CNN-PepPred: User's Guide

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Contents

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1 Installation

1.1 Installation with *conda*

In the folder *CNN-PepPred*, you will find environment files to create a python environment with all the required packages to run the model. There are two environment files *model_environment_gpu.yml* and *model_environment_cpu.yml*, the first one will create an environment to work with GPU and the second one with CPU. GPU computations will usually be faster than CPU. The environment contains the following packages:

- python version 3.6.10
- numpy version 1.19.1
- tensorflow-gpu or tensorflow (for CPU environment) version 2.0.0
- keras-gpu or keras (for CPU environment) version 2.3.1
- pandas version 1.1.3
- pathlib
- biopython version 1.78
- logomaker
- scikit-learn version 0.23.2
- seaborn version 0.11.0
- pillow version 8.0.0

To create the environment, set the working directory to be the folder *CNN-PepPred* and type in your Anaconda terminal

```
conda env create -f model_environment_gpu.yml
```

for the GPU environment and

```
conda env create -f model_environment_cpu.yml
```

for the CPU environment. This might take a few minutes.
Once the installation is finished, activate the environment using the command

```
conda activate CNNPepPred_Env_GPU
```

for GPU and

```
conda activate CNNPepPred_Env_CPU
```

for CPU.
At the end of the session, you can deactivate the environment using the command

```
conda deactivate
```

To remove the environment, use the command

```
conda remove --name CNNPepPred_Env_GPU --all
conda remove --name CNNPepPred_Env_CPU --all
```

1.2 Installation with *pip*

It is recommended to use the *conda* installation since an older version of python is required and creating environment in Anaconda is more convenient and more uniform through different operating system. However if you wish to do the installation using *pip*, make sure that you are using the version 3.6 of python and you can create an environment and install the required packages following the instructions below.
Set the main folder *CNN-PepPred* as working directory and create a python environment called *CNNPepPred_Env_GPU* or *CNNPepPred_Env_CPU* using the lines

```
python -m venv CNNPepPred_Env_GPU
python -m venv CNNPepPred_Env_CPU
```

Activate the environment on Linux or MacOS with

```
source CNNPepPred_Env_GPU/bin/activate
source CNNPepPred_Env_CPU/bin/activate
```

and on Windows with

```
.\CNNPepPred_Env_GPU\Scripts\activate
.\CNNPepPred_Env_CPU\Scripts\activate
```

To install the required packages, as listed in the previous subsection, use for the GPU environment

```
pip install -r requirements_GPU.txt
```

and for the CPU environment

```
pip install -r requirements_CPU.txt
```

To deactive the environment, run

```
deactivate
```

1.3 Test

To test the installation, call the main function with the template *test_template.txt* in the *Test* folder. It will apply a pre-trained model to the sequences *test_seq.fasta.* The template contains pathways to the pre-trained model and to the data; you will need to modify these pathways in the template to be adapted to the operating system of your computer and replace *[your_working_path]* by the pathway of the folder *CNN-PepPred.* The result file *HLA_DRB1_08_01_predictedOutcome.txt* will be saved in the same folder. Check that they match the results in the file *HLA_DRB1_08_01_predictedOutcome_to_obtain.txt.*
To apply the main script, activate the previously installed environment and set the working directory to be the folder *CNN-PepPred.* If you are working from the python console, execute the lines

```
import sys
model_from_template = open("model_from_template.py").read()
sys.argv = ['model_from_template.py','test_template.txt']
exec(model_from_template)
```

Alternatively, you can run

```
import model_from_template
modelCNN = model_from_template.main('test_template.txt')
```

Or, if you are working from Spyder, you can execute the line

```
runfile('model_from_template.py',args='test_template.txt')
```

2 Package description

The main folder *CNN-PepPred* contains two python scripts, *model_initializer.py* and *model_from_template.py*. The first contains the class *CNNPepPred* where all the functions for training and applying allele-specific models are defined, the second launches the analysis following a user-filled template.

2.1 The class *CNNPepPred*

The class *CNNPepPred* is in the python script *model_initializer.py* and contains the following methods.

2.1.1 *__init__*

Description
Initialize the class. The input arguments can be read from the template.

Usage

```
CNNPepPred(allele='no_allele_name',savePath=Path(os.getcwd()),
   doTraining=False,trainingData=None,trainingOutcome=None,
   doLogoSeq=False,doCV=False,cvPart=None,kFold=5,doApplyData=
   False,trainedModelsFile=None,applyData=None,applyDataName=
   None,epitopesLength=15,parametersFile='parameters.txt')
```

Arguments

`allele`

The name of the allele.

`savePath`

The pathway where to save the results.

`doTraining`

Whether or not to do the training.

`trainingData`

The training sequences, in a list.

`trainingOutcome`

The training outcome corresponding to the training sequences.

`doLogoSeq`

Whether or not to plot (logo plot) the core binding pattern of the trained model.

`doCV`

Whether or not to perform a cross-validation.

`kFold`

The number of fold for the cross-validation.

`doApplyData`

Whether or not to apply the trained model to new sequences.

`trainedModelsFile`

The file containing the trained model. This option is only valid if no training is selected. The file is a pickle saved file from a previous training using this class.

`applyData`

The new sequences for the application of the trained model.

`applyDataName`

The name of the new sequences.

`epitopesLength`

The length of the epitopes on which the trained model will be applied. Each new sequence will be cut into all overlapping *epitopesLength*-mers and a prediction will be made for each of them.

`parametersFile`

The name with extension of the file containing the parameters of the model.

2.1.2 ***getParameters***

Description

Get the parameters of the model as given by the parameters file of the template. The parameters will be saved as attributes. For more information about the parameters, see section 2.2.

Usage

```
CNNPepPred.getParameters()
```

2.1.3 *aa2int*

Description
Transform a sequence of amino acids to integers according to:

A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	-
0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20

where ”-” stands for the absence of amino acids. Any non-amino acid characters will be considered as ”-”.

Usage

```
CNNPepPred.aa2int(s)
```

Arguments

`s`

The amino acid sequences in a list.

Value
Returns `sInt`, a list with the sequences as integers.

2.1.4 *int2aa*

Description
Transform a sequence of integers to amino acids according to the table in section 2.1.3.

Usage

```
CNNPepPred.int2aa(sInt)
```

Arguments

`sInt`

The integer sequences in a list of numpy arrays. If all sequences have the same length, it can be a numpy array of shape (N, L) where N is the number of sequences and L their length.

Value
Returns `s`, a list with the sequences as amino acid characters.

2.1.5 *seqLength*

Description
Compute the maximal length *maxL* in a set of sequences, the length of each of them in *seqL* and the parameter *nMaxPool* which determines the pooling size of the maxpooling layer in the model.
For more information on *nMaxPool*, see Appendix A.2.

Usage

```
CNNPepPred.seqLength(s,saveOutput=False)
```

Arguments

`s`

The sequences, they can be either a list of amino acid sequences or a list of integer sequences.

`saveOutput`

Whether or not to save the outputs as attributes.

Value
Returns `seqL`, a numpy array with the length of the sequences; `maxL`, the maximal length and `nMaxPool`, the pooling size of the maxpooling layer.

2.1.6 *addEmptyPositions*

Description
Add the integer value 20 standing for the absence of amino acids to the given sequences so that they all have the same length as the maximal length in the training set. It will also add this value at the beginning, resp. the end, of the sequences *nbPrev*, resp. *nbAfter*, times. *nbPrev* and *nbAfter* parameters are set in the parameter file (section 2.2).

Usage

```
CNNPepPred.addEmptyPositions(sInt)
```

Arguments

`sInt`

The integer sequences in a list.

Value
Returns `sIntNew`, a list of the integer sequences with the added absence of amino acid values.

2.1.7 *getImages*

Description
Transform the sequences into images according to the given similarity matrix. For a given sequence, the height of the image corresponds to the residues of the sequence, the width corresponds to the 21 amino acids+absence of amino acids. The image is then filled with the similarity value between a residue of the sequence and an amino acid.
For more information on the peptide's encoding, see Appendix A.1.

Usage

```
CNNPepPred.getImages(sInt)
```

Arguments

`sInt`

The integer sequences in a numpy array as given by the output of *addEmptyPositions* (section 2.1.6), in particular all sequences must have the same length.

Value
Returns `IM`, a 4D numpy array with the images corresponding to the sequences. The first dimension corresponds to the number of sequences, the second to the height, the third to the width and the fourth to the channel (which is always 1 with this encoding).

2.1.8 *trainCNN*

Description
Train an ensemble convolutional neural network model. The base model consists of a *Conv2D* layer with *ReLu* activation, a *MaxPooling2D* layer and a

Dense (or fully connected) layer. The parameters are defined in the parameters file (section 2.2).
For more information on the model's architecture, see Appendix A.2.

Usage

`CNNPepPred.trainCNN(IM,out,saveModel=False)`

Arguments

`IM`

The training images, as given by the output of *getImages* (section 2.1.7).

`out`

The training outcome.

`saveModels`

Whether or not to save the trained model as an attribute and in the saving pathway *savePath* of the class. If *saveModels* is true, the computation time of the training will be an attribute of the class called *timeTrain*. A folder called *model_[allele]* (where [allele] is the allele name of the class) will be created, it will contains the parameters file of the model and a folder called *nets* where the trained nets will be saved.

Value
Returns `models`, a list containing all the Keras trained models.

2.1.9 *applyCNN*

Description
Apply the trained model.

Usage

`CNNPepPred.applyCNN(models,IM,saveOutcome=False)`

Arguments

`models`

The ensemble model as given by the output of *trainCNN* (section 2.1.8).

`IM`

The images on which the trained model will be applied.

`saveOutcome`

Whether or not to save the predicted outcome as an attribute.

Value
Returns `yhat`, a numpy array with the predicted outcome of each sample.

2.1.10 *crossValCNN*

Description
Perform the training in a cross-validation set up. The computation time of the cross-validation will be an attribute of the class called *timeCV*.

Usage

```
CNNPepPred.crossValCNN(IM,out)
```

Arguments

`IM`

The training images for the cross-validation.

`out`

The training outcome.

Value
Returns `yhatCV`, a numpy array containing the cross-validated predicted outcome of each sample and `modelCV`, a list containing the trained Keras models (as returned by *trainCNN*, section 2.1.8) for each fold.

2.1.11 *feedForwardAndGetScore*

Description
Apply the trained model of the class to new sequences and get the score for each of the overlapping l-mer of a sequence, where l is the parameter determining the length of the core binder (9 by default).
To control the memory usage, the application of the sequences will be by batches of *maxNbSamples2apply* which is a parameter (see section 2.2) with default value 50000.

For more information on the contribution score, see Appendix A.4.

Usage

`CNNPepPred.feedForwardAndGetScore(seq,saveOutcome=False)`

Arguments

`seq`

The sequences on which the trained model will be apply as given by the output of *addEmptyPositions* (section 2.1.6).

`saveOutcome`

Whether or not to save the predicted outcome as an attribute. If *saveOutcome* is true, the computation time to apply the model on the data will be an attribute of the class called *timeApply*.

Value

Returns `contributionScore`, a numpy array with the constribution score of all the overlapping *l*-mer of each sequence and `contributionScore`, a numpy array with the predicted outcome of each sequence.

