

UNIVERSITY OF SOUTHAMPTON
Faculty of Physical Sciences and Engineering
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A project report submitted for the award of
BSc Computer Science

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**Knowledge distillation and Model
compression on CNN for Protein
Secondary Structure Prediction**

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ABSTRACT

FACULTY OF PHYSICAL SCIENCES AND ENGINEERING

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Predicting the secondary structure of the protein is one of the most challenging problem in Bioinformatics. Experimentally determining the protein structure is costly and inefficient, therefore multiple machine learning algorithms have been published that predict the secondary structure from the amino-acid residues chain.

The purpose of the project will be to train different secondary structure predictors and to understand if there exists significant asymmetry in the inputs that explain the predictions. The aim of this work is to observe if systematic trends appear on large datasets - especially on Prokaryotes and Eukaryotes where the protein synthesis mechanism is different.

– MODIFY THIS ONCE THE REPORT IS DONE AND THE MAIN IDEA OF IT IS UNDERSTOOD

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Introduction

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Chapter 2

Background of the problem

2.1 Dictionary of protein secondary structure

Protein secondary structure is in essence a way of classifying each amino-acid present in the sequence as belonging to a particular class. The work of Wolfgang Kabsch and Christian Sander (1983) suggests that for a successful classification of the amino-acid sequence there must be a physical meaningful description of the secondary structure. In their paper, the problem of classification is seen as a pattern-recognition process on hydrogen-bonds and geometrical features that have been previously extracted from x-ray coordinates.

Prior to their work, other researchers have published different structure assignments. The assignments of the secondary structure appear in the Brookhaven Protein Data Bank [1] however, some of the results are incomplete and can be considered subjective. The final work proposes a set of patterns which are simple but powerful enough to discriminate among different types of secondary structures. The accuracy of the dictionary revolves around the resolution of each structure, therefore the process of assigning labels is determined by the accuracy (resolution) of the measurements taken from the x-ray. The most valuable information found in this paper is in regards to the idea that there are 21 different types of amino-acids and each one can be assigned one of 8 classes: 3 types of helices (H, G, I), 2 types of β -sheets (B, E), 3 types of coils (T, S, L). [2]

2.2 Generative Stochastic Network

The work of Jian Zhou and Olga G. Troyanskaya (2014) presents a supervised generative stochastic network which is fed by a 1D Convolutional Neural Network layer (1 protein sequence as input) and learns a Markov chain. The main advantage over a unsupervised

GSN is that it focuses the resources on dependencies that have higher importance on the desired output/prediction. An important aspect of this approach has to do with the hierarchical representation which enables the architecture to deal with long sequences of amino-acids - there are two channels considered as input, one for the features (X) and one for the labels (Y) and only the last one is being corrupted (injecting noise to input and intermediate computation).

The dataset used for training and testing the model was created using the PISCES Cull PDB server and the final result consisted of 6128 proteins (5600 Training, 256 Validation, 272 Testing). All the solved amino-acid sequences have a resolution better than 2.5Å and the length varies between 50 and 700. Apart from this, the PSSM values ($n \times b$ matrices, with n representing the sequence length and b the number of amino-acid types) have been computed using PSI-BLAST against UniRef90 database and the results have been normalised to a 0-1 range using the sigmoid function.

The Q8 accuracy on the test set was $72.1 \pm 0.6\%$ with high scores when it comes to predicting the states (H, E, L, T) and low scores on the states (S, G, B) - this is due to an imbalanced dataset (the state 'I' was not present in the test set so the accuracy was 0). Performing validation on the public benchmark dataset CB513 led to an accuracy of 0.664 which outperformed the current best. [3]

2.3 Deep Convolutional Neural Fields

Considerable improvement compared to GSN on the Q8 and Q3 accuracy has been made by Sheng Wang et al. (2016). They developed a new machine learning method called Deep Convolutional Neural Fields. DeepCNF introduces a combined version of conditional neural fields and Deep Convolutional Neural Networks which manages to capture relations between amino-acids at adjacent positions. The method finds complex relations between the input features and the output classes - this is due to the fact that a convolutional deep neural network will capture more information coming from longer amino-acid sequences than a normal deep neural network when using the same window size.

A few key differences from Jian Zhou and Olga G. Troyanskaya (2014) can be observed, starting with the fact that instead of having two channels as input (features and labels), DeepCNF only offers the secondary structure features to the visible layer. Apart from this, the DeepCNF model is explicitly learning the amino-acid interdependency while Sheng Wang et al. (2016) does not. This is due to the fact that each amino-acid

label probability is calculated directly compared to the sampling method of Zhou's work.

When it comes to accuracy, there is a clear improvement to the previous work especially on the Q3 classification. DeepCNF outperforms other state-of-the-art methods, but it also does a better job at labeling structure types that are known to be hard to predict such as (S, T, L).

The dataset used for training is similar to the one used by Zhou and it is publicly available (Cull PDB). The dataset is split differently for this work - there is a similarity less than 25% between training data (≈ 5600) and test data (≈ 500). Besides this dataset, a number of four other publicly available datasets have been used for testing purposes and for comparing the accuracy with other models: CB513(513 proteins), CASP10(123 proteins), CASP11(105 proteins) and CAMEO test proteins (175 after filtering) from the last 6 months (2014/12/05 - 2015/05/29). An important note here is that every dataset mentioned above is generated using the dictionary of protein secondary structure (Wolfgang Kabsch and Christian Sander). An interesting addition to the Q3 accuracy measurement is brought by the SOV score (Segment of overlap) which assigns a lower score to a prediction which had wrong labels at the middle of the sequence compared to one that made incorrect classification of the amino-acids at the terminals.

