ELIX

Federated Learning

Report v2.1

March 17, 2021

Report v2.1

March 17, 2021

Federated Learning

In this joined project between Elix Inc. and Kyoto University, we implement a small communication module called "Mila" for federated learning, following the implementations of NVIDIA Clara (as close as possible). To validate the results, we analyze the behavior of various datasets and architectures during the distributed learning process.

Contents

Theoretical Background

1.1 Federated Learning

Federated learning is a machine learning paradigm focused on distributed training across decentralized machines. As opposed to classic approaches where all the data is in one central location, during federated learning, the data is spread across multiple servers or edge devices. Each device (hereafter called "client") runs training for a number of epochs and sends the weights/checkpoints to a central location (hereafter called "server") which aggregates the information from all clients. The new aggregate model would then be sent to all participating clients, which then repeat the process using the latest model.

This way, each client's data remains private, and is not shared with any of the other clients, nor the server. For companies where data is a sensitive matter (as is the case for big pharmaceutical companies), this is a very attractive approach.

Additional details can be found in the original paper[42].

1.2 Datasets

We experiment with a large number of datasets, however, they can be grouped into 3 categories:

- Toxicity datasets
- ADME datasets (absorption, distribution, metabolism, and excretion)
- Protein-Ligand Affinity dataset

An overview of all datasets used can be visualized in Table 1.1.

The Tox21 dataset

The Tox21 dataset contains 7831 entries (SMILES[70] strings) for 12 different toxicological experiments (binary labels) representing activity (active/inactive). It should be noted that the dataset contains missing values, which we ignore in the loss function and during back-propagation. The dataset is very imbalanced, as the number of positive samples range between 186 and 942, depending on the target.

The AMES dataset

We received 3 different versions of the AMES dataset, however, the data structure is similar for all of them. The input format is a SMILES string and the output is a single, binary target.

For the federated learning experiments, we combined the "benchmark" and the "NTP PubChem" subsets, as all of the duplicates, except for one entry, had matching labels. The single entry with a different label was removed ("O=c1c2ccccc2c(=O)c2c1ccc1c2[nH]c2c3c(=O)c4ccccc4c(=O)c3c3[nH]c4c(ccc5c(=O)c6ccccc6c(=O)c54)c3c12"). The S9 Minus dataset was too different from the other 2, and was not merged into the final set.

ADME datasets

The ADME datasets were delivered as a combination of SDF files (structural information) and an Excel file (labels and target values). The excel file also described the molecules in InChI format, but upon further inspection, these did not always match the SDF entries when loaded with RdKit[34]. As a consequence, we matched the molecule IDs between the SDF files ("ID" property) and the excel files ("drumap_id" or "no_salt_drumap_id"), and entries outside the join.

Some of the datasets contain continuous values (regression) while some of them are reduced to binary labels (classification) either directly in the dataset, or manually by us. The final number of entries and the type of task for each dataset can be seen in Table 1.1.

For most datasets, we used the "value", or a numeric format of the "value.class" column directly, but there are a few exceptions. For the intrinsic clearance (CLint) dataset, the "value", "lower_value", and "upper_value" columns were combined into a single target. For the fraction excreted unchanged in urine (fe_human), the continuous "value" column was binarized using a threshold of 0.3, and 0.7 (for federated learning, we used the 0.7 threshold). For the P-gp Net Efflux Ratio (Ner LLC), the "value.class" column was decomposed into 3 classes (multi-class classification).

ChEMBL assays dataset

The Protein-Ligand Affinity dataset is a subset of the ChEMBL dataset and was delivered as an relational database (SQL) wrapped around an command-line interface (CLI). The CLI allows for exports of entries based on protein identifiers, affinity thresholds and metric types, however, we wanted to explore the dataset in more detail and select proteins based on certain criteria, not identifiers. Therefore, we operated directly on the SQL dataset, so updates to the CLI tool should not influence the structure of these datasets.

The input structures are pairs of protein (amino-acid sequences) and ligands (SMILES strings), and the goal is to compute the affinity between them (generally, a binary values and a classification task).

Name	Category	Samples	Task
Tox21	Toxicity	7831	Classification
AMES (Final)	Toxicity	7441	Classification
AMES (Benchmark)*	Toxicity	6512	Classification
AMES (NTP PubChem)*	Toxicity	7403	Classification
AMES (S9 Minus)*	Toxicity	2876	Classification
Clint Human	ADME	5216	Regression
Fe Human	ADME	340	Classification
Fu Brain	ADME	580	Regression
Fup Human	ADME	2559	Regression
Fup Rat	ADME	539	Regression
Ner LLC Human	ADME	445	Classification
PappCaco2	ADME	4294	Both
Papp LLC Human	ADME	461	Regression
Rb Rat	ADME	162	Regression
Solubility	ADME	514	Classification
ChEMBL Assays (v1)	Binding Affinity	574583	Classification
ChEMBL Assays (v2)*	Binding Affinity	947586	Both

Table 1.1: Datasets used for experiments (subsets marked with [*] were not analyzed through distributed learning)

Initially, we export a subset of this dataset where:

- the "valid" column was equal to 1
- the metric was one of "IC50", "Ki", "EC50", or "Kd"
- and the protein had at least 500 positive samples (where "positive" was classified as a value of 100 nM or less)

For each protein individually, we used the median value when duplicate ligand measures were encountered. This setup resulted in a dataset, referred to as version 1 (v1), containing 574,583 entries spread across 272 unique protein sequences, 390,467 unique ligands (represented as SMILES), and a roughly equal distribution of positive (292,144) and negative (282,439) samples.
After feedback, we created another export with a few slight variations:

- we used the pchembl_value ($-\log_{10}(x)$) instead of the value (affinity) and metric types ("IC50", "Ki", "EC50", or "Kd") when filtering
- the protein filtering was set to a minimum of 100 entries (positive or negative)

Duplicate entries were similarly averaged using the median value. This resulted in a much larger dataset (referred to as version 2, or v2), containing 947,586 entries spread across 1413 unique protein sequences, 583,624 unique ligands. Furthermore, we experimented with 3 different thresholds along with the raw (regression) values. The 3 thresholds suggested were 100 nM (pchembl=7), 1 uM (pchembl=6), and 10 um (pchembl=5), which obviously result in different distributions. The number of positive entries for the 3 splits were 404321, 645186, and 852925 respectively, which in turn meant 543265, 302400, and 94661 negative entries respectively.

The queries used to retrieve the subsets were as follows

```
# SQL query used to extract version 1

SELECT target_accession, target_sequence, standard_type, standard_value, smiles
FROM activities
WHERE standard_type IN ("IC50", "Ki", "EC50", "Kd")
AND valid = 1
AND target_accession IN (
    SELECT target_accession FROM activities
    WHERE valid = 1
    AND standard_value <= 100
    AND standard_type IN ("IC50", "Ki", "EC50", "Kd")
    GROUP BY target_accession
    HAVING COUNT(*) >= 500
)

# SQL query used to extract version 2 (thresholds were applied programmatically)

SELECT target_accession, target_sequence, standard_type, pchembl_value, smiles
FROM activities
WHERE standard_type IN ("IC50", "Ki", "EC50", "Kd")
AND valid = 1
AND target_accession IN (
    SELECT target_accession FROM activities
    WHERE valid = 1
    AND standard_type IN ("IC50", "Ki", "EC50", "Kd")
    GROUP BY target_accession
    HAVING COUNT(*) >= 100
)
```

One import matter to point out is the distribution of the metrics used in the dataset (column "standard_type"). The number of entries in the dataset for all metric types is listed in Table 1.2.

Metric	Samples
Potency	1026983
IC50	770361
Ki	379869
EC50	109957
AC50	58336
Kd	38456
XC50	5
pIC50	1

Table 1.2: Metric distribution in the ChEMBL dataset

We notice that among the metrics we focused, IC50 and Ki values are abundant, however, there is a "Potency" metric which contains almost 50% of the whole dataset. The "Potency" is generally an inexact metric used when we do not know what the actual measurement is. This can be problematic, because some metrics should be minimized while other metrics should be maximized. Furthermore, looking at the the distribution of samples, we clearly see that entries measured in "Potency" contain much larger entries, most of which would be classified as negative (although, we stress, this metric is ambiguous). As a consequence, we decided not to include these values in our subsets.

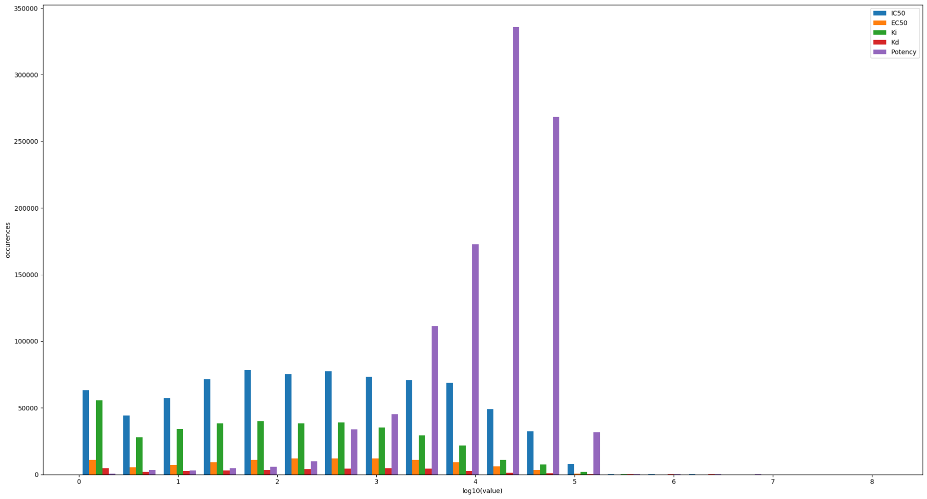


Figure 1.1: Distribution of each metric type

Finally, we should note that these datasets are large and the data formats are big and complex (ie: long amino-acid chains or molecular graph structures). It can take a long time to train a single model on these datasets, and for federated learning, we have to train these models hundreds of times over thousands of epochs. As we only recently started experimenting with version 2, all federated learning experiments were performed on version 1 of the dataset.

Additional Datasets

While no other datasets were used for federated learning experiments, we did test our models and optimization tools on a number of other publicly available ADME-Tox datasets. These datasets were accessed through the Therapeutics Data Commons (TDC) project, which accesses data from the Harward Dataverse.

A list of all datasets we experimented with and their references can be found in Table 1.3. Some of these datasets might be identical to the ones listed under the

"ADME datasets" section. it should also be noted that the Hydration Free Energy dataset (FreeSolv) cannot be used for commercial purposes.

Name	Category	References
Bioavailability	Absorption	[41]
Cell Effective Permeability (Caco-2)	Absorption	[67]
Human Intestinal Absorption	Absorption	[26]
Hydration Free Energy	Absorption	[45]
Lipophilicity	Absorption	[74]
P-glycoprotein Inhibition	Absorption	[9]
Solubility	Absorption	[48]
Blood-Brain Barrier	Distribution	[74]
Plasma Protein Binding Rate	Distribution	[71]
Volumn of Distribution at steady state	Distribution	[39]
CYP P450 1A2 Inhibition	Metabolism	[16]
CYP P450 2C19 Inhibition	Metabolism	[16]
CYP P450 2C9 Inhibition	Metabolism	[16]
CYP P450 2D6 Inhibition	Metabolism	[16]
CYP P450 3A4 Inhibition	Metabolism	[16]
CYP2C9 Substrate	Metabolism	[11]
CYP2D6 Substrate	Metabolism	[11]
CYP3A4 Substrate	Metabolism	[11]
Clearance	Excretion	[15]
Half Life	Excretion	[49]
Acute Toxicity (LD50)	Toxicity	[77]
Carcinogens	Toxicity	[33]
ClinTox	Toxicity	[20]
Drug Induced Liver Injury	Toxicity	[76]
hERG Blockers	Toxicity	[68]
Skin Reaction	Toxicity	[3]
ToxCast	Toxicity	[55]

Table 1.3: ADME-Tox datasets we experimented with.

1.3 Featurization

Molecules are complex structures and they need to be preprocessed and transformed to a machine learning readable format. This process is often referred to as featurization. Different models will support different featurized formats, however, we mainly focus on graph-based models in this project.

We generally use a graph featurization to encode ligands or small-molecules, however, we experimented with circular (Morgan[46]) fingerprints as well. Some of our architectures combine atom-level features with global (molecule) level features. For these features we generally used property descriptor fingerprints computed either with RdKit[34] or Mordred[53].

Amino-acid sequences have been featurized either through one-hot encoding or using an n-gram, bag-of-words approach. We focus on the models in the next section, but to understand the whole pipeline, we briefly introduce the featurizers we employed.

1.3.1 Graph Representation

A molecule can be thought of as an undirected graph, where each atom is a node/vertex, and each bond is an edge. Each node in turn can contain several atom related features like: a one-hot encoding of the chemical symbol or the atomic number, a similar encoding of the hybridization, the number of neighbours the atom has (ie: the degree of the node), or the valence. These features would be concatenated into a single array (similar to a fingerprint, for individual atoms) and fed as a matrix into a graph convolutional network (where each row is a separate atom, and each column an atom feature).

Additionally, an adjacency matrix which marks the connections (ie: bonds) between the atoms is also fed to the model. This matrix is symmetric, with both row and columns representing the index of each atom in the feature matrix, and the value of a cell being either "1" if there is a bond between the 2 atoms or "0" otherwise.

In Figure 2.2, we show a possible feature representation of Aspirin. On the left hand-side we have the atom features. Each row represents an atom, and each column is a feature of that atom (for example, column 3 marks whether the atom is a Carbon, while column 5 marks if it is an a Oxygen atom). On the right hand-side we have the adjacency matrix which marks the bonds between these atoms. For example, we see that the second row atom (which is the core of the carboxyl group) has 3 neighbors (atoms positioned as 1, 3 and 4).

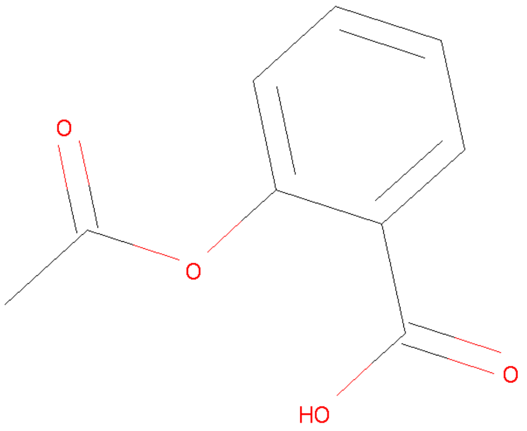
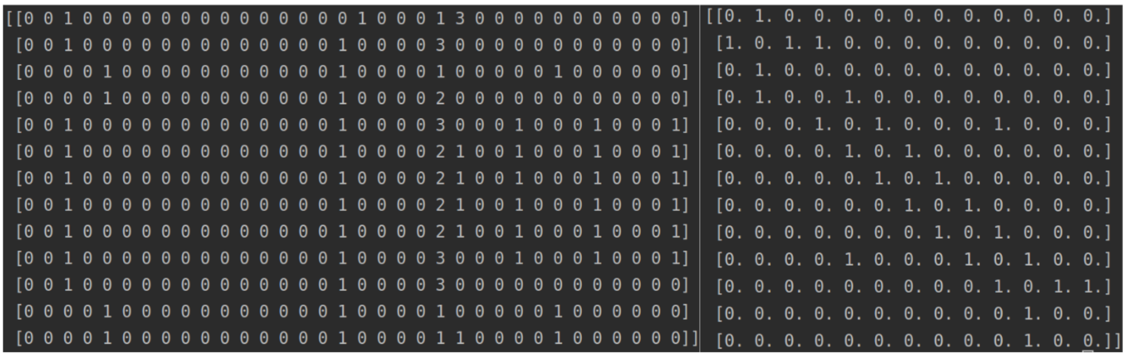


Figure 1.2: 2D structure of Aspirin



```
[[0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 1 3 0 0 0 0 0 0 0 0 0 0 0] [[0. 1. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 3 0 0 0 0 0 0 0 0 0 0 0 0]  [1. 0. 1. 1. 0. 0. 0. 0. 0. 0. 0. 0. 0.]
 [0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 1 0 0 0 0 0 1 0 0 0 0 0 0]  [0. 1. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.]
 [0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0 0]  [0. 1. 0. 0. 1. 0. 0. 0. 0. 0. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 3 0 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 1. 0. 1. 0. 0. 0. 1. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 2 1 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 0. 1. 0. 1. 0. 0. 0. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 2 1 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 0. 0. 1. 0. 1. 0. 0. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 2 1 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 0. 0. 0. 1. 0. 1. 0. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 2 1 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 0. 0. 0. 0. 1. 0. 1. 0. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 3 0 0 0 1 0 0 0 1 0 0 0 1]  [0. 0. 0. 0. 1. 0. 0. 0. 1. 0. 1. 0. 0.]
 [0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 3 0 0 0 0 0 0 0 0 0 0 0 0]  [0. 0. 0. 0. 0. 0. 0. 0. 0. 1. 0. 1. 1.]
 [0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 1 0 0 0 0 0 1 0 0 0 0 0 0]  [0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 1. 0. 0.]
 [0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 1 1 0 0 0 0 1 0 0 0 0 0 0]] [0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 1. 0. 0.]]
```

Figure 1.3: A graph representation of Aspirin. The feature matrix (left) encodes properties or descriptors (columns) for each individual atom (row), while the adjacency matrix (right) marks the connections (bonds) between the atoms.

1.3.2 Circular Fingerprints (Morgan)

Molecular fingerprints encode the structure of a compound as a series of binary digits (0 or 1), each of which represent the presence or absence of a particular substructure in the molecule. Circular fingerprints do this by considering substructures of atoms and their neighbours which are within a certain radius of the said atoms.

Morgan fingerprints[46] are similar to Extended-Connectivity Fingerprints (ECFPs)[57] in this sense. ECFPs however are a proprietary solution of Pipeline Pilot, and the hashing function is not publicly known. Morgan fingerprints on the other hand are implemented in RdKit[34], which is the software we used in generating them.

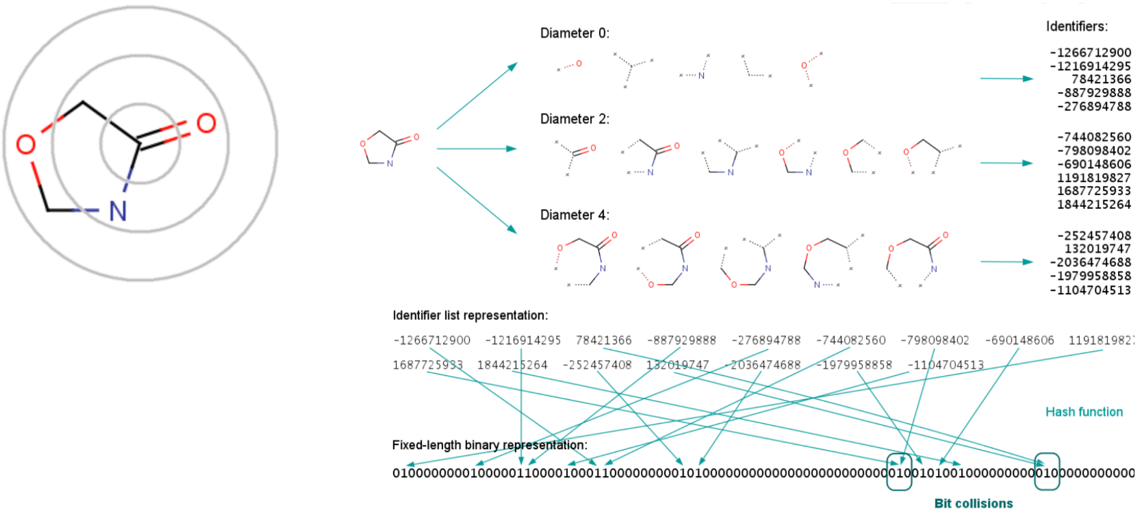


Figure 1.4: Circular Fingerprints. Substructures are created based on a preset radius and mapped to an identifier. A hash function is applied on top of the identifiers which map them to a certain position on the fingerprint vector. As the fingerprint size is fixed, collisions can occur (image source: chemaxon docs)

1.3.3 Property Descriptor Fingerprints

Similar to circular fingerprints, a list of properties of the given molecule can be computed an summarized in an array, which then can be easily fed to a model.

RdKit Descriptors

RdKit[34] provides implementations of many such properties. We concatenated 17 such of them to form our rdkit fingerprints:

- Descriptors.MolWt (the molecular weight)
- Descriptors.NumRadicalElectrons
- Descriptors.NumValenceElectrons
- rdMolDescriptors.CalcTPSA (the topological polar surface area (TPSA))
- MolSurf.LabuteASA (Labute's Approximate Surface Area[32])
- GraphDescriptors.BalabanJ (Balaban's J index[4])
- Lipinski.RingCount
- Lipinski.NumAliphaticRings
- Lipinski.NumSaturatedRings
- Lipinski.NumRotatableBonds
- Lipinski.NumHeteroatoms
- Lipinski.HeavyAtomCount
- Lipinski.NumHDonors[38]
- Lipinski.NumHAcceptors[38]
- Lipinski.NumAromaticRings
- Crippen.MolLogP (the partition coefficient)
- QED.qed (the quantitative estimate of drug-likeness[8])

Mordred Descriptors

We also experimented with Mordred Descriptors[53], which provides a list of 1826 molecular descriptors.

1.3.4 Sequence Featurizers

Amino-acid sequences are unlike small molecules represented as SMILES, and need different featurizers.

Tokenization

One approach is to use a one-hot encoding representation of each amino-acid, and concatenate these encodings into a matrix of shape (number of tokens, maximum sequence length). The number of tokens, of course, is equal to 21 (the number of distinct amino-acids we can have), and the maximum sequence length is the length of the longest amino-acid chain from the dataset. Shorter chains than the maximum entry are be 0-padded.

Bag-of-words Encoding

Bag-of-words approaches are generally applied to text data. Each sentence is split and the occurrence of each word is counted, thus a dictionary of all words present in the dataset is created. Although we are not dealing with words and sentences, our amino-acid sequences can be split by length. As an example, if we have a DNA sequence ATTGATTCG, we could extract all subsequences of length 6: ATTGAT, TTGATT, TGATTC, and GATTCG.

Normally, we would enumerate all possible substrings up to a certain length, count the number of times they occur, and use these counts to form a fingerprint. With DNA sequences, our vocabulary has a length of 4 (A, C, T, G). The unigram would also contain 4 options (A, C, T, G), but the bigram increases in size exponentially (AA, AC, AT, AG, CA, CC, CT, etc.), so there is a limit to the size of the substrings we are able to consider. For our vocabulary of 21 amino-acids, we went up to a length of 3, which resulted in a fingerprint of length 9723.

1.4 Models

As mentioned before, our work mainly focuses on graph-based models, however, certain datasets require additional strategies. For binding affinity prediction, we need to consider models which can handle sequence (amino-acid) information.

1.4.1 Graph Architectures

There are various graph-based architectures, but almost all of them rely on the base concept which we visualize in Figure 1.5.

As a first step, the input molecules are featurized and converted to a graph representation. These features are then past through a number of graph convolutional layers, which, in a sense, are very similar to classic convolutional layers where fixed size filters are applied in a sliding window fashion across the whole image, enabling the layer to learn features from neighboring pixels. Graph layers are doing the same thing, aggregating information from neighbouring nodes; the main difference is that they work on non-euclidean data formats. The graph layer is applied to each node (here atom), and the more layers are added, the further away information will be brought towards the central node (atom).

After a number of such layers are applied, generally, a graph pooling layer is used, which works very similar to a regular pooling layer, in that it summarizes and shrinks the feature space. These features are then flattened and passed through a shallow neural network.

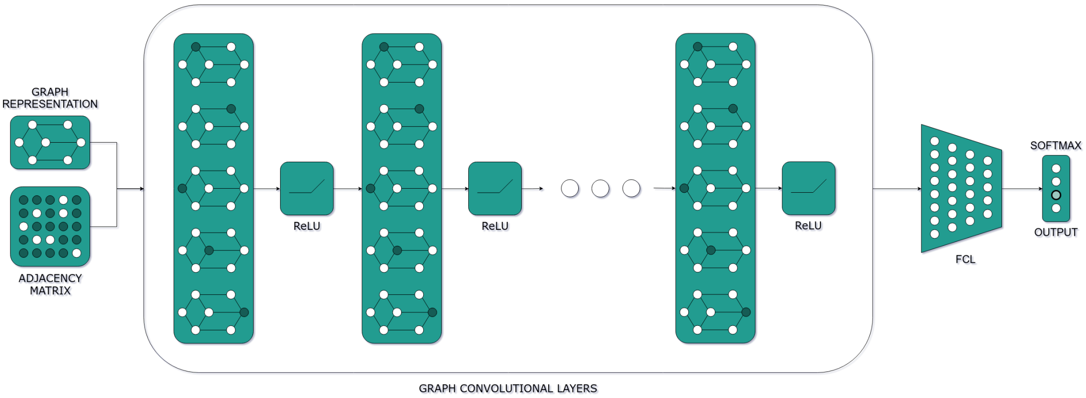


Figure 1.5: Graph convolutional networks aggregate information from neighbouring atoms. As more layers are added, further away information is brought towards the central node. In the end, the node features are downsized using a graph pooling layer, flattened, and passed through a final Multilayer Perceptron (MLP) block.

Different arhitectures perform the aggregation in different ways, which can be as simple as multiplying the input features with the set of training weights and the adjacency matrix. Going through the details of all available graph architectures is beyond the scope of this report, however, we refer the readers to Table 1.4, which lists all architectures we tried and their reference. As a note, our implementation is built upon Pytorch Geometric[19], which provides sparse implementations for many graph convolutional kernels.

Name	**Reference**
Classic Graph Network (Kipf & Welling)	[62]
Message Passing Network	[21]
Chebyshev Spectral Network	[13]
GraphSAGE Network	[22]
Weisfeiler-Leman Graph Network	[47]
Graph Isomorphism Network	[75]
ARMA Graph Network	[7]
Local Extremum Graph Network	[54]
GENeralized Graph Network	[35]
Cluster Graph Network	[12]
Feature-Steered Graph Netowrk	[65]
Graph Attention Network	[64]
Topology Adaptive Graph Network	[17]
Simple Graph Network	[72]
Triplet Message Passing Network (TrimNet)	[36]

Table 1.4: Graph Convolutional Networks we experimented with.

Our approach goes beyond classic graph convolutional networks which mainly just focus on atom features, and expect the graph convolutional operator to learn the global information from these lower level features. An overview of our architecture, which wraps most of the operators listed in Table 1.4, can be seen in Figure 1.6.

As an initial step, the input SMILES are converted using graph featurization and the generated atom features + adjacency matrix are then fed to a number of graph convolutional layers. For each layer, we can optionally append edge features to the atom features before passing them to the graph operator (listed in Table 1.4), then an optional residual layer[23], an optional batch normalization layer (we have support for BatchNorm[27], LayerNorm[63], and GraphNorm[10]), a Rectified Linear Unit activation[1] and a dropout[60] layer with configurable probability. The output of one layer acts as the input for the next one.

After the final layer is propagated through, 2 feature sets are generated; one using global max pooling (by taking the channel-wise maximum across the node dimension) and one using global add pooling (were node features are summed across the node dimension).

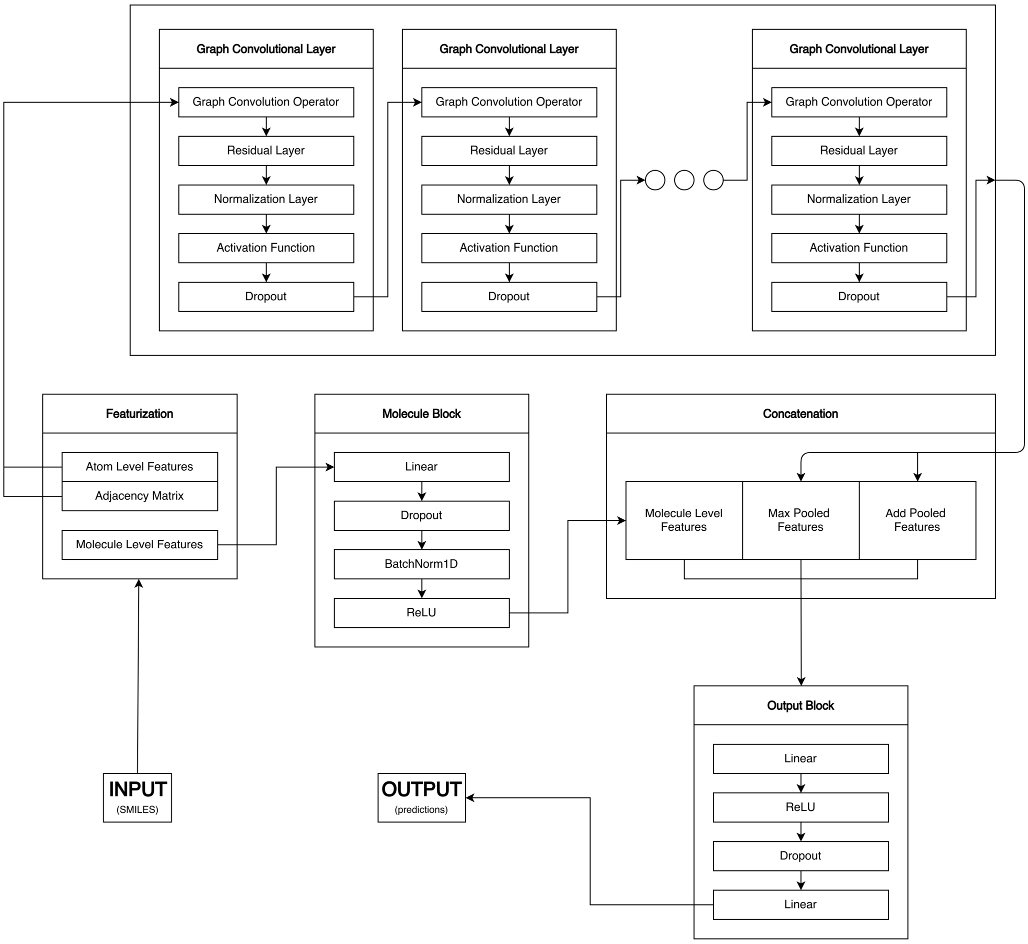


Figure 1.6: Overview of our Graph Network Wrapper

In the meantime, molecular level features (either RdKit or Mordred) are passed through a shallow network (one linear layer, a dropout[60] activation, a batch normalization layer, and a ReLu activation), and the output is concatenated with the above mentioned pooled features. Finally, the features pass through a final output block consisting of 2 linear layers, a ReLu activation and another dropout layer.

1.4.2 Multi-Modal Architectures

For ChEMBL assay dataset, while we can still use graph convolutional networks for the ligand encoding, we also have to deal with the amino-acid sequences.

Here, we either used classic 1D convolutions for the tokenized entries, or a shallow neural network for the bag-of-words encoded features. We also experimented with circular fingerprints as a ligand encoding, along with graph representations.

Bag-of-words encodings for the amino-acid and graph representations for the ligand seemed to work best.

1.5 Pipelines

Any operation within our framework has to pass through 2 processes:

- data preparation
- execution

Data preparation pipelines start from the raw data format (ie: a file on disk) and end when the data is featurized, normalized, and ready for training in Tensor formats. Execution pipelines contain everything that happens afterwards, including training and inference, but also optimization, learning rate scheduling, and metric computations.

1.5.1 Data Preprocessing

There are number of entities with various roles which help bring the data from raw format, to machine learning ready format. To better explain the pipeline, we borrow some terms from the DeepChem[74] library:

- **loaders**: load the raw data with various formats (ie: CSV) from disk into memory (ie: pandas DataFrame);
- **featurizers**: the input fields (ie: SMILES) are prepared by the featurizers (ie: fingerprint featurizer);
- **transformers**: the output fields (ie: toxicity) can be normalized by a transformer (ie: standardization);
- **cache manager**: featurization and transformation can be a lengthy process, so we make use of caching to save our progress and time;
- **splitters**: are used to create subsets of our dataset for various purposes;
- **streamers**: combine all to other elements and dictate how they should coordinate.

Loaders

We provide 3 types of loaders out of the box:

- **CSV Loader**: for comma-separated values
- **Excel Loader**: for spreadsheets
- **SDF Loader**: for SDF files (which also makes the SMILES string available for featurization)

Featurizers

Featurizers work on target columns/fields and it is possible to use more than 1 featurizer. These can be used in parallel, on different columns, or in series, for the same columns.

- **Graph Featurizer**: for graph convolutional networks, with configurable atom features and molecule level features;
- **Circular Fingerprint Featurizer**: for shallow networks and classic machine learning models like Random Forest[25];
- **One-Hot Encoder**;

- **Tokenizer**;
- **Bag of Words Featurizer**;
- **Transpose Featurizer**: if the model expects a matrix to be flipped and we do not want to write custom code;
- **Fixed Featurizer**: will divide the target input by a fixed value.

Transformers

Similar to featurizers, multiple transformers can be applied to the same target. Transformers are kept in memory after they are applied and are reverted after inference (only for direct inference, not for metric computations).

- **Log Normalizer**: will convert the targets to their log values;
- **Min-Max Normalizer**;
- **Fixed Normalizer**: will divide the targets by a fixed value;
- **Standardizer**: will perform Z-score normalization on the target value;
- **Cutoff Transformer**: will convert a continuous value to a binary value based on a user-specified threshold (note: this operation is destructive).

Splitters

The splitters can generate any number of subsets, not just 2 (train-test) or 3 (train-eval-test). We provide 3 ways to perform data splits:

- **Index Split**: will return the entries in the order they appear in the file;
- **Random Split**: will return the entries randomly;
- **Stratified Split**: will return random entries but will try to keep the proportion of a certain output value equal among splits (if the target value in continuous, it can be sorted in a number of configurable bins before sorting is done).

Streamers

The streamers are of little concern for most users, however we include them for completeness sake.

- **General Streamer**: A general purpose streamer which will use the "loader" to iterate through entries, featurizes and transforms them, then caches the solution before applying the splitter on top. In the end, users can specify which split to use, the batch size to collate, and whether to shuffle the data split before serving.
- **Subset Streamer**: Very useful for federated learning experiments, but for little else. It will basically apply an additional index split and return a subset of the data (for each client in the case of federated learning).
- **Cross Validation Streamer**: The cross-validation streamer overwrites the splitting functionality so it generates a number of user-specified folds instead of a single split. As an example, if a 5-fold split is requested, the specified splitter is applied to split the data into 5 (if possible) equal proportion subsets. When a fold is requested, the given fold will act as the test split and the remaining folds as the train split.

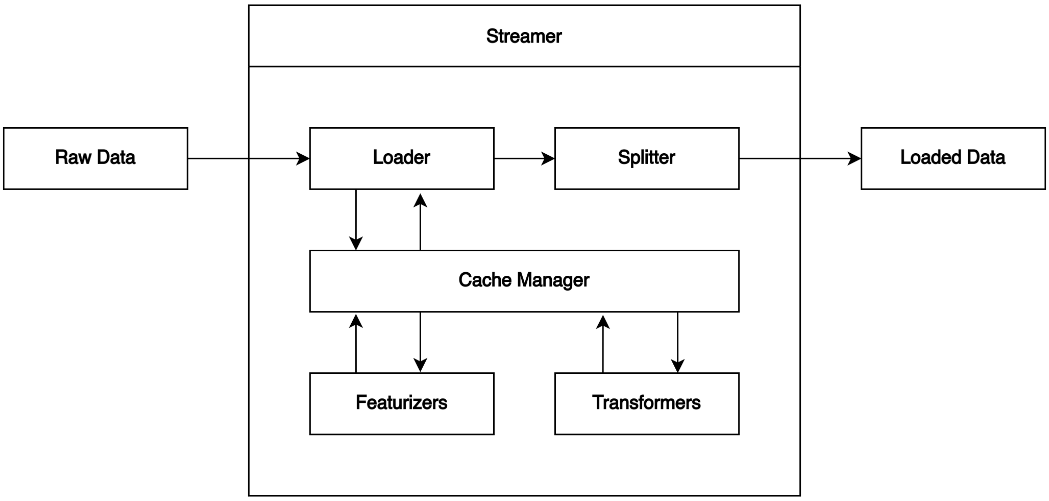


Figure 1.7: Overview of the Data Preparation Pipeline

1.5.2 Model Tuning

Similar to the graph convolutional model wrapper, the whole training process was designed to be highly customizable. That is, users should be able to achieve a lot of functionality without having to touch the code. While the details of how this is achieved is left for the technical part of this report, we briefly mention some of the customizable options.

Training Options

Loss functions (criterions) and optimizers can be directly specified in the configuration files as a module path (ie: "torch.nn.MSELoss"). As far as we are aware, most loss functions and optimizers can be used in this way without having to modify the code.

Additionally, it easy to add custom solutions in separate files, which then can be linked in a similar fashion. As an example, we implement a novel optimizer, the AdaBelief[78] optimizer, which outperformed Adam[30] in many experiments.

We are also making use of learning rate schedules which can be configured in a similar way.

Metrics

Metrics can be specified to both evaluation and logging purposes during training. These metrics can also be selected as target when using Bayesian Optimization[2]. All supported metrics are listed in Table 1.5

Name	Shorthand	Task
Mean Absolute Error	mae	Regression
Mean Squared Error	mse	Regression
Root Mean Squared Error	rmse	Regression
R2 Score	r2	Regression
Area Under the ROC Curve	roc_auc	Classification
Average Precision	pr_auc	Classification
Accuracy Score	accuracy	Classification
Precision Score	precision	Classification
Recall Score	recall	Classification
F1 Score	f1	Classification
Cohen's Kappa Coefficient	cohen_kappa	Classification
Jaccard Similarity	jaccard	Classification

Table 1.5: Supported Metrics

Bayesian Optimization

All configurable options can be tuned using Bayesian optimization. This includes model specific options like the model type, layer types, dropout rates or batch normalization layer types, but also training options like the optimizer, criterion, or the learning rate (the list is not exhaustive).

To be more specific, we use a Tree-structured Parzen Estimator (TPE)[5, 6] implemented with Optuna[2]. On each trial, for each parameter, TPE fits one Gaussian Mixture Model (GMM) $l(x)$ to the set of parameter values associated with the best objective values, and another GMM $g(x)$ to the remaining parameter values. It chooses the parameter value x that maximizes the ratio $\frac{l(x)}{g(x)}$.

1.6 Communication (Mila)

For the communication part of federated learning, we were planning to use NVIDIA's Clara, but it turned out that Clara only works with Tensorflow models (version 1.14). We, as well as Kyoto University would prefer working with PyTorch or at least Tensorflow 2.x, so we decided to rebuild the communication module, following in the steps of the NVIDIA Clara implementation.

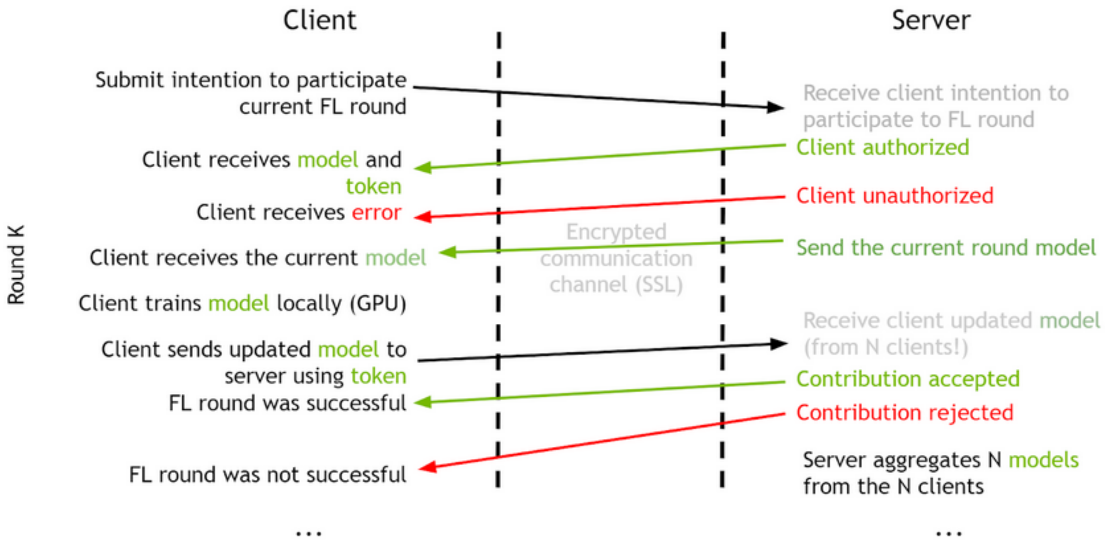

Client
Server
Round K
Submit intention to participate current FL round
Receive client intention to participate to FL round
Client authorized
Client receives model and token
Client unauthorized
Client receives error
Encrypted communication channel (SSL)
Send the current round model
Client receives the current model
Client trains model locally (GPU)
Receive client updated model (from N clients!)
Client sends updated model to server using token
Contribution accepted
FL round was successful
Contribution rejected
FL round was not successful
Server aggregates N models from the N clients
...
...

Figure 1.8: Federated Learning workflow followed by NVIDIA Clara and modeled by us (source: NVIDIA Blog)

We named the module "Mila", the greek word for speech. Similar to NVIDIA Clara, we use gRPC and protocol buffers to transmit information between the client and the servers.

Once the server is online, we wait for a number of clients to join before the training starts. The server then sends the latest model to each participant, which then train the model on their local data for a fixed number of epochs. After training finished, the latest checkpoint is sent back to the server, which will wait for all checkpoints before they are averaged. The new aggregate model is then used for the next round, and the process is repeated.

Each client sends a keepalive signal every minute, and in case one client goes offline or we stop receiving the heartbeat signal, the server halts the process. That is, if one client goes offline, the whole experiment has to be repeated.

