Prediction of MHC Class II-Peptide Interaction Using Fuzzy Neural Network

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1 Introduction

A major histocompatibility complex (MHC) molecule plays an essential role in the immune system. A MHC molecule binds a peptide derived from an antigen, and then displays it on a cell surface for recognition by T cells. Hence, it is important for therapy of autoimmune diseases and cancer to determine which peptides can bind to a given MHC molecule. However, it is difficult to predict the peptides bind to MHC class II molecules because of various amino acid lengths of them. In this study, the fuzzy neural network (FNN) based method was investigated for rule extraction and prediction of peptides bind to human MHC class II molecule HLA-DRB1*0401(DR4Dw4).

2 Materials and Methods

2.1 Data preprocessing

The initial data set consisted of 650 peptides known to bind or not bind to HLA-DRB1*0401. The peptides are classified into 4 categories (no-, low-, moderate- and high-affinity).

A quantitative matrix whose elements were optimized by an evolutionary algorithm (EA) was used to determine nine amino acids as a binding region of a peptide. An EA is an optimization method based on evolutionary principles. Using this optimized quantitative matrix, each score for every region in a peptide was calculated and the highest scoring region was determined as binding region. These data were divided into two sets as the data set for learning used for model construction and the data for evaluation used for model validation.

2.2 Amino acid index

When peptide binds to protein, hydrophobic interaction, electrostatic interaction and van der Waals force are concerned. Therefore, 3 indices of hydrophilicity (Hopp and Woods), electric charge and van der Waals volume for each amino acids were used for analysis.

2.3 Fuzzy neural network

An FNN is a method combined fuzzy reasoning with artificial neural network (ANN). By learning using a back propagation method, the relationship between input and output can be extracted automatically as the if-then rules. In this research, FNN Type-I [1] was used for modeling (Fig. 1). And a parameter increasing method (PIM) based on statistics was used for optimization of numbers of membership functions and for selection of essential input variables. Using this FNN, we have constructed a model to predict binding affinity from amino acid sequences of peptides.

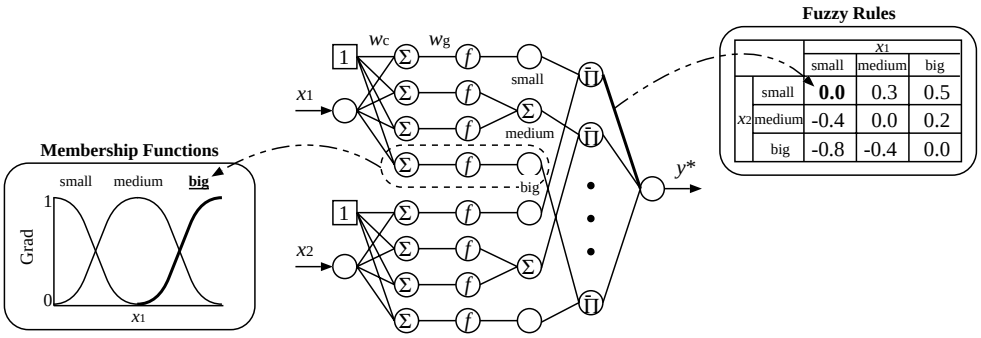

Figure 1: FNN Type-I

3 Results and Discussion

The result of the two-class classification (binder versus non-binder) using the FNN model is given in Table 1. Overall, the FNN model predicts binding affinity of peptides with high accuracy. Especially about non-binder and binder of high-affinity, about 90 percent of peptides were correctly classified. The prediction accuracy of our FNN model is better than those of other methods, including ANN [2].

The number of selected input variables by PIM and fuzzy rules are 8 and 576 respectively. The obtained fuzzy rules follow the results of previous experimental investigations. However, the structure of the obtained FNN model is too complex to grasp the detail of relationship between MHC molecule and peptide. We need to discuss about other methods for optimization of FNN and other amino acid indices which affect binding. Our future objects are reduction of the model complexity and extraction of the rules of MHC-peptide interaction.

Table 1: Results of two-class classification using FNN

	Data for Learning	Data for Evaluation
High	95.3%	88.2%
Moderate	88.0%	70.9%
Low	69.7%	55.3%
Non-binder	93.4%	89.4%

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References

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