The accuracy on the Q8 classification of DeepCNF on CullPDB results in a value of 75.2% which represents an increase of 3.1% compared to ICML2014, while the Q3 accuracy yields a value of 85.4%. In terms of SOV score, the model has an accuracy of 86.7% - that is, DeepCNF makes more meaningful predictions on the protein sequences and this is due to the use of deep neural networks.

Further work has been done on observing the differences in accuracy that appear when the models are tested on homologous information. Neff is a way of measuring how sparse the amino-acid sequence is - a small Neff value indicates that the test protein has a sparse sequence while a high Neff value indicates that the protein secondary structure contains a considerable amount of homologous information. The results of running the model on sparse sequences suggested that there is no significant improvement to other methods and that it is still complicated to predict secondary structure from the primary structure.[4]

2.4 Cascaded Convolutional and Recurrent Neural Networks

Zhen Li and Yizhou Yu (2016) introduced a method which also sets up a new benchmark in terms of accuracy for secondary structure prediction by proposing a combination of

CNN and RNN architectures - it is known that local contexts, in particular amino-acid neighbours, represent a good way to predict the labels and that CNNs have proven to be effective in picking up such patterns. RNNs are another type of neural networks that contain loop connections and in the case of secondary structure prediction are able to find dependencies that appear at a larger distance than the local contexts (global context) - this is particularly implemented using multiple bidirectional GRU (gate recurrent units) which represent the most important part of the model.

The input is represented by two channels, one containing the sequence features and one containing the profile features. Different from other approaches using 1 hot encoded values, here the first input is being transformed by the feature embedding layer - sparse sequences are mapped into denser feature vectors. The new input is then fed to the CNN structure which extracts the local features, then the concatenated local features become input to the three BGRU layers.

The data set used for training was CB6133 (PISCES CullPDB) which contains 6128 proteins, a number of which 256 represent the validation data and 272 the testing data. For testing and comparison reasons, the same datasets mentioned previously were used, one of which is the well known benchmark CB513. A filtered version of the CB6133 has been created in order to remove the proteins that shared more than 25% similarity with the test dataset. Training on the original CB6133 and testing on the 272 proteins gives a Q8 accuracy of $73.2 \pm 0.6\%$, 1.1% more accurate than GSN. Using the filtered version of the dataset and testing on CB513 gives a Q8 accuracy of $69.4 \pm 0.5\%$, 1.1% higher than the previous state of the art method, DeepCNF.[5]

2.5 Saliency Map on CNNS

Guillermo Romero Moreno et al. (2019) takes another approach to the well known Bioinformatics problem of secondary protein prediction. To this point, most of the efforts have been made to improve the accuracy of the predictions by introducing and training new deep neural architectures. In this paper, the main idea is to find a way of interpreting the decisions made by the architectures using Saliency map techniques. The model used in the paper has been trained using the dataset produced by Zhou and Troyanskaya and the Q8 accuracy yields a value of 69.23% - not far from the state-of-the-art methods (the model has been kept simple to keep saliency map calculations to low levels).

Every input to the model represents a amino-acid sequence where each element is represented by 42 features (21 features for representing the type of amino-acid in 1 hot encoded form and 21 values for the PSSM features). Furthermore, each position in the

protein sequence generates a Saliency map that spans across the entire feature space and 9 positions to each side - this has to do with the chosen window size which is 19. Each possible output label will then have a Saliency map value, so the final size is $8 \times 42 \times 19$.

This paper highlights the importance of PSSM values on predicting the secondary structure using Saliency maps. This is done by separating each Saliency map into sequence features and profile features and the results are summed to obtain an overall score. These score suggests that PSSM values have 4 times or more importance in the majority of positions. This finding is backed up by training a model with only PSSM values and the final results show an improvement of 0.14% compared to the original Q8 accuracy - this suggest that the one-hot-encoded amino-acids are of no importance in the presence of PSSM values.

Another useful insight that Saliency maps offer is the study of spatial importance, in other words, where the machine learning model looks when it makes predictions. In the paper, for every input labeled correctly, the Saliency map is summed together on the feature space and that generates a vector of dimension 19. For every class, all the values are averaged together and the final results suggest what were the positions most relevant when predictions were made. In the case of the class 'H' there is some periodicity appearing at the right side and large asymmetry - this can suggest a strong dependency that appears at the protein chain creation. These findings have been validated by running another version of the model which ignores the input from the left positions and then from the right positions (setting convolutional filters parameters to zero). Using the left positions gives an accuracy of 80.81% while the right positions achieves 86.60% (on H and non-H classification). [6]

2.6 CNN architecture overview

With the introduction of the previous deep learning techniques, current efforts in secondary protein structure are focused on convolutional/recurrent neural networks. – MAYBE WRITE HERE ABOUT SOME OF THE PAPERS AND CITE THEM–. This section is a technical overview of CNN based on the open course offered by the University of Stanford - CS231n: Convolutional Neural Networks for Visual Recognition.

CNN are similar to normal neural networks meaning that they contain neurons that have weights and biases that need to be learned. A neuron receives the input and performs a dot product with the current parameters and outputs the result that can be

followed by an activation function. The entire network uses a differentiable score function along with a loss function that is used in the last fully connected layer (eg. Softmax).