1.6.1 Security

Secure Communication

Communication is done through SSL/TLS with both server and client certificate chains. For development purposes, insecure connections are also allowed (no certs required).

When a client authenticates, it receives a token, which will subsequently be used for all operations. Machines not authenticates (ie: without a valid token), or dead clients (with an expired keeplive signal) will not be able to join the training process.

Furthermore, the server has the option to whitelist only a few trusted IP addresses which can join the process; blacklisting suspicious IPs is also possible.

Privacy Attacks

We generally think of machine learning models as a black box and expect that they would not reveal information about the original dataset they were trained on. In reality, membership inference attacks are possible, where an attacker tries to determine whether an input sample was used as part of the training set. While it is questionable how well research on privacy attacks transfers to large and complex models (let alone graph based models), we cannot ignore the possibility of such attacks.

Over-fitting is often exploited in inference attacks, and regularization tactics have been shown to reduce attack accuracies. Here we are talking about methods such as dropout, regularization, or normalization. The architecture type and complexity of the model and data can also affect attack accuracy.

An in-depth review of potential privacy attacks is beyond the score of this report, however, we would like to redirect curious readers to a recent survey paper on the topic[56]. It should be noted that research of such attacks on graph-based models is either sparse or nonexistent.

Differential Privacy

Differential privacy can be a useful asset for defence against privacy attacks. It is based on the idea of "learning nothing about an individual while learning useful information about a population"[18, 56]. The definition is based on the notion that if two databases differ only by one record and are used by the same model, the output of that algorithm should be similar.

Formally put, a randomized model M with output S is (ϵ, δ)-differentially private if for any adjacent inputs D and D' that differ in a single example:

$$\forall M, P[M(D) \in S] \leq e^{\epsilon} P[M(D') \in S] + \delta \tag{1.1}$$

where:

- ϵ: is the privacy budget.
- δ: is the probability of information accidentally being leaked. The term was introduced as a relaxation that allows some outputs not to be bounded by e^{ϵ}.

The privacy budget ϵ, measures the distance between the outputs of the model on the 2 datasets. Therefore, ϵ is a measure of the privacy loss.

It is important to note that differential privacy does not guarantee any privacy in itself, instead, it is a measure of privacy and informs us about how likely the model is to leak knowledge about certain samples from the dataset. With differential privacy, we can set a "privacy budget" and control how much privacy we are willing to give away. Actually making the solution more secure is generally achieved by adding Gaussian or Laplacian noise either to the weights or the gradients of the model, however, this will affect the quality of the trained model (sometimes drastically).

For our solution, we used Opacus[50] to implement differential privacy, however, it comes with limitations. Some layer types are not compatible for differential privacy, with the most prominent example being BatchNorm. As a solution we provide 2 solutions, either removing batch normalization layers, or replacing them with an alternative such as GroupNorm[73].

But more importantly, differential-privacy has a utility-privacy trade off. To make the model more secure, more noise will have to be added, but the more noise we add to the model, the worse it will perform.

1.6.2 Differences from NVIDIA Clara

The main advantage of our implementation is that it is framework independent. All models and checkpoints are transmitted as bytes and stored in the same way they are on the server. NVIDIA Clara transports directly (Tensorflow) Tensor objects, and so, only supports Tensorflow models and aggregators.

Another key difference is that our implementation does not require GPUs and can run with all participants (clients and servers) using CPU only, should they wish to do so.

In addition, we added support for IP whitelisting and blacklisting.

On the negative side, our implementation is new and didn't go through extensive testing as (presumably) NVIDIA Clara did.

Experiment Results

2.1 Introduction

The general pipeline for each dataset can be summarized as follows:

- we first use Bayesian Optimization for both architecture search and hyper-parameter tuning;
- we validate the best architecture using Cross-Validation
- we perform distributed experiments with the best architecture (federated learning)

For federated learning experiments, we analyze how the performance changes when we alter important properties like:

- the number of clients (from 2 to 20);
- the number of epochs trained per round (1, 2, 5, 10, or 20);
- the balance of the datasets between each client (from evenly distributed to highly skewed splits).

All reported metrics all the highest recorded independent values across all checkpoints. The reported mean absolute, mean squared, and root mean squared errors are based on normalized values.

Thresholds

We evaluate experiments on various metrics, depending on the task (classification or regression). For regression tasks we use the R^2 Score, the root mean squared error, and the mean absolute error. For classification, we make note of the area under the receiver operating characteristic curve (ROC-AUC, or AUROC), the average precision (PR-AUC, or mAP), the accuracy, the precision, the recall, and Cohen's Kappa Coefficient.

It is worth noting that some classification metrics are threshold based (ie: they are evaluated at a certain threshold), while other ones are threshold independent (ie: evaluated at various thresholds). Besides the ROC-AUC and PR-AUC (average precision) metrics, all classification metrics are threshold based. Threshold based metrics like the accuracy can be dangerous when analyzed individually if the dataset is imbalanced. For example, if we are working on a classification task on a cancer dataset, over 99% of entries are probably negative. If a model outputs "negative" predictions all the time, it would achieve a 99%+ accuracy without actually providing a discriminative effect.

As an attempt to get a more meaningful metric, the thresholds have been optimized using a precision-recall curve, and have been set to the value where the precision and recall lines intersect. As a consequence, threshold based metrics like the accuracy do not show the highest possible values we can register on the said metric, but the most useful and informative values.

2.2 Architecture & Hyper-Parameter Optimization

As a first step, we report the best architectures we found using Bayesian Optimization for each dataset. We considered the following options during the optimization phase:

- the model/layer type (Table 1.4)
- the number of hidden features (between 32 and 256)
- the dropout rate (between 0.0 and 0.7)
- the number of graph layers (between 2 and 12)
- the batch normalization layer (BatchNorm, LayerNorm, or GraphNorm)
- the optimizer (Stochastic Gradient Descent[29], Adam[30], AdamW[40], and AdaBelief[78])
- the learning rate (between 0.0001 and 0.01)
- the weight decay rate (between 0.00001 and 0.001)
- whether to use residual layers in the graph convolution (yes or no)
- whether to use edge features in the graph operation (yes or no)
- the type of molecular descriptors (none, rdKit[34] or Mordred[53])

2.2.1 Tox21

Although the Tox21 dataset contains 12 targets, it was taken as a single, multi-task dataset. The model would use the (featurized) SMILES as input and output a prediction for all 12 labels in one go.

The dataset is very imbalanced, so metrics such as accuracy should not be fully trusted (even with threshold tuning). Metrics such as the ROC-AUC and PR-AUC are more trustworthy when it comes to imbalanced datasets.

Furthermore, the Tox21 dataset contains many missing values. To handle these cases, we perform the forward pass of the model as usual, but we set the weight for the missing values to 0 when computing the loss. Similarly, when we compute the metrics, we ignore missing values.

Task	ROC-AUC	PR-AUC	Accuracy	Precision	Recall	Kappa
NR-AR	0.813	0.524	0.971	0.929	0.471	0.567
NR-AR-LBD	0.908	0.610	0.980	0.730	0.711	0.678
NR-AhR	0.900	0.659	0.909	0.655	0.840	0.579
NR-Aromatase	0.913	0.534	0.953	0.556	0.694	0.492
NR-ER	0.738	0.444	0.865	0.465	0.699	0.335
NR-ER-LBD	0.838	0.448	0.947	0.581	0.530	0.431
NR-PPAR-gamma	0.897	0.394	0.973	0.556	0.621	0.433
SR-ARE	0.844	0.553	0.844	0.491	0.842	0.446
SR-ATAD5	0.918	0.464	0.968	0.571	0.635	0.494
SR-HSE	0.855	0.435	0.949	0.625	0.662	0.481
SR-MMP	0.924	0.729	0.889	0.616	0.900	0.614
SR-p53	0.884	0.368	0.937	0.365	0.696	0.350
Minimum	0.738	0.368	0.844	0.365	0.471	0.335
Maximum	0.924	0.729	0.980	0.929	0.900	0.678
Mean	0.869	0.513	0.932	0.595	0.692	0.492
Median	0.890	0.494	0.948	0.576	0.695	0.487
Standard Deviation	0.052	0.105	0.043	0.135	0.120	0.099

Table 2.1: Baseline metrics on the Tox21 dataset

The best performing architecture registered was a Local Extremum Graph Network[54] with 7 graph layers, a hidden layer size of 96, activate residual layers, a dropout rate of 0.1, and BatchNorm as a normalization layer. We used an index split of 80% (training) 20% (test), and rdKit molecule level descriptors. The optimizer used was AdamW[40], with a learning rate of 0.01, and weight decay of 0.00056. As a criterion we used binary cross entropy loss with a mask for missing values. The batch size was set to 128, we trained for 200 epochs, and used a threshold of 0.216 for non-logit based metric computations. We also used a One Cycle Learning Rate Scheduler[59].

2.2.2 AMES

The AMES dataset has a single label, however we trained models on 4 versions of the dataset (see the datasets section). Bayesian optimization was performed on the final combo dataset (benchmark + NTP PubChem), and evaluated on all 4 versions.

The best performing architecture registered was a Classic Graph Convolutional Network[62] with 3 graph layers, a hidden layer size of 160, activate residual layers, a dropout rate of 0.1, and BatchNorm as a normalization layer. We used an stratified split of 80% (training) 20% (test). The split was performed with Scikit-Learn[52] and the random seed was set to 42.
The optimizer used was AdaBelief[78], with a learning rate of 0.01, and weight decay of 0.00036. As a criterion we used binary cross entropy loss, and again, a One Cycle Learning Rate Scheduler[59]. The batch size was set to 128, we trained for 200 epochs, and used a threshold of 0.499.

Task	ROC-AUC	PR-AUC	Accuracy	Precision	Recall	Kappa
Benchmark	0.871	0.876	0.804	0.833	0.906	0.603
NTP PubChem	0.890	0.899	0.830	0.865	0.889	0.659
S9 Minus	0.885	0.824	0.847	0.878	0.806	0.649
Combo/Final	0.903	0.908	0.837	0.879	0.897	0.674

Table 2.2: Baseline metrics on the AMES datasets

2.2.3 ADME

Each ADME related dataset was optimized separately. We present our results in Table 2.3 for classification tasks, and Table 2.4 for regression tasks.

Task	ROC-AUC	PR-AUC	Accuracy	Precision	Recall	Kappa
FeHuman (th=0.3)	0.835	0.897	0.721	0.702	0.921	0.505
FeHuman (th=0.7)	0.921	0.985	0.897	0.932	0.966	0.572
NER-LLC (low)	0.853	0.897	0.809	1.000	0.851	0.621
NER-LLC (medium)	0.782	0.574	0.607	0.441	1.000	0.298
NER-LLC (high)	0.829	0.488	0.876	1.000	1.000	0.415
NER-LLC (mean)	0.821	0.653	0.764	0.813	0.950	0.444
PappCaco2	0.860	0.781	0.799	0.739	0.991	0.581
Solubility	0.861	0.895	0.806	0.803	1.0	0.584

Table 2.3: ADME tasks (classification)

Task	R2	MAE	RMSE
CLint	0.489	0.806	1.536
FuBrain	0.591	1.309	2.545
FupHuman	0.690	0.090	0.156
FupRat	0.594	0.111	0.183
PappCaco2	0.451	1.090	1.411
Papp-LLC	0.577	0.071	0.124
RbRat	0.669	0.173	0.225

Table 2.4: ADME tasks (regression)

We also experimented with multi-task learning on the ADME dataset, however, the overlaps between them is small and the results were not very good. For the PappCaco2 dataset, we did both regression and classification experiments. We report the individual values, however, we experimented with a joined learning approach as well, where we train the classification and regression task in one experiment. For the fraction excreted unchanged in urine (FeHuman) dataset, with experimented with 2 thresholds, 0.3 and 0.7.

A list of the most important options are listed in Table 2.5. All architectures used residual layers, and most used BatchNorm[27] for normalization (exceptions are NER-LLC which used GraphNorm[10], and FupRat which used LayerNorm[63]). As optimizer, all experiments used AdamW[40]. For regression tasks we used random split, for classification we used a stratified split. The batch size was 64 on all experiments, except for RbRat, where we used a batch size of 24. Classification tasks used a binary cross entropy loss, while regression tasks relied on Smooth L1 Loss. Models were trained for 200 epochs, except for fuBrain (210), fupRat (230), and rbRat (230). We used log values for FuBrain, CLint, PappCaco2, and RbRat, while for PappLLC we used a fixed transformer and divided values by 300.

Dataset	Layer Type	n_layers	hidden	dropout	lr	decay
CLint	GENConv[35]	2	128	0.1	0.01	6e-6
FeHuman	GCNConv[62]	4	64	0.2	0.003	5e-4
FuBrain	TrimConv[36]	3	64	0.2	0.0045	1.6e-6
FupHuman	GINConv[75]	2	128	0.15	0.003	1.5e-6
FupRat	GENConv[35]	3	64	0.1	0.01	2e-6
NER-LLC	GINConv[75]	2	32	0.25	0.01	1e-4
PappCaco2	GINConv[75]	4	128	0.1	0.0008	2e-4
Papp-LLC	GCNConv[62]	2	32	0.2	0.01	8e-6
RbRat	GCNConv[62]	3	32	0.15	0.017	1e-5
Solubility	GINConv[75]	2	128	0.1	0.001	5e-5

Table 2.5: Hyper-parameters of ADME tasks (layer type, number of layers, number of hidden features, dropout rate, learning rate, weight decay)

2.2.4 ChEMBL

Parameters were tuned on the first version of the dataset (details in the datasets section), which was then evaluated on the second version subtasks as well.

Protein encoding was done with bag-of-words featurization, while ligand features were encoded as graphs. The protein features were passed through a multi-layer perceptron, with 9723 input features, 160 hidden features, and 16 output features. The ligand features were passed through a GENeralized Graph Network[35] with

5 layers, no dropout, no residual connections, and BatchNorm as normalization layer. The number of hidden features of the graph model was 192. Surprisingly, a Stochastic Gradient Descent[29] worked best, with the learning rate set to 0.0041 and the weight decay to 0.00001. For classification, again we rely on binary cross entropy loss, and for regression on the Smooth L1 loss. We also used a batch size of 128 and trained the models for 50 epochs. For the regression task, we used a log transformation of the target values.

Task	ROC-AUC	PR-AUC	Accuracy	Precision	Recall	Kappa
v1 (t=100nM)	0.882	0.882	0.800	0.807	0.810	0.600
v2 (t=100nM)	0.891	0.855	0.809	0.779	0.818	0.61
v2 (t=1um)	0.9	0.948	0.836	0.868	0.934	0.616
v2 (t=10um)	0.916	0.989	0.918	0.941	0.999	0.476

Table 2.6: Baseline Metrics for the ChEMBL Protein-Ligand Binding Affinity datasets (classification)

Task	R2	MAE	RMSE
v2	0.651	1.362	1.828

Table 2.7: Baseline Metrics for the ChEMBL Protein-Ligand Binding Affinity datasets (regression)

Initially, we used an index split on the first version (v1) which yielded better results than the ones we report in Table 2.6, with a register ROC-AUC of 0.956, PR-AUC of 0.959, and accuracy of 0.878. We later experimented with stratified splits which are the values reported in Table 2.6 and Table 2.7. The stratified split should contain a better representation of the target values, so we think these values are closer to reality.

2.2.5 Other Datasets

Finally, we report values registered on the additional ADME-Tox datasets for information purposes.

Dataset	ROC-AUC	PR-AUC	Acc	R2	MAE	RMSE
bbb adenot	0.987	0.996	0.955			
bbb martins	0.947	0.975	0.882			
bioavailability ma	0.787	0.899	0.804			
caco2 wang				0.760	0.375	0.485
carcinogens lagunin	0.948	0.875	0.910			
clearance edrug3d				0.028	0.303	1.547
clearance hepatocyte az				0.195	0.667	0.890
clearance microsome az				0.383	0.558	0.784
clintox	0.951	0.765	0.959			
cyp1a2 veith	0.943	0.938	0.874			
cyp2c19 veith	0.903	0.880	0.831			
cyp2c9 substrate	0.766	0.479	0.791			
cyp2c9 veith	0.900	0.805	0.828			
cyp2d6 substrate	0.812	0.678	0.783			
cyp2d6 veith	0.893	0.727	0.874			
cyp3a4 substrate	0.723	0.713	0.634			
cyp3a4 veith	0.915	0.878	0.839			
dili	0.927	0.902	0.852			
f20 edrug3d	0.782	0.956	0.814			
f30 edrug3d	0.806	0.948	0.728			
halflife edrug3d				0.501	0.106	0.271
half life obach				0.405	0.103	0.171
herg	0.914	0.957	0.839			
hia hou	0.998	0.999	0.982			
hydrationfreeenergy freesolv				0.930	0.165	0.283
ld50 zhu				0.669	0.418	0.578
lipophilicity astrazeneca				0.763	0.365	0.492
pgp broccatelli	0.955	0.966	0.762			

Table 2.8: Metrics for other datasets

Dataset	ROC-AUC	PR-AUC	Acc	R2	MAE	RMSE
ppbr az				0.641	0.375	0.605
ppbr edrug3d				0.732	0.381	0.515
ppbr ma	0.885	0.874	0.745			
skin reaction	0.896	0.947	0.802			
solubility aqsoldb				0.837	0.267	0.396
vd edrug3d				0.121	0.087	0.147
vdss lombardo				0.315	0.115	0.193

Table 2.8: Metrics for other datasets (continued)

dataset	model	optimizer	layers	dropout	residual
bbb adenot	SAGEConv	AdamW	7	0.2	yes
bbb martins	GENConv	AdaBelief	3	0.4	no
bioavailability ma	GCNConv	AdaBelief	2	0.3	no
caco2 wang	GraphConv	Adam	5	0.2	no
carcinogens lagunin	GENConv	AdamW	7	0.0	yes
clearance edrug3d	GCNConv	AdamW	4	0.0	no
clearance hepatocyte az	GCNConv	AdaBelief	3	0.2	yes
clearance microsome az	GraphConv	Adam	7	0.2	yes
clintox	GINConv	AdaBelief	7	0.2	no
cyp1a2 veith	SAGEConv	AdaBelief	7	0.1	no
cyp2c19 veith	GCNConv	Adam	7	0.1	no
cyp2c9 substrate	GraphConv	Adam	7	0.4	yes
cyp2c9 veith	GraphConv	AdaBelief	2	0.4	no
cyp2d6 substrate	SAGEConv	AdaBelief	5	0.0	no
cyp2d6 veith	SAGEConv	AdamW	6	0.1	no
cyp3a4 substrate	LEConv	SGD	4	0.0	no
cyp3a4 veith	GraphConv	Adam	3	0.1	yes
dili	GCNConv	SGD	6	0.4	no
f20 edrug3d	GENConv	AdamW	3	0.2	yes
f30 edrug3d	GraphConv	Adam	6	0.4	no

Table 2.9: Parameters for other datasets

dataset	model	optimizer	layers	dropout	residual
halflife edrug3d	GINConv	AdamW	6	0.2	yes
half life obach	GCNConv	AdamW	3	0.2	no
herg	LEConv	SGD	2	0.1	yes
hia hou	GINConv	AdamW	4	0.0	yes
hydrationfreeenergy freesolv	GENConv	AdaBelief	4	0.0	yes
ld50 zhu	LEConv	AdaBelief	3	0.1	no
lipophilicity astrazeneca	GENConv	AdamW	5	0.1	no
pgp broccatelli	SAGEConv	Adam	8	0.2	yes
ppbr az	GraphConv	AdamW	4	0.1	no
ppbr edrug3d	GCNConv	Adam	3	0.1	no
ppbr ma	GENConv	SGD	7	0.2	yes
skin reaction	GraphConv	SGD	4	0.0	yes
solubility aqsoldb	SAGEConv	Adam	4	0.0	yes
vd edrug3d	GCNConv	AdaBelief	3	0.2	yes
vdss lombardo	GENConv	Adam	2	0.3	yes

Table 2.9: Parameters for other datasets (continued)

It is interesting to see the distribution of these hyperparameters.

In terms of model architecture, Classic Graph Networks[62] and Weisfeiler-Leman Graph Networks[47] dominate with 8 counts for each, however GENeralized Graph Networks[35] are not far behind with 7 wins. For optimizers we see an equal distribution amoung AdaBelief, AdamW, and Adam, with 10 entries for each, while SGD is lagging behind with 5 wins. For the number of layers, it seems there is no clear winner, however 3 and 7 layers seem to be the most popular (with 8 wins for each). In terms of dropout, 0.2 (11 wins) and 0.1 (9 wins) is a sweet spot, followed by no dropout at all (8 wins). And finally, we see that some models work better with skip connections while others just do not.

2.3 Cross-Validation

Hyper-parameter tuning was done using the same data splits. That is, each set of hyper-parameters was evaluated on the same data samples. It is helpful to evaluate these baselines on multiple splits.

Dataset	ROC-AUC	PR-AUC	Accuracy
NR-AR	0.8358±0.0161	0.5594±0.0531	0.9757±0.0024
NR-AR-LBD	0.8998±0.0089	0.6538±0.0429	0.9795±0.0010
NR-AhR	0.9105±0.0075	0.6682±0.0164	0.9080±0.0043
NR-Aromatase	0.8871±0.0156	0.4955±0.0405	0.9498±0.0073
NR-ER	0.7627±0.0106	0.4937±0.0300	0.8769±0.0089
NR-ER-LBD	0.8604±0.0185	0.5402±0.0378	0.9592±0.0034
NR-PPAR-gamma	0.8972±0.0177	0.4292±0.0247	0.9719±0.0038
SR-ARE	0.8479±0.0118	0.5691±0.0265	0.8371±0.0064
SR-ATAD5	0.8911±0.0167	0.4344±0.0608	0.9640±0.0036
SR-HSE	0.8519±0.0097	0.4302±0.0282	0.9461±0.0038
SR-MMP	0.9228±0.0085	0.7563±0.0286	0.8965±0.0069
SR-p53	0.8803±0.0095	0.4332±0.0446	0.9309±0.0022
Tox21 (mean)	0.8706±0.0126	0.5386±0.0362	0.9330±0.0045
AMES (Benchmark)	0.8814±0.0034	0.8929±0.0064	0.8153±0.0069
AMES (NTP PubChem)	0.8950±0.0028	0.9051±0.0070	0.8302±0.0049
AMES (S9 Minux)	0.8972±0.0099	0.8469±0.0128	0.8561±0.0143
AMES (Final)	0.8927±0.0111	0.9000±0.0098	0.8277±0.0107
FeHuman (th=0.3)	0.8255±0.0176	0.8714±0.0415	0.7849±0.0587
FeHuman (th=0.7)	0.8650±0.0390	0.9710±0.0097	0.8673±0.0460
NER-LLC (low)	0.8283±0.0448	0.8177±0.0596	0.7884±0.0420
NER-LLC (medium)	0.7096±0.0484	0.6055±0.0427	0.5633±0.0444
NER-LLC (high)	0.8372±0.0306	0.5211±0.0856	0.8514±0.0198
NER-LLC (mean)	0.7917±0.0413	0.6481±0.0626	0.7344±0.0354
PappCaco2	0.8645±0.0053	0.8075±0.0081	0.8049±0.0097
Solubility	0.8726±0.0221	0.9035±0.0138	0.8152±0.0216
ChEMBL (v1)	0.8819±0.0010	0.8819±0.0011	0.8010±0.0009

Table 2.10: Cross-validation Results (classification tasks)

Dataset	Precision	Recall	Cohen’s Kappa
NR-AR	0.9509±0.0598	0.5315±0.0472	0.6116±0.0447
NR-AR-LBD	0.7630±0.0486	0.7296±0.0499	0.6744±0.0291
NR-AhR	0.6176±0.0396	0.8866±0.0268	0.5776±0.0158
NR-Aromatase	0.5440±0.0756	0.7221±0.0509	0.4467±0.0257
NR-ER	0.5376±0.0693	0.7728±0.0313	0.3902±0.0281
NR-ER-LBD	0.6481±0.0373	0.6419±0.0506	0.5101±0.0244
NR-PPAR-gamma	0.5040±0.0920	0.6515±0.0555	0.4454±0.0262
SR-ARE	0.4979±0.0285	0.9142±0.0209	0.4582±0.0177
SR-ATAD5	0.5119±0.0823	0.7219±0.0624	0.4596±0.0573
SR-HSE	0.5513±0.0494	0.7066±0.0431	0.4669±0.0188
SR-MMP	0.6566±0.0212	0.9370±0.0082	0.6322±0.0152
SR-p53	0.4464±0.0520	0.7924±0.0335	0.4278±0.0308
Tox21 (mean)	0.6024±0.0546	0.7507±0.0400	0.5084±0.0278
AMES (Benchmark)	0.8636±0.0095	0.9155±0.0153	0.6286±0.0142
AMES (NTP PubChem)	0.8941±0.0137	0.9106±0.0166	0.6593±0.0095
AMES (S9 Minux)	0.9026±0.0440	0.8607±0.0622	0.6666±0.0339
AMES (Final)	0.8787±0.0163	0.9031±0.0189	0.6545±0.0217
FeHuman (th=0.3)	0.7911±0.0878	1.0000±0.0000	0.5197±0.1025
FeHuman (th=0.7)	0.8895±0.0466	0.9965±0.0062	0.4459±0.0858
NER-LLC (low)	0.9778±0.0390	0.9498±0.0547	0.5666±0.0875
NER-LLC (medium)	0.5631±0.1945	1.0000±0.0000	0.2019±0.0756
NER-LLC (high)	1.0000±0.0000	0.9716±0.0313	0.3780±0.0730
NER-LLC (mean)	0.8470±0.0778	0.9738±0.0287	0.3821±0.0787
PappCaco2	0.7670±0.0242	0.9709±0.0176	0.5888±0.0178
Solubility	0.8815±0.0429	1.0000±0.0000	0.6130±0.0486
ChEMBL (v1)	0.8018±0.0024	0.8307±0.0083	0.6019±0.0019

Table 2.10: Cross-validation Results (classification tasks) (continued)

For this, we use cross-validation, where we divide the dataset into "n" equal splits. For each "fold", the subsample will act as a test set, and the remaining samples as the train set. Each fold is then evaluated and we report the average values for each metric.

For smaller datasets we performed multiple experiments with different random splits. All Tox21, AMES and ChEMBL tasks, along with the fupHuman, fuBrain, CLint, and PappCaco2 tasks were evaluated once on 5-fold split. The Solubility, fupRat, PappLLC, NER-LLC, and feHuman tasks were evaluated on 5 different 5-fold splits. The RbRat task was evaluated on 10 different 5-fold splits.

Dataset	R2	MAE	RMSE
CLint	0.4583±0.0280	1.9015±0.1890	0.8279±0.0480
FuBrain	0.6068±0.0770	2.066±0.5110	1.168±0.1800
FupHuman	0.6629±0.0330	0.1559±0.0110	0.0927±0.0060
FupRat	0.6019±0.0900	0.1954±0.0210	0.1218±0.0150
PappCaco2	0.5053±0.010	1.2707±0.0100	0.9552±0.0140
Papp-LLC	0.6044±0.080	0.1213±0.0180	0.0694±0.0120
RbRat	0.5205±0.1490	0.3842±0.1970	0.2642±0.0830

Table 2.11: Cross-validation Results (regression tasks)

2.4 Distributed Learning

To perform federated learning, we split the training set among the clients. For client-based an epoch-based experiments, the ratios are equal. As an example, for a 2 client experiment, both clients would get an equal 50/50 share of the training set, for a 10 client experiment, they would each receive 10% of the training set. For imbalanced experiments, we specify the ratios explicitly.

Before we present our findings, it is helpful to discuss the aggregation strategies we investigated. Training progress charts for all experiments can be found in the Appendix section.

All client-based and imbalanced split experiments were trained for 10 epochs per round, and all epoch-based experiments were trained on 2 client splits.

2.4.1 Aggregators

The aggregation process is an important part of the federated learning process. We experimented with 3 different strategies:

- plain averaging
- weighted averaging
- benchmarked averaging

With plain averaging, checkpoints are averaged as they are, however, this can be a naive approach.

Some clients will often have a lot more data and their contribution matters more. To account for these differences, we multiply the weights for each client by the ratio of samples they posses. We call this aggregation "weighted averaging".

Still, not all datasets are equal. Possession of a benchmark dataset for evaluation on the server side can be very helpful. For these experiments we use the test set to evaluate each checkpoint received by the client in each round. Then, we compute a user specified metric for them (the ROC-AUC for classification and the R2-score for regression in our case), and multiply the weights according to the performance of each one.

We expect this aggregator to perform much better, however, the benchmark should be evaluated carefully. If the dataset is too small, or if it is not representative of the overall distribution, it can negatively affect the federated learning process. Some clients might have very useful, but rare samples which score low on the benchmark dataset (and therefore, penalized). On the other hand, benchmarked aggregation can protect against security attacks such as model poisoning[69] or evasion attacks[37].

2.4.2 Tox21 - NR-AR

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.813	0.524	0.971	0.929	0.471	0.567
Clients 2	0.795	0.490	0.967	0.778	0.735	0.523
Clients 3	0.789	0.485	0.964	0.683	0.941	0.496
Clients 4	0.807	0.507	0.959	0.592	0.971	0.475
Clients 5	0.815	0.506	0.962	0.630	0.985	0.490
Clients 6	0.811	0.488	0.958	0.569	1.000	0.466

Clients 7	0.809	0.495	0.961	0.617	0.971	0.485
Clients 8	0.811	0.497	0.958	0.569	1.000	0.466
Clients 9	0.809	0.511	0.959	0.592	1.000	0.475
Clients 10	0.820	0.490	0.963	0.667	1.000	0.499
Clients 11	0.801	0.484	0.967	0.778	1.000	0.523
Clients 12	0.803	0.474	0.961	0.622	1.000	0.476
Clients 13	0.797	0.478	0.961	0.622	1.000	0.480
Clients 14	0.814	0.483	0.966	0.732	1.000	0.534
Clients 15	0.805	0.482	0.961	0.617	1.000	0.485
Clients 16	0.807	0.491	0.946	0.423	1.000	0.423
Clients 17	0.803	0.484	0.960	0.605	1.000	0.480
Clients 18	0.805	0.490	0.964	0.690	1.000	0.510
Clients 19	0.812	0.494	0.963	0.659	1.000	0.499
Clients 20	0.814	0.480	0.963	1.000	1.000	0.499
Epochs 1	0.803	0.485	0.968	0.800	0.441	0.529
Epochs 2	0.805	0.481	0.966	0.737	0.441	0.520
Epochs 5	0.820	0.500	0.969	0.848	0.456	0.540
Epochs 10	0.795	0.491	0.964	0.683	0.471	0.496
Epochs 20	0.799	0.497	0.962	0.659	0.956	0.486
Balanced 60|40	0.796	0.504	0.962	0.643	0.529	0.490
Balanced 67|33	0.810	0.497	0.963	0.667	0.676	0.494
Balanced 75|25	0.837	0.499	0.964	0.683	0.471	0.496
Balanced 80|20	0.806	0.514	0.965	0.718	0.662	0.507
Balanced 40|30|30	0.780	0.485	0.961	0.622	0.971	0.476
Balanced 60|20|20	0.798	0.484	0.964	0.674	1.000	0.505
Balanced 80|10|10	0.812	0.503	0.962	0.651	0.912	0.494
Balanced 60|30|10	0.806	0.504	0.962	0.636	0.971	0.481
Balanced 30|30|15|15|10	0.814	0.487	0.965	0.707	0.971	0.515
Balanced 60|10|10|10|10	0.797	0.496	0.966	0.750	0.971	0.503

Table 2.12: Best results for plain averaging on NR-AR (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.813	0.524	0.971	0.929	0.471	0.567

60|40	0.810	0.502	0.961	0.622	0.471	0.493
67|33	0.819	0.492	0.965	0.707	0.471	0.518
75|25	0.805	0.492	0.964	0.690	0.500	0.510
80|20	0.810	0.496	0.967	0.778	0.485	0.523
40|30|30	0.827	0.502	0.964	0.674	1.000	0.505
60|20|20	0.814	0.481	0.962	0.651	0.971	0.498
80|10|10	0.801	0.497	0.966	0.732	0.485	0.534
60|30|10	0.826	0.504	0.964	0.711	0.456	0.492
30|30|15|15|10	0.822	0.489	0.964	0.674	0.971	0.505
60|10|10|10|10	0.815	0.510	0.966	0.737	0.779	0.512

Table 2.13: Best results for weighted averaging on NR-AR (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.813	0.524	0.971	0.929	0.471	0.567
Clients 2	0.802	0.483	0.965	0.730	1.000	0.498
Clients 3	0.800	0.495	0.961	0.628	1.000	0.471
Clients 4	0.805	0.513	0.962	0.644	1.000	0.503
Clients 5	0.791	0.500	0.957	0.558	1.000	0.462
Clients 6	0.802	0.489	0.966	0.757	1.000	0.517
Clients 7	0.791	0.483	0.959	0.610	1.000	0.475
Clients 8	0.796	0.494	0.959	0.588	1.000	0.484
Clients 9	0.802	0.495	0.958	0.569	1.000	0.466
Clients 10	0.797	0.504	0.959	0.580	1.000	0.471
Clients 11	0.790	0.486	0.953	0.500	1.000	0.437
Clients 12	0.799	0.485	0.954	0.509	1.000	0.444
Clients 13	0.799	0.491	0.953	0.476	1.000	0.433
Clients 14	0.785	0.480	0.957	0.547	1.000	0.474
Clients 15	0.790	0.471	0.955	0.518	1.000	0.444
Clients 16	0.805	0.478	0.944	0.408	1.000	0.393
Clients 17	0.797	0.483	0.951	0.470	1.000	0.437
Clients 18	0.787	0.474	0.960	0.600	1.000	0.488
Clients 19	0.790	0.467	0.944	0.397	1.000	0.383

Clients 20	0.778	0.466	0.961	0.622	1.000	0.485
Epochs 1	0.803	0.492	0.968	0.844	0.471	0.529
Epochs 2	0.806	0.507	0.967	0.794	0.471	0.514
Epochs 5	0.788	0.487	0.968	0.818	0.662	0.523
Epochs 10	0.810	0.508	0.964	0.700	1.000	0.505
Epochs 20	0.797	0.499	0.967	0.763	1.000	0.531
Balanced 60|40	0.805	0.503	0.965	0.718	0.941	0.515
Balanced 67|33	0.795	0.501	0.966	0.737	0.971	0.512
Balanced 75|25	0.786	0.487	0.963	0.659	0.971	0.499
Balanced 80|20	0.789	0.499	0.966	0.730	0.956	0.520
Balanced 40|30|30	0.801	0.494	0.964	0.667	1.000	0.513
Balanced 60|20|20	0.799	0.499	0.962	0.630	1.000	0.490
Balanced 80|10|10	0.805	0.489	0.965	0.718	1.000	0.507
Balanced 60|30|10	0.793	0.503	0.961	0.622	1.000	0.476
Balanced 30|30|15|15|10	0.816	0.524	0.966	0.750	1.000	0.511
Balanced 60|10|10|10|10	0.803	0.483	0.962	0.659	1.000	0.477

Table 2.14: Best results for benchmarked averaging on NR-AR (Tox21)

2.4.3 Tox21 - NR-AR-LBD

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.908	0.610	0.980	0.730	0.711	0.678
Clients 2	0.896	0.594	0.976	0.630	0.711	0.625
Clients 3	0.899	0.591	0.973	0.577	1.000	0.605
Clients 4	0.906	0.593	0.972	0.554	1.000	0.599
Clients 5	0.893	0.633	0.976	0.620	1.000	0.640
Clients 6	0.872	0.593	0.972	0.569	1.000	0.598
Clients 7	0.884	0.585	0.972	0.554	1.000	0.599
Clients 8	0.893	0.576	0.967	0.500	1.000	0.555
Clients 9	0.873	0.613	0.972	0.564	1.000	0.606
Clients 10	0.875	0.572	0.972	0.558	1.000	0.593
Clients 11	0.877	0.570	0.977	0.646	1.000	0.655
Clients 12	0.872	0.576	0.969	0.526	1.000	0.581

Clients 13	0.884	0.613	0.967	0.500	1.000	0.565
Clients 14	0.888	0.594	0.974	0.596	1.000	0.627
Clients 15	0.879	0.596	0.970	0.536	1.000	0.581
Clients 16	0.894	0.571	0.959	0.395	1.000	0.474
Clients 17	0.863	0.575	0.969	0.518	1.000	0.558
Clients 18	0.883	0.598	0.972	0.556	1.000	0.591
Clients 19	0.892	0.572	0.973	0.583	1.000	0.591
Clients 20	0.866	0.589	0.970	1.000	1.000	0.579
Epochs 1	0.906	0.649	0.979	0.682	0.733	0.663
Epochs 2	0.892	0.624	0.977	0.659	0.733	0.655
Epochs 5	0.900	0.598	0.975	0.608	0.733	0.640
Epochs 10	0.906	0.652	0.975	0.622	0.733	0.626
Epochs 20	0.912	0.659	0.974	0.600	0.933	0.599
Balanced 60|40	0.901	0.602	0.977	0.633	0.711	0.648
Balanced 67|33	0.897	0.606	0.977	0.640	0.956	0.662
Balanced 75|25	0.887	0.613	0.978	0.674	0.756	0.648
Balanced 80|20	0.890	0.611	0.980	0.698	0.711	0.671
Balanced 40|30|30	0.889	0.591	0.976	0.625	1.000	0.633
Balanced 60|20|20	0.883	0.566	0.978	0.674	1.000	0.648
Balanced 80|10|10	0.895	0.601	0.976	0.630	0.689	0.625
Balanced 60|30|10	0.897	0.596	0.975	0.617	1.000	0.618
Balanced 30|30|15|15|10	0.883	0.602	0.979	0.682	1.000	0.663
Balanced 60|10|10|10|10	0.874	0.584	0.979	0.682	1.000	0.663

Table 2.15: Best results for plain averaging on NR-AR-LBD (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.908	0.610	0.980	0.730	0.711	0.678
60|40	0.889	0.589	0.976	0.625	0.689	0.633
67|33	0.909	0.612	0.977	0.644	0.711	0.640
75|25	0.911	0.605	0.976	0.625	0.733	0.633
80|20	0.901	0.599	0.977	0.638	0.711	0.640
40|30|30	0.901	0.630	0.974	0.592	0.689	0.603
60|20|20	0.906	0.600	0.975	0.612	1.000	0.625

80|10|10	0.919	0.619	0.980	0.714	0.733	0.671
60|30|10	0.896	0.582	0.974	0.592	0.667	0.605
30|30|15|15|10	0.885	0.616	0.977	0.638	1.000	0.640
60|10|10|10|10	0.898	0.616	0.978	0.683	0.978	0.640

Table 2.16: Best results for weighted averaging on NR-AR-LBD (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.908	0.610	0.980	0.730	0.711	0.678
Clients 2	0.893	0.587	0.975	0.612	1.000	0.625
Clients 3	0.899	0.626	0.970	0.536	1.000	0.587
Clients 4	0.900	0.590	0.974	0.585	1.000	0.619
Clients 5	0.918	0.612	0.974	0.593	1.000	0.633
Clients 6	0.889	0.595	0.969	0.517	1.000	0.567
Clients 7	0.890	0.577	0.967	0.500	1.000	0.555
Clients 8	0.890	0.607	0.966	0.492	1.000	0.557
Clients 9	0.890	0.597	0.968	0.508	1.000	0.561
Clients 10	0.886	0.595	0.972	0.556	1.000	0.591
Clients 11	0.877	0.576	0.969	0.517	1.000	0.567
Clients 12	0.879	0.602	0.964	0.463	1.000	0.535
Clients 13	0.866	0.616	0.967	0.500	1.000	0.563
Clients 14	0.885	0.601	0.973	0.574	1.000	0.612
Clients 15	0.878	0.578	0.966	0.484	1.000	0.543
Clients 16	0.900	0.564	0.964	0.462	1.000	0.527
Clients 17	0.870	0.598	0.966	0.420	1.000	0.488
Clients 18	0.860	0.593	0.973	0.583	1.000	0.588
Clients 19	0.858	0.571	0.964	0.408	1.000	0.491
Clients 20	0.895	0.599	0.974	0.609	1.000	0.602
Epochs 1	0.908	0.668	0.977	0.651	0.756	0.624
Epochs 2	0.901	0.627	0.978	0.675	0.733	0.655
Epochs 5	0.909	0.630	0.979	0.690	1.000	0.656
Epochs 10	0.903	0.606	0.976	0.625	1.000	0.633
Epochs 20	0.906	0.604	0.971	0.545	1.000	0.585

Balanced 60|40	0.885	0.624	0.976	0.625	1.000	0.640
Balanced 67|33	0.899	0.623	0.979	0.682	1.000	0.663
Balanced 75|25	0.897	0.583	0.974	0.604	1.000	0.610
Balanced 80|20	0.881	0.629	0.975	0.608	0.978	0.633
Balanced 40|30|30	0.921	0.643	0.973	0.574	1.000	0.612
Balanced 60|20|20	0.892	0.589	0.974	0.593	1.000	0.633
Balanced 80|10|10	0.878	0.601	0.977	0.633	1.000	0.648
Balanced 60|30|10	0.921	0.592	0.975	0.617	1.000	0.618
Balanced 30|30|15|15|10	0.907	0.618	0.978	0.667	1.000	0.655
Balanced 60|10|10|10|10	0.886	0.581	0.980	0.707	1.000	0.664

Table 2.17: Best results for benchmarked averaging on NR-AR-LBD (Tox21)

