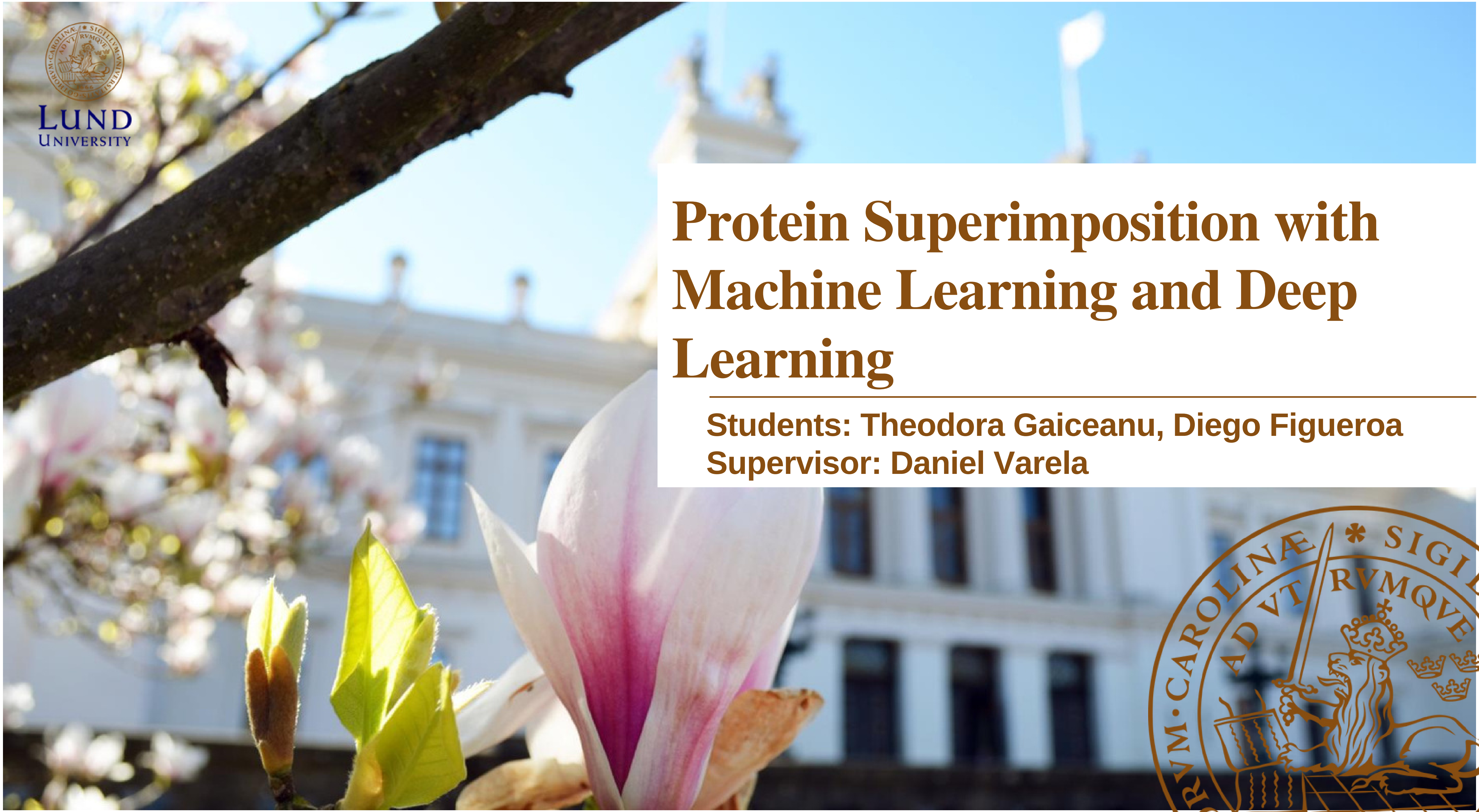


LUND UNIVERSITY

Protein Superimposition with Machine Learning and Deep Learning

Students: Theodora Gaiceanu, Diego Figueroa
Supervisor: Daniel Varela

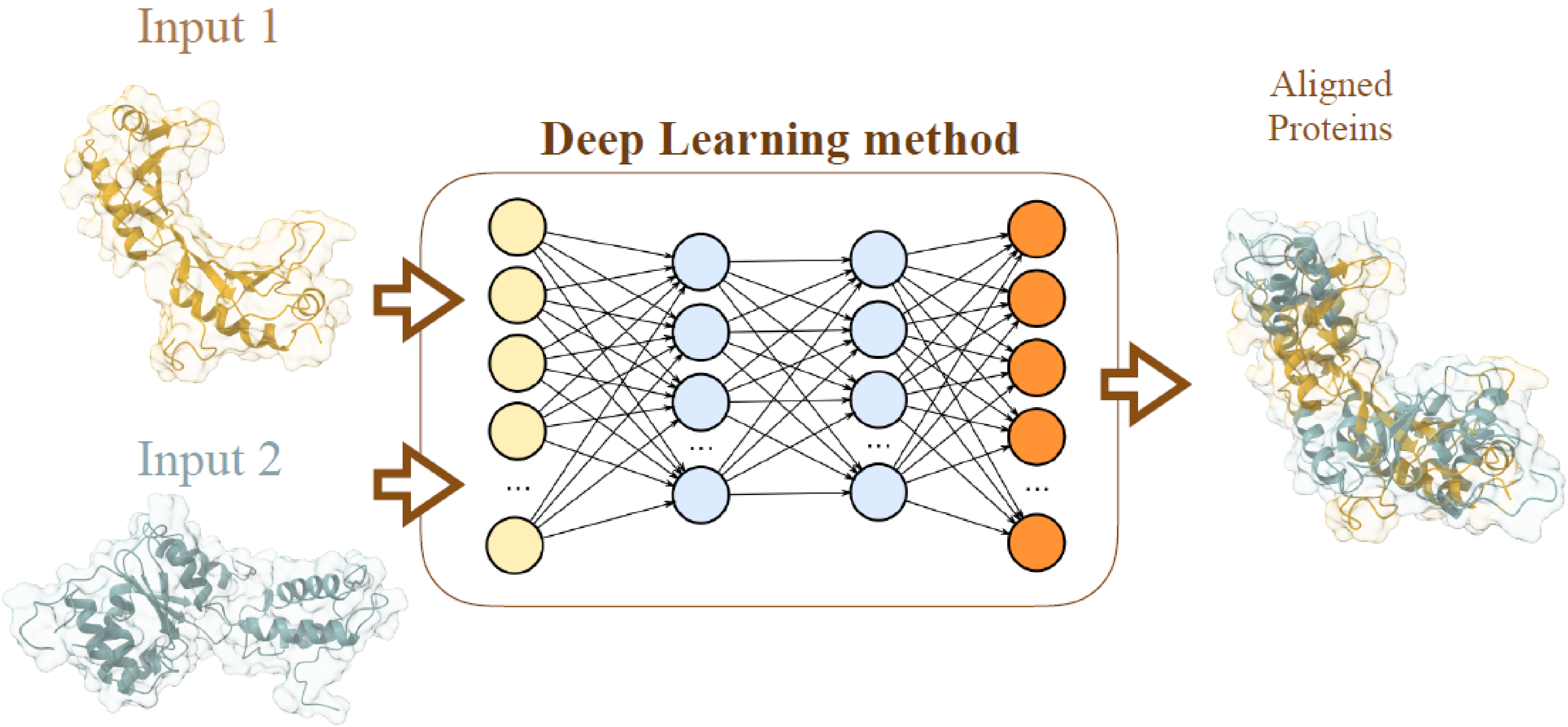
INTRODUCTION

Why this project?

