
- **DrugBank**: All drugs (under *COMPLETE DATABASE*) and DrugBank Vocabulary (under *OPEN DATA*).
- **SNOMED-CT**: [Download RF2 Files Now!](#).

These files will be later used in *Build Neo4j graph database*.

7.1.2 Software

- Java, version compatible with chosen Neo4j version (check Neo4j requirements)
- R >= 3.5.2
- Python 3.6
- Redis server
- Neo4j <= 3.15

7.1.3 Hardware

- Memory: 16Gb
- Disk space: >= 80Gb
- Stable internet connection

CHAPTER
EIGHT

API REFERENCE

8.1 CKG package API Reference

graphdb_connector
graphdb_builder
report_manager
analytics_core
notebooks

8.1.1 Graph Database Connector

connector.py

```
graphdb_connector.connector.getGraphDatabaseConnectionConfiguration(configuration=None,  
database=None)  
graphdb_connector.connector.connectToDB(host='localhost', port=7687, user='neo4j', pass-  
word='password')  
graphdb_connector.connector.removeRelationshipDB(entity1, entity2, relationship)  
graphdb_connector.connector.modifyEntityProperty(parameters)  
    parameters: tuple with entity name, entity id, property name to modify, and value  
graphdb_connector.connector.sendQuery(driver, query, parameters={})  
graphdb_connector.connector.getCursorData(driver, query, parameters={})  
graphdb_connector.connector.create_node(driver, node_type, **kwargs)  
graphdb_connector.connector.find_node(driver, node_type, **kwargs)
```

query_utils.py

```
graphdb_connector.query_utils.read_knowledge_queries(dataset_type='proteomics')  
graphdb_connector.query_utils.read_queries(queries_file)  
graphdb_connector.query_utils.list_queries(queries)  
graphdb_connector.query_utils.find_queries_involving_nodes(queries, nodes,  
print_pretty=False)
```

```
graphdb_connector.query_utils.find_queries_involving_relationships(queries,  
                           rels)  
  
graphdb_connector.query_utils.get_query(queries, query_id)  
graphdb_connector.query_utils.get_description(query)  
graphdb_connector.query_utils.get_nodes(query)  
graphdb_connector.query_utils.get_relationships(query)  
graphdb_connector.query_utils.map_node_name_to_id(driver, node, value)
```

8.1.2 Graph Database Builder

Ontology Databases

Ontologies Parsers

icdParser.py

```
graphdb_builder.ontologies.parsers.icdParser.parser(ICDfile)  
Parses and extracts relevant data from ICD-10 files (Classification of Diseases).
```

Parameters **ICDfile** – list of files downloaded from the ontology database and used to generate nodes and relationships to the graph database.

Returns

Three nested dictionaries: terms, relationships between terms, and definitions of the terms.

- terms: Dictionary where each key is an ontology identifier (*str*) and the values are lists of names and synonyms (*list[str]*).
- relationships: Dictionary of tuples (*str*). Each tuple contains two ontology identifiers (source and target) and the relationship type between them.
- definitions: Dictionary with ontology identifiers as keys (*str*), and definition of the terms as values (*str*).

oboParser.py

```
graphdb_builder.ontologies.parsers.oboParser.parser(ontology, files)  
Multiple ontology database parser. This function parses and extracts relevant data from: Disease Ontology, Tissues, Human Phenotype Ontology, HUPO-PSI and Gene Ontology databases.
```

Parameters

- **ontology** (*str*) – name of the ontology to be imported ('Disease', 'Tissue', 'Phenotype', 'Experiment', 'Modification', 'Molecular_interactions', 'Gene_ontology')
- **files** (*list*) – list of files downloaded from an ontology and used to generate nodes and relationships in the graph database.

Returns

Three nested dictionaries: terms, relationships between terms, and definitions of the terms.

- terms: Dictionary where each key is an ontology identifier (*str*) and the values are lists of names and synonyms (*list[str]*).

- relationships: Dictionary of tuples (*str*). Each tuple contains two ontology identifiers (source and target) and the relationship type between them.
- definitions: Dictionary with ontology identifiers as keys (*str*), and definition of the terms as values (*str*).

reflectParser.py

`graphdb_builder.ontologies.parsers.reflectParser.parser(files, filters, qtype=None)`
 Parses and extracts relevant data from REFLECT ontologies: Disease Ontology, Tissues, STITCH and Gene Ontology databases.

Parameters

- **files** (*list*) – list of files downloaded from an ontology and used to generate nodes and relationships in the graph database.
- **filters** (*list*) – list of ontology identifiers to be ignored.
- **qtype** (*int*) – ontology type code.

Returns

Three nested dictionaries: terms, relationships between terms, and definitions of the terms.

- terms: Dictionary where each key is an ontology identifier (*str*) and the values are lists of names and synonyms (*list[str]*).
- relationships: Dictionary of tuples (*str*). Each tuple contains two ontology identifiers (source and target) and the relationship type between them.
- definitions: Dictionary with ontology identifiers as keys (*str*), and definition of the terms as values (*str*).

snomedParser.py

`graphdb_builder.ontologies.parsers.snomedParser.parser(files, filters)`
 Parses and extracts relevant data from SNOMED CT database files.

Parameters

- **files** (*list*) – list of files downloaded from SNOMED CT and used to generate nodes and relationships in the graph database.
- **filters** (*list*) – list of SNOMED CT Identifiers to be ignored.

Returns

Three nested dictionaries: terms, relationships between terms, and definitions of the terms.

- terms: Dictionary where each key is a SNOMED CT Identifier (*str*) and the values are lists of names and synonyms (*list[str]*).
- relationships: Dictionary of tuples (*str*). Each tuple contains two SNOMED CT Identifiers (source and target) and the relationship type between them.
- definitions: Dictionary with SNOMED CT Identifiers as keys (*str*), and definition of the terms as values (*str*).

`graphdb_builder.ontologies.parsers.snomedParser.get_inactive_terms(concept_file)`

Parameters `concept_file` –

Return set inactive_terms inactive terms

Ontologies Controller

```
graphdb_builder.ontologies.ontologies_controller.entries_to_remove(entries,  
the_dict)
```

This function removes pairs from a given dictionary, based on a list of provided keys.

Parameters

- **entries** (*list*) – list of keys to be deleted from dictionary.
- **the_dict** (*dict*) – dictionary.

Returns The original dictionary minus the key,value pairs from the provided entries list.

```
graphdb_builder.ontologies.ontologies_controller.get_extra_entities_rels(ontology_directory)
```

```
graphdb_builder.ontologies.ontologies_controller.parse_ontology(ontology,  
down-  
load=True)
```

Parses and extracts data from a given ontology file(s), and returns a tuple with multiple dictionaries.

Parameters

- **ontology** (*str*) – acronym of the ontology to be parsed (e.g. Disease Ontology:'DO').
- **download** (*bool*) – wether database is to be downloaded.

Returns Tuple with three nested dictionaries: terms, relationships between terms, and definitions of the terms. For more information on the returned dictionaries, see the documentation for any ontology parser.

```
graphdb_builder.ontologies.ontologies_controller.generate_graphFiles(import_directory,  
ontolo-  
gies=None,  
down-  
load=True)
```

This function parses and extracts data from a given list of ontologies. If no ontologies are provided, all availables ontologies are used. Terms, relationships and definitions are saved as .tsv files to be loaded into the graph database.

Parameters

- **import_directory** (*str*) – relative path from current python module to ‘imports’ directory.
- **ontologies** (*list or None*) – list of ontologies to be imported. If None, all available ontologies are imported.
- **download** (*bool*) – wether database is to be downloaded.

Returns Dictionary of tuples. Each tuple corresponds to a unique label/relationship type, date, time, database, and number of nodes and relationships.

Biomedical Databases

Biomedical Databases Parsers

cancerGenomeInterpreterParser.py

```
graphdb_builder.databases.parsers.cancerGenomeInterpreterParser.parser(databases_directory,
                                                               down-
                                                               load=True)
```

corumParser.py

```
graphdb_builder.databases.parsers.corumParser.parser(databases_directory,      down-
                                                       load=True)
```

disgenetParser.py

```
graphdb_builder.databases.parsers.disgenetParser.parser(databases_directory,
                                                       download=True)
graphdb_builder.databases.parsers.disgenetParser.readDisGeNetProteinMapping(config,
                                                               di-
                                                               rec-
                                                               tory)
graphdb_builder.databases.parsers.disgenetParser.readDisGeNetDiseaseMapping(config,
                                                               di-
                                                               rec-
                                                               tory)
```

drugBankParser.py

```
graphdb_builder.databases.parsers.drugBankParser.parser(databases_directory)
graphdb_builder.databases.parsers.drugBankParser.extract_drugs(config,      direc-
                                                               tory)
graphdb_builder.databases.parsers.drugBankParser.parseDrugBankVocabulary(config,
                                                               di-
                                                               rec-
                                                               tory)
graphdb_builder.databases.parsers.drugBankParser.build_relationships_from_DrugBank(config,
                                                               drugs)
graphdb_builder.databases.parsers.drugBankParser.build_drug_entity(config,
                                                               drugs)
graphdb_builder.databases.parsers.drugBankParser.build_DrugBank_dictionary(config,
                                                               di-
                                                               rec-
                                                               tory,
                                                               drugs)
```

drugGeneInteractionDBParser.py

```
graphdb_builder.databases.parsers.drugGeneInteractionDBParser.parser(databases_directory,  
                           download=  
                           load=True)
```

exposomeParser.py

```
graphdb_builder.databases.parsers.exposomeParser.parser(databases_directory,  
                           download=True)  
graphdb_builder.databases.parsers.exposomeParser.parseBiomarkersFile(fhandler,  
                           file_name)  
graphdb_builder.databases.parsers.exposomeParser.parseCorrelationsFile(fhandler,  
                           file_name,  
                           biomark-  
                           ers,  
                           map-  
                           ping)
```

foodbParser.py

```
graphdb_builder.databases.parsers.foodbParser.parser(databases_directory,      down-  
                           load=True)  
graphdb_builder.databases.parsers.foodbParser.parseContents(fhandler)  
graphdb_builder.databases.parsers.foodbParser.parseFood(fhandler)  
graphdb_builder.databases.parsers.foodbParser.parseCompounds(fhandler)
```

goaParser.py

```
graphdb_builder.databases.parsers.goaParser.parser(databases_dir, download=True)  
graphdb_builder.databases.parsers.goaParser.parse_annotations_with_pandas(annotation_file,  
                           valid_proteins=None)
```

gwasCatalogParser.py

```
graphdb_builder.databases.parsers.gwasCatalogParser.parser(databases_directory,  
                           download=True)
```

hgncParser.py

```
graphdb_builder.databases.parsers.hgncParser.parser(databases_directory,      down-
load=True)
```

hmdbParser.py

```
graphdb_builder.databases.parsers.hmdbParser.parser(databases_directory,      down-
load=True)
graphdb_builder.databases.parsers.hmdbParser.extract_metabolites(config, direc-
tory,      down-
load=True)
graphdb_builder.databases.parsers.hmdbParser.build_metabolite_entity(config,
direc-
tory,
metabo-
lites)
graphdb_builder.databases.parsers.hmdbParser.build_relationships_from_HMDB(config,
metabo-
lites,
map-
ping)
graphdb_builder.databases.parsers.hmdbParser.build_HMDB_dictionary(directory,
metabo-
lites)
```

hpaParser.py

```
graphdb_builder.databases.parsers.hpaParser.parser(databases_directory,      down-
load=True)
graphdb_builder.databases.parsers.hpaParser.parsePathologyFile(config, fhandler,
file_name,      pro-
tein_mapping,
dis-
ease_mapping)
```

intactParser.py

```
graphdb_builder.databases.parsers.intactParser.parser(databases_directory,      down-
load=True)
```

internalDBsParser.py

```
graphdb_builder.databases.parsers.jensenlabParser.parser(databases_directory,  
download=True)  
graphdb_builder.databases.parsers.jensenlabParser.parsePairs(config,  
databases_directory,  
qtype, mapping,  
download=True)
```

mutationDsParser.py

```
graphdb_builder.databases.parsers.mutationDsParser.parser(databases_directory,  
download=True)
```

oncokbParser.py

```
graphdb_builder.databases.parsers.oncokbParser.parser(databases_directory, download=True)
```

pathwayCommonsParser.py

```
graphdb_builder.databases.parsers.pathwayCommonsParser.parser(databases_directory,  
download=True)
```

pfamParser.py

```
graphdb_builder.databases.parsers.pfamParser.parser(databases_directory, import_directory, download=True,  
updated_on=None)  
graphdb_builder.databases.parsers.pfamParser.print_files(data, header, outputfile,  
is_first, filter_for=None)
```

pspParser.py

```
graphdb_builder.databases.parsers.pspParser.parser(databases_directory)  
graphdb_builder.databases.parsers.pspParser.parseSites(fhandler, modifications)  
graphdb_builder.databases.parsers.pspParser.parseKinaseSubstrates(fhandler,  
modifications)  
graphdb_builder.databases.parsers.pspParser.parseRegulationAnnotations(fhandler,  
modifications, ca-  
tions, map-  
ping)
```

```
graphdb_builder.databases.parsers.pspParser.parseDiseaseAnnotations (fhandler,  
                                modifi-  
cations,  
                                map-  
ping)
```

reactomeParser.py

```
graphdb_builder.databases.parsers.reactomeParser.parser (databases_directory,  
                                         download=True)  
graphdb_builder.databases.parsers.reactomeParser.parsePathways (config,  
                                         databases_directory,  
                                         fhandler)  
graphdb_builder.databases.parsers.reactomeParser.parsePathwayHierarchy (fhandler)  
graphdb_builder.databases.parsers.reactomeParser.parsePathwayRelationships (config,  
                                         fhan-  
dler,  
                                         map-  
ping=None)
```

refseqParser.py

```
graphdb_builder.databases.parsers.refseqParser.parser (databases_directory, down-  
load=True)
```

siderParser.py

```
graphdb_builder.databases.parsers.siderParser.parser (databases_directory,  
                                         drug_source, download=True)  
graphdb_builder.databases.parsers.siderParser.parserIndications (databases_directory,  
                                         drugMap-  
ping, phe-  
notypeMap-  
ping, down-  
load=True)
```

smpdbParser.py

```
graphdb_builder.databases.parsers.smpdbParser.parser (databases_directory, down-  
load=True)  
graphdb_builder.databases.parsers.smpdbParser.parsePathways (config, fhandler)  
graphdb_builder.databases.parsers.smpdbParser.parsePathwayProteinRelationships (fhandler)  
graphdb_builder.databases.parsers.smpdbParser.parsePathwayMetaboliteDrugRelationships (fhandl)
```

stringParser.py

```
graphdb_builder.databases.parsers.stringParser.parser(databases_directory,  
importDirectory,  
drug_source=None, download=True, db='STRING')  
  
graphdb_builder.databases.parsers.stringParser.parseActions(databases_directory,  
importDirectory,  
proteinMap-  
ping, drugMap-  
ping=None,  
download=True,  
db='STRING')
```

textminingParser.py

```
graphdb_builder.databases.parsers.textminingParser.parser(databases_directory,  
importDirectory, download=True)  
  
graphdb_builder.databases.parsers.textminingParser.read_valid_pubs(organisms,  
organ-  
isms_file)  
  
graphdb_builder.databases.parsers.textminingParser.parse_PMC_list(config,  
directory,  
down-  
load=True,  
valid_pubs=None)  
  
graphdb_builder.databases.parsers.textminingParser.parse_mentions(config,  
directory,  
qtype,  
importDi-  
rectory,  
down-  
load=True)
```

uniprotParser.py

```
graphdb_builder.databases.parsers.uniprotParser.parser(databases_directory,  
import_directory,  
download=True, updated_on=None)  
  
graphdb_builder.databases.parsers.uniprotParser.parse_release_notes(databases_directory,  
config,  
down-  
load=True)  
  
graphdb_builder.databases.parsers.uniprotParser.parse_fasta(databases_directory,  
config, im-  
port_directory,  
download=True,  
updated_on=None)
```

```
graphdb_builder.databases.parsers.uniprotParser.parse_idmapping_file(databases_directory,  
                           config,  
                           im-  
                           port_directory,  
                           down-  
                           load=True,  
                           up-  
                           dated_on=None)  
  
graphdb_builder.databases.parsers.uniprotParser.format_output(proteins)  
  
graphdb_builder.databases.parsers.uniprotParser.print_single_file(data,  
                           header,  
                           output_file,  
                           data_type,  
                           data_object,  
                           is_first, up-  
                           dated_on)  
  
graphdb_builder.databases.parsers.uniprotParser.print_multiple_relationships_files(data,  
                           header,  
                           out-  
                           put_dir,  
                           is_first,  
                           up-  
                           dated_on)  
  
graphdb_builder.databases.parsers.uniprotParser.addUniProtTexts(textsFile, proteins)  
  
graphdb_builder.databases.parsers.uniprotParser.parseUniProtVariants(config,  
                           databases_directory,  
                           im-  
                           port_directory,  
                           down-  
                           load=True,  
                           up-  
                           dated_on=None)  
  
graphdb_builder.databases.parsers.uniprotParser.parseUniProtAnnotations(config,  
                           databases_directory,  
                           down-  
                           load=True)  
  
graphdb_builder.databases.parsers.uniprotParser.parseUniProtPeptides(config,  
                           databases_directory,  
                           down-  
                           load=True)
```

Databases Controller

```
graphdb_builder.databases.databases_controller.parseDatabase(importDirectory,  
database, down-  
load=True)  
graphdb_builder.databases.databases_controller.generateGraphFiles(importDirectory,  
databases=None,  
down-  
load=True,  
n_jobs=4)
```

Experimental Data

Experiments Parsers

Clinical parser

```
graphdb_builder.experiments.parsers.clinicalParser.parser(projectId)  
graphdb_builder.experiments.parsers.clinicalParser.project_parser(projectId,  
config,  
directory,  
separator)  
graphdb_builder.experiments.parsers.clinicalParser.experimental_design_parser(projectId,  
con-  
fig,  
di-  
rec-  
tory)  
graphdb_builder.experiments.parsers.clinicalParser.clinical_parser(projectId,  
config,  
directory,  
separa-  
tor)  
graphdb_builder.experiments.parsers.clinicalParser.parse_dataset(projectId,  
configura-  
tion, dataDir,  
key='project')
```

This function parses clinical data from subjects in the project Input: uri of the clinical data file. Format: Subjects as rows, clinical variables as columns Output: pandas DataFrame with the same input format but the clinical variables mapped to the right ontology (defined in config), i.e. type = -40 -> SNOMED CT

```
graphdb_builder.experiments.parsers.clinicalParser.extract_project_info(project_data)  
graphdb_builder.experiments.parsers.clinicalParser.extract_responsible_rels(project_data,  
sep-  
a-  
ra-  
tor='|')
```

```

graphdb_builder.experiments.parsers.clinicalParser.extract_participant_rels (project_data,
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_project_tissue_rels (project_data,
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_project_disease_rels (project_data,
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_project_intervention_rels (project_
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_project_rels (project_data,
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_timepoints (project_data,
    sep-
    a-
    ra-
    tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_project_subject_rels (projectId,
    de-
    sign_data)

graphdb_builder.experiments.parsers.clinicalParser.extract_subject_identifiers (design_data)

graphdb_builder.experiments.parsers.clinicalParser.extract_biosample_identifiers (design_data)

graphdb_builder.experiments.parsers.clinicalParser.extract_analytical_sample_identifiers (de
graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_subject_rels (cl
graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_analytical_sam
graphdb_builder.experiments.parsers.clinicalParser.extract_biological_samples_info (clinical_da
graphdb_builder.experiments.parsers.clinicalParser.extract_analytical_samples_info (clinical_da
graphdb_builder.experiments.parsers.clinicalParser.extract_biosample_analytical_sample_rel
graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_timepoint_rel
graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_tissue_rels (cl
graphdb_builder.experiments.parsers.clinicalParser.extract_subject_disease_rels (clinical_data,
    sep-
    a-
    ra-
    tor='|')

```

```
graphdb_builder.experiments.parsers.clinicalParser.extract_subject_intervention_rels(clinical_
                                         sep-
                                         a-
                                         ra-
                                         tor='|')

graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_group_rels(clin_
                                         graphdb_builder.experiments.parsers.clinicalParser.extract_biological_sample_clinical_varia
```

Proteomics parser

```
graphdb_builder.experiments.parsers.proteomicsParser.parser(projectId,  
                                data_type='proteomics')  
  
graphdb_builder.experiments.parsers.proteomicsParser.parse_dataset(projectId,  
                                config-  
                                uration,  
                                dataDir)  
  
graphdb_builder.experiments.parsers.proteomicsParser.check_columns(data,  
                                req_columns,  
                                gener-  
                                ated_columns)  
  
graphdb_builder.experiments.parsers.proteomicsParser.check_minimum_configuration(configuration)  
  
graphdb_builder.experiments.parsers.proteomicsParser.load_dataset(uri, config-  
                                uration)  
  
This function gets the molecular data from a proteomics experiment. Input: uri of the processed file resulting  
from MQ Output: pandas DataFrame with the columns and filters defined in config.py  
  
graphdb_builder.experiments.parsers.proteomicsParser.remove_contaminant_tag(column,  
                                tag='CON__')  
  
graphdb_builder.experiments.parsers.proteomicsParser.expand_groups(data,  
                                configura-  
                                tion)  
  
graphdb_builder.experiments.parsers.proteomicsParser.extract_modification_protein_rels(data,  
                                con-  
                                fig-  
                                u-  
                                ra-  
                                tion)  
  
graphdb_builder.experiments.parsers.proteomicsParser.extract_protein_modification_subject
```

```
graphdb_builder.experiments.parsers.proteomicsParser.extract_peptide_protein_modification_rels(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_protein_modifications_rels(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_protein_modifications_modifications(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_peptides(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_peptide_subject_rels(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_peptide_protein_rels(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_protein_subject_rels(data, config, fig, u, r, t)

graphdb_builder.experiments.parsers.proteomicsParser.extract_subject_replicates(data, regex)

graphdb_builder.experiments.parsers.proteomicsParser.extract_attributes(data, attributes)
```

```
graphdb_builder.experiments.parsers.proteomicsParser.merge_regex_attributes(data,  
at-  
tributes,  
in-  
dex,  
regex-  
Cols)  
graphdb_builder.experiments.parsers.proteomicsParser.merge_col_attributes(data,  
at-  
tributes,  
in-  
dex)  
graphdb_builder.experiments.parsers.proteomicsParser.calculate_median_replicates(data,  
log='log2')  
graphdb_builder.experiments.parsers.proteomicsParser.update_groups(data,  
groups)  
graphdb_builder.experiments.parsers.proteomicsParser.get_dataset_configuration(processing_forma  
data_type)
```

WES parser

```
graphdb_builder.experiments.parsers.wesParser.parser(projectId)  
graphdb_builder.experiments.parsers.wesParser.parseWESDataset(projectId, config-  
uration, dataDir)  
graphdb_builder.experiments.parsers.wesParser.loadWESDataset(uri, configuration)  
This function gets the molecular data from a Whole Exome Sequencing experiment. Input: uri of the pro-  
cessed file resulting from the WES analysis pipeline. The resulting Annovar annotated VCF file from Mutect  
(sampleID_mutect_anno.vcf) Output: pandas DataFrame with the columns and filters defined in config.py  
graphdb_builder.experiments.parsers.wesParser.extractWESRelationships(data,  
con-  
fig-  
ura-  
tion)
```

Experiments Controller

```
graphdb_builder.experiments.experiments_controller.generate_dataset_imports(projectId,  
dataType,  
dataset_import_dir)  
graphdb_builder.experiments.experiments_controller.generate_graph_files(data,  
dataType,  
pro-  
jec-  
tId,  
stats,  
ot='w',  
dataset_import_dir='experi
```

User Creation

Users Controller

```
graphdb_builder.users.users_controller.parseUsersFile(importDirectory, expiration=365)
```

Creates new user in the graph database and corresponding node, through the following steps:

1. Generates new user identifier
2. Checks if a user with given properties already exists in the database. If not:
3. Creates new local user (access to graph database)
4. Saves data to tab-delimited file.