A regular neural net consists of multiple fully connected layers. The input layer is followed by a series of "hidden layers" and the final output layer in a classification problem represents the class scores. Each layer is composed of a number of neurons that are fully connected to the previous layer and do not share any parameters with other neurons. The problem with this architecture is that the number of learnable parameters increases with the addition of new layers and soon this can become unmanageable - when working with images, an input image of resolution 200×200 pixels in the RGB colour space would require a neuron with a number of $200 \times 200 \times 3 = 120,000$ weights. On the other hand, CNN consider the input to be an image and all the following layers have the neurons arranged in 3 dimensions - height, width and depth. This allows neurons to be connected only to a specific region of the previous layer. (Figure 2.1)

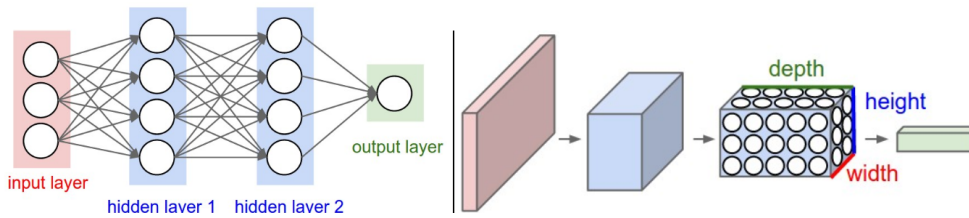


Figure 2.1: Comparison between a regular neural network and CNN, sourced from Stanford-University (CS231n)

One of the most important part of the CNN is the convolutional layer. It consists of a series of filters that represent a set of learnable parameters. Each filter is a spatial "patch" (width and height) that extends over the entire depth of the input - for example, the first layer of CNN that does image classification could contain a filter of size $5 \times 5 \times 3$ that has depth 3 in order to accommodate the entire depth of the input (RGB colour space). During the forward pass in the architecture, a filter would slide across the width and height of the input and perform a dot product with the current weights (convolution) - this would create a 2D activation map that contains the response of the filter at each position of the input. The idea behind this process is that the network would look for the same pattern over the entire span of the input and therefore use the same parameters (parameter sharing). Increasing the number of filters per convolutional layer would add new activation maps and the stacked result would be the depth of the output. (Figure 2.2)

Moving away from image classification, in protein secondary structure prediction, the data is represented by a chain of amino-acid residues that form the protein. The main key difference here is that for this particular problem 1D convolutional layers are used. In Figure 2.3, the filter (feature detector) spans across the entire representation of the

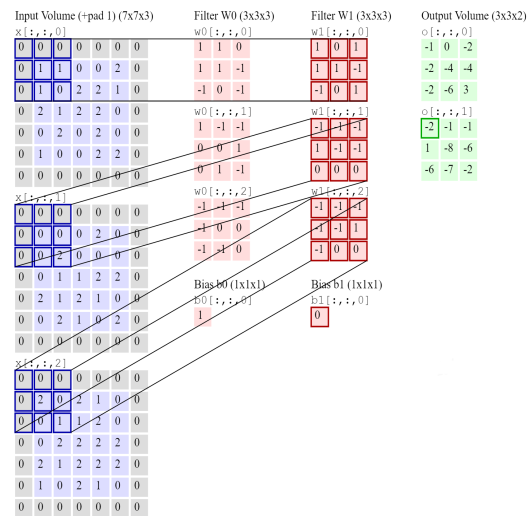


Figure 2.2: Convolution on a RGB image, sourced from Stanford-University (CS231n)

amino-acid and is of size 3, meaning that it convolves with the feature vectors of 3 amino-acids.

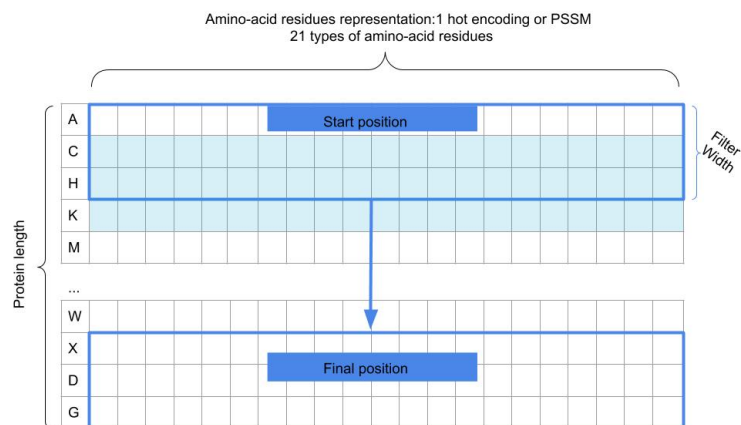


Figure 2.3: 1D convolution of a AA chain, –MADE WITH GOOGLE DRAWINGS???

Chapter 3

Final approach

3.1 Libraries and tools

This project has been build using Python and the *JupyterLab IDE*. The main libraries used for creating the model architectures and for training-testing the models are *Keras* [7] and *Tenserflow* [8]. From a hardware perspective, a combination of multiple machines and servers have been used to cope with the high number of experiments. At the beginning of the project, most of the training was done with the help of the Google Colab platform (Tesla K80 GPU - 2496 CUDA cores, 12GB GDDR5 VRAM). Two other computing resources used were offered by the University of Southampton and accessed through remote desktop connection (2 NVidia RTX2070 GPU cards with 2,304 CUDA cores each).

