INSTRUCTION FOR PROTEIN-PROTEIN COMPLEXES QUALITY ASSESSMENT USING GRAPH NEURAL NETWORKS

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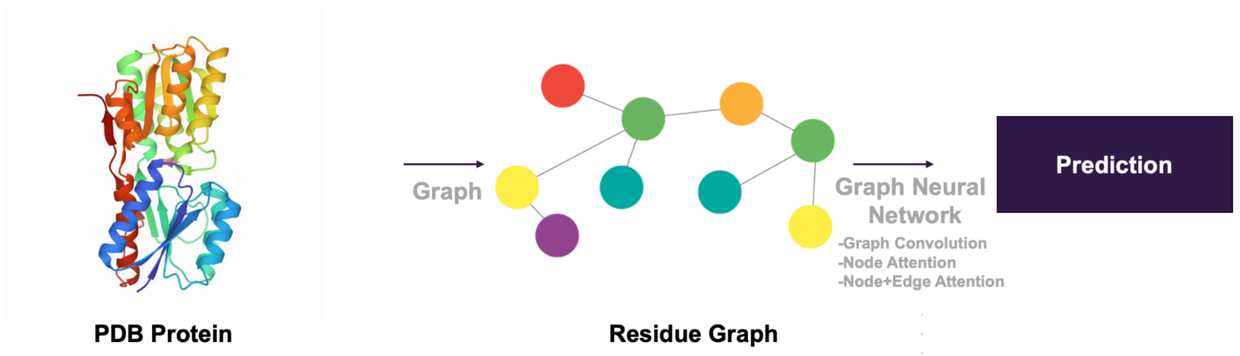


I - INITIAL SETUP :

Step 1: Fork and clone the repository

- **Option 1 (recommended) :**
    - 1. Fork repository from: https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes
    - 2. Clone repository from your Github on the cluster :

```
git clone  https://github.com/<YOUR_USER_NAME>/Graph_Neural_Net_Protein_Scoring.git
```

- **Option 2 (not recommended):**

```
scp -r <YOUR_CLUSTER_NAME>@<CLUSTER_IP>:/bgfs01/insite/yanis.tazi/Scoring_Project/
<YOUR_GRAPH_FOLDER/>
```

Step 2 : Create a dedicated environment compatible with the cluster

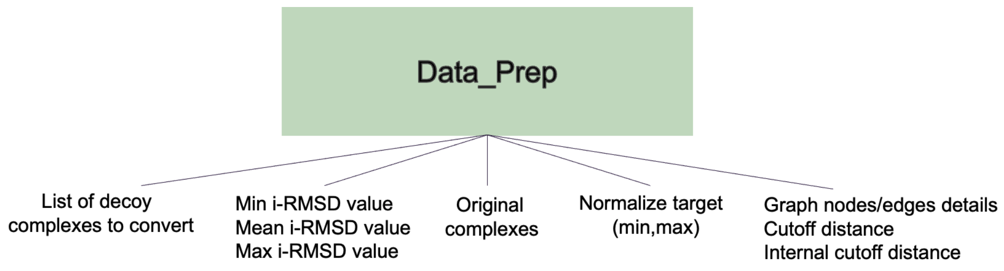
(after step 1 , you should be able to find environment_graph_predictions.yml)

```
conda env create --name <YOUR_ENV_NAME> --file=environment_graph_predictions.yml
```

Step 3 : Activate the dedicated environment

```
conda activate <YOUR_ENV_NAME>
```

II - DATA PREPARATION : FROM PDB FILES TO RESIDUE GRAPHS

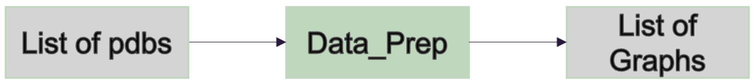


3 Steps process :

1.create_dict_selected_pdbs():
create a dictionary with the selected pdb files that follow the above criteria and their corresponding i-RMSD .
Example : {'1JTD_it1_complex_329.pdb': 14.98, '1JTD_it1_complex_359.pdb': 11.385}