Parameters

- **importDirectory** (*str*) – path to the directory where all the import files are generated.
- **expiration** (*int*) – number of days a user is given access.

Returns Writes relevant .tsv file for the users in the provided file.

```
graphdb_builder.users.users_controller.get_user_creation_queries()
```

Reads the YAML file containing the queries relevant to user creation, parses the given stream and returns a Python object (dict[dict]).

```
graphdb_builder.users.users_controller.get_new_user_identifier(driver)
```

Queries the database for the last user identifier and returns a new sequential identifier.

Parameters **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.

Returns User identifier.

Return type *str*

```
graphdb_builder.users.users_controller.check_if_node_exists(driver, node_property, value)
```

Queries the graph database and checks if a node with a specific property and property value already exists.

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **node_property** (*str*) – property of the node.
- **value** (*str, int, float or bool*) – property value.

Returns Pandas dataframe with user identifier if User with node_property and value already exists, if User does not exist, returns and empty dataframe.

```
graphdb_builder.users.users_controller.create_db_user(driver, data)
```

Creates and assigns role to new graph database user, if user not in list of local users.

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **data** (*Series*) – pandas Series with required user information (see set_arguments()).

```
graphdb_builder.users.users_controller.GenerateGraphFiles(data, output_file)
```

Saves pandas dataframe to users.tsv. If file already exists, appends new lines. Else, creates file and writes dataframe to it.

Parameters

- **data** – pandas dataframe to be written to .tsv file.
- **output_file** (*str*) – path to output csv file.

CKG Builder

User Creation Module

```
graphdb_builder.builder.create_user.create_user_node(driver, data)
```

Creates graph database node for new user and adds respective properties to node.

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **data** (*Series*) – pandas Series with new user identifier and required user information (see `set_arguments()`).

```
graphdb_builder.builder.create_user.create_user_from_command_line(args, expiration)
```

Creates new user in the graph database and corresponding node, from a terminal window (command line), and adds the new user information to the users excel and import files. Arguments as in `set_arguments()`.

Parameters

- **args** (*any object with __dict__ attribute*) – object. Contains all the parameters necessary to create a user ('username', 'name', 'email', 'secondary_email', 'phone_number' and 'affiliation').
- **expiration** (*int*) – number of days users is given access.

Note: This function can be used directly with `python create_user_from_command_line.py -u username -n user_name -e email -s secondary_email -p phone_number -a affiliation`.

```
graphdb_builder.builder.create_user.create_user_from_file(filepath, expiration)
```

Creates new user in the graph database and corresponding node, from an excel file. Rows in the file must be users, and columns must follow `set_arguments()` fields.

Parameters

- **filepath** (*str*) – filepath and filename containing users information.
- **output_file** (*str*) – path to output csv file.
- **expiration** (*int*) – number of days users is given access.

Note: This function can be used directly with `python create_user_from_file.py -f path_to_file`.

```
graphdb_builder.builder.create_user.create_user(data, output_file, expiration=365)
```

Creates new user in the graph database and corresponding node, through the following steps:

1. Checks if a user with given properties already exists in the database. If not:

2. Generates new user identifier
3. Creates new local user (access to graph database)
4. Creates new user node
5. Saves data to users.tsv

Parameters

- **data** – pandas dataframe with users as rows and arguments and columns.
- **output_file** (*str*) – path to output csv file.
- **expiration** (*int*) – number of days users is given access.

Returns Writes relevant .tsv file for the users in data.

```
graphdb_builder.builder.create_user.set_arguments()
```

This function sets the arguments to be used as input for **create_user.py** in the command line.

Importer Module

Generates all the import files: Ontologies, Databases and Experiments. The module is responsible for generating all the csv files that will be loaded into the Graph database and also updates a stats object (hdf table) with the number of entities and relationships from each dataset imported. A new stats object is created the first time a full import is run.

```
graphdb_builder.builder.importer.ontologiesImport(importDirectory, ontolo-
gues=None, download=True,
import_type='partial')
```

Generates all the entities and relationships from the provided ontologies. If the ontologies list is not provided, then all the ontologies listed in the configuration will be imported (full_import). This function also updates the stats object with numbers from the imported ontologies.

Parameters

- **importDirectory** (*str*) – path of the import directory where files will be created.
- **ontologies** (*list*) – a list of ontology names to be imported.
- **download** (*bool*) – whether database is to be downloaded.
- **import_type** (*str*) – type of import ('full' or 'partial').

```
graphdb_builder.builder.importer.databasesImport(importDirectory, databases=None,
n_jobs=1, download=True, import_type='partial')
```

Generates all the entities and relationships from the provided databases. If the databases list is not provided, then all the databases listed in the configuration will be imported (full_import). This function also updates the stats object with numbers from the imported databases.

Parameters

- **importDirectory** (*str*) – path of the import directory where files will be created.
- **databases** (*list*) – a list of database names to be imported.
- **n_jobs** (*int*) – number of jobs to run in parallel. 1 by default when updating one database.
- **import_type** (*str*) – type of import ('full' or 'partial').

```
graphdb_builder.builder.importer.experimentsImport(projects=None, n_jobs=1, import_type='partial')
```

Generates all the entities and relationships from the specified Projects. If the projects list is not provided, then all the projects the experiments directory will be imported (full_import). Calls function experimentImport.

Parameters

- **projects** (*list*) – list of project identifiers to be imported.
- **n_jobs** (*int*) – number of jobs to run in parallel. 1 by default when updating one project.
- **import_type** (*str*) – type of import ('full' or 'partial').

```
graphdb_builder.builder.importer.experimentImport(importDirectory, experimentsDirectory, project)
```

Generates all the entities and relationships from the specified Project. Called from function experimentsImport.

Parameters

- **importDirectory** (*str*) – path to the directory where all the import files are generated.
- **experimentDirectory** (*str*) – path to the directory where all the experiments are located.
- **project** (*str*) – identifier of the project to be imported.

```
graphdb_builder.builder.importer.usersImport(importDirectory, import_type='partial')
```

Generates User entities from excel file and grants access of new users to the database. This function also writes the relevant information to a tab-delimited file in the import directory.

Parameters

- **importDirectory** (*str*) – path to the directory where all the import files are generated.
- **import_type** (*str*) – type of import ('full' or 'partial').

```
graphdb_builder.builder.importer.fullImport(download=True, n_jobs=4)
```

Calls the different importer functions: Ontologies, databases, experiments. The first step is to check if the stats object exists and create it otherwise. Calls setupStats.

```
graphdb_builder.builder.importer.generateStatsDataFrame(stats)
```

Generates a dataframe with the stats from each import. :param list stats: a list with statistics collected from each importer function. :return: Pandas dataframe with the collected statistics.

```
graphdb_builder.builder.importer.setupStats(import_type)
```

Creates a stats object that will collect all the statistics collected from each import.

```
graphdb_builder.builder.importer.createEmptyStats(statsCols, statsFile, statsName)
```

Creates a HDFStore object with a empty dataframe with the collected stats columns.

Parameters

- **statsCols** (*list*) – a list of columns with the fields collected from the import statistics.
- **statsFile** (*str*) – path where the object should be stored.
- **statsName** (*str*) – name if the file containing the stats object.

```
graphdb_builder.builder.importer.writeStats(statsDf, import_type, stats_name=None)
```

Appends the new collected statistics to the existing stats object. :param statsDf: a pandas dataframe with the new statistics from the importing. :param str statsName: If the statistics should be stored with a specific name.

```
graphdb_builder.builder.importer.getStatsName(import_type)
```

Generates the stats object name where to store the importing statistics from the CKG version, which is defined in the configuration.

Returns statsName: key used to store in the stats object.

Return type str

Loader Module

Populates the graph database with all the files generated by the importer.py module: Ontologies, Databases and Experiments. The module loads all the entities and relationships defined in the importer files. It calls Cypher queries defined in the cypher.py module. Further, it generates an hdf object with the number of entities and relationships loaded for each Database, Ontology and Experiment. This module also generates a compressed backup file of all the loaded files.

There are two types of updates:

- Full: all the entities and relationships in the graph database are populated
- Partial: only the specified entities and relationships are loaded

The compressed files for each type of update are named accordingly and saved in the archive/ folder in data/.

```
graphdb_builder.builder.loader.load_into_database(driver, queries, requester)
```

This function runs the queries provided in the graph database using a py2neo driver.

Parameters

- **driver** (py2neo driver) – py2neo driver, which provides the connection to the neo4j graph database.
- **queries** (list [dict]) – list of queries to be passed to the database.
- **requester** (str) – identifier of the query.

```
graphdb_builder.builder.loader.updateDB(driver, imports=None, specific=[])
```

Populates the graph database with information for each Database, Ontology or Experiment specified in imports. If imports is not defined, the function populates the entire graph database based on the graph variable defined in the grapher_config.py module. This function also updates the graph stats object with numbers from the loaded entities and relationships.

Parameters

- **driver** (py2neo driver) – py2neo driver, which provides the connection to the neo4j graph database.
- **imports** (list) – a list of entities to be loaded into the graph.

```
graphdb_builder.builder.loader.fullUpdate()
```

Main method that controls the population of the graph database. Firstly, it gets a connection to the database (driver) and then initiates the update of the entire database getting all the graph entities to update from configuration. Once the graph database has been populated, the imports folder in data/ is compressed and archived in the archive/ folder so that a backup of the imports files is kept (full).

```
graphdb_builder.builder.loader.partialUpdate(imports, specific=[])
```

Method that controls the update of the graph database with the specified entities and relationships. Firstly, it gets a connection to the database (driver) and then initiates the update of the specified graph entities. Once the graph database has been populated, the data files uploaded to the graph are compressed and archived in the archive/ folder (partial).

Parameters **imports** (list) – list of entities to update

```
graphdb_builder.builder.loader.archiveImportDirectory(archive_type='full')
```

This function creates the compressed backup imports folder with either the whole folder (full update) or with only the files uploaded (partial update). The folder or files are compressed into a gzipped tarball file and stored in the archive/ folder defined in the configuration.

Parameters `archive_type` (`str`) – whether it is a full update or a partial update.

Builder Module

Builds the database in two main steps:

- 1) Imports all the data from ontologies, databases and experiments
- 2) Loads these data into the database

The module can perform full updates, executing both steps for all the ontologies, databases and experiments or a partial update. Partial updates can execute step 1 or step 2 for specific data.

`graphdb_builder.builder.builder.set_arguments()`

This function sets the arguments to be used as input for `builder.py` in the command line.

builder_utils.py

`graphdb_builder.builder_utils.readDataset(uri)`

`graphdb_builder.builder_utils.readDataFromCSV(uri)`

Read the data from csv file

`graphdb_builder.builder_utils.readDataFromTXT(uri)`

Read the data from tsv or txt file

`graphdb_builder.builder_utils.readDataFromExcel(uri)`

Read the data from Excel file

`graphdb_builder.builder_utils.get_files_by_pattern(regex_path)`

`graphdb_builder.builder_utils.get_extra_pairs(directory, extra_file)`

`graphdb_builder.builder_utils.parse_contents(contents, filename)`

Reads binary string files and returns a Pandas DataFrame.

`graphdb_builder.builder_utils.export_contents(data, dataDir, filename)`

Export Pandas DataFrame to file, with UTF-8 encoding.

`graphdb_builder.builder_utils.write_relationships(relationships, header, outputfile)`

Reads a set of relationships and saves them to a file.

Parameters

- `relationships` (`set`) – set of tuples with relationship data: source node, target node, relationship type, source and other attributes.
- `header` (`list`) – list of column names.
- `outputfile` (`str`) – path to file to be saved (including filename and extension).

`graphdb_builder.builder_utils.write_entities(entities, header, outputfile)`

Reads a set of entities and saves them to a file.

Parameters

- `entities` (`set`) – set of tuples with entities data: identifier, label, name and other attributes.
- `header` (`list`) – list of column names.
- `outputfile` (`str`) – path to file to be saved (including filename and extension).

`graphdb_builder.builder_utils.get_config(config_name, data_type='databases')`
Reads YAML configuration file and converts it into a Python dictionary.

Parameters

- **config_name** (`str`) – name of the configuration YAML file.
- **data_type** (`str`) – configuration type ('databases' or 'ontologies').

Returns Dictionary.

Note: Use this function to obtain configuration for individual database/ontology parsers.

`graphdb_builder.builder_utils.expand_cols(data, col, sep=',')`
Expands the rows of a dataframe by splitting the specified column

Parameters

- **data** – dataframe to be expanded
- **col** (`str`) – column that contains string to be expanded (i.e. 'P02788;E7EQB2;E7ER44;P02788-2;C9JCF5')
- **sep** (`str`) – separator (i.e. ',')

Returns expanded pandas dataframe

`graphdb_builder.builder_utils.setup_config(data_type='databases')`
Reads YAML configuration file and converts it into a Python dictionary.

Parameters `data_type` – configuration type ('databases', 'ontologies', 'experiments' or 'builder').

Returns Dictionary.

Note: This function should be used to obtain the configuration for databases_controller.py, ontologies_controller.py, experiments_controller.py and builder.py.

`graphdb_builder.builder_utils.get_full_path_directories()`
Reads Builder YAML configuration file and returns the full path of all directories. :return: Dictionary.

`graphdb_builder.builder_utils.list_ftp_directory(ftp_url, user='', password='')`
Lists all files present in folder from FTP server.

Parameters

- **ftp_url** (`str`) – link to access ftp server.
- **user** (`str`) – username to access ftp server if required.
- **password** (`str`) – password to access ftp server if required.

Returns List of files contained in ftp server folder provided with `ftp_url`.

`graphdb_builder.builder_utils.setup_logging(path='log.config', key=None)`
Setup logging configuration.

Parameters

- **path** (`str`) – path to file containing configuration for logging file.
- **key** (`str`) – name of the logger.

Returns Logger with the specified name from ‘key’. If key is *None*, returns a logger which is the root logger of the hierarchy.

```
graphdb_builder.builder_utils.downloadDB(databaseURL, directory=None, file_name=None,  
                                         user='', password='')
```

This function downloads the raw files from a biomedical database server when a link is provided.

Parameters

- **databaseURL** (*str*) – link to access biomedical database server.
- **directory** (*str or None*) –
- **file_name** (*str or None*) – name of the file to download. If *None*, ‘databaseURL’ must contain filename after the last ‘/’.
- **user** (*str*) – username to access biomedical database server if required.
- **password** (*str*) – password to access biomedical database server if required.

```
graphdb_builder.builder_utils.searchPubMed(searchFields, sortby='relevance', num='10',  
                                            resultsFormat='json')
```

Searches PubMed database for MeSH terms and other additional fields (‘searchFields’), sorts them by relevance and returns the top ‘num’.

Parameters

- **searchFields** (*list*) – list of search fields to query for.
- **sortby** (*str*) – parameter to use for sorting.
- **num** (*str*) – number of PubMed identifiers to return.
- **resultsFormat** (*str*) – format of the PubMed result.

Returns Dictionary with total number of PubMed ids, and top ‘num’ ids.

```
graphdb_builder.builder_utils.is_number(s)
```

This function checks if given input is a float and returns True if so, and False if it is not.

Parameters **s** – input

Returns Boolean.

```
graphdb_builder.builder_utils.getMedlineAbstracts(idList)
```

This function accesses NCBI over the WWW and returns Medline data as a handle object, which is parsed and converted to a Pandas DataFrame.

Parameters **idList** (*str or list*) – single identifier or comma-delimited list of identifiers.
All the identifiers must be from the database PubMed.

Returns Pandas DataFrame with columns: ‘title’, ‘authors’, ‘journal’, ‘keywords’, ‘abstract’, ‘PMID’ and ‘url’.

```
graphdb_builder.builder_utils.remove_directory(directory)
```

```
graphdb_builder.builder_utils.listDirectoryFiles(directory)
```

Lists all files in a specified directory.

Parameters **directory** (*str*) – path to folder.

Returns List of file names.

```
graphdb_builder.builder_utils.listDirectoryFolders(directory)
```

Lists all directories in a specified directory.

Parameters **directory** (*str*) – path to folder.

Returns List of folder names.

`graphdb_builder.builder_utils.listDirectoryFoldersNotEmpty(directory)`
Lists all directories in a specified directory.

Parameters `directory (str)` – path to folder.

Returns List of folder names.

`graphdb_builder.builder_utils.checkDirectory(directory)`
Checks if given directory exists and if not, creates it.

Parameters `directory (str)` – path to folder.

`graphdb_builder.builder_utils.flatten(t)`

Code from: <https://gist.github.com/shaxbee/0ada767debf9eefbdb6e> Acknowledgements: Zbigniew Mandziejewicz (shaxbee) Generator flattening the structure

```
>>> list(flatten([2, [2, (4, 5, [7], [2, [6, 2, 6, [6, 4]], 6]]]))  
[2, 2, 4, 5, 7, 2, 6, 2, 6, 6, 4, 6]
```

`graphdb_builder.builder_utils.pretty_print(data)`

This function provides a capability to “pretty-print” arbitrary Python data structures in a forma that can be used as input to the interpreter. For more information visit <https://docs.python.org/2/library/pprint.html>.

Parameters `data` – python object.

`graphdb_builder.builder_utils.convertOBOToNet(ontologyFile)`

Takes an .obo file and returns a NetworkX graph representation of the ontology, that holds multiple edges between two nodes.

Parameters `ontologyFile (str)` – path to ontology file.

Returns NetworkX graph.

`graphdb_builder.builder_utils.getCurrentTime()`

Returns current date (Year-Month-Day) and time (Hour-Minute-Second).

Returns Two strings: date and time.

`graphdb_builder.builder_utils.convert_bytes(num)`

This function will convert bytes to MB.... GB... etc.

Parameters `num` – float, integer or pandas.Series.

`graphdb_builder.builder_utils.copytree(src, dst, symlinks=False, ignore=None)`

`graphdb_builder.builder_utils.file_size(file_path)`

This function returns the file size.

Parameters `file_path (str)` – path to file.

Returns Size in bytes of a plain file.

Return type str

`graphdb_builder.builder_utils.buildStats(count, otype, name, dataset, filename, updated_on=None)`

Returns a tuple with all the information needed to build a stats file.

Parameters

- `count (int)` – number of entities/relationships.
- `otype (str)` – ‘entity’ or ‘relationsgips’.

- **name** (*str*) – entity/relationship label.
- **dataset** (*str*) – database/ontology.
- **filename** (*str*) – path to file where entities/relationships are stored.

Returns Tuple with date, time, database name, file where entities/relationships are stored, file size, number of entities/relationships imported, type and label.

```
graphdb_builder.builder_utils.compress_directory(folder_to_backup, dest_folder,  
                                                file_name)
```

Compresses folder to .tar.gz to create data backup archive file.

Parameters

- **folder_to_backup** (*str*) – path to folder to compress and backup.
- **dest_folder** (*str*) – path where to save compressed folder.
- **file_name** (*str*) – name of the compressed file.

```
graphdb_builder.builder_utils.read_gzipped_file(filepath)
```

Opens an underlying process to access a gzip file through the creation of a new pipe to the child.

Parameters **filepath** (*str*) – path to gzip file.

Returns A bytes sequence that specifies the standard output.

```
graphdb_builder.builder_utils.parse_fasta(file_handler)
```

Using BioPython to read fasta file as SeqIO objects

Parameters **file_handler** (*file_handler*) – opened fasta file

Return iterator records iterator of sequence objects

```
graphdb_builder.builder_utils.batch_iterator(iterator, batch_size)
```

Returns lists of length batch_size.

This can be used on any iterator, for example to batch up SeqRecord objects from Bio.SeqIO.parse(...), or to batch Alignment objects from Bio.AlignIO.parse(...), or simply lines from a file handle.

This is a generator function, and it returns lists of the entries from the supplied iterator. Each list will have batch_size entries, although the final list may be shorter.

Parameters

- **iterator** (*iterator*) – batch to be extracted
- **batch_size** (*integer*) – size of the batch

Return list batch list with the batch elements of size batch_size

source: https://biopython.org/wiki/Split_large_file

mapping.py

```
graphdb_builder.mapping.reset_mapping(entity)
```

Checks if mapping.tsv file exists and removes it.

Parameters **entity** (*str*) – entity label as defined in databases_config.yml

```
graphdb_builder.mapping.mark_complete_mapping(entity)
```

Checks if mapping.tsv file exists and renames it to complete_mapping.tsv.

Parameters **entity** (*str*) – entity label as defined in databases_config.yml

```
graphdb_builder.mapping.getMappingFromOntology(ontology, source=None)
```

Converts .tsv file with complete list of ontology identifiers and aliases, to dictionary with aliases as keys and ontology identifiers as values.

Parameters

- **ontology** (*str*) – ontology label as defined in ontologies_config.yml.
- **source** (*str* or *None*) – name of the source database for selecting aliases.

Returns Dictionary of aliases (keys) and ontology identifiers (values).

```
graphdb_builder.mapping.getMappingFromDatabase(id_list, node, attribute_from='id', attribute_to='name')
```

```
graphdb_builder.mapping.getMappingForEntity(entity)
```

Converts .tsv file with complete list of entity identifiers and aliases, to dictionary with aliases as keys and entity identifiers as values.

Parameters **entity** (*str*) – entity label as defined in databases_config.yml.

Returns Dictionary of aliases (keys) and entity identifiers (value).

```
graphdb_builder.mapping.getMultipleMappingForEntity(entity)
```

Converts .tsv file with complete list of entity identifiers and aliases, to dictionary with aliases to other databases as keys and entity identifiers as values.

Parameters **entity** (*str*) – entity label as defined in databases_config.yml.

Returns Dictionary of aliases (keys) and set of unique entity identifiers (values).

```
graphdb_builder.mapping.get_STRING_mapping_url(db='STRING')
```

Get the url for downloading the mapping file from either STRING or STITCH

Parameters **db** (*str*) – Which database to get the url from: STRING or STITCH

Returns url where to download the mapping file

```
graphdb_builder.mapping.getSTRINGMapping(source='BLAST_UniProt_AC', download=True, db='STRING')
```

Parses database (db) and extracts relationships between identifiers to order databases (source).

Parameters

- **url** (*str*) – link to download database raw file.
- **source** (*str*) – name of the source database for selecting aliases.
- **download** (*bool*) – whether to download the file or not.
- **db** (*str*) – name of the database to be parsed.

Returns Dictionary of database identifiers (keys) and set of unique aliases to other databases (values).

```
graphdb_builder.mapping.buildMappingFromOBO(obofile, ontology)
```

Parses and extracts ontology idnetifiers, names and synonyms from raw file, and writes all the information to a .tsv file. :param str obofile: path to ontology raw file. :param str ontology: ontology database acronym as defined in ontologies_config.yml.

```
graphdb_builder.mapping.map_experiment_files(project_id, datasetPath, mapping)
```

```
graphdb_builder.mapping.map_experimental_data(data, mapping)
```

```
graphdb_builder.mapping.get_mapping_analytical_samples(project_id)
```

8.1.3 Report Manager

Report Dash Apps

Basic App

Data Upload App

Data Upload

```
report_manager.apps.dataUpload.get_data_upload_queries()
```

Reads the YAML file containing the queries relevant to parsing of clinical data and returns a Python object (dict[dict]).

Returns Nested dictionary.

```
report_manager.apps.dataUpload.get_new_subject_identifier(driver)
```

Queries the database for the last subject identifier and returns a new sequential identifier.

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **projectId** (*str*) – external project identifier (from the graph database).

Returns Subject identifier.

Return type str

```
report_manager.apps.dataUpload.get_new_biosample_identifier(driver)
```

Queries the database for the last biological sample internal identifier and returns a new sequential identifier.

Parameters **driver** – py2neo driver, which provides the connection to the neo4j graph database.

Returns Biological sample identifier.

```
report_manager.apps.dataUpload.get_new_analytical_sample_identifier(driver)
```

Queries the database for the last analytical sample internal identifier and returns a new sequential identifier.
:param driver: py2neo driver, which provides the connection to the neo4j graph database.

Returns Analytical sample identifier.

```
report_manager.apps.dataUpload.get_subjects_enrolled_in_project(driver, projectId)
```

Extracts the number of subjects included in a given project.