3.2 Dataset

Two main datasets are used for developing the architecture in this report - CULLPDB and CB513 that are made available by Jian Zhou and Olga G. Troyanskaya (2014). CULLPDB contains protein sequences that have been downloaded from Protein data bank [9] using the PISCES Cull PDB server [10]. The final result consists of solved proteins structures that have a resolution better that 2.5 Å and share a similarity of less than 30%. The protein length has been limited to the range [50, 700] and no discontinuous chains appear in the dataset.

CullPDB contains 6128 proteins and this has been further filtered to remove those chains that share more than 25% similarity with the test set CB513. The final configuration consists of 5534 proteins split into 5278 training and 256 validation similar to [11] [12]. CB513 is the test set that is usually used as benchmark for model comparison - it contains 513 protein chains but with 514 entries because the last protein is split in two.

The following structure shows the dimensionality of the filtered dataset.

$$\begin{array}{c}
 \text{5534 proteins(N)} \left\{ \begin{array}{c} \overbrace{\begin{pmatrix} p_{11} & p_{12} & \cdot & \cdot & \cdot & p_{1,a-1} & p_{1,a} \\ p_{21} & p_{22} & \cdot & \cdot & \cdot & p_{2,a-1} & p_{2,a} \\ \cdot & & & & & & \\ \cdot & & & & & & \\ \cdot & & & & & & \\ p_{n,1} & p_{n,2} & \cdot & \cdot & \cdot & p_{n,a-1} & p_{n,a} \end{pmatrix}}^{700 \text{ amino-acids(A)}} \end{array} \right. \text{(Dataset dimensions)}
 \end{array}$$

where each p value in the matrix represents one amino-acid that has the following 57 features:

[0 : 22): amino-acid residues that appear in one hot encoded form

[22 : 31): secondary structure labels - (L,B,E,G,I,H,S,T)

[31 : 33): N and C terminals - not used

[33 : 35): relative and absolute solvent accessibility - not used

[35 : 57): sequence profile (PSSM) - the values belong to the range [0, 1]

The elements found at positions 21 and 30 mark the end of the protein sequence. Each protein has a sequence which ranges from 50 to 700 amino-acids and zero padding is used such that each protein has the same length.[3]

3.2.1 PSSM - position-specific scoring matrix

PSSMs are used in bioinformatics as representations of motifs that appear in biological sequences. Each row in the PSSM represents 1 type of amino acid (20 types) and each column is for each position present in the pattern (700 in CullPDB dataset). The first step in obtaining the PSSM is to create the position frequency matrix PFM that counts the occurrence of each AA at every location. Then, the position probability matrix PBM is computed by dividing the number of occurrences by the number of sequences such that the final values are normalised. Equation 3.1 offers the formal definition of the matrix for a set P of size N aligned sequences (proteins in our case) of length l (700).

$$M_{k,j} = \frac{1}{N} \sum_{i=1}^N T(P_{i,j} = k) \quad (3.1)$$

Where:

- k : is one 20 types of amino-acids
- $M_{k,j}$: is the value for amino-acid k at position j .
- $P_{i,j}$: is the amino-acid found at position j in protein P_i .
- $T()$: is a function that denotes the ground truth and returns 0 or 1

Finally, PSSM are obtained by transforming the raw probabilities into log likelihoods using a background model b that assumes how frequently each-amino acid appears in the set. The simplest form of the model is to assume that each AA appears equally, $b_k = \frac{1}{|k|}$.

$$M_{k,j} = \log_2 \frac{M_{k,j}}{b_k} \quad (3.2)$$

If the set of sequences is too small, values of 0 could appear in the matrix (no occurrences) and after applying the logarithm we are left with values of ∞ and $-\infty$ - this can be solved by using pseudocounts (applying a Dirichlet distribution to each column).

[13]

PSSM found in the CullPDB dataset has been generated using PSI-BLAST against UniRef90 database and the final results was transformed using the sigmoid function. One interesting point is that there are 21 entries for the amino-acids, 1 more than the known types - there is one extra encoding "X" that denotes an unknown type.[3]

It is important to see how balanced the data is before moving on to training. In Figure 3.1(a) we can observe how heavily imbalanced the entire dataset is. The labels 'B', 'G' appear in a low number compared to the others while the number of amino-acids labeled as 'T' represents a really small fraction (212 labels).

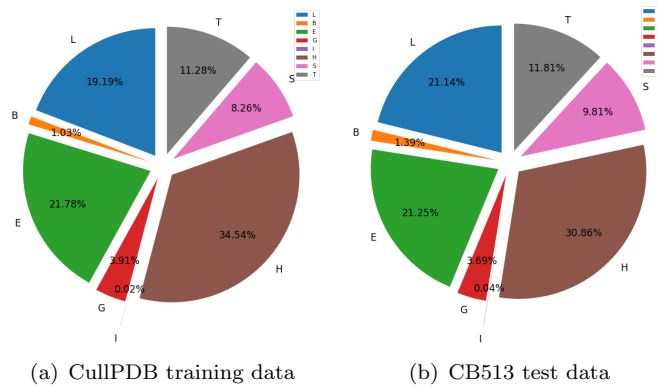


Figure 3.1: Dataset distribution

3.3 Evaluation methods

Throughout the report, different models are evaluated and multiple types of performance metrics appear, so it is important to highlight how they are computed.