2.prepare_pdb_selected_data(): Prepare pdb files and corresponding output (normalized)

3.prepare_hdf5_graphs(): *Create the hdf5 graphs corresponding to the inputs*



Step 1 *(Optional)* : Get the complete DB5 docking dataset (~600K pdb files)

- **Option 1 (recommended) :** https://data.sbgrid.org/dataset/131/

```
rsync -av rsync://data.sbgrid.org/10.15785/SBGRID/131
```

- **Option 2 (not recommended) :**

  Make a copy from my directory to your new pdb data folder

```
cp -r /bgfs01/insite02/yanis.tazi/data/graph_project_data/131/
<YOUR_INITIAL_PDB_DATA_FOLDER>/
```

Step 2 *(Optional)* : Residue Graph Preparation from pdb files :

Fully Automated data preparation pipeline that creates balanced graph datasets from PDB protein complexes and decoys files. It is a 3 step process that:

1. creates a balanced dataset of pdb files based on the [min,mean,max] i-RMSD values provided, and on the minimum number of decoys per stage.
2. prepares a folder with the selected pdb files and their corresponding i-RMSD and input complexes if provided.
3. creates the residue graphs with the nodes/edges based on the nodes cutoff distance , edges internal cutoff distance, nodes and edges features provided , the normalized i-RMSD and can also add input complexes to the graphs

Tutorial :
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Tutorials/Data_Prep_Tutorial.ipynb

OR

Also available in : Graph_Project/Tutorial/Data_Prep_Tutorial.ipynb

Data preparation functions with detailed explanations :
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Model_Functions/Data_Preparation.py

OR

Also available in : Graph_Project/Model_Functions/Data_Preparation.py

Additional Information :

The user can directly make a copy of all the data from pdb files to .hdf5 graphs and their replicates.
The copy will of course be dependent on the parameters that were chosen to create the graphs to include i-RMSD (min,mean,max), nodes/edges features and node cutoff distance as well as edge internal cutoff distance,...

```
cp -r /bgfs01/insite02/yanis.tazi/data/graph_project_data/
<YOUR_INITIAL_DATA_FOLDER>/
```

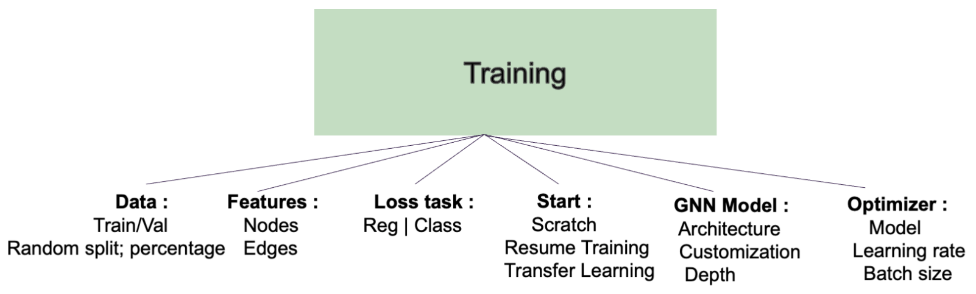
Dataset balanced around 10 A : (you will get multiple copies of the graph so that you can use them for gridsearch without interference of reading hdf5 files)

```
cp -r /bgfs01/insite02/yanis.tazi/data/graph_project_data/hdf5_replicates/
<YOUR_HDF5_target_10_replicates>/
```