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **projectId** (*str*) – external project identifier (from the graph database).

Returns Number of subjects.

Return type Numpy ndarray

```
report_manager.apps.dataUpload.check_samples_in_project(driver, projectId)
```

```
report_manager.apps.dataUpload.check_external_ids_in_db(driver, projectId)
```

```
report_manager.apps.dataUpload.remove_samples_nodes_db(driver, projectId)
```

```
report_manager.apps.dataUpload.create_new_subjects(driver, data, projectId)
```

Parameters

- **driver** – py2neo driver, which provides the connection to the neo4j graph database.
- **data** – pandas Dataframe with clinical data as columns and samples as rows.
- **projectId** (*string*) – project identifier.

Returns Pandas DataFrame where new biological sample internal identifiers have been added.

```
report_manager.apps.dataUpload.create_new_biosamples(driver, data)
```

Parameters

- **driver** – py2neo driver, which provides the connection to the neo4j graph database.
- **data** – pandas Dataframe with clinical data as columns and samples as rows.

Returns Pandas DataFrame where new biological sample internal identifiers have been added.

```
report_manager.apps.dataUpload.create_new_ansamples(driver, data)
```

Parameters

- **driver** – py2neo driver, which provides the connection to the neo4j graph database.
- **data** – pandas Dataframe with clinical data as columns and samples as rows.

Returns Pandas DataFrame where new analytical sample internal identifiers have been added.

```
report_manager.apps.dataUpload.create_experiment_internal_identifiers(driver,  
pro-  
jec-  
tId,  
data,  
direc-  
tory,  
file-  
name)
```

```
report_manager.apps.dataUpload.create_mapping_cols_clinical(driver, data, direc-  
tory, filename, sepa-  
rator='|')
```

Parameters

- **driver** (*py2neo driver*) – py2neo driver, which provides the connection to the neo4j graph database.
- **data** – pandas Dataframe with clinical data as columns and samples as rows.
- **separator** (*str*) – character used to separate multiple entries in an attribute.

Returns Pandas Dataframe with all clinical data and graph database internal identifiers.

HomePage Stats App

HomePage Stats

```
report_manager.apps.homepageStats.size_converter(value)
```

Converts a given value to the highest possible unit, maintaining two decimals.

Parameters or float value(*int*) –

Returns String with converted value and units.

```
report_manager.apps.homepageStats.get_query()
```

Reads the YAML file containing the queries relevant for graph database stats, parses the given stream and returns a Python object (dict[dict]).

Returns Nested dictionary.

```
report_manager.apps.homepageStats.get_db_schema()
```

Retrieves the database schema

Returns network with all the database nodes and how they are related

```
report_manager.apps.homepageStats.get_db_stats_data()
```

Retrieves all the stats data from the graph database and returns them as a dictionary.

Returns Dictionary of dataframes.

```
report_manager.apps.homepageStats.plot_store_size_components(dfs, title, args)
```

Plots the store size of different components of the graph database, as a Pie Chart.

Parameters

- **dfs** (*dict*) – dictionary of json objects.
- **title** (*str*) – title of the Dash div where plot is located.
- **args** (*dict*) – see below.

Arguments

- **valueCol** (str) – name of the column with the values to be plotted.
- **textCol** (str) – name of the column containing information for the hoverinfo parameter.
- **height** (str) – height of the plot.
- **width** (str) – width of the plot.

Returns New Dash div containing title and pie chart.

```
report_manager.apps.homepageStats.plot_node_rel_per_label(dfs, title, args, focus='nodes')
```

Plots the number of nodes or relationships (depending on ‘focus’) per label, contained in the grapha database.

Parameters

- **dfs** (*dict*) – dictionary of json objects.
- **title** (*str*) – title of the Dash div where plot is located.

Pacem str focus plot number of nodes per label (‘nodes’) or the number of relationships per type (‘relationships’).

Returns New Dash div containing title and barplot.

```
report_manager.apps.homepageStats.indicator(color, text, id_value)
```

Builds a new Dash div styled as a container, with borders and background.

Parameters

- **color** (*str*) – background color of the container (RGB or Hex colors).
- **text** (*str*) – name to be plotted inside the container.
- **id_value** (*str*) – identifier of the container.

Returns Dash div containing title and an html.P element.

```
report_manager.apps.homepageStats.quick_numbers_panel()
```

Creates a panel of Dash containers where an overview of the graph database numbers can be plotted.

Returns List of Dash components.

DB Imports Stats App

DB Imports Stats

```
report_manager.apps.imports.get_stats_data(filename, n=3)
```

Reads graph database stats file and filters for the last ‘n’ full and partial independent imports, returning a Pandas DataFrame.

Parameters

- **filename** (*str*) – path to stats file (including filename and ‘.hdf’ extension).
- **n** (*int*) – number of independent imports to plot.

Returns Pandas Dataframe with different entities and relationships as rows and columns:

```
report_manager.apps.imports.select_last_n_imports(stats_file, n=3)
```

Selects which independent full and partial imports should be plotted based on n.

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **n** (*int*) – number of independent imports to select.

Returns List of import ids to be plotted according to selection criterion.

```
report_manager.apps.imports.remove_legend_duplicates(figure)
```

Removes duplicated legend items.

Parameters **figure** – plotly graph object figure.

```
report_manager.apps.imports.get_databases_entities_relationships(stats_file,
                                                               key='full',
                                                               op-
                                                               tions='databases')
```

Builds dictionary from stats file. Depending on ‘options’, keys and values can differ. If *options* is set to ‘dates’, keys are dates of the imports and values are databases imported at each date; if ‘databases’, keys are databases and values are entities and relationships created from each database; if ‘entities’, keys are databases and values are entities created from each database; if ‘relationships’, keys are databases and values are relationships created from each database.

Parameters

- **stats_file** – pandas DataFrame with stats data.

- **key** (`str`) – use only full, partial or both kinds of imports ('full', 'partial', 'all').
- **options** (`str`) – name of the variables to be used as keys in the output dictionary ('dates', 'databases', 'entities' or 'relationships').

Returns Dictionary.

```
report_manager.apps.imports.set_colors(dictionary)
```

This function takes the values in a dictionary and attributes them an RGB color.

Parameters `dictionary` (`dict`) – dictionary with variables to be attributed a color, as values.

Returns Dictionary where 'dictionary' values are keys and random RGB colors are the values.

```
report_manager.apps.imports.get_dropdown_menu(fig, options_dict, add_button=True, equal_traces=True, number_traces=2)
```

Builds a list for the dropdown menu, based on a plotly figure traces and a dictionary with the options to be used in the dropdown.

Parameters

- **fig** – plotly graph object figure.
- **options_dict** – dictionary where keys are used as dropdown options and values data points.
- **add_button** (`bool`) – add option to display all dropdown options simultaneously.
- **equal_traces** (`bool`) – defines if all dropdown options have the same number of traces each. If True, define 'number_traces' as well. If False, number of traces will be the same as the number of values for each 'options_dict' key.
- **number_traces** (`int`) – number of traces created for each 'options_dict' key.

Returns List of nested structures. Each dictionary within `updatemenus[0]['buttons'][0]` corresponds to one dropdown menu options and contains information on which traces are visible, label and method.

```
report_manager.apps.imports.get_totals_per_date(stats_file, key='full', import_types=False)
```

Summarizes stats file to a Pandas DataFrame with import dates and total number of imported entities and relationships.

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **key** (`str`) – use only full or partial imports ('full', 'partial').
- **import_types** (`bool`) – breakdown importing stats into entities or relationships related.

Returns Pandas DataFrame with independent import dates as rows and imported numbers as columns.

```
report_manager.apps.imports.get_imports_per_database_date(stats_file)
```

Summarizes stats file to a Pandas DataFrame with import dates, databases and total number of imported entities and relationships per database.

Parameters `stats_file` – pandas DataFrame with stats data.

Returns Pandas DataFrame with independent import dates and databases as rows and imported numbers as columns.

```
report_manager.apps.imports.plot_total_number_imported(stats_file, plot_title)
```

Creates plot with overview of imports numbers per date.

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **plot_title** (*str*) – title of the plot.

Returns Line plot figure within the <div id=”_dash-app-content”>.

```
report_manager.apps.imports.plot_total_numbers_per_date(stats_file, plot_title)
```

Plots number of entities and relationships imported per date, with scaled markers reflecting numbers ratios.

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **plot_title** (*str*) – title of the plot.

Returns Scatter plot figure within the <div id=”_dash-app-content”>, with scaled markers.

```
report_manager.apps.imports.plot_databases_numbers_per_date(stats_file, plot_title,
key='full', dropdown=False, dropdown_options='dates')
```

Grouped horizontal barplot showing the number of entities and relationships imported from each biomedical database.

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **plot_title** (*str*) – title of the plot.
- **key** (*str*) – use only full or partial imports ('full', 'partial').
- **dropdown** (*bool*) – add dropdown menu to figure or not.
- **dropdown_options** (*str*) – name of the variables to be used as options in the dropdown menu ('dates', 'databases', 'entities' or 'relationships').

Returns Horizontal barplot figure within the <div id=”_dash-app-content”>.

```
report_manager.apps.imports.plot_import_numbers_per_database(stats_file, plot_title,
key='full', subplot_titles=("", ), colors=True, plots_1='entities', plots_2='relationships', dropdown=True, dropdown_options='databases')
```

Creates plotly multiplot figure with breakdown of imported numbers and size of the respective files, per database and import type (entities or relationships).

Parameters

- **stats_file** – pandas DataFrame with stats data.
- **plot_title** (*str*) – title of the plot.
- **key** (*str*) – use only full or partial imports ('full', 'partial').
- **subplot_titles** (*tuple*) – title of the subplots (tuple of strings, one for each subplot).
- **colors** (*bool*) – define standard colors for entities and for relationships.
- **plots_1** (*str*) – name of the variable plotted.

- **plots_2** (`str`) – name of the variable plotted.
- **dropdown** (`bool`) – add dropdown menu to figure or not.
- **dropdown_options** (`str`) – name of the variables to be used as options in the dropdown menu ('dates', 'databases', 'entities' or 'relationships').

Returns Multi-scatterplot figure within the <div id=”_dash-app-content”>.

Initial App

Login App

Project App

Project Creation App

Project Creation

```
report_manager.apps.projectCreation.get_project_creation_queries()
```

Reads the YAML file containing the queries relevant to user creation, parses the given stream and returns a Python object (dict[dict]).

Returns Nested dictionary.

```
report_manager.apps.projectCreation.check_if_node_exists(driver, node, node_property, value)
```

Queries the graph database and checks if a node with a specific property and property value already exists.
:param driver: py2neo driver, which provides the connection to the neo4j graph database. :type driver: py2neo driver
:param str node: node to be matched in the database. :param str node_property: property of the node.
:param value: property value. :type value: str, int, float or bool :return: Pandas dataframe with user identifier if User with node_property and value already exists, if User does not exist, returns an empty dataframe.

```
report_manager.apps.projectCreation.get_new_project_identifier(driver, projectId)
```

Queries the database for the last project external identifier and returns a new sequential identifier.

Parameters

- **driver** (`py2neo driver`) – py2neo driver, which provides the connection to the neo4j graph database.
- **projectId** (`str`) – internal project identifier (CPxxxxxxxxxxxx).

Returns Project external identifier.

Return type str

```
report_manager.apps.projectCreation.get_subject_number_in_project(driver, projectId)
```

Extracts the number of subjects included in a given project.

Parameters

- **driver** (`py2neo driver`) – py2neo driver, which provides the connection to the neo4j graph database.
- **projectId** (`str`) – external project identifier (from the graph database).

Returns Integer with the number of subjects.

```
report_manager.apps.projectCreation.create_new_project(driver, projectId, data, separator='|')
```

Creates a new project in the graph database, following the steps:

1. Retrieves new project external identifier and creates project node and relationships in the graph database.
2. Creates subjects, timepoints and intervention nodes.
3. Saves all the entities and relationships to tab-delimited files.
4. Returns the number of projects created and the project external identifier.

Parameters

- **driver** (`py2neo driver`) – py2neo driver, which provides the connection to the neo4j graph database.
- **projectId** (`str`) – internal project identifier (CPxxxxxxxxxxxx).
- **data** – pandas Dataframe with project as row and other attributes as columns.
- **separator** (`str`) – character used to separate multiple entries in a project attribute.

Returns Two strings: number of projects created and the project external identifier.

app.py

dataset.py

```
class report_manager.dataset.Dataset(identifier, dataset_type, configuration=None, data={}, analyses={}, analysis_queries={}, report=None)
Bases: object

property identifier
property dataset_type
property data
property analyses
property configuration
property analysis_queries
property report
generate_dataset()
update_report(report)
update_analysis_queries(query)
get_dataframe(dataset_name)
get_dataframes(dataset_names)
list_dataframes()
get_analysis(analysis)
update_data(new)
update_analyses(new)
set_configuration_from_file(configuration_file)
```

```
update_configuration_from_file(configuration_file)
get_dataset_data_directory(directory='../../data/reports')
query_data()
send_query(query)
extract_configuration(configuration)
add_configuration_to_report(report_pipeline)
generate_report()
save_dataset_recursively(dset, group, dt)
save_dataset(dataset_directory)
save_dataset_recursively_to_file(dset, dataset_directory, base_name='')
save_dataset_to_file(dataset_directory)
save_report(dataset_directory)
load_dataset_recursively(dset, loaded_dset={})
load_dataset(dataset_directory)
load_dataset_report(report_dir)
generate_knowledge()

class report_manager.dataset.MultiOmicsDataset(identifier, data, configuration=None,
                                               analyses={}, analysis_queries={}, report=None)
Bases: report_manager.dataset.Dataset

get_dataframes(datasets)
generate_knowledge()

class report_manager.dataset.ProteomicsDataset(identifier, dataset_type='proteomics',
                                                data={}, configuration=None, analyses={},
                                                analysis_queries={}, report=None)
Bases: report_manager.dataset.Dataset

generate_dataset()
process_dataset()
processing()
generate_knowledge()

class report_manager.dataset.PTMDataset(identifier, data={}, configuration=None, analyses={},
                                         analysis_queries={}, report=None)
Bases: report_manager.dataset.ProteomicsDataset

class report_manager.dataset.PhosphoproteomicsDataset(identifier, data={}, configuration=None,
                                                       analyses={}, analysis_queries={}, report=None)
Bases: report_manager.dataset.PTMDataset
```

```

class report_manager.dataset.InteractomicsDataset (identifier, data={}, configuration=None, analyses={}, analysis_queries={}, report=None)
    Bases: report_manager.dataset.ProteomicsDataset

class report_manager.dataset.LongitudinalProteomicsDataset (identifier, data={}, configuration=None, analyses={}, analysis_queries={}, report=None)
    Bases: report_manager.dataset.ProteomicsDataset

class report_manager.dataset.ClinicalDataset (identifier, data={}, configuration=None, analyses={}, analysis_queries={}, report=None)
    Bases: report_manager.dataset.Dataset

    generate_dataset ()
    process_dataset ()
    widen_original_dataset ()
    processing ()
    generate_knowledge ()

class report_manager.dataset.DNAseqDataset (identifier, dataset_type, data={}, configuration=None, analyses={}, analysis_queries={}, report=None)
    Bases: report_manager.dataset.Dataset
    generate_dataset ()

class report_manager.dataset.RNAseqDataset (identifier, data={}, configuration=None, analyses={}, analysis_queries={}, report=None)
    Bases: report_manager.dataset.Dataset
    generate_dataset ()

```

index.py

knowledge.py

```

class report_manager.knowledge.Knowledge (identifier, data, nodes={}, relationships={}, queries_file=None, colors={}, graph=None, report={})
    Bases: object

    property identifier
    property data
    property entities
    property nodes
    property relationships
    property queries_file
    property colors
    property default_color

```

```
property report
property graph
generate_knowledge_from_regulation(entity)
generate_knowledge_from_correlation(entity_node1, entity_node2, filter, cutoff=0.5)
generate_knowledge_from_wgcna(data, entity1, entity2, cutoff=0.2)
generate_knowledge_from_annotations(entity1, entity2, filter=None)
generate_knowledge_from_similarity(entity='Project')
generate_knowledge_from_queries(entity, queries_results)
send_query(query)
query_data(replace)
generate_cypher_nodes_list()
generate_knowledge_graph()
reduce_to_subgraph(nodes)
get_knowledge_graph_plot()
generate_report(visualization='sankey')
save_report(directory)

class report_manager.knowledge.ProjectKnowledge(identifier, data, nodes={}, relationships={}, colors={}, graph=None, report={})
Bases: report_manager.knowledge.Knowledge
    generate_knowledge()

class report_manager.knowledge.ProteomicsKnowledge(identifier, data, nodes={}, relationships={}, colors={}, graph=None, report={})
Bases: report_manager.knowledge.Knowledge
    generate_knowledge()

class report_manager.knowledge.ClinicalKnowledge(identifier, data, nodes={}, relationships={}, colors={}, graph=None, report={})
Bases: report_manager.knowledge.Knowledge
    generate_knowledge()

class report_manager.knowledge.MultiOmicsKnowledge(identifier, data, nodes={}, relationships={}, colors={}, graph=None, report={})
Bases: report_manager.knowledge.Knowledge
    generate_knowledge()
```

project.py

```
class report_manager.project.Project (identifier, configuration_files={}, datasets={}, knowledge=None, report={})
Bases: object
```

A project class that defines an experimental project. A project can be of different types, contain several datasets and reports.

Example:

```
p = Project(identifier="P0000001", datasets=None, report=None)
p.show_report(environment="notebook")
```

```
property identifier
property configuration_files
property queries_file
property name
property acronym
property data_types
append_data_type (data_type)
property responsible
property description
property status
property num_subjects
property datasets
property knowledge
property report
property similar_projects
property overlap
get_dataset (dataset)
update_dataset (dataset)
update_report (new)
remove_project (host='localhost', port=7687, user='neo4j', password='password')
get_report_directory ()
get_downloads_directory ()
set_attributes (project_info)
from_dict (attributes)
to_dict ()
to_dataframe ()
list_datasets ()
to_json ()
```

```
from_json(json_str)
query_data()
check_report_exists()
load_project_report()
load_project(directory)
load_project_data()
build_project(force=False)
get_projects_overlap(project_info)
get_similar_projects(project_info)
generate_project_attributes_plot()
generate_project_similarity_plots()
generate_overlap_plots()
get_similarity_network_style()
get_similarity_network()
generate_knowledge()
generate_project_info_report()
generate_report()
notify_project_ready(message_type='slack')
empty_report()
save_project_report()
save_project_datasets_reports()
save_project()
save_project_datasets_data()
show_report(environment)
download_project()
download_project_report()
download_knowledge(directory)
download_project_datasets()
```

report.py

```
class report_manager.report.Report(identifier, plots={})
Bases: object
property identifier
property plots
get_plot(plot)
update_plots(plot)
```

```

list_plots()
print_report(directory, plot_format='pdf')
save_report(directory)
read_report(directory)
visualize_report(environment)
visualize_plot(environment, plot_type)
download_report(directory)

```

user.py

```

class report_manager.user.User(username)
    Bases: object

    find()
    register(password)
    verify_password(password)

```

utils.py

```

report_manager.utils.copy_file_to_destination(cfile, destination)
report_manager.utils.send_message_to_slack_webhook(message, message_to, user-
    name='albsantosdel')
report_manager.utils.send_email(message, subject, message_from, message_to)
report_manager.utils.compress_directory(name, directory, compression_format='zip')
report_manager.utils.get_markdown_date(extra_text)
report_manager.utils.convert_html_to_dash(el, style=None)
report_manager.utils.extract_style(el)
report_manager.utils.is_jsonable(x)
report_manager.utils.convert_dash_to_json(dash_object)
report_manager.utils.get_image(figure, width, height)
report_manager.utils.parse_html(html_snippet)
report_manager.utils.hex2rgb(color)
report_manager.utils.getNumberText(num)
report_manager.utils.get_rgb_colors(n)
report_manager.utils.get_hex_colors(n)
report_manager.utils.convert_html_to_pdf(source_html, output_filename)

class report_manager.utils.NumpyEncoder(*, skipkeys=False, ensure_ascii=True,
    check_circular=True, allow_nan=True, sort_keys=False, indent=None, separators=None,
    default=None)
    Bases: json.encoder.JSONEncoder

```

default (obj)

Implement this method in a subclass such that it returns a serializable object for `o`, or calls the base implementation (to raise a `TypeError`).

For example, to support arbitrary iterators, you could implement `default` like this:

```
def default(self, o):
    try:
        iterable = iter(o)
    except TypeError:
        pass
    else:
        return list(iterable)
    # Let the base class default method raise the TypeError
    return JSONEncoder.default(self, o)
```

```
class report_manager.utils.DictDFEncoder(*, skipkeys=False, ensure_ascii=True,
                                         check_circular=True, allow_nan=True,
                                         sort_keys=False, indent=None, separators=None, default=None)
```

Bases: `json.encoder.JSONEncoder`

default (obj)

Implement this method in a subclass such that it returns a serializable object for `o`, or calls the base implementation (to raise a `TypeError`).

For example, to support arbitrary iterators, you could implement `default` like this:

```
def default(self, o):
    try:
        iterable = iter(o)
    except TypeError:
        pass
    else:
        return list(iterable)
    # Let the base class default method raise the TypeError
    return JSONEncoder.default(self, o)
```

worker.py

8.1.4 Analytics Core

Analysis

Analytics

```
analytics_core.analytics.analytics.unit_vector(vector)
```

Returns the unit vector of the vector. :param tuple `vector`: vector :return tuple `unit_vector`: unit vector

```
analytics_core.analytics.analytics.flatten(t, my_list=[])
```

Code from: <https://gist.github.com/shaxbee/0ada767deb9eefbdb6e> Acknowledgements: Zbigniew Mandziejewicz (shaxbee) Generator flattening the structure

```
>>> list(flatten([2, [2, (4, 5, [7], [2, [6, 2, 6, [6], 4]], 6)]]))  
[2, 2, 4, 5, 7, 2, 6, 2, 6, 6, 4, 6]
```

```
analytics_core.analytics.analytics.angle_between(v1, v2)
    Returns the angle in radians between vectors 'v1' and 'v2'
```

Parameters

- **v1** (*tuple*) – vector 1
- **v2** (*tuple*) – vector 2

Returns float angle angle between two vectors in radians

Example:: angle = angle_between((1, 0, 0), (0, 1, 0))

```
analytics_core.analytics.analytics.transform_into_wide_format(data,           index,
                                                               columns,   values,
                                                               extra=[])
    This function converts a Pandas DataFrame from long to wide format using pandas pivot_table() function.
```

Parameters

- **data** – long-format Pandas DataFrame
- **index** (*list*) – columns that will be converted into the index
- **columns** (*str*) – column name whose unique values will become the new column names
- **values** (*str*) – column to aggregate
- **extra** (*list*) – additional columns to be kept as columns

Returns Wide-format pandas DataFrame

Example:

```
result = transform_into_wide_format(df, index='index', columns='x', values='y',
                                     extra='group')
```

```
analytics_core.analytics.analytics.transform_into_long_format(data,
                                                               drop_columns,
                                                               group,
                                                               columns=['name',
                                                               'y'])
    Converts a Pandas DataDrame from wide to long format using pd.melt() function.
```

Parameters

- **data** – wide-format Pandas DataFrame
- **drop_columns** (*list*) – columns to be deleted
- **group** (*str or list*) – column(s) to use as identifier variables
- **columns** (*list*) – names to use for the 1)variable column, and for the 2)value column

Returns Long-format Pandas DataFrame.

Example:

```
result = transform_into_long_format(df, drop_columns=['sample', 'subject'],
                                     group='group', columns=['name', 'y'])
```

```
analytics_core.analytics.analytics.get_ranking_with_markers(data, drop_columns,
                                                               group,      columns,
                                                               list_markers, annotation={})
```

This function creates a long-format dataframe with features and values to be plotted together with disease biomarker annotations.