2.4.4 Tox21 - NR-AhR

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.900	0.659	0.909	0.655	0.840	0.579
Clients 2	0.893	0.645	0.899	0.565	0.994	0.543
Clients 3	0.894	0.669	0.907	0.598	1.000	0.569
Clients 4	0.896	0.645	0.895	0.545	1.000	0.555
Clients 5	0.890	0.673	0.897	0.555	1.000	0.551
Clients 6	0.888	0.647	0.901	0.571	1.000	0.550
Clients 7	0.886	0.673	0.898	0.556	1.000	0.548
Clients 8	0.896	0.647	0.883	0.505	1.000	0.525
Clients 9	0.894	0.638	0.886	0.512	1.000	0.537
Clients 10	0.883	0.632	0.892	0.532	1.000	0.538
Clients 11	0.886	0.650	0.889	0.521	1.000	0.536
Clients 12	0.884	0.621	0.889	0.522	1.000	0.532
Clients 13	0.888	0.649	0.894	0.540	1.000	0.551
Clients 14	0.886	0.650	0.895	0.547	1.000	0.544
Clients 15	0.887	0.619	0.882	0.500	1.000	0.525
Clients 16	0.890	0.619	0.847	0.418	1.000	0.456
Clients 17	0.890	0.651	0.898	0.554	1.000	0.555

Clients 18	0.889	0.633	0.883	0.504	1.000	0.531
Clients 19	0.886	0.613	0.897	0.556	1.000	0.564
Clients 20	0.886	0.628	0.895	0.547	1.000	0.537
Epochs 1	0.901	0.671	0.914	0.631	0.968	0.590
Epochs 2	0.896	0.672	0.905	0.583	1.000	0.573
Epochs 5	0.897	0.660	0.899	0.564	0.840	0.546
Epochs 10	0.896	0.651	0.901	0.573	0.968	0.562
Epochs 20	0.888	0.648	0.907	0.615	1.000	0.566
Balanced 60|40	0.894	0.681	0.903	0.573	0.801	0.577
Balanced 67|33	0.888	0.638	0.904	0.597	1.000	0.559
Balanced 75|25	0.894	0.663	0.908	0.604	0.782	0.566
Balanced 80|20	0.896	0.680	0.906	0.596	0.763	0.562
Balanced 40|30|30	0.899	0.663	0.905	0.591	1.000	0.564
Balanced 60|20|20	0.889	0.658	0.903	0.579	1.000	0.562
Balanced 80|10|10	0.890	0.664	0.902	0.578	1.000	0.548
Balanced 60|30|10	0.893	0.632	0.905	0.586	1.000	0.575
Balanced 30|30|15|15|10	0.892	0.681	0.904	0.584	1.000	0.564
Balanced 60|10|10|10|10	0.882	0.646	0.889	0.523	1.000	0.521

Table 2.18: Best results for plain averaging on NR-AhR (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.900	0.659	0.909	0.655	0.840	0.579
60|40	0.897	0.688	0.904	0.584	0.929	0.575
67|33	0.891	0.646	0.911	0.624	0.962	0.576
75|25	0.893	0.663	0.905	0.590	0.897	0.566
80|20	0.895	0.645	0.902	0.575	0.814	0.550
40|30|30	0.887	0.657	0.906	0.587	1.000	0.582
60|20|20	0.892	0.674	0.903	0.582	1.000	0.566
80|10|10	0.891	0.645	0.900	0.568	0.897	0.550
60|30|10	0.887	0.655	0.910	0.612	0.776	0.578
30|30|15|15|10	0.900	0.668	0.895	0.543	1.000	0.551
60|10|10|10|10	0.901	0.678	0.905	0.585	0.776	0.582

Table 2.19: Best results for weighted averaging on NR-AhR (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.900	0.659	0.909	0.655	0.840	0.579
Clients 2	0.884	0.660	0.910	0.616	1.000	0.575
Clients 3	0.888	0.657	0.890	0.530	1.000	0.527
Clients 4	0.885	0.653	0.897	0.552	1.000	0.553
Clients 5	0.889	0.634	0.885	0.510	1.000	0.527
Clients 6	0.888	0.657	0.885	0.509	1.000	0.525
Clients 7	0.888	0.654	0.892	0.535	1.000	0.542
Clients 8	0.895	0.667	0.892	0.534	1.000	0.545
Clients 9	0.891	0.650	0.896	0.548	1.000	0.555
Clients 10	0.889	0.678	0.886	0.514	1.000	0.528
Clients 11	0.891	0.649	0.889	0.522	1.000	0.534
Clients 12	0.894	0.645	0.885	0.509	1.000	0.529
Clients 13	0.893	0.662	0.869	0.465	1.000	0.491
Clients 14	0.887	0.646	0.882	0.500	1.000	0.525
Clients 15	0.887	0.634	0.888	0.519	1.000	0.532
Clients 16	0.890	0.653	0.873	0.478	1.000	0.518
Clients 17	0.889	0.635	0.875	0.480	1.000	0.519
Clients 18	0.888	0.650	0.883	0.502	1.000	0.523
Clients 19	0.897	0.646	0.871	0.470	1.000	0.508
Clients 20	0.889	0.615	0.889	0.525	1.000	0.532
Epochs 1	0.903	0.682	0.905	0.587	0.853	0.562
Epochs 2	0.893	0.660	0.902	0.575	0.814	0.555
Epochs 5	0.892	0.667	0.903	0.575	1.000	0.571
Epochs 10	0.891	0.675	0.906	0.593	1.000	0.577
Epochs 20	0.889	0.662	0.908	0.616	1.000	0.576
Balanced 60|40	0.889	0.663	0.901	0.565	1.000	0.573
Balanced 67|33	0.890	0.664	0.899	0.562	1.000	0.566
Balanced 75|25	0.900	0.659	0.905	0.584	1.000	0.580
Balanced 80|20	0.896	0.661	0.904	0.584	1.000	0.559
Balanced 40|30|30	0.889	0.646	0.903	0.574	1.000	0.573
Balanced 60|20|20	0.884	0.634	0.888	0.519	1.000	0.530
Balanced 80|10|10	0.900	0.669	0.905	0.587	1.000	0.573

Balanced 60|30|10	0.894	0.665	0.886	0.514	1.000	0.537
Balanced 30|30|15|15|10	0.891	0.662	0.888	0.519	1.000	0.545
Balanced 60|10|10|10|10	0.896	0.659	0.895	0.548	1.000	0.545

Table 2.20: Best results for benchmarked averaging on NR-AhR (Tox21)

2.4.5 Tox21 - NR-Aromatase

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.913	0.534	0.953	0.556	0.694	0.492
Clients 2	0.893	0.523	0.946	0.485	0.968	0.479
Clients 3	0.881	0.530	0.942	0.451	0.984	0.450
Clients 4	0.875	0.518	0.942	0.451	1.000	0.453
Clients 5	0.859	0.499	0.934	0.407	1.000	0.439
Clients 6	0.878	0.508	0.940	0.443	0.984	0.465
Clients 7	0.870	0.478	0.931	0.383	1.000	0.398
Clients 8	0.867	0.486	0.926	0.341	1.000	0.361
Clients 9	0.884	0.499	0.931	0.375	1.000	0.389
Clients 10	0.876	0.503	0.939	0.362	1.000	0.378
Clients 11	0.872	0.494	0.927	0.330	1.000	0.375
Clients 12	0.856	0.453	0.926	0.315	1.000	0.357
Clients 13	0.858	0.476	0.941	0.295	1.000	0.337
Clients 14	0.838	0.441	0.941	0.306	1.000	0.332
Clients 15	0.865	0.427	0.911	0.264	1.000	0.304
Clients 16	0.870	0.472	0.911	0.227	1.000	0.284
Clients 17	0.845	0.431	0.943	0.280	1.000	0.327
Clients 18	0.848	0.421	0.945	0.286	1.000	0.291
Clients 19	0.855	0.458	0.937	0.298	1.000	0.342
Clients 20	0.871	0.419	0.948	0.500	1.000	0.371
Epochs 1	0.893	0.498	0.939	0.421	0.645	0.431
Epochs 2	0.903	0.532	0.941	0.444	0.613	0.446
Epochs 5	0.879	0.543	0.946	0.487	0.629	0.508
Epochs 10	0.889	0.519	0.945	0.474	0.629	0.439

Epochs 20	0.881	0.540	0.947	0.493	1.000	0.483
Balanced 60|40	0.876	0.500	0.942	0.453	1.000	0.466
Balanced 67|33	0.906	0.552	0.942	0.453	1.000	0.466
Balanced 75|25	0.882	0.512	0.940	0.440	0.645	0.461
Balanced 80|20	0.871	0.533	0.940	0.437	0.597	0.434
Balanced 40|30|30	0.883	0.497	0.942	0.455	1.000	0.446
Balanced 60|20|20	0.876	0.511	0.947	0.492	0.968	0.460
Balanced 80|10|10	0.869	0.510	0.942	0.457	0.903	0.458
Balanced 60|30|10	0.874	0.531	0.941	0.449	1.000	0.469
Balanced 30|30|15|15|10	0.871	0.482	0.933	0.384	1.000	0.390
Balanced 60|10|10|10|10	0.867	0.536	0.947	0.493	1.000	0.498

Table 2.21: Best results for plain averaging on NR-Aromatase (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.913	0.534	0.953	0.556	0.694	0.492
60|40	0.887	0.489	0.946	0.485	0.839	0.471
67|33	0.869	0.476	0.943	0.456	0.871	0.407
75|25	0.874	0.484	0.946	0.484	0.581	0.455
80|20	0.881	0.520	0.937	0.419	0.613	0.427
40|30|30	0.884	0.496	0.933	0.395	0.968	0.413
60|20|20	0.881	0.509	0.936	0.405	0.935	0.407
80|10|10	0.872	0.473	0.943	0.458	0.597	0.426
60|30|10	0.873	0.528	0.948	0.508	0.581	0.477
30|30|15|15|10	0.864	0.447	0.942	0.453	1.000	0.435
60|10|10|10|10	0.892	0.505	0.943	0.462	0.871	0.443

Table 2.22: Best results for weighted averaging on NR-Aromatase (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.913	0.534	0.953	0.556	0.694	0.492
Clients 2	0.883	0.529	0.937	0.418	1.000	0.435

Clients 3	0.885	0.461	0.937	0.416	1.000	0.431
Clients 4	0.890	0.536	0.942	0.451	1.000	0.450
Clients 5	0.879	0.462	0.926	0.337	1.000	0.348
Clients 6	0.874	0.417	0.904	0.284	1.000	0.340
Clients 7	0.873	0.459	0.921	0.343	1.000	0.383
Clients 8	0.878	0.452	0.931	0.375	1.000	0.386
Clients 9	0.887	0.456	0.922	0.337	1.000	0.363
Clients 10	0.869	0.415	0.899	0.258	1.000	0.305
Clients 11	0.876	0.416	0.926	0.305	1.000	0.329
Clients 12	0.887	0.441	0.904	0.289	1.000	0.349
Clients 13	0.873	0.449	0.928	0.300	1.000	0.334
Clients 14	0.861	0.434	0.937	0.295	1.000	0.334
Clients 15	0.871	0.402	0.909	0.261	1.000	0.299
Clients 16	0.861	0.409	0.904	0.272	1.000	0.323
Clients 17	0.840	0.410	0.946	0.333	1.000	0.284
Clients 18	0.860	0.456	0.944	0.268	1.000	0.297
Clients 19	0.859	0.440	0.925	0.248	1.000	0.299
Clients 20	0.854	0.398	0.937	0.241	1.000	0.280
Epochs 1	0.909	0.520	0.942	0.455	0.645	0.438
Epochs 2	0.907	0.544	0.940	0.434	0.710	0.464
Epochs 5	0.902	0.535	0.947	0.492	0.645	0.476
Epochs 10	0.880	0.485	0.942	0.449	1.000	0.442
Epochs 20	0.887	0.529	0.949	0.517	1.000	0.481
Balanced 60|40	0.894	0.477	0.939	0.429	1.000	0.439
Balanced 67|33	0.901	0.542	0.942	0.463	1.000	0.491
Balanced 75|25	0.906	0.539	0.950	0.523	0.984	0.509
Balanced 80|20	0.894	0.537	0.941	0.433	1.000	0.431
Balanced 40|30|30	0.889	0.459	0.943	0.453	1.000	0.410
Balanced 60|20|20	0.882	0.481	0.925	0.341	1.000	0.369
Balanced 80|10|10	0.877	0.511	0.934	0.392	1.000	0.392
Balanced 60|30|10	0.886	0.498	0.933	0.387	1.000	0.390
Balanced 30|30|15|15|10	0.891	0.493	0.928	0.371	1.000	0.411
Balanced 60|10|10|10|10	0.893	0.517	0.932	0.393	1.000	0.418

Table 2.23: Best results for benchmarked averaging on NR-Aromatase (Tox21)

2.4.6 Tox21 - NR-ER

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.738	0.444	0.865	0.465	0.699	0.335
Clients 2	0.728	0.437	0.818	0.340	1.000	0.283
Clients 3	0.719	0.443	0.816	0.340	1.000	0.294
Clients 4	0.713	0.430	0.807	0.322	1.000	0.273
Clients 5	0.716	0.440	0.841	0.367	1.000	0.293
Clients 6	0.724	0.445	0.827	0.356	1.000	0.307
Clients 7	0.719	0.439	0.825	0.359	1.000	0.302
Clients 8	0.726	0.410	0.827	0.305	1.000	0.259
Clients 9	0.734	0.431	0.838	0.346	1.000	0.275
Clients 10	0.734	0.416	0.860	0.379	1.000	0.261
Clients 11	0.727	0.416	0.820	0.338	1.000	0.270
Clients 12	0.721	0.408	0.807	0.321	1.000	0.265
Clients 13	0.721	0.416	0.861	0.414	1.000	0.273
Clients 14	0.726	0.405	0.828	0.319	1.000	0.261
Clients 15	0.730	0.426	0.803	0.319	1.000	0.273
Clients 16	0.723	0.403	0.765	0.260	1.000	0.226
Clients 17	0.710	0.411	0.847	0.330	1.000	0.254
Clients 18	0.723	0.410	0.834	0.353	1.000	0.290
Clients 19	0.721	0.411	0.837	0.322	1.000	0.248
Clients 20	0.729	0.396	0.860	0.419	1.000	0.270
Epochs 1	0.718	0.442	0.829	0.363	0.957	0.296
Epochs 2	0.732	0.424	0.819	0.333	0.939	0.282
Epochs 5	0.725	0.441	0.826	0.360	0.939	0.298
Epochs 10	0.723	0.444	0.823	0.361	0.951	0.310
Epochs 20	0.731	0.427	0.833	0.367	0.994	0.309
Balanced 60|40	0.716	0.430	0.827	0.360	0.693	0.295
Balanced 67|33	0.722	0.436	0.835	0.381	1.000	0.314
Balanced 75|25	0.718	0.439	0.813	0.330	1.000	0.277
Balanced 80|20	0.734	0.407	0.792	0.301	1.000	0.249
Balanced 40|30|30	0.702	0.428	0.829	0.343	1.000	0.273

Balanced 60|20|20	0.709	0.446	0.834	0.380	0.988	0.329
Balanced 80|10|10	0.714	0.423	0.816	0.330	1.000	0.261
Balanced 60|30|10	0.714	0.427	0.818	0.338	1.000	0.273
Balanced 30|30|15|15|10	0.714	0.430	0.834	0.353	1.000	0.262
Balanced 60|10|10|10|10	0.720	0.406	0.810	0.318	1.000	0.249

Table 2.24: Best results for plain averaging on NR-ER (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.738	0.444	0.865	0.465	0.699	0.335
60|40	0.732	0.456	0.830	0.369	0.926	0.304
67|33	0.727	0.429	0.819	0.347	0.914	0.291
75|25	0.723	0.446	0.822	0.348	0.546	0.284
80|20	0.724	0.441	0.865	0.451	0.558	0.299
40|30|30	0.716	0.426	0.806	0.315	1.000	0.264
60|20|20	0.705	0.419	0.826	0.344	1.000	0.261
80|10|10	0.714	0.452	0.834	0.372	0.564	0.297
60|30|10	0.708	0.430	0.816	0.329	0.975	0.282
30|30|15|15|10	0.712	0.437	0.818	0.342	1.000	0.292
60|10|10|10|10	0.706	0.427	0.829	0.361	0.945	0.302

Table 2.25: Best results for weighted averaging on NR-ER (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.738	0.444	0.865	0.465	0.699	0.335
Clients 2	0.727	0.432	0.815	0.332	1.000	0.279
Clients 3	0.723	0.446	0.800	0.320	1.000	0.276
Clients 4	0.717	0.425	0.796	0.312	1.000	0.264
Clients 5	0.720	0.450	0.799	0.318	1.000	0.276
Clients 6	0.717	0.410	0.761	0.274	1.000	0.227
Clients 7	0.720	0.422	0.809	0.325	1.000	0.276
Clients 8	0.724	0.421	0.811	0.332	1.000	0.286

Clients 9	0.714	0.416	0.794	0.302	1.000	0.246
Clients 10	0.730	0.418	0.797	0.313	1.000	0.264
Clients 11	0.718	0.404	0.819	0.328	1.000	0.280
Clients 12	0.719	0.407	0.793	0.291	1.000	0.237
Clients 13	0.723	0.393	0.794	0.274	1.000	0.217
Clients 14	0.719	0.406	0.819	0.300	1.000	0.254
Clients 15	0.726	0.398	0.809	0.312	1.000	0.247
Clients 16	0.720	0.395	0.738	0.253	1.000	0.213
Clients 17	0.716	0.410	0.845	0.291	1.000	0.243
Clients 18	0.722	0.396	0.828	0.315	1.000	0.254
Clients 19	0.719	0.398	0.744	0.273	1.000	0.238
Clients 20	0.711	0.393	0.815	0.339	1.000	0.284
Epochs 1	0.724	0.438	0.817	0.343	0.632	0.286
Epochs 2	0.743	0.446	0.816	0.351	0.975	0.312
Epochs 5	0.727	0.439	0.811	0.338	0.988	0.293
Epochs 10	0.722	0.423	0.829	0.349	1.000	0.269
Epochs 20	0.740	0.432	0.830	0.358	1.000	0.286
Balanced 60|40	0.720	0.431	0.820	0.346	1.000	0.285
Balanced 67|33	0.732	0.431	0.819	0.332	1.000	0.272
Balanced 75|25	0.741	0.450	0.815	0.344	1.000	0.292
Balanced 80|20	0.731	0.431	0.800	0.316	1.000	0.270
Balanced 40|30|30	0.733	0.447	0.803	0.324	1.000	0.285
Balanced 60|20|20	0.723	0.427	0.797	0.312	1.000	0.261
Balanced 80|10|10	0.717	0.426	0.801	0.302	1.000	0.253
Balanced 60|30|10	0.732	0.431	0.792	0.314	1.000	0.276
Balanced 30|30|15|15|10	0.721	0.434	0.801	0.300	1.000	0.250
Balanced 60|10|10|10|10	0.715	0.442	0.800	0.311	1.000	0.253

Table 2.26: Best results for benchmarked averaging on NR-ER (Tox21)

2.4.7 Tox21 - NR-ER-LBD

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa

Baseline	0.838	0.448	0.947	0.581	0.530	0.431
Clients 2	0.817	0.479	0.941	0.500	0.952	0.427
Clients 3	0.814	0.449	0.933	0.432	0.952	0.413
Clients 4	0.830	0.452	0.934	0.433	0.988	0.415
Clients 5	0.804	0.457	0.936	0.457	1.000	0.424
Clients 6	0.820	0.459	0.935	0.446	1.000	0.411
Clients 7	0.803	0.459	0.936	0.459	1.000	0.443
Clients 8	0.813	0.460	0.934	0.414	1.000	0.413
Clients 9	0.803	0.447	0.934	0.412	1.000	0.407
Clients 10	0.817	0.466	0.937	0.459	1.000	0.430
Clients 11	0.807	0.456	0.929	0.410	1.000	0.410
Clients 12	0.801	0.428	0.934	0.385	1.000	0.388
Clients 13	0.788	0.411	0.939	0.412	1.000	0.357
Clients 14	0.800	0.426	0.936	0.336	1.000	0.351
Clients 15	0.798	0.410	0.924	0.361	1.000	0.366
Clients 16	0.801	0.362	0.922	0.236	1.000	0.268
Clients 17	0.775	0.398	0.938	0.370	1.000	0.348
Clients 18	0.809	0.429	0.939	0.383	1.000	0.398
Clients 19	0.792	0.403	0.934	0.322	1.000	0.336
Clients 20	0.791	0.413	0.941	1.000	1.000	0.383
Epochs 1	0.824	0.478	0.941	0.493	0.566	0.451
Epochs 2	0.827	0.481	0.931	0.430	0.795	0.434
Epochs 5	0.821	0.454	0.938	0.468	0.554	0.436
Epochs 10	0.838	0.444	0.935	0.442	0.506	0.396
Epochs 20	0.830	0.432	0.939	0.481	0.988	0.430
Balanced 60|40	0.830	0.490	0.937	0.465	0.976	0.440
Balanced 67|33	0.818	0.487	0.943	0.512	0.976	0.473
Balanced 75|25	0.817	0.490	0.938	0.473	0.976	0.464
Balanced 80|20	0.824	0.469	0.936	0.456	0.976	0.431
Balanced 40|30|30	0.822	0.470	0.934	0.449	1.000	0.451
Balanced 60|20|20	0.819	0.474	0.942	0.506	0.976	0.463
Balanced 80|10|10	0.820	0.493	0.943	0.513	0.976	0.469
Balanced 60|30|10	0.804	0.453	0.932	0.424	0.976	0.392
Balanced 30|30|15|15|10	0.817	0.458	0.936	0.455	0.988	0.442

Balanced 60|10|10|10|10	0.809	0.469	0.941	0.493	1.000	0.430

Table 2.27: Best results for plain averaging on NR-ER-LBD (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.838	0.448	0.947	0.581	0.530	0.431
60|40	0.837	0.460	0.936	0.457	0.711	0.452
67|33	0.799	0.471	0.943	0.515	0.542	0.427
75|25	0.797	0.452	0.936	0.458	0.566	0.451
80|20	0.819	0.454	0.937	0.398	0.542	0.392
40|30|30	0.817	0.465	0.934	0.441	0.988	0.431
60|20|20	0.808	0.463	0.935	0.448	0.952	0.424
80|10|10	0.807	0.467	0.941	0.481	0.566	0.443
60|30|10	0.812	0.434	0.934	0.442	0.506	0.415
30|30|15|15|10	0.834	0.483	0.942	0.507	1.000	0.475
60|10|10|10|10	0.789	0.462	0.940	0.488	0.904	0.453

Table 2.28: Best results for weighted averaging on NR-ER-LBD (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.838	0.448	0.947	0.581	0.530	0.431
Clients 2	0.841	0.478	0.934	0.430	1.000	0.436
Clients 3	0.819	0.442	0.930	0.417	1.000	0.410
Clients 4	0.813	0.463	0.928	0.404	1.000	0.404
Clients 5	0.840	0.472	0.927	0.400	1.000	0.417
Clients 6	0.795	0.480	0.912	0.331	1.000	0.350
Clients 7	0.804	0.431	0.921	0.362	1.000	0.374
Clients 8	0.816	0.433	0.934	0.343	1.000	0.353
Clients 9	0.811	0.428	0.923	0.375	1.000	0.376
Clients 10	0.812	0.411	0.923	0.377	1.000	0.383
Clients 11	0.815	0.436	0.934	0.380	1.000	0.383
Clients 12	0.807	0.428	0.919	0.342	1.000	0.359

Clients 13	0.794	0.424	0.931	0.342	1.000	0.364
Clients 14	0.801	0.430	0.932	0.354	1.000	0.376
Clients 15	0.801	0.430	0.930	0.368	1.000	0.359
Clients 16	0.793	0.394	0.931	0.303	1.000	0.333
Clients 17	0.788	0.377	0.939	0.349	1.000	0.353
Clients 18	0.787	0.406	0.941	0.369	1.000	0.381
Clients 19	0.801	0.345	0.935	0.301	1.000	0.321
Clients 20	0.795	0.402	0.936	0.342	1.000	0.353
Epochs 1	0.822	0.461	0.935	0.414	0.771	0.413
Epochs 2	0.820	0.460	0.934	0.442	0.566	0.415
Epochs 5	0.824	0.457	0.934	0.438	0.988	0.415
Epochs 10	0.825	0.455	0.941	0.493	1.000	0.443
Epochs 20	0.827	0.447	0.935	0.448	0.964	0.424
Balanced 60|40	0.814	0.471	0.938	0.463	0.952	0.418
Balanced 67|33	0.813	0.469	0.936	0.453	0.988	0.427
Balanced 75|25	0.840	0.475	0.936	0.456	1.000	0.445
Balanced 80|20	0.823	0.460	0.932	0.432	0.988	0.425
Balanced 40|30|30	0.818	0.481	0.931	0.420	1.000	0.415
Balanced 60|20|20	0.832	0.442	0.928	0.406	1.000	0.407
Balanced 80|10|10	0.841	0.478	0.945	0.535	1.000	0.465
Balanced 60|30|10	0.826	0.454	0.923	0.380	1.000	0.401
Balanced 30|30|15|15|10	0.830	0.457	0.927	0.396	1.000	0.395
Balanced 60|10|10|10|10	0.808	0.480	0.936	0.462	1.000	0.457

Table 2.29: Best results for benchmarked averaging on NR-ER-LBD (Tox21)

2.4.8 Tox21 - NR-PPAR-gamma

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.897	0.394	0.973	0.556	0.621	0.433
Clients 2	0.863	0.414	0.967	0.429	0.973	0.439
Clients 3	0.884	0.425	0.961	0.362	0.973	0.422
Clients 4	0.832	0.366	0.964	0.311	0.973	0.365
Clients 5	0.845	0.375	0.960	0.310	0.973	0.357

Clients 6	0.844	0.345	0.963	0.312	0.973	0.349
Clients 7	0.828	0.350	0.960	0.296	0.973	0.335
Clients 8	0.849	0.347	0.966	0.262	1.000	0.302
Clients 9	0.849	0.378	0.964	0.333	0.973	0.375
Clients 10	0.844	0.382	0.969	0.359	1.000	0.384
Clients 11	0.835	0.428	0.965	0.263	0.973	0.317
Clients 12	0.828	0.280	0.968	0.286	1.000	0.335
Clients 13	0.822	0.292	0.969	0.290	1.000	0.340
Clients 14	0.845	0.284	0.966	0.302	1.000	0.323
Clients 15	0.840	0.308	0.968	0.295	1.000	0.308
Clients 16	0.843	0.343	0.966	0.239	1.000	0.288
Clients 17	0.802	0.278	0.969	0.350	1.000	0.356
Clients 18	0.814	0.294	0.970	0.304	1.000	0.343
Clients 19	0.838	0.340	0.969	0.314	1.000	0.342
Clients 20	0.841	0.263	0.972	1.000	1.000	0.329
Epochs 1	0.869	0.464	0.969	0.439	0.622	0.445
Epochs 2	0.868	0.384	0.970	0.450	0.622	0.435
Epochs 5	0.859	0.407	0.962	0.349	0.568	0.361
Epochs 10	0.871	0.384	0.965	0.385	0.838	0.377
Epochs 20	0.848	0.313	0.959	0.293	0.919	0.317
Balanced 60|40	0.841	0.417	0.968	0.366	0.595	0.388
Balanced 67|33	0.848	0.352	0.963	0.324	0.838	0.342
Balanced 75|25	0.827	0.368	0.952	0.286	0.730	0.342
Balanced 80|20	0.867	0.369	0.962	0.362	0.946	0.388
Balanced 40|30|30	0.859	0.353	0.959	0.319	0.973	0.350
Balanced 60|20|20	0.837	0.400	0.966	0.409	0.784	0.427
Balanced 80|10|10	0.840	0.340	0.960	0.326	0.649	0.341
Balanced 60|30|10	0.852	0.351	0.969	0.423	0.919	0.375
Balanced 30|30|15|15|10	0.819	0.387	0.968	0.311	1.000	0.365
Balanced 60|10|10|10|10	0.845	0.343	0.962	0.324	0.973	0.323

Table 2.30: Best results for plain averaging on NR-PPAR-gamma (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa

Baseline	0.897	0.394	0.973	0.556	0.621	0.433
60|40	0.845	0.405	0.969	0.444	0.919	0.431
67|33	0.854	0.405	0.972	1.000	0.595	0.394
75|25	0.855	0.348	0.972	0.500	0.595	0.396
80|20	0.863	0.389	0.969	0.346	0.541	0.384
40|30|30	0.877	0.388	0.957	0.310	0.865	0.361
60|20|20	0.840	0.399	0.963	0.340	0.568	0.403
80|10|10	0.843	0.366	0.967	0.394	0.568	0.354
60|30|10	0.866	0.372	0.968	0.347	0.622	0.375
30|30|15|15|10	0.824	0.400	0.966	0.346	0.973	0.365
60|10|10|10|10	0.850	0.359	0.966	0.375	0.892	0.346

Table 2.31: Best results for weighted averaging on NR-PPAR-gamma (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.897	0.394	0.973	0.556	0.621	0.433
Clients 2	0.879	0.340	0.963	0.364	1.000	0.376
Clients 3	0.877	0.354	0.963	0.350	1.000	0.361
Clients 4	0.850	0.356	0.957	0.292	1.000	0.313
Clients 5	0.851	0.328	0.944	0.227	1.000	0.273
Clients 6	0.876	0.359	0.936	0.224	1.000	0.283
Clients 7	0.839	0.344	0.957	0.263	1.000	0.305
Clients 8	0.838	0.324	0.964	0.217	1.000	0.265
Clients 9	0.881	0.312	0.950	0.277	1.000	0.329
Clients 10	0.859	0.331	0.947	0.234	1.000	0.289
Clients 11	0.852	0.317	0.961	0.241	1.000	0.311
Clients 12	0.868	0.338	0.950	0.253	1.000	0.328
Clients 13	0.825	0.337	0.967	0.213	1.000	0.266
Clients 14	0.856	0.327	0.963	0.230	1.000	0.279
Clients 15	0.836	0.351	0.964	0.256	1.000	0.322
Clients 16	0.849	0.292	0.956	0.242	1.000	0.277
Clients 17	0.825	0.268	0.970	0.176	1.000	0.230
Clients 18	0.816	0.336	0.971	0.350	1.000	0.344

Clients 19	0.841	0.315	0.966	0.209	1.000	0.267
Clients 20	0.827	0.259	0.967	0.217	1.000	0.272
Epochs 1	0.907	0.410	0.972	0.500	0.649	0.399
Epochs 2	0.885	0.439	0.967	0.393	0.595	0.380
Epochs 5	0.885	0.391	0.967	0.372	0.649	0.381
Epochs 10	0.840	0.360	0.962	0.348	1.000	0.383
Epochs 20	0.872	0.350	0.957	0.293	0.973	0.335
Balanced 60|40	0.866	0.370	0.962	0.362	1.000	0.387
Balanced 67|33	0.869	0.391	0.960	0.347	0.649	0.379
Balanced 75|25	0.885	0.423	0.966	0.400	0.973	0.413
Balanced 80|20	0.868	0.407	0.955	0.317	1.000	0.370
Balanced 40|30|30	0.896	0.414	0.953	0.269	1.000	0.333
Balanced 60|20|20	0.860	0.374	0.949	0.282	1.000	0.369
Balanced 80|10|10	0.864	0.334	0.954	0.283	0.973	0.314
Balanced 60|30|10	0.887	0.373	0.957	0.328	0.973	0.385
Balanced 30|30|15|15|10	0.872	0.360	0.952	0.260	1.000	0.320
Balanced 60|10|10|10|10	0.886	0.423	0.960	0.361	1.000	0.429

Table 2.32: Best results for benchmarked averaging on NR-PPAR-gamma (Tox21)

2.4.9 Tox21 - SR-ARE

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.844	0.553	0.844	0.491	0.842	0.446
Clients 2	0.845	0.550	0.836	0.472	1.000	0.437
Clients 3	0.840	0.546	0.832	0.462	1.000	0.418
Clients 4	0.830	0.563	0.837	0.475	1.000	0.448
Clients 5	0.836	0.537	0.831	0.460	1.000	0.434
Clients 6	0.834	0.537	0.824	0.445	1.000	0.419
Clients 7	0.830	0.520	0.838	0.476	1.000	0.436
Clients 8	0.838	0.521	0.810	0.426	1.000	0.420
Clients 9	0.836	0.527	0.836	0.474	1.000	0.457
Clients 10	0.834	0.553	0.837	0.476	1.000	0.457

Clients 11	0.826	0.515	0.834	0.469	1.000	0.445
Clients 12	0.823	0.518	0.825	0.442	1.000	0.409
Clients 13	0.826	0.525	0.837	0.475	1.000	0.462
Clients 14	0.832	0.520	0.830	0.459	1.000	0.446
Clients 15	0.832	0.503	0.810	0.421	1.000	0.408
Clients 16	0.815	0.432	0.740	0.344	1.000	0.336
Clients 17	0.826	0.499	0.839	0.479	1.000	0.443
Clients 18	0.836	0.506	0.831	0.462	1.000	0.442
Clients 19	0.826	0.516	0.840	0.481	1.000	0.434
Clients 20	0.829	0.506	0.827	0.454	1.000	0.429
Epochs 1	0.847	0.561	0.827	0.450	0.831	0.425
Epochs 2	0.846	0.565	0.822	0.447	0.944	0.438
Epochs 5	0.832	0.558	0.840	0.481	0.977	0.437
Epochs 10	0.841	0.557	0.839	0.477	1.000	0.444
Epochs 20	0.835	0.547	0.837	0.474	1.000	0.441
Balanced 60|40	0.824	0.525	0.832	0.463	0.966	0.423
Balanced 67|33	0.846	0.571	0.825	0.450	1.000	0.441
Balanced 75|25	0.842	0.534	0.820	0.438	1.000	0.432
Balanced 80|20	0.851	0.562	0.833	0.466	1.000	0.436
Balanced 40|30|30	0.830	0.549	0.832	0.460	1.000	0.422
Balanced 60|20|20	0.838	0.543	0.835	0.468	0.977	0.431
Balanced 80|10|10	0.833	0.547	0.822	0.443	1.000	0.431
Balanced 60|30|10	0.834	0.551	0.831	0.461	1.000	0.431
Balanced 30|30|15|15|10	0.834	0.541	0.835	0.470	1.000	0.437
Balanced 60|10|10|10|10	0.829	0.557	0.834	0.465	1.000	0.419

Table 2.33: Best results for plain averaging on SR-ARE (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.844	0.553	0.844	0.491	0.842	0.446
60|40	0.842	0.550	0.835	0.468	1.000	0.451
67|33	0.845	0.528	0.829	0.455	0.989	0.423
75|25	0.847	0.546	0.839	0.479	0.972	0.433
80|20	0.844	0.515	0.820	0.438	0.785	0.428

40|30|30	0.837	0.532	0.829	0.455	1.000	0.413
60|20|20	0.839	0.548	0.826	0.450	1.000	0.423
80|10|10	0.857	0.567	0.835	0.468	0.791	0.465
60|30|10	0.850	0.566	0.836	0.471	0.915	0.433
30|30|15|15|10	0.833	0.541	0.834	0.463	1.000	0.412
60|10|10|10|10	0.841	0.557	0.836	0.469	1.000	0.428

Table 2.34: Best results for weighted averaging on SR-ARE (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.844	0.553	0.844	0.491	0.842	0.446
Clients 2	0.832	0.527	0.844	0.491	1.000	0.444
Clients 3	0.839	0.521	0.826	0.449	1.000	0.425
Clients 4	0.834	0.521	0.828	0.455	1.000	0.423
Clients 5	0.838	0.514	0.806	0.412	1.000	0.401
Clients 6	0.832	0.524	0.795	0.404	1.000	0.401
Clients 7	0.837	0.543	0.811	0.424	1.000	0.406
Clients 8	0.834	0.528	0.809	0.421	1.000	0.403
Clients 9	0.841	0.532	0.815	0.432	1.000	0.416
Clients 10	0.825	0.504	0.793	0.396	1.000	0.380
Clients 11	0.833	0.507	0.807	0.415	1.000	0.397
Clients 12	0.832	0.509	0.801	0.413	1.000	0.410
Clients 13	0.822	0.494	0.813	0.422	1.000	0.391
Clients 14	0.841	0.521	0.818	0.438	1.000	0.425
Clients 15	0.831	0.499	0.804	0.410	1.000	0.402
Clients 16	0.819	0.488	0.785	0.387	1.000	0.380
Clients 17	0.828	0.501	0.775	0.376	1.000	0.368
Clients 18	0.825	0.504	0.813	0.428	1.000	0.420
Clients 19	0.833	0.469	0.796	0.407	1.000	0.406
Clients 20	0.828	0.466	0.796	0.403	1.000	0.395
Epochs 1	0.844	0.551	0.823	0.444	1.000	0.420
Epochs 2	0.848	0.566	0.826	0.452	1.000	0.438
Epochs 5	0.841	0.542	0.832	0.462	1.000	0.436

Epochs 10	0.834	0.555	0.839	0.480	1.000	0.439
Epochs 20	0.829	0.557	0.822	0.440	1.000	0.413
Balanced 60|40	0.833	0.533	0.822	0.445	1.000	0.428
Balanced 67|33	0.836	0.530	0.829	0.457	1.000	0.430
Balanced 75|25	0.842	0.538	0.830	0.457	1.000	0.420
Balanced 80|20	0.846	0.537	0.826	0.452	1.000	0.443
Balanced 40|30|30	0.843	0.545	0.813	0.425	1.000	0.412
Balanced 60|20|20	0.849	0.546	0.816	0.428	1.000	0.406
Balanced 80|10|10	0.851	0.541	0.815	0.428	1.000	0.423
Balanced 60|30|10	0.836	0.559	0.832	0.463	1.000	0.439
Balanced 30|30|15|15|10	0.838	0.538	0.821	0.441	1.000	0.414
Balanced 60|10|10|10|10	0.839	0.515	0.813	0.424	1.000	0.390

Table 2.35: Best results for benchmarked averaging on SR-ARE (Tox21)

2.4.10 Tox21 - SR-ATAD5

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.918	0.464	0.968	0.571	0.635	0.494
Clients 2	0.899	0.457	0.957	0.418	0.769	0.415
Clients 3	0.911	0.473	0.951	0.382	0.962	0.429
Clients 4	0.895	0.442	0.957	0.418	0.981	0.431
Clients 5	0.883	0.457	0.950	0.366	0.981	0.406
Clients 6	0.876	0.413	0.948	0.326	1.000	0.382
Clients 7	0.885	0.441	0.950	0.354	0.981	0.401
Clients 8	0.880	0.399	0.955	0.295	1.000	0.342
Clients 9	0.892	0.434	0.949	0.298	1.000	0.367
Clients 10	0.873	0.436	0.960	0.346	1.000	0.389
Clients 11	0.877	0.407	0.954	0.309	1.000	0.347
Clients 12	0.848	0.377	0.947	0.300	1.000	0.334
Clients 13	0.878	0.441	0.956	0.281	1.000	0.334
Clients 14	0.893	0.441	0.957	0.299	1.000	0.345
Clients 15	0.860	0.381	0.956	0.272	1.000	0.316
Clients 16	0.865	0.336	0.946	0.206	1.000	0.254

Clients 17	0.860	0.366	0.959	0.346	1.000	0.389
Clients 18	0.875	0.382	0.961	0.293	1.000	0.345
Clients 19	0.848	0.391	0.957	0.301	1.000	0.329
Clients 20	0.863	0.350	0.964	1.000	1.000	0.335
Epochs 1	0.917	0.509	0.958	0.431	0.769	0.437
Epochs 2	0.908	0.511	0.959	0.436	0.654	0.461
Epochs 5	0.904	0.481	0.957	0.419	0.673	0.473
Epochs 10	0.913	0.436	0.957	0.429	0.692	0.448
Epochs 20	0.890	0.432	0.960	0.456	1.000	0.456
Balanced 60|40	0.896	0.445	0.954	0.394	0.673	0.417
Balanced 67|33	0.893	0.456	0.960	0.444	0.712	0.453
Balanced 75|25	0.889	0.505	0.957	0.429	0.962	0.457
Balanced 80|20	0.904	0.507	0.962	0.472	0.673	0.475
Balanced 40|30|30	0.919	0.480	0.952	0.390	1.000	0.441
Balanced 60|20|20	0.893	0.451	0.955	0.417	0.942	0.461
Balanced 80|10|10	0.910	0.500	0.949	0.367	0.846	0.417
Balanced 60|30|10	0.888	0.482	0.953	0.389	0.981	0.435
Balanced 30|30|15|15|10	0.892	0.455	0.958	0.310	1.000	0.353
Balanced 60|10|10|10|10	0.881	0.416	0.948	0.333	0.981	0.381

Table 2.36: Best results for plain averaging on SR-ATAD5 (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.918	0.464	0.968	0.571	0.635	0.494
60|40	0.897	0.472	0.957	0.422	0.712	0.446
67|33	0.909	0.473	0.958	0.438	0.962	0.461
75|25	0.899	0.453	0.956	0.397	0.615	0.413
80|20	0.906	0.487	0.960	0.456	0.654	0.456
40|30|30	0.908	0.484	0.952	0.373	0.962	0.410
60|20|20	0.898	0.491	0.957	0.422	0.962	0.443
80|10|10	0.908	0.467	0.962	0.467	0.635	0.469
60|30|10	0.895	0.473	0.957	0.417	0.962	0.424
30|30|15|15|10	0.898	0.460	0.949	0.346	0.981	0.394
60|10|10|10|10	0.887	0.481	0.955	0.409	0.865	0.435