It seems a bit counter intuitive, but the main idea behind protein secondary structure prediction is not to label correctly the entire protein - for example, the test dataset CB513 contains 513 proteins and the number of AAs is 84,765 (Figure 3.1(b)), therefore the accuracy found in Equation 3.3 uses the number of AAs and not the number of proteins in the dataset. That is, a model performs well if it manages to predict how the AAs are going to interact with each other and stabilise into a secondary state.

$$accuracy = \frac{\text{number of correct predictions}}{\text{total number of cases}} \quad (3.3)$$

Depending on the number of secondary structure classes each AA needs to be assigned we depict three types of accuracies: Q2,Q3,Q8

$$Q2 : AA \in \text{class } \{\text{Helix (H), non-Helix (G,I,B,E,T,S,L)}\} \quad (3.4)$$

$$Q3 : AA \in \text{class } \{\text{Helix (H,G,I), } \beta\text{-sheets (B,E), coils (T,S,L)}\} \quad (3.5)$$

$$Q8 : AA \in \text{class } \{H, G, I, B, E, T, S, L\} \quad (3.6)$$

Equation 3.3 is the default one used by the *Keras* library. Here we present in a detailed manner how the class scores returned by a model are labeled correct or incorrect.

As we mentioned in literature review, the last layer of a convolutional architecture is represented by a dense layer that has a number of neurons equal to the number of classes of the clasification problem. These nodes output the class scores followed by an activation function. Let the score of a input X_i be denoted with $s = f(X_i; W)$, where W represents the weights of the network. A *softmax function* can act as an activation function and takes these unnormalised log probabilities of the classes and normalizes them such that they add up to 1.(Equation 3.7)

$$P(Y = y_i | X = X_i) = \frac{e^{s_{y_i}}}{\sum_j e^{s_j}} \quad (3.7)$$

That is, for the Q8 classification, the final results represent a probability distribution over 8 classes, showing how 'confident' the network is. *Keras library* chooses the class with the highest probability as the final results. (Equation 3.8)

$$T(y_i) = \begin{cases} \text{correct,} & \text{if } \textit{argmax}(y_i) = \textit{argmax}(\textit{target}) \\ \text{incorrect,} & \text{otherwise} \end{cases} \quad (3.8)$$

Where:

target: is the true class label in 1 hot encoding

Chapter 4

Implementation, experiments and results

4.1 Data prepossessing and input discussion

Thankfully, the work of Jian Zhou and Olga G. Troyanskaya (2014) on the CullPDB dataset has been made available to the public - this saved hours of work for filtering the AA chains and computational time for computing the PSSM values.

When it comes to proteins secondary structure, the neural networks have to label AA that have local and long-range dependencies. Many techniques have been published where the concept of a sliding window is used in order to capture local and intermediate interactions. Using CNN this can be implemented by applying a filter (window) over the input in the first convolutional layer - essentially, the protein is segmented in smaller parts. It is known that in order to improve the Q8 accuracy there is a need to introduce global information[3]. Therefore, most of the recent approaches make use of deep CNN networks ([14], [15], [11], [5]) or a combination of local feature extraction using CNN and other deep learning techniques such as long short term memory networks([16], [17], [3], [12], [4],).

When using a convolutional layer to segment the original input, the window parameters are still subjective to change according to the gradients from the loss function. It can become unclear whether the performance comes from local or long-range interactions as further convolutions combine these results and can disregard parts of the AA chain while training. In this report we focus mainly on local and intermediate range interactions by reshaping the dataset such that each AA appears in the center of an odd length window. In work of Matt Spencer et al. [18] multiple sizes of windows are tested and

the peak accuracy is achieved at 19. Our final dataset contains windows of size 19 with the prediction label of the AA in the center - for the terminal AA, further experiments have been made to decide the best type of padding and this will be discussed in a further section.

Finally, the following developed architectures all use input of size 19x21 (19 amino acids with 21 features each) - vanilla approach where in order to make a prediction we gather information from 9 adjacent positions on the left and right.

4.2 CNN depth exploration

Taking in consideration that the average length of an alpha helix is 5 [19] and that of β -strand is 6 [20], our input can capture this information. The next step is to discover the best architecture, in particular at what the depth(number of convolutional layers) we obtain the best accuracy.

To keep the computational time low, we have decided to use the smallest filter size that can capture some context (3), and a number of 64 filters per layer - the stride is set to one, meaning that a filter moves by 1 position and padding (zeros) is used to preserve the dimensionality of the input. The loss function used is a combination of the *cross-entropy loss* that uses the softmax scores and an additional factor which is the regularization parameter.

$$L_i = -\log\left(\frac{e^{s_{y_i}}}{\sum_j e^{s_j}}\right) \quad (4.1)$$

$$R(W) = \sum_k \sum_l W_{k,l}^2 \quad (4.2)$$

$$Loss = \frac{1}{N} \sum_i L_i + \lambda R(W) \quad (4.3)$$

(4.1) is the *cross entropy loss* between the true distribution(p) and our predicted distribution(q) which can be written as $H(p, q) = -\sum_x p(x) \log q(x)$ - what this means is that this part of the loss function "forces" the network to distribute the probability mass such that it matches the 1 hot target. (4.2) is called the L2 norm and is added such that the model is kept as simple as possible by penalising large weights.

In the following experiments, we use a lambda value of $\lambda = 10^{-4}$. For optimising the weights, we use TensorFlow's ADAM optimizer [21] (default initialisation parameters)

with a learning rate value of $LR = 5 \cdot 10^{-4}$. The networks that we train all have different number of convolutional layers that are followed by Batch Normalisation [22] layers such that we overcome the problem of gradient vanishing; at the end of the networks we have 2 Dense layers of size 16 and 8 (Softmax layer).