Parameters

- **data** – wide-format Pandas DataFrame with samples as rows and features as columns
- **drop_columns** (*list*) – columns to be deleted
- **group** (*str*) – column to use as identifier variables
- **columns** (*list*) – names to use for the 1)variable column, and for the 2)value column
- **list_markers** (*list*) – list of features from data, known to be markers associated to disease.
- **annotation** (*dict*) – markers, from list_markers, and associated diseases.

Returns Long-format pandas DataFrame with group identifiers as rows and columns: ‘name’ (identifier), ‘y’ (LFQ intensity), ‘symbol’ and ‘size’.

Example:

```
result = get_ranking_with_markers(data, drop_columns=['sample', 'subject'], group=
                                   ↪'group', columns=['name', 'y'], list_markers, annotation={})
```

```
analytics_core.analytics.analytics.extract_number_missing(data,           min_valid,
                                                               drop_cols=['sample'],
                                                               group='group')
```

Counts how many valid values exist in each column and filters column labels with more valid values than the minimum threshold defined.

Parameters

- **data** – pandas DataFrame with group as rows and protein identifier as column.
- **group** (*str*) – column label containing group identifiers. If None, number of valid values is counted across all samples, otherwise is counted per unique group identifier.
- **min_valid** (*int*) – minimum number of valid values to be filtered.
- **drop_columns** (*list*) – column labels to be dropped.

Returns List of column labels above the threshold.

Example:

```
result = extract_number_missing(data, min_valid=3, drop_cols=['sample'], group=
                                   ↪'group')
```

```
analytics_core.analytics.analytics.extract_percentage_missing(data,           miss-
                                                               ing_max,
                                                               drop_cols=['sample'],
                                                               group='group')
```

Extracts ratio of missing/valid values in each column and filters column labels with lower ratio than the minimum threshold defined.

Parameters

- **data** – pandas dataframe with group as rows and protein identifier as column.

- **group** (*str*) – column label containing group identifiers. If None, ratio is calculated across all samples, otherwise is calculated per unique group identifier.
- **missing_max** (*float*) – maximum ratio of missing/valid values to be filtered.

Returns List of column labels below the threshold.

Example:

```
result = extract_percentage_missing(data, missing_max=0.3, drop_cols=['sample'],  
group='group')
```

```
analytics_core.analytics.analytics.imputation_KNN(data, drop_cols=['group', 'sample', 'subject'], group='group',  
cutoff=0.6, alone=True)
```

k-Nearest Neighbors imputation for pandas dataframes with missing data. For more information visit <https://github.com/iskandr/fancyimpute/blob/master/fancyimpute/knn.py>.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **group** (*str*) – column label containing group identifiers.
- **drop_cols** (*list*) – column labels to be dropped. Final dataframe should only have gene/protein/etc identifiers as columns.
- **cutoff** (*float*) – minimum ratio of missing/valid values required to impute in each column.
- **alone** (*boolean*) – if True removes all columns with any missing values.

Returns Pandas dataframe with samples as rows and protein identifiers as columns.

Example:

```
result = imputation_KNN(data, drop_cols=['group', 'sample', 'subject'], group=  
group='group', cutoff=0.6, alone = True)
```

```
analytics_core.analytics.analytics.imputation_mixed_norm_KNN(data, index_cols=['group',  
'sample', 'subject'], shift=1.8,  
nstd=0.3, group='group',  
cutoff=0.6)
```

Missing values are replaced in two steps: 1) using k-Nearest Neighbors we impute protein columns with a higher ratio of missing/valid values than the defined cutoff, 2) the remaining missing values are replaced by random numbers that are drawn from a normal distribution.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **group** (*str*) – column label containing group identifiers.
- **index_cols** (*list*) – list of column labels to be set as dataframe index.
- **shift** (*float*) – specifies the amount by which the distribution used for the random numbers is shifted downwards. This is in units of the standard deviation of the valid data.

- **nstd** (*float*) – defines the width of the Gaussian distribution relative to the standard deviation of measured values. A value of 0.5 would mean that the width of the distribution used for drawing random numbers is half of the standard deviation of the data.
- **cutoff** (*float*) – minimum ratio of missing/valid values required to impute in each column.

Returns Pandas dataframe with samples as rows and protein identifiers as columns.

Example:

```
result = imputation_mixed_norm_KNN(data, index_cols=['group', 'sample', 'subject'],
                                     shift = 1.8, nstd = 0.3, group='group', cutoff=0.6)
```

```
analytics_core.analytics.analytics.imputation_normal_distribution(data, index_cols=['group', 'sample', 'subject'],
                                                               shift=1.8,
                                                               nstd=0.3)
```

Missing values will be replaced by random numbers that are drawn from a normal distribution. The imputation is done for each sample (across all proteins) separately. For more information visit <http://www.coxdocs.org/doku.php?id=perseus:user:activities:matrixprocessing:imputation:replacemissingfromgaussian>.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **index_cols** (*list*) – list of column labels to be set as dataframe index.
- **shift** (*float*) – specifies the amount by which the distribution used for the random numbers is shifted downwards. This is in units of the standard deviation of the valid data.
- **nstd** (*float*) – defines the width of the Gaussian distribution relative to the standard deviation of measured values. A value of 0.5 would mean that the width of the distribution used for drawing random numbers is half of the standard deviation of the data.

Returns Pandas dataframe with samples as rows and protein identifiers as columns.

Example:

```
result = imputation_normal_distribution(data, index_cols=['group', 'sample',
                                                          'subject'], shift = 1.8, nstd = 0.3)
```

```
analytics_core.analytics.analytics.normalize_data(data, method='median_polish')
```

This function normalizes the data using the selected method

Parameters

- **data** – DataFrame with the data to be normalized (samples x features)
- **method** (*string*) – normalization method to choose among: median_polish, median, quantile, linear

Returns Pandas dataframe.

Example:

```
result = normalize_data(data, method='median_polish')
```

```
analytics_core.analytics.analytics.median_normalization(data)
```

This function normalizes each sample by using its median.

Parameters `data` –**Returns** Pandas dataframe.

Example:

```
result = median_normalization(data)
```

`analytics_core.analytics.analytics.zscore_normalization(data)`

This function normalizes each sample by using its mean and standard deviation (mean=0, std=1).

Parameters `data` –**Returns** Pandas dataframe.

Example:: `data = pd.DataFrame({'a': [2,5,4,3,3], 'b':[4,4,6,5,3], 'c':[4,14,8,8,9]}) result = zscore_normalization(data)`

a	b	c
0 -1.154701	0.577350	0.577350
1 -0.484182	-0.665750	1.149932
2 -1.000000	0.000000	
3 -0.927173	-0.132453	1.059626
4 -0.577350	-0.577350	1.154701

0 -1.154701	0.577350	0.577350	1 -0.484182	-0.665750	1.149932	2 -1.000000	0.000000
1.000000	3 -0.927173	-0.132453	1.059626	4 -0.577350	-0.577350	1.154701	

`analytics_core.analytics.analytics.median_polish_normalization(data,`

max_iter=250

This function iteratively normalizes each sample and each feature to its median until medians converge.

Parameters

- `data` –

- `max_iter` (`int`) – number of maximum iterations to prevent infinite loop.

Returns Pandas dataframe.

Example:

```
result = median_polish_normalization(data, max_iter = 10)
```

`analytics_core.analytics.analytics.quantile_normalization(data)`

Applies quantile normalization to each column in pandas dataframe.

Parameters `data` – pandas dataframe with features as rows and samples as columns.**Returns** Pandas dataframe

Example:

```
result = quantile_normalization(data)
```

`analytics_core.analytics.analytics.linear_normalization(data, method='l1', axis=0)`

This function scales input data to a unit norm. For more information visit <https://scikit-learn.org/stable/modules/generated/sklearn.preprocessing.normalize.html>.

Parameters

- `data` – pandas dataframe with samples as rows and features as columns.

- `method` (`str`) – norm to use to normalize each non-zero sample or non-zero feature (depends on axis).

- `axis` (`int`) – axis used to normalize the data along. If 1, independently normalize each sample, otherwise (if 0) normalize each feature.

Returns Pandas dataframe

Example:

```
result = linear_normalization(data, method = "11", axis = 0)
```

analytics_core.analytics.analytics.**remove_group**(data)

Removes column with label ‘group’.

Parameters **data** – pandas dataframe with one column labelled ‘group’

Returns Pandas dataframe

Example:

```
result = remove_group(data)
```

analytics_core.analytics.analytics.**calculate_coefficient_variation**(values)

Compute the coefficient of variation, the ratio of the biased standard deviation to the mean, in percentage. For more information visit <https://docs.scipy.org/doc/scipy/reference/generated/scipy.stats.variation.html>.

Parameters **values** (*ndarray*) – numpy array

Returns The calculated variation along rows.

Return type ndarray

Example:

```
result = calculate_coefficient_variation()
```

analytics_core.analytics.analytics.**get_coefficient_variation**(data,

drop_columns,

group,

columns=[‘name’,

‘y’])

Extracts the coefficients of variation in each group.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **drop_columns** (*list*) – column labels to be dropped from the dataframe
- **group** (*str*) – column label containing group identifiers.
- **columns** (*list*) – names to use for the variable column(s), and for the value column(s)

Returns Pandas dataframe with columns ‘name’ (protein identifier), ‘x’ (coefficient of variation), ‘y’ (mean) and ‘group’.

Exmaple:

```
result = get_coefficient_variation(data, drop_columns=['sample', 'subject'],  
group='group')
```

```
analytics_core.analytics.analytics.get_proteomics_measurements_ready(df, index_cols=['group', 'sample', 'subject', 'identifier'], drop_cols=['sample'], group='group', identifier='identifier', extra_identifier='name', imputation=True, method='distribution', missing_method='percentage', missing_per_group=True, missing_max=0.3, min_valid=1, value_col='LFQ_intensity', shift=1.8, nstd=0.3, knn_cutoff=0.6)
```

Processes proteomics data extracted from the database: 1) filter proteins with high number of missing values (> missing_max or min_valid), 2) impute missing values. For more information on imputation method visit <http://www.coxdocs.org/doku.php?id=perseus:user:activities:matrixprocessing:filterrows:filtervalidvaluesrows>.

Parameters

- **df** – long-format pandas dataframe with columns ‘group’, ‘sample’, ‘subject’, ‘identifier’ (protein), ‘name’ (gene) and ‘LFQ_intensity’.
- **index_cols** (*list*) – column labels to be kept as index identifiers.
- **drop_cols** (*list*) – column labels to be dropped from the dataframe.
- **group** (*str*) – column label containing group identifiers.
- **identifier** (*str*) – column label containing feature identifiers.
- **extra_identifier** (*str*) – column label containing additional protein identifiers (e.g. gene names).
- **imputation** (*bool*) – if True performs imputation of missing values.
- **method** (*str*) – method for missing values imputation ('KNN', 'distribution', or 'mixed')
- **missing_method** (*str*) – defines which expression rows are counted to determine if a column has enough valid values to survive the filtering process.
- **missing_per_group** (*bool*) – if True filter proteins based on valid values per group; if False filter across all samples.
- **missing_max** (*float*) – maximum ratio of missing/valid values to be filtered.
- **min_valid** (*int*) – minimum number of valid values to be filtered.

- **value_col** (*str*) – column label containing expression values.
- **shift** (*float*) – when using distribution imputation, the down-shift
- **nstd** (*float*) – when using distribution imputation, the width of the distribution
- **knn_cutoff** (*float*) – when using KNN imputation, the minimum percentage of valid values for which to use KNN imputation (i.e. 0.6 -> if 60% valid values use KNN, otherwise MinProb)

Returns Pandas dataframe with samples as rows and protein identifiers (UniprotID~GeneName) as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).

Example 1:

```
result = get_proteomics_measurements_ready(df, index_cols=['group', 'sample',
    ↪ 'subject'], drop_cols=['sample'], group='group', identifier='identifier', extra_
    ↪ identifier='name', imputation = True, method = 'distribution', missing_method =
    ↪ 'percentage', missing_per_group=True, missing_max = 0.3, value_col='LFO_
    ↪ intensity')
```

Example 2:

```
result = get_proteomics_measurements_ready(df, index_cols=['group', 'sample',
    ↪ 'subject'], drop_cols=['sample'], group='group', identifier='identifier', extra_
    ↪ identifier='name', imputation = True, method = 'mixed', missing_method = 'at_
    ↪ least_x', missing_per_group=False, min_valid=5, value_col='LFO_intensity')
```

```
analytics_core.analytics.analytics.get_clinical_measurements_ready(df, sub-
    ↪ ject_id='subject',
    ↪ sam-
    ↪ ple_id='biological_sample',
    ↪ group_id='group',
    ↪ columns=['clinical_variable'],
    ↪ val-
    ↪ ues='values',
    ↪ ex-
    ↪ tra=['group'],
    ↪ imputa-
    ↪ tion=True,
    ↪ imputa-
    ↪ tion_method='KNN')
```

Processes clinical data extracted from the database by converting dataframe to wide-format and imputing missing values.

Parameters

- **df** – long-format pandas dataframe with columns ‘group’, ‘biological_sample’, ‘subject’, ‘clinical_variable’, ‘value’.
- **subject_id** (*str*) – column label containing subject identifiers.
- **sample_id** (*str*) – column label containing biological sample identifiers.
- **group_id** (*str*) – column label containing group identifiers.
- **columns** (*list*) – column name whose unique values will become the new column names
- **values** (*str*) – column label containing clinical variable values.
- **extra** (*list*) – additional column labels to be kept as columns

- **imputation** (`bool`) – if True performs imputation of missing values.
- **imputation_method** (`str`) – method for missing values imputation ('KNN', 'distribution', or 'mixed').

Returns Pandas dataframe with samples as rows and clinical variables as columns (with additional columns 'group', 'subject' and 'biological_sample').

Example:

```
result = get_clinical_measurements_ready(df, subject_id='subject', sample_id=
                                         'biological_sample', group_id='group', columns=['clinical_variable'], values=
                                         'values', extra=['group'], imputation=True, imputation_method='KNN')
```

`analytics_core.analytics.analytics.get_summary_data_matrix(data)`

Returns some statistics on the data matrix provided.

Parameters `data` – pandas dataframe.

Returns dictionary with the type of statistics as key and the statistic as value in the shape of a pandas data frame

Example:

```
result = get_summary_data_matrix(data)
```

```
analytics_core.analytics.analytics.check_equal_variances(data, drop_cols=['group',
                                         'sample', 'subject'],
                                         group_col='group',
                                         alpha=0.05)
```

```
analytics_core.analytics.analytics.check_normality(data, drop_cols=['group', 'sample',
                                         'subject'], group_col='group',
                                         alpha=0.05)
```

```
analytics_core.analytics.analytics.run_pca(data, drop_cols=['sample', 'subject'],
                                         group='group', components=2, dropna=True)
```

Performs principal component analysis and returns the values of each component for each sample and each protein, and the loadings for each protein. For information visit <https://scikit-learn.org/stable/modules/generated/sklearn.decomposition.PCA.html>.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns 'group', 'sample' and 'subject').
- **drop_cols** (`list`) – column labels to be dropped from the dataframe.
- **group** (`str`) – column label containing group identifiers.
- **components** (`int`) – number of components to keep.
- **dropna** (`bool`) – if True removes all columns with any missing values.

Returns Two dictionaries: 1) two pandas dataframes (first one with components values, the second with the components vectors for each protein), 2) xaxis and yaxis titles with components loadings for plotly.

Example:

```
result = run_pca(data, drop_cols=['sample', 'subject'], group='group', components=2, dropna=True)
```

```
analytics_core.analytics.analytics.run_tsne(data,      drop_cols=['sample',      'subject'],
                                             group='group',      components=2,      per-
                                             perplexity=40,      n_iter=1000,      init='pca',
                                             dropna=True)
```

Performs t-distributed Stochastic Neighbor Embedding analysis. For more information visit <https://scikit-learn.org/stable/modules/generated/sklearn.manifold.TSNE.html>.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **drop_cols** (*list*) – column labels to be dropped from the dataframe.
- **group** (*str*) – column label containing group identifiers.
- **components** (*int*) – dimension of the embedded space.
- **perplexity** (*int*) – related to the number of nearest neighbors that is used in other manifold learning algorithms. Consider selecting a value between 5 and 50.
- **n_iter** (*int*) – maximum number of iterations for the optimization (at least 250).
- **init** (*str*) – initialization of embedding (‘random’, ‘pca’ or numpy array of shape n_samples x n_components).
- **dropna** (*bool*) – if True removes all columns with any missing values.

Returns Two dictionaries: 1) pandas dataframe with embedding vectors, 2) xaxis and yaxis titles for plotly.

Example:

```
result = run_tsne(data, drop_cols=['sample', 'subject'], group='group', ↵
                    components=2, perplexity=40, n_iter=1000, init='pca', dropna=True)
```

```
analytics_core.analytics.analytics.run_umap(data,      drop_cols=['sample',      'sub-
                                              ject'],      group='group',      n_neighbors=10,
                                              min_dist=0.3,      metric='cosine',
                                              dropna=True)
```

Performs Uniform Manifold Approximation and Projection. For more information vist <https://umap-learn.readthedocs.io>.

Parameters

- **data** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **drop_cols** (*list*) – column labels to be dropped from the dataframe.
- **group** (*str*) – column label containing group identifiers.
- **n_neighbors** (*int*) – number of neighboring points used in local approximations of manifold structure.
- **min_dist** (*float*) – controls how tightly the embedding is allowed compress points together.
- **metric** (*str*) – metric used to measure distance in the input space.
- **dropna** (*bool*) – if True removes all columns with any missing values.

Returns Two dictionaries: 1) pandas dataframe with embedding of the training data in low-dimensional space, 2) xaxis and yaxis titles for plotly.

Example:

```
result = run_umap(data, drop_cols=['sample', 'subject'], group='group', n_
↳neighbors=10, min_dist=0.3, metric='cosine', dropna=True)
```

`analytics_core.analytics.analytics.calculate_correlations(x, y, method='pearson')`

Calculates a Spearman (nonparametric) or a Pearson (parametric) correlation coefficient and p-value to test for non-correlation.

Parameters

- **x** (*ndarray*) – array 1
- **y** (*ndarray*) – array 2
- **method** (*str*) – chooses which kind of correlation method to run

Returns Tuple with two floats, correlation coefficient and two-tailed p-value.

Example:

```
result = calculate_correlations(x, y, method='pearson')
```

`analytics_core.analytics.analytics.apply_pvalue_correction(pvalues, alpha=0.05, method='bonferroni')`

Performs p-value correction using the specified method. For more information visit <https://www.statsmodels.org/dev/generated/statsmodels.stats.multitest.multipletests.html>.

Parameters

- **pvalues** (*ndarray*) – et of p-values of the individual tests.
- **alpha** (*float*) – error rate.
- **method** (*str*) – method of p-value correction: - bonferroni : one-step correction - sidak : one-step correction - holm-sidak : step down method using Sidak adjustments - holm : step-down method using Bonferroni adjustments - simes-hochberg : step-up method (independent) - hommel : closed method based on Simes tests (non-negative) - fdr_bh : Benjamini/Hochberg (non-negative) - fdr_by : Benjamini/Yekutieli (negative) - fdr_tsbh : two stage fdr correction (non-negative) - fdr_tsbky : two stage fdr correction (non-negative)

Returns Tuple with two arrays, boolean for rejecting H0 hypothesis and float for adjusted p-value.

Exmaple:

```
result = apply_pvalue_correction(pvalues, alpha=0.05, method='bonferroni')
```

`analytics_core.analytics.analytics.apply_pvalue_fdrCorrection(pvalues, alpha=0.05, method='indep')`

Performs p-value correction for false discovery rate. For more information visit <https://www.statsmodels.org/devel/generated/statsmodels.stats.multitest.fdrCorrection.html>.

Parameters

- **pvalues** (*ndarray*) – et of p-values of the individual tests.
- **alpha** (*float*) – error rate.
- **method** (*str*) – method of p-value correction ('indep', 'negcorr').

Returns Tuple with two arrays, boolean for rejecting H0 hypothesis and float for adjusted p-value.

Exmaple:

```
result = apply_pvalue_fdrCorrection(pvalues, alpha=0.05, method='indep')
```

```
analytics_core.analytics.analytics.apply_pvalue_twostage_fdrCorrection(pvalues,
al-
pha=0.05,
method='bh')
```

Iterated two stage linear step-up procedure with estimation of number of true hypotheses. For more information visit https://www.statsmodels.org/dev/generated/statsmodels.stats.multitest.fdrCorrection_twostage.html.

Parameters

- **pvalues** (*ndarray*) – et of p-values of the individual tests.
- **alpha** (*float*) – error rate.
- **method** (*str*) – method of p-value correction ('bky', 'bh').

Returns Tuple with two arrays, boolean for rejecting H0 hypothesis and float for adjusted p-value.

Exmaple:

```
result = apply_pvalue_twostage_fdrCorrection(pvalues, alpha=0.05, method='bh')
```

```
analytics_core.analytics.analytics.apply_pvalue_permutation_fdrCorrection(df,
ob-
served_pvalues,
group,
al-
pha=0.05,
per-
mu-
ta-
tions=50)
```

This function applies multiple hypothesis testing correction using a permutation-based false discovery rate approach.

Parameters

- **df** – pandas dataframe with samples as rows and features as columns.
- **observed_pvalues** – pandas Series with p-values calculated on the originally measured data.
- **group** (*str*) – name of the column containing group identifiers.
- **alpha** (*float*) – error rate. Values below alpha are considered significant.
- **permutations** (*int*) – number of permutations to be applied.

Returns Pandas dataframe with adjusted p-values and rejected columns.

Example:

```
result = apply_pvalue_permutation_fdrCorrection(df, observed_pvalues, group='group
↪', alpha=0.05, permutations=50)
```

```
analytics_core.analytics.analytics.get_counts_permutation_fdr(value, random,
observed, n,
alpha)
```

Calculates local FDR values (q-values) by computing the fraction of accepted hits from the permuted data over accepted hits from the measured data normalized by the total number of permutations.

Parameters

- **value** (`float`) – computed p-value on measured data for a feature.
- **random** (`ndarray`) – p-values computed on the permuted data.
- **observed** – pandas Series with p-values calculated on the originally measured data.
- **n** (`int`) – number of permutations to be applied.
- **alpha** (`float`) – error rate. Values below alpha are considered significant.

Returns Tuple with q-value and boolean for H0 rejected.

Example:

```
result = get_counts_permutation_fdr(value, random, observed, n=250, alpha=0.05)
```

`analytics_core.analytics.analytics.convertToEdgeList (data, cols)`

This function converts a pandas dataframe to an edge list where index becomes the source nodes and columns the target nodes.

Parameters

- **data** – pandas dataframe.
- **cols** (`list`) – names for dataframe columns.

Returns Pandas dataframe with columns cols.

```
analytics_core.analytics.analytics.run_correlation(df, alpha=0.05, subject='subject',
                                                 group='group', method='pearson',
                                                 correction='fdr_bh')
```

This function calculates pairwise correlations for columns in dataframe, and returns it in the shape of a edge list with ‘weight’ as correlation score, and the adjusted p-values.

Parameters

- **df** – pandas dataframe with samples as rows and features as columns.
- **subject** (`str`) – name of column containing subject identifiers.
- **group** (`str`) – name of column containing group identifiers.
- **method** (`str`) – method to use for correlation calculation (‘pearson’, ‘spearman’).
- **alpha** (`float`) – error rate. Values below alpha are considered significant.
- **correction** (`string`) – type of correction see apply_pvalue_correction for methods

Returns Pandas dataframe with columns: ‘node1’, ‘node2’, ‘weight’, ‘padj’ and ‘rejected’.

Example:

```
result = run_correlation(df, alpha=0.05, subject='subject', group='group', method=
                           'pearson', correction='fdr_bh')
```

```
analytics_core.analytics.analytics.run_multi_correlation(df_dict, alpha=0.05,
                                                       subject='subject',
                                                       on=['subject', 'biological_sample'],
                                                       group='group',
                                                       method='pearson',
                                                       correction='fdr_bh')
```

This function merges all input dataframes and calculates pairwise correlations for all columns.