Table 2.37: Best results for weighted averaging on SR-ATAD5 (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.918	0.464	0.968	0.571	0.635	0.494
Clients 2	0.912	0.456	0.954	0.391	1.000	0.429
Clients 3	0.897	0.427	0.951	0.371	1.000	0.401
Clients 4	0.892	0.419	0.947	0.354	1.000	0.406
Clients 5	0.891	0.464	0.938	0.297	0.981	0.374
Clients 6	0.884	0.417	0.931	0.276	1.000	0.344
Clients 7	0.882	0.397	0.943	0.310	1.000	0.372
Clients 8	0.890	0.436	0.942	0.324	1.000	0.400
Clients 9	0.893	0.399	0.933	0.277	1.000	0.334
Clients 10	0.867	0.375	0.939	0.266	1.000	0.341
Clients 11	0.887	0.407	0.952	0.248	1.000	0.318
Clients 12	0.873	0.422	0.946	0.277	1.000	0.346
Clients 13	0.867	0.412	0.948	0.238	1.000	0.301
Clients 14	0.888	0.350	0.956	0.245	1.000	0.299
Clients 15	0.863	0.357	0.950	0.301	1.000	0.341
Clients 16	0.864	0.358	0.945	0.206	1.000	0.254
Clients 17	0.880	0.401	0.962	0.269	1.000	0.330
Clients 18	0.861	0.454	0.963	0.315	1.000	0.368
Clients 19	0.865	0.444	0.956	0.227	1.000	0.285
Clients 20	0.881	0.445	0.958	0.318	1.000	0.379
Epochs 1	0.905	0.487	0.963	0.400	0.673	0.414
Epochs 2	0.896	0.468	0.957	0.424	0.635	0.452
Epochs 5	0.902	0.445	0.958	0.420	0.962	0.418
Epochs 10	0.909	0.445	0.952	0.387	0.981	0.432
Epochs 20	0.896	0.422	0.956	0.407	1.000	0.433
Balanced 60|40	0.884	0.435	0.952	0.373	1.000	0.396
Balanced 67|33	0.907	0.454	0.955	0.403	0.885	0.420
Balanced 75|25	0.910	0.481	0.956	0.418	1.000	0.448
Balanced 80|20	0.911	0.471	0.955	0.403	0.981	0.416
Balanced 40|30|30	0.911	0.461	0.946	0.346	1.000	0.394
Balanced 60|20|20	0.903	0.444	0.940	0.307	1.000	0.376
Balanced 80|10|10	0.920	0.470	0.954	0.400	1.000	0.436

Balanced 60|30|10	0.919	0.442	0.948	0.347	0.981	0.388
Balanced 30|30|15|15|10	0.909	0.450	0.941	0.330	1.000	0.396
Balanced 60|10|10|10|10	0.891	0.449	0.952	0.380	1.000	0.415

Table 2.38: Best results for benchmarked averaging on SR-ATAD5 (Tox21)

2.4.11 Tox21 - SR-HSE

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.855	0.435	0.949	0.625	0.662	0.481
Clients 2	0.842	0.431	0.938	0.481	1.000	0.421
Clients 3	0.840	0.432	0.943	0.528	1.000	0.480
Clients 4	0.859	0.389	0.935	0.460	1.000	0.453
Clients 5	0.835	0.417	0.942	0.517	1.000	0.455
Clients 6	0.831	0.424	0.940	0.500	1.000	0.451
Clients 7	0.820	0.387	0.927	0.404	1.000	0.395
Clients 8	0.824	0.413	0.930	0.420	1.000	0.415
Clients 9	0.821	0.374	0.930	0.411	1.000	0.375
Clients 10	0.794	0.322	0.938	0.403	1.000	0.364
Clients 11	0.806	0.401	0.930	0.420	1.000	0.396
Clients 12	0.808	0.371	0.937	0.471	1.000	0.408
Clients 13	0.807	0.373	0.930	0.418	1.000	0.386
Clients 14	0.824	0.379	0.935	0.398	1.000	0.373
Clients 15	0.810	0.350	0.920	0.367	1.000	0.372
Clients 16	0.822	0.365	0.920	0.270	1.000	0.307
Clients 17	0.806	0.337	0.935	0.372	1.000	0.334
Clients 18	0.808	0.346	0.938	0.354	1.000	0.320
Clients 19	0.802	0.341	0.924	0.353	1.000	0.334
Clients 20	0.806	0.307	0.940	1.000	1.000	0.297
Epochs 1	0.836	0.435	0.937	0.473	0.571	0.430
Epochs 2	0.840	0.433	0.935	0.455	0.714	0.433
Epochs 5	0.861	0.450	0.935	0.466	0.610	0.464
Epochs 10	0.852	0.455	0.937	0.474	1.000	0.443

Epochs 20	0.840	0.445	0.937	0.474	1.000	0.444
Balanced 60|40	0.828	0.436	0.933	0.437	0.675	0.414
Balanced 67|33	0.857	0.444	0.942	0.519	1.000	0.466
Balanced 75|25	0.842	0.423	0.936	0.464	0.545	0.405
Balanced 80|20	0.835	0.441	0.945	0.544	0.922	0.481
Balanced 40|30|30	0.847	0.390	0.931	0.432	1.000	0.433
Balanced 60|20|20	0.840	0.393	0.937	0.468	1.000	0.398
Balanced 80|10|10	0.848	0.447	0.943	0.534	1.000	0.434
Balanced 60|30|10	0.824	0.406	0.939	0.492	1.000	0.413
Balanced 30|30|15|15|10	0.837	0.423	0.937	0.470	1.000	0.415
Balanced 60|10|10|10|10	0.822	0.394	0.938	0.481	1.000	0.401

Table 2.39: Best results for plain averaging on SR-HSE (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.855	0.435	0.949	0.625	0.662	0.481
60|40	0.828	0.403	0.940	0.500	0.636	0.422
67|33	0.840	0.432	0.930	0.416	0.597	0.383
75|25	0.833	0.427	0.938	0.478	0.636	0.412
80|20	0.815	0.425	0.930	0.429	0.558	0.427
40|30|30	0.828	0.363	0.938	0.481	1.000	0.460
60|20|20	0.848	0.452	0.938	0.478	1.000	0.427
80|10|10	0.830	0.423	0.938	0.483	0.545	0.416
60|30|10	0.846	0.451	0.944	0.535	0.896	0.484
30|30|15|15|10	0.824	0.402	0.932	0.438	1.000	0.410
60|10|10|10|10	0.837	0.419	0.939	0.493	0.805	0.448

Table 2.40: Best results for weighted averaging on SR-HSE (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.855	0.435	0.949	0.625	0.662	0.481
Clients 2	0.826	0.407	0.932	0.444	1.000	0.443

Clients 3	0.827	0.434	0.935	0.457	1.000	0.427
Clients 4	0.855	0.424	0.935	0.455	1.000	0.430
Clients 5	0.826	0.364	0.919	0.348	1.000	0.357
Clients 6	0.830	0.413	0.916	0.360	1.000	0.382
Clients 7	0.817	0.389	0.925	0.391	1.000	0.377
Clients 8	0.813	0.410	0.922	0.384	1.000	0.391
Clients 9	0.820	0.359	0.917	0.347	1.000	0.345
Clients 10	0.822	0.381	0.908	0.315	1.000	0.332
Clients 11	0.809	0.364	0.918	0.351	1.000	0.373
Clients 12	0.820	0.388	0.910	0.314	1.000	0.335
Clients 13	0.809	0.369	0.928	0.405	1.000	0.380
Clients 14	0.831	0.383	0.931	0.370	1.000	0.397
Clients 15	0.802	0.329	0.916	0.310	1.000	0.331
Clients 16	0.821	0.330	0.913	0.320	1.000	0.335
Clients 17	0.800	0.328	0.936	0.312	1.000	0.344
Clients 18	0.825	0.370	0.936	0.394	1.000	0.372
Clients 19	0.820	0.343	0.925	0.322	1.000	0.351
Clients 20	0.806	0.311	0.934	0.315	1.000	0.340
Epochs 1	0.836	0.419	0.935	0.453	0.610	0.414
Epochs 2	0.855	0.454	0.938	0.481	0.623	0.454
Epochs 5	0.836	0.401	0.931	0.421	1.000	0.415
Epochs 10	0.838	0.396	0.931	0.429	1.000	0.410
Epochs 20	0.822	0.430	0.938	0.478	1.000	0.443
Balanced 60|40	0.843	0.434	0.937	0.470	1.000	0.427
Balanced 67|33	0.841	0.424	0.942	0.514	0.987	0.472
Balanced 75|25	0.829	0.410	0.935	0.444	1.000	0.391
Balanced 80|20	0.835	0.450	0.942	0.515	1.000	0.452
Balanced 40|30|30	0.831	0.399	0.938	0.481	1.000	0.401
Balanced 60|20|20	0.839	0.454	0.934	0.451	1.000	0.430
Balanced 80|10|10	0.846	0.441	0.935	0.463	1.000	0.447
Balanced 60|30|10	0.871	0.464	0.939	0.492	1.000	0.456
Balanced 30|30|15|15|10	0.838	0.425	0.931	0.425	1.000	0.409
Balanced 60|10|10|10|10	0.831	0.398	0.931	0.420	1.000	0.390

Table 2.41: Best results for benchmarked averaging on SR-HSE (Tox21)

2.4.12 Tox21 - SR-MMP

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.924	0.729	0.889	0.616	0.900	0.614
Clients 2	0.921	0.736	0.888	0.612	0.989	0.604
Clients 3	0.905	0.704	0.874	0.569	1.000	0.567
Clients 4	0.914	0.744	0.875	0.563	1.000	0.593
Clients 5	0.908	0.705	0.886	0.601	1.000	0.604
Clients 6	0.911	0.702	0.866	0.543	1.000	0.557
Clients 7	0.911	0.720	0.877	0.570	1.000	0.591
Clients 8	0.900	0.686	0.856	0.520	1.000	0.544
Clients 9	0.914	0.712	0.868	0.548	1.000	0.572
Clients 10	0.909	0.692	0.870	0.553	1.000	0.570
Clients 11	0.911	0.719	0.864	0.538	1.000	0.561
Clients 12	0.899	0.651	0.855	0.517	1.000	0.534
Clients 13	0.909	0.695	0.867	0.546	1.000	0.555
Clients 14	0.897	0.679	0.862	0.534	1.000	0.552
Clients 15	0.901	0.667	0.856	0.519	1.000	0.534
Clients 16	0.896	0.616	0.779	0.398	1.000	0.425
Clients 17	0.906	0.670	0.866	0.544	1.000	0.551
Clients 18	0.904	0.674	0.848	0.502	1.000	0.530
Clients 19	0.892	0.642	0.852	0.512	1.000	0.508
Clients 20	0.903	0.658	0.862	0.534	1.000	0.554
Epochs 1	0.928	0.744	0.881	0.583	1.000	0.605
Epochs 2	0.919	0.749	0.879	0.581	1.000	0.599
Epochs 5	0.920	0.741	0.889	0.606	0.944	0.615
Epochs 10	0.915	0.719	0.884	0.601	0.989	0.593
Epochs 20	0.912	0.693	0.886	0.601	1.000	0.604
Balanced 60|40	0.920	0.734	0.888	0.612	0.961	0.598
Balanced 67|33	0.919	0.741	0.872	0.561	0.861	0.567
Balanced 75|25	0.917	0.730	0.879	0.583	0.978	0.580
Balanced 80|20	0.914	0.722	0.879	0.581	0.911	0.595
Balanced 40|30|30	0.913	0.731	0.884	0.604	1.000	0.592

Balanced 60|20|20	0.918	0.720	0.880	0.588	0.989	0.585
Balanced 80|10|10	0.920	0.739	0.873	0.561	1.000	0.572
Balanced 60|30|10	0.922	0.740	0.889	0.610	1.000	0.609
Balanced 30|30|15|15|10	0.907	0.712	0.880	0.584	1.000	0.586
Balanced 60|10|10|10|10	0.905	0.703	0.875	0.568	1.000	0.581

Table 2.42: Best results for plain averaging on SR-MMP (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.924	0.729	0.889	0.616	0.900	0.614
60|40	0.913	0.720	0.885	0.604	0.856	0.601
67|33	0.918	0.726	0.881	0.585	0.928	0.593
75|25	0.923	0.737	0.884	0.596	0.872	0.591
80|20	0.920	0.728	0.890	0.623	0.856	0.608
40|30|30	0.915	0.715	0.871	0.558	1.000	0.563
60|20|20	0.917	0.696	0.876	0.571	1.000	0.577
80|10|10	0.916	0.714	0.883	0.589	0.867	0.599
60|30|10	0.921	0.723	0.885	0.600	0.911	0.598
30|30|15|15|10	0.910	0.721	0.879	0.582	1.000	0.579
60|10|10|10|10	0.914	0.721	0.879	0.586	0.961	0.580

Table 2.43: Best results for weighted averaging on SR-MMP (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.924	0.729	0.889	0.616	0.900	0.614
Clients 2	0.916	0.723	0.887	0.608	1.000	0.601
Clients 3	0.911	0.687	0.867	0.547	1.000	0.564
Clients 4	0.910	0.720	0.877	0.576	1.000	0.577
Clients 5	0.913	0.673	0.857	0.521	1.000	0.555
Clients 6	0.905	0.669	0.859	0.526	1.000	0.549
Clients 7	0.900	0.692	0.846	0.498	1.000	0.524
Clients 8	0.905	0.657	0.849	0.504	1.000	0.530

Clients 9	0.915	0.701	0.862	0.532	1.000	0.569
Clients 10	0.905	0.681	0.867	0.543	1.000	0.572
Clients 11	0.908	0.677	0.857	0.522	1.000	0.544
Clients 12	0.898	0.653	0.839	0.484	1.000	0.516
Clients 13	0.899	0.661	0.859	0.526	1.000	0.548
Clients 14	0.900	0.668	0.862	0.534	1.000	0.554
Clients 15	0.900	0.653	0.856	0.518	1.000	0.544
Clients 16	0.889	0.659	0.860	0.530	1.000	0.534
Clients 17	0.886	0.647	0.838	0.481	1.000	0.505
Clients 18	0.890	0.636	0.850	0.505	1.000	0.532
Clients 19	0.891	0.638	0.839	0.483	1.000	0.502
Clients 20	0.906	0.653	0.856	0.520	1.000	0.549
Epochs 1	0.918	0.746	0.870	0.555	0.906	0.569
Epochs 2	0.919	0.735	0.878	0.573	0.900	0.591
Epochs 5	0.914	0.719	0.889	0.607	0.989	0.614
Epochs 10	0.913	0.712	0.888	0.608	1.000	0.605
Epochs 20	0.914	0.727	0.878	0.574	1.000	0.588
Balanced 60|40	0.913	0.729	0.887	0.606	0.989	0.601
Balanced 67|33	0.911	0.708	0.886	0.605	1.000	0.597
Balanced 75|25	0.917	0.719	0.879	0.581	1.000	0.595
Balanced 80|20	0.920	0.709	0.879	0.577	1.000	0.593
Balanced 40|30|30	0.912	0.710	0.881	0.584	1.000	0.594
Balanced 60|20|20	0.918	0.694	0.869	0.550	1.000	0.573
Balanced 80|10|10	0.919	0.728	0.870	0.553	1.000	0.572
Balanced 60|30|10	0.907	0.666	0.864	0.538	1.000	0.563
Balanced 30|30|15|15|10	0.914	0.705	0.867	0.544	1.000	0.577
Balanced 60|10|10|10|10	0.909	0.697	0.872	0.558	1.000	0.577

Table 2.44: Best results for benchmarked averaging on SR-MMP (Tox21)

2.4.13 Tox21 - SR-p53

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa

Baseline	0.884	0.368	0.937	0.365	0.696	0.350
Clients 2	0.868	0.371	0.936	0.386	0.855	0.387
Clients 3	0.874	0.384	0.927	0.340	1.000	0.361
Clients 4	0.865	0.328	0.927	0.337	0.971	0.357
Clients 5	0.846	0.331	0.935	0.316	1.000	0.332
Clients 6	0.879	0.365	0.927	0.296	0.986	0.332
Clients 7	0.867	0.342	0.928	0.280	1.000	0.316
Clients 8	0.864	0.320	0.933	0.248	1.000	0.299
Clients 9	0.865	0.375	0.928	0.301	1.000	0.343
Clients 10	0.864	0.352	0.941	0.289	1.000	0.321
Clients 11	0.839	0.280	0.929	0.252	1.000	0.282
Clients 12	0.839	0.280	0.928	0.274	1.000	0.288
Clients 13	0.822	0.318	0.941	0.263	1.000	0.303
Clients 14	0.835	0.320	0.944	0.288	1.000	0.334
Clients 15	0.819	0.293	0.913	0.239	1.000	0.273
Clients 16	0.829	0.234	0.917	0.189	1.000	0.229
Clients 17	0.837	0.260	0.945	0.286	1.000	0.295
Clients 18	0.841	0.253	0.946	0.252	1.000	0.269
Clients 19	0.835	0.290	0.934	0.264	1.000	0.285
Clients 20	0.844	0.284	0.949	0.279	1.000	0.319
Epochs 1	0.895	0.419	0.930	0.352	0.681	0.375
Epochs 2	0.867	0.359	0.931	0.337	0.609	0.379
Epochs 5	0.873	0.394	0.930	0.352	0.667	0.388
Epochs 10	0.875	0.371	0.928	0.337	0.638	0.357
Epochs 20	0.855	0.332	0.925	0.330	1.000	0.347
Balanced 60|40	0.869	0.363	0.928	0.330	0.739	0.358
Balanced 67|33	0.868	0.366	0.926	0.318	0.652	0.349
Balanced 75|25	0.874	0.435	0.930	0.362	0.855	0.381
Balanced 80|20	0.888	0.372	0.941	0.410	0.913	0.402
Balanced 40|30|30	0.859	0.341	0.930	0.352	0.971	0.363
Balanced 60|20|20	0.853	0.348	0.939	0.397	0.884	0.362
Balanced 80|10|10	0.867	0.371	0.931	0.356	0.971	0.371
Balanced 60|30|10	0.861	0.430	0.935	0.372	1.000	0.364
Balanced 30|30|15|15|10	0.861	0.380	0.939	0.365	1.000	0.367

Balanced 60|10|10|10|10	0.865	0.339	0.923	0.320	0.957	0.344

Table 2.45: Best results for plain averaging on SR-p53 (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.884	0.368	0.937	0.365	0.696	0.350
60|40	0.869	0.423	0.937	0.390	0.594	0.378
67|33	0.867	0.382	0.933	0.366	0.855	0.383
75|25	0.886	0.398	0.929	0.333	0.768	0.363
80|20	0.870	0.424	0.946	0.365	0.638	0.368
40|30|30	0.881	0.376	0.923	0.327	0.913	0.354
60|20|20	0.876	0.384	0.929	0.341	1.000	0.345
80|10|10	0.879	0.374	0.932	0.322	0.681	0.362
60|30|10	0.885	0.367	0.929	0.321	0.623	0.358
30|30|15|15|10	0.869	0.357	0.922	0.301	0.957	0.319
60|10|10|10|10	0.850	0.331	0.927	0.326	0.870	0.329

Table 2.46: Best results for weighted averaging on SR-p53 (Tox21)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.884	0.368	0.937	0.365	0.696	0.350
Clients 2	0.884	0.366	0.917	0.305	1.000	0.343
Clients 3	0.871	0.388	0.921	0.304	1.000	0.334
Clients 4	0.847	0.340	0.916	0.275	1.000	0.297
Clients 5	0.869	0.311	0.916	0.298	1.000	0.338
Clients 6	0.852	0.273	0.884	0.240	1.000	0.291
Clients 7	0.864	0.340	0.898	0.253	1.000	0.302
Clients 8	0.841	0.289	0.913	0.229	1.000	0.256
Clients 9	0.847	0.276	0.894	0.247	1.000	0.289
Clients 10	0.866	0.306	0.900	0.258	1.000	0.312
Clients 11	0.849	0.316	0.924	0.250	1.000	0.300
Clients 12	0.839	0.319	0.903	0.212	1.000	0.247

Clients 13	0.836	0.313	0.930	0.244	1.000	0.300
Clients 14	0.829	0.289	0.938	0.243	1.000	0.284
Clients 15	0.832	0.272	0.915	0.254	1.000	0.287
Clients 16	0.836	0.270	0.889	0.214	1.000	0.244
Clients 17	0.830	0.265	0.946	0.205	1.000	0.239
Clients 18	0.850	0.261	0.947	0.243	1.000	0.273
Clients 19	0.823	0.255	0.927	0.199	1.000	0.232
Clients 20	0.838	0.288	0.942	0.252	1.000	0.297
Epochs 1	0.872	0.398	0.925	0.313	0.681	0.350
Epochs 2	0.898	0.437	0.930	0.355	0.739	0.373
Epochs 5	0.879	0.422	0.931	0.360	0.913	0.369
Epochs 10	0.870	0.410	0.931	0.349	1.000	0.378
Epochs 20	0.861	0.339	0.920	0.311	1.000	0.344
Balanced 60|40	0.843	0.399	0.933	0.358	1.000	0.351
Balanced 67|33	0.876	0.396	0.931	0.356	1.000	0.371
Balanced 75|25	0.893	0.376	0.920	0.328	1.000	0.371
Balanced 80|20	0.878	0.421	0.918	0.316	1.000	0.357
Balanced 40|30|30	0.876	0.425	0.918	0.303	1.000	0.332
Balanced 60|20|20	0.876	0.385	0.911	0.290	1.000	0.334
Balanced 80|10|10	0.877	0.424	0.920	0.318	1.000	0.352
Balanced 60|30|10	0.871	0.402	0.931	0.363	1.000	0.377
Balanced 30|30|15|15|10	0.862	0.369	0.906	0.263	1.000	0.306
Balanced 60|10|10|10|10	0.872	0.347	0.919	0.295	1.000	0.322

Table 2.47: Best results for benchmarked averaging on SR-p53 (Tox21)

2.4.14 Tox21 - Mean

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.869	0.513	0.932	0.595	0.692	0.492
Clients 2	0.838	0.482	0.914	0.431	0.908	0.420
Clients 3	0.844	0.481	0.912	0.425	0.984	0.420
Clients 4	0.837	0.478	0.912	0.428	0.990	0.426
Clients 5	0.832	0.484	0.915	0.444	0.995	0.430

Clients 6	0.836	0.478	0.910	0.422	0.995	0.416
Clients 7	0.832	0.475	0.910	0.406	0.994	0.403
Clients 8	0.836	0.462	0.896	0.376	1.000	0.385
Clients 9	0.836	0.480	0.903	0.396	0.998	0.405
Clients 10	0.831	0.479	0.914	0.415	1.000	0.410
Clients 11	0.827	0.474	0.904	0.410	0.998	0.406
Clients 12	0.818	0.444	0.900	0.383	1.000	0.386
Clients 13	0.827	0.466	0.911	0.390	1.000	0.395
Clients 14	0.828	0.459	0.908	0.397	1.000	0.394
Clients 15	0.824	0.442	0.894	0.368	1.000	0.378
Clients 16	0.828	0.420	0.865	0.280	1.000	0.304
Clients 17	0.818	0.437	0.904	0.388	1.000	0.385
Clients 18	0.828	0.444	0.899	0.383	1.000	0.383
Clients 19	0.826	0.450	0.901	0.392	1.000	0.385
Clients 20	0.822	0.431	0.916	0.588	1.000	0.386
Epochs 1	0.846	0.502	0.913	0.447	0.623	0.426
Epochs 2	0.845	0.496	0.908	0.427	0.630	0.425
Epochs 5	0.841	0.492	0.916	0.439	0.628	0.434
Epochs 10	0.845	0.488	0.914	0.441	0.666	0.425
Epochs 20	0.842	0.470	0.912	0.422	0.982	0.418
Balanced 60|40	0.833	0.486	0.914	0.430	0.610	0.421
Balanced 67|33	0.843	0.491	0.914	0.441	0.848	0.430
Balanced 75|25	0.836	0.491	0.912	0.439	0.762	0.434
Balanced 80|20	0.843	0.487	0.914	0.469	0.733	0.432
Balanced 40|30|30	0.835	0.481	0.912	0.431	0.993	0.422
Balanced 60|20|20	0.835	0.476	0.917	0.456	0.959	0.438
Balanced 80|10|10	0.839	0.488	0.913	0.439	0.890	0.425
Balanced 60|30|10	0.834	0.484	0.916	0.441	0.987	0.429
Balanced 30|30|15|15|10	0.835	0.490	0.910	0.424	0.997	0.413
Balanced 60|10|10|10|10	0.830	0.470	0.911	0.436	0.990	0.417

Table 2.48: Best results for plain averaging on Tox21 (average)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa

Baseline	0.869	0.513	0.932	0.595	0.692	0.492
60|40	0.846	0.487	0.916	0.453	0.619	0.436
67|33	0.841	0.474	0.912	0.441	0.620	0.423
75|25	0.842	0.472	0.912	0.429	0.636	0.415
80|20	0.841	0.478	0.907	0.420	0.601	0.412
40|30|30	0.841	0.483	0.909	0.424	0.941	0.421
60|20|20	0.835	0.488	0.910	0.422	0.938	0.413
80|10|10	0.844	0.476	0.913	0.447	0.617	0.428
60|30|10	0.844	0.478	0.914	0.441	0.610	0.426
30|30|15|15|10	0.837	0.484	0.912	0.421	0.990	0.417
60|10|10|10|10	0.837	0.481	0.913	0.437	0.875	0.422

Table 2.49: Best results for weighted averaging on Tox21 (average)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.869	0.513	0.932	0.595	0.692	0.492
Clients 2	0.839	0.474	0.913	0.427	1.000	0.422
Clients 3	0.843	0.470	0.907	0.407	1.000	0.409
Clients 4	0.838	0.469	0.905	0.395	1.000	0.398
Clients 5	0.841	0.457	0.899	0.378	0.998	0.388
Clients 6	0.832	0.453	0.887	0.345	1.000	0.365
Clients 7	0.832	0.464	0.895	0.368	1.000	0.379
Clients 8	0.834	0.464	0.896	0.364	1.000	0.380
Clients 9	0.839	0.451	0.894	0.363	1.000	0.376
Clients 10	0.836	0.449	0.894	0.371	1.000	0.376
Clients 11	0.833	0.450	0.896	0.356	1.000	0.373
Clients 12	0.833	0.456	0.883	0.338	1.000	0.364
Clients 13	0.824	0.458	0.889	0.348	1.000	0.367
Clients 14	0.831	0.451	0.897	0.373	1.000	0.385
Clients 15	0.823	0.442	0.893	0.349	1.000	0.362
Clients 16	0.825	0.426	0.879	0.324	1.000	0.340
Clients 17	0.817	0.434	0.905	0.318	1.000	0.336
Clients 18	0.816	0.453	0.896	0.368	1.000	0.372

Clients 19	0.819	0.433	0.875	0.313	1.000	0.337
Clients 20	0.825	0.434	0.891	0.369	1.000	0.373
Epochs 1	0.847	0.493	0.903	0.415	0.616	0.405
Epochs 2	0.848	0.496	0.909	0.432	0.622	0.420
Epochs 5	0.847	0.481	0.911	0.438	0.885	0.428
Epochs 10	0.838	0.480	0.913	0.444	0.998	0.426
Epochs 20	0.844	0.478	0.911	0.422	0.995	0.413
Balanced 60|40	0.837	0.477	0.912	0.434	0.990	0.428
Balanced 67|33	0.846	0.482	0.911	0.431	0.957	0.429
Balanced 75|25	0.847	0.491	0.912	0.430	0.994	0.427
Balanced 80|20	0.842	0.489	0.911	0.440	0.992	0.430
Balanced 40|30|30	0.848	0.494	0.907	0.416	1.000	0.413
Balanced 60|20|20	0.844	0.477	0.899	0.395	1.000	0.396
Balanced 80|10|10	0.845	0.486	0.911	0.437	0.998	0.424
Balanced 60|30|10	0.853	0.486	0.906	0.417	0.996	0.413
Balanced 30|30|15|15|10	0.848	0.476	0.899	0.407	1.000	0.400
Balanced 60|10|10|10|10	0.841	0.476	0.907	0.421	1.000	0.413

Table 2.50: Best results for benchmarked averaging on Tox21 (average)

2.4.15 ADME - CLint

experiment	r2	mae	rmse
Baseline	0.489	0.806	1.536
Clients 2	0.508	2.877	3.392
Clients 3	0.492	3.670	4.092
Clients 4	0.493	2.871	3.392
Clients 5	0.496	3.357	3.814
Clients 6	0.450	3.426	3.876
Clients 7	0.456	3.253	3.721
Clients 8	0.373	3.505	3.947
Clients 9	0.415	3.345	3.803
Clients 10	0.336	3.428	3.877
Clients 11	0.367	3.464	3.910

Clients 12	0.255	3.487	3.932
Clients 13	0.344	3.431	3.880
Clients 14	0.327	3.501	3.944
Clients 15	0.292	3.463	3.909
Clients 16	0.227	3.534	3.973
Clients 17	0.311	3.465	3.911
Clients 18	0.191	3.451	3.899
Clients 19	0.269	3.474	3.920
Clients 20	0.121	3.471	3.916
Epochs 1	0.470	3.446	3.896
Epochs 2	0.507	3.570	3.996
Epochs 5	0.510	2.998	3.498
Epochs 10	0.525	3.379	3.837
Epochs 20	0.484	2.524	3.096
Balanced 60|40	0.517	2.358	2.957
Balanced 67|33	0.492	3.065	3.555
Balanced 75|25	0.522	3.297	3.759
Balanced 80|20	0.497	3.095	3.578
Balanced 40|30|30	0.504	3.590	4.022
Balanced 60|20|20	0.494	3.507	3.951
Balanced 80|10|10	0.507	3.115	3.600
Balanced 60|30|10	0.519	3.109	3.598
Balanced 30|30|15|15|10	0.479	3.305	3.766
Balanced 60|10|10|10|10	0.468	3.560	3.997

Table 2.51: Best results for plain averaging on CLint (ADME)

experiment	r2	mae	rmse
Baseline	0.489	0.806	1.536
60|40	0.510	1.673	2.408
67|33	0.505	3.200	3.669
75|25	0.504	1.921	2.602
80|20	0.513	1.627	2.367
40|30|30	0.499	3.356	3.814

60|20|20	0.513	2.601	3.158
80|10|10	0.506	2.001	2.653
60|30|10	0.492	3.250	3.723
30|30|15|15|10	0.499	3.376	3.831
60|10|10|10|10	0.494	3.191	3.662

Table 2.52: Best results for weighted averaging on CLint (ADME)

experiment	r2	mae	rmse
Baseline	0.489	0.806	1.536
Clients 2	0.510	2.236	2.859
Clients 3	0.379	1.174	2.242
Clients 4	0.477	3.374	3.830
Clients 5	0.496	3.340	3.800
Clients 6	0.480	3.428	3.879
Clients 7	0.442	3.482	3.927
Clients 8	0.462	3.410	3.862
Clients 9	0.484	3.363	3.820
Clients 10	0.194	1.242	2.009
Clients 11	0.384	3.467	3.913
Clients 12	0.379	3.465	3.911
Clients 13	0.402	3.434	3.883
Clients 14	0.413	3.377	3.832
Clients 15	0.396	3.477	3.923
Clients 16	0.370	3.513	3.954
Clients 17	0.351	3.511	3.953
Clients 18	0.345	3.330	3.790
Clients 19	0.312	3.465	3.911
Clients 20	0.370	1.237	2.029
Epochs 1	0.515	2.266	2.883
Epochs 2	0.527	3.237	3.709
Epochs 5	0.498	2.132	2.772
Epochs 10	0.486	2.015	2.674
Epochs 20	0.493	2.551	3.124

Balanced 60|40	0.510	2.294	2.906
Balanced 67|33	0.466	1.062	2.022
Balanced 75|25	0.518	2.733	3.283
Balanced 80|20	0.483	1.723	2.387
Balanced 40|30|30	0.498	2.982	3.486
Balanced 60|20|20	0.520	2.752	3.290
Balanced 80|10|10	0.492	2.182	2.818
Balanced 60|30|10	0.494	3.321	3.789
Balanced 30|30|15|15|10	0.503	3.587	4.020
Balanced 60|10|10|10|10	0.476	1.067	2.269

Table 2.53: Best results for benchmarked averaging on CLint (ADME)

2.4.16 ADME - FeHuman

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.921	0.985	0.897	0.932	0.966	0.572
Clients 2	0.871	0.977	0.912	0.919	1.000	0.579
Clients 3	0.847	0.973	0.882	0.903	1.000	0.438
Clients 4	0.874	0.978	0.897	0.918	1.000	0.531
Clients 5	0.853	0.975	0.882	0.917	1.000	0.489
Clients 6	0.800	0.962	0.853	0.909	1.000	0.327
Clients 7	0.843	0.972	0.897	0.917	1.000	0.489
Clients 8	0.843	0.970	0.897	0.918	1.000	0.531
Clients 9	0.850	0.974	0.897	0.918	1.000	0.531
Clients 10	0.822	0.967	0.882	0.909	1.000	0.376
Clients 11	0.819	0.968	0.868	0.914	1.000	0.414
Clients 12	0.817	0.966	0.868	0.925	1.000	0.369
Clients 13	0.829	0.967	0.882	0.912	1.000	0.438
Clients 14	0.831	0.971	0.868	0.911	1.000	0.398
Clients 15	0.810	0.964	0.868	0.900	1.000	0.361
Clients 16	0.790	0.956	0.882	0.909	1.000	0.398
Clients 17	0.812	0.966	0.882	0.914	1.000	0.414

Clients 18	0.774	0.953	0.853	0.900	1.000	0.298
Clients 19	0.774	0.955	0.868	0.907	1.000	0.296
Clients 20	0.776	0.958	0.868	0.898	1.000	0.335
Epochs 1	0.847	0.973	0.882	0.915	1.000	0.450
Epochs 2	0.850	0.975	0.868	0.915	1.000	0.450
Epochs 5	0.845	0.972	0.882	0.914	1.000	0.438
Epochs 10	0.881	0.978	0.882	0.917	1.000	0.489
Epochs 20	0.852	0.974	0.868	0.912	1.000	0.381
Balanced 60|40	0.845	0.969	0.882	0.917	1.000	0.489
Balanced 67|33	0.847	0.972	0.868	0.915	1.000	0.450
Balanced 75|25	0.883	0.979	0.897	0.915	1.000	0.483
Balanced 80|20	0.891	0.982	0.882	0.917	1.000	0.489
Balanced 40|30|30	0.814	0.966	0.868	0.915	1.000	0.450
Balanced 60|20|20	0.819	0.965	0.882	0.914	1.000	0.414
Balanced 80|10|10	0.807	0.966	0.853	0.909	1.000	0.322
Balanced 60|30|10	0.852	0.975	0.897	0.911	1.000	0.483
Balanced 30|30|15|15|10	0.819	0.966	0.868	0.915	1.000	0.450
Balanced 60|10|10|10|10	0.824	0.970	0.882	0.914	1.000	0.438

Table 2.54: Best results for plain averaging on FeHuman with a 0.7 threshold (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.921	0.985	0.897	0.932	0.966	0.572
60|40	0.872	0.977	0.897	0.918	1.000	0.531
67|33	0.841	0.971	0.897	0.918	1.000	0.531
75|25	0.834	0.966	0.882	0.917	1.000	0.489
80|20	0.891	0.981	0.882	0.917	1.000	0.489
40|30|30	0.866	0.975	0.868	0.915	1.000	0.450
60|20|20	0.878	0.977	0.912	0.919	1.000	0.579
80|10|10	0.874	0.979	0.882	0.914	1.000	0.438
60|30|10	0.879	0.978	0.912	0.919	1.000	0.579
30|30|15|15|10	0.862	0.975	0.912	0.919	1.000	0.579
60|10|10|10|10	0.855	0.974	0.882	0.903	1.000	0.438

Table 2.55: Best results for weighted averaging on FeHuman with a 0.7 threshold (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.921	0.985	0.897	0.932	0.966	0.572
Clients 2	0.862	0.976	0.882	0.914	1.000	0.438
Clients 3	0.867	0.977	0.868	0.900	1.000	0.361
Clients 4	0.855	0.974	0.897	0.918	1.000	0.531
Clients 5	0.843	0.970	0.897	0.918	1.000	0.531
Clients 6	0.841	0.973	0.882	0.903	1.000	0.438
Clients 7	0.864	0.977	0.868	0.887	1.000	0.298
Clients 8	0.847	0.970	0.897	0.918	1.000	0.531
Clients 9	0.841	0.971	0.897	0.905	1.000	0.483
Clients 10	0.852	0.973	0.868	0.902	1.000	0.398
Clients 11	0.843	0.973	0.868	0.889	1.000	0.335
Clients 12	0.834	0.970	0.868	0.911	1.000	0.350
Clients 13	0.843	0.972	0.882	0.911	1.000	0.438
Clients 14	0.855	0.975	0.897	0.914	1.000	0.483
Clients 15	0.822	0.967	0.868	0.914	1.000	0.414
Clients 16	0.828	0.970	0.897	0.925	1.000	0.483
Clients 17	0.834	0.971	0.897	0.922	1.000	0.531
Clients 18	0.826	0.969	0.897	0.918	1.000	0.531
Clients 19	0.762	0.954	0.882	0.909	1.000	0.376
Clients 20	0.840	0.973	0.882	0.917	1.000	0.489
Epochs 1	0.845	0.972	0.882	0.917	1.000	0.489
Epochs 2	0.891	0.982	0.868	0.915	1.000	0.450
Epochs 5	0.876	0.978	0.882	0.891	1.000	0.376
Epochs 10	0.836	0.970	0.868	0.915	1.000	0.450
Epochs 20	0.864	0.976	0.912	0.919	1.000	0.579
Balanced 60|40	0.853	0.974	0.868	0.902	1.000	0.398
Balanced 67|33	0.852	0.974	0.868	0.915	1.000	0.450
Balanced 75|25	0.831	0.967	0.897	0.918	1.000	0.531
Balanced 80|20	0.862	0.975	0.882	0.915	1.000	0.450
Balanced 40|30|30	0.805	0.959	0.882	0.914	1.000	0.438
Balanced 60|20|20	0.817	0.964	0.868	0.915	1.000	0.450

Balanced 80|10|10	0.866	0.977	0.853	0.907	1.000	0.327
Balanced 60|30|10	0.828	0.967	0.868	0.911	1.000	0.350
Balanced 30|30|15|15|10	0.833	0.971	0.882	0.923	1.000	0.450
Balanced 60|10|10|10|10	0.828	0.963	0.882	0.917	1.000	0.489

Table 2.56: Best results for benchmarked averaging on FeHuman with a 0.7 threshold (ADME)

2.4.17 ADME - FuBrain

experiment	r2	mae	rmse
Baseline	0.591	1.309	2.545
Clients 2	0.504	3.274	5.045
Clients 3	0.483	3.859	5.525
Clients 4	0.315	3.891	5.552
Clients 5	0.322	3.926	5.582
Clients 6	0.294	3.900	5.563
Clients 7	0.462	3.837	5.509
Clients 8	0.164	3.982	5.627
Clients 9	0.335	3.966	5.619
Clients 10	0.394	3.894	5.558
Clients 11	0.226	3.948	5.602
Clients 12	0.311	3.934	5.591
Clients 13	0.381	3.950	5.603
Clients 14	0.219	3.974	5.621
Clients 15	0.275	3.932	5.589
Clients 16	0.185	3.979	5.625
Clients 17	0.145	3.961	5.613
Clients 18	0.179	3.960	5.612
Clients 19	0.173	3.966	5.616
Clients 20	0.203	3.970	5.620
Epochs 1	0.457	3.944	5.597
Epochs 2	0.483	3.883	5.548
Epochs 5	0.495	3.883	5.550

Epochs 10	0.520	3.863	5.532
Epochs 20	0.577	3.521	5.243
Balanced 60|40	0.492	3.702	5.395
Balanced 67|33	0.512	3.781	5.460
Balanced 75|25	0.514	3.719	5.412
Balanced 80|20	0.483	3.677	5.369
Balanced 40|30|30	0.474	3.639	5.348
Balanced 60|20|20	0.453	3.776	5.458
Balanced 80|10|10	0.462	3.633	5.339
Balanced 60|30|10	0.458	3.941	5.596
Balanced 30|30|15|15|10	0.404	3.988	5.634
Balanced 60|10|10|10|10	0.385	3.879	5.548

Table 2.57: Best results for plain averaging on FuBrain (ADME)

experiment	r2	mae	rmse
Baseline	0.591	1.309	2.545
60|40	0.551	3.304	5.071
67|33	0.506	3.455	5.184
75|25	0.560	3.481	5.215
80|20	0.561	3.380	5.126
40|30|30	0.433	3.827	5.501
60|20|20	0.422	3.851	5.527
80|10|10	0.565	3.257	5.022
60|30|10	0.460	4.154	5.768
30|30|15|15|10	0.347	4.002	5.645
60|10|10|10|10	0.488	3.415	5.163

Table 2.58: Best results for weighted averaging on FuBrain (ADME)

experiment	r2	mae	rmse
Baseline	0.591	1.309	2.545

Clients 2	0.516	3.787	5.461
Clients 3	0.492	3.794	5.476
Clients 4	0.398	3.960	5.607
Clients 5	0.386	3.907	5.567
Clients 6	0.446	3.890	5.554
Clients 7	0.351	4.006	5.645
Clients 8	0.358	3.935	5.590
Clients 9	0.362	3.957	5.610
Clients 10	0.357	3.972	5.620
Clients 11	0.240	3.961	5.612
Clients 12	0.289	3.948	5.602
Clients 13	0.271	3.977	5.624
Clients 14	0.347	156.747	172.060
Clients 15	0.362	3.989	5.634
Clients 16	0.388	49.924	54.748
Clients 17	0.328	5.844	6.592
Clients 18	0.270	55.438	67.088
Clients 19	0.280	52.190	55.873
Clients 20	0.328	3.970	5.620
Epochs 1	0.453	3.951	5.611
Epochs 2	0.499	4.049	5.677
Epochs 5	0.462	3.785	5.464
Epochs 10	-	-	-
Epochs 20	-0.488	2804.875	4961.508
Balanced 60|40	0.536	3.456	5.199
Balanced 67|33	0.504	2.194	3.955
Balanced 75|25	-0.016	73.116	90.772
Balanced 80|20	0.522	3.599	5.298
Balanced 40|30|30	0.481	4.006	5.647
Balanced 60|20|20	0.496	3.832	5.501
Balanced 80|10|10	-0.370	3.990	5.634
Balanced 60|30|10	0.463	3.735	5.423
Balanced 30|30|15|15|10	0.352	4.081	5.708
Balanced 60|10|10|10|10	0.390	4.047	5.680