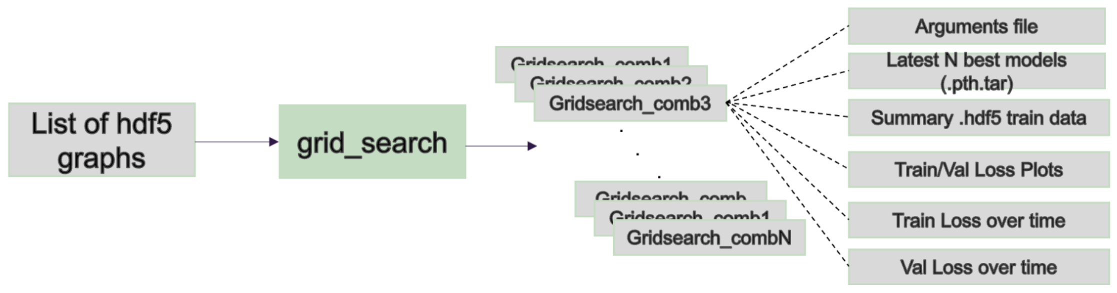
Dataset balanced around 5 A : (you will get multiple copies of the graph so that you can use them for gridsearch without interference of reading hdf5 files)

```
cp -r /bgfs01/insite02/yanis.tazi/data/graph_project_data/hdf5_target_5_replicates/
<YOUR_HDF5_target_5_replicates>/
```

III - TRAINING OF THE GRAPH NEURAL NETWORK



grid_search(): performs training for all possible parameter combinations. It creates one folder per combinations and help in the optimal model selection by evaluating validation loss.



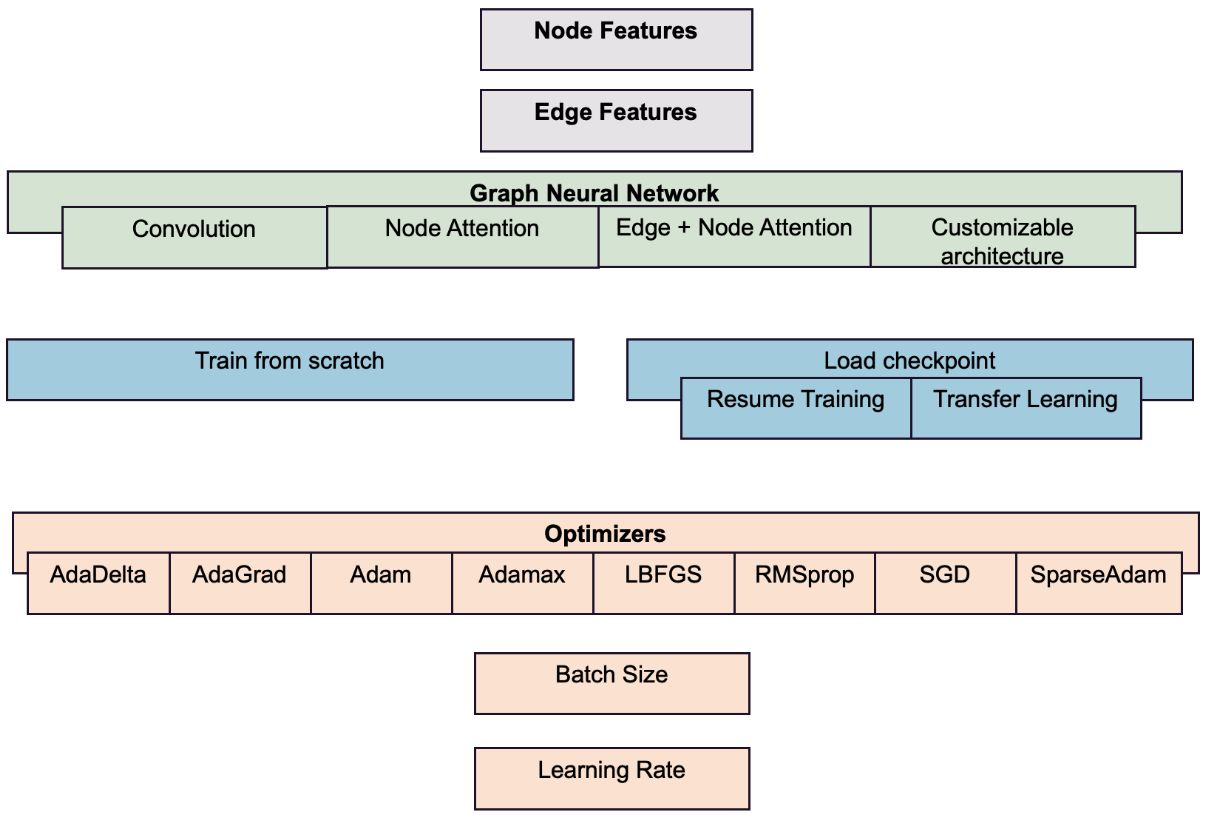
Tutorial :
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Tutorials/Model_Training_Tutorial.ipynb