Parameters

- **df_dict** (*dict*) – dictionary of pandas dataframes with samples as rows and features as columns.
- **subject** (*str*) – name of the column containing subject identifiers.
- **group** (*str*) – name of the column containing group identifiers.
- **on** (*list*) – column names to join dataframes on (must be found in all dataframes).
- **method** (*str*) – method to use for correlation calculation ('pearson', 'spearman').
- **alpha** (*float*) – error rate. Values below alpha are considered significant.
- **correction** (*string*) – type of correction see apply_pvalue_correction for methods

Returns Pandas dataframe with columns: 'node1', 'node2', 'weight', 'padj' and 'rejected'.

Example:

```
result = run_multi_correlation(df_dict, alpha=0.05, subject='subject', on=[  
    ↪ 'subject', 'biological_sample'], group='group', method='pearson', correction=  
    ↪ 'fdr_bh')
```

`analytics_core.analytics.analytics.calculate_rm_correlation(df, x, y, subject)`

Computes correlation and p-values between two columns a and b in df.

Parameters

- **df** – pandas dataframe with subjects as rows and two features and columns.
- **x** (*str*) – feature a name.
- **y** (*str*) – feature b name.
- **subject** – column name containing the covariate variable.

Returns Tuple with values for: feature a, feature b, correlation, p-value and degrees of freedom.

Example:

```
result = calculate_rm_correlation(df, x='feature a', y='feature b', subject=  
    ↪ 'subject')
```

`analytics_core.analytics.analytics.run_rm_correlation(df, alpha=0.05, subject='subject', correction='fdr_bh')`

Computes pairwise repeated measurements correlations for all columns in dataframe, and returns results as an edge list with 'weight' as correlation score, p-values, degrees of freedom and adjusted p-values.

Parameters

- **df** – pandas dataframe with samples as rows and features as columns.
- **subject** (*str*) – name of column containing subject identifiers.
- **alpha** (*float*) – error rate. Values below alpha are considered significant.
- **correction** (*string*) – type of correction type see apply_pvalue_correction for methods

Returns Pandas dataframe with columns: 'node1', 'node2', 'weight', 'pvalue', 'dof', 'padj' and 'rejected'.

Example:

```
result = run_rm_correlation(df, alpha=0.05, subject='subject', correction='fdr_bh
                           ←')
```

`analytics_core.analytics.analytics.run_efficient_correlation(data,
 method='pearson')`

Calculates pairwise correlations and returns lower triangle of the matrix with correlation values and p-values.

Parameters

- **data** – pandas dataframe with samples as index and features as columns (numeric data only).
- **method** (*str*) – method to use for correlation calculation ('pearson', 'spearman').

Returns Two numpy arrays: correlation and p-values.

Example:

```
result = run_efficient_correlation(data, method='pearson')
```

`analytics_core.analytics.analytics.calculate_ttest_samr(df, labels, n=2, s0=0,
 paired=False)`

Calculates modified T-test using 'samr' R package.

Parameters

- **df** – pandas dataframe with group as columns and protein identifier as rows
- **labels** (*list*) – integers reflecting the group each sample belongs to (e.g. group1 = 1, group2 = 2)
- **n** (*int*) – number of samples
- **s0** (*float*) – exchangeability factor for denominator of test statistic
- **paired** (*bool*) – True if samples are paired

Returns Pandas dataframe with columns 'identifier', 'group1', 'group2', 'mean(group1)', 'mean(group1)', 'log2FC', 'FC', 't-statistics', 'p-value'.

Example:

```
result = calculate_ttest_samr(df, labels, n=2, s0=0.1, paired=False)
```

`analytics_core.analytics.analytics.calculate_ttest(df, condition1, condition2,
 paired=False, is_logged=True,
 non_par=False, tail='two-sided',
 correction='auto', r=0.707)`

Calculates the t-test for the means of independent samples belonging to two different groups. For more information visit https://docs.scipy.org/doc/scipy/reference/generated/scipy.stats.ttest_ind.html.

Parameters

- **df** – pandas dataframe with groups and subjects as rows and protein identifier as column.
- **condition1** (*str*) – identifier of first group.
- **condition2** (*str*) – identifier of second group.
- **is_logged** (*bool*) – data is logged transformed
- **non_par** (*bool*) – if True, normality and variance equality assumptions are checked and non-parametric test Mann Whitney U test if not passed

Returns Tuple with t-statistics, two-tailed p-value, mean of first group, mean of second group and logfc.

Example:

```
result = calculate_ttest(df, 'group1', 'group2')
```

```
analytics_core.analytics.analytics.calculate_THSD(df, column, group='group', alpha=0.05, is_logged=True)
```

Pairwise Tukey-HSD posthoc test using pingouin stats. For more information visit https://pingouin-stats.org/generated/pingouin.pairwise_tukey.html

Parameters

- **df** – pandas dataframe with group and protein identifier as columns
- **column** (*str*) – column containing the protein identifier
- **group** (*str*) – column label containing the between factor
- **alpha** (*float*) – significance level

Returns Pandas dataframe.

Example:

```
result = calculate_THSD(df, column='HBG2~P69892', group='group', alpha=0.05)
```

```
analytics_core.analytics.analytics.calculate_pairwise_ttest(df, column, subject='subject', group='group', correction='none', is_logged=True)
```

Performs pairwise t-test using pingouin, as a posthoc test, and calculates fold-changes. For more information visit https://pingouin-stats.org/generated/pingouin.pairwise_ttests.html.

Parameters

- **df** – pandas dataframe with subject and group as rows and protein identifier as column.
- **column** (*str*) – column label containing the dependant variable
- **subject** (*str*) – column label containing subject identifiers
- **group** (*str*) – column label containing the between factor
- **correction** (*str*) – method used for testing and adjustment of p-values.

Returns Pandas dataframe with means, standard deviations, test-statistics, degrees of freedom and effect size columns.

Example:

```
result = calculate_pairwise_ttest(df, 'protein a', subject='subject', group='group', correction='none')
```

```
analytics_core.analytics.analytics.complement_posthoc(posthoc, identifier, is_logged)
```

Calculates fold-changes after posthoc test.

Parameters

- **posthoc** – pandas dataframe from posthoc test. Should have at least columns ‘mean(group1)’ and ‘mean(group2)’.

- **identifier** (*str*) – feature identifier.

Returns Pandas dataframe with additional columns ‘identifier’, ‘log2FC’ and ‘FC’.

```
analytics_core.analytics.analytics.calculate_dabest(df, idx, x, y, paired=False,
                                                id_col=None, test='mean_diff')
```

Parameters

- **df** –
- **idx** –
- **x** –
- **y** –
- **paired** –
- **id_col** –
- **test** –

Returns

```
analytics_core.analytics.analytics.calculate_anova_samr(df, labels, s0=0)
```

Calculates modified one-way ANOVA using ‘samr’ R package.

Parameters

- **df** – pandas dataframe with group as columns and protein identifier as rows
- **labels** (*list*) – integers reflecting the group each sample belongs to (e.g. group1 = 1, group2 = 2, group3 = 3)
- **s0** (*float*) – exchangeability factor for denominator of test statistic

Returns Pandas dataframe with protein identifiers and F-statistics.

Example:

```
result = calculate_anova_samr(df, labels, s0=0.1)
```

```
analytics_core.analytics.analytics.calculate_anova(df, column, group='group')
```

Calculates one-way ANOVA using pingouin.

Parameters

- **df** – pandas dataframe with group as rows and protein identifier as column
- **column** (*str*) – name of the column in df to run ANOVA on
- **group** (*str*) – column with group identifiers

Returns Tuple with t-statistics and p-value.

```
analytics_core.analytics.analytics.calculate_repeated_measures_anova(df, col-
                                                                umn,
                                                                sub-
                                                                ject='subject',
                                                                group='group')
```

One-way and two-way repeated measures ANOVA using pingouin stats.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifier as column. Data must be in long-format for two-way repeated measures.

- **column** (*str*) – column label containing the dependant variable
- **subject** (*str*) – column label containing subject identifiers
- **group** (*str*) – column label containing the within factor

Returns Tuple with protein identifier, t-statistics and p-value.

Example:

```
result = calculate_repeated_measures_anova(df, 'protein a', subject='subject',  
                                         group='group')
```

`analytics_core.analytics.analytics.get_max_permutations(df, group='group')`
Get maximum number of permutations according to number of samples.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns
- **group** (*str*) – column with group identifiers

Returns Maximum number of permutations.

Return type `int`

`analytics_core.analytics.analytics.check_is_paired(df, subject, group)`
Check if samples are paired.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **subject** (*str*) – column with subject identifiers
- **group** (*str*) – column with group identifiers

Returns True if paired samples.

Return type `bool`

`analytics_core.analytics.analytics.run_dabest(df, drop_cols=['sample'], subject='subject', group='group', test='mean_diff')`

Parameters

- **df** –
- **drop_cols** (*list*) –
- **subject** (*str*) –
- **group** (*str*) –
- **test** (*str*) –

Returns Pandas dataframe

`analytics_core.analytics.analytics.run_anova(df, alpha=0.05, drop_cols=['sample', 'subject'], subject='subject', group='group', permutations=0, correction='fdr_bh', is_logged=True, non_par=False)`

Performs statistical test for each protein in a dataset. Checks what type of data is the input (paired, unpaired or repeated measurements) and performs posthoc tests for multiclass data. Multiple hypothesis correction uses permutation-based if permutations>0 and Benjamini/Hochberg if permutations=0.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **subject** (*str*) – column with subject identifiers
- **group** (*str*) – column with group identifiers
- **drop_cols** (*list*) – column labels to be dropped from the dataframe
- **alpha** (*float*) – error rate for multiple hypothesis correction
- **permutations** (*int*) – number of permutations used to estimate false discovery rates.
- **non_par** (*bool*) – if True, normality and variance equality assumptions are checked and non-parametric test Mann Whitney U test if not passed

Returns Pandas dataframe with columns ‘identifier’, ‘group1’, ‘group2’, ‘mean(group1)’, ‘mean(group2)’, ‘Log2FC’, ‘std_error’, ‘tail’, ‘t-statistics’, ‘posthoc pvalue’, ‘effsize’, ‘efftype’, ‘FC’, ‘rejected’, ‘F-statistics’, ‘p-value’, ‘correction’, ‘-log10 p-value’, and ‘method’.

Example:

```
result = run_anova(df, alpha=0.05, drop_cols=["sample", "subject"], subject=
↳ 'subject', group='group', permutations=50)
```

```
analytics_core.analytics.analytics.correct_pairwise_ttest(df, alpha, correction='fdr_bh')
analytics_core.analytics.analytics.run_repeated_measurements_anova(df, alpha=0.05,
drop_cols=['sample'], subject='subject', group='group', permutations=50,
correction='fdr_bh', is_logged=True)
```

Performs repeated measurements anova and pairwise posthoc tests for each protein in dataframe.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **subject** (*str*) – column with subject identifiers
- **group** (*str*) – column with group identifiers
- **drop_cols** (*list*) – column labels to be dropped from the dataframe
- **alpha** (*float*) – error rate for multiple hypothesis correction
- **permutations** (*int*) – number of permutations used to estimate false discovery rates

Returns Pandas dataframe

Example:

```
result = run_repeated_measurements_anova(df, alpha=0.05, drop_cols=['sample'], subject='subject', group='group', permutations=50)
```

```
analytics_core.analytics.analytics.format_anova_table(df, aov_results, pairwise_results, pairwise_cols, group, permutations, alpha, correction)
```

Performs p-value correction (permutation-based and FDR) and converts pandas dataframe into final format.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **aov_results** (`list[tuple]`) – list of tuples with anova results (one tuple per feature).
- **pairwise_results** (`list[dataframes]`) – list of pandas dataframes with posthoc tests results
- **group** (`str`) – column with group identifiers
- **alpha** (`float`) – error rate for multiple hypothesis correction
- **permutations** (`int`) – number of permutations used to estimate false discovery rates

Returns

Pandas dataframe

```
analytics_core.analytics.analytics.run_ttest(df, condition1, condition2, alpha=0.05, drop_cols=['sample'], subject='subject', group='group', paired=False, correction='fdr_bh', permutations=50, is_logged=True, non_par=False)
```

Runs t-test (paired/unpaired) for each protein in dataset and performs permutation-based (if permutations>0) or Benjamini/Hochberg (if permutations=0) multiple hypothesis correction.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **condition1** (`str`) – first of two conditions of the independent variable
- **condition2** (`str`) – second of two conditions of the independent variable
- **subject** (`str`) – column with subject identifiers
- **group** (`str`) – column with group identifiers (independent variable)
- **drop_cols** (`list`) – column labels to be dropped from the dataframe
- **paired** (`bool`) – paired or unpaired samples
- **correction** (`str`) – method of pvalue correction see apply_pvalue_correction for methods
- **alpha** (`float`) – error rate for multiple hypothesis correction
- **permutations** (`int`) – number of permutations used to estimate false discovery rates.
- **is_logged** (`bool`) – data is log-transformed
- **non_par** (`bool`) – if True, normality and variance equality assumptions are checked and non-parametric test Mann Whitney U test if not passed

Returns

Pandas dataframe with columns ‘identifier’, ‘group1’, ‘group2’, ‘mean(group1)’, ‘mean(group2)’, ‘std(group1)’, ‘std(group2)’, ‘Log2FC’, ‘FC’, ‘rejected’, ‘T-statistics’, ‘p-value’, ‘correction’, ‘-log10 p-value’, and ‘method’.

Example:

```
result = run_ttest(df, condition1='group1', condition2='group2', alpha = 0.05, ↵
    ↵drop_cols=['sample'], subject='subject', group='group', paired=False, ↵
    ↵correction='fdr_bh', permutations=50)
```

`analytics_core.analytics.analytics.define_samr_method(df, subject, group, drop_cols)`
Method to identify the correct problem type to run with SAMR

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **subject** (*str*) – column with subject identifiers
- **group** (*str*) – column with group identifiers
- **drop_cols** (*str*) – columns to be dropped

Returns tuple with the method to be used (One Class, Two class paired, Two class unpaired or Multiclass) and the labels (conditions)

Example:

```
method, labels = define_samr_method(df, subject, group)
```

`analytics_core.analytics.analytics.calculate_pvalue_from_tstats(tstat, dfn, dfk)`
Calculate two-tailed p-values from T- or F-statistics.

tstat: T/F distribution
dfn: degrees of freedom n (values) per protein (keys), i.e. number of observations - number of groups (dict)
dfk: degrees of freedom n (values) per protein (keys), i.e. number of groups - 1 (dict)

`analytics_core.analytics.analytics.run_samr(df, subject='subject', group='group', drop_cols=['subject', 'sample'], alpha=0.05, s0='null', permutations=250, fc=0, is_logged=True, localfdr=False)`

Python adaptation of the ‘samr’ R package for statistical tests with permutation-based correction and s0 parameter. For more information visit <https://cran.r-project.org/web/packages/samr/samr.pdf>. The method only runs if R is installed and permutations is higher than 0, otherwise ANOVA.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns (with additional columns ‘group’, ‘sample’ and ‘subject’).
- **subject** (*str*) – column with subject identifiers
- **group** (*str*) – column with group identifiers
- **drop_cols** (*list*) – columnlabels to be dropped from the dataframe
- **alpha** (*float*) – error rate for multiple hypothesis correction
- **s0** (*float*) – exchangeability factor for denominator of test statistic
- **permutations** (*int*) – number of permutations used to estimate false discovery rates. If number of permutations is equal to zero, the function will run anova with FDR Benjamini/Hochberg correction.
- **fc** (*float*) – minimum fold change to define practical significance (needed when computing delta table)

Returns Pandas dataframe with columns ‘identifier’, ‘group1’, ‘group2’, ‘mean(group1)’, ‘mean(group2)’, ‘Log2FC’, ‘FC’, ‘T-statistics’, ‘p-value’, ‘padj’, ‘correction’, ‘-log10 p-value’, ‘rejected’ and ‘method’

Example:

```
result = run_samr(df, subject='subject', group='group', drop_cols=['subject',
    ↪'sample'], alpha=0.05, s0=1, permutations=250, fc=0)
```

```
analytics_core.analytics.analytics.calculate_discriminant_lines(result)
analytics_core.analytics.analytics.run_fisher(group1, group2, alternative='two-sided')
    annotated not-annotated group1 a b group2 c d
    group1 = [a, b] group2 = [c, d]
    odds, pvalue = stats.fisher_exact([[a, b], [c, d]])
analytics_core.analytics.analytics.run_site_regulation_enrichment(regulation_data,
    annotation,
    identi-
    fier='identifier',
    groups=['group1',
    'group2'],
    annota-
    tion_col='annotation',
    re-
    ject_col='rejected',
    group_col='group',
    method='fisher',
    regex='(\w+~+)\_\w\w+d+\-\w+',
    correc-
    tion='fdr_bh')
```

This function runs a simple enrichment analysis for significantly regulated protein sites in a dataset.

Parameters

- **regulation_data** – pandas dataframe resulting from differential regulation analysis.
- **annotation** – pandas dataframe with annotations for features (columns: ‘annotation’, ‘identifier’ (feature identifiers), and ‘source’).
- **identifier** (*str*) – name of the column from annotation containing feature identifiers.
- **groups** (*list*) – column names from regulation_data containing group identifiers.
- **annotation_col** (*str*) – name of the column from annotation containing annotation terms.
- **reject_col** (*str*) – name of the column from regulation_data containing boolean for rejected null hypothesis.
- **group_col** (*str*) – column name for new column in annotation dataframe determining if feature belongs to foreground or background.
- **method** (*str*) – method used to compute enrichment (only ‘fisher’ is supported currently).
- **regex** (*str*) – how to extract the annotated identifier from the site identifier

Returns Pandas dataframe with columns: ‘terms’, ‘identifiers’, ‘foreground’, ‘background’, ‘pvalue’, ‘padj’ and ‘rejected’.

Example:

```
result = run_site_regulation_enrichment(regulation_data, annotation, identifier=
    ↪'identifier', groups=['group1', 'group2'], annotation_col='annotation', reject_
    ↪col='rejected', group_col='group', method='fisher', match="(\w+~+)\_\w\w+d+\-\w+")
    (continues on next page)
```

(continued from previous page)

```
analytics_core.analytics.analytics.run_regulation_enrichment(regulation_data,
annotation, identifier='identifier',
groups=['group1', 'group2'], annotation_col='annotation',
reject_col='rejected', group_col='group',
method='fisher',
correction='fdr_bh')
```

This function runs a simple enrichment analysis for significantly regulated features in a dataset.

Parameters

- **regulation_data** – pandas dataframe resulting from differential regulation analysis.
- **annotation** – pandas dataframe with annotations for features (columns: ‘annotation’, ‘identifier’ (feature identifiers), and ‘source’).
- **identifier** (*str*) – name of the column from annotation containing feature identifiers.
- **groups** (*list*) – column names from regulation_data containing group identifiers.
- **annotation_col** (*str*) – name of the column from annotation containing annotation terms.
- **reject_col** (*str*) – name of the column from regulation_data containing boolean for rejected null hypothesis.
- **group_col** (*str*) – column name for new column in annotation dataframe determining if feature belongs to foreground or background.
- **method** (*str*) – method used to compute enrichment (only ‘fisher’ is supported currently).

Returns Pandas dataframe with columns: ‘terms’, ‘identifiers’, ‘foreground’, ‘background’, ‘pvalue’, ‘padj’ and ‘rejected’.

Example:

```
result = run_regulation_enrichment(regulation_data, annotation, identifier=
'identifier', groups=['group1', 'group2'], annotation_col='annotation', reject_
col='rejected', group_col='group', method='fisher')
```

```
analytics_core.analytics.analytics.run_enrichment(data, foreground_id,
background_id, annotation_col='annotation',
group_col='group', identifier_col='identifier',
method='fisher', correction='fdr_bh')
```

Computes enrichment of the foreground relative to a given background, using Fisher’s exact test, and corrects for multiple hypothesis testing.

Parameters

- **data** – pandas dataframe with annotations for dataset features (columns: ‘annotation’, ‘identifier’, ‘source’, ‘group’).
- **foreground_id** (*str*) – group identifier of features that belong to the foreground.
- **background_id** (*str*) – group identifier of features that belong to the background.
- **annotation_col** (*str*) – name of the column containing annotation terms.
- **group_col** (*str*) – name of column containing the group identifiers.
- **identifier_col** (*str*) – name of column containing dependent variables identifiers.
- **method** (*str*) – method used to compute enrichment (only ‘fisher’ is supported currently).

Returns Pandas dataframe with annotation terms, features, number of foreground/background features in each term, p-values and corrected p-values (columns: ‘terms’, ‘identifiers’, ‘foreground’, ‘background’, ‘pvalue’, ‘padj’ and ‘rejected’).

Example:

```
result = run_enrichment(data, foreground='foreground', background='background',  
    ↪foreground_pop=len(foreground_list), background_pop=len(background_list),  
    ↪annotation_col='annotation', group_col='group', identifier_col='identifier',  
    ↪method='fisher')
```

`analytics_core.analytics.analytics.calculate_fold_change(df, condition1, condition2)`

Calculates fold-changes between two groups for all proteins in a dataframe.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns.
- **condition1** (*str*) – identifier of first group.
- **condition2** (*str*) – identifier of second group.

Returns Numpy array.

Example:

```
result = calculate_fold_change(data, 'group1', 'group2')
```

`analytics_core.analytics.analytics.cohen_d(df, condition1, condition2, ddof=0)`

Calculates Cohen’s d effect size based on the distance between two means, measured in standard deviations. For more information visit <https://docs.scipy.org/doc/scipy/reference/generated/scipy.stats.nanstd.html>.

Parameters

- **df** – pandas dataframe with samples as rows and protein identifiers as columns.
- **condition1** (*str*) – identifier of first group.
- **condition2** (*str*) – identifier of second group.
- **ddof** (*int*) – means Delta Degrees of Freedom.

Returns Numpy array.

Example:

```
result = cohen_d(data, 'group1', 'group2', ddof=0)
```

`analytics_core.analytics.analytics.hedges_g(df, condition1, condition2, ddof=0)`

Calculates Hedges' g effect size (more accurate for sample sizes below 20 than Cohen's d). For more information visit <https://docs.scipy.org/doc/numpy/reference/generated/numpy.nanstd.html>.

Parameters

- `df` – pandas dataframe with samples as rows and protein identifiers as columns.
- `condition1` (`str`) – identifier of first group.
- `condition2` (`str`) – identifier of second group.
- `ddof` (`int`) – means Delta Degrees of Freedom.

Returns

Numpy array.

Example:

```
result = hedges_g(data, 'group1', 'group2', ddof=0)
```

`analytics_core.analytics.analytics.run_mapper(data, lenses=['l2norm'], n_cubes=15, overlap=0.5, n_clusters=3, linkage='complete', affinity='correlation')`

Parameters

- `data` –
- `lenses` –
- `n_cubes` –
- `overlap` –
- `n_clusters` –
- `linkage` –
- `affinity` –

Returns

`analytics_core.analytics.analytics.run_WGCNA(data, drop_cols_exp, drop_cols_cli, RsquaredCut=0.8, networkType='unsigned', minModuleSize=30, deepSplit=2, pamRespectsDendro=False, merge_modules=True, MEDissThres=0.25, verbose=0, sd_cutoff=0)`

Runs an automated weighted gene co-expression network analysis (WGCNA), using input proteomics/transcriptomics/genomics and clinical variables data.

Parameters

- `data` (`dict`) – dictionary of pandas dataframes with processed clinical and experimental datasets
- `drop_cols_exp` (`list`) – column names to be removed from the experimental dataset.
- `drop_cols_cli` (`list`) – column names to be removed from the clinical dataset.
- `RquaredCut` (`float`) – desired minimum scale free topology fitting index R^2.
- `networkType` (`str`) – network type ('unsigned', 'signed', 'signed hybrid', 'distance').
- `minModuleSize` (`int`) – minimum module size.

- **deepSplit** (*int*) – provides a rough control over sensitivity to cluster splitting, the higher the value (with ‘hybrid’ method) or if True (with ‘tree’ method), the more and smaller modules.
- **pamRespectsDendro** (*bool*) – only used for method ‘hybrid’. Objects and small modules will only be assigned to modules that belong to the same branch in the dendrogram structure.
- **merge_modules** (*bool*) – if True, very similar modules are merged.
- **MEDissThres** (*float*) – maximum dissimilarity (i.e., 1-correlation) that qualifies modules for merging.
- **verbose** (*int*) – integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.