Table 2.59: Best results for benchmarked averaging on FuBrain (ADME)

2.4.18 ADME - FupHuman

experiment	r2	mae	rmse
Baseline	0.690	0.090	0.156
Clients 2	0.661	0.353	0.377
Clients 3	0.646	0.278	0.306
Clients 4	0.667	0.436	0.466
Clients 5	0.588	0.236	0.282
Clients 6	0.640	0.332	0.356
Clients 7	0.641	0.364	0.388
Clients 8	0.636	0.374	0.398
Clients 9	0.650	0.380	0.405
Clients 10	0.589	0.297	0.323
Clients 11	0.623	0.370	0.395
Clients 12	0.636	0.370	0.395
Clients 13	0.614	0.362	0.386
Clients 14	0.598	0.356	0.380
Clients 15	0.630	0.378	0.403
Clients 16	0.626	0.384	0.409
Clients 17	0.604	0.365	0.389
Clients 18	0.617	0.373	0.398
Clients 19	0.601	0.376	0.400
Clients 20	0.611	0.369	0.393
Epochs 1	0.661	0.240	0.278
Epochs 2	0.672	0.264	0.296
Epochs 5	0.661	0.384	0.410
Epochs 10	0.665	0.336	0.360
Epochs 20	0.692	0.309	0.333
Balanced 60|40	0.647	0.256	0.287
Balanced 67|33	0.670	0.410	0.437
Balanced 75|25	0.660	0.346	0.370
Balanced 80|20	0.645	0.269	0.298
Balanced 40|30|30	0.681	0.335	0.358

Balanced 60|20|20	0.649	0.372	0.397
Balanced 80|10|10	0.623	0.138	0.212
Balanced 60|30|10	0.653	0.310	0.334
Balanced 30|30|15|15|10	0.655	0.318	0.342
Balanced 60|10|10|10|10	0.646	0.328	0.352

Table 2.60: Best results for plain averaging on FupHuman (ADME)

experiment	r2	mae	rmse
Baseline	0.690	0.090	0.156
60|40	0.685	0.253	0.286
67|33	0.667	0.274	0.302
75|25	0.668	0.250	0.281
80|20	0.645	0.266	0.297
40|30|30	0.671	0.396	0.422
60|20|20	0.260	0.348	0.371
80|10|10	0.264	0.396	0.426
60|30|10	0.664	0.353	0.377
30|30|15|15|10	0.521	0.299	0.324
60|10|10|10|10	0.271	0.401	0.430

Table 2.61: Best results for weighted averaging on FupHuman (ADME)

experiment	r2	mae	rmse
Baseline	0.690	0.090	0.156
Clients 2	0.687	0.362	0.386
Clients 3	0.684	0.248	0.283
Clients 4	0.665	0.388	0.414
Clients 5	0.658	0.402	0.429
Clients 6	0.645	0.142	0.224
Clients 7	0.673	0.146	0.216
Clients 8	0.651	0.153	0.223

Clients 9	-0.571	0.233	0.381
Clients 10	0.645	0.152	0.228
Clients 11	0.611	0.197	0.326
Clients 12	0.495	0.210	0.350
Clients 13	-0.093	0.210	0.350
Clients 14	0.018	0.485	0.611
Clients 15	0.654	0.154	0.231
Clients 16	0.630	0.155	0.236
Clients 17	0.624	0.384	0.410
Clients 18	0.616	0.338	0.362
Clients 19	0.600	0.317	0.341
Clients 20	0.617	0.337	0.360
Epochs 1	0.115	0.210	0.349
Epochs 2	0.707	0.151	0.244
Epochs 5	0.667	0.234	0.270
Epochs 10	0.680	0.303	0.327
Epochs 20	0.642	0.300	0.326
Balanced 60|40	0.663	0.281	0.307
Balanced 67|33	0.662	0.408	0.434
Balanced 75|25	0.672	0.397	0.424
Balanced 80|20	0.651	0.284	0.310
Balanced 40|30|30	0.679	0.136	0.206
Balanced 60|20|20	0.651	0.137	0.204
Balanced 80|10|10	-0.262	0.207	0.345
Balanced 60|30|10	0.632	0.134	0.206
Balanced 30|30|15|15|10	0.639	0.284	0.311
Balanced 60|10|10|10|10	0.664	0.375	0.400

Table 2.62: Best results for benchmarked averaging on FupHuman (ADME)

2.4.19 ADME - FupRat

experiment	r2	mae	rmse

Baseline	0.594	0.111	0.183
Clients 2	0.577	0.211	0.310
Clients 3	0.550	0.356	0.388
Clients 4	0.584	0.317	0.343
Clients 5	0.486	0.242	0.285
Clients 6	0.511	0.387	0.425
Clients 7	0.521	0.272	0.299
Clients 8	0.542	0.333	0.361
Clients 9	0.398	0.311	0.336
Clients 10	0.529	0.278	0.321
Clients 11	0.572	0.347	0.375
Clients 12	0.561	0.358	0.388
Clients 13	0.474	0.362	0.394
Clients 14	0.482	0.319	0.345
Clients 15	0.494	0.381	0.416
Clients 16	0.483	0.319	0.345
Clients 17	0.408	0.314	0.339
Clients 18	0.441	0.345	0.373
Clients 19	0.509	0.363	0.395
Clients 20	0.384	0.336	0.363
Epochs 1	0.608	0.267	0.315
Epochs 2	0.557	0.241	0.284
Epochs 5	0.614	0.434	0.481
Epochs 10	0.520	0.228	0.268
Epochs 20	0.584	0.234	0.267
Balanced 60|40	0.609	0.209	0.313
Balanced 67|33	0.521	0.199	0.281
Balanced 75|25	0.574	0.217	0.277
Balanced 80|20	0.553	0.217	0.267
Balanced 40|30|30	0.536	0.199	0.275
Balanced 60|20|20	0.463	0.255	0.304
Balanced 80|10|10	0.590	0.217	0.272
Balanced 60|30|10	0.591	0.367	0.402
Balanced 30|30|15|15|10	0.295	0.245	0.337

Balanced 60|10|10|10|10	0.500	0.401	0.442

Table 2.63: Best results for plain averaging on FupRat (ADME)

experiment	r2	mae	rmse
Baseline	0.594	0.111	0.183
60|40	0.552	0.208	0.253
67|33	0.653	0.208	0.279
75|25	0.528	0.277	0.303
80|20	0.525	0.200	0.283
40|30|30	0.563	0.266	0.294
60|20|20	0.607	0.488	0.542
80|10|10	0.513	0.232	0.270
60|30|10	0.617	0.245	0.275
30|30|15|15|10	0.553	0.236	0.280
60|10|10|10|10	0.607	0.247	0.272

Table 2.64: Best results for weighted averaging on FupRat (ADME)

experiment	r2	mae	rmse
Baseline	0.594	0.111	0.183
Clients 2	0.632	0.221	0.264
Clients 3	0.619	0.231	0.366
Clients 4	0.621	0.257	0.285
Clients 5	-	-	-
Clients 6	0.170	0.208	0.276
Clients 7	0.640	0.352	0.418
Clients 8	0.433	0.450	0.497
Clients 9	0.163	0.460	0.511
Clients 10	0.561	0.641	0.723
Clients 11	0.267	0.299	0.323
Clients 12	-0.012	0.509	0.568

Clients 13	0.158	0.452	0.500
Clients 14	0.228	0.339	0.368
Clients 15	0.192	0.610	0.677
Clients 16	0.600	0.729	0.787
Clients 17	-0.009	0.617	0.683
Clients 18	0.220	0.614	0.701
Clients 19	0.414	0.562	0.645
Clients 20	-0.190	0.735	0.794
Epochs 1	0.639	0.482	0.536
Epochs 2	0.652	0.448	0.533
Epochs 5	0.541	0.554	0.640
Epochs 10	0.568	0.217	0.347
Epochs 20	0.652	0.204	0.274
Balanced 60|40	0.575	0.165	0.252
Balanced 67|33	0.578	0.208	0.259
Balanced 75|25	0.558	0.432	0.477
Balanced 80|20	0.529	0.174	0.247
Balanced 40|30|30	0.500	0.238	0.373
Balanced 60|20|20	-0.162	0.481	0.601
Balanced 80|10|10	-0.361	0.331	0.468
Balanced 60|30|10	0.655	0.163	0.243
Balanced 30|30|15|15|10	0.611	0.234	0.367
Balanced 60|10|10|10|10	0.578	0.435	0.537

Table 2.65: Best results for benchmarked averaging on FupRat (ADME)

2.4.20 ADME - NER-LLC

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.821	0.653	0.764	0.813	0.950	0.444
Clients 2	0.786	0.617	0.655	0.731	0.775	0.347
Clients 3	0.794	0.594	0.644	0.740	0.810	0.271
Clients 4	0.762	0.561	0.659	0.725	1.000	0.282
Clients 5	0.793	0.603	0.652	0.738	1.000	0.337

Clients 6	0.784	0.595	0.652	0.735	1.000	0.312
Clients 7	0.780	0.568	0.663	0.746	1.000	0.295
Clients 8	0.786	0.604	0.652	0.751	1.000	0.294
Clients 9	0.790	0.591	0.670	0.717	0.952	0.365
Clients 10	0.791	0.579	0.652	0.733	1.000	0.306
Clients 11	0.784	0.586	0.644	0.734	1.000	0.272
Clients 12	0.760	0.559	0.644	0.733	0.857	0.281
Clients 13	0.776	0.575	0.659	0.730	1.000	0.264
Clients 14	0.785	0.575	0.655	0.723	1.000	0.273
Clients 15	0.776	0.564	0.678	0.738	1.000	0.345
Clients 16	0.777	0.570	0.652	0.775	1.000	0.300
Clients 17	0.777	0.563	0.652	0.736	1.000	0.294
Clients 18	0.764	0.557	0.659	0.728	1.000	0.323
Clients 19	0.775	0.578	0.663	0.743	1.000	0.317
Clients 20	0.782	0.571	0.655	0.715	1.000	0.341
Epochs 1	0.808	0.635	0.663	0.762	0.820	0.347
Epochs 2	0.802	0.600	0.655	0.738	1.000	0.338
Epochs 5	0.786	0.608	0.670	0.748	0.773	0.320
Epochs 10	0.801	0.610	0.648	0.677	0.789	0.316
Epochs 20	0.795	0.586	0.652	0.564	1.000	0.310
Balanced 60|40	0.794	0.616	0.640	0.732	0.782	0.261
Balanced 67|33	0.793	0.596	0.640	0.719	0.917	0.312
Balanced 75|25	0.811	0.637	0.670	0.751	0.905	0.306
Balanced 80|20	0.809	0.610	0.674	0.729	0.806	0.306
Balanced 40|30|30	0.782	0.578	0.678	0.738	0.751	0.273
Balanced 60|20|20	0.815	0.653	0.667	0.734	0.976	0.279
Balanced 80|10|10	0.785	0.575	0.685	0.740	0.915	0.343
Balanced 60|30|10	0.795	0.641	0.644	0.732	1.000	0.238
Balanced 30|30|15|15|10	0.798	0.621	0.655	0.722	0.787	0.336
Balanced 60|10|10|10|10	0.790	0.589	0.655	0.731	0.965	0.315

Table 2.66: Best results for plain averaging on NER-LLC (average) (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa

Baseline	0.821	0.653	0.764	0.813	0.950	0.444
60|40	0.804	0.597	0.633	0.730	0.765	0.272
67|33	0.796	0.602	0.652	0.699	0.808	0.296
75|25	0.806	0.616	0.719	0.729	0.803	0.338
80|20	0.807	0.621	0.648	0.724	0.986	0.331
40|30|30	0.808	0.625	0.648	0.738	0.804	0.309
60|20|20	0.811	0.628	0.655	0.772	0.787	0.319
80|10|10	0.796	0.596	0.663	0.741	0.818	0.343
60|30|10	0.805	0.623	0.670	0.720	0.869	0.333
30|30|15|15|10	0.796	0.597	0.640	0.731	0.908	0.279
60|10|10|10|10	0.802	0.683	0.663	0.746	0.940	0.309

Table 2.67: Best results for weighted averaging on NER-LLC (average) (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.821	0.653	0.764	0.813	0.950	0.444
Clients 2	0.801	0.599	0.644	0.738	0.825	0.283
Clients 3	0.796	0.602	0.648	0.734	0.787	0.286
Clients 4	0.790	0.624	0.652	0.736	0.857	0.296
Clients 5	0.803	0.601	0.652	0.739	1.000	0.304
Clients 6	0.793	0.593	0.678	0.722	1.000	0.345
Clients 7	0.795	0.600	0.670	0.734	1.000	0.325
Clients 8	0.790	0.601	0.682	0.739	1.000	0.373
Clients 9	0.791	0.588	0.670	0.739	1.000	0.362
Clients 10	0.799	0.584	0.655	0.735	1.000	0.333
Clients 11	0.803	0.604	0.655	0.729	1.000	0.330
Clients 12	0.783	0.570	0.655	0.743	1.000	0.306
Clients 13	0.794	0.608	0.674	0.730	1.000	0.342
Clients 14	0.776	0.575	0.648	0.726	1.000	0.309
Clients 15	0.759	0.533	0.659	0.740	1.000	0.288
Clients 16	0.755	0.553	0.652	0.716	1.000	0.264
Clients 17	0.787	0.572	0.685	0.741	1.000	0.361
Clients 18	0.789	0.609	0.670	0.735	1.000	0.321

Clients 19	0.772	0.573	0.655	0.742	1.000	0.303
Clients 20	0.787	0.583	0.648	0.741	1.000	0.319
Epochs 1	0.797	0.605	0.655	0.740	0.763	0.324
Epochs 2	0.785	0.604	0.667	0.740	0.833	0.312
Epochs 5	0.797	0.606	0.659	0.732	0.808	0.331
Epochs 10	0.784	0.614	0.652	0.772	0.773	0.319
Epochs 20	0.785	0.604	0.655	0.610	0.929	0.303
Balanced 60|40	0.810	0.644	0.618	0.701	0.768	0.281
Balanced 67|33	0.802	0.645	0.652	0.741	0.758	0.304
Balanced 75|25	0.799	0.626	0.648	0.696	0.785	0.285
Balanced 80|20	0.803	0.619	0.682	0.734	0.765	0.316
Balanced 40|30|30	0.805	0.625	0.674	0.726	0.801	0.385
Balanced 60|20|20	0.800	0.608	0.655	0.756	0.782	0.305
Balanced 80|10|10	0.784	0.593	0.655	0.746	1.000	0.271
Balanced 60|30|10	0.795	0.599	0.644	0.725	0.803	0.303
Balanced 30|30|15|15|10	0.803	0.594	0.648	0.734	1.000	0.279
Balanced 60|10|10|10|10	0.786	0.604	0.659	0.740	0.773	0.328

Table 2.68: Best results for benchmarked averaging on NER-LLC (average) (ADME)

2.4.21 ADME - PappCaco2 (Classification)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.860	0.781	0.799	0.739	0.991	0.581
Clients 2	0.867	0.793	0.794	0.717	1.000	0.575
Clients 3	0.855	0.775	0.757	0.650	1.000	0.513
Clients 4	0.848	0.768	0.728	0.606	1.000	0.471
Clients 5	0.853	0.777	0.769	0.674	1.000	0.532
Clients 6	0.838	0.741	0.746	0.633	1.000	0.498
Clients 7	0.840	0.751	0.705	0.583	1.000	0.433
Clients 8	0.832	0.748	0.695	0.573	1.000	0.414
Clients 9	0.834	0.740	0.716	0.596	1.000	0.447
Clients 10	0.823	0.734	0.652	0.532	1.000	0.355

Clients 11	0.826	0.741	0.614	0.504	1.000	0.301
Clients 12	0.811	0.721	0.536	0.457	1.000	0.191
Clients 13	0.817	0.724	0.686	0.563	1.000	0.401
Clients 14	0.813	0.710	0.601	0.495	1.000	0.283
Clients 15	0.805	0.708	0.586	0.486	1.000	0.261
Clients 16	0.795	0.694	0.532	0.455	1.000	0.186
Clients 17	0.807	0.698	0.593	0.490	1.000	0.272
Clients 18	0.795	0.690	0.558	0.470	1.000	0.223
Clients 19	0.794	0.694	0.536	0.457	1.000	0.192
Clients 20	0.795	0.691	0.561	0.471	1.000	0.222
Epochs 1	0.853	0.766	0.756	0.643	1.000	0.515
Epochs 2	0.851	0.769	0.752	0.640	0.991	0.507
Epochs 5	0.858	0.776	0.778	0.679	0.991	0.552
Epochs 10	0.851	0.756	0.782	0.717	1.000	0.549
Epochs 20	0.854	0.777	0.789	0.758	0.997	0.551
Balanced 60|40	0.861	0.780	0.794	0.704	1.000	0.583
Balanced 67|33	0.859	0.786	0.794	0.721	0.988	0.573
Balanced 75|25	0.863	0.787	0.788	0.696	0.997	0.569
Balanced 80|20	0.860	0.786	0.782	0.697	1.000	0.554
Balanced 40|30|30	0.854	0.784	0.763	0.661	1.000	0.528
Balanced 60|20|20	0.850	0.764	0.765	0.660	1.000	0.532
Balanced 80|10|10	0.866	0.789	0.794	0.708	1.000	0.578
Balanced 60|30|10	0.855	0.772	0.780	0.671	1.000	0.561
Balanced 30|30|15|15|10	0.847	0.769	0.728	0.606	1.000	0.472
Balanced 60|10|10|10|10	0.851	0.764	0.717	0.594	1.000	0.460

Table 2.69: Best results for plain averaging on PappCaco2 (ADME) (classification)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.860	0.781	0.799	0.739	0.991	0.581
60|40	0.874	0.795	0.789	0.699	1.000	0.571
67|33	0.863	0.790	0.783	0.719	0.958	0.556
75|25	0.851	0.773	0.779	0.702	0.985	0.542

80|20	0.863	0.784	0.790	0.722	1.000	0.564
40|30|30	0.860	0.777	0.768	0.656	1.000	0.540
60|20|20	0.854	0.786	0.781	0.711	1.000	0.548
80|10|10	0.854	0.783	0.783	0.711	1.000	0.551
60|30|10	0.853	0.775	0.771	0.689	1.000	0.535
30|30|15|15|10	0.841	0.762	0.728	0.607	1.000	0.470
60|10|10|10|10	0.847	0.778	0.758	0.663	1.000	0.510

Table 2.70: Best results for weighted averaging on PappCaco2 (ADME) (classification)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.860	0.781	0.799	0.739	0.991	0.581
Clients 2	0.862	0.785	0.788	0.702	1.000	0.568
Clients 3	0.855	0.781	0.786	0.730	1.000	0.550
Clients 4	0.847	0.775	0.763	0.649	1.000	0.529
Clients 5	0.834	0.750	0.750	0.652	1.000	0.498
Clients 6	0.833	0.754	0.715	0.596	1.000	0.444
Clients 7	0.781	0.664	0.705	0.591	1.000	0.421
Clients 8	0.836	0.763	0.701	0.579	1.000	0.424
Clients 9	0.833	0.750	0.671	0.547	1.000	0.384
Clients 10	0.826	0.738	0.659	0.538	1.000	0.367
Clients 11	0.815	0.717	0.619	0.508	1.000	0.306
Clients 12	0.826	0.743	0.681	0.558	1.000	0.395
Clients 13	0.814	0.713	0.629	0.514	1.000	0.324
Clients 14	0.820	0.735	0.686	0.563	1.000	0.403
Clients 15	0.809	0.711	0.587	0.487	1.000	0.266
Clients 16	0.813	0.722	0.631	0.516	1.000	0.323
Clients 17	0.786	0.677	0.523	0.450	1.000	0.173
Clients 18	0.794	0.692	0.552	0.466	1.000	0.212
Clients 19	0.798	0.694	0.573	0.478	1.000	0.243
Clients 20	0.796	0.692	0.569	0.476	1.000	0.237
Epochs 1	0.861	0.782	0.769	0.665	1.000	0.543
Epochs 2	0.859	0.787	0.767	0.667	0.988	0.531

Epochs 5	0.867	0.795	0.800	0.740	1.000	0.587
Epochs 10	0.871	0.799	0.793	0.712	1.000	0.577
Epochs 20	0.850	0.783	0.794	0.743	1.000	0.569
Balanced 60|40	0.851	0.770	0.779	0.708	0.991	0.547
Balanced 67|33	0.861	0.788	0.800	0.747	1.000	0.581
Balanced 75|25	0.853	0.781	0.780	0.707	1.000	0.544
Balanced 80|20	0.868	0.785	0.797	0.725	1.000	0.581
Balanced 40|30|30	0.858	0.783	0.775	0.699	0.997	0.546
Balanced 60|20|20	0.857	0.777	0.760	0.654	1.000	0.523
Balanced 80|10|10	0.865	0.788	0.788	0.691	1.000	0.571
Balanced 60|30|10	0.855	0.780	0.785	0.723	1.000	0.552
Balanced 30|30|15|15|10	0.845	0.764	0.771	0.680	1.000	0.532
Balanced 60|10|10|10|10	0.858	0.779	0.785	0.696	1.000	0.560

Table 2.71: Best results for benchmarked averaging on PappCaco2 (ADME) (classification)

2.4.22 ADME - PappCaco2 (Regression)

experiment	r2	mae	rmse
Baseline	0.451	1.090	1.411
Clients 2	0.367	2.511	2.914
Clients 3	0.389	2.948	3.352
Clients 4	0.337	3.693	4.064
Clients 5	0.328	3.676	4.048
Clients 6	0.331	3.366	3.751
Clients 7	0.231	3.591	3.965
Clients 8	0.062	3.826	4.193
Clients 9	-0.187	3.800	4.168
Clients 10	0.101	3.697	4.068
Clients 11	-0.134	3.708	4.079
Clients 12	-0.141	3.749	4.119
Clients 13	0.016	3.822	4.188
Clients 14	-0.067	3.637	4.010

Clients 15	-0.251	3.768	4.137
Clients 16	-0.213	3.747	4.116
Clients 17	-0.165	3.751	4.121
Clients 18	-0.161	3.730	4.100
Clients 19	-0.277	3.784	4.153
Clients 20	-0.111	3.738	4.108
Epochs 1	0.321	3.558	3.933
Epochs 2	0.400	2.820	3.227
Epochs 5	0.447	2.900	3.308
Epochs 10	0.446	3.138	3.529
Epochs 20	0.448	2.183	2.561
Balanced 60|40	0.396	2.690	3.096
Balanced 67|33	0.435	2.441	2.838
Balanced 75|25	0.400	2.531	2.932
Balanced 80|20	0.373	3.332	3.714
Balanced 40|30|30	0.341	2.998	3.400
Balanced 60|20|20	0.381	3.187	3.576
Balanced 80|10|10	0.413	2.977	3.377
Balanced 60|30|10	0.417	3.556	3.931
Balanced 30|30|15|15|10	0.318	3.691	4.063
Balanced 60|10|10|10|10	0.268	3.987	4.344

Table 2.72: Best results for plain averaging on PappCaco2 (ADME) (regression)

experiment	r2	mae	rmse
Baseline	0.451	1.090	1.411
60|40	0.448	2.429	2.825
67|33	0.350	2.710	3.115
75|25	0.396	2.214	2.589
80|20	0.409	2.918	3.303
40|30|30	0.412	3.145	3.538
60|20|20	0.473	2.180	2.567
80|10|10	0.390	2.269	2.653
60|30|10	0.343	4.296	4.635

30|30|15|15|10	0.256	3.501	3.880
60|10|10|10|10	0.412	2.663	3.067

Table 2.73: Best results for weighted averaging on PappCaco2 (ADME) (regression)

experiment	r2	mae	rmse
Baseline	0.451	1.090	1.411
Clients 2	0.366	1.680	2.019
Clients 3	0.349	1.592	1.954
Clients 4	0.350	3.838	4.202
Clients 5	0.393	3.819	4.186
Clients 6	0.302	3.687	4.059
Clients 7	0.270	3.030	3.432
Clients 8	0.285	3.499	3.877
Clients 9	0.264	3.627	4.001
Clients 10	0.256	3.760	4.130
Clients 11	-0.216	3.731	4.101
Clients 12	-0.337	3.676	4.048
Clients 13	-0.206	3.899	4.261
Clients 14	-0.227	3.759	4.128
Clients 15	-0.209	3.725	4.095
Clients 16	-0.273	3.810	4.177
Clients 17	-0.277	3.764	4.133
Clients 18	-0.235	3.801	4.170
Clients 19	-0.267	3.870	6.011
Clients 20	-0.288	3.821	4.187
Epochs 1	0.401	2.302	2.700
Epochs 2	0.398	3.018	3.421
Epochs 5	0.381	2.485	2.887
Epochs 10	0.391	1.461	1.830
Epochs 20	0.495	2.648	3.035
Balanced 60|40	0.346	1.403	1.717

Balanced 67|33	0.406	1.408	1.756
Balanced 75|25	-666.924	865.534	1131.583
Balanced 80|20	0.387	2.907	3.741
Balanced 40|30|30	0.389	3.151	3.544
Balanced 60|20|20	0.247	1.975	2.415
Balanced 80|10|10	-0.242	2.236	2.651
Balanced 60|30|10	0.406	2.310	2.713
Balanced 30|30|15|15|10	0.370	3.801	4.168
Balanced 60|10|10|10|10	-0.125	6.013	7.276

Table 2.74: Best results for benchmarked averaging on PappCaco2 (ADME) (regression)

2.4.23 ADME - Papp-LLC

experiment	r2	mae	rmse
Baseline	0.577	0.071	0.124
Clients 2	0.559	0.292	0.310
Clients 3	0.578	0.203	0.223
Clients 4	0.577	0.279	0.297
Clients 5	0.492	0.186	0.207
Clients 6	0.591	0.275	0.293
Clients 7	0.632	0.365	0.387
Clients 8	0.507	0.362	0.384
Clients 9	0.571	0.372	0.395
Clients 10	0.553	0.375	0.398
Clients 11	0.495	0.381	0.404
Clients 12	0.616	0.369	0.391
Clients 13	0.519	0.377	0.400
Clients 14	0.537	0.359	0.381
Clients 15	0.494	0.371	0.394
Clients 16	0.543	0.380	0.403
Clients 17	0.562	0.382	0.405
Clients 18	0.523	0.394	0.419

Clients 19	0.550	0.386	0.411
Clients 20	0.476	0.390	0.415
Epochs 1	0.548	0.324	0.343
Epochs 2	0.540	0.187	0.209
Epochs 5	0.588	0.338	0.359
Epochs 10	0.565	0.120	0.168
Epochs 20	0.529	0.299	0.322
Balanced 60|40	0.618	0.344	0.368
Balanced 67|33	0.541	0.147	0.177
Balanced 75|25	0.566	0.235	0.257
Balanced 80|20	0.563	0.286	0.305
Balanced 40|30|30	0.606	0.288	0.306
Balanced 60|20|20	0.526	0.201	0.221
Balanced 80|10|10	0.584	0.239	0.258
Balanced 60|30|10	0.601	0.328	0.347
Balanced 30|30|15|15|10	0.529	0.384	0.408
Balanced 60|10|10|10|10	0.577	0.323	0.342

Table 2.75: Best results for plain averaging on Papp-LLC (ADME)

experiment	r2	mae	rmse
Baseline	0.577	0.071	0.124
60|40	0.523	0.196	0.217
67|33	0.533	0.254	0.271
75|25	0.522	0.193	0.214
80|20	0.497	0.199	0.219
40|30|30	0.596	0.193	0.213
60|20|20	0.560	0.279	0.297
80|10|10	0.522	0.166	0.189
60|30|10	0.559	0.335	0.356
30|30|15|15|10	0.542	0.240	0.258
60|10|10|10|10	0.512	0.304	0.323

Table 2.76: Best results for weighted averaging on Papp-LLC (ADME)

experiment	r2	mae	rmse
Baseline	0.577	0.071	0.124
Clients 2	-0.502	0.135	0.233
Clients 3	0.572	0.266	0.284
Clients 4	-0.502	0.135	0.233
Clients 5	0.612	0.237	0.256
Clients 6	-0.227	0.865	0.886
Clients 7	0.583	0.319	0.394
Clients 8	0.561	0.159	0.192
Clients 9	0.358	0.577	0.683
Clients 10	0.544	0.117	0.165
Clients 11	-0.064	0.135	0.233
Clients 12	-0.502	0.135	0.233
Clients 13	-0.016	0.217	0.282
Clients 14	0.438	0.220	0.307
Clients 15	0.420	0.404	0.430
Clients 16	0.474	0.403	0.429
Clients 17	0.556	0.381	0.404
Clients 18	0.459	0.379	0.402
Clients 19	0.575	0.379	0.402
Clients 20	0.507	0.502	0.534
Epochs 1	0.486	0.275	0.297
Epochs 2	-	-	-
Epochs 5	0.516	0.104	0.181
Epochs 10	-0.471	0.135	0.233
Epochs 20	0.646	0.224	0.241
Balanced 60|40	0.459	0.133	0.230
Balanced 67|33	0.603	0.134	0.233
Balanced 75|25	0.485	0.104	0.161
Balanced 80|20	0.547	0.204	0.222
Balanced 40|30|30	0.541	0.102	0.159
Balanced 60|20|20	0.468	0.097	0.161
Balanced 80|10|10	0.462	0.104	0.159

Balanced 60|30|10	-0.502	0.135	0.233
Balanced 30|30|15|15|10	0.295	0.655	0.724
Balanced 60|10|10|10|10	0.268	0.138	0.236

Table 2.77: Best results for benchmarked averaging on Papp-LLC (ADME)

2.4.24 ADME - RbRat

Baseline	0.669	0.173	0.225
Clients 2	0.388	0.603	0.745
Clients 3	0.596	0.309	0.382
Clients 4	0.651	0.382	0.471
Clients 5	0.585	0.346	0.452
Clients 6	0.729	0.320	0.389
Clients 7	0.604	0.350	0.405
Clients 8	0.394	0.324	0.429
Clients 9	0.650	0.323	0.395
Clients 10	0.611	0.323	0.396
Clients 11	0.619	0.334	0.411
Clients 12	0.706	0.328	0.397
Clients 13	0.625	0.336	0.400
Clients 14	0.565	0.332	0.399
Clients 15	0.627	0.361	0.422
Clients 16	0.564	0.372	0.440
Clients 17	0.547	0.369	0.439
Clients 18	0.508	0.327	0.399
Clients 19	0.631	0.327	0.397
Clients 20	0.427	0.325	0.392
Epochs 1	0.582	0.443	0.845
Epochs 2	0.570	0.399	0.635
Epochs 5	0.408	0.464	0.629
Epochs 10	0.499	0.351	0.454
Epochs 20	0.549	0.386	0.557

Balanced 60|40	0.404	0.329	0.584
Balanced 67|33	0.613	0.381	0.464
Balanced 75|25	0.554	0.608	0.693
Balanced 80|20	0.649	0.326	0.516
Balanced 40|30|30	0.628	0.666	0.791
Balanced 60|20|20	0.476	0.380	0.667
Balanced 80|10|10	0.507	0.328	0.450
Balanced 60|30|10	0.593	0.341	0.465
Balanced 30|30|15|15|10	0.420	0.331	0.488
Balanced 60|10|10|10|10	0.634	0.331	0.404

Table 2.78: Best results for plain averaging on RbRat (ADME)

experiment	r2	mae	rmse
Baseline	0.669	0.173	0.225
60|40	0.524	0.344	0.604
67|33	0.536	0.417	0.516
75|25	0.424	0.359	0.609
80|20	0.495	0.342	0.580
40|30|30	0.675	0.324	0.410
60|20|20	0.483	0.418	0.700
80|10|10	0.320	0.340	0.584
60|30|10	0.492	0.360	0.460
30|30|15|15|10	0.611	0.330	0.408
60|10|10|10|10	0.412	0.402	0.718

Table 2.79: Best results for weighted averaging on RbRat (ADME)

experiment	r2	mae	rmse
Baseline	0.669	0.173	0.225
Clients 2	0.616	0.575	0.834
Clients 3	0.522	1.371	2.282

Clients 4	0.137	0.807	1.006
Clients 5	0.580	1.073	1.520
Clients 6	0.210	0.714	1.305
Clients 7	0.346	1.555	1.936
Clients 8	0.354	0.990	1.328
Clients 9	0.050	0.398	0.507
Clients 10	0.108	1.714	2.184
Clients 11	0.131	0.626	1.049
Clients 12	0.111	0.697	1.125
Clients 13	-0.030	1.393	1.580
Clients 14	0.279	0.784	1.118
Clients 15	0.528	1.111	1.392
Clients 16	-0.118	0.868	1.419
Clients 17	0.441	0.634	0.850
Clients 18	-0.048	1.142	1.734
Clients 19	0.301	1.374	1.607
Clients 20	-0.014	0.628	1.128
Epochs 1	-0.100	0.856	0.982
Epochs 2	0.587	0.744	0.866
Epochs 5	0.708	0.582	0.707
Epochs 10	0.396	0.812	1.229
Epochs 20	0.464	11.679	15.911
Balanced 60|40	0.529	121.003	129.052
Balanced 67|33	0.589	1425.939	1513.100
Balanced 75|25	0.692	0.517	0.701
Balanced 80|20	0.532	1.420	1.865
Balanced 40|30|30	-0.109	0.483	0.726
Balanced 60|20|20	0.731	2.234	4.891
Balanced 80|10|10	-0.588	0.833	0.942
Balanced 60|30|10	0.603	2.110	2.277
Balanced 30|30|15|15|10	0.332	0.982	1.785
Balanced 60|10|10|10|10	-0.112	0.842	0.993

Table 2.80: Best results for benchmarked averaging on RbRat (ADME)

2.4.25 ADME - Solubility

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.861	0.895	0.806	0.803	1.0	0.584
Clients 2	0.837	0.867	0.806	0.810	1.000	0.590
Clients 3	0.831	0.850	0.806	0.797	1.000	0.587
Clients 4	0.824	0.859	0.796	0.788	1.000	0.568
Clients 5	0.848	0.872	0.816	0.789	1.000	0.606
Clients 6	0.831	0.852	0.806	0.800	1.000	0.587
Clients 7	0.823	0.848	0.806	0.803	1.000	0.593
Clients 8	0.830	0.860	0.816	0.797	1.000	0.609
Clients 9	0.814	0.832	0.816	0.806	1.000	0.612
Clients 10	0.832	0.863	0.796	0.767	1.000	0.562
Clients 11	0.805	0.827	0.806	0.770	1.000	0.581
Clients 12	0.822	0.850	0.786	0.764	1.000	0.543
Clients 13	0.822	0.843	0.786	0.788	1.000	0.552
Clients 14	0.827	0.856	0.796	0.800	1.000	0.574
Clients 15	0.803	0.840	0.777	0.750	1.000	0.517
Clients 16	0.813	0.845	0.806	0.778	1.000	0.584
Clients 17	0.823	0.849	0.786	0.750	1.000	0.536
Clients 18	0.826	0.863	0.786	0.750	1.000	0.536
Clients 19	0.809	0.846	0.786	0.771	1.000	0.546
Clients 20	0.824	0.865	0.757	0.727	1.000	0.471
Epochs 1	0.821	0.855	0.816	0.786	1.000	0.604
Epochs 2	0.835	0.860	0.816	0.794	1.000	0.604
Epochs 5	0.849	0.872	0.816	0.766	1.000	0.598
Epochs 10	0.832	0.851	0.825	0.818	1.000	0.633
Epochs 20	0.835	0.872	0.796	0.825	1.000	0.568
Balanced 60|40	0.833	0.867	0.806	0.794	1.000	0.590
Balanced 67|33	0.835	0.856	0.806	0.783	1.000	0.584
Balanced 75|25	0.834	0.874	0.816	0.781	1.000	0.604
Balanced 80|20	0.831	0.851	0.786	0.779	1.000	0.549
Balanced 40|30|30	0.851	0.884	0.825	0.800	1.000	0.628
Balanced 60|20|20	0.820	0.839	0.786	0.771	1.000	0.546
Balanced 80|10|10	0.829	0.862	0.777	0.761	1.000	0.524

Balanced 60|30|10	0.830	0.869	0.777	0.768	1.000	0.527
Balanced 30|30|15|15|10	0.830	0.868	0.786	0.771	1.000	0.546
Balanced 60|10|10|10|10	0.837	0.870	0.777	0.753	1.000	0.520

Table 2.81: Best results for plain averaging on Solubility (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.861	0.895	0.806	0.803	1.0	0.584
60|40	0.843	0.862	0.816	0.825	1.000	0.617
67|33	0.834	0.871	0.806	0.794	1.000	0.590
75|25	0.829	0.862	0.796	0.800	1.000	0.574
80|20	0.823	0.851	0.806	0.770	1.000	0.581
40|30|30	0.837	0.867	0.806	0.778	1.000	0.584
60|20|20	0.837	0.866	0.796	0.791	1.000	0.571
80|10|10	0.833	0.856	0.796	0.810	1.000	0.577
60|30|10	0.824	0.845	0.796	0.781	1.000	0.565
30|30|15|15|10	0.832	0.855	0.786	0.781	1.000	0.549
60|10|10|10|10	0.837	0.876	0.816	0.797	1.000	0.609

Table 2.82: Best results for weighted averaging on Solubility (ADME)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.861	0.895	0.806	0.803	1.0	0.584
Clients 2	0.839	0.870	0.806	0.794	1.000	0.590
Clients 3	0.840	0.864	0.806	0.814	1.000	0.593
Clients 4	0.810	0.823	0.796	0.787	1.000	0.565
Clients 5	0.834	0.866	0.806	0.800	1.000	0.587
Clients 6	0.826	0.849	0.816	0.797	1.000	0.609
Clients 7	0.828	0.852	0.806	0.783	1.000	0.581
Clients 8	0.816	0.846	0.786	0.768	1.000	0.543
Clients 9	0.822	0.839	0.796	0.783	1.000	0.568
Clients 10	0.837	0.873	0.786	0.750	1.000	0.536

Clients 11	0.831	0.861	0.806	0.786	1.000	0.587
Clients 12	0.825	0.853	0.796	0.767	1.000	0.562
Clients 13	0.822	0.851	0.786	0.785	1.000	0.546
Clients 14	0.828	0.853	0.825	0.809	1.000	0.631
Clients 15	0.812	0.843	0.806	0.794	1.000	0.590
Clients 16	0.828	0.862	0.786	0.764	1.000	0.543
Clients 17	0.820	0.857	0.786	0.750	1.000	0.536
Clients 18	0.825	0.858	0.806	0.770	1.000	0.581
Clients 19	0.810	0.849	0.777	0.753	1.000	0.520
Clients 20	0.832	0.876	0.757	0.722	1.000	0.468
Epochs 1	0.829	0.867	0.816	0.783	1.000	0.604
Epochs 2	0.855	0.887	0.806	0.786	1.000	0.587
Epochs 5	0.831	0.857	0.796	0.783	1.000	0.568
Epochs 10	0.857	0.881	0.796	0.800	1.000	0.574
Epochs 20	0.849	0.877	0.786	0.781	1.000	0.549
Balanced 60|40	0.836	0.859	0.806	0.788	1.000	0.579
Balanced 67|33	0.832	0.854	0.806	0.806	1.000	0.576
Balanced 75|25	0.831	0.852	0.796	0.788	1.000	0.556
Balanced 80|20	0.830	0.861	0.825	0.784	1.000	0.623
Balanced 40|30|30	0.861	0.896	0.825	0.800	1.000	0.628
Balanced 60|20|20	0.846	0.856	0.825	0.818	1.000	0.633
Balanced 80|10|10	0.819	0.866	0.757	0.778	1.000	0.496
Balanced 60|30|10	0.854	0.876	0.796	0.767	1.000	0.562
Balanced 30|30|15|15|10	0.826	0.850	0.786	0.779	1.000	0.549
Balanced 60|10|10|10|10	0.821	0.866	0.767	0.746	1.000	0.498

Table 2.83: Best results for benchmarked averaging on Solubility (ADME)

2.4.26 AMES

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.903	0.908	0.837	0.879	0.897	0.674
Clients 2	0.900	0.908	0.830	0.866	0.842	0.660
Clients 3	0.894	0.902	0.827	0.870	0.977	0.653

Clients 4	0.898	0.907	0.840	1.000	0.864	0.680
Clients 5	0.895	0.902	0.834	0.870	0.860	0.667
Clients 6	0.890	0.896	0.828	0.861	0.863	0.656
Clients 7	0.896	0.905	0.827	1.000	0.861	0.654
Clients 8	0.892	0.902	0.827	0.836	1.000	0.652
Clients 9	0.892	0.901	0.824	0.848	0.999	0.648
Clients 10	0.892	0.904	0.822	1.000	0.858	0.643
Clients 11	0.887	0.894	0.823	0.851	1.000	0.647
Clients 12	0.889	0.898	0.815	1.000	0.878	0.627
Clients 13	0.890	0.903	0.818	0.835	1.000	0.635
Clients 14	0.886	0.896	0.814	0.814	0.992	0.626
Clients 15	0.881	0.893	0.813	0.812	1.000	0.623
Clients 16	0.884	0.895	0.816	0.828	1.000	0.631
Clients 17	0.882	0.890	0.821	0.821	1.000	0.641
Clients 18	0.885	0.891	0.820	0.832	1.000	0.638
Clients 19	0.880	0.885	0.812	0.810	1.000	0.621
Clients 20	0.886	0.893	0.819	0.822	0.989	0.637
Epochs 1	0.902	0.913	0.838	0.885	0.879	0.675
Epochs 2	0.901	0.911	0.839	0.877	0.863	0.677
Epochs 5	0.906	0.914	0.838	1.000	0.849	0.676
Epochs 10	0.898	0.904	0.831	0.862	0.859	0.661
Epochs 20	0.898	0.902	0.838	0.862	0.912	0.676
Balanced 60|40	0.899	0.904	0.832	0.868	0.936	0.662
Balanced 67|33	0.896	0.906	0.834	0.869	0.875	0.669
Balanced 75|25	0.892	0.901	0.830	0.873	0.839	0.659
Balanced 80|20	0.897	0.902	0.834	0.870	0.867	0.667
Balanced 40|30|30	0.901	0.909	0.832	0.876	0.933	0.664
Balanced 60|20|20	0.894	0.904	0.830	1.000	0.869	0.660
Balanced 80|10|10	0.896	0.903	0.832	0.856	0.922	0.664
Balanced 60|30|10	0.895	0.903	0.827	0.876	0.875	0.656
Balanced 30|30|15|15|10	0.894	0.901	0.834	0.860	0.865	0.668
Balanced 60|10|10|10|10	0.899	0.910	0.825	0.847	0.878	0.648