- The shape of a protein - an essential role in drug discovery
- Aligning proteins - function & relationships between proteins
- Increasing dataset - ANN model

Goal of the project

- Use DL and ML to align 2 proteins
- Input: original protein + rotated one
- Output:
  - Rotation values or,
  - Zeal score



Input 1

Input 2

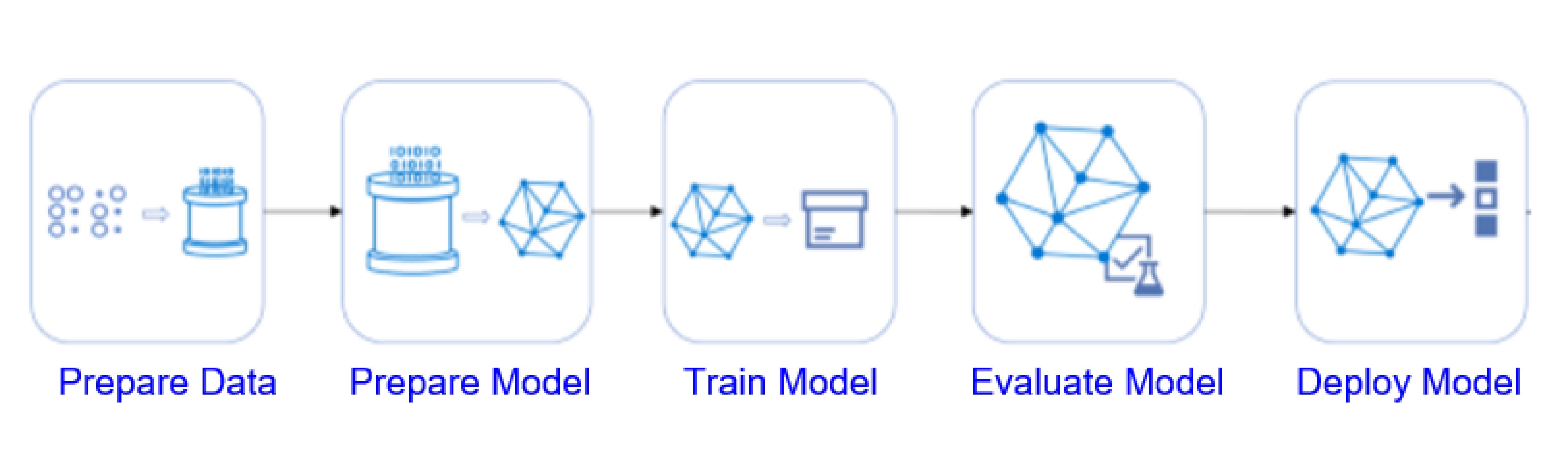
Deep Learning method

Aligned Proteins

EDAN70 Project in Computer Science