Returns Tuple with multiple pandas dataframes.

Example:

```
result = run_WGCNA(data, drop_cols_exp=['subject', 'sample', 'group', 'index'],  
                    drop_cols_cli=['subject', 'biological_sample', 'group', 'index'], RsquaredCut=0.  
                    8, networkType='unsigned', minModuleSize=30, deepSplit=2,  
                    pamRespectsDendro=False, merge_modules=True, MEDissThres=0.25, verbose=0)
```

`analytics_core.analytics.analytics.most_central_edge(G)`

Compute the eigenvector centrality for the graph G, and finds the highest value.

Parameters **G** (*graph*) – networkx graph

Returns Highest eigenvector centrality value.

Return type *float*

`analytics_core.analytics.analytics.get_louvain_partitions(G, weight)`

Computes the partition of the graph nodes which maximises the modularity (or try..) using the Louvain heuristics. For more information visit <https://python-louvain.readthedocs.io/en/latest/api.html>.

Parameters

- **G** (*graph*) – networkx graph which is decomposed.
- **weight** (*str*) – the key in graph to use as weight.

Returns The partition, with communities numbered from 0 to number of communities.

Return type *dict*

`analytics_core.analytics.analytics.get_network_communities(graph, args)`

Finds communities in a graph using different methods. For more information on the methods visit:

- https://networkx.github.io/documentation/latest/reference/algorithms/generated/networkx.algorithms.community.modularity_max.greedy_modularity_communities.html
- https://networkx.github.io/documentation/networkx-2.0/reference/algorithms/generated/networkx.algorithms.community.asyn_lpa.asyn_lpa_communities.html
- https://networkx.github.io/documentation/latest/reference/algorithms/generated/networkx.algorithms.community.centrality.girvan_newman.html
- https://networkx.github.io/documentation/latest/reference/generated/networkx.convert_matrix.to_pandas_adjacency.html

Parameters

- **graph** (*graph*) – networkx graph
- **args** (*dict*) – config file arguments

Returns Dictionary of nodes and which community they belong to (from 0 to number of communities).

```
analytics_core.analytics.analytics.get_publications_abstracts(data, publication_col='publication', join_by=['publication', 'Proteins', 'Diseases'], index='PMID')
```

Accesses NCBI PubMed over the WWW and retrieves the abstracts corresponding to a list of one or more PubMed IDs.

Parameters

- **data** – pandas dataframe of diseases and publications linked to a list of proteins (columns: ‘Diseases’, ‘Proteins’, ‘linkout’ and ‘publication’).
- **publication_col** (*str*) – column label containing PubMed ids.
- **join_by** (*list*) – column labels to be kept from the input dataframe.
- **index** (*str*) – column label containing PubMed ids from the NCBI retrieved data.

Returns Pandas dataframe with publication information and columns ‘PMID’, ‘abstract’, ‘authors’, ‘date’, ‘journal’, ‘keywords’, ‘title’, ‘url’, ‘Proteins’ and ‘Diseases’.

Example:

```
result = get_publications_abstracts(data, publication_col='publication', join_by=['publication', 'Proteins', 'Diseases'], index='PMID')
```

analytics_core.analytics.analytics.eta_squared(*aov*)

Calculates the effect size using Eta-squared.

Parameters **aov** – pandas dataframe with anova results from statsmodels.

Returns Pandas dataframe with additional Eta-squared column.

analytics_core.analytics.analytics.omega_squared(*aov*)

Calculates the effect size using Omega-squared.

Parameters **aov** – pandas dataframe with anova results from statsmodels.

Returns Pandas dataframe with additional Omega-squared column.

```
analytics_core.analytics.analytics.run_two_way_anova(df, drop_cols=['sample'], subject='subject', group=['group', 'secondary_group'])
```

Run a 2-way ANOVA when data[‘secondary_group’] is not empty

Parameters

- **df** – processed pandas dataframe with samples as rows, and proteins and groups as columns.
- **drop_cols** (*list*) – column names to drop from dataframe
- **subject** (*str*) – column name containing subject identifiers.
- **group** (*list*) – column names corresponding to independent variable groups

Returns Two dataframes, anova results and residuals.

Example:

```
result = run_two_way_anova(data, drop_cols=['sample'], subject='subject', group=[  
    ↪'group', 'secondary_group'])
```

```
analytics_core.analytics.analytics.merge_for_polar(regulation_data, regulators,  
                                                identifier_col='identifier',  
                                                group_col='group',  
                                                theta_col='modifier',  
                                                aggr_func='mean',      normalize=  
                                                True)  
  
analytics_core.analytics.analytics.run_qc_markers_analysis(data, qc_markers,  
                                                       sample_col='sample',  
                                                       group_col='group',  
                                                       drop_cols=['subject'],  
                                                       identifier_col='identifier',  
                                                       qcidenti-  
                                                       fier_col='identifier',  
                                                       qcclass_col='class')  
  
analytics_core.analytics.analytics.run_snf(df_dict, clusters, distance_metric, K_affinity,  
                                           mu_affinity)
```

Parameters

- **df_dict** -
- **clusters** -

```
analytics_core.analytics.analytics.run_km(data, time_col, event_col, group_col, args={})
```

WGCNA analytics

```
analytics_core.analytics.wgcnaAnalysis.get_data(data, drop_cols_exp=['subject',  
                     'group', 'sample', 'index'],  
                     drop_cols_cli=['subject', 'group', 'bio-  
logical_sample', 'index'], sd_cutoff=0)
```

This function cleans up and formats experimental and clinical data into similarly shaped dataframes.

Parameters

- **data** (*dict*) – dictionary with processed clinical and proteomics datasets.
- **drop_cols_exp** (*list*) – list of columns to drop from processed experimental (proteomics/rna-seq/dna-seq) dataframe.
- **drop_cols_cli** (*list*) – list of columns to drop from processed clinical dataframe.

Returns Dictionary with experimental and clinical dataframes (keys are the same as in the input dictionary).

```
analytics_core.analytics.wgcnaAnalysis.get_dendrogram(df, labels, distfun='euclidean',  
                                                    linkagefun='ward',  
                                                    div_clusters=False, fcluster_method='distance',  
                                                    fcluster_cutoff=15)
```

This function calculates the distance matrix and performs hierarchical cluster analysis on a set of dissimilarities and methods for analyzing it.

Parameters

- **df** – pandas dataframe with samples/subjects as index and features as columns.
- **labels** (*list*) – labels for the leaves of the tree.
- **distfun** (*str*) – distance measure to be used ('euclidean', 'maximum', 'manhattan', 'canberra', 'binary', 'minkowski' or 'jaccard').
- **linkagefun** (*str*) – hierarchical/agglomeration method to be used ('single', 'complete', 'average', 'weighted', 'centroid', 'median' or 'ward').
- **div_clusters** (*bool*) – dividing dendrogram leaves into clusters (True or False).
- **fcluster_method** (*str*) – criterion to use in forming flat clusters.
- **fcluster_cutoff** (*int*) – maximum cophenetic distance between observations in each cluster.

Returns Dictionary of data structures computed to render the dendrogram. Keys: 'icoords', 'dcoords', 'ivl' and 'leaves'. If div_clusters is used, it will also return a dictionary of each cluster and respective leaves.

```
analytics_core.analytics.wgcnaAnalysis.get_clusters_elements(linkage_matrix,
                                                               fcluster_method,
                                                               fcluster_cutoff,
                                                               labels)
```

This function implements the generation of flat clusters from an hierarchical clustering with the same interface as `scipy.cluster.hierarchy.fcluster`.

Parameters

- **linkage_matrix** (*ndarray*) – hierarchical clustering encoded with a linkage matrix.
- **fcluster_method** (*str*) – criterion to use in forming flat clusters ('inconsistent', 'distance', 'maxclust', 'monocrit', 'maxclust_monocrit').
- **fcluster_cutoff** (*float*) – maximum cophenetic distance between observations in each cluster.
- **labels** (*list*) – labels for the leaves of the dendrogram.

Returns A dictionary where keys are the cluster numbers and values are the dendrogram leaves.

```
analytics_core.analytics.wgcnaAnalysis.filter_df_by_cluster(df, clusters, number)
```

Select only the members of a defined cluster.

Parameters

- **df** – pandas dataframe with samples/subjects as index and features as columns.
- **clusters** (*dict*) – clusters dictionary from `get_dendrogram` function if div_clusters option was True.
- **number** (*int*) – cluster number (key).

Returns Pandas dataframe with all the features (columns) and samples/subjects belonging to the defined cluster (index).

```
analytics_core.analytics.wgcnaAnalysis.df_sort_by_dendrogram(df, Z_dendrogram)
```

Reorders pandas dataframe by index and according to the dendrogram list of leaf nodes labels.

Parameters

- **df** – pandas dataframe with the labels to be reordered as index.

- **`z_dendrogram`** (`dict`) – dictionary of data structures computed to render the dendrogram. Keys: ‘icoords’, ‘dcoords’, ‘ivl’ and ‘leaves’.

Returns Reordered pandas dataframe.

```
analytics_core.analytics.wgcnaAnalysis.get_percentiles_heatmap(df,
                                                               Z_dendrogram,
                                                               bydendro=True,
                                                               bycols=False)
```

This function transforms the absolute values in each row or column (option ‘bycols’) into relative values.

Parameters

- **`df`** – pandas dataframe with samples/subjects as index and features as columns.
- **`z_dendrogram`** (`dict`) – dictionary of data structures computed to render the dendrogram. Keys: ‘icoords’, ‘dcoords’, ‘ivl’ and ‘leaves’.
- **`bydendro`** (`bool`) – if labels should be ordered according to dendrogram list of leaf nodes labels set to True, otherwise set to False.
- **`bycols`** (`bool`) – relative values calculated across rows (samples) then set to False. Calculation performed across columns (features) set to True.

Returns Pandas dataframe.

```
analytics_core.analytics.wgcnaAnalysis.get_miss_values_df(data)
```

Processes pandas dataframe so missing values can be plotted in heatmap with specific color.

Parameters `data` – pandas dataframe.

Returns Pandas dataframe with missing values as integer 1, and originally valid values as NaN.

```
analytics_core.analytics.wgcnaAnalysis.paste_matrices(matrix1, matrix2, rows, cols)
```

Takes two matrices with analog shapes and concatenates each value in matrix 1 with corresponding one in matrix 2, returning a single pandas dataframe.

Parameters

- **`matrix1`** (`ndarray`) – input 1
- **`matrix2`** (`ndarray`) – input 2

Returns Pandas dataframe.

```
analytics_core.analytics.wgcnaAnalysis.cutreeDynamic(distmatrix, linkage=fun='average', minModuleSize=50, method='hybrid', deepSplit=2, pamRespectsDendro=False, distfun=None)
```

This function implements the R `cutreeDynamic` wrapper in Python, providing an access point for methods of adaptive branch pruning of hierarchical clustering dendograms.

Parameters

- **`data`** – pandas dataframe.
- **`distfun`** (`str`) – distance measure to be used (‘euclidean’, ‘maximum’, ‘manhattan’, ‘canberra’, ‘binary’, ‘minkowski’ or ‘jaccard’).
- **`linkagefun`** (`str`) – hierarchical/agglomeration method to be used (‘single’, ‘complete’, ‘average’, ‘weighted’, ‘centroid’, ‘median’ or ‘ward’).
- **`minModuleSize`** (`int`) – minimum module size.
- **`method`** (`str`) – method to use (‘hybrid’ or ‘tree’).

- **deepSplit** (*int*) – provides a rough control over sensitivity to cluster splitting, the higher the value (with ‘hybrid’ method) or if True (with ‘tree’ method), the more and smaller modules.
- **pamRespectsDendro** (*bool*) – only used for method ‘hybrid’. Objects and small modules will only be assigned to modules that belong to the same branch in the dendrogram structure.

Returns Numpy array of numerical labels giving assignment of objects to modules. Unassigned objects are labeled 0, the largest module has label 1, next largest 2 etc.

```
analytics_core.analytics.wgcnaAnalysis.build_network(data, softPower=6, networkType='unsigned', linkagefun='average', method='hybrid', minModuleSize=50, deepSplit=2, pamRespectsDendro=False, merge_modules=True, MEDissThres=0.4, verbose=0)
```

Weighted gene network construction and module detection. Calculates co-expression similarity and adjacency, topological overlap matrix (TOM) and clusters features in modules.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **softPower** (*int*) – soft-thresholding power.
- **networkType** (*str*) – network type (‘unsigned’, ‘signed’, ‘signed hybrid’, ‘distance’).
- **linkagefun** (*str*) – hierarchical/agglomeration method to be used (‘single’, ‘complete’, ‘average’, ‘weighted’, ‘centroid’, ‘median’ or ‘ward’).
- **method** (*str*) – method to use (‘hybrid’ or ‘tree’).
- **minModuleSize** (*int*) – minimum module size.
- **pamRespectsDendro** (*bool*) – only used for method ‘hybrid’. Objects and small modules will only be assigned to modules that belong to the same branch in the dendrogram structure.
- **merge_modules** (*bool*) – if True, very similar modules are merged.
- **MEDissThres** (*float*) – maximum dissimilarity (i.e., 1-correlation) that qualifies modules for merging.
- **verbose** (*int*) – integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.

Parameter int deepSplit provides a rough control over sensitivity to cluster splitting, the higher the value (with ‘hybrid’ method) or if True (with ‘tree’ method), the more and smaller modules.

Returns Tuple with TOM dissimilarity pandas dataframe, numpy array with module colors per experimental feature.

```
analytics_core.analytics.wgcnaAnalysis.pick_softThreshold(data, RsquaredCut=0.8, networkType='unsigned', verbose=0)
```

Analysis of scale free topology for multiple soft thresholding powers. Aids the user in choosing a proper soft-thresholding power for network construction.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **RsquareCut** (`float`) – desired minimum scale free topology fitting index R^2.
- **networkType** (`str`) – network type ('unsigned', 'signed', 'signed hybrid', 'distance').
- **verbose** (`int`) – integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.

Returns Estimated appropriate soft-thresholding power: the lowest power for which the scale free topology fit R^2 exceeds RsquareCut.

Return type `int`

```
analytics_core.analytics.wgcnaAnalysis.identify_module_colors(matrix, linkage-
fun='average',
method='hybrid',
minModule-
Size=30, deep-
Split=2, pam-
RespectsDen-
dro=False)
```

Identifies co-expression modules and converts the numeric labels into colors.

Parameters

- **matrix** – dissimilarity structure as produced by R.stats dist.
- **minModuleSize** (`int`) – minimum module size.
- **deepSplit** (`int`) – provides a rough control over sensitivity to cluster splitting, the higher the value (with 'hybrid' method) or if True (with 'tree' method), the more and smaller modules.
- **pamRespectsDendro** (`bool`) – only used for method 'hybrid'. Objects and small modules will only be assigned to modules that belong to the same branch in the dendrogram structure.

Returns Numpy array of strings with module color of each experimental feature.

```
analytics_core.analytics.wgcnaAnalysis.calculate_module_eigengenes(data,
mod-
Colors,
soft-
Power=6,
dissim-
ilar-
ity=True)
```

Calculates modules eigengenes to quantify co-expression similarity of entire modules.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **modColors** (`ndarray`) – array (numeric, character or a factor) attributing module colors to each feature in the experimental dataframe.
- **softPower** (`int`) – soft-thresholding power.
- **dissimilarity** – calculates dissimilarity of module eigengenes.

Returns Pandas dataframe with calculated module eigengenes. If dissimilarity is set to True, returns a tuple with two pandas dataframes, the first with the module eigengenes and the second with the eigengenes dissimilarity.

```
analytics_core.analytics.wgcnaAnalysis.merge_similar_modules(data, modColors,
                                                               MEDissThres=0.4,
                                                               verbose=0)
```

Merges modules in co-expression network that are too close as measured by the correlation of their eigengenes.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **modColors** (*ndarray*) – array (numeric, character or a factor) attributing module colors to each feature in the experimental dataframe.
- **verbose** (*int*) – integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.

Para, float MEDissThres maximum dissimilarity (i.e., 1-correlation) that qualifies modules for merging.

Returns Tuple containing pandas dataframe with eigengenes of the new merged modules, and array with module colors of each expeirmental feature.

```
analytics_core.analytics.wgcnaAnalysis.calculate_ModuleTrait_correlation(df_exp,
                                                                       df_traits,
                                                                       MEs)
```

Correlates eigengenes with external traits in order to identify the most significant module-trait associations.

Parameters

- **df_exp** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **df_traits** – pandas dataframe containing clinical data, with samples/subjects as rows and clinical traits as columns.
- **MEs** – pandas dataframe with module eigengenes.

Returns Tuple with two pandas datafames, first the correlation between all module eigengenes and all clinical traits, second a dataframe with concatenated correlation and p-value used for heatmap annotation.

```
analytics_core.analytics.wgcnaAnalysis.calculate_ModuleMembership(data, MEs)
```

For each module, calculates the correlation of the module eigengene and the feature expression profile (quantitative measure of module membership (MM)).

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **MEs** – pandas dataframe with module eigengenes.

Returns Tuple with two pandas dataframes, one with module membership correlations and another with p-values.

```
analytics_core.analytics.wgcnaAnalysis.calculate_FeatureTraitSignificance(df_exp,
                                                                           df_traits)
```

Quantifies associations of individual experimental features with the measured clinical traits, by defining Feature Significance (FS) as the absolute value of the correlation between the feature and the trait.

Parameters

- **df_exp** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **df_traits** – pandas dataframe containing clinical data, with samples/subjects as rows and clinical traits as columns.

Returns Tuple with two pandas dataframes, one with feature significance correlations and another with p-values.

```
analytics_core.analytics.wgcnaAnalysis.get_FeaturesPerModule(data, modColors, mode='dictionary')
```

Groups all experimental features by the co-expression module they belong to.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **modColors** (*ndarray*) – array (numeric, character or a factor) attributing module colors to each feature in the experimental dataframe.
- **mode** (*str*) – type of the value returned by the function ('dictionary' or 'dataframe').

Returns Depending on selected mode, returns a dictionary or dataframe with module color per experimental feature.

```
analytics_core.analytics.wgcnaAnalysis.get_ModuleFeatures(data, modColors, modules=[])
```

Groups and returns a list of the experimental features clustered in specific co-expression modules.

Parameters

- **data** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **modColors** (*ndarray*) – array (numeric, character or a factor) attributing module colors to each feature in the experimental dataframe.
- **modules** (*list*) – list of module colors of interest.

Returns List of lists with experimental features in each selected module.

```
analytics_core.analytics.wgcnaAnalysis.get_EigengenesTrait_correlation(MEs, data)
```

Eigengenes are used as representative profiles of the co-expression modules, and correlation between them is used to quantify module similarity. Clinical traits are added to the eigengenes to see how the traits fit into the eigengene network.

Parameters

- **MEs** – pandas dataframe with module eigengenes.
- **data** – pandas dataframe containing clinical data, with samples/subjects as rows and clinical traits as columns.

Returns Tuple with two pandas dataframes, one with features and traits recalculates module eigengenes dissimilarity, and another with all the overall correlations.

Vizualization

Viz module

```
analytics_core.viz.viz.getPlotTraces(data, key='full', type='lines', div_factor=10010.0, horizontal=False)
```

This function returns traces for different kinds of plots.

Parameters

- **data** – Pandas DataFrame with one variable as data.index (i.e. ‘x’) and all others as columns (i.e. ‘y’).
- **type** (*str*) – ‘lines’, ‘scaled markers’, ‘bars’.
- **div_factor** (*float*) – relative size of the markers.
- **horizontal** (*bool*) – bar orientation.

Returns

list of traces.

Exmaple 1:

```
result = getPlotTraces(data, key='full', type = 'lines', horizontal=False)
```

Example 2:

```
result = getPlotTraces(data, key='full', type = 'scaled markers', div_
factor=float(10^3000), horizontal=True)
```

`analytics_core.viz.viz.get_markdown(text, args={})`

Converts a given text into a Dash Markdown component. It includes a syntax for things like bold text and italics, inline code snippets, lists, quotes, and more. For more information visit <https://dash.plot.ly/dash-core-components/markdown>.

Parameters

- **text** (*str*) – markdown string (or array of strings) that adhreres to the CommonMark spec.
- **args** (*dict*) – dictionary with items from <https://dash.plot.ly/dash-core-components/markdown>.

Returns

dash Markdown component.

`analytics_core.viz.viz.get_pieplot(data, identifier, args)`

This function plots a simple Pie plot.

Parameters

- **data** – pandas DataFrame with values to plot as columns and labels as index.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **valueCol** (*str*) – name of the column with the values to be plotted.
- **textCol** (*str*) – name of the column containing information for the hoverinfo parameter.
- **height** (*str*) – height of the plot.
- **width** (*str*) – width of the plot.

Returns Pieplot figure within the <div id=”_dash-app-content”>.

`analytics_core.viz.viz.get_distplot(data, identifier, args)`

Parameters

- **data** –
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below.

Arguments

- **group** (str) – name of the column containing the group.

`analytics_core.viz.viz.get_boxplot_grid(data, identifier, args)`

This function plots a boxplot in a grid based on column values.

Parameters

- **data** – pandas DataFrame with columns: ‘x’ values and ‘y’ values to plot, ‘color’ and ‘facet’ (color and facet can be the same).
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below.

Arguments

- **title** (str) – plot title.
- **x** (str) – name of column with x values.
- **y** (str) – name of column with y values.
- **color** (str) – name of column with colors
- **facet** (str) – name of column specifying grouping
- **height** (str) – plot height.
- **width** (str) – plot width.

Returns boxplot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_boxplot_grid(data, identifier='Boxplot', args={"Title": "Boxplot", 'x': 'sample', 'y': 'identifier', 'color': 'group', 'facet': 'qc_class', 'axis': 'cols'})
```

`analytics_core.viz.viz.get_barplot(data, identifier, args)`

This function plots a simple barplot.

Parameters

- **data** – pandas DataFrame with three columns: ‘name’ of the bars, ‘x’ values and ‘y’ values to plot.
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below.

Arguments

- **title** (str) – plot title.
- **x_title** (str) – plot x axis title.

- **y_title** (str) – plot y axis title.
- **height** (str) – plot height.
- **width** (str) – plot width.

Returns barplot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_barplot(data, identifier='barplot', args={'title':'Figure with',
    ↵Barplot'})
```

`analytics_core.viz.viz.get_facet_grid_plot(data, identifier, args)`

This function plots a scatterplot matrix where we can plot one variable against another to form a regular scatter plot, and we can pick a third faceting variable to form panels along the columns to segment the data even further, forming a bunch of vertical panels. For more information visit <https://plot.ly/python/facet-trellis/>.

Parameters

- **data** – pandas dataframe with format: ‘group’, ‘name’, ‘type’, and ‘x’ and ‘y’ values to be plotted.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **x** (str) – name of the column containing values to plot in the x axis.
- **y** (str) – name of the column containing values to plot in the y axis.
- **group** (str) – name of the column containing the group.
- **class** (str) – name of the column to be used as ‘facet’ column.
- **plot_type** (str) – decides the type of plot to appear in the facet grid. The options are ‘scatter’, ‘scattergl’, ‘histogram’, ‘bar’, and ‘box’.
- **title** (str) – plot title.

Returns facet grid figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_facet_grid_plot(data, identifier='facet_grid', args={'x':'a', 'y':'b',
    ↵'group':'group', 'class':'type', 'plot_type':'bar', 'title':'Facet Grid Plot
    ↵'})
```

`analytics_core.viz.viz.get_ranking_plot(data, identifier, args)`

Creates abundance multiplots (one per sample group).

Parameters

- **data** – long-format pandas dataframe with group as index, ‘name’ (protein identifiers) and ‘y’ (LFQ intensities) as columns.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below

Arguments

- **group** (str) – name of the column containing the group.

- **index** (bool) – set to True when multi samples per group. Calculates the mean intensity for each protein in each group.
- **x_title** (str) – title of plot x axis.
- **y_title** (str) – title of plot y axis.
- **title** (str) – plot title.
- **width** (int) – plot width.
- **height** (int) – plot height.
- **annotations** (dict, optional) – dictionary where data points names are the keys and descriptions are the values.

Returns multi abundance plot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_ranking_plot(data, identifier='ranking', args={'group':'group',
    ↪'index':'', 'x_title':'x_axis', 'y_title':'y_axis',
    ↪'title':'Ranking Plot', 'width':100, 'height':150, 'annotations': {'GPT~
    ↪P24298': 'liver disease', 'CP~P00450': 'Wilson disease'}})
```

`analytics_core.viz.viz.get_scatterplot_matrix(data, identifier, args)`

This function plots a multi scatterplot (one for each unique element in args[‘group’]).