Table 2.84: Best results for plain averaging on AMES (final)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.903	0.908	0.837	0.879	0.897	0.674
60|40	0.896	0.908	0.828	0.871	0.836	0.655
67|33	0.895	0.903	0.831	0.871	0.855	0.662
75|25	0.894	0.903	0.827	0.871	0.854	0.653
80|20	0.897	0.907	0.829	0.872	0.849	0.658
40|30|30	0.896	0.905	0.836	0.873	0.851	0.670
60|20|20	0.896	0.904	0.832	0.877	0.870	0.665
80|10|10	0.902	0.907	0.831	0.871	0.920	0.662
60|30|10	0.899	0.905	0.832	0.872	0.848	0.664
30|30|15|15|10	0.901	0.905	0.830	0.860	0.867	0.659
60|10|10|10|10	0.898	0.905	0.828	0.876	0.841	0.656

Table 2.85: Best results for weighted averaging on AMES (final)

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.903	0.908	0.837	0.879	0.897	0.674
Clients 2	0.872	0.883	0.804	1.000	0.866	0.605
Clients 3	0.886	0.898	0.814	1.000	0.884	0.624
Clients 4	0.877	0.886	0.807	1.000	0.906	0.612
Clients 5	0.886	0.896	0.815	0.843	0.893	0.629
Clients 6	0.869	0.879	0.809	1.000	0.862	0.615
Clients 7	0.874	0.886	0.804	0.824	0.987	0.605
Clients 8	0.881	0.890	0.812	0.827	0.889	0.621
Clients 9	0.872	0.886	0.804	0.814	1.000	0.603
Clients 10	0.877	0.888	0.806	1.000	0.897	0.609
Clients 11	0.875	0.888	0.806	0.815	0.894	0.609
Clients 12	0.868	0.882	0.800	0.817	1.000	0.597
Clients 13	0.876	0.885	0.805	1.000	0.904	0.607
Clients 14	0.876	0.890	0.798	1.000	0.900	0.593
Clients 15	0.875	0.887	0.797	0.809	1.000	0.590
Clients 16	0.874	0.880	0.797	1.000	0.893	0.587
Clients 17	0.874	0.885	0.810	1.000	0.892	0.618

Clients 18	0.882	0.891	0.800	0.805	1.000	0.596
Clients 19	0.873	0.882	0.805	1.000	0.903	0.606
Clients 20	0.869	0.880	0.800	0.799	1.000	0.595
Epochs 1	0.883	0.897	0.816	0.839	0.867	0.629
Epochs 2	0.883	0.892	0.814	0.846	0.887	0.627
Epochs 5	0.879	0.892	0.810	0.837	0.859	0.616
Epochs 10	0.879	0.887	0.804	0.827	0.879	0.606
Epochs 20	0.877	0.884	0.809	0.857	0.887	0.616
Balanced 60|40	0.874	0.885	0.808	0.843	0.916	0.614
Balanced 67|33	0.876	0.887	0.806	0.841	0.854	0.611
Balanced 75|25	0.877	0.887	0.807	0.836	0.854	0.612
Balanced 80|20	0.873	0.881	0.815	0.831	0.856	0.628
Balanced 40|30|30	0.879	0.884	0.808	0.839	0.866	0.615
Balanced 60|20|20	0.879	0.891	0.808	0.830	0.863	0.614
Balanced 80|10|10	0.872	0.884	0.808	0.829	0.884	0.614
Balanced 60|30|10	0.877	0.888	0.807	0.852	0.989	0.611
Balanced 30|30|15|15|10	0.881	0.892	0.812	0.832	0.886	0.622
Balanced 60|10|10|10|10	0.874	0.884	0.804	0.829	0.866	0.606

Table 2.86: Best results for benchmarked averaging on AMES (final)

2.4.27 ChEMBL

experiment	roc_auc	pr_auc	accuracy	precision	recall	kappa
Baseline	0.882	0.882	0.800	0.807	0.810	0.600
Clients 2	0.877	0.875	0.799	0.810	0.817	0.597
Clients 3	0.878	0.878	0.799	1.000	0.835	0.598
Clients 4	0.878	0.877	0.799	1.000	0.818	0.598
Clients 5	0.879	0.877	0.800	1.000	0.830	0.600
Clients 6	0.879	0.880	0.799	1.000	0.863	0.598
Clients 7	0.879	0.878	0.800	1.000	0.821	0.600
Clients 8	0.878	0.877	0.798	1.000	0.934	0.595
Clients 9	0.876	0.876	0.796	1.000	0.816	0.591
Clients 10	0.873	0.874	0.794	1.000	0.810	0.588

Clients 11	0.871	0.872	0.792	1.000	0.848	0.583
Clients 12	0.870	0.870	0.790	1.000	0.881	0.581
Clients 13	0.867	0.868	0.787	1.000	0.865	0.573
Clients 14	0.865	0.866	0.786	1.000	0.869	0.571
Clients 15	0.867	0.868	0.788	1.000	0.886	0.576
Clients 16	0.865	0.865	0.786	1.000	0.801	0.572
Clients 17	0.860	0.860	0.780	1.000	0.853	0.560
Clients 18	0.861	0.862	0.781	1.000	0.843	0.562
Clients 19	0.857	0.857	0.777	1.000	0.856	0.554
Clients 20	0.855	0.856	0.774	1.000	0.792	0.549
Epochs 1	0.867	0.864	0.789	0.800	0.941	0.577
Epochs 2	0.869	0.869	0.790	1.000	0.814	0.579
Epochs 5	0.882	0.882	0.800	1.000	0.828	0.600
Epochs 10	0.877	0.876	0.799	1.000	0.818	0.598
Epochs 20	0.870	0.870	0.791	1.000	0.803	0.582
Balanced 60|40	0.878	0.878	0.798	1.000	0.824	0.596
Balanced 67|33	0.879	0.879	0.799	1.000	0.823	0.598
Balanced 75|25	0.878	0.877	0.799	1.000	0.825	0.597
Balanced 80|20	0.879	0.877	0.801	1.000	0.826	0.602
Balanced 40|30|30	0.880	0.880	0.801	1.000	0.819	0.601
Balanced 60|20|20	0.881	0.879	0.801	1.000	0.836	0.602
Balanced 80|10|10	0.881	0.881	0.803	1.000	0.839	0.605
Balanced 60|30|10	0.880	0.880	0.801	0.808	0.831	0.602
Balanced 30|30|15|15|10	0.880	0.879	0.801	1.000	0.828	0.601
Balanced 60|10|10|10|10	0.879	0.879	0.799	0.880	0.818	0.598

Table 2.87: Best results for plain averaging on ChEMBL (v1)

2.4.28 Discussion

The first thing we notice is that some of the smaller datasets are more chaotic when we look at metrics and are less trustworthy in general. This makes sense. If the dataset has only 200 samples, it will result in a training set with only 10 samples for each client when we split it among 20 parties. Smaller ADME datasets should therefore be analyzed with caution.

We ran over 1000 experiments totaling over 20000 epochs, so it is difficult to find common behaviors. For almost any trend we observe we also find exceptions for it. But one prevalent behavior is that the ROC-AUC metric and especially the PR-AUC metric need longer time to converge as the number of clients increases. This effect is clearly visible on most Tox21 tasks, on AMES, on ChEMBL, as well as some ADME datasets like PappCaco2 and Solubility.

Regression tasks are affected a lot more by the federated learning process. Even for larger datasets like CLint the losses in R2 can surpass 50%, and in case of PappCaco2, it can even fail to converge. Other datasets like FupHuman, FupRat, or even the very small RbRat seem to be less affected, but the differences are still much bigger when compared to classification tasks. These effects seemed to be smaller when using benchmarked aggregation (ie: on CLint), but on small or difficult datasets, this method fails in several rounds because the intermediate checkpoints diverge in early phases (ie: on FuBrain, PappCaco2, PappLLC, or RbRat).

Classification tasks work very well on the other hand on almost all tasks, with small losses registered even with large number of clients. This is especially so for the ROC-AUC metric, which is more stable in general compared to PR-AUC and Cohen's Kappa.

Occasionally, we notice a clear sign that the performance decreases as the number of clients increases, but other times, the scores a scrambled, and there is no clear indication if more or less clients work better. This might seem like a strange occurrence because, we would expect the performance to get worse as the local dataset becomes smaller, even if we later aggregate the result, however, it would seem that the federation process can actually be beneficial and acts as a sort of regularization. What we are doing is very similar to what is often referred to in the literature as Stochastic Weight Averaging[28] which has been shown to lead to better generalization. When the effect is not clear in client-based experiments, the differences are likely just random occurrences, similar to what we would get if we trained the model locally with various random splits.

Looking at the number of epochs trained per round, metrics are generally not significantly affected for the most part, but training for too many epochs (20 per round) does sometimes adversely affect the outcome. Otherwise, plain aggregation generally seemed to prefer higher epoch rounds, while benchmarked aggregation worked scored better on fewer rounds.

Another matter worth mentioning is that recall (and sometimes precision) values in the tables presented do not seem to offer any insight by themselves. This is because early in the training process many models often just predict the same value for any input, which often leads to a perfect recall score. As we only show the best values registered in these tables, readers are referred to the Appendix to see how recall and precision values change throughout the training progress.

More importantly, the aggregation method we use does not seem to make that much of a difference, especially on classification tasks. Balancing weights by the number of samples often increased performance, but the differences where much smaller than we expected. Also, there were several exceptions where plain, naive averaging worked better.

Weighting the checkpoints by their performance on a metric was surely expected to outperform naive aggregation, but that was not always the case. We should of course remember the difficulties of evaluating checkpoints on difficult and small datasets, which makes this approach even less attractive (as we can see from the large number of gaps in the line plots from the Appendix). Benchmarked aggregation slightly outperforms plain or, occasionally, even weighted aggregation on classification tasks as well, but the difference is seldom significant. However, client-based and imbalanced split experiments were executed with 10 epochs trained per round. Often times we noticed that benchmarked averaging performed better when we train for fewer epochs per round, so decreasing the number of epochs for these experiments might be worth checking out.

2.5 Performance Analysis

The time it takes to featurize a dataset and to train one epoch will depend on the architecture and the size of the dataset. We report in Table 2.88 our recorded time for featurizing the training set and the time it takes to train 1 epoch on the traning set.

Dataset	Featurization	Training
Tox21	49.682	14.194
AMES	48.530	7.945
CLint	43.739	12.333
FeHuman	5.129	3.281
FuBrain	6.848	4.576
FupHuman	21.483	4.483
FupRat	6.675	3.334
NER-LLC	5.866	3.200
PappCaco2 (cls)	38.291	6.691
PappCaco2 (reg)	38.400	7.204
PappLLC	6.311	2.989
RbRat	4.138	2.901
Solubility	6.893	3.145
ChEMBL (v1)	8147.601	5171.256
ChEMBL (v2)	13436.784	8528.283

Table 2.88: Registered time (in seconds) for featurizing the training set and for training one epoch on CPU.

Technical Documentation

3.1 Installing Dependencies

In order to perform experiments, some preliminary steps must be taken. Namely, we must install all dependencies which we support with conda. If conda is not installed locally, one may follow the online installation guides.

As a first step, we create a new environment using the provided snapshot. Then, we install additional dependencies for PyTorch Geometric (which are downloaded as wheel files).

```
conda env create -f environment.yml
conda activate federated
bash install_additional_dependencies.sh
```

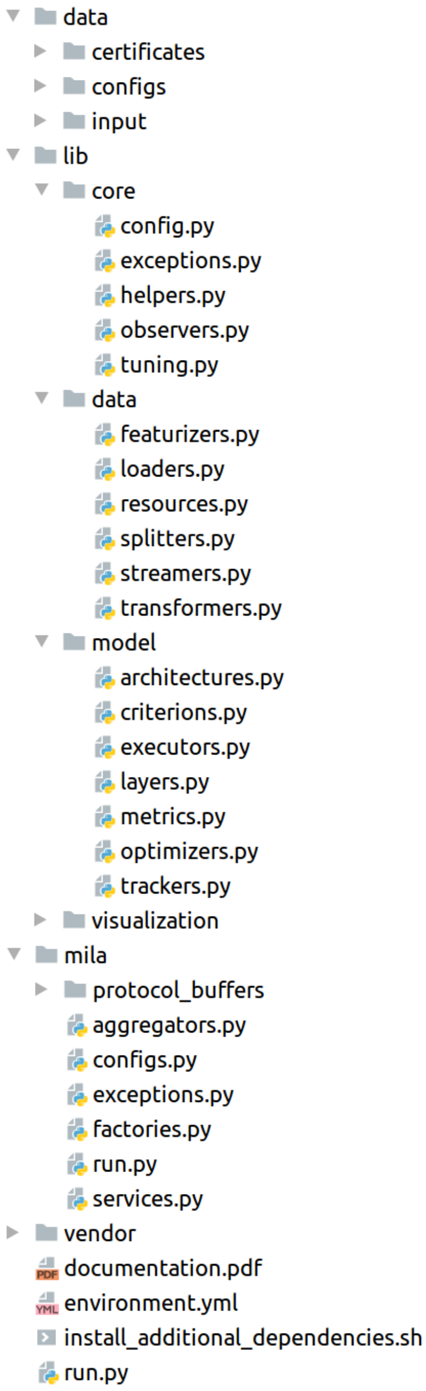
This step has to be performed only one time. Once the environment is created and the depencies installed, one may use the new environment at any time by activating it.

```
conda activate federated
```

3.2 Project Structure

Our code is split into several folders:

- **data**: contains datasets, checkpoints, certificates, logs, and everything else data related. This folder is not fixed. Data can be stored anywhere else on the disk.
- **lib**: contains all the custom code implemented for data preprocessing, training, inference, and experimenting with models in general.
- **mila**: contains the communication module (federated learning)
- **vendor**: contains chunks of code from 3rd party libraries
- **run.py**: is the entry point for experiments (models, not federated learning)
- **environment.yml, install_additional_dependencies.sh**: are installation environments and scripts



```
▼ data
    ▶ certificates
    ▶ configs
    ▶ input
▼ lib
    ▼ core
        config.py
        exceptions.py
        helpers.py
        observers.py
        tuning.py
    ▼ data
        featurizers.py
        loaders.py
        resources.py
        splitters.py
        streamers.py
        transformers.py
    ▼ model
        architectures.py
        criterions.py
        executors.py
        layers.py
        metrics.py
        optimizers.py
        trackers.py
    ▶ visualization
▼ mila
    ▶ protocol_buffers
    aggregators.py
    configs.py
    exceptions.py
    factories.py
    run.py
    services.py
▶ vendor
  documentation.pdf
  environment.yml
  install_additional_dependencies.sh
  run.py
```

Figure 3.9: Project Structure

- **documentation.pdf**: is this file

The main codebase (**lib**) is furthermore split into 4 folders:

- **core**: contains often used functionality and helper functions
- **data**: contains data handles and pre-processing tools
- **model**: contains architectures, metrics, and modeling tools
- **visualization**: contains functionality from visualizing results

In the **core** folder we have:

- **config.py**: for configuration parsing
- **exceptions.py**: for exception handling
- **helpers.py**: for functionality like caching, time tracking, reflection, and dependency injection
- **observers.py**: for event management
- **tuning.py**: for bayesian optimization

In **data** we have:

- **featurizers.py**: for preparing input fields
- **loaders.py**: for loading raw data formats from disk

- **resources.py**: for common structures
- **splitters.py**: for data splitting
- **streamers.py**: where we combine data loading and preprocessing tools
- **transformers.py**: for preparing output fields

In **model** we have:

- **architectures.py**: for model architectures
- **criterions.py**: for custom loss functions
- **executors.py**: for pipelines (ie: training, inference, evaluation)
- **layers.py**: for custom layers
- **metrics.py**: for handling and computing metrics
- **optimizers.py**: for custom optimizers
- **trackers.py**: for tracking running averages

In **mila** we have:

- **protocol_buffers**: for service contracts and gRPC messages
- **aggregators.py**: for aggregator implementations
- **configs.py**: for server and client configuration parsing
- **exceptions.py**: for exception handling
- **factories.py**: for abstractions
- **run.py**: is the entry point for federated learning (both server and clients)
- **services.py**: implements the communication between server and clients

3.3 Framework

Our vision and efforts for the provided solution are centered are 3 key points:

- good quality and clean code
- extensible with minimum effort
- highly configurable and easy to use
-

We rely on several concepts and design patterns improve these characteristics. We briefly describe some of the major components.

3.3.1 Abstractions

Most of our components, like loaders, featurizers, networks, or execution pipelines are designed by contract. For each group of components, we first design an abstract class (ie: AbstractLoader) with common functionality, but more importantly, common methods. The abstract classes are then extended to implement detailed solutions (ie: CsvLoader).

Then, if high level components (like the streamers) rely on low level ones (like the loaders), it is enough for us to specify the abstraction, and the high level module will be able to handle all subtypes of it (it acts as a contract). In object-oriented design, this is referred to as dependency inversion.

3.3.2 Dependency Injection

Dependency injection makes a class independent of its dependencies (ie: input arguments). We achieve this by decoupling the use of a component from its instantiation.

Among other things, this means we can change the code of a lower level objects without having to modify higher level objects which depend on it. This can be a very powerful concept, because it allows us to easily add new functionality without having to write a lot of additional code.

For a more visual way to see the benefits of this concept, see the next section.

3.3.3 Dynamic Configuration

To run experiments, we require a configuration file in JSON format (details in a later section). While some of the structure is rigid, for the most part, configurable options are directly linked to the argument lists of the components constructor. This is achieved with dependency injection.

For example, let us assume we have a "Calculator" object we want to make use of:

```
# file: custom/helpers.py

class Calculator:
    def __init__(self, x: int, y: int):
        self._x = x
        self._y = y

    def sum(self) -> int:
        return self._x + self._y
```

To make use of this object, no changes have to be made to the configuration parsing logic whatsoever. We just point to the class we want to use and specify its arguments:

```
{
    "helper": {
        "type": custom.helpers.Calculator,
        "x": 2,
        "y": 3
    }
}
```

Input arguments do not have to be numeric though, we can use any objects whatsoever. If additional classes are required, they will be instantiated recursively. As an example, this would also work:

```
# file: custom/computers.py

from custom.helpers import Calculator

class Computer:

    def __init__(self, calculator: Calculator, constants: list):
        self._calculator = calculator
        self._constants = constants
    def sum(self, x: int, y: int) -> int:
        return self._calculator.sum(x, y)
```

```
{
    "computer": {
        "type": "custom.computers.Computer",
        "calculator": {
            "type": custom.helpers.Calculator,
            "x": 2,
            "y": 3
        },
        "constants": [1, 5]
    }
}
```

We make use of this functionality a lot and it makes it very easy to use already implemented features like loss functions from the core Pytorch library[51] or graph convolutional operators from Pytorch Geometric[19]. More importantly, we can make use of them without having to write large chunks of complicated logic, or any code at all for most cases.

On the negative side, the compatibility can make the configuration less straight forward and require a level of knowledge about the underlying arguments. We make this easier by providing plenty of examples on how to configure experiments (see the `data/configs/` folder).

3.3.4 Events & Observer

Not everything can be solved with dependency injection. Some areas of any framework are just inherently complicated, complicated code is never good because it is messy, hard to maintain and more error prone.

One good example is the training pipeline. Even for minimal functionality, we need to load checkpoints, initiate data loaders, perform forward and backward passes, log progress, and compute metrics. However, as a central area where many components connect, usually things do not stop there and extra functionality continue to pile up in the area.

To somewhat mitigate this problem, we introduced an event manager, also called an observer pattern. In an observer pattern, we keep track of a list of dependents which are automatically notified when important events happen. In case of the training pipeline for example, we can define such a dependent to receive a payload containing the model and optimizer right before backpropagation happens. Of course, we can then add any changes we want using that payload.

There are several benefits to this approach.

- we will not have an ever growing training script for one
- due to dynamic configuration, anyone can add their own event handlers without having to touch the core codebase at all
- this is very useful for backwards compatibility as well, because changes will not be overwritten upon update

However, adding too many observers which modify the original behavior can hide or cause dependency issues, and make the functionality harder to debug.

The list of dispatchers (events that can be listened to) are listen in the configuration section below. An example of how to write a custom handler is described in the customization section.

3.4 Models

Models live under the `lib/` folder.

Each experiment requires a configuration file to run, which we describe in the next section. Furthermore, for the models to be compatible with Mila, it has to extend 2 abstract classes from the Mila library.

- the **AbstractConfiguration** class - responsible for configuration handling
- and the **AbstractExecutor** class - responsible for starting the train, validation, and inference processes.

3.4.1 Configuration

Configuration files are stored in JSON format and parsed by a class extending `AbstractConfiguration` . When using Mila with a BenchmarkedAggregator, the extended configuration must also include a "checkpoint_path" argument.

All experiments and operations make use of the same configuration file. Certain fields are dynamic and used for dependency injection. In these cases a "type" subfield will specify the desired class type, while all other subfields will be considered arguments for that class. Class arguments themselves can contain a "type" subfield, in which case additional objects will be instantiated recursively.

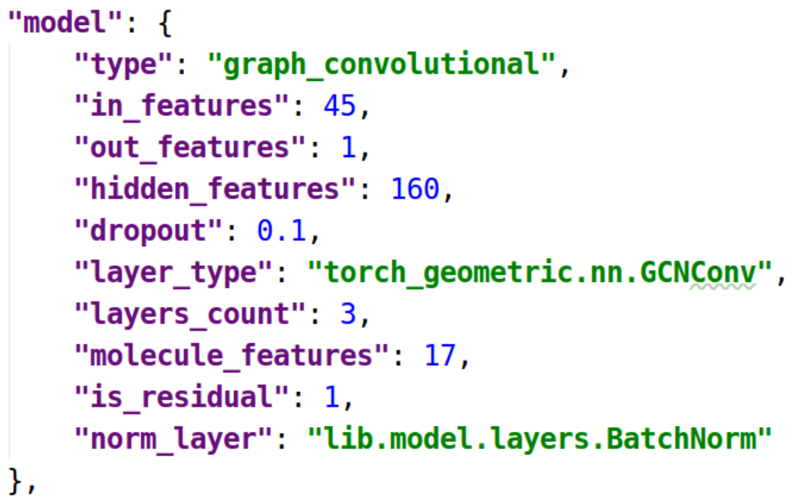
The configurable options are as follows.

model (no default)

The model option is used to specify which model architecture to use and the options of that model. It is a dynamic field and used to instantiate torch modules which extend `lib.model.architectures.AbstractNetwork` .

As a dynamic field, the "type" argument is used to specify which class to use. At the moment, we support 6 architectures as input for the "type" option:

- **graph_convolutional**
- **message_passing**
- **triplet_message_passing**
- **linear**
- **convolutional**
- **protein_ligand**



```
"model": {
    "type": "graph_convolutional",
    "in_features": 45,
    "out_features": 1,
    "hidden_features": 160,
    "dropout": 0.1,
    "layer_type": "torch_geometric.nn.GCNConv",
    "layers_count": 3,
    "molecule_features": 17,
    "is_residual": 1,
    "norm_layer": "lib.model.layers.BatchNorm"
},
```

Figure 3.10: An example of how to configure a Graph Convolutional Network

The `graph_convolutional` is by far the most configurable architecture. Customizable arguments for this model are as follows:

- **in_features**: the number of input features. This value will depend on the options configured for graph featurizer, but should be "45" by default.
- **hidden_features**: number of hidden features used in the graph convolutional operation.
- **out_features**: the number of output features. This should coincide with the number of concurrent tasks we are trying to predict (ie: 12 for Tox21, and 1 for AMES).
- **molecule_features**: how many molecule level features are we expecting? This should be set to "17" for RdKit descriptors and "1613" for Mordred descriptors.
- **dropout**: the dropout rate
- **layer_type**: The graph convolutional operator (defaults to "torch_geometric.nn.GCNConv"). We leverage implementations from Pytorch Geometric and support a large number of layers listen in torch_geometric.nn. Layers which have been tested to work are as follows:

  - torch_geometric.nn.GCNConv
  - torch_geometric.nn.ChebConv
  - torch_geometric.nn.SAGEConv
  - torch_geometric.nn.GraphConv
  - torch_geometric.nn.ARMAConv
  - torch_geometric.nn.LEConv
  - torch_geometric.nn.GENConv
  - torch_geometric.nn.ClusterGCNConv
  - torch_geometric.nn.FeaStConv
  - torch_geometric.nn.GATConv
  - torch_geometric.nn.TAGConv
  - torch_geometric.nn.SGConv
  - lib.model.layers.GINConvolution
  - lib.model.layers.TrimConvolution

- **layers_count**: The number of graph layers to use (defaults to "2")
- **is_residual**: Whether to apply a residual connection to the graph operation (defaults to "True")
- **norm_layer**: Which normalization layer to apply after the graph operation (defaults to "None"). The available options are:
  - None
  - lib.model.layers.BatchNorm
  - lib.model.layers.GraphNorm
  - torch_geometric.nn.LayerNorm
- **activation**: What activation function to use? (defaults to "torch.nn.ReLU"[1]). For a list of options, please check the PyTorch documentation on non-linear activations.
- **edge_features**: The number of edge features (defaults to 0). At the moment, the only working options are "0" or "12". If set to 12, edge features will be concatenated with atom features.

This is my no means an exhaustive list, as the options are dynamic. Should someone wish to implement custom models, the input arguments will be automatically passed from the configuration file.

Each graph convolutional operator can have additional options configured based on the input argument lists. We point curious readers to the PyTorch Geometric docs for a list of all available options. As an example, for GENConv, one might easily specify the initial inverse temperature or the initial power for mean aggregation by passing and additional "t" or "p" argument in the configuration file.

As a note, when the "layer_type" is set to "lib.model.layers.TrimConvolution", 2 additional options should be specified. Namely, "propagate_edge_features" should be set to "True" and "in_edge_features" should be set to "12".
The `message_passing` [21][58] architecture accepts the following options:

- **in_features**: the number of input features. This value will depend on the options configured for graph featurizer, but should be "45" by default.
- **hidden_features**: number of hidden features used in the graph convolutional kernel.
- **out_features**: the number of output features.
- **edge_features**: The number of edge features. At the moment, the only working option is 12.
- **edge_hidden**: the number of hidden features for the edge block.
- **steps**: number of processing steps to run
- **dropout**: the dropout rate (defaults to 0)
- **aggregation**: the aggregation scheme to use. (Options are: "add", "mean", or "max") (defaults to "add")
- **set2set_layers**: number of recurrent layers to use in the the global pooling operator[66] (defaults to "3")
- **set2set_steps**: processing steps for the global pooling operator[66] (defaults to "6")

The triplet_message_passing [36] architecture accepts the following options:

- **in_features**: the number of input features. This value will depend on the options configured for graph featurizer, but should be "45" by default.
- **hidden_features**: number of hidden features used in the graph convolutional kernel.
- **out_features**: the number of output features.
- **edge_features**: the number of edge features. At the moment, the only working option is 12.
- **layers_count**: the number of Triplet Message Passing layers to use
- **dropout**: the dropout rate (defaults to 0)
- **set2set_layers**: number of recurrent layers to use in the the global pooling operator[66] (defaults to "1")
- **set2set_steps**: processing steps for the global pooling operator[66] (defaults to "6")

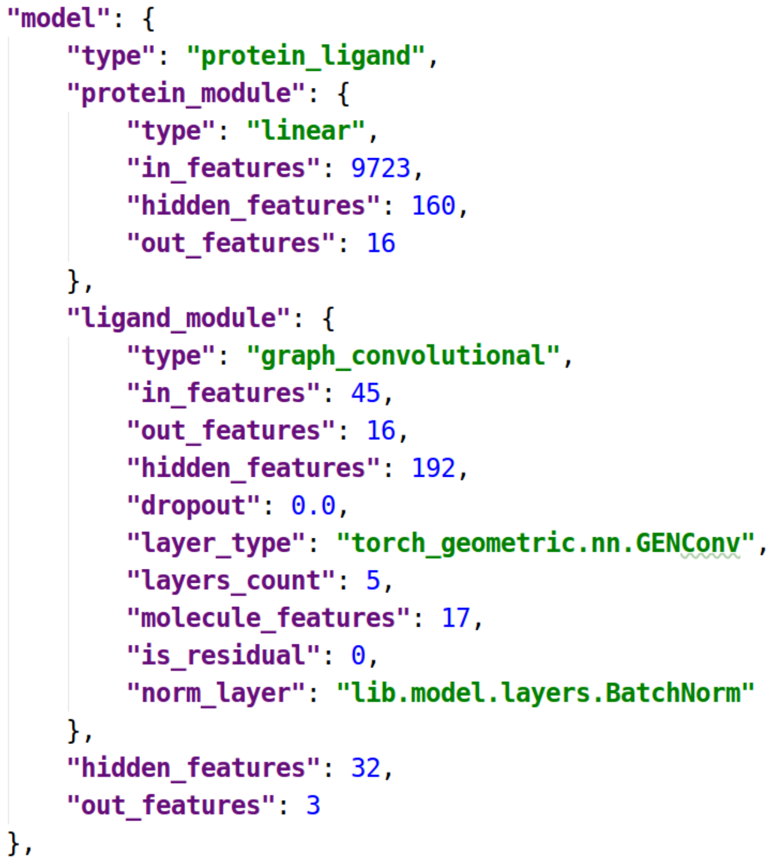
The linear architecture is a simple Shallow Neural Network with 2 linear layers.

- **in_features**: the number of input features.
- **hidden_features**: the number of hidden features
- **out_features**: the number of output features
- **activation**: the activation type (defaults to "torch.nn.ReLU"[1])

The convolutional architecture is a simple Convolutional Network with a single 1D convolutional layer, and a max pooling layer, followed by a linear block as describe above:

- **in_features**: the number of input features.
- **hidden_features**: the number of hidden features
- **out_features**: the number of output features

The `protein_ligand` is a composite architecture. That is, it takes 2 other modules as input, one for the ligand and one for the protein features. Dependency injection again makes our work easy.



```
"model": {
    "type": "protein_ligand",
    "protein_module": {
        "type": "linear",
        "in_features": 9723,
        "hidden_features": 160,
        "out_features": 16
    },
    "ligand_module": {
        "type": "graph_convolutional",
        "in_features": 45,
        "out_features": 16,
        "hidden_features": 192,
        "dropout": 0.0,
        "layer_type": "torch_geometric.nn.GENConv",
        "layers_count": 5,
        "molecule_features": 17,
        "is_residual": 0,
        "norm_layer": "lib.model.layers.BatchNorm"
    },
    "hidden_features": 32,
    "out_features": 3
},
```

Figure 3.11: An example of how to configure a Protein-Ligand Architecture

- **protein_module**: a list set of options for the protein module. Supported options include a *convolutional* architecture for tokenized inputs, or a *linear* architecture for bag-of-words featurized inputs.

- **ligand_module**: a list set of options for the ligand module. Supported options include a *graph_convolutional*, *message_passing*, or *triplet_message_passing* architecture for graph featurized ligands, or a *linear* architecture for circular fingerprints.

- **hidden_features**: the number of hidden features

- **out_features**: the number of output features

After the individual blocks are passed through, the outputs are concatenated and passed through a final "linear" block.

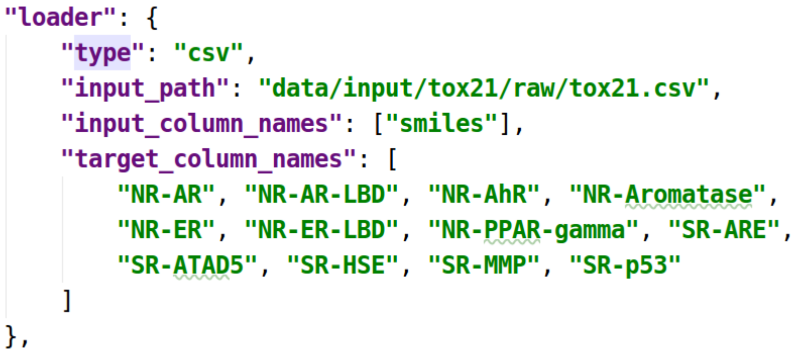
loader (no default)

The loader option is used to configure how raw data files are loaded. It is a dynamic field used to instantiate components which extend `lib.data.loaders.AbstractLoader` .
We support 3 loaders at this time, which are specified in the "type":

- **csv**: For comma-separated values
- **excel**: For excel spreadsheets (only one spreadsheet can be loaded at a time)
- **sdf**: For SDF files (where the whole dataset is stored in a single SDF file)

The additional arguments are identical for the most part at this time. One exception is the `excel` loader, which accepts a numeric "sheet_index" to specify which sheet to load (numbering starts from 0 for the first sheet in the file). Otherwise, all loaders are expected to receive 3 fields:

- **input_path**: the relative or absolute path to the input file
- **input_column_names**: a list of columns or properties which should be mapped as input features
- **target_column_names**: a list of columns or properties which should be mapped as output features



```
"loader": {
    "type": "csv",
    "input_path": "data/input/tox21/raw/tox21.csv",
    "input_column_names": ["smiles"],
    "target_column_names": [
        "NR-AR", "NR-AR-LBD", "NR-AhR", "NR-Aromatase",
        "NR-ER", "NR-ER-LBD", "NR-PPAR-gamma", "SR-ARE",
        "SR-ATAD5", "SR-HSE", "SR-MMP", "SR-p53"
    ]
},
```

Figure 3.12: An example of how to configure a CSV loader for the AMES dataset

featurizers (no default)

Featurizers prepare the input features for the training or inference. The expected input is a list, and therefore we can specify more than one featurizer per experiment. Featurizers are dynamic fields used to instantiate components extending `lib.data.featurizers.AbstractFeaturizer` .

As any dynamic field, the featurizer to be used is specified with the "type" option. The supported featurizers are as follows:

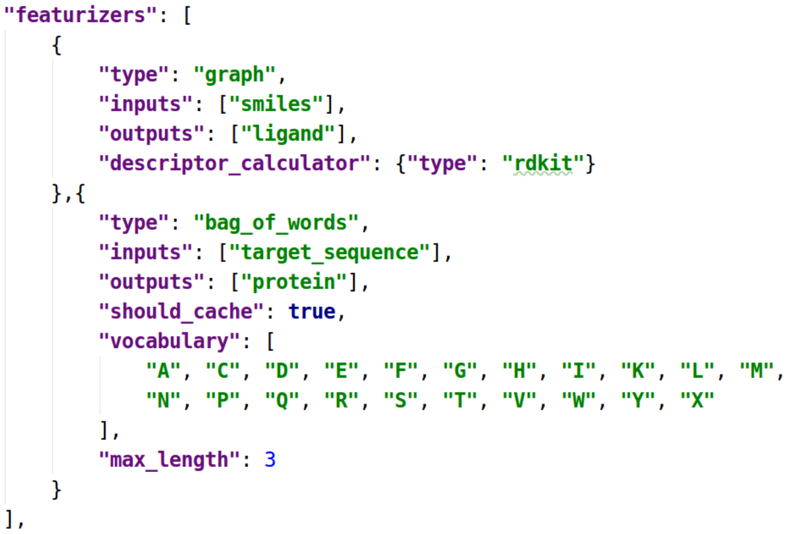
- **graph**: for graph featurization. This featurizer expects a SMILES[70] string for input, and the generated features can be used by graph architectures (*graph_convolutional*, *message_passing*, or *triplet_message_passing*)

- **circular_fingerprint**: for fingerprint featurization. This featurizer expects a SMILES[70] string for input, and the generated features can be used by the *linear* architecture.

- **token**: similar to the one-hot encoder, but will tokenize a whole sentence (like an amino-sequence). The expected input is a sequence (string), and the output can be used by the *convolutional* architecture.

- **bag_of_words**: performs an n-gram, bag-of-words featurization. The expected input is a sequence (string), and the generated features can be used by the *linear* architecture.

- **one_hot_encoder**: can one-hot encode categorical features. The expected input is a string. No architectures make direct use of this featurizer at this point, however, it could be used in a featurization pipeline to prepare inputs for other featurizers.
- **transpose**: is an intermediary featurizer. It expects a Torch Tensor as input and will output a transposed version of it. This of course can be done in a model directly, however, featurized outputs are cached, and can save valuable computational time.
- **fixed**: is an intermediary featurizer. It expects a single float as input and will return that value divided by a user specified value.



```
"featurizers": [
    {
        "type": "graph",
        "inputs": ["smiles"],
        "outputs": ["ligand"],
        "descriptor_calculator": {"type": "rdkit"}
    },{
        "type": "bag_of_words",
        "inputs": ["target_sequence"],
        "outputs": ["protein"],
        "should_cache": true,
        "vocabulary": [
            "A", "C", "D", "E", "F", "G", "H", "I", "K", "L", "M",
            "N", "P", "Q", "R", "S", "T", "V", "W", "Y", "X"
        ],
        "max_length": 3
    }
],
```

Figure 3.13: An example of how to configure featurizers for protein-ligand affinity prediction

Featurizers have custom arguments which can be configured, but all of them will have at least 3 parameters:

- **inputs**: a list of input targets. These values should match the ones specified in the "input_column_names" option of the loader.
- **outputs**: a list of output targets. These values should match the arguments expected by the network architectures. The list of arguments expected by each model is listed in Table 3.1.

- **should_cache**: whether we should perform sample level caching. Note that this is different from global caching, which is performed after featurization. When this option is set to true, each input will be cached in-memory and will not be processed again. This can be very helpful when we are dealing with many duplicates in a certain column which are expensive to compute, like amino-acid sequences. (defaults to "False")

Architecture	Dependency Name	Compatible Featurizers
graph_convolutional	graph	graph
message_passing	graph	graph
triplet_message_passing	graph	graph
linear	features	circular_fingerprint, bag_of_words
convolutional	features	token
protein_ligand	ligand	graph, circular_fingerprint
protein_ligand	protein	token, bag_of_words

Table 3.1: List of featurizers and what architectures they empower. The featurizer "outputs" option should include the "Dependency Name". The "protein_ligand" architecture has 2 dependencies, both of which have to be satisfied.

All featurizers will have these configurable options, and the "inputs" and "outputs" arguments are mandatory. However, most featurizers will have additional configurable options.

The `graph` featurizer supports:

- **descriptor_calculator**: specify how and what molecule level features to compute. The supported options include "rdkit"[34] and "mordred"[53].
- **allowed_atom_types**: specify which atom types should be considered explicitly for (one-hot) encoding. Other atoms will be grouped as a general "other" feature. The default option includes: B, C, N, O, F, Na, Si, P, S, Cl, K, Br, and I.

In additional to symbol based encoding, the graph featurizer also encodes a one-hot atom degree encoding (from 0 to 10), one-hot implicit valence encoding (form 0 to 6), the formal charge, the number of radical electrons, one-hot encoded hybridization, an aromaticity flag, and the total number of Hydrogen atoms. By default, these amounts to 45 input features. If additional atom types are specified, the input features settings should reflect those changes.

For bond level features, we compute a bond type one-hot encoding (single, double, triple, or aromatic), a conjucation flag, a ring membership flag, a stereo configuration encoding. All these amount to 12 edge features.
The `circular_fingerprint` featurizer supports:

- **fingerprint_size**: the number of bits (defaults to 2048)
- **radius**: which defaults to 2

The `one_hot_encoder` featurizer requires:

- **classes**: a list of all possible tokens (ie: "male", "female")

The `token` featurizer supports:

- **vocabulary**: a list of all possible tokens (ie: "A", "C", "T", "G")
- **max_length**: the length of the largest sequence (smaller sequences will be 0-padded)
- **separator**: a separator for the tokens. If an empty string "" is specified, the string will be split character-by-character (defaults to "")

The `bad_of_words` featurizer supports:

- **vocabulary**: a list of all possible tokens (ie: "A", "C", "T", "G")
- **max_length**: the length of the largest sequence (smaller sequences will be 0-padded)

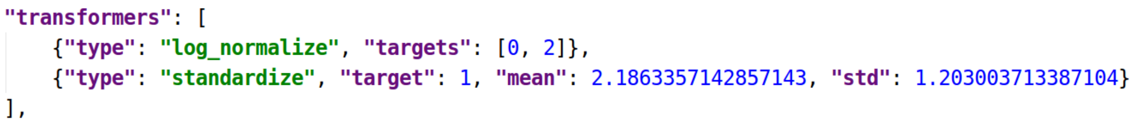
The `fixed` featurizer requires:

- **value**: the value to divide the input by

transformers (no default)

Are very similar featurizers, expect they are applied to output features, and are generally used to normalize values. Transformers are dynamic fields used to instantiate components extending `lib.data.transformers.AbstractTransformer` .

Each transformer implements an "apply" and a "reverse" operation, which converts the values back after inference (for prediction only, does not apply to metrics). Similar to featurizers, multiple transformers can be used in the same experiment



```
"transformers": [
    {"type": "log_normalize", "targets": [0, 2]},
    {"type": "standardize", "target": 1, "mean": 2.1863357142857143, "std": 1.203003713387104}
],
```

Figure 3.14: An example of how to 2 transformers

As a dynamic field, the transformer type is again specified with the "type" argument:

- **log_normalize**: Converts the target to its log value. This transformer expects a `targets` argument, which is a list of (0-based) indices mapping to the "target_column_names" argument of the loader.

- **min_max_normalize**: performs min-max normalization. This transformer has a `target` argument similar to the log transformer, however, in this case, we expect a single value instead of a list. The "minimum" and "maximum" arguments are also mandatory, which should reflect the smallest and largest values recorded for the column/property.