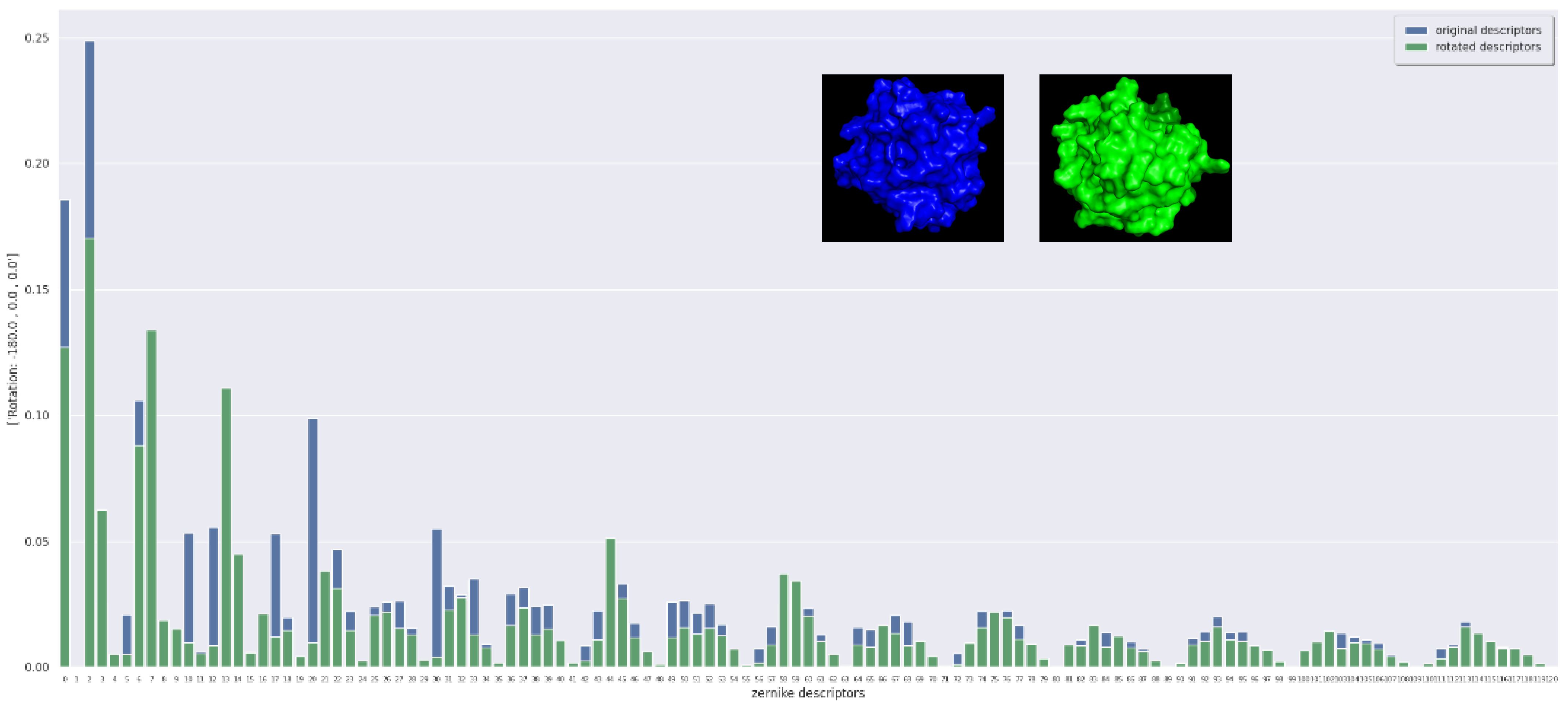
WORKFLOW

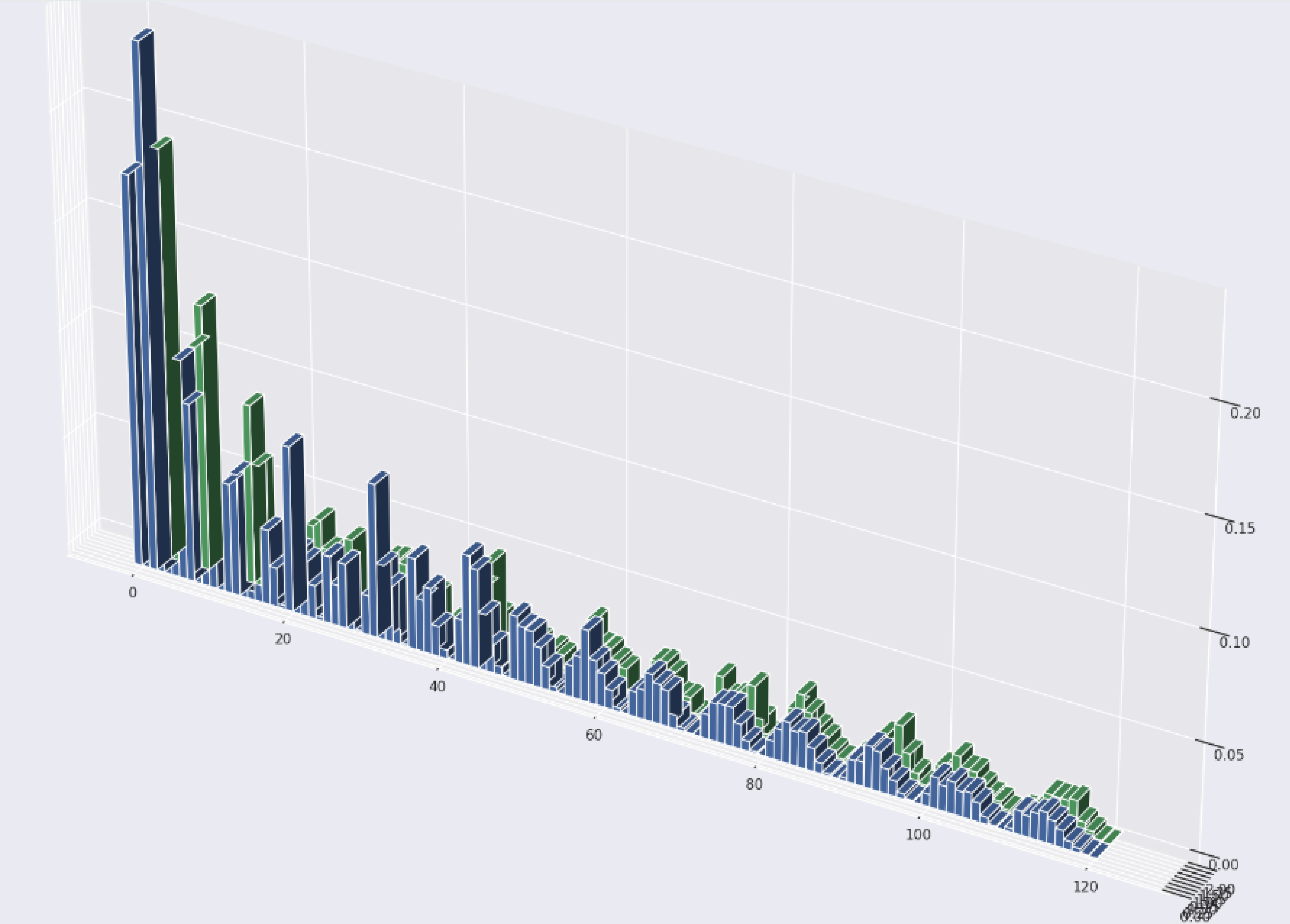
Workflow of the project

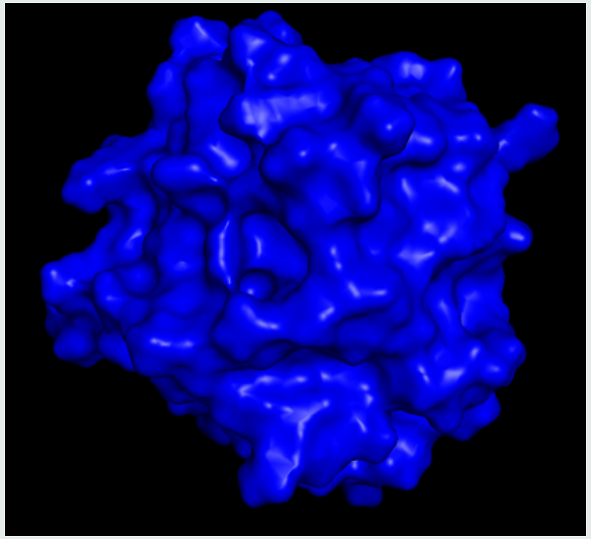


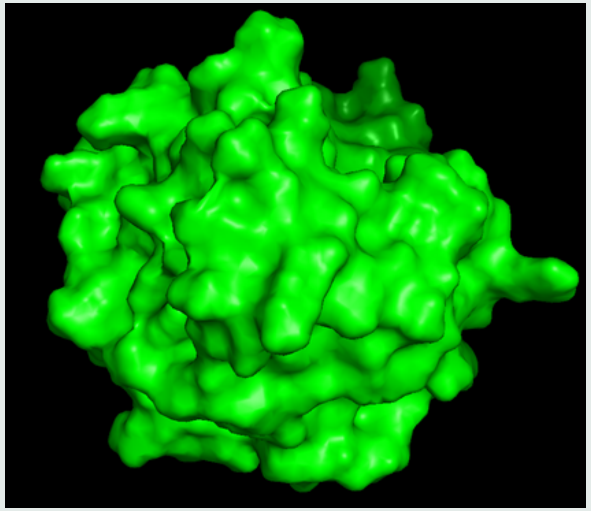
DATA PREPARATION & PREPROCESSING

Zernike descriptors









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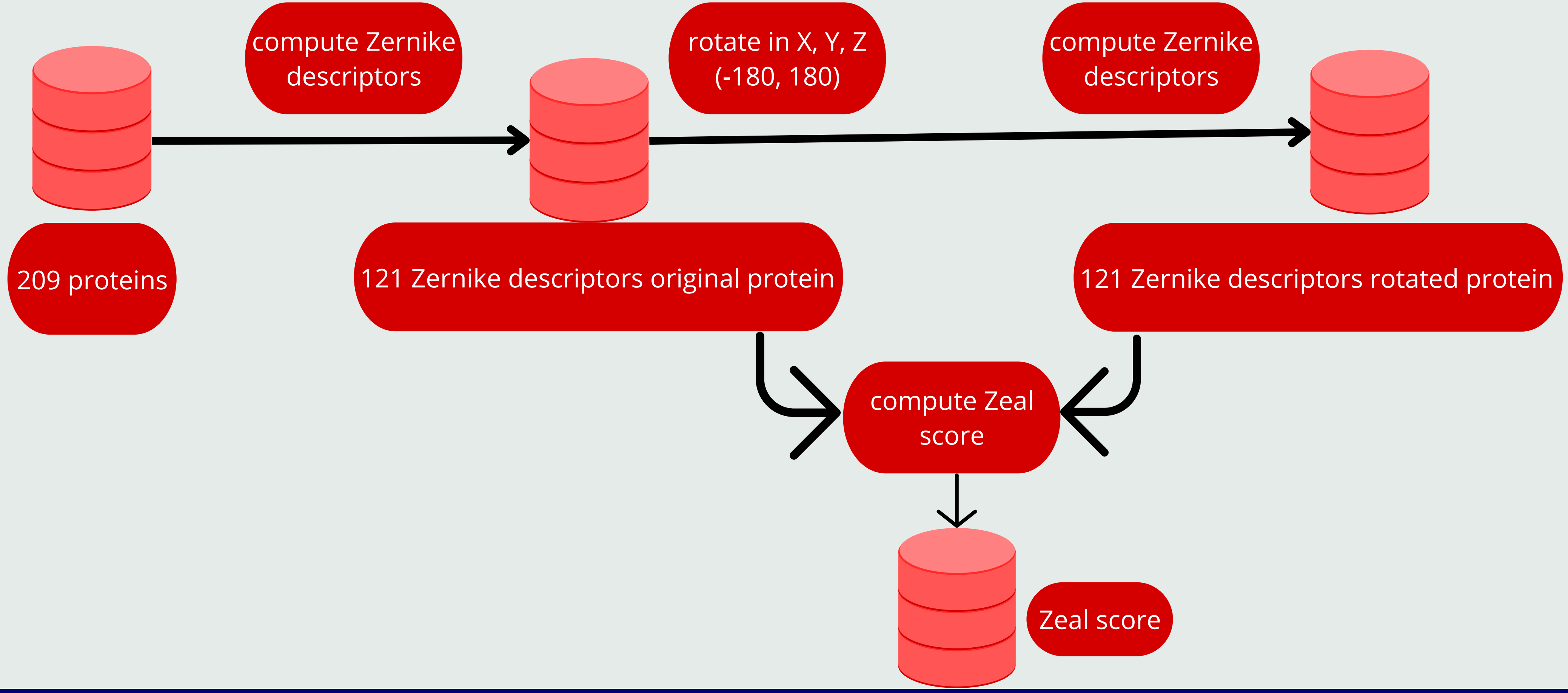
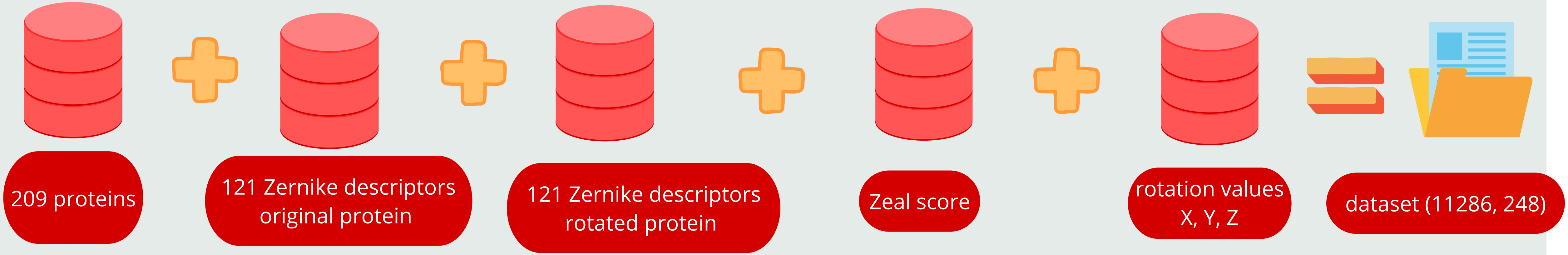
Data preparation