OR

Also available in : Graph_Project/Tutorial/Model_Training_Tutorial.ipynb

Follow Training tutorial that performs gridsearch and optimal search of parameter combinations. Users can train the model from scratch , load a preexisting trained model to resume training or perform transfer learning, they can choose among different existing/new customized model/architectures (details in the next section), chose the edges/nodes features, optimizers, learning rates, …

The gridsearch will also save the train/val loss plots over time , the N best saved models, the train/val loss values over time, provide a file with all the arguments to keep track of the parameters used and a summary of the training data over time with the predicted values every <e> epochs where e is also a hyperparameter.



For details about all the hyperparameters and the gridsearch, please consult the documentation: (you will find all the information and detailed explanation there, so please read it)
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Model_Functions/Model_Training.py

OR

Also available in : Graph_Project/Model_Functions/Model_Training.py

Customizable architecture :

Users can either use one of the preexisting architecture or create a new class with their own architecture that they can just import before training the model,

1. Chose from one of the existing architectures : GINet, EGAT_Net, FoutNet available in https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/tree/main/DeepRank-GNN/deeprank_gnn/{ginet.py,foutnet.py,EGAT_GNN.py}

OR

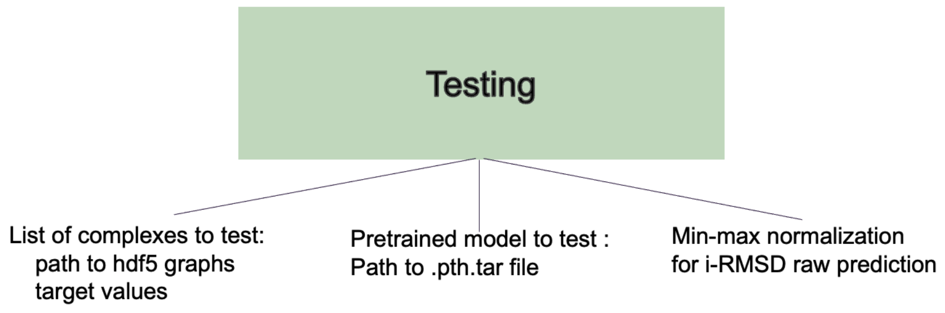
Also available in :
Graph_Project/DeepRank-GNN/deeprank_gnn/{ginet.py,foutnet.py,EGAT_GNN.py}

2. Create a customized architecture such as the 2 examples provided :
   (DO NOT FORGET TO IMPORT THEM)
   GINet_deeper and GINet_deeper_attention_fc available in
   https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/tree/main/DeepRank-GNN/deeprank_gnn/ginet.py