In Figure 4.1 we can observe the performance of networks with different depth where we use the same number of filters per layer - note, the number of parameters is different: $\approx 24k, \approx 50k, \approx 75k, \approx 100k$ and $\approx 125k$. There is a clear difference in training and validation accuracy as the models with more depth perform better despite over-fitting the data. CB513 accuracy is close to other publications and it follows the same trend - it is 4% lower than the validation accuracy.

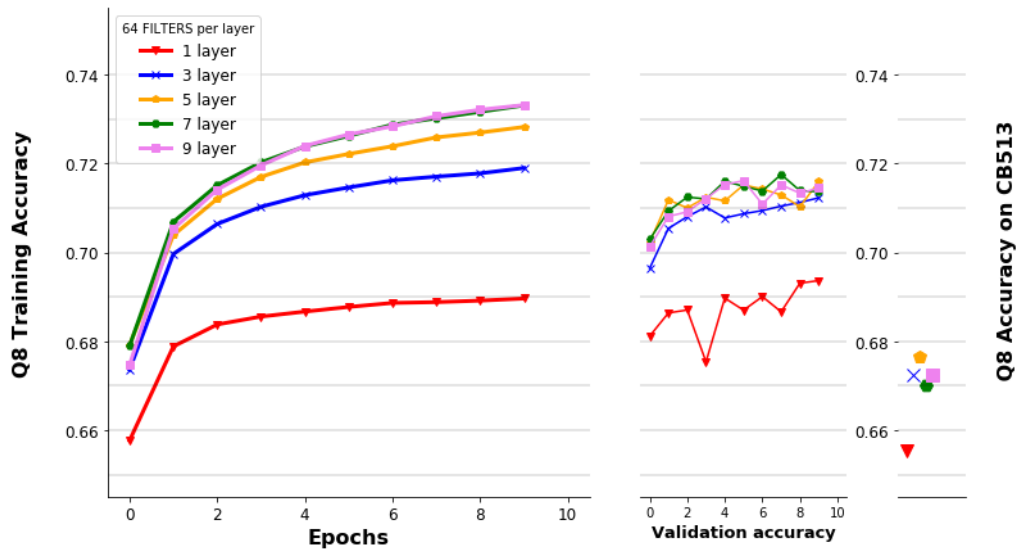


Figure 4.1: Q8 accuracy of models with different numbers of layers that use the same window

We can observe that increasing the number of convolutional layers above 7 does not bring any noticeable contribution to the overall performance.

To see if the performance comes from the depth of the network and not from the increased number of parameters, we have retrained other architectures each with $\approx 125k$ parameters such that the only difference is the depth.

In Figure 4.2 we can see some improvement for the network with one layer, but the overall learning trend seems to stagnate. The other networks seem to be quite similar, with the same over-fitting problem as before. We believe that choosing the right regularization factor for each network would have made the performance difference clearer but using the information provided by the training accuracy, the network with 5 layers has the most descriptive power. The accuracy on the test set CB513 could suggest that a network with 3 layers has the same performance - taking into consideration that we intend to further improve the accuracy using other methods, we choose the network with 5 layers as it offers the best trade-off between performance and training time.

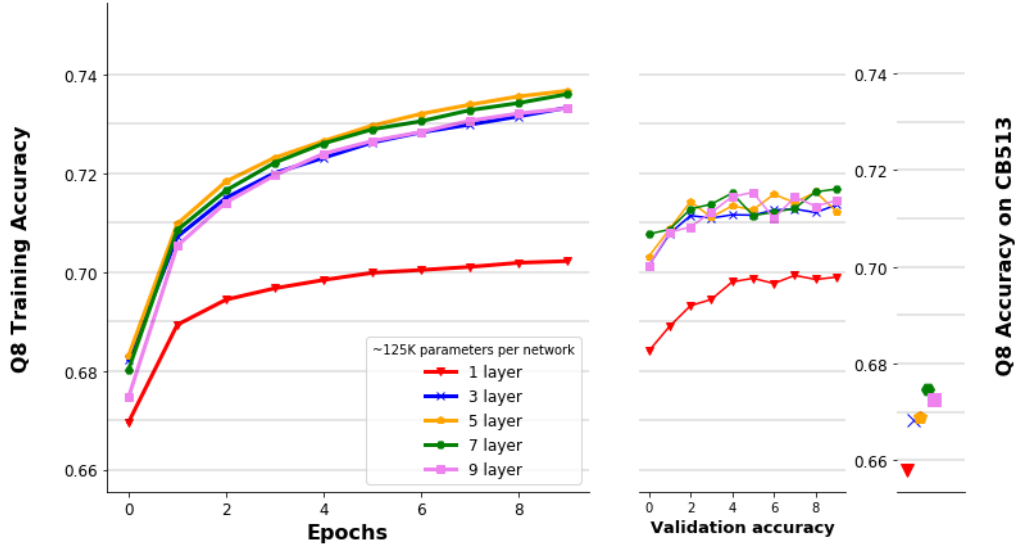


Figure 4.2: Q8 accuracy of models with the same numbers of layers

We further study the effect of the number of filters on the 5 layer network to see if it is possible to shrink the number of parameters to keep the model as simple as possible. In Figure 4.3, the networks with a decreased number of filters tend to generalise better on unseen data (validation) but still perform worse than the one with 64 filters that overfits. We can observe that the 5 layer architecture performs the best on the CB513 and it has enough descriptive power which means that there is no need to increase the number of parameters.