compute Zernike descriptors
rotate in X, Y, Z (-180, 180)
compute Zernike descriptors
209 proteins
121 Zernike descriptors original protein
121 Zernike descriptors rotated protein
compute Zeal score
Zeal score

Data preparation

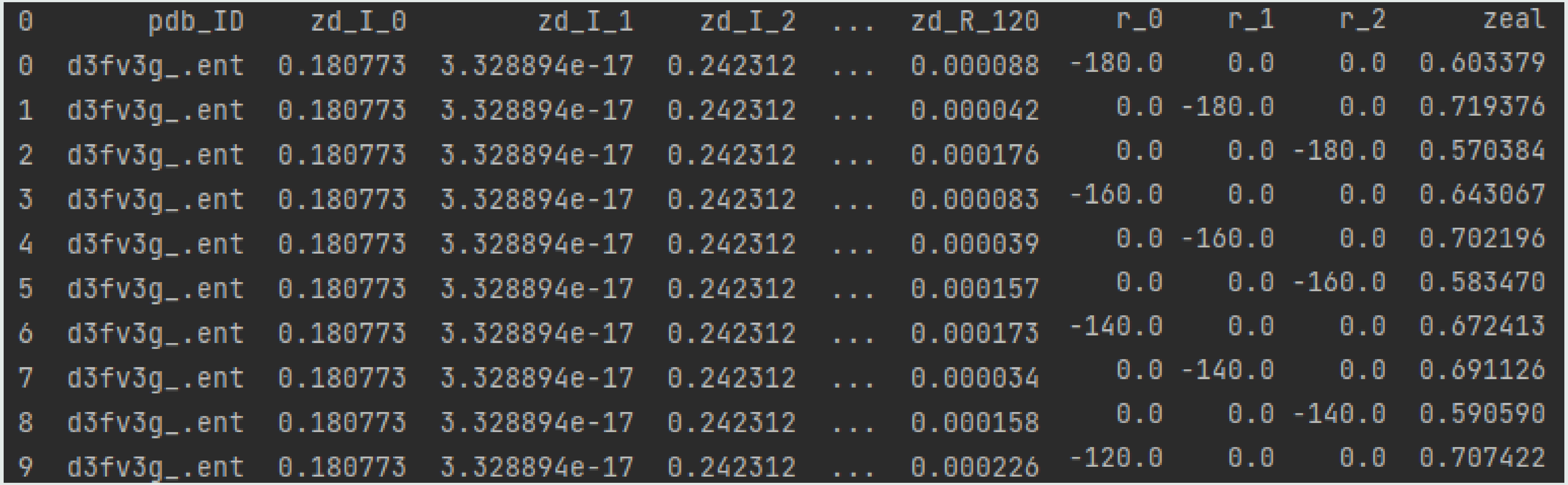


209 proteins + 121 Zernike descriptors original protein + 121 Zernike descriptors rotated protein + Zeal score + rotation values X, Y, Z = dataset (11286, 248)