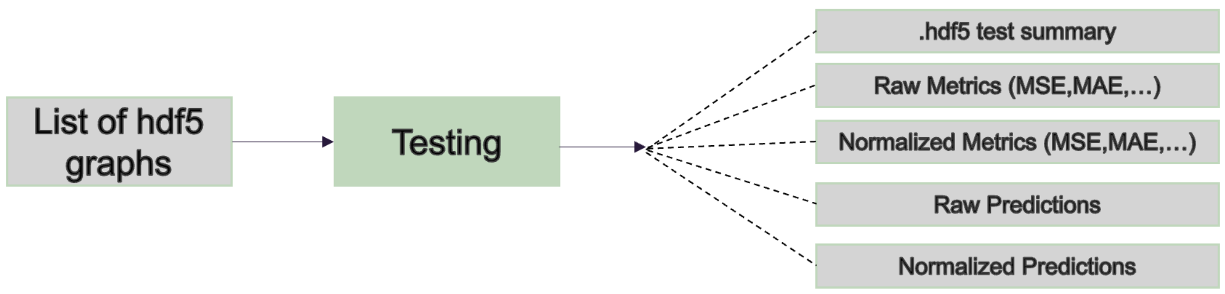
   OR

   Also available in : Graph_Project/DeepRank-GNN/deeprank_gnn/ginet.py

IV - TESTING



model_testing(): test any trained model and return summary , predictions and metrics



Tutorial :
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Tutorials/Model_Testing_Tutorial.ipynb

OR

Also available in : Graph_Project/Tutorial/Model_Testing_Tutorial.ipynb

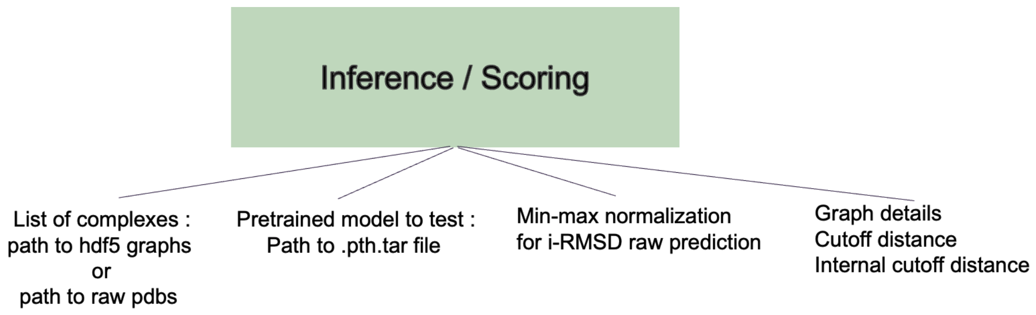
Follow Testing tutorial (part 1) that tests the models on new graphs data. You just need to provide the path to the checkpoint of the model you want to test , specify the architecture that was used , specify whether or not you want the raw predicted values by giving the min-max normalization values and provide the path to the test .hdf5 data. The model will then return a summary of the data (predictions and targets), lots of raw and normalized metric results (MAE,R^2, MSE, RMSE,...) , the raw and normalized predicted values.

For details about all the arguments, please consult the documentation:
(you will find all the information and detailed explanation there, so please read it)
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Model_Functions/Model_Testing_Predictions.py

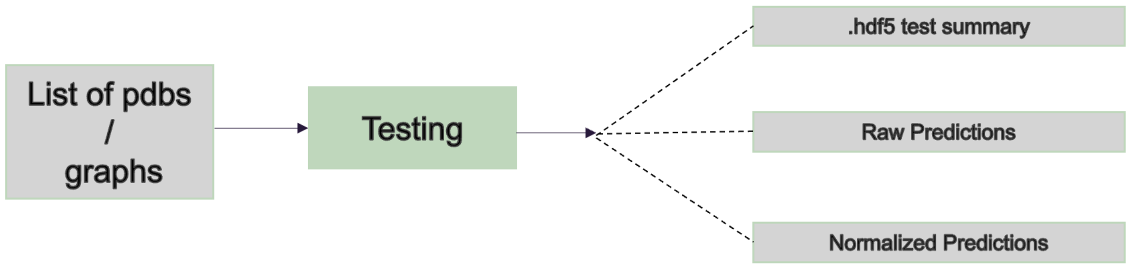
OR

Also available in : Graph_Project/Model_Functions/Model_Testing_Predictions.py

V - INFERENCE ON NEW PDB STRUCTURE


Inference / Scoring
List of complexes : path to hdf5 graphs or path to raw pdbs
Pretrained model to test : Path to .pth.tar file
Min-max normalization for i-RMSD raw prediction
Graph details
Cutoff distance
Internal cutoff distance

model_new_predictions(): it returns normalized and raw predicted i-RMSD values from the raw pdbs or the .hdf5 graphs



Follow Testing tutorial (part 2) that takes raw pdb files , converts them into graphs (or can take graphs directly) and predicts the i-RMSD. It returns the raw and normalized (if normalization is provided) predictions.