2.1.12 *generateRandomSeq*

Description

Generate integers random sequences. The number of random sequences to generate is set in the parameters file (section 2.2).

Usage

`CNNPepPred.generateRandomSeq(followLengthDistr=False)`

Arguments

`followLengthDistr`

If `False`, all the random sequences will have the same length *lengthRandSeq* as given in the parameters file (section 2.2). If `True`, the length distribution of the random sequences will follow the length distribution of the training data saved as an attribute called *seqL* with the function *seqLength* (section 2.1.5)

Value
Returns `sR`, a list with the randomly generated integer sequences.

2.1.13 *plotLogoSeq*

Description
Generate a logo plot (using the package *logomaker*) of the highest scoring core binders. The plot will be saved in the saving pathway *savePath* of the class. The number of best scoring sequences used in the logo plot is set in the parameters file (section 2.2).

Usage

```
CNNPepPred.plotLogoSeq(contributionScore,yhatR)
```

Arguments

`contributionScore`

The contribution score of each overlapping l-mers in all of the sequences to which the trained model has been applied, as given by the output of *feedForwardAndGetScore* (section 2.1.11).

`yhatR`

The predicted score of each sequences.

Value
Returns `h`, the plot handle of the logo plot; `sBchar`, a list with the amino acids sequences used to generate the plot and `pim`, the information matrix corresponding to the logo plot.

2.1.14 *computationTime*

Description
Save the computation time as an attribute called *timeTotal*.

Usage

```
CNNPepPred.computationTime(time_elapsed)
```

Arguments

`time_elapsed`

The time elapsed to save.

2.1.15 *getCVresults*

Description
Get the cross-validation results. The scores are: PC (Pearson correlation), AUC (area under the curve), RMSE (root mean square error), MCC (Matthews correlation coefficient), ACC (accuracy), BACC (balanced accuracy), F1 (F1-score). The result will be saved as a txt file *'cross_validation_results.txt* in the saving pathway *savePath* of the class.

Usage

```
CNNPepPred.getCVresults()
```

2.1.16 *printApplyOutcome*

Description
Print the predicted outcome of the apply sequences as a txt file *[allele]_predictedOutcome.txt* where [allele] is the allele name of the class. The file will be saved in the saving pathway *savePath* of the class. Note that only the unique core binders will be printed; if there are different peptides with the same core, the one with the highest predicted outcome will be printed.

Usage

```
CNNPepPred.printApplyOutcome(saveTable = False)
```

Arguments

`saveTable`

Whether or not to save the output table as an attribute.

Value
Returns `table`, a pandas data frame with the predicted outcome of the sequences on which a trained model was applied. Only unique core binders are in the table.

2.1.17 *seq2Lmer*

Description
Cut sequences into all overlapping *epitopesLength*-mers where *epitopesLength* is as given in the template (section 2.3).

Usage

```
CNNPepPred.seq2Lmer(seq,nameSeq=None,takeUniqueLmer=True,
   saveLmer=False)
```

Arguments

`seq`

The integer amino acid sequences in a list of numpy arrays.

`nameSeq`

The name of the sequences.

`takeUniqueLmer`

Whether or not to only select the unique overlapping *epitopesLength*-mers.

`saveLmer`

Whether or not to save the output sequences as an attribute.

Value
Returns `sLmer`, a list with all the overlapping *epitopesLength*-mers as integers; `nameSeqLmer`, the name of the sequences each element of `sLmer` belongs to and `indLmer`, the indices of the sequences each element of `sLmer` belongs to.

2.1.18 *getCoreBinder*

Description
Get the core binders of the sequences.

Usage

```
CNNPepPred.getCoreBinder(seq,contributionScore,applyDataName=
   None,saveCoreBinders=False)
```

Arguments

`seq`

The amino acid sequences in a list. The sequences must all have the same length, i.e. use *int2aa* (section 2.1.4) to the output of *addEmptyPositions* (section 2.1.6).

`contributionScore`

The contribution score of each overlapping *l*-mers in all of the sequences to which the trained model has been applied, as given by the output of *feedForwardAndGetScore* (section 2.1.11).

`applyDataName`

The name of the sequences.

`saveCoreBinders`

Whether or not to save the core binders as an attribute.

Value

Returns `sCore`, a numpy array with the core binder of each sequence (as amino acids).

2.1.19 *save_object*

Description

Save with *pickle* the object class. It will be saved in the saving pathway *savePath* of the class with the file name given as argument or by default *[allele]_ModelCNN.pkl* where [allele] is the allele name of the class.
In order to avoid loading problem if the object is loaded from another OS, the attribute *savePath* is deleted upon saving.
If the class contains a list of trained Keras neural networks, it will be deleted as these nets are saved separately with the saving option of *trainCNN* (section 2.1.8).

Usage

```
CNNPepPred.save_object(name=None)
```

Arguments

`name`

Name of the file.

2.1.20 *load_object*

Description
Load another object class. This is meant to load previously trained models. As the attribute *savePath* is deleted upon saving (section 2.1.19), this function will reset it to be the parent directory of the argument *filename*.

Usage

```
CNNPepPred.load_object(filename)
```

Arguments

`filename`

Complete pathway to the object to load.

Value
Returns `obj`, the loaded object.

2.1.21 *feedForwardVisualization*

Description
Visualization of the feed forward pass of the trained model on the set of sequences *s*. It will create a folder (in the saving pathway *savePath* of the class) called *feed_forward_visualization* which will contains two folders: *nets* and *sequences*. The folder *nets* will contain a folder for each net of the trained model with each of its corresponding convolutional layer's filters and dense layer's weights represented as images. The folder *sequences* will contains one folder for each of the input argument sequences with an image of their encoding and a folder for each net containing the convolutional layer's output and the maxpooling layer's output represented as images.
For each input sequence, many images will be saved; it is therefore recommended to only run this function on a small pre-selected set of sequences.
For more information on the visualization of the feedforward pass, see Appendix A.3.

Usage

```
CNNPepPred.feedForwardVisualization(s,fontSize=4,dpi=300)
```

Arguments

`s`

The amino acid sequences in a list.

`fontSize`

The font size of the x and y ticks labels. Default is 4.

`dpi`

The dpi of the images. Default is 300.

Value
Returns `yhat`, a numpy array with the predicted outcome of each sequence.

2.1.22 *generateCVpartWithLeastLmerOverlap*

Description
Generate a cross-validation partition for the training data such that the number of shared *l*-mers between folds is reduced, where *l* is the length of the core binders as given in the parameters (section 2.2).
For more information on the way the partition is generated, see Appendix B.2.

Usage

```
CNNPepPred.generateCVpartWithLeastLmerOverlap(kFold,saveCVPart=
   False)
```

Arguments

`kFold`

The number of folds, as an integer.

`saveCVPart`

Whether or not to save the cross-validation partition as an attribute of the class called *cvPart*. If true, the average number of shared *l*-mers between each of the `kFold` train/test partitions (within each positive and negative class) will also be saved as an attribute of the class called *averageLmersOverlappingCV*.

Value
Returns `cvPart`, a numpy array with the cross-validation partition and

`averageLmersOverlappingCV`, the average number of shared l-mers between each of the `kFold` train/test partitions (within each positive and negative class).

2.2 The parameters file

When initializing the class, the parameters will be set from the file given with full path in the template or, by default, the file in the working directory called *parameters.txt*. This file consists of two columns (separated by a comma), one with the name of the parameter and one with the value of the parameter. Only the parameter values can be changed if needed. If a parameter value is left empty, the default value will be set (if left empty, check that the comma separating the columns is still there). The parameters are the following.

- *bindingThr*. Default: 0.5.
  The binding threshold for the predicted values. The default is 0.5.

- *similarityMat*. Default: blosum62.txt
  The similarity matrix to use for the sequences encoding. It must be symmetric and be of the same format, with the same amino acids order, as the default file.

- *l*. Default: 9
  The length of the core binder.

- *maxNbSamples2apply*. Default: 50000
  The maximum number of sequences on which a trained model can be applied in one batch. This is only for the application of the model through the function *feedForwardAndGetScore* (section 2.1.11). Increase if you have enough memory and decrease if you don't have enough memory.

- *nbPrev*. Default: 2
  The number of empty positions (corresponding to the absence of amino acids) to add at the beginning of a sequence.

- *nbAfter*. Default: 2
  The number of empty positions (corresponding to the absence of amino acids) to add at the end of a sequence.

- *F*. Default: 5/10/20/30
  The number of filters of the convolutional layer. Different number of filters can be given, separated by a slash "/". In that case the final model will be an -equally weighted- ensemble of models with different number of filters.

- *rep*. Default: 10
  The number of models to train with different initial weights per number of filters. For each number of filters given in the parameter *F*, *rep* number of models will be trained. The final model will be an equally weighted ensemble of *rep* times the number of different number of filters, i.e. $40 = 10 \cdot 4$ with the default parameters.

- *nMaxPool*. Default: see Appendix A.2.
  The pooling size of the Maxpooling layer will be *nMaxPool*$\times 1$. The default value is set by a formula given in the Appendix A.2 and will be such that the output layer has size $L_{freq} \times F$ where L_{freq} is the most frequent sequence length in the training data set and F is the number of filters.

- *initializeStd*. Default: 0.01
  The standard deviation of the initial weights (randomly generated from the normal distribution with zero mean). The same value will be used for the convolutional and the dense layers.

- *alpha*. Default: 0.005
  The learning rate of the stochastic gradient descent.

- *gamma*. Default: 0.9
  The momentum of the stochastic gradient descent.

- *l2_fact*. Default: 0.0001
  The L2 regularization factor. The same value will be used for the convolutional and the dense layers.

- *maxEpochs*. Default: 30
  The number of epochs.

- *miniBatchSize*. Default: 128
  The size of the mini batch for the stochastic gradient descent.

- *useBias*. Default: 1
  Whether or not to use bias. The same value will be used for the convolutional and the dense layers.

- *activationFctDenseLayer*. Default: linear
  The activation function of the last layer (the *Dense* layer). Possible values are to choose among *keras*'s activation functions.

- *lossFct*. Default: mean_squared_error
  The loss function. Be aware that if changed, some parameter tuning might be needed. For example if for a classification problem you would rather use the *binary_crossentropy* loss function, you should change the activation function of the *Dense* layer to be the *sigmoid* function. Possible values are to choose among *keras*'s loss functions.

- *nbRandSeq*. Default: 200000
  The number of random sequences to be generated in the function *generateRandomSeq* (section 2.1.12).

- *nbBest*. Default: 2000
  The number of best scoring sequences to select for the generation of the logo plot with *plotLogoSeq* (section 2.1.13)

- *lengthRandSeq*. Default: 15
  The length of the random sequences generated in the function *generateRandomSeq* (section 2.1.12).

2.3 The template file

Fill the template file given the main folder *CNN-PepPred* according to the desired analysis. This template consists of two columns (separated by a comma), one with the name of the template's inputs and one with their values. Only the input values can be changed if needed. If an input value is left empty, the default value will be set (if left empty, check that the comma separating the columns is still there). The inputs are the following.