Parameters

- **data** – pandas dataframe with four columns: ‘name’ of the data points, ‘x’ and ‘y’ values to plot, and ‘group’ they belong to.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below

Arguments

- **group** (str) – name of the column containing the group.
- **title** (str) – plot title.
- **x_title** (str) – plot x axis title.
- **y_title** (str) – plot y axis title.
- **height** (int) – plot height.
- **width** (int) – plot width.
- **annotations** (dict, optional) – dictionary where data points names are the keys and descriptions are the values.

Returns multi scatterplot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_scatterplot_matrix(data, identifier='scatter matrix', args={'group':
    ↪'group', 'title':'Scatter Plot Matrix', 'x_title':'x_axis',
    ↪'y_title':'y_axis', 'height':100, 'width':100, 'annotations':
    ↪': {'GPT~P24298': 'liver disease', 'CP~P00450': 'Wilson disease'}})
```

`analytics_core.viz.viz.get_simple_scatterplot(data, identifier, args)`

Plots a simple scatterplot with the possibility of including in-plot annotations of data points.

Parameters

- **data** – long-format pandas dataframe with columns: ‘x’ (ranking position), ‘group’ (original dataframe position), ‘name’ (protein identifier), ‘y’ (LFQ intensity), ‘symbol’ (data point shape) and ‘size’ (data point size).
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **annotations** (*dict*) – dictionary where data points names are the keys and descriptions are the values.
- **title** (*str*) – plot title.
- **x_title** (*str*) – plot x axis title.
- **y_title** (*str*) – plot y axis title.
- **height** (*int*) – plot height.
- **width** (*int*) – plot width.

Returns annotated scatterplot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_scatterplot_matrix(data, identifier='scatter plot', args={
    ↪ 'annotations': {'GPT~P24298': 'liver disease', 'CP~P00450': 'Wilson disease'},
    ↪ 'title': 'Scatter Plot', 'x_title': 'x_axis',
    ↪ 'y_title': 'y_axis', 'height': 100, 'width': 100})
```

`analytics_core.viz.viz.get_scatterplot (data, identifier, args)`

This function plots a simple Scatterplot.

Parameters

- **data** – is a Pandas DataFrame with four columns: “name”, x values and y values (provided as variables) to plot.
- **identifier** (*str*) – is the id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **title** (*str*) – title of the figure.
- **x_title** (*str*) – plot x axis title.
- **y_title** (*str*) – plot y axis title.
- **height** (*int*) – plot height.
- **width** (*int*) – plot width.

Returns scatterplot figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_scatterplot(data, identifier='scatter plot', 'title': 'Scatter Plot',
    ↪ 'x_title': 'x_axis', 'y_title': 'y_axis', 'height': 100, 'width': 100}))
```

`analytics_core.viz.viz.get_volcanoplot (results, args)`

This function plots volcano plots for each internal dictionary in a nested dictionary.

Parameters

- **results** (`dict [dict]`) – nested dictionary with pairwise group comparisons as keys and internal dictionaries containing ‘x’ (log2FC values), ‘y’ (-log10 p-values), ‘text’, ‘color’, ‘pvalue’ and ‘annotations’ (number of hits to be highlighted).
- **args** (`dict`) – see below.

Arguments

- **fc** (float) – fold change threshold.
- **range_x** (list) – list with minimum and maximum values for x axis.
- **range_y** (list) – list with minimum and maximum values for y axis.
- **x_title** (str) – plot x axis title.
- **y_title** (str) – plot y axis title.
- **colorscale** (str) – string for predefined plotly colorscales or dict containing one or more of the keys listed in <https://plot.ly/python/reference/#layout-colorscale>.
- **showscale** (bool) – determines whether or not a colorbar is displayed for a trace.
- **marker_size** (int) – sets the marker size (in px).

Returns list of volcano plot figures within the <div id=”_dash-app-content”>.

Example:

```
result = get_volcanoplot(results, args={'fc':2.0, 'range_x':[0, 1], 'range_y':[-1, 1], 'x_title':'x_axis', 'y_title':'y_title', 'colorscale':'Blues', 'showscale':True, 'marker_size':7})
```

```
analytics_core.viz.viz.run_volcano(data, identifier, args={'alpha': 0.05, 'colorscale': 'Blues', 'fc': 2, 'marker_size': 8, 'num_annotations': 10, 'showscale': False, 'x_title': 'log2FC', 'y_title': '-log10(pvalue)'})
```

This function parses the regulation data from statistical tests and creates volcano plots for all distinct group comparisons. Significant hits with lowest adjusted p-values are highlighted.

Parameters

- **data** – pandas dataframe with format: ‘identifier’, ‘group1’, ‘group2’, ‘mean(group1)’, ‘mean(group2)’, ‘log2FC’, ‘std_error’, ‘tail’, ‘t-statistics’, ‘padj_THSD’, ‘effsize’, ‘efftype’, ‘FC’, ‘rejected’, ‘F-statistics’, ‘pvalue’, ‘padj’, ‘correction’, ‘-log10 pvalue’ and ‘Method’.
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below.

Arguments

- **alpha** (float) – adjusted p-value threshold for significant hits.
- **fc** (float) – fold change threshold.
- **colorscale** (str or dict) – name of predefined plotly colorscale or dictionary containing one or more of the keys listed in <https://plot.ly/python/reference/#layout-colorscale>.
- **showscale** (bool) – determines whether or not a colorbar is displayed for a trace.
- **marker_size** (int) – sets the marker size (in px).
- **x_title** (str) – plot x axis title.

- **y_title** (str) – plot y axis title.
- **num_annotations** (int) – number of hits to be highlighted (if num_annotations = 10, highlights 10 hits with lowest adjusted p-value).

Returns list of volcano plot figures within the <div id="“_dash-app-content”">.

Example:

```
result = run_volcano(data, identifier='volvano data', args={'alpha':0.05, 'fc':2,
                                                               'colorscale':'Blues', 'showscale':False, 'marker_size':6, 'x_title':'log2FC',
                                                               'y_title':'-log10(pvalue)', 'num_annotations':10})
```

`analytics_core.viz.viz.get_heatmapplot (data, identifier, args)`

This function plots a simple Heatmap.

Parameters

- **data** – is a Pandas DataFrame with the shape of the heatmap where index corresponds to rows and column names corresponds to columns, values in the heatmap corresponds to the row values.
- **identifier** (*str*) – is the id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **format** (str) – defines the format of the input dataframe.
- **source** (str) – name of the column containing the source.
- **target** (str) – name of the column containing the target.
- **values** (str) – name of the column containing the values to be plotted.
- **title** (str) – title of the figure.

Returns heatmap figure within the <div id="“_dash-app-content”">.

Example:

```
result = get_heatmapplot(data, identifier='heatmap', args={'format':'edgelist',
                                                               'source':'node1', 'target':'node2', 'values':'score', 'title':'Heatmap Plot'})
```

`analytics_core.viz.viz.get_complex_heatmapplot (data, identifier, args)`

`analytics_core.viz.viz.get_notebook_network_pyvis (graph, args={})`

This function converts a Networkx graph into a PyVis graph supporting Jupyter notebook embedding.

Parameters

- **graph** (*graph*) – networkX graph.
- **args** (*dict*) – see below.

Arguments

- **height** (int) – network canvas height.
- **width** (int) – network canvas width.

Returns PyVis graph.

Example:

```
result = get_notebook_network_pyvis(graph, args={'height':100, 'width':100})
```

`analytics_core.viz.viz.get_notebook_network_web(graph, args)`

This function converts a networkX graph into a webweb interactive network in a browser.

Parameters `graph` (`graph`) – networkX graph.

Returns web network.

`analytics_core.viz.viz.network_to_tables(graph)`

Creates the graph edge list and node list and returns them as separate Pandas DataFrames.

Parameters `graph` – networkX graph used to construct the Pandas DataFrame.

Returns two Pandas DataFrames.

`analytics_core.viz.viz.generate_configuration_tree(report_pipeline, dataset_type)`

This function retrieves the analysis pipeline from a dataset .yml file and creates a Cytoscape network, organized hierarchically.

Parameters

- `report_pipeline` (`dict`) – dictionary with dataset type analysis and visualization pipeline (conversion of .yml files to python dictionary).
- `dataset_type` (`str`) – type of dataset ('clinical', 'proteomics', 'DNAseq', 'RNAseq', 'multomics').

Returns new Dash div with title and Cytoscape network, summarizing analysis pipeline.

`analytics_core.viz.viz.get_network(data, identifier, args)`

This function filters an input dataframe based on a threshold score and builds a cytoscape network. For more information on 'node_size' parameter, visit https://networkx.github.io/documentation/networkx-1.10/reference/generated/networkx.algorithms.centrality.betweenness_centrality.html and https://networkx.github.io/documentation/networkx-1.10/reference/generated/networkx.algorithms.centrality.eigenvector_centrality_numpy.html.

Parameters

- `data` – long-format pandas dataframe with at least three columns: source node, target node and value (e.g. weight, score).
- `identifier` (`str`) – id used to identify the div where the figure will be generated.
- `args` (`dict`) – see below.

Arguments

- `source` (str) – name of the column containing the source.
- `target` (str) – name of the column containing the target.
- `cutoff` (float) – value threshold for network building.
- `cutoff_abs` (bool) – if True will take both positive and negative sides of the cutoff value.
- `values` (str) – name of the column containing the values to be plotted.
- `node_size` (str) – method used to determine node radius ('betweenness', 'ev_centrality', 'degree').
- `title` (str) – plot title.
- `color_weight` (bool) – if True, edges in network are colored red if score > 0 and blue if score < 0.

Returns dictionary with the network in multiple formats: jupyter-notebook compatible, web browser compatibles, data table, and json.

Example:

```
result = get_network(data, identifier='network', args={'source':'node1', 'target':  
    ↪ 'node2', 'cutoff':0.5, 'cutoff_abs':True, 'values':'weight',  
    ↪ 'node_size':'degree', 'title':'Network Figure', 'color_weight': True})
```

`analytics_core.viz.viz.get_network_style(node_colors, color_edges)`

This function uses a dictionary of nodes and colors and creates a stylesheet and layout for a network.

Parameters

- **node_colors** (`dict`) – dictionary with node names as keys and colors as values.
- **color_edges** (`bool`) – if True, add edge coloring to stylesheet (red for positive width, blue for negative).

Returns stylesheet (list of dictionaries specifying the style for a group of elements, a class of elements, or a single element) and layout (dictionary specifying how the nodes should be positioned on the canvas).

`analytics_core.viz.viz.visualize_notebook_network(network, notebook_type='jupyter',
 layout={'height': '700px', 'width': '100%'})`

This function returns a Cytoscape network visualization for Jupyter notebooks

Parameters

- **network** (`tuple`) – tuple with two dictionaries: network data and stylesheet (see `get_network(data, identifier, args)`).
- **notebook_type** (`str`) – the type of notebook where the network will be visualized (currently only jupyter notebook is supported)
- **layout** (`dict`) – specific layout properties (see <https://dash.plot.ly/cytoscape/layout>)

Returns cyjupyter.cytoscape.Cytoscape object

Example:

```
net = get_network(clincorr.dropna(), identifier='corr', args={'source':'node1',  
    ↪ 'target':'node2',  
    ↪ 'cutoff':0, 'cutoff_abs':True,  
    ↪ 'values':'weight', 'node_size':  
    ↪ 'degree',  
    ↪ 'title':'Network Figure',  
    ↪ 'color_weight': True})  
visualize_notebook_network(net['notebook'], notebook_type='jupyter', layout={  
    ↪ 'width':'100%', 'height':'700px'})
```

`analytics_core.viz.viz.visualize_notebook_path(path, notebook_type='jupyter')`

This function returns a Cytoscape network visualization for Jupyter notebooks

Parameters

- **object** (`path`) – dash_html_components object with the cytoscape network (returned by `get_cytoscape_network()`)
- **notebook_type** (`str`) – the type of notebook where the network will be visualized (currently only jupyter notebook is supported)
- **layout** (`dict`) – specific layout properties (see <https://dash.plot.ly/cytoscape/layout>)

Returns cyjupyter.cytoscape.Cytoscape object

Example:

```
net = get_cytoscape_network(G, identifier='corr', args={'title':'Cytoscape path',
                                                       'stylesheet':stylesheet,
                                                       'layout': layout})
visualize_notebook_path(net, notebook_type='jupyter')
```

`analytics_core.viz.viz.get_pca_plot(data, identifier, args)`

This function creates a pca plot with scores and top “args[‘loadings’]” loadings.

Parameters

- **data** (`tuple`) – tuple with two pandas dataframes: scores and loadings.
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below

Arguments

- **loadings** (int) – number of features with highest loading values to be displayed in the pca plot
- **title** (str) – title of the figure
- **x_title** (str) – plot x axis title
- **y_title** (str) – plot y axis title
- **height** (int) – plot height
- **width** (int) – plot width

Returns PCA figure within the <div id=”_dash-app-content”>.

Example:

```
result = get_pca_plot(data, identifier='pca', args={'loadings':15, 'title':'PCA_Plot',
                                                    'x_title':'PC1', 'y_title':'PC2', 'height':100, 'width':100})
```

`analytics_core.viz.viz.get_sankey_plot(data, identifier, args={'font': 12, 'height': 800, 'orientation': 'h', 'source': 'source', 'source_colors': 'source_colors', 'target': 'target', 'target_colors': 'target_colors', 'title': 'Sankey plot', 'valueformat': '.0f', 'weight': 'weight', 'width': 800})`

This function generates a Sankey plot in Plotly.

Parameters

- **data** – Pandas DataFrame with the format: source target weight.
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below

Arguments

- **source** (str) – name of the column containing the source
- **target** (str) – name of the column containing the target
- **weight** (str) – name of the column containing the weight
- **source_colors** (str) – name of the column in data that contains the colors of each source item

- **target_colors** (str) – name of the column in data that contains the colors of each target item
- **title** (str) – plot title
- **orientation** (str) – whether to plot horizontal ('h') or vertical ('v')
- **valueformat** (str) – how to show the value ('.0f')
- **width** (int) – plot width
- **height** (int) – plot height
- **font** (int) – font size

Returns dcc.Graph

Example:

```
result = get_sankey_plot(data, identifier='sankeyplot', args={'source':'source',
← 'target':'target', 'weight':'weight', 'source_colors':'source_colors',
← 'target_colors':'target_colors', 'orientation': 'h',
← 'valueformat': '.0f', 'width':800, 'height':800, 'font':12, 'title':'Sankey plot
← })
```

```
analytics_core.viz.viz.get_table(data, identifier, title, colors=('#C2D4FF', '#F5F8FF'), subset=None, plot_attr={'font': 12, 'height': 2500, 'width': 1500}, subplot=False)
```

This function converts a pandas dataframe into an interactive table for viewing, editing and exploring large datasets. For more information visit <https://dash.plot.ly/datatable>.

Parameters

- **data** – pandas dataframe.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **title** (*str*) – table title.
- **subset** – selects columns from dataframe to be used. If None, the entire dataframe is used.

Returns new Dash div containing title and interactive table.

Example:

```
result = get_table(data, identifier='table', title='Table Figure', subset = None)
```

```
analytics_core.viz.viz.get_multi_table(data, identifier, title)
```

```
analytics_core.viz.viz.get_violinplot(data, identifier, args)
```

This function creates a violin plot for all columns in the input dataframe.

Parameters

- **data** – pandas dataframe with samples as rows and dependent variables as columns.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below

Arguments

- **drop_cols** (list) – column labels to be dropped from the dataframe.
- **group** (str) – name of the column containing the group.

Returns list of violin plots within the <div id="_dash-app-content">.

Example:

```
result = get_violinplot(data, identifier='violinplot', args={'drop_cols': ['sample',  
    ↴ 'subject'], 'group': 'group'})
```

`analytics_core.viz.viz.create_violinplot(df, variable, group_col='group')`

This function creates traces for a simple violin plot.

Parameters

- **df** – pandas dataframe with samples as rows and dependent variables as columns.
- **variable** (`str`) – name of the column with the dependent variable.

Pram (str) group_col name of the column containing the group.

Returns list of traces to be used as data for plotly figure.

Example:

```
result = create_violinplot(df, 'prptein a', group_col='group')
```

`analytics_core.viz.viz.get_clustergrammer_plot(data, identifier, args)`

This function takes a pandas dataframe, calculates clustering, and generates the visualization json. For more information visit <https://github.com/MaayanLab/clustergrammer-py>.

Parameters

- **data** – long-format pandas dataframe with columns ‘node1’ (source), ‘node2’ (target) and ‘weight’
- **identifier** (`str`) – id used to identify the div where the figure will be generated
- **args** (`dict`) – see below

Arguments

- **format** (str) – defines if dataframe needs to be converted from ‘edgelist’ to matrix
- **title** (str) – plot title

Returns Dash Div with heatmap plot from Clustergrammer web-based tool

`analytics_core.viz.viz.get_parallel_plot(data, identifier, args)`

This function creates a parallel coordinates plot, with sample groups as the different dimensions.

Parameters

- **data** – pandas dataframe with groups as rows and dependent variables as columns.
- **identifier** (`str`) – id used to identify the div where the figure will be generated.
- **args** (`dict`) – see below.

Arguments

- **group** (str) – name of the column containing the groups.
- **zscore** (bool) – if True, calculates the z score of each values in the row, relative to the row mean and standard deviation.
- **color** (str) – line color.
- **title** (str) – plot title.

Returns parallel plot figure within <div id=”_dash-app-content”> .

Example:

```
result = get_parallel_plot(data, identifier='parallel plot', args={'group':'group
→', 'zscore':True, 'color':'blue', 'title':'Parallel Plot'})
```

`analytics_core.viz.viz.get_WGCNAPlots (data, identifier)`

Takes data from runWGCNA function and builds WGCNA plots.

Parameters

- `data` – tuple with multiple pandas dataframes.
- `identifier (str)` – is the id used to identify the div where the figure will be generated.

`Returns` list of `dcc.Graph`.

`analytics_core.viz.viz.getMapperFigure (data, identifier, title)`

This function uses the KeplerMapper python package to visualize high-dimensional data and generate a FigureWidget that can be shown or edited. This method is suitable for use in Jupyter notebooks. For more information visit <https://kepler-mapper.scikit-tda.org/reference/stubs/kmappert.plotlyviz.plotlyviz.html>.

Parameters

- `data` – dictionary. Simplicial complex output from the KeplerMapper map method.
- `identifier (str)` – id used to identify the div where the figure will be generated.
- `title (str)` – plot title.

`Returns` plotly FigureWidget within `<div id=_dash-app-content>`.

`analytics_core.viz.viz.get_2_venn_diagram (data, identifier, cond1, cond2, args)`

This function extracts the exclusive features in cond1 and cond2 and their common features, and build a two-circle venn diagram.

Parameters

- `data` – pandas dataframe with features as rows and group identifiers as columns.
- `identifier (str)` – id used to identify the div where the figure will be generated.
- `cond1 (str)` – identifier of first group.
- `cond2 (str)` – identifier of second group.
- `args (dict)` – see below.

Arguments

- `colors (dict)` – dictionary with cond1 and cond2 as keys, and color codes as values.
- `title (str)` – plot title.

`Returns` two-circle venn diagram figure within `<div id=_dash-app-content>`.

Example:

```
result = get_2_venn_diagram(data, identifier='venn2', cond1='group1', cond2=
→'group2', args={'color': {'group1':'blue', 'group2':'red'},
→ 'title':'Two-circle Venn diagram'})
```

`analytics_core.viz.viz.plot_2_venn_diagram (cond1, cond2, unique1, unique2, intersection,
→ identifier, args)`

This function creates a simple non area-weighted two-circle venn diagram.

Parameters

- `cond1 (str)` – label of the first circle.

- **cond2** (*str*) – label of the second circle.
- **unique1** (*int*) – number of features exclusive to cond1.
- **unique2** (*int*) – number of features exclusive to cond2.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Parm int intersection number of features common to cond1 and cond2.

Arguments

- **colors** (*dict*) – dictionary with cond1 and cond2 as keys, and color codes as values.
- **title** (*str*) – plot title.

Returns two-circle venn diagram figure within <div id=”_dash-app-content”>.

Example:

```
result = plot_2_venn_diagram(cond1='group1', cond2='group2', unique1=10, ↵
    ↵unique2=15, intersection=8, identifier='vennplot', ↵
    ↵    args={'color':{'group1':'blue', 'group2':'red'}}, 'title':'Two-circle ↵
    ↵Venn diagram')}
```

```
analytics_core.viz.viz.get_wordcloud(data, identifier, args={'height': 700, 'margin': 1, ↵
    ↵    'max_font_size': 100, 'max_words': 400, 'stopwords': ↵
    ↵    []}, 'width': 700})
```

This function generates a Wordcloud based on the natural text in a pandas dataframe column.

Parameters

- **data** – pandas dataframe with columns: ‘PMID’, ‘abstract’, ‘authors’, ‘date’, ‘journal’, ‘keywords’, ‘title’, ‘url’, ‘Proteins’, ‘Diseases’.
- **identifier** (*str*) – id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **text_col** (*str*) – name of column containing the natural text used to generate the wordcloud.
- **stopwords** (*list*) – list of words that will be eliminated.
- **max_words** (*int*) – maximum number of words.
- **max_font_size** (*int*) – maximum font size for the largest word.
- **margin** (*int*) – plot margin size.
- **width** (*int*) – width of the plot.
- **height** (*int*) – height of the plot.
- **title** (*str*) – plot title.

Returns wordcloud figure within <div id=”_dash-app-content”>.

Example:

```
result = get_wordcloud(data, identifier='wordcloud', args={'stopwords': [ ↵
    ↵    'BACKGROUND', 'CONCLUSION', 'RESULT', 'METHOD', 'CONCLUSIONS', 'RESULTS', 'METHODS'], ↵
    ↵    'max_words': 400, 'max_font_size': 100, 'width' ↵
    ↵    ': 700, 'height': 700, 'margin': 1})
```

```
analytics_core.viz.viz.get_cytoscape_network(net, identifier, args)
```

This function creates a Cytoscape network in dash. For more information visit <https://dash.plot.ly/cytoscape>.

Parameters

- **net** (*dict*) – dictionary in which each element (key) is defined by a dictionary with ‘id’ and ‘label’ (if it is a node) or ‘source’, ‘target’ and ‘label’ (if it is an edge).
- **identifier** (*str*) – is the id used to identify the div where the figure will be generated.
- **args** (*dict*) – see below.

Arguments

- **title** (str) – title of the figure.
- **stylesheet** (list[dict]) – specifies the style for a group of elements, a class of elements, or a single element (accepts two keys ‘selector’ and ‘style’).
- **layout** (dict) – specifies how the nodes should be positioned on the screen.

Returns network figure within <div id=”_dash-app-content”>.