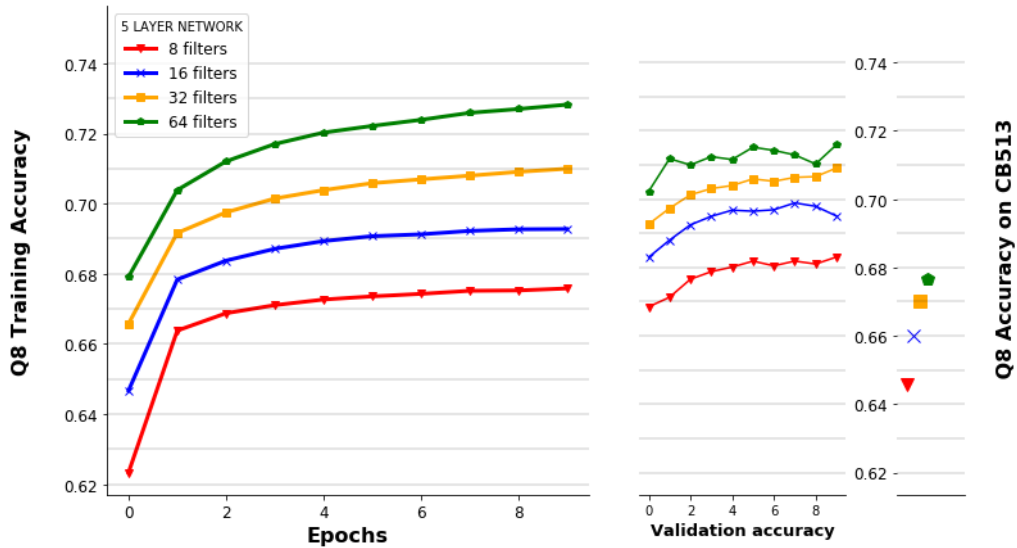


Figure 4.3: Q8 accuracy of the 5 layer network with various number of filters

4.3 K-fold accuracy

In this section we perform 10 fold-cross-validation test on the training data to see the variation of the accuracy on the test set - in particular, we divide the entire dataset in 10 and use a subset of 9 for training and the one left out for testing. Two types of input are used: windows of size 19 in PSSM and 1 hot encoding. The following experiments are run with the same parameters on the the architecture with depth 5 from the previous section. An additional change to the dataset is made to reshape the target labels from Q8 to Q3 and Q2 in order to provide the following accuracies.

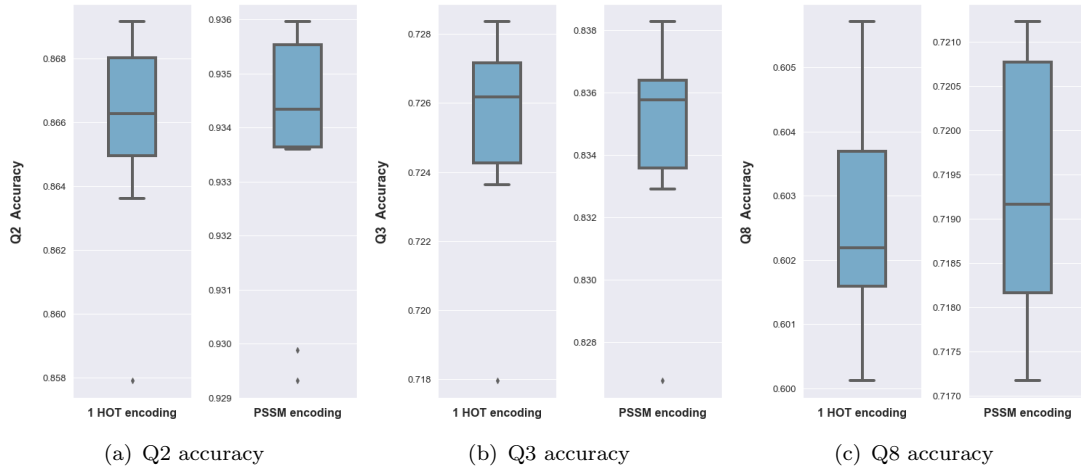


Figure 4.4: Accuracy variation on 10 fold cross validation

The accuracy variation highlighted Figure 4.6 is quite small across all problem types with a small number of outliers - this suggests that the network manages to perform well in general and not because of a "lucky" initialisation. Another important idea suggested by these results is that using PSSM values instead of 1 hot encoding format, we can boost the accuracy up to 10% - for the Q2 class this is only 5% as it is a simple classification problem where the label can be H or non-H. We can observe that the Q8 classification is much harder than Q3(10% accuracy difference), and that it has a higher variance of %0.01 compared to %0.001 - we believe that this is due to the network having problems predicting those AA that have long-interactions. That is, for each different run with random initialisation the model has a slightly different way of understanding the Q8 classification problem.

To validate the findings of Guillermo Romero Moreno et al. (2019), where it is stated that the right side of the window holds more information, we have reshaped the dataset to windows of size 9 where the target class label belongs to the AA on the right or the left side of the window.(Figure 4.5)

The idea that α -helices hold a large asymmetry can be seen in Figure 4.6 (a). It is indeed easier to predict the label using the information from the right side - as it is mentioned in

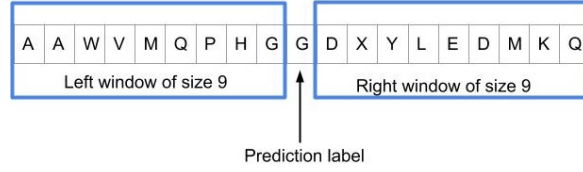


Figure 4.5: Example of a window of size 19 split into two windows of size 9

the paper, this asymmetry can point to a strong dependency on the previous (posterior) AAs. In other words, the information found at the right side is more valuable because we can "infer" knowledge about previous amino-acids. What is more interesting is that we can see the same dependency when it comes to Q3 and Q8 classification where the difference between accuracies $\approx \%0.04$ is similar compared to $\approx \%0.05$ in Q2.