- *allele*.
  The name of the allele. This name can be thought of as a job name for the run. If the training option is not selected and no trained model

is given as input, then *allele* corresponds to the name of a pre-trained model (section 2.5).

- *savePath*. Default: os.getcwd()
  The pathway where to save the results.

- *doTraining*. Default: 0
  Whether or not to do the training.

- *trainingDataPath*. Default: None
  The file with the training data. It must be a *.txt* file, with at least two columns (with headers) separated by a comma. The first column contains the sequences and the second the outcome. For regression, the outcome must be already normalized. A third column containing a cross-validation partition can be added. If the cross-validation option is selected and no partition is given here, it will be generated following the function *generateCVpartWithLeastLmerOverlap* (section 2.1.22).

- *doLogoSeq*. Default: 0
  Whether or not to plot (logo plot) the core binding pattern of the trained model.

- *doCV*. Default: 0
  Whether or not to do the cross-validation.

- *kFold*. Default: 5
  The number of folds for the cross-validation. If a partition is given in the training data file, this input will be ignored and the *kFold* value will be the number of partitions.

- *doApplyData*. Default: 0
  Whether or not to apply the trained model to new sequences.

- *trainedModelsFile*. Default: None
  Either the file containing the trained model (a *.pkl* file) or the pathway of the folder containing the *parameters* file and the *nets* folder with the trained nets (as saved with the function *trainCNN*, see section 2.1.8). If the input is a *.pkl* file, the parent folder must contain the *nets* folder. This option is only valid if no training is selected.
  If the apply or the logoseq option are selected with no training and

trainedModelsFile is left empty, then a pre-trained model will be selected based on the *allele*. For available alleles, see section 2.5.
If a trained model is given as input, the parameters file *parametersFile* given in the template will be ignored.

- *applyDataPath*. Default: None
  The file containing the data on which the trained model will be applied. It must be a FASTA file.

- *epitopesLength*. Default: 15
  The length of the epitopes on which the trained model will be applied. Each new sequence will be cut into all overlapping *epitopesLength*-mers and a prediction will be made for each of them.

- *parametersFile*. Default: parameters.txt (in the working directory)
  The full path file with extension of the file containing the parameters of the model. This file is ignored if a trained model is given as input in *trainedModelsFile*.

- *saveClassObject*. Default: 0
  Whether or not to save the class generated following the template in *savePath*. If the class contains a list of trained Keras neural networks, it will be deleted as these nets are saved separately with the saving option of *trainCNN* (section 2.1.8).

2.4 The script *model_from_template.py*

The argument of the script *model_from_template.py* is the template file. By default this file is called *template.txt* and is located in the working directory, the name and pathway can be modified but need to be given with full pathway as a system argument.
The script will first read the system argument to obtain the name of the template and call the main function with this template as an argument.

```
tmplName = sys.argv
if len(tmplName)==1:
   tmplName = 'template.txt'
else:
   tmplName = tmplName[1]
main(tmplName)
```

The *main* function will run the desired analysis following the template. First the start time is recorded and the template is read,

```
time_start = time.perf_counter()
file = Path(tmplName)
allele,savePath,doTraining,trainingData,trainingOutcome,
   doLogoSeq,doCV,cvPart,kFold,doApplyData,trainedModelsFile,
   applyData,applyDataName,epitopesLength,parametersFile,
   saveClassObject = readTemplate(file)
```

then, the class *CNNPepPred* is initialized

```
modelCNN = CNNPepPred(allele,savePath,doTraining,trainingData,
   trainingOutcome,doLogoSeq,doCV,cvPart,kFold,doApplyData,
   trainedModelsFile,applyData,applyDataName,epitopesLength,
   parametersFile)
```

and the desired analysis will be performed following the template. If the training option is selected, the images *IM* encoding the sequences and training outcome *out* are first retrieved.

```
sInt = modelCNN.aa2int(modelCNN.trainingData)
modelCNN.seqLength(sInt,saveOutput=True)
sInt = modelCNN.addEmptyPositions(sInt)
IM = modelCNN.getImages(sInt)
out = modelCNN.trainingOutcome
```

Cross-validation with the training data is performed as follows.

```
modelCNN.crossValCNN(IM,out)
modelCNN.getCVresults()
```

The final model, to be saved in the object *modelCNN*, will be trained with all of the training data.

```
modelCNN.trainCNN(IM,out,saveModel=True)
```

To obtain the logoplot with the binding core, the script generate random sequences,

```
sR = modelCNN.generateRandomSeq()
```

apply the model to obtain the predicted outcomes and contribution scores of the random sequences' overlapping *modelCNN.l*-mers

```
contributionScore,yhatR = modelCNN.feedForwardAndGetScore(sR)
```

and finally generates the logoplot.

```
modelCNN.plotLogoSeq(contributionScore,yhatR)
```

The sequences on which the trained model must be applied are first cut into all the overlapping *epitopesLength*-mers.

```
sIntApply,sApplyName = modelCNN.seq2Lmer(modelCNN.aa2int(
   modelCNN.applyData),L=None,nameSeq=modelCNN.applyDataName,
   saveLmer = True)[0:2]
```

Then the amino acid sequences are prepared for the application of the trained model into the required format.

```
sIntApply = modelCNN.addEmptyPositions(sIntApply)
```

The trained model is then applied to obtain the predicted outcomes and the contribution scores which are used to find the binding cores and the results are printed in the saving pathway.

```
modelCNN.feedForwardAndGetScore(sIntApply,saveOutcome = True)
modelCNN.getCoreBinder(modelCNN.int2aa(sIntApply),modelCNN.
   contributionScore,sApplyName,saveCoreBinders = True)
modelCNN.printApplyOutcome()
```

Finally the computation time is saved in the object and the object is saved in the saving pathway if selected in the template.

```
time_elapsed = (time.perf_counter() - time_start)
modelCNN.computationTime(time_elapsed)
if saveClassObject:
   modelCNN.save_object()
```

2.5 The pre-trained models

The user can use models available for some alleles which were trained with the IEDB data (Appendix B.1). The models are in a folder called *trainedIEDB-models* of the main directory *CNN-PepPred*. In this case, the template must contain the name of the allele, the data to apply, no training must be selected and the trained model file (*trainedModelsFile*) must be left empty. An example template called *template_pretrained_model_example.txt* in the main directory has been pre-filled for the allele *HLA_DRB1_01_01*. The location where to save the results and the fasta file on which to apply the pre-trained model

must be filled (*[your_path_to_save_the_results]* and *[fasta_file_for_prediction]* in the example template).
Available alleles are:

HLA_DPA1_01_03_DPB1_02_01,	HLA_DPA1_01_03_DPB1_03_01,	HLA_DPA1_01_03_DPB1_04_01,
HLA_DPA1_01_03_DPB1_04_02,	HLA_DPA1_01_03_DPB1_06_01,	HLA_DPA1_01_03_DPB1_104_01,
HLA_DPA1_02_01_DPB1_01_01,	HLA_DPA1_02_01_DPB1_09_01,	HLA_DPA1_02_01_DPB1_10_01,
HLA_DPA1_02_01_DPB1_14_01,	HLA_DPA1_02_01_DPB1_17_01,	HLA_DPA1_02_01__DPB1_13_01,
HLA_DPA1_02_02_DPB1_05_01,	HLA_DQA1_01_01_DQB1_05_01,	HLA_DQA1_01_02_DQB1_05_01,
HLA_DQA1_01_02_DQB1_06_02,	HLA_DQA1_02_01_DQB1_02_02,	HLA_DQA1_02_01_DQB1_03_01,
HLA_DQA1_03_01_DQB1_03_02,	HLA_DQA1_03_02_DQB1_04_01,	HLA_DQA1_05_01_DQB1_02_01,
HLA_DQA1_05_01_DQB1_03_01,	HLA_DQA1_05_05_DQB1_03_01,	HLA_DRB1_01_01,
HLA_DRB1_03_01,	HLA_DRB1_04_01,	HLA_DRB1_04_02,
HLA_DRB1_04_04,	HLA_DRB1_04_05,	HLA_DRB1_07_01,
HLA_DRB1_08_01,	HLA_DRB1_08_02,	HLA_DRB1_09_01,
HLA_DRB1_10_01,	HLA_DRB1_11_01,	HLA_DRB1_11_03,
HLA_DRB1_12_01,	HLA_DRB1_13_01,	HLA_DRB1_13_02,
HLA_DRB1_13_03,	HLA_DRB1_14_01,	HLA_DRB1_14_54,
HLA_DRB1_15_01,	HLA_DRB1_16_01,	HLA_DRB3_01_01,
HLA_DRB3_02_02,	HLA_DRB3_03_01,	HLA_DRB4_01_01,
HLA_DRB4_01_03,	HLA_DRB5_01_01,	HLA_DRB5_02_02.

2.6 Random generation of non-binders

The majority of experimental results only report binding peptides, so that most sets are too imbalanced to properly train a model. Therefore, we provide a separate script for the generation of randomly selected peptides that act as non-binders.
The script will simply select at random peptides from a user given folder with fasta files, respecting the length distribution of the binders in the training set. These files should contain enough natural random sequences so that there shouldn't be any patterns that would relate them to one another.
The script is in the main folder *CNN-PepPred*, it is called *generateRandomNonBinders.py* and contain a unique function with the same name. Therefore, to import it, use

```
from generateRandomNonBinders import generateRandomNonBinders
```

The function is

```
generateRandomNonBinders(fastaSeqLoc,seqL=None,seq=None,prop=1,
    N=None,maxFiles=None)
```

with arguments:

`fastaSeqLoc`

The location of the folder containing the fasta files to select from.

`seqL`

A numpy array with the lengths of the binding peptides in the training set.

`seq`

A list of amino acids sequences corresponding the binding peptides in the training set. If `seqL` is not given, it will be computed from this list. If `seqL` is given, this argument is ignored.

`prop`

The proportion of peptides to select. The number of selected peptides will be around `prop`·`N` where `N` is either the number of binding peptides or the argument `N`.
`prop` is 1 by default.

`N`

The number of peptides to select. The final number will be `prop`·`N`. Note that due to the nature of the algorithm, it is possible that the number of peptides in the output differs slightly from this number.
If no sequences or length of sequences is given, `N` will be 2000 by default.

`maxFiles`

The maximum number of files to read in the given folder `fastaSeqLoc`.
We recommend dividing the sequences to select from into many files in `fastaSeqLoc` and using the parameter `maxFiles` instead of having one big file. In this way, the computational time will be lower since the algorithm will only read few smaller files rather than a big one and there won't be any memory issues.

The function will return `seqNeg`, a list of amino acids sequences respecting the number of sequences and their length distribution accordingly to the given input arguments.
The function can be called as follows, with `myfolderwithsequences` being the pathway to the folder containing the sequences to select from.

```
seqNeg = generateRandomNonBinders(myfolderwithsequencesaSeqLoc,
   seqL=bindersLength,prop=1.3,maxFiles=3)
```

The output `seqNeg` will have around 1.3 times the number of elements in `bindersLength` sequences whose lengths are ditributed like in `bindersLength` and which are selected from 3 randomly selected fasta files in the folder `myfolderwithsequences`.

```
seqNeg = generateRandomNonBinders(myfolderwithsequencesaSeqLoc,
   seq=bindersSeq,N=2500,maxFiles=1)
```

will return around 2500 peptides respecting the length distribution of the amino acids sequences in `bindersSeq` and randomly selected from 1 file in the folder `myfolderwithsequences`.