Preprocessing:

- scale Zernike descriptors - MinMax scaler
- check null values

Dataset



```
0        pdb_ID    zd_I_0        zd_I_1    zd_I_2  ...  zd_R_120    r_0    r_1    r_2      zeal
0  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000088 -180.0    0.0    0.0  0.603379
1  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000042    0.0 -180.0    0.0  0.719376
2  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000176    0.0    0.0 -180.0  0.570384
3  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000083 -160.0    0.0    0.0  0.643067
4  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000039    0.0 -160.0    0.0  0.702196
5  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000157    0.0    0.0 -160.0  0.583470
6  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000173 -140.0    0.0    0.0  0.672413
7  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000034    0.0 -140.0    0.0  0.691126
8  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000158    0.0    0.0 -140.0  0.590590
9  d3fv3g_.ent  0.180773  3.328894e-17  0.242312  ...  0.000226 -120.0    0.0    0.0  0.707422
```

MODELS

Models

- 80% training + 20% testing

- First approach
    - Input: zernike descriptors original protein + zernike descriptors rotated protein
    - Output: rotation values

- Second approach
    - Input: zernike descriptors original protein + zernike descriptors rotated protein + rotation values
    - Output: zeal score

Models

- Considered models:
  - Multioutput Random Forest Regressor
  - Multioutput MLP Regressor
  - CNN Regressor (three outputs)

Multioutput Random Forest

Multioutput Random Forest Regressor - output - rotation values:

- 100 trees
- MSE: 0.0426

Models - Multioutput MLP Regressor

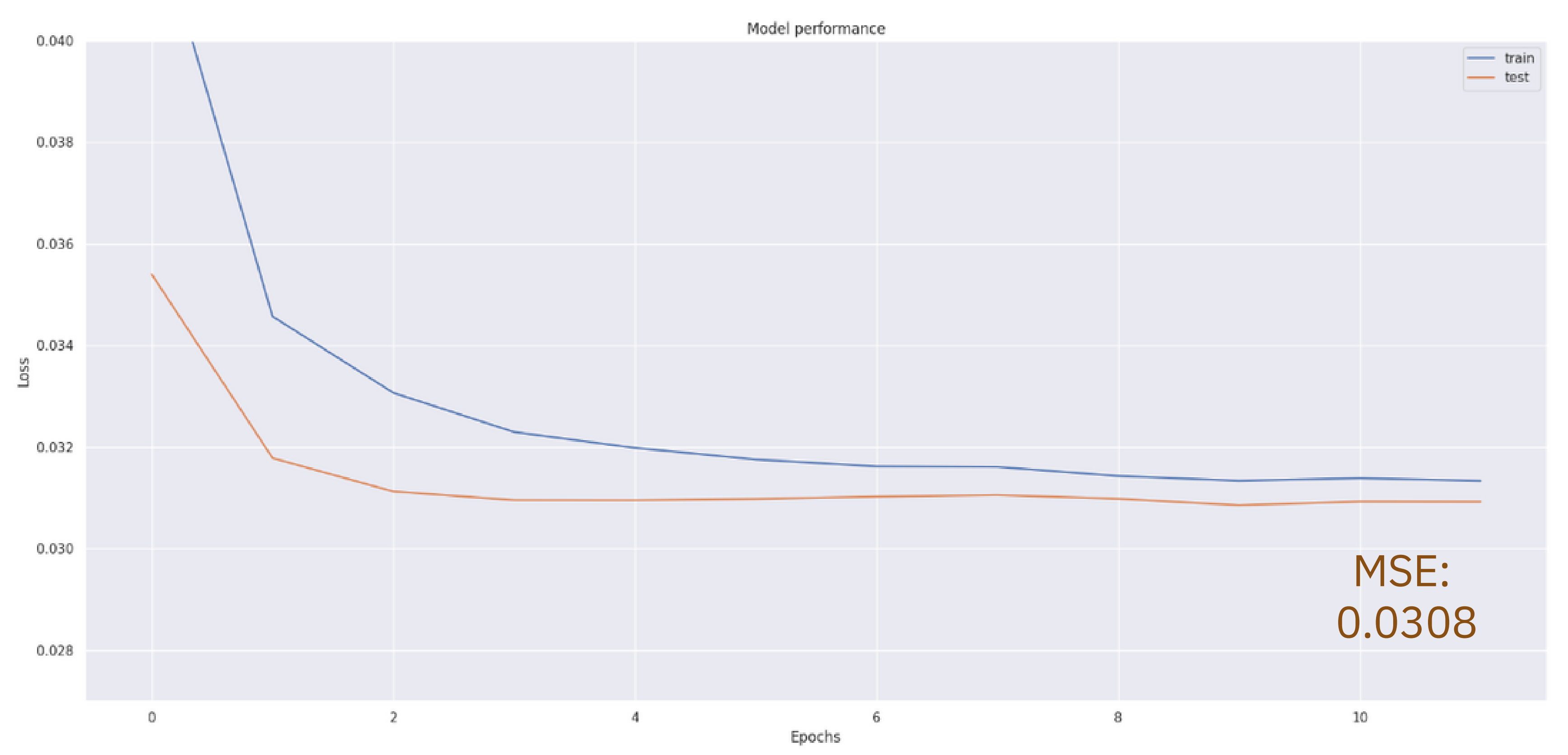
- Multioutput MLP Regressor - output - rotation values
  - 43 hidden layers
  - 200 max iterations
  - Early stopping