For details about all the arguments, please consult the documentation:
(you will find all the information and detailed explanation there, so please read it)
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Model_Functions/Model_Testing_Predictions.py

OR

Also available in : Graph_Project/Model_Functions/Model_Testing_Predictions.py

VI - INITIAL RESULTS

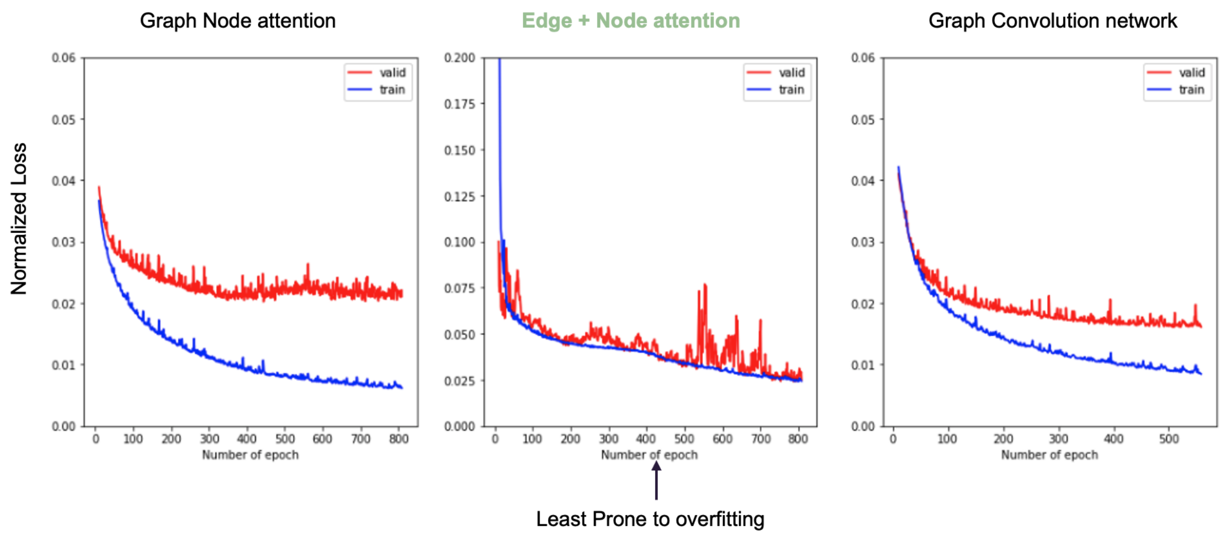
The initial results were promising and we demonstrated that a model leveraging edge and node information with attention mechanism on a dataset that has been provided independently (11K pdb files) can reach a precision of 2A.

Results Analysis available :
https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/Graph_Project/Results_Analysis.ipynb