3 Examples

Three different templates were prepared as examples in the main folder *ModelCNN*. To use them, you will need to change the pathways in the templates to be adapted to the operating system of your computer and replace *[your_working_path]* by the pathway of the folder *ModelCNN*.
To run the template files, set your working directory to be *ModelCNN* and type in your console

```
import sys
model_from_template = open("model_from_template.py").read()
sys.argv = ['model_from_template.py','full_path_to_any_template
   .txt']
exec(model_from_template)
```

Or alternatively,

```
import model_from_template
modelCNN = model_from_template.main('full_path_to_any_template.
   txt')
```

3.1 Template 1: Train+CV+logoPlot+Apply

The first template, *template1_Train_CV_logoPlot_Apply.txt*, will perform cross-validation and train a model from the example training data set of the allele *HLA_DRB1_08_01* in the folder *Example*. It will also generate the logo plot representing the binding characteristics of the trained model and apply it to new sequences *uniprot-proteome_UP000000605_100.fasta* in the same folder. The results will be saved in the folder *Template1_results* of the *Example* folder.
Here are the cross-validation results obtained after runing this template (note that there might small diffrences between runs):

```
Allele,#Peptide,#Binder,PC,AUC,RMSE,MCC,ACC,BACC,F1
HLA_DRB1_08_01
   ,1118,559,0.783,0.962,0.312,0.834,0.917,0.917,0.917
```

The different scores are: PC (Pearson correlation), AUC (area under the curve), RMSE (root mean square error), MCC (Matthews correlation coefficient), ACC (accuracy), BACC (balanced accuracy), F1 (F1-score).
Figure 1 contains the logo plot of the trained model:

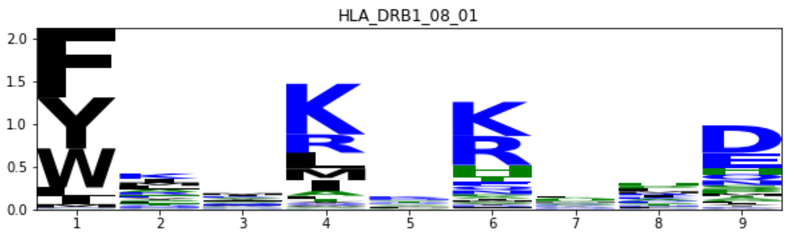


Figure 1: Logo plot of the first template.

Here is a list of some of the highest predicted binders:

```
Peptide_Source,Start,End,Peptide,Binding_Core,Predicted_Outcome
spQ63PT2SAHH_BURPS,168,182,EVALFKSIERHLEID,FKSIERHLE,1.454
spQ63Q03RPOB_BURPS,1069,1083,VKVYLAVKRRLQPGD,YLAVKRRLQ,1.392
spQ63UT2SYH_BURPS,346,360,REQAFIVAERLRDTG,FIVAERLRD,1.375
spQ63PT2SAHH_BURPS,103,117,GTPVFAFKGESLDEY,FAFKGESLD,1.371
spQ63NC4ACSA_BURPS,572,586,VVAFVVLKRSRPEGE,FVVLKRSRP,1.327
spQ63Y06SYR_BURPS,440,454,AVRFFLISRKADTEF,FFLISRKAD,1.303
spQ63WM0RS20_BURPS,28,42,FRTAIKAVRKAIDAG,IKAVRKAID,1.289
spQ63WM0RS20_BURPS,47,61,AAELFKAATKTIDTI,FKAATKTID,1.278
spQ63TM2SYT_BURPS,575,589,EKISYKIREHTLEKV,YKIREHTLE,1.236
spQ63UY6RS6_BURPS,85,99,LRHLIVKMKKAETGP,LIVKMKKAE,1.232
```

The first column is the name of the sequence, as written in the FASTA file. The second and third columns are respectively the start and end position of the peptide in the sequence. The fourth column is the peptide and the fifth column its binding core. The fifth colum is the model's predicted outcome.

3.2 Template 2: Train

The second template, *template2_Train.txt*, will train a model from the example training data set of the allele *HLA_DRB1_08_01* in the folder *Example*. The results will be saved in the folder *Template2_results* of the *Example* folder.

3.3 Template 3: Apply with template 2 trained model

The third template, *template3_Apply.txt*, apply the pre-trained model of *HLA_DRB1_08_01* to new sequences *uniprot-proteome_UP000000605_100seq.fasta* in the *Example* folder. The results will be saved in the folder *Template3_results* of the *Example* folder. Here is a list of some of the highest predicted binders:

```
Peptide_Source,Start,End,Peptide,Binding_Core,Predicted_Outcome
spQ63PT2SAHH_BURPS,168,182,EVALFKSIERHLEID,FKSIERHLE,1.449
spQ63UT2SYH_BURPS,346,360,REQAFIVAERLRDTG,FIVAERLRD,1.391
spQ63Q03RPOB_BURPS,1069,1083,VKVYLAVKRRLQPGD,LAVKRRLQP,1.369
spQ63PT2SAHH_BURPS,103,117,GTPVFAFKGESLDEY,FAFKGESLD,1.351
spQ63Y06SYR_BURPS,440,454,AVRFFLISRKADTEF,FFLISRKAD,1.327
spQ63WM0RS20_BURPS,29,43,RTAIKAVRKAIDAGD,IKAVRKAID,1.309
spQ63NC4ACSA_BURPS,572,586,VVAFVVLKRSRPEGE,FVVLKRSRP,1.305
spQ63T53ALLC1_BURPS,34,48,DDFFAPKERMLNPEP,FAPKERMLN,1.301
spQ63WM0RS20_BURPS,47,61,AAELFKAATKTIDTI,FKAATKTID,1.272
spQ63TM2SYT_BURPS,575,589,EKISYKIREHTLEKV,YKIREHTLE,1.269
```

Appendix A: A convolutional neural network architecture for the prediction of peptide's binding

A.1 Peptide's encoding

The peptides are encoded using the *blosum62* similarity matrix below [4].

```
,A,R,N,D,C,Q,E,G,H,I,L,K,M,F,P,S,T,W,Y,V,-
A,4,-1,-2,-2,0,-1,-1,0,-2,-1,-1,-1,-1,-2,-1,1,0,-3,-2,0,-4
R,-1,5,0,-2,-3,1,0,-2,0,-3,-2,2,-1,-3,-2,-1,-1,-3,-2,-3,-4
N,-2,0,6,1,-3,0,0,0,1,-3,-3,0,-2,-3,-2,1,0,-4,-2,-3,-4
D,-2,-2,1,6,-3,0,2,-1,-1,-3,-4,-1,-3,-3,-1,0,-1,-4,-3,-3,-4
C,0,-3,-3,-3,9,-3,-4,-3,-3,-1,-1,-3,-1,-2,-3,-1,-1,-2,-2,-1,-4
Q,-1,1,0,0,-3,5,2,-2,0,-3,-2,1,0,-3,-1,0,-1,-2,-1,-2,-4
E,-1,0,0,2,-4,2,5,-2,0,-3,-3,1,-2,-3,-1,0,-1,-3,-2,-2,-4
G,0,-2,0,-1,-3,-2,-2,6,-2,-4,-4,-2,-3,-3,-2,0,-2,-2,-3,-3,-4
H,-2,0,1,-1,-3,0,0,-2,8,-3,-3,-1,-2,-1,-2,-1,-2,-2,2,-3,-4
I,-1,-3,-3,-3,-1,-3,-3,-4,-3,4,2,-3,1,0,-3,-2,-1,-3,-1,3,-4
L,-1,-2,-3,-4,-1,-2,-3,-4,-3,2,4,-2,2,0,-3,-2,-1,-2,-1,1,-4
K,-1,2,0,-1,-3,1,1,-2,-1,-3,-2,5,-1,-3,-1,0,-1,-3,-2,-2,-4
M,-1,-1,-2,-3,-1,0,-2,-3,-2,1,2,-1,5,0,-2,-1,-1,-1,-1,1,-4
F,-2,-3,-3,-3,-2,-3,-3,-3,-1,0,0,-3,0,6,-4,-2,-2,1,3,-1,-4
P,-1,-2,-2,-1,-3,-1,-1,-2,-2,-3,-3,-1,-2,-4,7,-1,-1,-4,-3,-2,-4
S,1,-1,1,0,-1,0,0,0,-1,-2,-2,0,-1,-2,-1,4,1,-3,-2,-2,-4
T,0,-1,0,-1,-1,-1,-1,-2,-2,-1,-1,-1,-1,-2,-1,1,5,-2,-2,0,-4
W,-3,-3,-4,-4,-2,-2,-3,-2,-2,-3,-2,-3,-1,1,-4,-3,-2,11,2,-3,-4
Y,-2,-2,-2,-3,-2,-1,-2,-3,2,-1,-1,-2,-1,3,-3,-2,-2,2,7,-1,-4
V,0,-3,-3,-3,-1,-2,-2,-3,-3,3,1,-2,1,-1,-2,-2,0,-3,-1,4,-4
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
```

The symbol "-" stands for the absence of amino acids. A similar type of encoding is used in the models of the netMHCII family [5].
With the template, you can set your own similarity matrix keeping the above format and amino acids order.
A peptide will then be encoded as an "image" for the input of the convolutional neural network. This image can be though of as a table where the rows are the residues of the peptide and the columns are the 20 amino acids +

the absence of amino acid. This table is then filled using the corresponding similarity value. To take into account for the difference in peptides' lengths, the absence of amino acid character "-" will be added at the end of each peptide until its length matches the maximal length in the training data set. Moreover, a fixed number of character "-" will be added at the beginning and at the end of the peptide; this step can be thought of as a sequence equivalent to an image zero-padding. The exact number of additional characters "-" at the beginning, resp. at the end, of the sequence is determined by the parameter *nbPrev*, resp. *nbAfter*; both of them are 2 by default. Therefore, the number of rows, i.e. the length of the input peptide, will be the length of the maximal peptide in the training data set + *nbPrev* + *nbAfter*.
For example, the peptide *MSAIESVLHERRQFA*, in a model where the maximal length is 20, will be encoded as:

```
,A,R,N,D,C,Q,E,G,H,I,L,K,M,F,P,S,T,W,Y,V,-
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
M,-1,-1,-2,-3,-1,0,-2,-3,-2,1,2,-1,5,0,-2,-1,-1,-1,-1,1,-4
S,1,-1,1,0,-1,0,0,0,-1,-2,-2,0,-1,-2,-1,4,1,-3,-2,-2,-4
A,4,-1,-2,-2,0,-1,-1,0,-2,-1,-1,-1,-1,-2,-1,1,0,-3,-2,0,-4
I,-1,-3,-3,-3,-1,-3,-3,-4,-3,4,2,-3,1,0,-3,-2,-1,-3,-1,3,-4
E,-1,0,0,2,-4,2,5,-2,0,-3,-3,1,-2,-3,-1,0,-1,-3,-2,-2,-4
S,1,-1,1,0,-1,0,0,0,-1,-2,-2,0,-1,-2,-1,4,1,-3,-2,-2,-4
V,0,-3,-3,-3,-1,-2,-2,-3,-3,3,1,-2,1,-1,-2,-2,0,-3,-1,4,-4
L,-1,-2,-3,-4,-1,-2,-3,-4,-3,2,4,-2,2,0,-3,-2,-1,-2,-1,1,-4
H,-2,0,1,-1,-3,0,0,-2,8,-3,-3,-1,-2,-1,-2,-1,-2,-2,2,-3,-4
E,-1,0,0,2,-4,2,5,-2,0,-3,-3,1,-2,-3,-1,0,-1,-3,-2,-2,-4
R,-1,5,0,-2,-3,1,0,-2,0,-3,-2,2,-1,-3,-2,-1,-1,-3,-2,-3,-4
R,-1,5,0,-2,-3,1,0,-2,0,-3,-2,2,-1,-3,-2,-1,-1,-3,-2,-3,-4
Q,-1,1,0,0,-3,5,2,-2,0,-3,-2,1,0,-3,-1,0,-1,-2,-1,-2,-4
F,-2,-3,-3,-3,-2,-3,-3,-3,-1,0,0,-3,0,6,-4,-2,-2,1,3,-1,-4
A,4,-1,-2,-2,0,-1,-1,0,-2,-1,-1,-1,-1,-2,-1,1,0,-3,-2,0,-4
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
```

```
-,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,-4,1
```