```
analytics_core.viz.viz.save_DASH_plot(plot, name, plot_format='svg', directory='')
```

This function saves a plotly figure to a specified directory, in a determined format.

Parameters

- **plot** – plotly figure (dictionary with data and layout)
- **name** (*str*) – name of the figure
- **plot_format** (*str*) – suffix of the saved file (‘svg’, ‘pdf’, ‘png’, ‘jpeg’, ‘jpg’)
- **directory** (*str*) – folder where figure is to be saved

Returns figure saved in directory

Example:

```
result = save_DASH_plot(plot, name='Plot example', plot_format='svg', directory='/
˓→data/plots')
```

```
analytics_core.viz.viz.mpl_to_plotly(fig, ci=True, legend=True)
```

```
analytics_core.viz.viz.get_km_plot(data, identifier, args)
```

```
analytics_core.viz.viz.get_polar_plot(df, identifier, args)
```

This function creates a Polar plot with data aggregated for a given group.

Parameters

- **df** (*dataframe*) – dataframe with the data to plot
- **identifier** (*str*) – identifier to be used in the app
- **args** (*dict*) – dictionary containing the arguments needed to plot the figure (value_col (value to aggregate), group_col (group by), color_col (color by))

Returns Dash Graph

Example:: figure = get_polar_plot(df, identifier='polar', args={‘value_col’:‘intensity’, ‘group_col’:‘modifier’, ‘color_col’:‘group’})

WGCNA viz

```
analytics_core.viz.wgcnaFigures.get_module_color_annotation(map_list,
                                                               col_annotation=False,
                                                               row_annotation=False,
                                                               bygene=False, module_colors=[],
                                                               dendrogram=[])
```

This function takes a list of values, converts them into colors, and creates a new plotly object to be used as an annotation. Options module_colors and dendrogram only apply when map_list is a list of experimental features used in module eigenegenes calculation.

Parameters

- **map_list** (*list*) – dendrogram leaf labels.
- **col_annotation** (*bool*) – if True, adds color annotations as a row.
- **row_annotation** (*bool*) – if True, adds color annotations as a column.
- **bygene** (*bool*) – determines whether annotation colors have to be reordered to match dendrogram leaf labels.
- **module_colors** (*list*) – dendrogram leaf module color.
- **dendrogram** (*dict*) – dendrogram represented as a plotly object figure.

Returns Plotly object figure.

Note: map_list and module_colors must have the same length.

```
analytics_core.viz.wgcnaFigures.get_heatmap(df, colorscale=None, color_missing=True)
```

This function plots a simple Plotly heatmap.

Parameters

- **df** – pandas dataframe containing experimental data, with samples/subjects as rows and features as columns.
- **colorscale** (*list[list]*) – heatmap colorscale (e.g. [[0,’#67a9cf’],[0.5,’#f7f7f7’],[1,’#ef8a62’]]). If colorscale is not defined, will take [[0, ‘rgb(255,255,255)’], [1, ‘rgb(255,51,0)’]] as default.
- **color_missing** (*bool*) – if set to True, plots missing values as grey in the heatmap.

Returns Plotly object figure.

```
analytics_core.viz.wgcnaFigures.plot_labeled_heatmap(df, textmatrix, title, colorscale=[[0, 'rgb(0,255,0)'), [0.5, 'rgb(255,255,255)'), [1, 'rgb(255,0,0)']], width=1200, height=800, row_annotation=False, col_annotation=False)
```

This function plots a simple Plotly heatmap with column and/or row annotations and heatmap annotations.

Parameters

- **df** – pandas dataframe containing data to be plotted in the heatmap.
- **textmatrix** – pandas dataframe with heatmap annotations as values.

- **title** (*str*) – the title of the figure.
- **colorscale** (*list[list]*) – heatmap colorscale (e.g. `[[0,rgb(0,255,0)], [0.5,rgb(255,255,255)], [1,rgb(255,0,0)]]`)
- **width** (*int*) – the width of the figure.
- **height** (*int*) – the height of the figure.
- **row_annotation** (*bool*) – if True, adds a color-coded column at the left of the heatmap.
- **col_annotation** (*bool*) – if True, adds a color-coded row at the bottom of the heatmap.

Returns Plotly object figure.

```
analytics_core.viz.wgcnaFigures.plot_dendrogram_guidelines(Z_tree, dendrogram)
```

This function takes a dendrogram tree dictionary and its plotly object and creates shapes to be plotted as vertical dashed lines in the dendrogram.

Parameters

- **Z_tree** (*dict*) – dictionary of data structures computed to render the dendrogram. Keys: ‘icoords’, ‘dcoords’, ‘ivl’ and ‘leaves’.
- **dendrogram** – dendrogram represented as a plotly object figure.

Returns List of dictionaries.

```
analytics_core.viz.wgcnaFigures.plot_intramodular_correlation(MM, FS, feature_module_df, title, width=1000, height=800)
```

This function uses the Feature significance and Module Membership measures, and plots a multi-scatter plot of all modules against all clinical traits.

Parameters

- **MM** – pandas dataframe with module membership data
- **FS** – pandas dataframe with feature significance data
- **feature_module_df** – pandas DataFrame of experimental features and module colors (use mode='dataframe' in get_FeaturesPerModule)
- **title** (*str*) – plot title
- **width** (*int*) – plot width
- **height** (*int*) – plot height

Returns Plotly object figure.

Example:

```
plot = plot_intramodular_correlation(MM, FS, feature_module_df, title='Plot', width=1000, height=800):
```

Note: There is a limit in the number of subplots one can make in Plotly. This function limits the number of modules shown to 5.

```
analytics_core.viz.wgcnaFigures.plot_complex_dendrogram(dendro_df, subplot_df, title, dendro_labels=[], distfun='euclidean', linkagefun='average', hang=0.04, subplot='module colors', subplot_colorscale=[], color_missingvals=True, row_annotation=False, col_annotation=False, width=1000, height=800)
```

This function plots a dendrogram with a subplot below that can be a heatmap (annotated or not) or module colors.

Parameters

- **dendro_df** – pandas dataframe containing data used to generate dendrogram, columns will result in dendrogram leaves.
- **subplot_df** – pandas dataframe containing data used to generate plot below dendrogram.
- **title (str)** – the title of the figure.
- **dendro_labels (list)** – list of strings for dendrogram leaf nodes labels.
- **distfun (str)** – distance measure to be used ('euclidean', 'maximum', 'manhattan', 'canberra', 'binary', 'minkowski' or 'jaccard').
- **linkagefun (str)** – hierarchical/agglomeration method to be used ('single', 'complete', 'average', 'weighted', 'centroid', 'median' or 'ward').
- **hang (float)** – height at which the dendrogram leaves should be placed.
- **subplot (str)** – type of plot to be shown below the dendrogram ('module colors' or 'heatmap').
- **subplot_colorscale (list)** – colorscale to be used in the subplot.
- **color_missingvals (bool)** – if set to *True*, plots missing values as grey in the heatmap.
- **row_annotation (bool)** – if *True*, adds a color-coded column at the left of the heatmap.
- **col_annotation (bool)** – if *True*, adds a color-coded row at the bottom of the heatmap.
- **width (int)** – the width of the figure.
- **height (int)** – the height of the figure.

Returns Plotly object figure.

Dendrogram

```
analytics_core.viz.Dendrogram.plot_dendrogram(Z_dendrogram, cutoff_line=True, value=15, orientation='bottom', hang=30, hide_labels=False, labels=None, colorscale=None, hovertext=None, color_threshold=None)
```

Modified version of Plotly _dendrogram.py that returns a dendrogram Plotly figure object with cutoff line.

Parameters

- **Z_dendrogram (ndarray)** – Matrix of observations as array of arrays

- **cutoff_line** (*boolean*) – plot distance cutoff line
- **value** (*float or int*) – dendrogram distance for cutoff line
- **orientation** (*str*) – ‘top’, ‘right’, ‘bottom’, or ‘left’
- **hang** (*float*) – dendrogram distance of leaf lines
- **hide_labels** (*boolean*) – show leaf labels
- **labels** (*list*) – List of axis category labels(observation labels)
- **colorscale** (*list*) – Optional colorscale for dendrogram tree
- **hovertext** (*list [list]*) – List of hovertext for constituent traces of dendrogram clusters
- **color_threshold** (*double*) – Value at which the separation of clusters will be made

Returns Plotly figure object

Example:

```
figure = plot_dendrogram(dendro_tree, hang=0.9, cutoff_line=False)
```

```
class analytics_core.viz.Dendrogram.Dendrogram(Z_dendrogram, orientation='bottom',
                                               hang=1, hide_labels=False, labels=None,
                                               colorscale=None, hovertext=None,
                                               color_threshold=None,
                                               width=inf, height=inf, xaxis='xaxis',
                                               yaxis='yaxis')
```

Bases: *object*

Refer to `plot_dendrogram()` for docstring.

get_color_dict (*colorscale*)

Returns colorscale used for dendrogram tree clusters.

Parameters **colorscale** (*list*) – colors to use for the plot in rgb format

Return (dict) default colors mapped to the user colorscale

set_axis_layout (*axis_key, hide_labels*)

Sets and returns default axis object for dendrogram figure.

Parameters **axis_key** (*str*) – E.g., ‘xaxis’, ‘xaxis1’, ‘yaxis’, ‘yaxis1’, etc.

Return (dict) An axis_key dictionary with set parameters.

set_figure_layout (*width, height, hide_labels*)

Sets and returns default layout object for dendrogram figure.

Parameters

- **width** (*int*) – plot width
- **height** (*int*) – plot height
- **hide_labels** (*boolean*) – show leaf labels

Returns Plotly layout

get_dendrogram_traces (*Z_dendrogram, hang, colorscale, hovertext, color_threshold*)

Calculates all the elements needed for plotting a dendrogram.

Parameters

- **`z_dendrogram`** (`ndarray`) – Matrix of observations as array of arrays
- **`hang`** (`float`) – dendrogram distance of leaf lines
- **`colorscale`** (`list`) – Color scale for dendrogram tree clusters
- **`hovertext`** (`list`) – List of hovertext for constituent traces of dendrogram

Return (tuple) Contains all the traces in the following order:

- a. `trace_list`: List of Plotly trace objects for dendrogram tree
- b. `icoord`: All X points of the dendrogram tree as array of arrays with length 4
- c. `dcoord`: All Y points of the dendrogram tree as array of arrays with length 4
- d. `ordered_labels`: leaf labels in the order they are going to appear on the plot
- e. `Z_dendrogram['leaves']`: left-to-right traversal of the leaves

Colors

Code for handling color names and RGB codes.

This module is part of Swampy, and used in Think Python and Think Complexity, by Allen Downey.

<http://greenteapress.com>

Copyright 2013 Allen B. Downey. Distributed under the GNU General Public License at gnu.org/licenses/gpl.html.

```
analytics_core.viz.color_list.make_color_dict(colors='n141 211 199\nturquoise\n31
120 180\ntblue\n139 69
19\tsaddlebrown\n177 89
40\tbrown\n51 160 44\tgreen\n255
237 111\tyellow\n173 255
47\tpreblue\n255 0 0\ltredd\n255
255 255\white\n0 0\tnblack\n255 192
203\tpink\n255 0 255\tmagenta\n160
32 240\tpurple\n210 180
140\tan\n250 128 114\tsalmon\n166
206 227\tcyan\n25 25
112\tnightblue\n224
255 255\lightcyan\n153
153 153 \tgrey60\n144
238 144\lightgreen\n255
255 224\lightyellow\n65
105 225\royalblue\n139 0
0\tdarkred\n0 100 0\tdarkgreen\n0
206 209\darkturquoise\n169
169 169\darkgrey\n255
165 0\torange\n255 140
0\tdarkorange\n135 206
235\tskyblue\n70 130
180\steelblue\n175 238
238\paleturquoise\n238
130 238\vviolet\n85 107
47\tdarkolivegreen\n139 0
139\darkmagenta\n190 190
190\gray\n190 190 190\grey\n')
```

Returns a dictionary that maps color names to RGB strings.

The format of RGB strings is '#RRGGBB'.

```
analytics_core.viz.color_list.read_colors()
    Returns color information in two data structures.
```

The format of RGB strings is '#RRGGBB'.

color_dict: map from color name to RGB string rgbs: list of (rgb, names) pairs, where rgb is an RGB code and names is a sorted list of color names

```
analytics_core.viz.color_list.invert_dict(d)
    Returns a dictionary that maps from values to lists of keys.
```

d: dict

returns: dict

R wrapper

```
analytics_core.R_wrapper.call_Rpackage(call='function', designation='aov')
analytics_core.R_wrapper.R_matrix2Py_matrix(r_matrix, index, columns)
```

Analytics factory

```
class analytics_core.analytics_factory.Analysis(identifier, analysis_type, args, data, result=None)
    Bases: object
    property identifier
    property analysis_type
    property args
    property data
    property result
    generate_result()
    get_plot(name, identifier)
```

Utils

```
analytics_core.utils.generate_html(network)
```

This method gets the data structures supporting the nodes, edges, and options and updates the pyvis html template holding the visualization.

```
analytics_core.utils.append_to_list(mylist, myappend)
analytics_core.utils.neo4j_path_to_networkx(paths, key='path')
analytics_core.utils.neo4j_schema_to_networkx(schema)
analytics_core.utils.networkx_to_cytoscape(graph)
analytics_core.utils.networkx_to_gml(graph, path)
analytics_core.utils.json_network_to_gml(graph_json, path)
```

```
analytics_core.utils.json_network_to_networkx(graph_json)
analytics_core.utils.get_clustergrammer_link(net, filename=None)
analytics_core.utils.generator_to_dict(genvar)
analytics_core.utils.parse_html(html_snippet)
analytics_core.utils.hex2rgb(color)
analytics_core.utils.get_rgb_colors(n)
analytics_core.utils.get_hex_colors(n)
analytics_core.utils.getMedlineAbstracts(idList)
```

8.1.5 Notebooks

vis.py

```
notebooks.development.vis.vis_network(nodes, edges, physics=False)
notebooks.development.vis.draw(graph, options, physics=False, limit=100)
```

PROJECT INFO

9.1 Credits

9.1.1 Development Leads

- Alberto Santos Delgado (@albsantosdel)
- Ana Rita Colaço (@arcolaco)
- Annelaura Bach Nielsen (@aannelaura)

9.1.2 Core Committers

9.1.3 Contributors

9.2 Backers

We would like to thank the following people for supporting us in our efforts to maintain and improve the Clinical Knowledge Graph:

-
-

9.3 Contributing

Contributions are welcome, and they are greatly appreciated! Every little bit helps, and credit will always be given.

- Types of Contributions *Types of Contributions*
- Contributor Setup *Setting Up the Code for Local Development*
- Contributor Guidelines *Contributor Guidelines*
- Core Committer Guide *Core Committer Guide*

9.3.1 Types of Contributions

You can contribute in many ways:

Create Analysis or Visualization methods

If you develop new ways of analysing or visualizing data, please feel free to add to the Analytics Core.

Report Bugs

Report bugs at <https://github.com/MannLabs/CKG/issues>.

If you are reporting a bug, please include:

- Your operating system name and version.
- Any details about your local setup that might be helpful in troubleshooting.
- If you can, provide detailed steps to reproduce the bug.
- If you don't have steps to reproduce the bug, just note your observations in as much detail as you can. Questions to start a discussion about the issue are welcome.

Fix Bugs

Look through the GitHub issues for bugs. Anything tagged with "bug" is open to whoever wants to implement it.

Implement Features

Look through the GitHub issues for features. Anything tagged with "enhancement" and "please-help" is open to whoever wants to implement it.

Please do not combine multiple feature enhancements into a single pull request.

Write Documentation

The Clinical Knowledge Graph could always use more documentation, whether as part of the official docs, in doc-strings, or even on the web in blog posts, articles, and such.

If you want to review your changes on the documentation locally, you can do:

This will compile the documentation, open it in your browser and start watching the files for changes, recompiling as you save.

Submit Feedback

The best way to send feedback is to file an issue at <https://github.com/MannLabs/CKG/issues>.

If you are proposing a feature:

- Explain in detail how it would work.
- Keep the scope as narrow as possible, to make it easier to implement.
- Remember that this is a volunteer-driven project, and that contributions are welcome :)

9.3.2 Setting Up the Code for Local Development

Here's how to set up CKG for local development.

1. Fork the CKG repo on GitHub.
2. Clone your fork locally:
3. Install your local copy into a virtualenv. Assuming you have virtualenvwrapper installed, this is how you set up your fork for local development:

FINISH THIS PART!!!!!!

4. Create a branch for local development:

Now you can make your changes locally.

5. When you're done making changes, check that your changes pass
6. Commit your changes and push your branch to GitHub:
7. Submit a pull request through the GitHub website.

9.3.3 Contributor Guidelines

Pull Request Guidelines

Before you submit a pull request, check that it meets these guidelines:

1. If the pull request adds functionality, the docs should be updated. Put your new functionality into a function with a docstring, and describe it.
2. The pull request should work for Python 3.5, 3.6 and 3.7.

Coding Standards

- PEP8
- Functions over classes except in tests
- Quotes via <http://stackoverflow.com/a/56190/5549>
 - Use double quotes around strings that are used for interpolation or that are natural language messages
 - Use single quotes for small symbol-like strings (but break the rules if the strings contain quotes)
 - Use triple double quotes for docstrings and raw string literals for regular expressions even if they aren't needed.
 - Example:

```
LIGHT_MESSAGES = {
    'English': "There are %(number_of_lights)s lights.",
    'Pirate': "Arr! Thar be %(number_of_lights)s lights."
}
def lights_message(language, number_of_lights):
    """Return a language-appropriate string reporting the light count."""
    return LIGHT_MESSAGES[language] % locals()
def is_pirate(message):
    """Return True if the given message sounds piratical."""
    return re.search(r"(?i)(arr|avast|yohoho)!", message) is not None
```

- Write new code in Python 3.

9.3.4 Core Committer Guide

Vision and Scope

Core committers, use this section to:

- Guide your instinct and decisions as a core committer
- Limit the codebase from growing infinitely

Command-Line and API Accessible

- Provides command-line utilities that launch a dash app to browse projects, statistics and others, create new users, and import and load data into the database.
- Extremely easy to use without having to think too hard
- Flexible for more complex use via optional arguments

Extensible

Being extendable by people with different ideas.

- Entirely function-based
- Aim for statelessness
- Lets anyone write more opinionated tools

Freedom for CKG users to build and extend.

- Community-based project, all contributions to improve and/or extend the code are welcome.

Inclusive

- Cross-platform support.
- Fixing Windows bugs even if it's a pain, to allow for use by the entire community.

Process: Pull Requests

If a pull request is untriaged:

- Look at the roadmap
- Set it for the milestone where it makes the most sense
- Add it to the roadmap

How to prioritize pull requests, from most to least important:

- Fixes for broken code. Broken means broken on any supported platform or Python version.
- Features.
- Bug fixes.

- Major edits to docs.
- Extra tests to cover corner cases.
- Minor edits to docs.

Ensure that each pull request meets all requirements in [checklist](#).

Process: Issues

If an issue is a bug that needs an urgent fix, mark it for the next patch release. Then either fix it or mark as please-help.

For other issues: encourage friendly discussion, moderate debate, offer your thoughts.

New features require a +1 from 2 other core committers (besides yourself).

Process: Pull Request merging and HISTORY.md maintenance

If you merge a pull request, you're responsible for updating AUTHORS.rst and HISTORY.rst

When you're processing the first change after a release, create boilerplate following the existing pattern:

```
## x.y.z (Development)

The goals of this release are TODO: release summary of features

Features:

* Feature description, thanks to [@contributor] (https://github.com/contributor) (#PR).

Bug Fixes:

* Bug fix description, thanks to [@contributor] (https://github.com/contributor) (#PR).

Other changes:

* Description of the change, thanks to [@contributor] (https://github.com/contributor) ↵
  (#PR).
```

Process: Accepting New Features Pull Requests

- Run the feature to generate the output.
- Attempt to include it in the standard pipeline and run an example project dataset.
- Merge the feature in.
- Update the history file.

note: Adding features doesn't give authors credit.

Process: Your own code changes

All code changes, regardless of who does them, need to be reviewed and merged by someone else. This rule applies to all the core committers.

Exceptions:

- Minor corrections and fixes to pull requests submitted by others.
- While making a formal release, the release manager can make necessary, appropriate changes.
- Small documentation changes that reinforce existing subject matter. Most commonly being, but not limited to spelling and grammar corrections.

Responsibilities

- Ensure cross-platform compatibility for every change that's accepted. Windows, Mac, Debian & Ubuntu Linux.
- Ensure that code that goes into core meets all requirements in this checklist: <https://gist.github.com/audreyr/4feef90445b9680475f2>
- Create issues for any major changes and enhancements that you wish to make. Discuss things transparently and get community feedback.
- Keep feature versions as small as possible, preferably one new feature per version.
- Be welcoming to newcomers and encourage diverse new contributors from all backgrounds. Look at *Code of Conduct* :ref:code-of-conduct.

9.4 History

9.4.1 0.1.0 (2019-12-10)

- First release on GitHub.

9.5 Code of Conduct

Everyone interacting in the Clinical Knowledge Graph codebases, issue trackers, chat rooms, and mailing lists is expected to follow the [PyPA Code of Conduct](#).

**CHAPTER
TEN**

INDEX

- genindex
- modindex
- search

PYTHON MODULE INDEX

a

analytics_core.analytics.analytics, ??
analytics_core.analytics.wgcnaAnalysis, ??
analytics_core.analytics_factory, ??
analytics_core.R_wrapper, ??
analytics_core.utils, ??
analytics_core.viz.color_list, ??
analytics_core.viz.Dendrogram, ??
analytics_core.viz.viz, ??
analytics_core.viz.wgcnaFigures, ??

g

graphdb_builder.builder.builder, ??
graphdb_builder.builder.create_user, ??
graphdb_builder.builder.importer, ??
graphdb_builder.builder.loader, ??
graphdb_builder.builder_utils, ??
graphdb_builder.databases.databases_controller, ??
graphdb_builder.databases.parsers.cancerGenomeInterpreterParser, ??
graphdb_builder.databases.parsers.corumParser, ??
graphdb_builder.databases.parsers.disgenetParser, ??
graphdb_builder.databases.parsers.drugBankParser, ??
graphdb_builder.databases.parsers.drugGeInteractionDBParser, ??
graphdb_builder.databases.parsers.exposomeParser, ??
graphdb_builder.databases.parsers.foodbParser, ??
graphdb_builder.databases.parsers.goaParser, ??
graphdb_builder.databases.parsers.gwasCatalogParser, ??
graphdb_builder.databases.parsers.hgncParser, ??
graphdb_builder.databases.parsers.hmdbParser, ??
graphdb_builder.databases.parsers.hpaParser, ??
graphdb_builder.databases.parsers.intactParser, ??
graphdb_builder.databases.parsers.jensenlabParser, ??
graphdb_builder.databases.parsers.mutationDsParser, ??
graphdb_builder.databases.parsers.oncokbParser, ??
graphdb_builder.databases.parsers.pathwayCommonsParser, ??
graphdb_builder.databases.parsers.pfamParser, ??
graphdb_builder.databases.parsers.pspParser, ??
graphdb_builder.databases.parsers.reactomeParser, ??
graphdb_builder.databases.parsers.refseqParser, ??
graphdb_builder.databases.parsers.siderParser, ??
graphdb_builder.databases.parsers.smpdbParser, ??
graphdb_builder.databases.parsers.stringParser, ??
graphdb_builder.databases.parsers.textminingParser, ??
graphdb_builder.databases.parsers.uniprotParser, ??
graphdb_builder.experiments.experiments_controller, ??
graphdb_builder.experiments.parsers.clinicalParser, ??
graphdb_builder.experiments.parsers.proteomicsParser, ??
graphdb_builder.experiments.parsers.wesParser, ??
graphdb_builder.mapping, ??
graphdb_builder.ontologies.ontologies_controller, ??
graphdb_builder.ontologies.parsers.icdParser, ??

```
??  
graphdb_builder.ontologies.parsers.oboParser,  
??  
graphdb_builder.ontologies.parsers.reflectParser,  
??  
graphdb_builder.ontologies.parsers.snomedParser,  
??  
graphdb_builder.users.users_controller,  
??  
graphdb_connector.connector, ??  
graphdb_connector.query_utils, ??
```

n

```
notebooks.development.vis, ??
```

r

```
report_manager.apps.dataUpload, ??  
report_manager.apps.homepageStats, ??  
report_manager.apps.imports, ??  
report_manager.apps.initialApp, ??  
report_manager.apps.projectCreation, ??  
report_manager.dataset, ??  
report_manager.knowledge, ??  
report_manager.project, ??  
report_manager.report, ??  
report_manager.user, ??  
report_manager.utils, ??  
report_manager.worker, ??
```