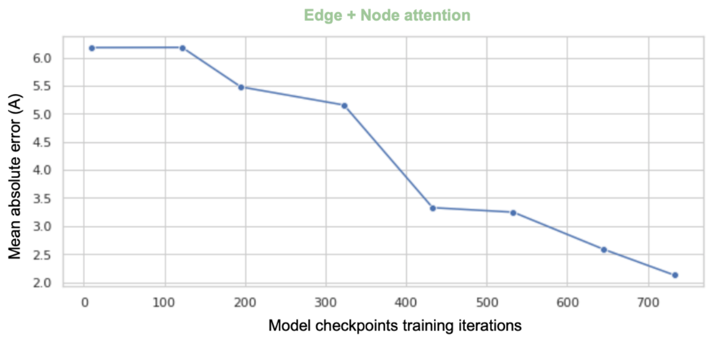
OR

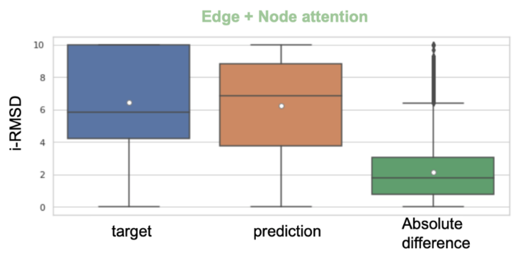
Also available in : Graph_Project/Results_Analysis.ipynb

Comparison of three architectures



Results on Testing set ~ 11K pdb files
(Training+validation on 15K pdb files from 52 complexes)





VII - SLURM JOBS ON CLUSTER

To run a gridsearch, it will be easier to launch the jobs directly on the cluster in order to have access to more computational power (more cores and processes, multiple GPUs , more memory,...) . Therefore, we provide an example slurm job for each part of the pipeline (preparation of the data, training/gridsearch and testing) with its corresponding python function for :

1. **Data Preparation**

   https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/tree/main/example_slurm_jobs_cluster/prepare_data

   OR

   example_slurm_jobs_cluster/prepare_data/

You can modify the slurm job through the .py file to update specific arguments of the customizable data preparation pipeline. Similarly, you can modify the .sh file dedicated to technical and scientific computing on the cluster.

Launch the job :

```
sbatch prepare_hdf5_data-slurm.sh
```

2. **Gridsearch training :**

   https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/tree/main/example_slurm_jobs_cluster/training_gridsearch_irmsd_5/

   OR

   example_slurm_jobs_cluster/training_gridsearch_irmsd_5/

You can modify the jobs based on the gridsearch's customizable parameters you are opting for. Similarly, you can modify the .sh file for more technical/scientific computing specifications.

Launch the job :

```
sbatch train_gridsearch-slurm.sh
```

3. **Testing on new data:**

   https://github.com/yanistazi/Graph_Neural_Net_Protein-Protein-Complexes/blob/main/example_slurm_jobs_cluster/Testing_model_slurms/

OR

example_slurm_jobs_cluster/Testing_model_slurms/

You can modify the jobs based on the model and the data you want to test.
Similarly, you can modify the .sh file for more technical/scientific computing specifications.
Launch the job:

```
sbatch Testing_models-slurm.sh
```

VIII - JUPYTER NOTEBOOK ON THE CLUSTER

1. Go on cluster:

```
ssh -i /Users/<USER_NAME>/.ssh/id_rsa <USER_NAME>@<CLUSTER_IP>
```

2. On Cluster terminal window (you can change arguments based on your needs):

```
srun -N 1 -n 1 -c 2 -p project --gres=gpu:1 --qos=maxjobs
--reservation=<RESERVATION_NAME> --pty /bin/bash -i
```

At this point , we also know the compute node name. `COMPUTENODE_NAME`

3. On Cluster terminal window:

```
cd /bgfs01/insite/<USER_NAME>
```

4. On Cluster terminal window:

```
conda activate <YOUR_ENV_NAME>
```

5. On Cluster terminal window make sure it is a unique port by initially running :
Optional (returns VALUE): `echo $((8000+$(id -u)))`

```
jupyter notebook --ip=0.0.0.0 --no-browser --port=<VALUE>
```

6. Open a new terminal (local):

```
ssh -i /Users/<USER_NAME>/.ssh/id_rsa -NL <VALUE>:<COMPUTENODE_NAME>:<VALUE>
<USER_NAME>@<CLUSTER_IP>
```

7. On web browser :

Replace `COMPUTENODE_NAME` by localhost: http://localhost:<VALUE>/?token=<TOKEN>