- MSE: 0.0325

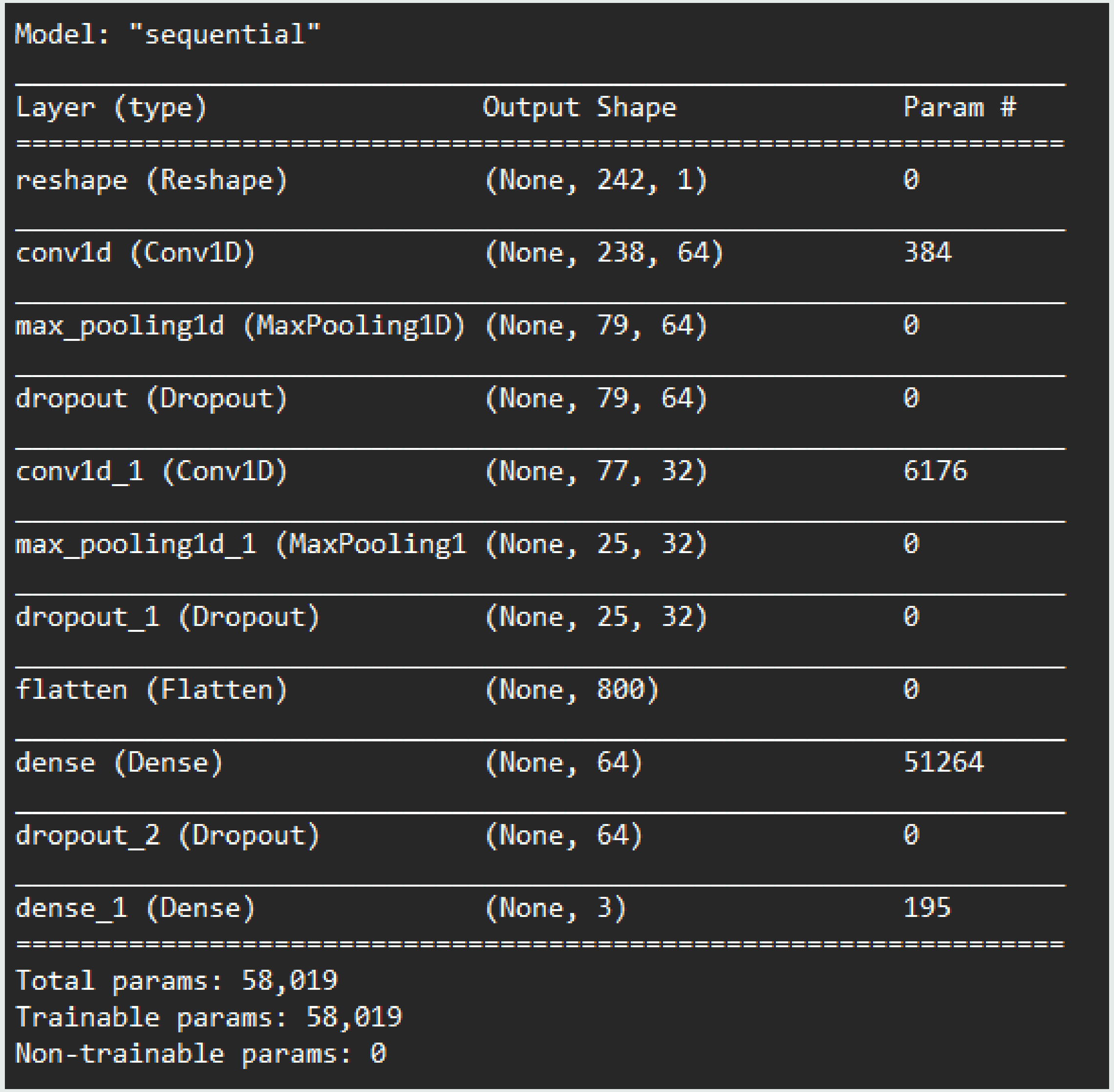
Models - CNN Regressor

- CNN Regressor - output - rotation values
  - 2 1D convolutional layers
  - Flatten layer
  - Dense layer
  - Output layer
  - 200 max epochs
  - Early stopping

CNN Regressor



Loss function (MSE) for the CNN Regressor (output rotation values)



```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
reshape (Reshape)            (None, 242, 1)            0
_________________________________________________________________
conv1d (Conv1D)              (None, 238, 64)           384
_________________________________________________________________
max_pooling1d (MaxPooling1D) (None, 79, 64)            0
_________________________________________________________________
dropout (Dropout)            (None, 79, 64)            0
_________________________________________________________________
conv1d_1 (Conv1D)            (None, 77, 32)            6176
_________________________________________________________________
max_pooling1d_1 (MaxPooling1 (None, 25, 32)            0
_________________________________________________________________
dropout_1 (Dropout)          (None, 25, 32)            0
_________________________________________________________________
flatten (Flatten)            (None, 800)               0
_________________________________________________________________
dense (Dense)                (None, 64)                51264
_________________________________________________________________
dropout_2 (Dropout)          (None, 64)                0
_________________________________________________________________
dense_1 (Dense)              (None, 3)                 195
=================================================================
Total params: 58,019
Trainable params: 58,019
Non-trainable params: 0
```

Models - CNN Regressor

CNN Regressor (output: rotation values) model configuration

Models

- Considered models:
  - Random Forest Regressor
  - MLP Regressor
  - CNN Regressor (one output)

Random Forest

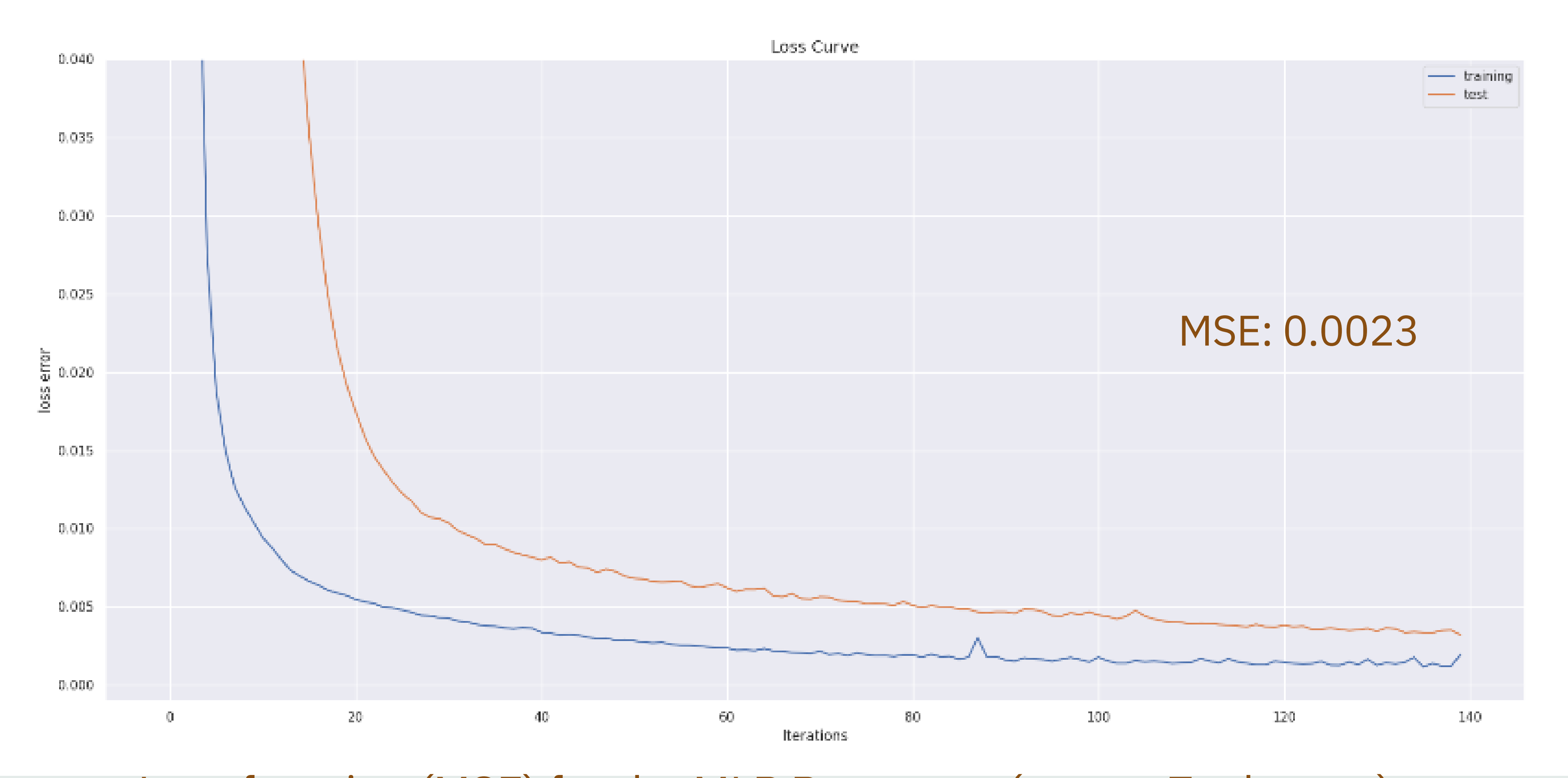
Random Forest Regressor - output - Zeal score:

- 100 trees
- MSE: 0.0016

Models - MLP Regressor

- MLP Regressor - output -Zeal score
  - 43 hidden layers
  - 200 max iterations
  - Early stopping

MLP Regressor

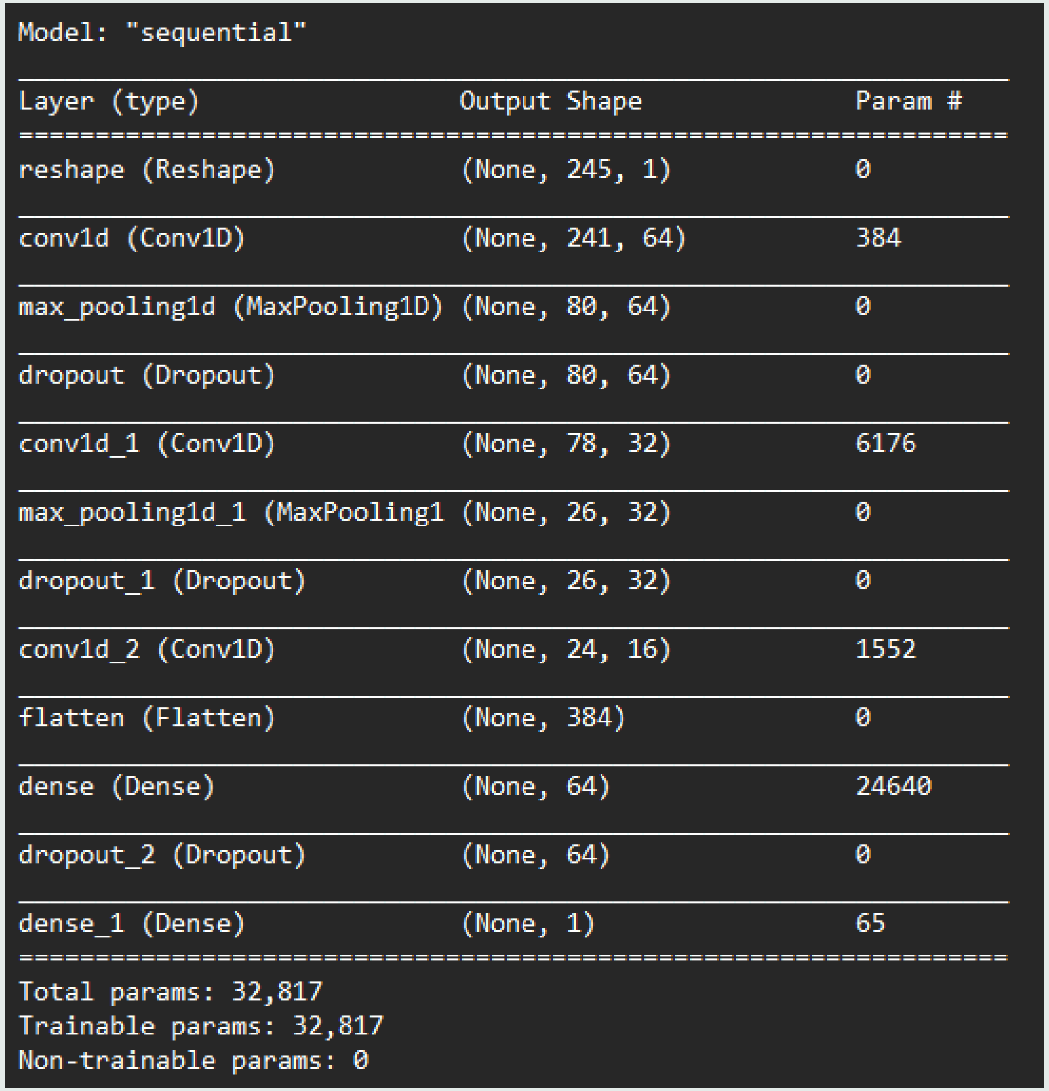


MSE: 0.0023

Loss function (MSE) for the MLP Regressor (output Zeal score)

Models - CNN Regressor

- CNN Regressor - output - Zeal score
  - 3 1D convolutional layers
  - Flatten layer
  - Dense layer
  - Output layer
  - 100 max epochs
  - Early stopping