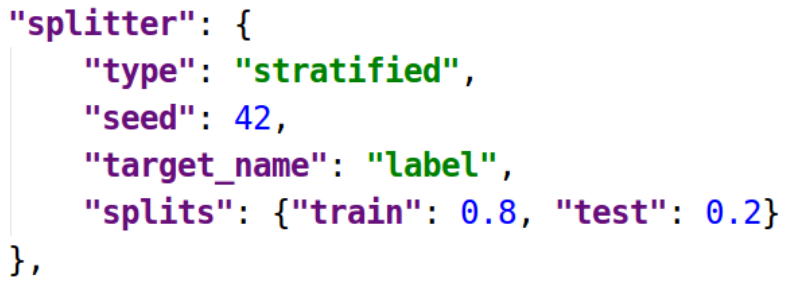
- **fixed_normalize**: Divides the target values by a fixed number. This transformer expects a `targets` argument, which is a list in this case. The "value" argument is used to specify the value used for the division.

- **standardize**: performs z-score normaliztion. This transformer has a `target` argument which is a single 0-based index (not a list). The "mean" and "std" options are also mandatory which denote the average value and the standard deviation for the target.

- **cutoff**: converts a continuous value to a discrete one, using a user-specified cutoff. Note that this operation is destructive and cannot be reversed. We expect a `target` argument with a single 0-based index, and a "cutoff" argument denoting the threshold for binarization.

splitter (no default)

The last of the major abstraction based dynamic settings, the "splitter" specifies how to split the dataset. These options are used to instantiate components extending `lib.data.splitters.AbstractSplitter` .



```
"splitter": {
    "type": "stratified",
    "seed": 42,
    "target_name": "label",
    "splits": {"train": 0.8, "test": 0.2}
},
```

Figure 3.15: An example configuration for a stratified splitter

As a dynamic option, splitter classes are specified using the "type" argument. We have the following splitter types:

- **index**: for index-based splitting
- **random**: for random splits
- **stratified**: for stratified splits based on a certain output column/property

All splits require a `splits` argument in a dictionary (key-value) format. The keys denote the name of the split and can be any users-specified value (we generally used "train" and "test"). The values represent the proportions for each split and should add up to 1. Users can specify any number of splits, not only 2.

The "random" and "stratified" splitters also require a "seed" argument which is used to set the random state for reproducible splits.

Finally, the "stratified" split requires a "target_name" argument, which should be an entry of the loader’s "target_column_names" argument. The split will be performed based on this column. If the "target_name" contains continuous values, they can be grouped into a number of bins using quantile-based discretization (ie: equal-sized buckets based on rank). Users can specify the number of bins using the "bins_count" argument.

criterion (no default)

The criterion option is used to specify the loss function. It is a dynamic option, however, it is not rely on abstractions.

Users can specify any native Torch or custom written loss functions:

```
"criterion": {
    "type": "torch.nn.BCEWithLogitsLoss"
},
```

We also provide a custom built masked loss function, which wrapps around a regular loss function, but ignores missing labels. Using the masked loss is easy with dependency injection:

```
"criterion": {
    "type": "lib.model.criterions.MaskedLoss",
    "loss": {"type": "torch.nn.BCEWithLogitsLoss"}
},
```

As a dynamic setting, of course, users can specify any additional input arguments for their loss function. For a list of all criterions, we point readers to the pytorch documentation.

optimizer (no default)

Is a dynamic option used to specify and configure the optimizer. As any other fynamic option, the class is specified with the "type" argument, and everything else is injected into the constructor:

```
"optimizer": {
    "type": "torch.optim.Adam",
    "lr": 0.01,
    "weight_decay": 0.00056
},
```

For a list of native PyTorch optimizers, please see the pytorch documentaiton. Of course, custom optimizers can be used as well. As an example, we provide support for the recent AdaBelief[78] optimizer:

```
"optimizer": {
    "type": "lib.model.optimizers.AdaBelief",
    "weight_decay": 0,
    "betas": [0.9, 0.999]
},
```

scheduler (no default)

Schedulers are used to adjust the learning rate during training. This is a dynamic option very similar to the criterion or the optimizer.

For a list of native pytorch learning rate schedulers, please visit the pytorch documentation.

```
"scheduler": {
    "type": "torch.optim.lr_scheduler.OneCycleLR",
    "max_lr": 0.01,
    "epochs": 200,
    "pct_start": 0.3,
    "div_factor": 25,
    "final_div_factor": 1000
},
```

is_stepwise_scheduler (default: True)

A static field. If true, we perform scheduler updates after every forward pass. Otherwise, we perform the update after every epoch.

is_finetuning (default: False)

A static field. This should remain "False" if one wishes to continue training after a reboot, and be set to "True" when we wish to train on a new dataset using a previous checkpoint. When this option is "True", only model weights will be loaded, otherwise we also load the optimizer, scheduler, and epoch tracking information.

output_path (no default)

Points to the location where checkpoints will be saved to.

checkpoint_path (default: None)

A static field marking the path to a checkpoint. Some operations like single checkpoint evaluation or inference require a fixed checkpoint. One can also specify a checkpoint path if they wish to continue training on a previous task, or for fine-tuning on another dataset.

threshold (default: 0.5)

Specifies what threshold to use when converting logits to predictions. This is going to affect certain metrics (like accuracy) and predicted values (when running inference).

Of course, the threshold is used only for classification tasks.

cross_validation_folds (default: 5)

How many folds to split the data into when performing cross-validation?

train_split (default: "train")

Specify which split to use for training. This should be one of the keys specified in the "splits" option of the "splitter".

test_split (default: "test")

Specify which split to use for evaluation and inference. This should be one of the keys specified in the "splits" option of the "splitter".

train_metrics (default: [])

Specify which metrics to report during training. This option is expected to be a list of strings, thus multiple metrics can be specified. But please note that metric computations can slow down the training process.

For a list of supported metrics, please use the shorthand code from Table 1.5.

test_metrics (default: [])

Specify which metrics to report during evaluation. This option is expected to be a list of strings, thus multiple metrics can be specified.

For a list of supported metrics, please use the shorthand code from Table 1.5.

epochs (default: 200)

How many epochs to train the model?

batch_size (default: 32)

What batch size to use (in all operations).

use_cuda (default=true)

If true, and if an NVIDIA graphics card is available, the model will use GPU acceleration.

cache_location (default: "/tmp/federated/")

A folder where cached objects will be stored in. It is recommended to monitor the size of this directory.

clear_cache (default: False)

When set to "True", cached data for the specific experiment will be flushed.

log_frequency (default: 20)

After how many iterations should an update be printed when training the model.

log_level (default: "info")

How many logs should be printed. The available options are: "debug", "info", "warn", "error", and "critical".

log_format (default: "")

Can be used to include additional details for logged messages, like timestamps.

target_metric (default: "roc_auc")

Specify which metric to use as feedback for bayesian optimization. This option is also used when to find best performing checkpoints.

optuna_trials (default: 1000)

How many trials should be perform when running Bayesian Optimization?

subset (default: None)

The subset is a static, but composite setting. It expects a dictionary containing an "id" and a "distribution" field.

The option is used to run experiments on a subset of the whole dataset, and is very helpful for distributed learning experiments. Otherwise, it provides little use, as the specific subsets can be optained using the regular splitter functionality.

The "distribution" setting specifies a list of fractions the dataset should be split into and the expected value is a list of floating point values which sum up to 1. The "id" setting specifies which subset should be used from the list of "distribution"s and is a 0-based index.

As an example, the below setting will split the dataset into 2 equal proportions, and will use the first half of the split for training.

```
"subset": {
    "id": 0,
    "distribution": [0.5, 0.5]
}
```

visualizer (default: None)

Another static, but composite option. This setting is used by the visualization operation.

The setting should contain 2 subfields:

- **targets**: is a list of target columns which will be explained. The values are 0-based indices mapping to the "target_column_names" option of the loader
- **output_path**: a folder where visualized drawings will be saved to

```
"visualizer": {
    "targets": [0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11],
    "output_path": "tmp/visualization/"
}
```

differential_privacy (default: {"enabled": False})

A static, but composite option used to control differential privacy.

The "enabled" option is a boolean value acting as a switch for differential privacy. The "options" argument is a dictionary of configurable options:

- **delta**: The target delta used when reporting the computed (epsilon, delta)-privacy budget spent so far.
- **alphas**: instructs the privacy engine what Renyi Differential Privacy[43, 44] orders to use for tracking privacy expenditure. (the default value is set to [1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8.0, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, 10.0, 10.1, 10.2, 10.3, 10.4, 10.5, 10.6, 10.7, 10.8, 10.9,

12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63]).

- **noise_multiplier**: The ratio of the standard deviation of the Gaussian noise to the L2-sensitivity of the function to which the noise is added.
- **max_grad_norm**: The maximum norm of the per-sample gradients. Any gradient with norm higher than this will be clipped to this value.
- **secure_rng**: If on, it will use torchcsprng for secure random number generation. This comes with a significant performance cost, therefore it is recommended to turn off when experimenting.

Differential privacy was implemented using Opacus[50].

```
"differential_privacy": {
    "enabled": true,
    "options": {
        "delta": 1e-5,
        "alphas": [10, 100],
        "noise_multiplier": 1.5,
        "max_grad_norm": 1.0,
        "secure_rng": false
    }
}
```

Caution! Not all layer types support differential privacy. Of especial note is that BatchNorm layers are not supported. As a workaround, we dynamically replace BatchNorm layers with GroupNorm[73] layers, which can affect the training results.

observers (default: {})

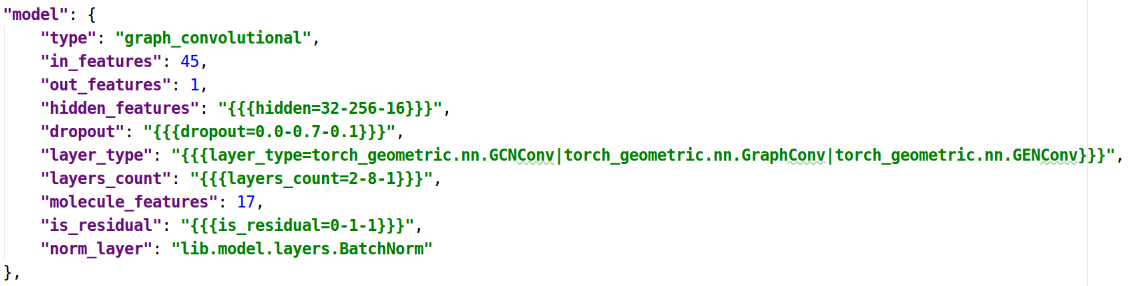
Observers are handlers which listen for and handle incoming events. We set up various event dispatchers throughout the framework like before a checkpoint is loaded, before training starts, or after training finished. A full list of event dispatchers and their payload is listed in Table 3.2.

Event listeners watch the dispatchers and act on the payload. Features like differential privacy are implemented entirely with observers. As for user specified handlers, the `add_sigmoid` handler is one of the only useful ones, which adds an additional sigmoid activation to the output of a model. It should be attached to "before_criterion", and "before_predict" dispatchers.

```
"observers": {
    "before_criterion": ["lib.core.observers.AddSigmoidHandler"],
    "after_predict": ["lib.core.observers.AddSigmoidHandler"]
},
```

3.4.2 Bayesian Optimization

To perform Bayesian Optimization, an experiment configuration file (in JSON format) must be first parameterized. An example of how this looks like is presented below.



```
"model": {
    "type": "graph_convolutional",
    "in_features": 45,
    "out_features": 1,
    "hidden_features": "{{{hidden=32-256-16}}}",
    "dropout": "{{{dropout=0.0-0.7-0.1}}}",
    "layer_type": "{{{layer_type=torch_geometric.nn.GCNConv|torch_geometric.nn.GraphConv|torch_geometric.nn.GENConv}}}",
    "layers_count": "{{{layers_count=2-8-1}}}",
    "molecule_features": 17,
    "is_residual": "{{{is_residual=0-1-1}}}",
    "norm_layer": "lib.model.layers.BatchNorm"
},
```

Figure 3.16: An example configuration with parameterized options.

Parameterized options are wrapped in triple curly brackets and must be enclosed within quotes "{{{}}}". These options are also referenced in the code as "placeholders". We use a parsing mechanism before we pass the options to Optuna[2] for suggestion generation:

- Each placeholder should have a name and some options, separated by an equal sign (ie: **"{{{name=options}}}"**)
- Options separated by a pipe "|" will be categorical (ie: **"{{{aggregate=mean|sum|max}}}"**)
- Numeric values should have 3 options separated by a dash "-" (ie: **"{{{dropout=min-max-step**}}}")

  - The first value is the minimum value
  - The second value is the maximum value
  - The the third value is the incremental step between the minimum and the maximum
  - The [minimum, maximum] is a closed interval

- if numeric values contain a dot ".", a float value will be suggested (ie: **"{{{dropout=0.0-0.7-0.1}}}"**)
- if numeric values do not contain a dot ".", an integer will be suggested (ie: **"{{{layers=2-5-1}}}**")

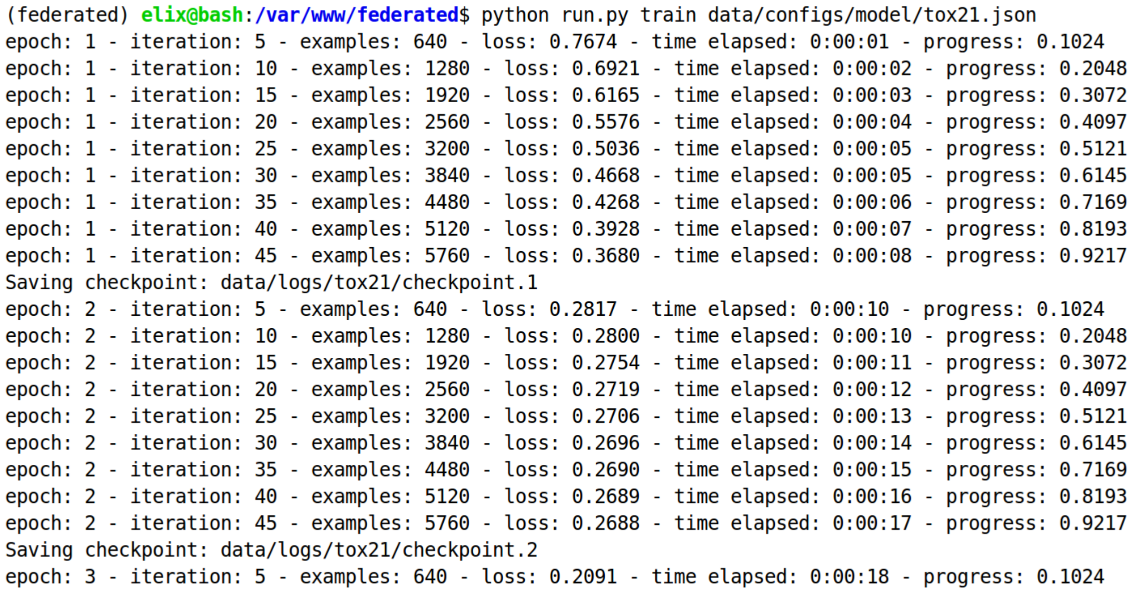
We present an example for the model arguments, but any option from the configuration file can be parameterized.

3.4.3 Commands

Training

To train a model, the following command can be used:

```
python run.py train {config_path}
```



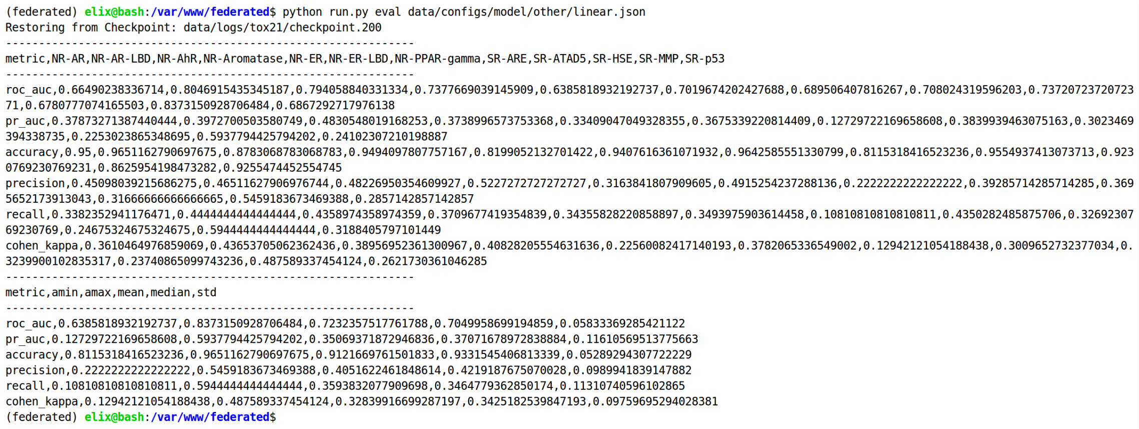
```
(federated) elix@bash:/var/www/federated$ python run.py train data/configs/model/tox21.json
epoch: 1 - iteration: 5 - examples: 640 - loss: 0.7674 - time elapsed: 0:00:01 - progress: 0.1024
epoch: 1 - iteration: 10 - examples: 1280 - loss: 0.6921 - time elapsed: 0:00:02 - progress: 0.2048
epoch: 1 - iteration: 15 - examples: 1920 - loss: 0.6165 - time elapsed: 0:00:03 - progress: 0.3072
epoch: 1 - iteration: 20 - examples: 2560 - loss: 0.5576 - time elapsed: 0:00:04 - progress: 0.4097
epoch: 1 - iteration: 25 - examples: 3200 - loss: 0.5036 - time elapsed: 0:00:05 - progress: 0.5121
epoch: 1 - iteration: 30 - examples: 3840 - loss: 0.4668 - time elapsed: 0:00:05 - progress: 0.6145
epoch: 1 - iteration: 35 - examples: 4480 - loss: 0.4268 - time elapsed: 0:00:06 - progress: 0.7169
epoch: 1 - iteration: 40 - examples: 5120 - loss: 0.3928 - time elapsed: 0:00:07 - progress: 0.8193
epoch: 1 - iteration: 45 - examples: 5760 - loss: 0.3680 - time elapsed: 0:00:08 - progress: 0.9217
Saving checkpoint: data/logs/tox21/checkpoint.1
epoch: 2 - iteration: 5 - examples: 640 - loss: 0.2817 - time elapsed: 0:00:10 - progress: 0.1024
epoch: 2 - iteration: 10 - examples: 1280 - loss: 0.2800 - time elapsed: 0:00:10 - progress: 0.2048
epoch: 2 - iteration: 15 - examples: 1920 - loss: 0.2754 - time elapsed: 0:00:11 - progress: 0.3072
epoch: 2 - iteration: 20 - examples: 2560 - loss: 0.2719 - time elapsed: 0:00:12 - progress: 0.4097
epoch: 2 - iteration: 25 - examples: 3200 - loss: 0.2706 - time elapsed: 0:00:13 - progress: 0.5121
epoch: 2 - iteration: 30 - examples: 3840 - loss: 0.2696 - time elapsed: 0:00:14 - progress: 0.6145
epoch: 2 - iteration: 35 - examples: 4480 - loss: 0.2690 - time elapsed: 0:00:15 - progress: 0.7169
epoch: 2 - iteration: 40 - examples: 5120 - loss: 0.2689 - time elapsed: 0:00:16 - progress: 0.8193
epoch: 2 - iteration: 45 - examples: 5760 - loss: 0.2688 - time elapsed: 0:00:17 - progress: 0.9217
Saving checkpoint: data/logs/tox21/checkpoint.2
epoch: 3 - iteration: 5 - examples: 640 - loss: 0.2091 - time elapsed: 0:00:18 - progress: 0.1024
```

Figure 3.17: Sample output of the training command.

Evaluating a Single Checkpoint

To evaluate the performance of the "checkpoint_path" specified in the configuration file, use the following command:

```
python run.py eval {config_path}
```



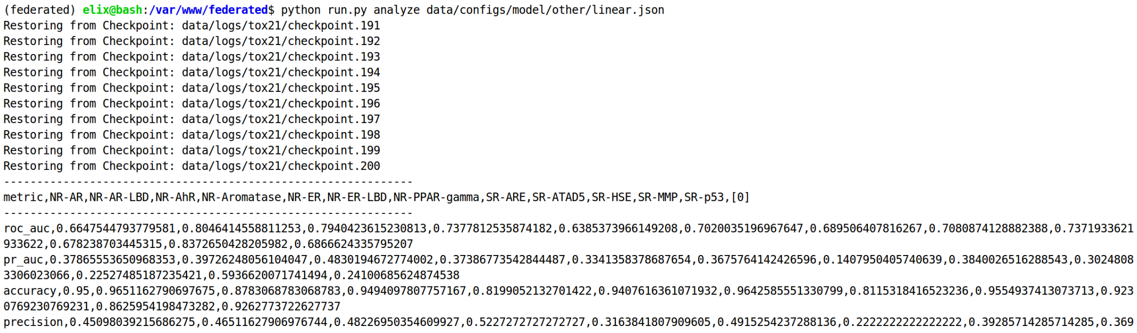
```
(federated) elix@bash:/var/www/federated$ python run.py eval data/configs/model/other/linear.json
Restoring from Checkpoint: data/logs/tox21/checkpoint.200
--------------------------------------------------------------
metric,NR-AR,NR-AR-LBD,NR-AhR,NR-Aromatase,NR-ER,NR-ER-LBD,NR-PPAR-gamma,SR-ARE,SR-ATAD5,SR-HSE,SR-MMP,SR-p53
--------------------------------------------------------------
roc_auc,0.66490238336714,0.8046915435345187,0.794058840331334,0.7377669039145909,0.6385818932192737,0.7019674202427688,0.689506407816267,0.708024319596203,0.73720723720723
71,0.678077074165503,0.8373150928706484,0.686729271797613 8
pr_auc,0.37873271387440444,0.3972700503580749,0.4830548019168253,0.3738996573753368,0.33409047049328355,0.3675339220814409,0.12729722169658608,0.3839939463075163,0.3023469
394338735,0.2253023865348695,0.5937794425794202,0.24102307210198887
accuracy,0.95,0.9651162790697675,0.8783068783068783,0.9494097807757167,0.8199052132701422,0.9407616361071932,0.9642585551330799,0.811531841652323 6,0.9554937413073713,0.923
0769230769231,0.8625954198473282,0.9255474452554745
precision,0.45098039215686275,0.46511627906976744,0.48226950354609927,0.5227272727272727,0.3163841807909605,0.4915254237288136,0.2222222222222222,0.3928571428571428 5,0.369
5652173913043,0.31666666666666665,0.5459183673469388,0.2857142857142857
recall,0.3382352941176471,0.4444444444444444,0.4358974358974359,0.3709677419354839,0.34355828220858897,0.3493975903614458,0.10810810810810811,0.4350282485875706,0.32692307
69230769,0.24675324675324675,0.5944444444444444,0.3188405797101449
cohen_kappa,0.3610464976859069,0.43653705062362436,0.38956952361300967,0.40828205554631636,0.22560082417140193,0.3782065336549002,0.12942121054188438,0.3009652732377034,0.
3239900102835317,0.23740865099743236,0.487589337454124,0.2621730361046285
--------------------------------------------------------------
metric,amin,amax,mean,median,std
--------------------------------------------------------------
roc_auc,0.6385818932192737,0.8373150928706484,0.7232357517761788,0.7049958699194859,0.0583336928542112 2
pr_auc,0.12729722169658608,0.5937794425794202,0.35069371872946836,0.37071678972838884,0.11610569513775663
accuracy,0.8115318416523236,0.9651162790697675,0.9121669761501833,0.9331545406813339,0.0528929430772222 9
precision,0.2222222222222222,0.5459183673469388,0.4051622461848614,0.4219187675070028,0.0989941839147882
recall,0.10810810810810811,0.5944444444444444,0.3593832077909698,0.3464779362850174,0.11310740596102865
cohen_kappa,0.12942121054188438,0.487589337454124,0.32839916699287197,0.3425182539847193,0.09759695294028381
(federated) elix@bash:/var/www/federated$
```

Figure 3.18: Sample output of the evaluation command.

Evaluating Multiple Checkpoints

To evaluate all checkpoints found in the "output_path" folder specified in the configuration file, use the following command:

```
python run.py eval {config_path}
```



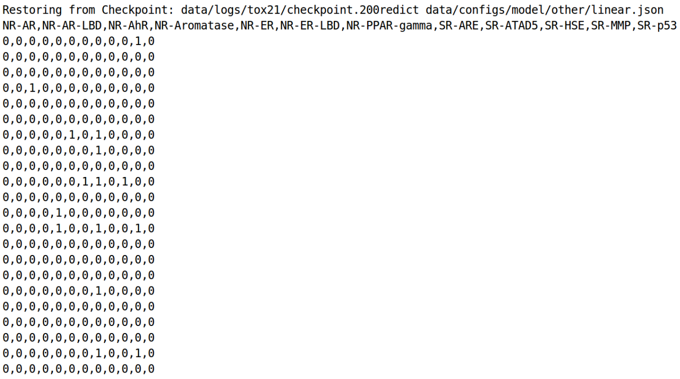
```
(federated) elix@bash:/var/www/federated$ python run.py analyze data/configs/model/other/linear.json
Restoring from Checkpoint: data/logs/tox21/checkpoint.191
Restoring from Checkpoint: data/logs/tox21/checkpoint.192
Restoring from Checkpoint: data/logs/tox21/checkpoint.193
Restoring from Checkpoint: data/logs/tox21/checkpoint.194
Restoring from Checkpoint: data/logs/tox21/checkpoint.195
Restoring from Checkpoint: data/logs/tox21/checkpoint.196
Restoring from Checkpoint: data/logs/tox21/checkpoint.197
Restoring from Checkpoint: data/logs/tox21/checkpoint.198
Restoring from Checkpoint: data/logs/tox21/checkpoint.199
Restoring from Checkpoint: data/logs/tox21/checkpoint.200
-------------------------------------------------------------
metric,NR-AR,NR-AR-LBD,NR-AhR,NR-Aromatase,NR-ER,NR-ER-LBD,NR-PPAR-gamma,SR-ARE,SR-ATAD5,SR-HSE,SR-MMP,SR-p53,[0]
-------------------------------------------------------------
roc_auc,0.6647544793779581,0.8046414558811253,0.7940423615230813,0.7377812535874182,0.6385373966149208,0.7020035196967647,0.689506407816267,0.7080874128882388,0.7371933621
933622,0.678238703445315,0.8372650428205982,0.6866624335795207
pr_auc,0.3786555365096835З,0.39726248056104047,0.4830194672774002,0.37386773542844487,0.3341358378687654,0.3675764142426596,0.1407950405740639,0.3840026516288543,0.3024808
3306023066,0.22527485187235421,0.5936620071741494,0.24100685624874538
accuracy,0.95,0.9651162790697675,0.8783068783068783,0.9494097807757167,0.8199052132701422,0.9407616361071932,0.9642585551330799,0.8115318416523236,0.9554937413073713,0.923
0769230769231,0.8625954198473282,0.9262773722627737
precision,0.45098039215686275,0.46511627906976744,0.48226950354609927,0.5227272727272727,0.3163841807909605,0.4915254237288136,0.2222222222222222,0.39285714285714285,0.369
```

Figure 3.19: Sample output of the analyze command.

Inference

To run inference using the "checkpoint_path" specified in the configuration file, the following command can be used:

```
python run.py predict {config_path}
```



```
Restoring from Checkpoint: data/logs/tox21/checkpoint.200redict data/configs/model/other/linear.json
NR-AR,NR-AR-LBD,NR-AhR,NR-Aromatase,NR-ER,NR-ER-LBD,NR-PPAR-gamma,SR-ARE,SR-ATAD5,SR-HSE,SR-MMP,SR-p53
0,0,0,0,0,0,0,0,0,0,1,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,1,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,1,0,1,0,0,0,0
0,0,0,0,0,0,0,1,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,1,1,0,1,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,1,0,0,0,0,0,0,0
0,0,0,0,1,0,0,1,0,0,1,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,1,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,0,0,0,0,0
0,0,0,0,0,0,0,1,0,0,1,0
0,0,0,0,0,0,0,0,0,0,0,0
```

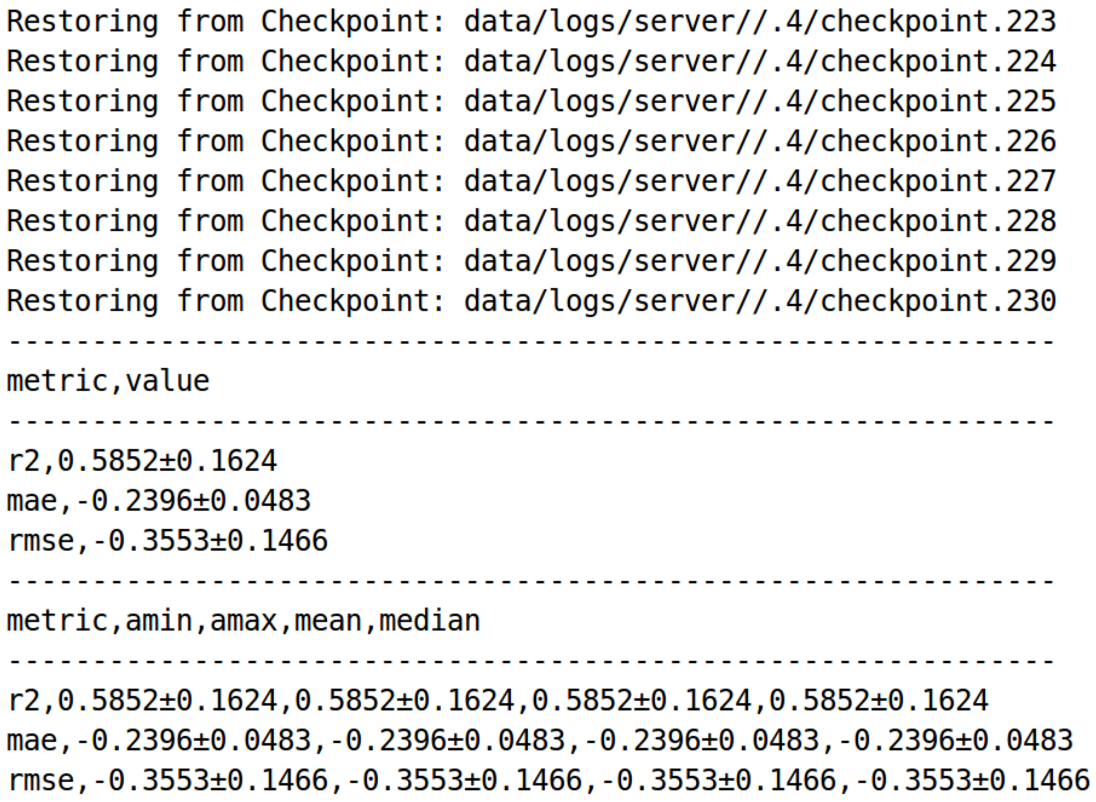
Figure 3.20: Sample output of the inference command.

Cross-Validation

We support 3 different ways to perform cross-validation:

- **mean cross-validation**: for each fold we train, then evaluate the fold. We store the best performing metrics and perform fold-wise aggregation of the metrics.
- **full cross-validation**: for each fold we train and retrieve the logits for the fold. These are stored and metrics are computed on the whole dataset after each fold finished training.
- **step cross-validation**: we train each fold one epoch at a time. After an epoch is trained on for each fold, we perform full cross-validation on for the last checkpoints only.

```
python run.py mean_cv {config_path}
python run.py full_cv {config_path}
python run.py step_cv {config_path}
```



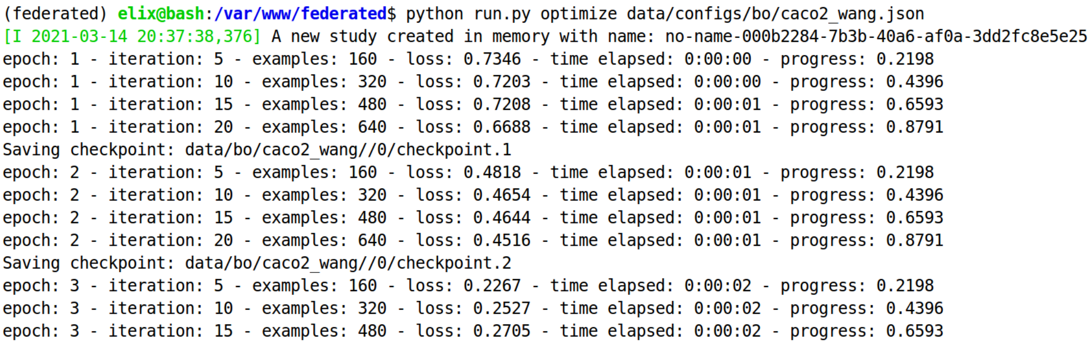
```
Restoring from Checkpoint: data/logs/server//.4/checkpoint.223
Restoring from Checkpoint: data/logs/server//.4/checkpoint.224
Restoring from Checkpoint: data/logs/server//.4/checkpoint.225
Restoring from Checkpoint: data/logs/server//.4/checkpoint.226
Restoring from Checkpoint: data/logs/server//.4/checkpoint.227
Restoring from Checkpoint: data/logs/server//.4/checkpoint.228
Restoring from Checkpoint: data/logs/server//.4/checkpoint.229
Restoring from Checkpoint: data/logs/server//.4/checkpoint.230
--------------------------------------------------------------
metric,value
--------------------------------------------------------------
r2,0.5852±0.1624
mae,-0.2396±0.0483
rmse,-0.3553±0.1466
--------------------------------------------------------------
metric,amin,amax,mean,median
--------------------------------------------------------------
r2,0.5852±0.1624,0.5852±0.1624,0.5852±0.1624,0.5852±0.1624
mae,-0.2396±0.0483,-0.2396±0.0483,-0.2396±0.0483,-0.2396±0.0483
rmse,-0.3553±0.1466,-0.3553±0.1466,-0.3553±0.1466,-0.3553±0.1466
```

Figure 3.21: Sample output of mean cross-validation command.

Bayesian Optimization

Bayesian optimization requires a parameterized configuration file as input. Otherwise, we use the "optimize" command.

```
python run.py optimize {config_path}
```



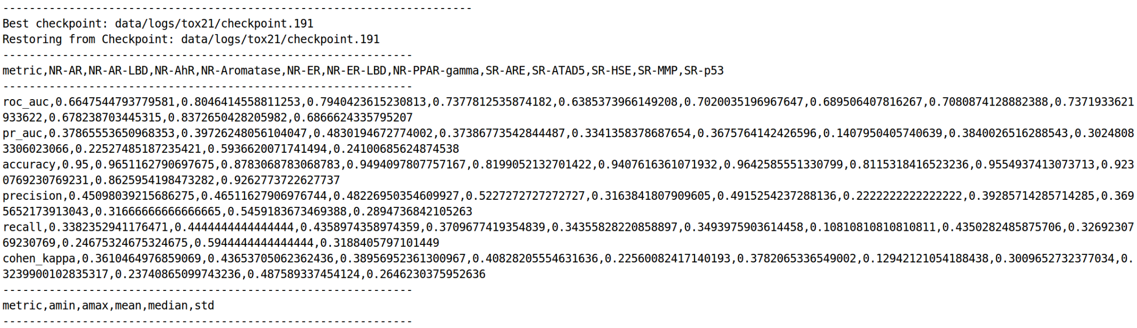
```
(federated) elix@bash:/var/www/federated$ python run.py optimize data/configs/bo/caco2_wang.json
[I 2021-03-14 20:37:38,376] A new study created in memory with name: no-name-000b2284-7b3b-40a6-af0a-3dd2fc8e5e25
epoch: 1 - iteration: 5 - examples: 160 - loss: 0.7346 - time elapsed: 0:00:00 - progress: 0.2198
epoch: 1 - iteration: 10 - examples: 320 - loss: 0.7203 - time elapsed: 0:00:00 - progress: 0.4396
epoch: 1 - iteration: 15 - examples: 480 - loss: 0.7208 - time elapsed: 0:00:01 - progress: 0.6593
epoch: 1 - iteration: 20 - examples: 640 - loss: 0.6688 - time elapsed: 0:00:01 - progress: 0.8791
Saving checkpoint: data/bo/caco2_wang//0/checkpoint.1
epoch: 2 - iteration: 5 - examples: 160 - loss: 0.4818 - time elapsed: 0:00:01 - progress: 0.2198
epoch: 2 - iteration: 10 - examples: 320 - loss: 0.4654 - time elapsed: 0:00:01 - progress: 0.4396
epoch: 2 - iteration: 15 - examples: 480 - loss: 0.4644 - time elapsed: 0:00:01 - progress: 0.6593
epoch: 2 - iteration: 20 - examples: 640 - loss: 0.4516 - time elapsed: 0:00:01 - progress: 0.8791
Saving checkpoint: data/bo/caco2_wang//0/checkpoint.2
epoch: 3 - iteration: 5 - examples: 160 - loss: 0.2267 - time elapsed: 0:00:02 - progress: 0.2198
epoch: 3 - iteration: 10 - examples: 320 - loss: 0.2527 - time elapsed: 0:00:02 - progress: 0.4396
epoch: 3 - iteration: 15 - examples: 480 - loss: 0.2705 - time elapsed: 0:00:02 - progress: 0.6593
```

Figure 3.22: Sample output of the bayesian optimization command.

Finding the Best Checkpoint

This functionality relies on the "analyze" command. It will evaluate all checkpoints and return the best one according to the "targe_metric" specified.

```
python run.py find_best_checkpoint {config_path}
```



```
----------------------------------------------------------------------
Best checkpoint: data/logs/tox21/checkpoint.191
Restoring from Checkpoint: data/logs/tox21/checkpoint.191
-------------------------------------------------------------
metric,NR-AR,NR-AR-LBD,NR-AhR,NR-Aromatase,NR-ER,NR-ER-LBD,NR-PPAR-gamma,SR-ARE,SR-ATAD5,SR-HSE,SR-MMP,SR-p53
-------------------------------------------------------------
roc_auc,0.6647544793779581,0.8046414558811253,0.7940423615230813,0.7377812535874182,0.6385373966149208,0.7020035196967647,0.689506407816267,0.7080874128882388,0.7371933621
933622,0.678238703445315,0.8372650428205982,0.6866624335795207
pr_auc,0.37865553650968353,0.39726248056104047,0.4830194672774002,0.37386773542844487,0.3341358378687654,0.3675764142426596,0.1407950405740639,0.3840026516288543,0.3024808
3306023066,0.22527485187235421,0.5936620071741494,0.24100685624874538
accuracy,0.95,0.9651162790697675,0.8783068783068783,0.9494097807757167,0.8199052132701422,0.9407616361071932,0.9642585551330799,0.8115318416523236,0.9554937413073713,0.923
0769230769231,0.8625954198473282,0.9262773722627737
precision,0.45098039215686275,0.46511627906976744,0.48226950354609927,0.5227272727272727,0.3163841807909605,0.4915254237288136,0.2222222222222222,0.39285714285714285,0.369
5652173913043,0.31666666666666665,0.5459183673469388,0.2894736842105263
recall,0.3382352941176471,0.4444444444444444,0.4358974358974359,0.3709677419354839,0.34355828220858897,0.3493975903614458,0.10810810810810811,0.4350282485875706,0.32692307
69230769,0.24675324675324675,0.5944444444444444,0.3188405797101449
cohen_kappa,0.3610464976859069,0.43653705062362436,0.38956952361300967,0.40828205554631636,0.22560082417140193,0.3782065336549002,0.12942121054188438,0.3009652732377034,0.
3239900102835317,0.23740865099743236,0.487589337454124,0.2646230375952636
-------------------------------------------------------------
metric,amin,amax,mean,median,std
-------------------------------------------------------------
```

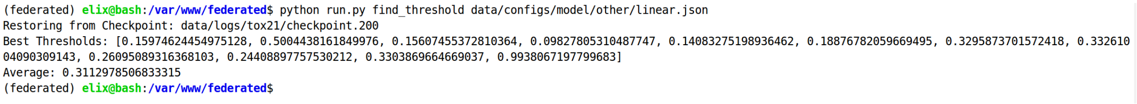
Figure 3.23: Sample output of the best checkpoint finder command.

Finding the Best Threshold

When traning a classifier, different thresholds will yield different predictions. If the dataset is imbalanced, some metrics like "accuracy" become less trustworthy.

One way to get more reliable results is to plot a precision-recall curve and pick the threshold where the 2 lines intersect. This threshold can be calculated for a certain "checkpoint_path" using the following command:

```
python run.py find_threshold {config_path}
```



```
(federated) elix@bash:/var/www/federated$ python run.py find_threshold data/configs/model/other/linear.json
Restoring from Checkpoint: data/logs/tox21/checkpoint.200
Best Thresholds: [0.15974624454975128, 0.5004438161849976, 0.15607455372810364, 0.09827805310487747, 0.14083275198936462, 0.18876782059669495, 0.3295873701572418, 0.332610
04090309143, 0.26095089316368103, 0.24408897757530212, 0.3303869664669037, 0.9938067197799683]
Average: 0.3112978506833315
(federated) elix@bash:/var/www/federated$
```

Figure 3.24: Sample output of the best threshold finder command.