A.2 The model's architecture

The neural networks are implemented as *Keras* [3] sequential models with the following architecture:

1. Convolutional layer with *ReLu* activation.
2. Maxpooling layer.
3. Dense (or fully connected) layer with parameter-defined activation function.

The initial weights of both the first and third layers are randomly generated from a normal distribution with zero mean and a standard deviation defined by the parameter *initializeStd* (0.01 by default).
The filters of the convolutional layers are of size $l \times 21$ where l is defined in the parameters (9 by default) and 21 are the 20 amino acids plus the absence of amino acids. The strides are of size 1×21, so that, in practice, the filters will only convolute along the first dimension with stride 1. The model therefore optimizes the search for l-mer core binders contained within a peptide.
The number of filters is defined in the parameters. Multiple different numbers can be chosen and *rep* neural networks will be trained for each number of filters, where *rep* is the number of repetitions so that the final model is trained from different initial configurations. By default, the final model will be an equally weighted ensemble of 40 neural networks: 10 of them with 5 filters, 10 with 10 filters, 10 with 20 filters and 10 with 30 filters.
The pooling size of the maxpooling layer is of size $m \times 1$ with stride 1×1. The parameter m can be set as *nMaxPool* in the parameters file (section 2.2). By default m is defined as follows:

$$m := \max(\{6, L_{max} - l - L_{freq} + nbPrev + nbAfter + 2\})$$

where L_{max} is the maximal peptide's length in the training data set, L_{freq} the most frequent one and *nbPrev* and *nbAfter* are the number of characters "-" added at the beginning and end of each sequence (see A.1). The formula for m is defined to make sure that it will neither be too small (the minimal value is 6) nor too big compared to L_{max} which changes from data set to

data set; it will control the size of the maxpooling layer's output to be equal to $L_{freq} \times F$ where F is the number of filters. Indeed, the height of the input image is $h := L_{max} + nbPrev + nbAfter$, therefore the size of the convolutional layer's output is $(h - l + 1) \times F$ and the size of the maxpooling layer's output is $(h - l - m + 2) \times F = L_{freq} \times F$. However, m has a minimum value of 6 to avoid having a pool size too small, therefore the first dimension of the maxpooling layer's output might be smaller.
The weight optimization is done with a mini batch stochastic gradient descent with parameters defined in the parameters file (section 2.2).

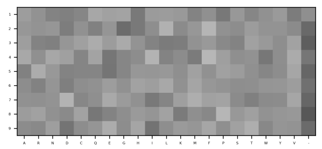
A.3 Visualization of the feed forward pass

Calling the function *feedForwardVisualization* (section 2.1.21) will generate images to visualize the feedforward pass of each net in the trained model on the sequences given as input of the function. The results will be saved in a folder called *feed_forward_visualization* in the saving pathway *savePath* of the class.
You can call this function through a class with a trained model. It can be applied to a previously trained and saved model in the following way:

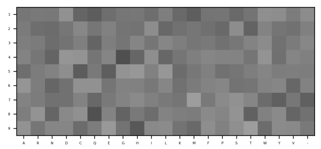
```
from model_initializer import CNNPepPred
path_to_trained_model = ...
s = ['KPTHFTVLTKGAGK', 'SEIQYKILTQKEDD', 'TAVFLAAGVGMRL']
myModel = CNNPepPred(trainedModelsFile=path_to_trained_model,
   doApplyData=True,applyData=s)
yhat = myModel.feedForwardVisualization(myModel.applyData)
```

where *path_to_trained_model* is either a *.pkl* saved class object or the path of the saved model (like the input *trainedModelsFile* in the template, see section 2.3).

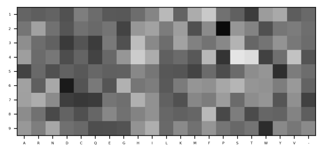
We present an example of this visualization. Below (Figure 2) are the 5 filters of the convolutional layer of one net.



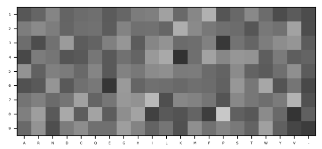
(a) filter_1



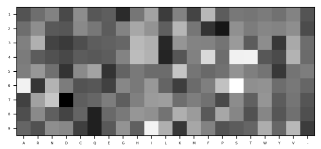
(b) filter_2



(c) filter_3



(d) filter_4



(e) filter_5

Figure 2: The 5 filters of the convolutional layer.

These filters are of size 9×21, where the columns are the amino acids *ARNDCQEGHILKMFPSTWYV-* and 9 is the length of the l-mers that the filters will highlight. Pixels with higher values are in white.
The encoded image of the peptide sequence *VLVKEIRSLGIDIDL* is printed below in Figure 3,

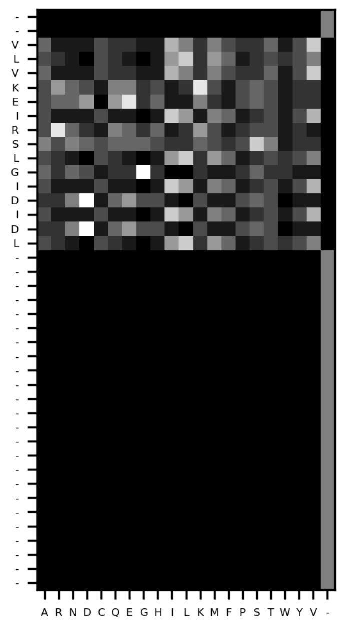


Figure 3: The encoded input image

with *nbPrev* and *nbAfter* equal to 2 and the maximal length in the training data set is 37.
After the convolution of the filters on the peptide's encoding image, the output is printed in Figure 4,

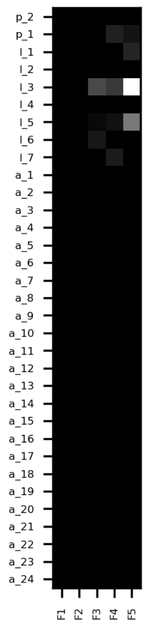
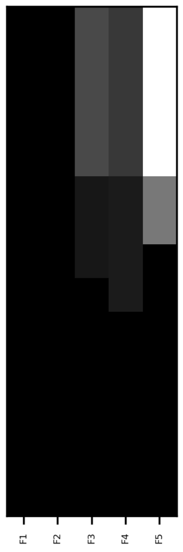
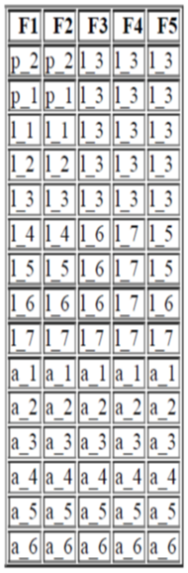


Figure 4: The output of the convolutional layer.

where each column represents the output after the convolution of each filter $F1$, $F2$, $F3$, $F4$ and $F5$. The rows corresponds to the application of each filter on an overlapping nonamer of the sequence - -*VLVKEIRSLGIDIDL*- -. The overlapping nonamers of the original peptide *VLVKEIRSLGIDID* are labelled l_x where x is the start position of the nonamer in this sequence. The overlapping nonamers containing the characters '-' which were added before the first residue of the original peptide are labelled p_x where x is an integer which decreases when approaching the first nonamer fully composed of the original peptide's residues, i.e. without special characters added. Similarly, the overlapping nonamers containg the added characters after the last residue of the peptide are labelled a_x where x increases when moving away from the last nonamer fully composed of the original peptide's resiudes.
The output of the maxpooling layer is printed in Figure 5,





F1	F2	F3	F4	F5
p_2	p_2	l_3	l_3	l_3
p_1	p_1	l_3	l_3	l_3
l_1	l_1	l_3	l_3	l_3
l_2	l_2	l_3	l_3	l_3
l_3	l_3	l_3	l_3	l_3
l_4	l_4	l_6	l_7	l_5
l_5	l_5	l_6	l_7	l_5
l_6	l_6	l_6	l_7	l_6
l_7	l_7	l_7	l_7	l_7
a_1	a_1	a_1	a_1	a_1
a_2	a_2	a_2	a_2	a_2
a_3	a_3	a_3	a_3	a_3
a_4	a_4	a_4	a_4	a_4
a_5	a_5	a_5	a_5	a_5
a_6	a_6	a_6	a_6	a_6

Figure 5: Left: the output of the MaxPool layer. Right: the argument of each pixel in the output.

where the image on the left is the output of the maxpooling layer with each column corresponding to a filter and the table on the right corresponds to the argument of each pixel in the image. In other words, each cell of the table corresponds to a pixel in the output image and the content of this cell is the overlapping nonamer (labelled as described above) which was selected during the maxpooling layer. The table will be saved as an html table.
Finally, the dense layer with the below weights (Figure 6) is applied to this output to obtain the net's prediction.

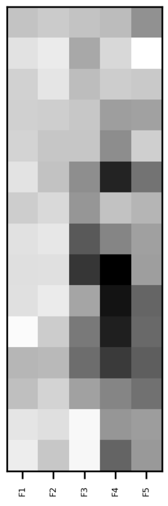


Figure 6: The weights of the dense layer.

Note that the biases of the net are not represented in this visualization. The feed forward pass visualization will generate many images; it is therefore recommended to first select a small subset of peptides of interest and only then call the function with this subset.