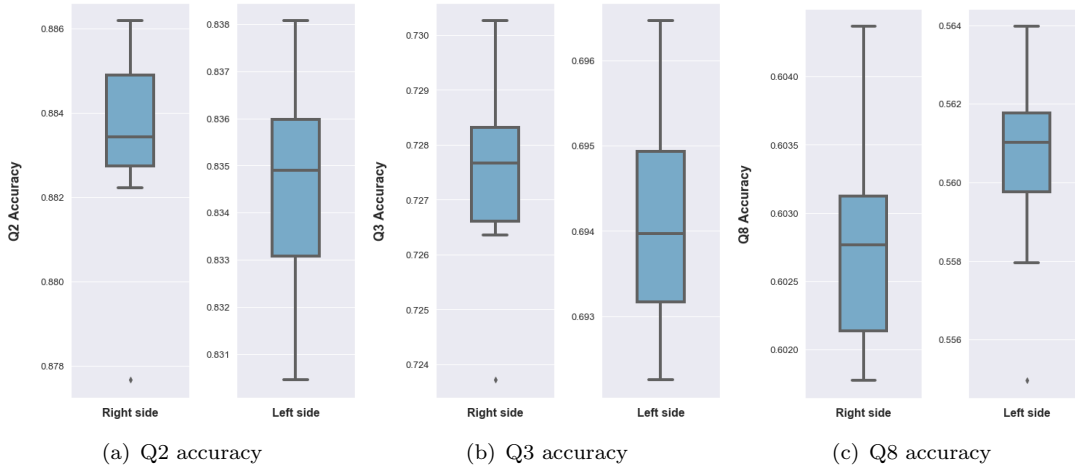


Figure 4.6: Accuracy variation on 10 fold cross validation with a window of size 9

One advantage over the previous reported results is that here we are limiting the model to learn local interactions and we can be confident that the difference in accuracy does not come from information found further across the AA chain.

4.4 Improving the architecture

Motivated by the previous findings and the work of Akosua Busia and Navdeep Jaitly [11] that achieved the state-of-the-art accuracy on CB513 benchmark using the CullPDB training set, we have decided to further investigate possible improvements to our network. The CNN constructed by Akousa Busia et. al, uses some recent findings in the field of Deep Learning especially from Computer Vision (image classification) to boost the performance - towards the end of the paper, it is mentioned that the vast majority of the information used for protein secondary structure prediction comes from local interactions (different from what was believed in the past). In this section, we use some of these new techniques but what is different from the other published approaches is that we are

trying to use the depth of the network only for local interactions that appear in the span of 19 AA. We are not going to go in depth of every new addition to the network as this goes beyond the purpose of this report, but a general overview will be provided.

The Inception network that is designed for image classification [23], introduces multi-scale convolutions that apply different filters on the input that compute different features at various scales. In Figure 4.7(a), our multiscale convolution uses three types of filters that slide on the same input. Here we decided to keep the previous window of 3 as it performed relatively well, and we introduce two new filters of size 11 and 19. The filter of size 19 might seem odd, with a size way larger than a typical kernel - considering that our input is only a fraction of the AA chain, the parameters for a filter of size 19 is still manageable ($19 \times 21 \times 19$ instead of $700 \times 21 \times 19$). The intuition of using a filter size the same as the input is to "build" global context (entire AA chain) from a small window. Thinking about how a typical deep CNN manages to use information from the entire sequence, here we are extending the information of the window by "diluting" the ends with staked convolutions that use padding. In other words, we are trying to infer knowledge about the surrounding AAs that the network cannot "see" from a small context input.

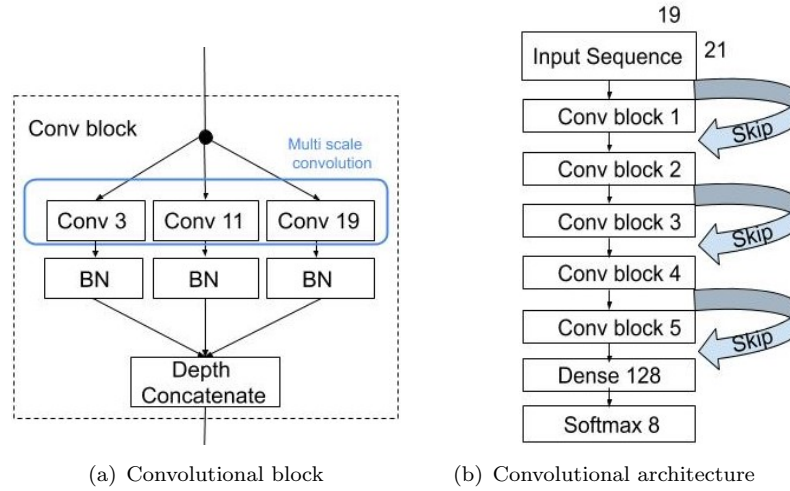


Figure 4.7: Accuracy variation on 10 fold cross validation with a window of size 9

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