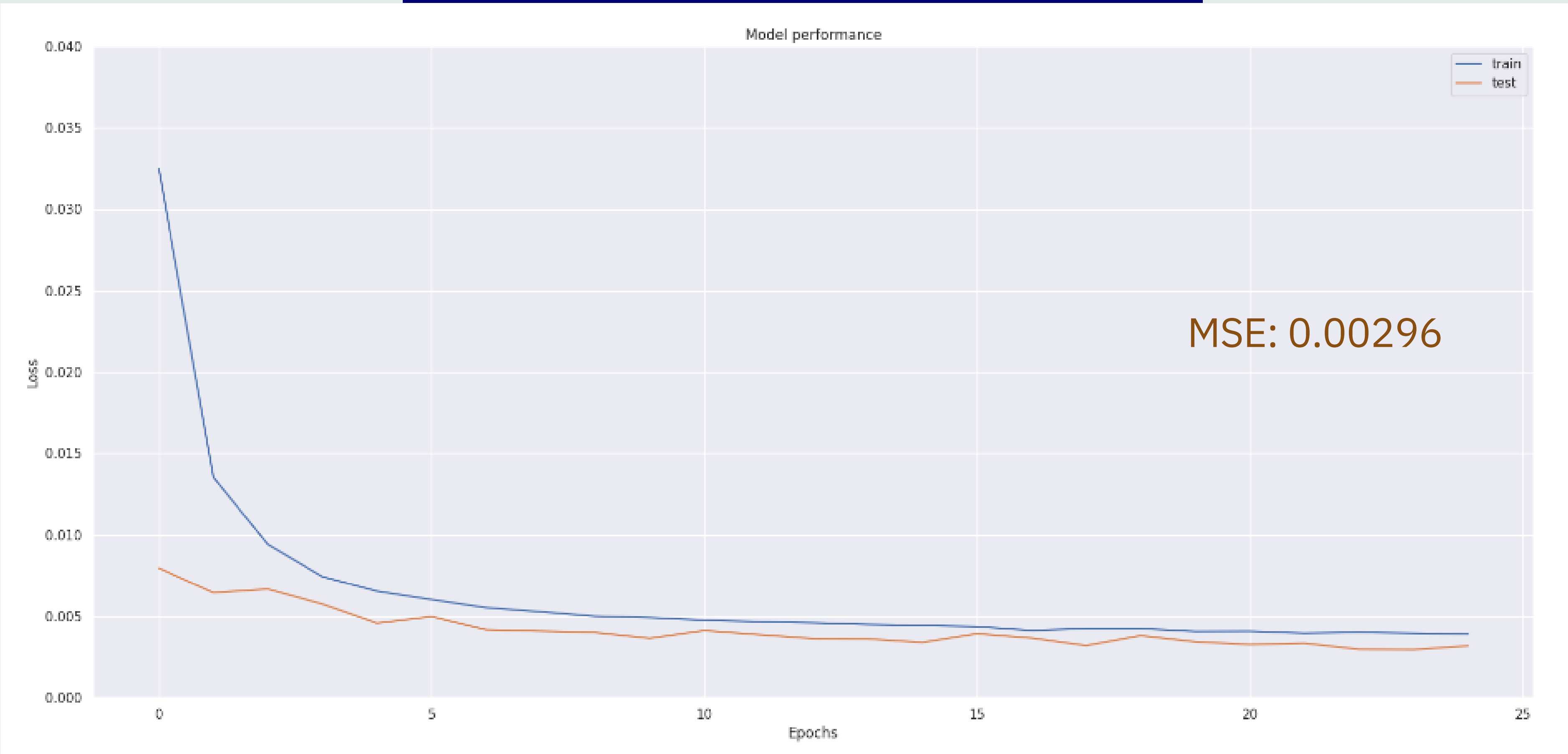


```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
reshape (Reshape)            (None, 245, 1)            0
_________________________________________________________________
conv1d (Conv1D)              (None, 241, 64)           384
_________________________________________________________________
max_pooling1d (MaxPooling1D) (None, 80, 64)            0
_________________________________________________________________
dropout (Dropout)            (None, 80, 64)            0
_________________________________________________________________
conv1d_1 (Conv1D)            (None, 78, 32)            6176
_________________________________________________________________
max_pooling1d_1 (MaxPooling1 (None, 26, 32)            0
_________________________________________________________________
dropout_1 (Dropout)          (None, 26, 32)            0
_________________________________________________________________
conv1d_2 (Conv1D)            (None, 24, 16)            1552
_________________________________________________________________
flatten (Flatten)            (None, 384)               0
_________________________________________________________________
dense (Dense)                (None, 64)                24640
_________________________________________________________________
dropout_2 (Dropout)          (None, 64)                0
_________________________________________________________________
dense_1 (Dense)              (None, 1)                 65
=================================================================
Total params: 32,817
Trainable params: 32,817
Non-trainable params: 0
```

Models - CNN Regressor

CNN Regressor (output: Zeal score) model configuration

CNN Regressor

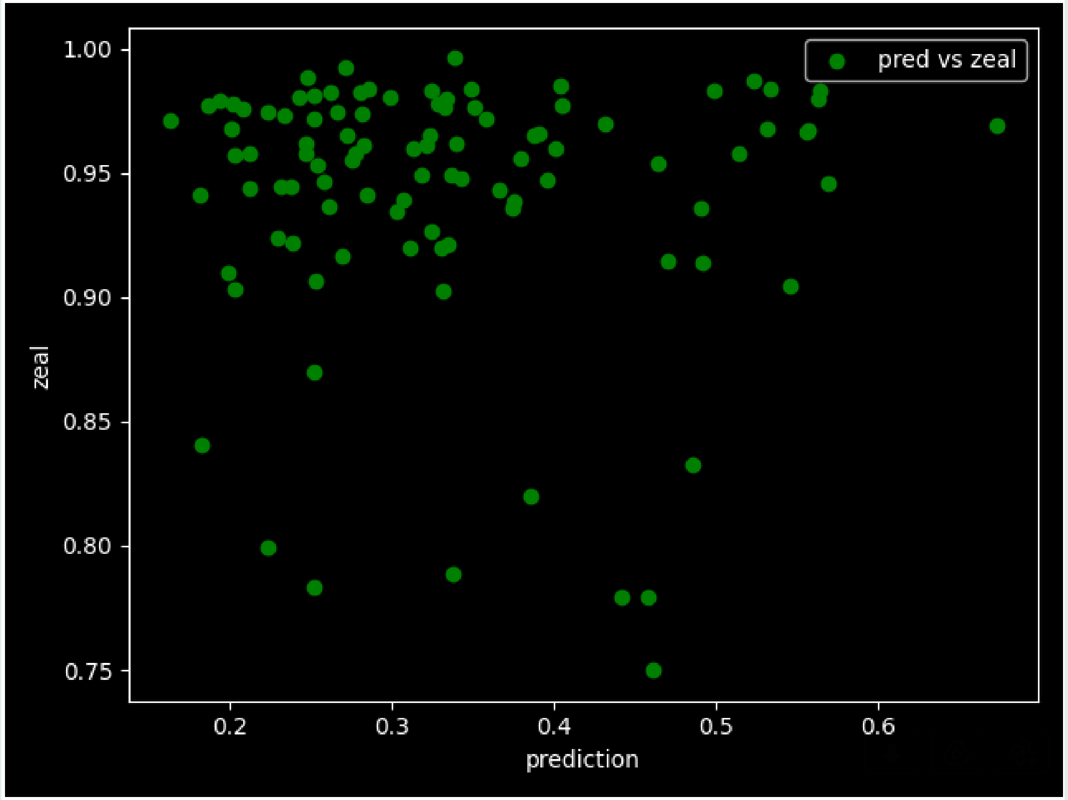


MSE: 0.00296

Loss function (MSE) for the CNN Regressor (output Zeal score)

DEPLOYMENT

Validating in real case



Performance of the models with real data

CONCLUSIONS

Conclusions

- data generation - computational expensive, tedious process
- more data is needed
- the models outputting the Zeal score work better
- 2D convolutional layers - possible improvement

THANK YOU

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