A.4 The contribution score

Let l be the length of the core binder. We define here the *contribution score* associated to each of the overlapping l-mers of a peptide sequence. This score can be understood as the relative importance of an l-mer to the predicted outcome of the corresponding peptide.
For a fixed peptide, let s be any of its overlapping l-mer and we will give a brief description of how the model is applied with respect to s.
The first layer of the model is a convolutional layer with F filters and the corresponding output layer consists of one value for each overlapping l-mer and each filter, i.e. each filter is applied to each overlapping l-mer to obtain an output layer with size the number of overlapping l-mers times the number of filters. Let $x_i^{(s)}$ denote the output value after the application of the filter i to the l-mer s for $i = 1, ..., F$. The activation function of this layer is the

ReLu activation, i.e. $x_i^{(s)}$ will be mapped to 0 if it is negative and will remain unchanged otherwise. For ease of notation, let $x_i^{(s)}$ be the output value after the *ReLu* activation.
The second layer is a maxpooling layer, therefore only the maximal values will remain with possible repetitions, i.e. for filter i, the value of the application of the model so far to s will be $m_i \cdot x_i^{(s)}$ where m_i is a positive integer (including zero).
The final layer is a dense layer with a parameter-defined activation function σ. This layer will multiply all the values by the weights $d_i^{(s)}$ of the layer and sum them to obtain one remaining value. Keeping only the terms related to s, we define

$$w^{(s)} := \sum_i d_i^{(s)} \cdot m_i \cdot x_i^{(s)}$$

which corresponds to the application of the model restricted to s. In particular, the predicted outcome $\hat{y}$ will be

$$\hat{y} = \sigma\left(\sum_{s'} w^{(s')} + b\right)$$

where b is the bias of the dense layer.
Therefore, the relative contribution of s, with respect to the other l-mers, to the predicted outcome can be thought of as

$$\phi^{(s)} := \frac{w^{(s)}}{\sum_{s'} w^{(s')}}$$

where we define $\phi^{(s)}$ to be the contribution score of s. Note that this value can be smaller than 0 and bigger than 1.
The final model is an ensemble of N convolutional neural networks. Let $w_n^{(s)}$ be the above defined value for the net n and let b_n be its last layer's bias, then the predicted outcome is

$$\hat{y} = \frac{1}{N}\sum_n \sigma\left(\sum_{s'} w_n^{(s')} + b_n\right)$$

and we define the contribution score of s for an ensemble of nets to be

$$\phi^{(s)} := \frac{\sum_n w_n^{(s)}}{\sum_n \sum_{s'} w_n^{(s')}}.$$

Note that $\sum_{s'} \phi^{(s')} = 1$ and, if σ is the linear activation, then $\phi^{(s)} = \frac{\sum_n w_n^{(s)}}{N\hat{y} - \sum_n b_n}$. The predicted binding core, s_{core}, is then defined to be the overlapping l-mer of the peptipe with the highest contribution score, i.e.

$$s_{\text{core}} \in \text{argmax}_{s'}(\phi^{(s')}).$$

Appendix B: IEDB data

B.1 Data preparation

We extracted the data from the IEDB web page `https://www.iedb.org/mhcdetails_v3.php` in the *Assays* tab with filters *Epitope Structure Type: Linear Epitopes*, *Host Organism: Homo sapiens (human)* and *assay-mhc_allele-mhc_Blass: II*. The outcome was taken from the column *qualitative_measure*, the sequences with value *Positive* and *Positive-High* were tagged as binders (1), the ones with value *Positive-Low* and *Positive-Intermediate* were ignored as they might be too weak binders and the rest of the sequences with value *Negative* were tagged as non-binders (0). For each allele's data set, if there were more non-binders than binders, a subset of non-binders was selected at random to balance the data set. If there were more binders than non-binders, the set was balanced using the script *generateRandomNonBinders.py* (section 2.6). This script generates a given number of non-binders selected from FASTA sequences in a given folder. The sequences used to randomly select non-binders were retrieved from `https://www.uniprot.org/uniparc/`. To improve the computational speed, we only downloaded some batches of sequences from UniParc, namely all the entries starting with *UPI00XX* where *XX*$= 00, 01, 02, ..., 10, 11$. There were then more than 70 millions sequences.
In order to avoid repetitive sequences in an allele's data set, which can bias the training and testing of the model, for each of the unique overlapping 11-mers contained in one class (binding or non-binding) of the allele's data, only the shortest peptide containing the 11-mer was included. The length 11 was selected because it can remove most of the repetitive sequences without being as restrictive as the length 9 (i.e. the length of the binding core).
Moreover, the cross-validation partition was set to avoid testing with peptides containing too many nonamers also contained in the training data (see next subsection).
Only alleles containing at least 100 positive peptides were included.

B.2 Cross-validation result

We performed a k-fold cross-validation with k$= 5$ on the allele specific data retrieved as described in the previous subsection. The cross-validation partition was generated using a simple approach in order to reduce the number of l-mers present in both the training and testing data, where l is the length

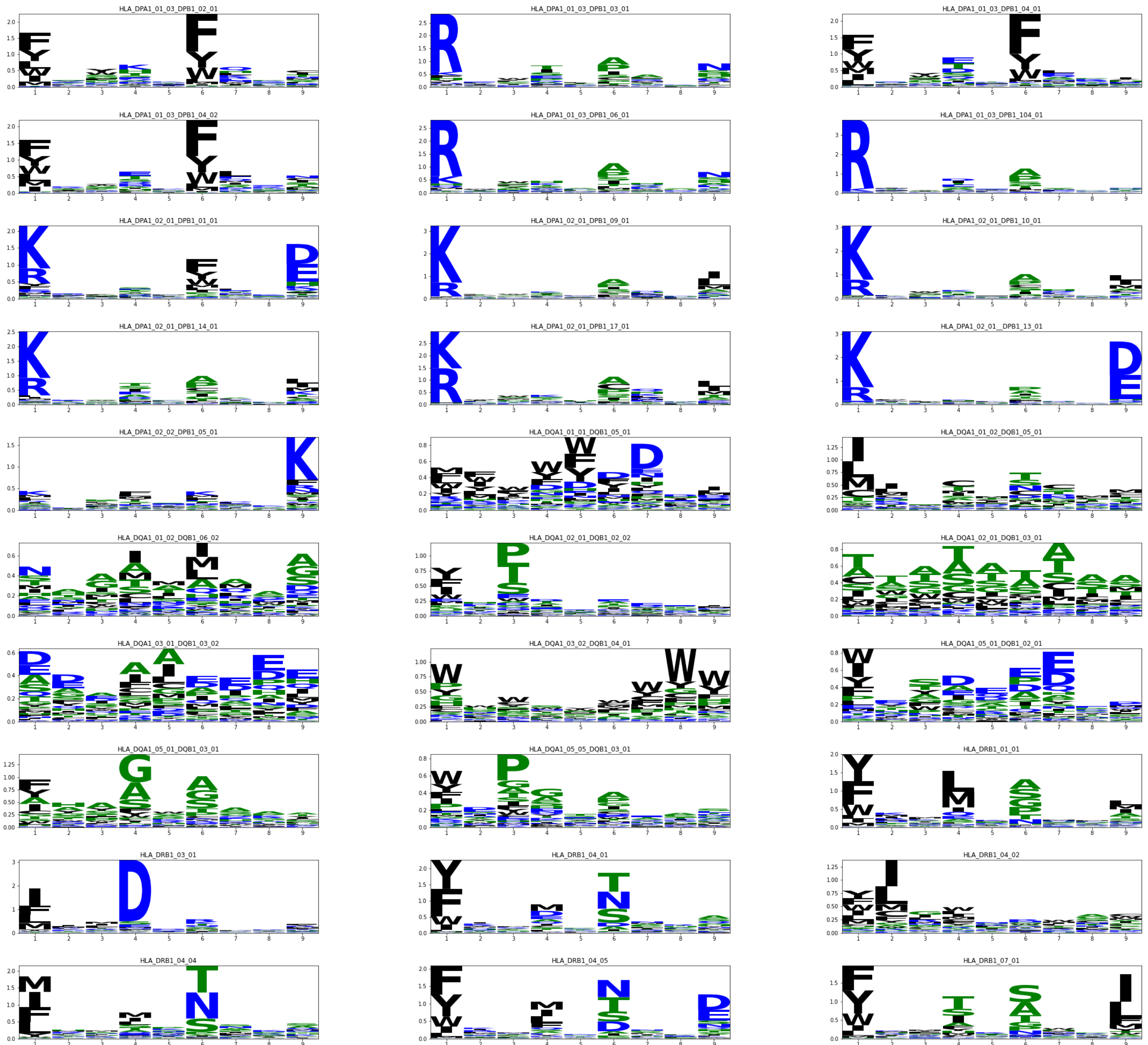
of the core binder (l= 9 here).
Firstly, a random cross-validation partition is generated. Then the l-mers shared between the training and testing splits of the random cross-validation partition (within each positive or negative class) are selected. Finally, the peptides containing each of the previously selected l-mers are re-assigned to the fold which occurs the most in the set of peptides sharing the same l-mer. In this way, the number of l-mers shared between folds is greatly reduced compared to a random assignment and all of the cross-validation partitions have a similar number of peptides. Note that this procedure doesn't guarantee that the folds won't share any l-mers. Such a procedure would likely be computationally expensive and could lead to very imbalanced partitions.
This procedure was implemented as *generateCVpartWithLeastLmerOverlap* (section 2.1.22) and if cross-validation is selected in the template and no partition is given with the training data, the model assign one using this procedure. Moreover, this function will also count the number of overlapping l-mers between each of the training and testing splits and return the average count per split; it will be saved as an attribute called *averageLmersOverlappingCV*.
The cross-validation results are reported in the table below with the following scores: AUC (area under the curve), MCC (Matthews correlation coefficient), ACC (accuracy), F1 (F1-score).
We also include the results with the same cross-validation folds using the NNAlign method (see Appendix C for more details on NNAlign). We used NNAlign with its default parameters, except for the cross-validation folds which were given as input and the rescaling of the outcome which we set to "No rescale", since the outcome was binary. Note that while NNAlign was rather meant for regression on a quantitative outcome, our model was also set to optimize the mean squared error (this can be set in the parameters), so that it could have been used with the exact same parameters on a quantitative outcome, just like NNAlign.
The best scores are highlighted in bold. For all alleles except one (with respect to the MCC/ACC/F1 score), CNN-PepPred outperformed NNAlign.