Finding the Best Learning Rate

The following command will use an exponential learning rate scheduler to analyze various learning rates and plots a chart to help decide on a good one.

```
python run.py find_learning_rate {config_path}
```

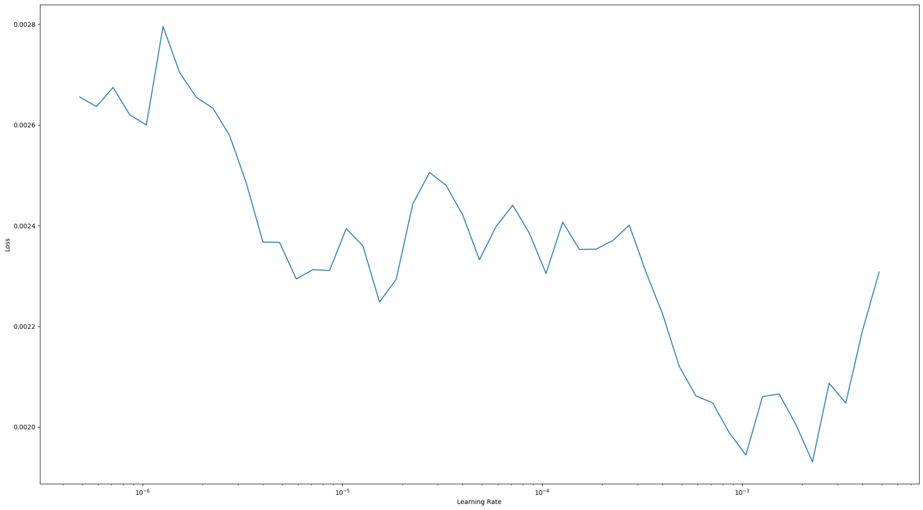


Figure 3.25: Sample output of the best learning rate finder command.

Visualizing Graphs

The following command uses model interpretability and understanding tools like Integrated Gradients[61] to plot graphs for molecules in the test set. Analysis will be performed on the "checkpoint_path" specified.

Implementations rely on the Captum library.

```
python run.py visualize {config_path}
```

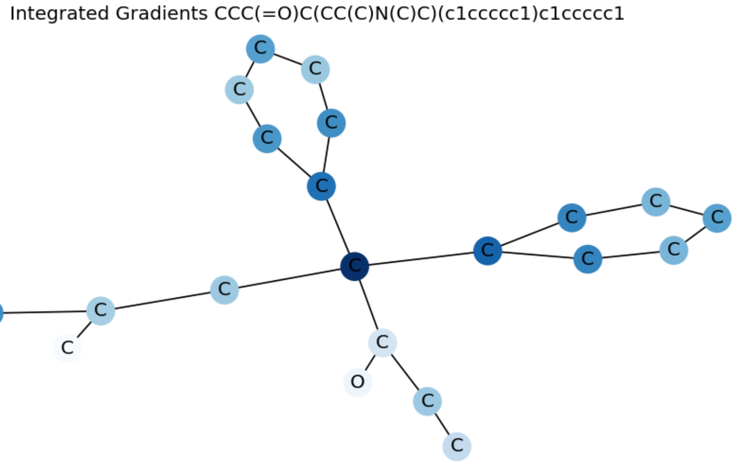


Figure 3.26: Sample output of the visualize command.

3.4.4 Customization

Extending the core functionality is can be easy and clean with the provided features. Dependency injection and observers allow anyone to add custom functionality without them having to touch any of the original code.

Indeed, we would recommend developers try to avoid modifying the original files as much as possible, unless absolutely necessary. Keeping custom code decoupled has several advantages. For one, it makes upgrading to a never version much easier, as the original files do not change. But more importantly it helps keep the manageability and maintainability of the library.

In what follows we provide a few examples on how one might add custom functionality, should they desire to do so.

Making Good use of Dependency Injection

Dependency injection helps with maintainability a lot, because our functionality can be anywhere. For example, maybe our dataset contains InChI[24] strings instead of SMILES[70]. One could dive into the code and start modifying all the featurizers, but there is a much easier and cleaner way. We write our own featurizer for it

We will be adding all our code to a folder called "custom/". Since we are writing a featurizer, we should override the associated abstract class to make sure we follow the expected contract. We see that the abstract class requires us to implement a single method called "$_{p}rocess$".

```
# in custom/featurizers.py
from lib.data.featurizers import AbstractFeaturizer

class InchiFeaturizer(AbstractFeaturizer):

    def _process(self, data: Any) -> Any:
        raise NotImplementedError
```

We will be connecting our featurizer directly to the loader, so we expect the input to be a string. However, we could easily connect multiple featurizers and use the output of one as input to the next one. To keep things simple, we will convert our InChI strings to SMILES, as most featurizers are already using SMILES.

```
# in custom/featurizers.py

from lib.data.featurizers import AbstractFeaturizer
from rdkit import Chem

class InchiFeaturizer(AbstractFeaturizer):

    def _process(self, data: str) -> str:
        return Chem.MolToSmiles(Chem.MolFromInchi(data))
```

We don’t even have to worry about exception handling, as problematic entries are filtered at the Streamer level. With this featurizer in place, we can now easily convert all InChI inputs and connect the output to other featurizers.

```
"featurizers": [
    {
        "type": "custom.featurizers.InchiFeaturizer",
        "inputs": ["inchi"],
        "outputs": ["our_custom_generated_smiles"]
    },
    {
        "type": "graph",
        "inputs": ["our_custom_generated_smiles"],
        "outputs": ["graph"],
        "descriptor_calculator": {"type": "rdkit"}
    }
],
```

Use Inheritance

In the previous section we created a general solution which can be plug in to every other featurizer, however, we don’t always have to think big. The same thing can be achieved by overriding one of the implemented featurizers:

```
# in custom/featurizers.py

from lib.data.featurizers import GraphFeaturizer

class InchiGraphFeaturizer(GraphFeaturizer):

    def _process(self, data: str):
        data = Chem.MolToSmiles(Chem.MolFromInchi(data))
        return super()._process(data)
```

When we pass the "GraphFeaturizer" as argument to the "InchiGraphFeaturizer", we are basically saying "start this class as a copy of GraphFeaturizer". We then alter only the "_process" method, while everything else stays the same. And even in the "_process", all we do is to convert the InChI strings to SMILES, then we pass the input to the parent object to do its job as usual.

All that is left is to use our custom featurizer.

```
"featurizers": [
    {
        "type": "custom.featurizers.InchiGraphFeaturizer",
        "inputs": ["inchi"],
        "outputs": ["graph"],
        "descriptor_calculator": {"type": "rdkit"}
    }
],
```

Spying on Pipelines with Observers

Observers are handlers which listen for and handle incoming events. We set up various event dispatchers throughout the framework which are summarized in Table 3.2 below.

Event Name	Payload Content
before_checkpoint_load	executor, loaded checkpoint
after_checkpoint_load	executor
after_network_create	executor, config
before_train_start	executor, data iterator
before_criterion	ground truth, logits
after_train_end	executor, data iterator
before_checkpoint_save	content to be saved
before_train_progress_log	logging information
after_predict	ground truth, logits, input features

Table 3.2: List of event dispatchers and the payload they transmit.

Event listeners watch dispatchers and act on their payload. Some of the core functionality is implemented with observers, however, someone can write custom event handlers and listen in on any of the dispatchers listed above.

Maybe we would like to modify a checkpoint before it is loaded, or we might wish to analyze the logits before they are passed to the loss function. For this example, we will show how one might go about logging the training process to an additional medium like Tensorboard, without having to touch any of the core files at all.

First, we extend from the abstract event handler to make sure we are implementing all expected methods. Again, it looks like we only have one named "run".

```
# in custom/observers.py

from lib.core.observers import EventHandler

class TensorboardLogHandler(EventHandler):

    def run(self, payload: Namespace):
        raise NotImplementedError
```

Next, we try to identify a dispatcher which contains the information we need. It would seem like "before_train_progress_log" is our best fit. We also see that it transmits a "message" argument in its payload, which is the string printed in the console. Not the best format, but we can work with it.

```
# in custom/observers.py

from lib.core.observers import EventHandler
import re

class TensorboardLogHandler(EventHandler):

    def _extract_information(self, message: str, desired_metric: str) -> float:
        regular_expression = "{}:\ ([0-9\.]*)".format(desired_metric)
        metric = re.findall(regular_expression, message)

        return float(metric[0])

    def run(self, payload: Namespace):
        message = payload.message

        roc_auc = self._extract_information(message, "roc_auc")
        loss = self._extract_information(message, "loss")

        self._print_to_tensorboard(roc_auc, loss, payload.epoch, payload.iteration)

    def _print_to_tensorboard(
            self, roc_auc: float, loss: float, epoch: float, iteration: float
    ) -> None:
        raise NotImplementedError
```

With the desired data extracted, logging the values to any medium is a trivial task. All we have to do now is to plug in the event handler in the configuration file:

```
"observers": {
    "before_train_progress_log": ["custom.observers.TensorboardLogHandler"],
}
```

This of course will print updates after every few iterations, based on the configured log frequency. If we wanted to evaluate the model after each epoch, the "before_checkpoint_save" event might have been a better choice.

3.5 Federated Learning (Mila)

Server and client processes are started similar to how models work. Each servicer and consumer requires a configuration file, which is fed to the entry point. In what follows, we describe the options for servers and clients separately.

3.5.1 Server Configurations

Server configuration files are expected to be in JSON format. The available options include:

task_configuration_file (no default)

Path to the model configuration file. This will be sent to each client along with the checkpoint.

config_type: (no default)

Module path to the configuration class (ie: "lib.config.Config")

executor_type: (no default)

Module path to the executor class (ie: "run.Executor")

aggregator_type (no default)

Which aggregator to use? Options include:

- **mila.aggregators.PlainTorchAggregator**

- **mila.aggregators.WeightedTorchAggregator**
- **mila.aggregators.BenchmarkedTorchAggregator**

aggregator_options (default={})

Input parameters for the aggregator (the expected value is a dictionary).

The "PlainTorchAggregator" does not expect any additional options.

The "WeightedTorchAggregator" expects a "weights" options which is a mapping between the client's "name" parameter and the expected weight. For example, if we have 2 clients named "tester1" and "tester2", this option could be set as follows:

```
"aggregator_options": {
    "weights": {
        "tester1": 0.67,
        "tester2": 0.33
    }
}
```

The "BenchmarkedTorchAggregator" needs additional options to determine how checkpoints are evaluated.

- **config_type**: specifies the configuration parser to use (which should extend "AbstractConfiguration")
- **config_path**: is the path to the actual JSON configuration
- **executor_type**: specifies which executor to use (which should extend "AbstractExecutor")
- **target_metric**: specifies which metric to use for checkpoint evaluation
- **minimized_metric**: should be set to "true" if the "target_metric" should be minimized instead of maximized (ie: "mae", "mse", or "rmse")

```
"aggregator_options": {
    "config_type": "lib.core.config.Config",
    "config_path": "data/configs/model/tox21.json",
    "executor_type": "run.Executor",
    "target_metric": "roc_auc"
```

```
  }
```

target (default="localhost:8024")

The gRPC service location URL (that is, the server address).

rounds_count (default=10)

How many rounds to perform

save_path (default="data/logs/server/")

Where to checkpoints received from clients and the aggregate models?

start_point (default=null)

Optionally, specify a checkpoint for the first round. If nothing is specified, clients will start training from scratch.

workers (default=2)

Maximum number of processes handling client requests

minimum_clients (default=2)

Minimum number of clients required to start federated learning. The server won't start the first round until this number is reached.

maximum_clients (default=100)

Maximum number of clients allowed to join the federated learning process.

client_wait_time (default=10)

Once the "minimum_clients" number is reach, the server will wait this many seconds for additional clients before the process starts. After this time expires, no new members will be allowed to join.

heartbeat_timeout (default=300)

How long to wait for a keepalive signal from clients before declaring them "dead"?

use_secure_connection (default=false)

When true, the communication will be performed through HTTPS protocol. The 3 SSL files specified below must be valid for this to work.

ssl_private_key (default="data/certificates/server.key")

gRPC secure communication private key

ssl_cert (default="data/certificates/server.crt")

gRPC secure communication SSL certificate

ssl_root_cert (default="data/certificates/rootCA.pem")

gRPC secure communication trusted root certificate

options

Additional gRPC options. "grpc.max_send_message_length" represents the maximum length of a sent message, and "grpc.max_receive_message_length" the maximum length of a received message. Since we are using peer-to-peer connections, we also disable host name checks of the certificates with "ssl_target_name_override".

The default value for this option is:

```
[
    ("grpc.max_send_message_length", 1000000000),
    ("grpc.max_receive_message_length", 1000000000),
    ("grpc.ssl_target_name_override", "localhost")
```

```
        ]
```

blacklist (default=[])

A list of IP addresses which will be declined upon authentication.

whitelist (default=[])

A list of IP addresses which will be allowed to join the federated learning process. If "use_whitelist" is True, these will be the only IP addresses allowed to join.

use_whitelist (default=false)

Enables whitelist filtering.

3.5.2 Client Configurations

Client configuration files are also expected to be in JSON format. The available options include:

name (no default)

A unique identifier for this client (could be a company name for example)

save_path (default="data/logs/client/")

Where to save checkpoints received from the client?

heartbeat_frequency (default=60)

How often to send keepalive signals to the client?

retry_timeout (default=1)

If a request failes because the server is under heavy load, we retry the connection after this many seconds.

model_overwrites

Used to override model configuration options. Generally, clients might want to change the path where local (model) checkpoints are stored. The default value for this option is:

```
{
    "output_path": "data/logs/local/",
    "epochs": 5
}
```

config_type: (no default)

Module path to the configuration class (ie: "lib.config.Config")

executor_type: (no default)

Module path to the executor class (ie: "run.Executor")

target (default="localhost:8024")

The gRPC service location URL (that is, the server address).

use_secure_connection (default=false)

When true, the communication will be performed through HTTPS protocol. The 3 SSL files specified below must be valid for this to work.

ssl_private_key (default="data/certificates/client.key")

gRPC secure communication private key

ssl_cert (default="data/certificates/client.crt")

gRPC secure communication SSL certificate

ssl_root_cert (default="data/certificates/rootCA.pem")

gRPC secure communication trusted root certificate

options

Additional gRPC options. "grpc.max_send_message_length" represents the maximum length of a sent message, and "grpc.max_receive_message_length" the maximum length of a received message. Since we are using peer-to-peer connections, we also disable host name checks of the certificates with "ssl_target_name_override".

The default value for this option is:

```
[
    ("grpc.max_send_message_length", 1000000000),
    ("grpc.max_receive_message_length", 1000000000),
    ("grpc.ssl_target_name_override", "localhost")
]
```

3.5.3 Creating SSL Certificates

We first need to create the root private key and a self-signed root certificate

```
openssl genrsa -des3 -out rootCA.key 2048

openssl req -x509 -new -nodes -key rootCA.key
-sha256 -days 1024 -out rootCA.pem
```

Next, we create a server private key, a server certificate signing request (CSR), and we sign the CSR using the root certificate:

```
openssl genrsa -out server.key 2048

openssl req -new -key server.key -out server.csr

openssl x509 -req -in server.csr -CA rootCA.pem
-CAkey rootCA.key -CAcreateserial -out server.crt
-days 500 -sha256
```

The client creates the client private key, a client certificate signing request (CSR). A common name should be specified when creating the CSR.

```
openssl genrsa -out client.key 2048
openssl req -new -key client.key -out client3.csr
```

The client sends the CSR to the server which wigns it using the root certificate. The server sends "client.crt" back to the client.

```
openssl x509 -req -in client.csr -CA rootCA.pem
-CAkey rootCA.key -CAcreateserial -out client3.crt
-days 500 -sha256
```

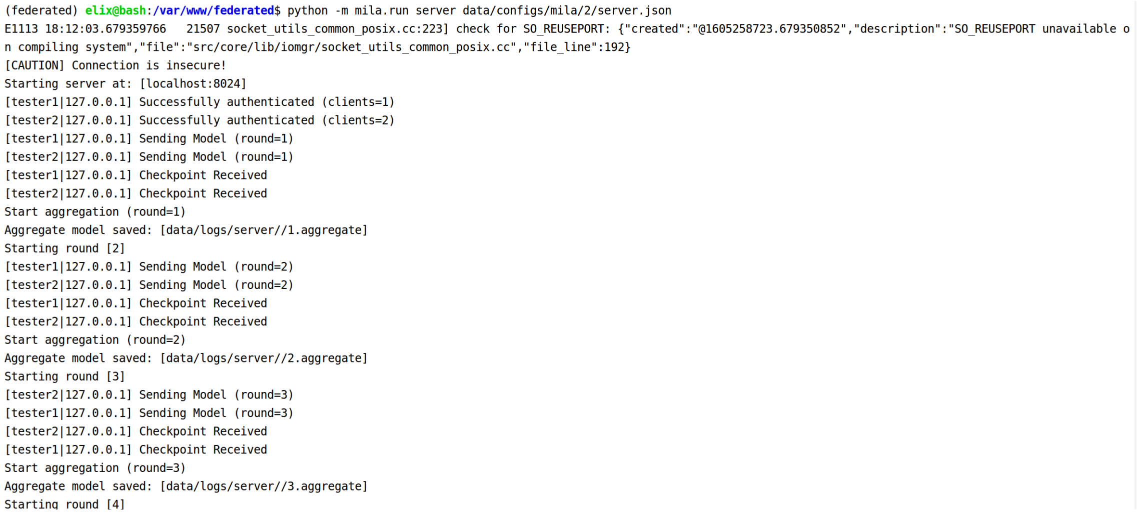
3.5.4 Commands

Starting the server can be done using following command:

```
python -m mila.run server {config_path}
```

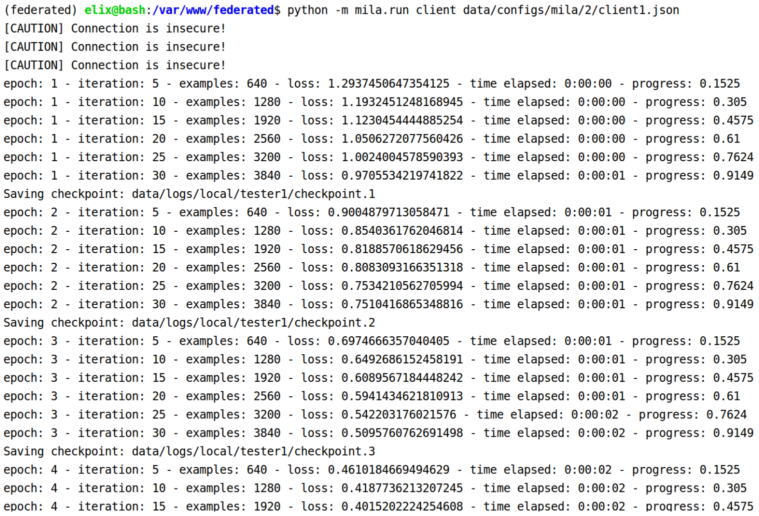
Starting a client process is very similar:

```
python -m mila.run client {config_path}
```



```
(federated) elix@bash:/var/www/federated$ python -m mila.run server data/configs/mila/2/server.json
E1113 18:12:03.679359766   21507 socket_utils_common_posix.cc:223] check for SO_REUSEPORT: {"created":"@1605258723.679350852","description":"SO_REUSEPORT unavailable o
n compiling system","file":"src/core/lib/iomgr/socket_utils_common_posix.cc","file_line":192}
[CAUTION] Connection is insecure!
Starting server at: [localhost:8024]
[tester1|127.0.0.1] Successfully authenticated (clients=1)
[tester2|127.0.0.1] Successfully authenticated (clients=2)
[tester1|127.0.0.1] Sending Model (round=1)
[tester2|127.0.0.1] Sending Model (round=1)
[tester1|127.0.0.1] Checkpoint Received
[tester2|127.0.0.1] Checkpoint Received
Start aggregation (round=1)
Aggregate model saved: [data/logs/server//1.aggregate]
Starting round [2]
[tester1|127.0.0.1] Sending Model (round=2)
[tester2|127.0.0.1] Sending Model (round=2)
[tester1|127.0.0.1] Checkpoint Received
[tester2|127.0.0.1] Checkpoint Received
Start aggregation (round=2)
Aggregate model saved: [data/logs/server//2.aggregate]
Starting round [3]
[tester2|127.0.0.1] Sending Model (round=3)
[tester1|127.0.0.1] Sending Model (round=3)
[tester2|127.0.0.1] Checkpoint Received
[tester1|127.0.0.1] Checkpoint Received
Start aggregation (round=3)
Aggregate model saved: [data/logs/server//3.aggregate]
Starting round [4]
```

Figure 3.27: Sample output of from the server.



```
(federated) elix@bash:/var/www/federated$ python -m mila.run client data/configs/mila/2/client1.json
[CAUTION] Connection is insecure!
[CAUTION] Connection is insecure!
[CAUTION] Connection is insecure!
epoch: 1 - iteration: 5 - examples: 640 - loss: 1.2937450647354125 - time elapsed: 0:00:00 - progress: 0.1525
epoch: 1 - iteration: 10 - examples: 1280 - loss: 1.1932451248168945 - time elapsed: 0:00:00 - progress: 0.305
epoch: 1 - iteration: 15 - examples: 1920 - loss: 1.1230454444885254 - time elapsed: 0:00:00 - progress: 0.4575
epoch: 1 - iteration: 20 - examples: 2560 - loss: 1.0506272077560426 - time elapsed: 0:00:00 - progress: 0.61
epoch: 1 - iteration: 25 - examples: 3200 - loss: 1.0024004578590393 - time elapsed: 0:00:00 - progress: 0.7624
epoch: 1 - iteration: 30 - examples: 3840 - loss: 0.9705534219741822 - time elapsed: 0:00:01 - progress: 0.9149
Saving checkpoint: data/logs/local/tester1/checkpoint.1
epoch: 2 - iteration: 5 - examples: 640 - loss: 0.9004879713058471 - time elapsed: 0:00:01 - progress: 0.1525
epoch: 2 - iteration: 10 - examples: 1280 - loss: 0.8540361762046814 - time elapsed: 0:00:01 - progress: 0.305
epoch: 2 - iteration: 15 - examples: 1920 - loss: 0.8188570618629456 - time elapsed: 0:00:01 - progress: 0.4575
epoch: 2 - iteration: 20 - examples: 2560 - loss: 0.8083093166351318 - time elapsed: 0:00:01 - progress: 0.61
epoch: 2 - iteration: 25 - examples: 3200 - loss: 0.7534210562705994 - time elapsed: 0:00:01 - progress: 0.7624
epoch: 2 - iteration: 30 - examples: 3840 - loss: 0.7510416865348816 - time elapsed: 0:00:01 - progress: 0.9149
Saving checkpoint: data/logs/local/tester1/checkpoint.2
epoch: 3 - iteration: 5 - examples: 640 - loss: 0.6974666357040405 - time elapsed: 0:00:01 - progress: 0.1525
epoch: 3 - iteration: 10 - examples: 1280 - loss: 0.6492686152458191 - time elapsed: 0:00:01 - progress: 0.305
epoch: 3 - iteration: 15 - examples: 1920 - loss: 0.6089567184448242 - time elapsed: 0:00:01 - progress: 0.4575
epoch: 3 - iteration: 20 - examples: 2560 - loss: 0.5941434621810913 - time elapsed: 0:00:01 - progress: 0.61
epoch: 3 - iteration: 25 - examples: 3200 - loss: 0.542203176021576 - time elapsed: 0:00:02 - progress: 0.7624
epoch: 3 - iteration: 30 - examples: 3840 - loss: 0.5095760762691498 - time elapsed: 0:00:02 - progress: 0.9149
Saving checkpoint: data/logs/local/tester1/checkpoint.3
epoch: 4 - iteration: 5 - examples: 640 - loss: 0.4610184669494629 - time elapsed: 0:00:02 - progress: 0.1525
epoch: 4 - iteration: 10 - examples: 1280 - loss: 0.4187736213207245 - time elapsed: 0:00:02 - progress: 0.305
epoch: 4 - iteration: 15 - examples: 1920 - loss: 0.4015202224254608 - time elapsed: 0:00:02 - progress: 0.4575
```

Figure 3.28: Sample output of from the client.

3.6 Environment Information

List of 3rd party libraries and frameworks used:

- **Pytorch**[51]: base framework
- **Pytorch Geometric**[19]: graph architectures
- **Scikit-Learn**[52]: metrics
- **Optuna**[2]: Bayesian optimization
- **Opacus**[50]: differential privacy
- **RdKit**[34]: molecule handling and descriptors
- **Mordred**[53]: molecular descriptors
- **DGL-LifeSci**[14]: featurizers
- **Captum**[31]: integrated gradients

Versioning:

- **OS**: Ubuntu 20.04.1 LTS

- **Python Version**: 3.8.3
- **PyTorch Version**: 1.6.0
- **CUDA Toolkit Version**: 10.2.89
- **cuDNN Version**: 7.6.5

Bibliography

[1] Abien Fred Agarap. Deep learning using rectified linear units (relu), 2019.

[2] Takuya Akiba, Shotaro Sano, Toshihiko Yanase, Takeru Ohta, and Masanori Koyama. Optuna: A next-generation hyperparameter optimization framework, 2019.

[3] Vinicius M. Alves, Eugene Muratov, Denis Fourches, Judy Strickland, Nicole Kleinstreuer, Carolina H. Andrade, and Alexander Tropsha. Predicting chemically-induced skin reactions. part i: Qsar models of skin sensitization and their application to identify potentially hazardous compounds. *Toxicology and Applied Pharmacology*, 284(2):262–272, 2015.

[4] Alexandru T. Balaban. Highly discriminating distance-based topological index. *Chemical Physics Letters*, 89(5):399–404, 1982.

[5] James Bergstra, Rémi Bardenet, Yoshua Bengio, and Balázs Kégl. Algorithms for hyper-parameter optimization. In *Proceedings of the 24th International Conference on Neural Information Processing Systems*, NIPS'11, page 2546âĂŞ2554, Red Hook, NY, USA, 2011. Curran Associates Inc.

[6] James Bergstra, Daniel Yamins, and David Cox. Making a science of model search: Hyperparameter optimization in hundreds of dimensions for vision architectures. In Sanjoy Dasgupta and David McAllester, editors, *Proceedings of the 30th International Conference on Machine Learning*, volume 28 of *Proceedings of Machine Learning Research*, pages 115–123, Atlanta, Georgia, USA, 17–19 Jun 2013. PMLR.

[7] Filippo Maria Bianchi, Daniele Grattarola, Lorenzo Livi, and Cesare Alippi. Graph neural networks with convolutional arma filters, 2021.

[8] G. Richard Bickerton, Gaia V. Paolini, Jeremy Besnard, Sorel Muresan, and Andrew L. Hopkins. Quantifying the chemical beauty of drugs. *Nature News*, Jan 2012.

[9] Fabio Broccatelli, Emanuele Carosati, Annalisa Neri, Maria Frosini, Laura Goracci, Tudor I. Oprea, and Gabriele Cruciani. A novel approach for predicting p-glycoprotein (abcb1) inhibition using molecular interaction fields. *Journal of Medicinal Chemistry*, 54(6):1740–1751, 2011. PMID: 21341745.

[10] Tianle Cai, Shengjie Luo, Keyulu Xu, Di He, Tie-Yan Liu, and Liwei Wang. Graphnorm: A principled approach to accelerating graph neural network training, 2021.

[11] Miriam Carbon-Mangels and Michael C. Hutter. Selecting relevant descriptors for classification by bayesian estimates: A comparison with decision trees and support vector machines approaches for disparate data sets. *Molecular Informatics*, 30(10):885–895, 2011.

[12] Wei-Lin Chiang, Xuanqing Liu, Si Si, Yang Li, Samy Bengio, and Cho-Jui Hsieh. Cluster-gcn: An efficient algorithm for training deep and large graph convolutional networks. *Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery Data Mining*, Jul 2019.

[13] MichaÃńl Defferrard, Xavier Bresson, and Pierre Vandergheynst. Convolutional neural networks on graphs with fast localized spectral filtering, 2017.

[14] Dgl-lifesci library. Available from lifesci.dgl.ai.

[15] Li Di, Christopher Keefer, Dennis O. Scott, Timothy J. Strelevitz, George Chang, Yi-An Bi, Yurong Lai, Jonathon Duckworth, Katherine Fenner, Matthew D. Troutman, and R. Scott Obach. Mechanistic insights from comparing intrinsic clearance values between human liver microsomes and hepatocytes to guide drug design. *European Journal of Medicinal Chemistry*, 57:441–448, 2012.

[16] Veith H;Southall N;Huang R;James T;Fayne D;Artemenko N;Shen M;Inglese J;Austin CP;Lloyd DG;Auld DS;. Comprehensive characterization of cytochrome p450 isozyme selectivity across chemical libraries.

[17] Jian Du, Shanghang Zhang, Guanhang Wu, Jose M. F. Moura, and Soummya Kar. Topology adaptive graph convolutional networks, 2018.

[18] Cynthia Dwork and Aaron Roth. The algorithmic foundations of differential privacy. *Foundations and TrendsÂő in Theoretical Computer Science*, 9(3âĂŞ4):211–407, 2014.

[19] Matthias Fey and Jan Eric Lenssen. Fast graph representation learning with pytorch geometric, 2019.

[20] Kaitlyn M. Gayvert, Neel S. Madhukar, and Olivier Elemento. A data-driven approach to predicting successes and failures of clinical trials. *Cell Chemical Biology*, 23(10):1294–1301, Oct 2016.

[21] Justin Gilmer, Samuel S. Schoenholz, Patrick F. Riley, Oriol Vinyals, and George E. Dahl. Neural message passing for quantum chemistry, 2017.

[22] William L. Hamilton, Rex Ying, and Jure Leskovec. Inductive representation learning on large graphs, 2018.

[23] Kaiming He, Xiangyu Zhang, Shaoqing Ren, and Jian Sun. Deep residual learning for image recognition, 2015.

[24] Stephen R. Heller, Alan McNaught, Igor Pletnev, Stephen Stein, and Dmitrii Tchekhovskoi. Inchi, the iupac international chemical identifier. *Journal of Cheminformatics*, 7(1):23, May 2015.

[25] Tin Kam Ho. Random decision forests. In *Proceedings of 3rd International Conference on Document Analysis and Recognition*, volume 1, pages 278–282 vol.1, 1995.

[26] Tingjun Hou, Junmei Wang, Wei Zhang, and Xiaojie Xu. Adme evaluation in drug discovery. 7. prediction of oral absorption by correlation and classification. *Journal of Chemical Information and Modeling*, 47(1):208–218, 2007. PMID: 17238266.

[27] Sergey Ioffe and Christian Szegedy. Batch normalization: Accelerating deep network training by reducing internal covariate shift, 2015.

[28] Pavel Izmailov, Dmitrii Podoprikhin, Timur Garipov, Dmitry Vetrov, and Andrew Gordon Wilson. Averaging weights leads to wider optima and better generalization, 2019.

[29] J. Kiefer and J. Wolfowitz. Stochastic estimation of the maximum of a regression function. *The Annals of Mathematical Statistics*, 23(3):462–466, 2021/02/26/ 1952. Full publication date: Sep., 1952.

[30] Diederik P. Kingma and Jimmy Ba. Adam: A method for stochastic optimization, 2017.

[31] Narine Kokhlikyan, Vivek Miglani, Miguel Martin, Edward Wang, Bilal Alsallakh, Jonathan Reynolds, Alexander Melnikov, Natalia Kliushkina, Carlos Araya, Siqi Yan, and Orion Reblitz-Richardson. Captum: A unified and generic model interpretability library for pytorch, 2020.

[32] Paul Labute. A widely applicable set of descriptors. *Journal of Molecular Graphics and Modelling*, 18(4):464–477, 2000.

[33] Alexey Lagunin, Dmitrii Filimonov, Alexey Zakharov, Wei Xie, Ying Huang, Fucheng Zhu, Tianxiang Shen, Jianhua Yao, and Vladimir Poroikov. Computer-aided prediction of rodent carcinogenicity by pass and cisoc-psct. *QSAR & Combinatorial Science*, 28(8):806–810, 2009.

[34] Greg Landrum. Rdkit: Open-source cheminformatics.

[35] Guohao Li, Chenxin Xiong, Ali Thabet, and Bernard Ghanem. Deepergcn: All you need to train deeper gcns, 2020.

[36] Pengyong Li, Yuquan Li, Chang-Yu Hsieh, Shengyu Zhang, Xianggen Liu, Huanxiang Liu, Sen Song, and Xiaojun Yao. TrimNet: learning molecular representation from triplet messages for biomedicine. *Briefings in Bioinformatics*, 11 2020. bbaa266.

[37] Yiming Li, Baoyuan Wu, Yong Jiang, Zhifeng Li, and Shu-Tao Xia. Backdoor learning: A survey, 2021.

[38] Christopher A Lipinski, Franco Lombardo, Beryl W Dominy, and Paul J Feeney. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings1pii of original

article: S0169-409x(96)00423-1. the article was originally published in advanced drug delivery reviews 23 (1997) 3âĂŞ25.1. *Advanced Drug Delivery Reviews*, 46(1):3–26, 2001. Special issue dedicated to Dr. Eric Tomlinson, Advanced Drug Delivery Reviews, A Selection of the Most Highly Cited Articles, 1991-1998.

[39] Franco Lombardo and Yankang Jing. In silico prediction of volume of distribution in humans. extensive data set and the exploration of linear and nonlinear methods coupled with molecular interaction fields descriptors. *Journal of Chemical Information and Modeling*, 56(10):2042–2052, 2016. PMID: 27602694.

[40] Ilya Loshchilov and Frank Hutter. Decoupled weight decay regularization, 2019.

[41] Chang-Ying Ma, Sheng-Yong Yang, Hui Zhang, Ming-Li Xiang, Qi Huang, and Yu-Quan Wei. Prediction models of human plasma protein binding rate and oral bioavailability derived by using gaâĂŞcgâĂŞsvm method. *Journal of Pharmaceutical and Biomedical Analysis*, 47(4):677–682, 2008.

[42] H. Brendan McMahan, Eider Moore, Daniel Ramage, Seth Hampson, and Blaise AgÃijera y Arcas. Communication-efficient learning of deep networks from decentralized data, 2017.

[43] Ilya Mironov. RÃľnyi differential privacy. *2017 IEEE 30th Computer Security Foundations Symposium (CSF)*, Aug 2017.

[44] Ilya Mironov, Kunal Talwar, and Li Zhang. Rényi differential privacy of the sampled gaussian mechanism, 2019.

[45] Guthrie J. Peter Mobley David L. Freesolv: a database of experimental and calculated hydration free energies, with input files.

[46] H. L. Morgan. The generation of a unique machine description for chemical structures-a technique developed at chemical abstracts service. *Journal of Chemical Documentation*, 5(2):107–113, 1965.

[47] Christopher Morris, Martin Ritzert, Matthias Fey, William L. Hamilton, Jan Eric Lenssen, Gaurav Rattan, and Martin Grohe. Weisfeiler and leman go neural: Higher-order graph neural networks, 2020.

[48] Abhishek Khetan Suleyman Er Murat Cihan Sorkun. Aqsoldb, a curated reference set of aqueous solubility and 2d descriptors for a diverse set of compounds.

[49] R. Scott Obach, Franco Lombardo, and Nigel J. Waters. Trend analysis of a database of intravenous pharmacokinetic parameters in humans for 670 drug compounds. *Drug Metabolism and Disposition*, 36(7):1385–1405, 2008.

[50] Opacus PyTorch library. Available from opacus.ai.

[51] Adam Paszke, Sam Gross, Francisco Massa, Adam Lerer, James Bradbury, Gregory Chanan, Trevor Killeen, Zeming Lin, Natalia Gimelshein, Luca Antiga, Alban Desmaison, Andreas Kopf, Edward Yang, Zachary DeVito, Martin Raison, Alykhan Tejani, Sasank Chilamkurthy, Benoit Steiner, Lu Fang, Junjie Bai, and Soumith Chintala. Pytorch: An imperative style, high-performance deep learning library. In H. Wallach, H. Larochelle, A. Beygelzimer, F. dAlché-Buc, E. Fox, and R. Garnett, editors, *Advances in Neural Information Processing Systems 32*, pages 8024–8035. Curran Associates, Inc., 2019.

[52] Fabian Pedregosa, Gaël Varoquaux, Alexandre Gramfort, Vincent Michel, Bertrand Thirion, Olivier Grisel, Mathieu Blondel, Peter Prettenhofer, Ron Weiss, Vincent Dubourg, Jake Vanderplas, Alexandre Passos, David Cournapeau, Matthieu Brucher, Matthieu Perrot, and Édouard Duchesnay. Scikit-learn: Machine learning in python. *Journal of Machine Learning Research*, 12(85):2825–2830, 2011.

[53] V. Consonni R. Todeschini, Y. Fu R. Wang, GM. Crippen AK. Ghose, R. Goswami V. Sharma, PC. Jurs DT. Stanton, CW. Yap, Q-S. Xu D-S. Cao, Y-Z. Liang D-S. Cao, N. Xiao D-S. Cao, GR. Hutchison NM. OâĂŹBoyle, and et al. Mordred: a molecular descriptor calculator. *Journal of Cheminformatics*, Jan 1970.

[54] Ekagra Ranjan, Soumya Sanyal, and Partha Pratim Talukdar. Asap: Adaptive structure aware pooling for learning hierarchical graph representations, 2020.

[55] Ann M. Richard, Richard S. Judson, Keith A. Houck, Christopher M. Grulke, Patra Volarath, Inthirany Thillainadarajah, Chihae Yang, James Rathman, Matthew T. Martin, John F. Wambaugh, Thomas B. Knudsen, Jayaram Kancherla, Kamel Mansouri, Grace Patlewicz, Antony J. Williams, Stephen B. Little, Kevin M. Crofton, and Russell S. Thomas. Toxcast chemical landscape: Paving the road to 21st century toxicology. *Chemical Research in Toxicology*, 29(8):1225–1251, 2016. PMID: 27367298.

[56] Maria Rigaki and Sebastian Garcia. A survey of privacy attacks in machine learning, 2020.

[57] David Rogers and Mathew Hahn. Extended-connectivity fingerprints. *Journal of Chemical Information and Modeling*, 50(5):742–754, 2010. PMID: 20426451.

[58] Martin Simonovsky and Nikos Komodakis. Dynamic edge-conditioned filters in convolutional neural networks on graphs, 2017.

[59] Leslie N. Smith and Nicholay Topin. Super-convergence: Very fast training of neural networks using large learning rates, 2018.

[60] Nitish Srivastava, Geoffrey Hinton, Alex Krizhevsky, Ilya Sutskever, and Ruslan Salakhutdinov. Dropout: A simple way to prevent neural networks from overfitting. *Journal of Machine Learning Research*, 15(56):1929–1958, 2014.

[61] Mukund Sundararajan, Ankur Taly, and Qiqi Yan. Axiomatic attribution for deep networks, 2017.

[62] Max Welling Thomas N. Kipf. Semi-supervised classification with graph convolutional networks. *Arxiv*, 2017.

[63] Dmitry Ulyanov, Andrea Vedaldi, and Victor Lempitsky. Instance normalization: The missing ingredient for fast stylization, 2017.

[64] Petar VeliÄ■koviÄĞ, Guillem Cucurull, Arantxa Casanova, Adriana Romero, Pietro LiÃš, and Yoshua Bengio. Graph attention networks, 2018.

[65] Nitika Verma, Edmond Boyer, and Jakob Verbeek. Feastnet: Feature-steered graph convolutions for 3d shape analysis, 2018.

[66] Oriol Vinyals, Samy Bengio, and Manjunath Kudlur. Order matters: Sequence to sequence for sets, 2016.

[67] Ning-Ning Wang, Jie Dong, Yin-Hua Deng, Min-Feng Zhu, Ming Wen, Zhi-Jiang Yao, Ai-Ping Lu, Jian-Bing Wang, and Dong-Sheng Cao. Adme properties evaluation in drug discovery: Prediction of caco-2 cell permeability using a combination of nsga-ii and boosting. *Journal of Chemical Information and Modeling*, 56(4):763–773, 2016. PMID: 27018227.

[68] Shuangquan Wang, Huiyong Sun, Hui Liu, Dan Li, Youyong Li, and Tingjun Hou. Admet evaluation in drug discovery. 16. predicting herg blockers by combining multiple pharmacophores and machine learning approaches. *Molecular Pharmaceutics*, 13(8):2855–2866, 2016. PMID: 27379394.

[69] Kang Wei, Jun Li, Ming Ding, Chuan Ma, Yo-Seb Jeon, and H. Vincent Poor. Covert model poisoning against federated learning: Algorithm design and optimization, 2021.

[70] David Weininger. Smiles, a chemical language and information system. 1. introduction to methodology and encoding rules. *Journal of Chemical Information and Computer Sciences*, 28(1):31–36, 1988.

[71] Mark Wenlock and Nicholas Tomkinson. Experimental in vitro dmpk and physicochemical data on a set of publicly disclosed compounds.

[72] Felix Wu, Tianyi Zhang, Amauri Holanda de Souza Jr. au2, Christopher Fifty, Tao Yu, and Kilian Q. Weinberger. Simplifying graph convolutional networks, 2019.

[73] Yuxin Wu and Kaiming He. Group normalization, 2018.

[74] Zhenqin Wu, Bharath Ramsundar, Evan N. Feinberg, Joseph Gomes, Caleb Geniesse, Aneesh S. Pappu, Karl Leswing, and Vijay Pande. Moleculenet: A benchmark for molecular machine learning, 2018.

[75] Keyulu Xu, Weihua Hu, Jure Leskovec, and Stefanie Jegelka. How powerful are graph neural networks?, 2019.

[76] Youjun Xu, Ziwei Dai, Fangjin Chen, Shuaishi Gao, Jianfeng Pei, and Luhua Lai. Deep learning for drug-induced liver injury. *Journal of Chemical Information and Modeling*, 55(10):2085–2093, 2015. PMID: 26437739.

[77] Hao Zhu, Todd M. Martin, Lin Ye, Alexander Sedykh, Douglas M. Young, and Alexander Tropsha. Quantitative structureâĹŠactivity relationship modeling of rat acute toxicity by oral exposure. *Chemical Research in Toxicology*, 22(12):1913–1921, 2009. PMID: 19845371.

[78] Juntang Zhuang, Tommy Tang, Yifan Ding, Sekhar Tatikonda, Nicha Dvornek, Xenophon Papademetris, and James S. Duncan. Adabelief optimizer: Adapting stepsizes by the belief in observed gradients, 2020.