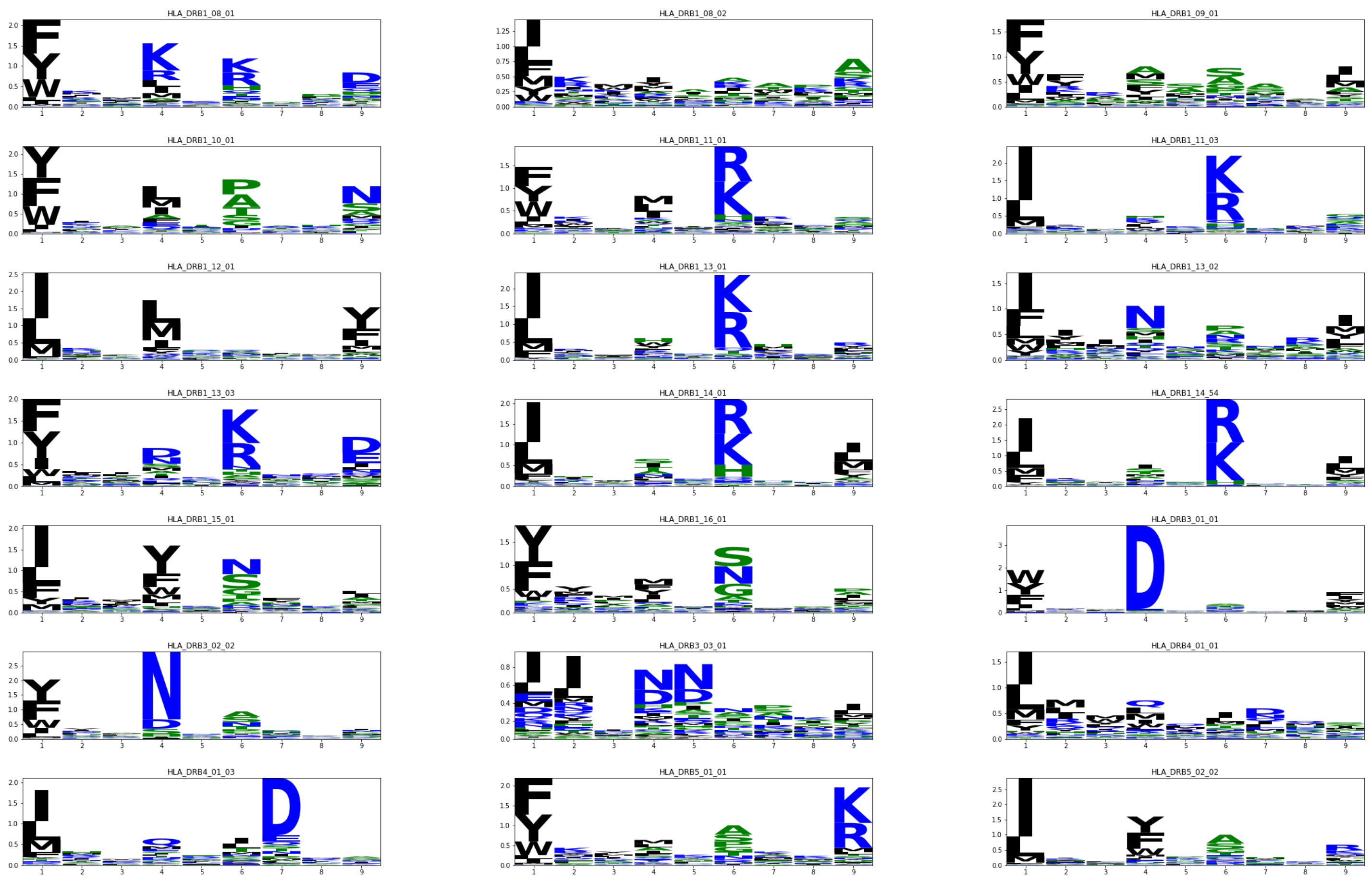
Allele	#Peptide	#Binder	CNN-PepPred				NNAlign			
			AUC	MCC	ACC	F1	AUC	MCC	ACC	F1
HLA_DPA1_01_03_DPB1_02_01	5177	2589	**0,951**	**0,763**	**0,88**	**0,874**	0,926	0,715	0,857	0,855
HLA_DPA1_01_03_DPB1_03_01	5025	2512	**0,959**	**0,803**	**0,901**	**0,898**	0,927	0,727	0,863	0,862
HLA_DPA1_01_03_DPB1_04_01	7984	3993	**0,946**	**0,747**	**0,872**	**0,865**	0,912	0,678	0,839	0,836
HLA_DPA1_01_03_DPB1_04_02	4643	2322	**0,971**	**0,839**	**0,919**	**0,917**	0,947	0,776	0,888	0,888
HLA_DPA1_01_03_DPB1_06_01	946	473	**0,965**	**0,784**	**0,891**	**0,887**	0,944	0,761	0,881	0,88
HLA_DPA1_01_03_DPB1_104_01	300	150	**0,99**	**0,887**	**0,943**	**0,944**	0,973	0,835	0,917	0,919
HLA_DPA1_02_01_DPB1_01_01	4292	2146	**0,969**	**0,829**	**0,914**	**0,913**	0,94	0,742	0,871	0,871
HLA_DPA1_02_01_DPB1_09_01	2692	1346	**0,972**	**0,835**	**0,917**	**0,916**	0,953	0,773	0,886	0,887
HLA_DPA1_02_01_DPB1_10_01	3628	1814	**0,97**	**0,822**	**0,911**	**0,909**	0,939	0,742	0,871	0,869
HLA_DPA1_02_01_DPB1_14_01	6035	3018	**0,966**	**0,808**	**0,904**	**0,902**	0,924	0,703	0,852	0,852
HLA_DPA1_02_01_DPB1_17_01	2170	1085	**0,974**	**0,839**	**0,919**	**0,918**	0,953	0,78	0,89	0,89
HLA_DPA1_02_01__DPB1_13_01	1968	984	**0,975**	**0,845**	**0,922**	**0,919**	0,961	0,809	0,904	0,905
HLA_DPA1_02_02_DPB1_05_01	7889	3945	**0,96**	**0,799**	**0,899**	**0,898**	0,914	0,689	0,845	0,845
HLA_DQA1_01_01_DQB1_05_01	208	104	**0,94**	**0,741**	**0,87**	**0,867**	0,898	0,635	0,817	0,816
HLA_DQA1_01_02_DQB1_05_01	410	206	**0,764**	**0,362**	**0,68**	**0,668**	0,699	0,254	0,627	0,622
HLA_DQA1_01_02_DQB1_06_02	1498	749	**0,915**	**0,672**	**0,835**	**0,829**	0,866	0,6	0,8	0,797
HLA_DQA1_02_01_DQB1_02_02	5772	2886	**0,901**	**0,653**	**0,826**	**0,82**	0,832	0,526	0,763	0,762
HLA_DQA1_02_01_DQB1_03_01	256	128	**0,884**	**0,603**	**0,801**	**0,794**	0,873	0,57	0,785	0,786
HLA_DQA1_03_01_DQB1_03_02	350	175	**0,783**	**0,402**	**0,7**	**0,685**	0,729	0,332	0,666	0,67
HLA_DQA1_03_02_DQB1_04_01	206	103	**0,792**	**0,488**	**0,743**	**0,728**	0,758	0,389	0,694	0,701
HLA_DQA1_05_01_DQB1_02_01	4051	2025	**0,872**	**0,574**	**0,786**	**0,776**	0,803	0,47	0,735	0,734
HLA_DQA1_05_01_DQB1_03_01	617	307	**0,909**	**0,668**	**0,833**	**0,825**	0,866	0,589	0,794	0,789
HLA_DQA1_05_05_DQB1_03_01	5882	2941	**0,889**	**0,63**	**0,815**	**0,811**	0,815	0,482	0,741	0,739
HLA_DRB1_01_01	12412	6208	**0,824**	**0,492**	**0,744**	**0,73**	0,773	0,405	0,702	0,698
HLA_DRB1_03_01	2178	1089	**0,866**	**0,553**	**0,775**	**0,763**	0,829	0,519	0,758	0,748
HLA_DRB1_04_01	5110	2557	**0,846**	**0,544**	**0,77**	**0,755**	0,809	0,479	0,739	0,733
HLA_DRB1_04_02	256	128	**0,764**	**0,469**	**0,734**	**0,73**	0,712	0,306	0,652	0,634
HLA_DRB1_04_04	3076	1538	**0,801**	**0,447**	**0,723**	**0,716**	0,714	0,315	0,657	0,651
HLA_DRB1_04_05	3972	1986	**0,913**	**0,676**	**0,837**	**0,83**	0,87	0,603	0,801	0,797
HLA_DRB1_07_01	4466	2233	**0,916**	**0,684**	**0,841**	**0,835**	0,894	0,639	0,82	0,817
HLA_DRB1_08_01	1118	559	**0,96**	**0,827**	**0,913**	**0,911**	0,933	0,726	0,863	0,865
HLA_DRB1_08_02	838	419	**0,829**	0,49	0,745	0,737	0,823	**0,509**	**0,754**	**0,746**
HLA_DRB1_09_01	1056	528	**0,906**	**0,672**	**0,836**	**0,835**	0,872	0,589	0,795	0,794
HLA_DRB1_10_01	2582	1291	**0,969**	**0,833**	**0,917**	**0,916**	0,959	0,811	0,905	0,906
HLA_DRB1_11_01	4180	2089	**0,917**	**0,665**	**0,832**	**0,826**	0,894	0,636	0,818	0,818
HLA_DRB1_11_03	422	211	**0,956**	**0,853**	**0,927**	**0,926**	0,934	0,763	0,882	0,883
HLA_DRB1_12_01	992	496	**0,966**	**0,809**	**0,904**	**0,903**	0,954	0,792	0,896	0,897
HLA_DRB1_13_01	1287	643	**0,935**	**0,74**	**0,869**	**0,865**	0,907	0,691	0,845	0,847
HLA_DRB1_13_02	1460	731	**0,885**	**0,607**	**0,803**	**0,802**	0,853	0,562	0,781	0,782
HLA_DRB1_13_03	1966	983	**0,986**	**0,894**	**0,947**	**0,947**	0,976	0,857	0,928	0,93
HLA_DRB1_14_01	681	340	**0,988**	**0,918**	**0,959**	**0,959**	0,978	0,88	0,94	0,94
HLA_DRB1_14_54	788	394	**0,998**	**0,959**	**0,98**	**0,98**	0,99	0,912	0,956	0,956
HLA_DRB1_15_01	4400	2201	**0,887**	**0,615**	**0,806**	**0,796**	0,862	0,573	0,786	0,783
HLA_DRB1_16_01	423	211	**0,959**	**0,822**	**0,91**	**0,907**	0,932	0,74	0,87	0,869
HLA_DRB3_01_01	1280	640	**0,951**	**0,819**	**0,905**	**0,899**	0,938	0,78	0,889	0,886

HLA_DRB3_02_02	1386	694	**0,979**	**0,865**	**0,932**	**0,931**	0,965	0,818	0,909	0,909
HLA_DRB3_03_01	210	105	**0,963**	**0,803**	**0,9**	**0,896**	0,903	0,619	0,81	0,813
HLA_DRB4_01_01	1316	658	**0,914**	**0,654**	**0,827**	**0,822**	0,871	0,582	0,791	0,792
HLA_DRB4_01_03	856	428	**0,971**	**0,824**	**0,911**	**0,908**	0,957	0,794	0,897	0,897
HLA_DRB5_01_01	3329	1664	**0,913**	**0,676**	**0,837**	**0,833**	0,898	0,655	0,827	0,828
HLA_DRB5_02_02	926	463	**0,989**	**0,92**	**0,96**	**0,96**	0,979	0,888	0,944	0,945
Average			**0,921**	**0,716**	**0,857**	**0,853**	0,889	0,647	0,824	0,822
Average weighted by #Binder			**0,918**	**0,702**	**0,850**	**0,845**	0,882	0,628	0,814	0,812

B.3 Binding motive

The binding motives are obtained by generating 200000 random 15-mer peptides and by plotting, with the package *logomaker* [10], the core binders of the top 2000 highest predictions.
Here are the binding motives of the alleles retrieved from the IEDB website.


HLA_DPA1_01_03_DPB1_02_01
HLA_DPA1_01_03_DPB1_03_01
HLA_DPA1_01_03_DPB1_04_01
HLA_DPA1_01_03_DPB1_04_02
HLA_DPA1_01_03_DPB1_06_01
HLA_DPA1_01_03_DPB1_104_01
HLA_DPA1_02_01_DPB1_01_01
HLA_DPA1_02_01_DPB1_09_01
HLA_DPA1_02_01_DPB1_10_01
HLA_DPA1_02_01_DPB1_14_01
HLA_DPA1_02_01_DPB1_17_01
HLA_DPA1_02_01__DPB1_13_01
HLA_DPA1_02_02_DPB1_05_01
HLA_DQA1_01_01_DQB1_05_01
HLA_DQA1_01_02_DQB1_05_01
HLA_DQA1_01_02_DQB1_06_02
HLA_DQA1_02_01_DQB1_02_02
HLA_DQA1_02_01_DQB1_03_01
HLA_DQA1_03_01_DQB1_03_02
HLA_DQA1_03_02_DQB1_04_01
HLA_DQA1_05_01_DQB1_02_01
HLA_DQA1_05_01_DQB1_03_01
HLA_DQA1_05_05_DQB1_03_01
HLA_DRB1_01_01
HLA_DRB1_03_01
HLA_DRB1_04_01
HLA_DRB1_04_02
HLA_DRB1_04_04
HLA_DRB1_04_05
HLA_DRB1_07_01


HLA_DRB1_08_01
HLA_DRB1_08_02
HLA_DRB1_09_01
HLA_DRB1_10_01
HLA_DRB1_11_01
HLA_DRB1_11_03
HLA_DRB1_12_01
HLA_DRB1_13_01
HLA_DRB1_13_02
HLA_DRB1_13_03
HLA_DRB1_14_01
HLA_DRB1_14_54
HLA_DRB1_15_01
HLA_DRB1_16_01
HLA_DRB3_01_01
HLA_DRB3_02_02
HLA_DRB3_03_01
HLA_DRB4_01_01
HLA_DRB4_01_03
HLA_DRB5_01_01
HLA_DRB5_02_02

Appendix C: NetMHCII data

In this appendix, we will benchmark the convolutional neural network approach with the state-of-the-art methods from the netMHCII family [5]. The netMHCII family consists of two main methods: one allele specific (netMHCII) and one pan specific (netMHCIIpan). They both have the same core algorithm NNAlign ([7], [6]) which consists of a two steps procedure that first estimates the core (nonamer) binder and then the weight configuration for the binding prediction. The pan specific method is trained with all of the peptides of all of the alleles and can make prediction for all alleles with known alpha and beta chains. The pan specific version is therefore more adequate for alleles with few training data, however, for alleles with enough training data, the authors report [5] that the allele specific method outperforms the pan specific one.

More modern versions of netMHCII include the possibility of training with multi-alleles peptides [9]. While this is an interesting recent research direction ([1],[8],[2]), our method aims at making available the full code of an efficient core algorithm for the local training of peptide sets which could then be modified to fit other purposes.

The convolutional neural network approach is similar to the strategy of netMHCII, since both uses similar blosum encoding and rely on ensemble of neural networks. The main difference is that NNAlign is a two steps procedure that first identifies a core nonamer and apply it (with flanking region) to a weight configuration. Our model uses convolution to slide through the possible nonamers contained within a peptide, therefore using the peptide in its full length. This strategy is also convenient to implement since it only requires building a sequential convolution neural networks using user friendly libraries such as Keras.

NetMHCII methods are only web based and meant to be used to predict binding with pre-trained models. While the executable is available upon request, the core algorithm training the models (NNAlign) is not open-source. NNAlign can however be used as an executable to train with specific data sets.

We implemented this method to show full transparency of the algorithm, giving the freedom to the user to tune it and train it with different source of data, as well as applying trained models on new sequences.

C.1 Cross-validation result

The data and the 5 fold cross-validation partition for this set-up were taken from the paper presenting netMHCIIpan-3.2, which is the latest version of the model not including multiple allele data. The results of netMHCIIpan-3.2 and netMHCII-2.3 were taken from the supplementary file, Suppl Table 3, of [5]. The authors only reported the AUC score but we also included the Pearson correlation (PC) and root mean squared error (RMSE) scores of our model for further information. The best AUC score for each allele is highlighted in bold.

As it can be seen in the table, if we also include the alleles with few training data (for which allele specific methods are clearly not fitted), netMHCIIpan outperforms (on average) the two allele specific methods. However, considering different set of alleles with different minimum numbers of binding training peptides, our model outperforms (on average) the models from the netMHCII family. In any cases, the performances are overall similar.

Allele	#Peptide	#Binder	CNN-PepPred			NetMHCII-2.3	NetMHCIIPan-3.2
			PC	AUC	RMSE	AUC	AUC
DRB1_0101	10412	6376	0,690	**0,837**	0,195	0,829	0,832
DRB1_0103	42	4	-0,231	0,204	0,208	0,250	**0,678**
DRB1_0301	5352	1457	0,646	**0,836**	0,181	0,816	0,816
DRB1_0401	6317	3022	0,613	**0,811**	0,198	0,798	0,809
DRB1_0402	53	19	0,419	0,669	0,249	0,633	**0,701**
DRB1_0403	59	14	0,511	0,703	0,152	0,644	**0,841**
DRB1_0404	3657	1852	0,636	0,803	0,189	0,787	**0,812**
DRB1_0405	3962	1653	0,669	**0,841**	0,171	0,839	0,827
DRB1_0701	6325	3456	0,748	**0,884**	0,171	0,877	0,875
DRB1_0801	937	390	0,658	0,836	0,165	0,834	**0,844**
DRB1_0802	4465	2036	0,673	**0,838**	0,184	0,834	0,834
DRB1_0901	4318	2164	0,657	**0,833**	0,175	0,832	**0,833**
DRB1_1001	2066	1521	0,754	0,915	0,157	0,912	**0,923**
DRB1_1101	6045	2667	0,734	0,866	0,174	**0,867**	0,864
DRB1_1201	2384	759	0,771	**0,894**	0,141	0,891	0,868
DRB1_1301	1034	520	0,673	0,851	0,220	0,828	**0,857**
DRB1_1302	4477	2249	0,774	**0,890**	0,176	0,889	0,885
DRB1_1501	4850	2107	0,679	**0,839**	0,187	0,833	0,834
DRB1_1602	1699	989	0,778	**0,886**	0,151	0,879	0,883
DRB3_0101	4633	1415	0,813	**0,912**	0,149	0,898	0,888
DRB3_0202	3334	1055	0,808	**0,889**	0,171	0,887	0,869
DRB3_0301	884	510	0,646	0,826	0,192	0,824	**0,840**
DRB4_0101	3961	1540	0,706	**0,851**	0,171	0,837	0,822
DRB4_0103	846	525	0,670	**0,849**	0,197	0,839	0,841
DRB5_0101	5125	2430	0,714	**0,855**	0,191	0,849	0,849
H_2_IAb	1794	431	0,703	0,885	0,163	0,884	**0,894**
H_2_IAd	774	321	0,611	0,813	0,202	**0,819**	**0,819**
H_2_IAk	115	4	0,332	0,619	0,137	0,628	**0,635**
H_2_IAs	190	48	0,534	0,815	0,195	0,761	**0,825**
H_2_IAu	56	22	0,603	**0,898**	0,262	0,830	0,765
H_2_IEd	245	28	0,400	0,706	0,180	0,730	**0,754**
H_2_IEk	68	40	0,633	0,754	0,216	0,836	**0,853**
HLA_DPA10103_DPB10201	787	141	0,720	0,903	0,146	0,910	**0,917**
HLA_DPA10103_DPB10301	1563	575	0,796	**0,914**	0,166	**0,914**	0,902
HLA_DPA10103_DPB10401	2725	786	0,882	**0,939**	0,140	0,935	0,935
HLA_DPA10103_DPB10402	45	9	0,194	0,596	0,180	0,497	**0,710**
HLA_DPA10103_DPB10601	584	282	0,958	0,995	0,116	**0,996**	0,995
HLA_DPA10201_DPB10101	2447	859	0,833	0,897	0,149	**0,903**	**0,903**
HLA_DPA10201_DPB10501	2470	713	0,806	0,913	0,154	**0,914**	0,911
HLA_DPA10201_DPB11401	2302	849	0,851	**0,942**	0,151	0,937	0,930
HLA_DPA10301_DPB10402	2641	921	0,834	0,903	0,157	**0,906**	0,904
HLA_DQA10101_DQB10501	2946	815	0,813	**0,917**	0,138	**0,917**	0,900
HLA_DQA10102_DQB10501	833	458	0,662	0,865	0,194	**0,867**	0,839
HLA_DQA10102_DQB10502	800	158	0,675	**0,851**	0,159	0,850	0,835
HLA_DQA10102_DQB10602	2747	1256	0,814	0,902	0,148	**0,905**	0,890
HLA_DQA10103_DQB10603	462	90	0,503	0,803	0,199	0,816	**0,861**
HLA_DQA10104_DQB10503	883	105	0,635	0,837	0,143	**0,844**	0,805
HLA_DQA10201_DQB10202	944	119	0,644	**0,860**	0,131	0,851	0,814
HLA_DQA10201_DQB10301	827	374	0,696	**0,876**	0,187	0,864	0,849
HLA_DQA10201_DQB10303	761	265	0,721	0,886	0,152	0,887	**0,894**
HLA_DQA10201_DQB10402	768	241	0,638	0,854	0,181	0,858	**0,860**
HLA_DQA10301_DQB10301	207	66	0,591	0,774	0,195	0,761	**0,839**
HLA_DQA10301_DQB10302	3111	568	0,702	0,846	0,126	**0,849**	0,810
HLA_DQA10303_DQB10402	567	117	0,632	**0,844**	0,168	0,836	0,820
HLA_DQA10401_DQB10402	2890	928	0,794	**0,903**	0,116	0,894	0,883
HLA_DQA10501_DQB10201	2897	874	0,780	**0,889**	0,131	**0,889**	0,876
HLA_DQA10501_DQB10301	3585	1812	0,812	**0,926**	0,143	0,922	0,915
HLA_DQA10501_DQB10302	847	203	0,600	0,820	0,139	**0,831**	0,822
HLA_DQA10501_DQB10303	564	179	0,680	0,869	0,138	**0,884**	0,876
HLA_DQA10501_DQB10402	749	337	0,718	**0,877**	0,157	0,857	0,868

HLA_DQA10601_DQB10402	565	133	0,622	**0,854**	0,180	0,845	0,848
Average			0,666	0,839	0,170	0,833	**0,847**
Average weighted by #Binder			0,722	**0,865**	0,172	0,860	0,858
Average over alleles with >=100binders			0,723	**0,872**	0,164	0,869	0,864
Average over alleles with >=500binders			0,745	**0,876**	0,165	0,871	0,867
Average over alleles with >=1000binders			0,719	**0,863**	0,174	0,856	0,854

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