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Mining Structural Patterns for Automatic Protein Function Prediction

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To

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Abstract

Protein function prediction is a challenging problem in bioinformatics. It has a great impact on the areas of diseases treatment and drug industry. Structure-based proteins representation plays an important role in proteins function prediction process. Three aspects of protein functions prediction have been considered: Predicting enzymes family and superfamily, classifying enzymes versus non-enzymes proteins and discriminating DNA-binding and non DNA-binding proteins. The thesis presents a modification to an existing protein representation approach which utilizes distance patterns between protein residues and a maximum cutoff. Also, the thesis presents a new protein structure representation for efficient protein function prediction. The new representation is based on three-dimensional patterns of protein residues. It utilizes atoms coordinates of protein residues, including the angles and distance patterns. This thesis also presents a study of the proposed protein representation and other protein-derived sequence, psychochemical and structure features to enhance the prediction of DNA-binding proteins and their classes.

Summary

One of the challenging problems in bioinformatics is the prediction of protein function. Protein function is the main key that can be used to classify different proteins. The analysis of proteins and their functions is an important research area. Such analysis affects many applications like clarification of the living body mechanism, treatment of diseases and drug industry. Protein function can be inferred experimentally with very small throughput and high cost or computationally with very high throughput and lower cost. Many of protein sequences and structures are available but with no knowledge about their function. Therefore, methods for protein function prediction are highly and continuously required. Computational methods are based on protein sequences or structures. Protein functions are highly related to their structures. Therefore, structure-based proteins representation plays an important role in the prediction process.

This thesis presents a modification to an existing protein representation approach which utilizes distance patterns between protein residues and a maximum cutoff. The proposed modified representation considers the whole protein instead of using cutoff. Comparative analysis was done to evaluate the proposed representation method and the existing method. The aspect of protein function considered is based on enzyme activity. The results show that the proposed representation outperforms the existing representation with a prediction accuracy of 90.12% and 80.27% for superfamily and family level, respectively, with accuracy improvement of about 5% in average.

This thesis also presents a new structure-based protein representation for efficient protein function prediction. The new representation is based on three-dimensional patterns of protein residues. It utilizes atoms coordinates of protein residues, including the angles and distance patterns. The proposed representation uses protein structure only with no need to any sequence information. Besides, it does not need any prior alignment process. The aspects of protein functions considered using different datasets: Predicting enzymes family and superfamily and classifying enzymes versus non-enzymes proteins. The prediction accuracy of the proposed representation using various classification methods outperforms a recently introduced representation that is based only on the distance patterns. The results show that the proposed representation achieved prediction accuracy of 98.3% in predicting superfamily, 91% in predicting family and 79.25% in predicting enzyme proteins, with improvement of about 10% on average.

Finally, the thesis presents a study of different protein-derived sequence, psychochemical and structure features. The objective was to enhance the prediction of DNA-binding proteins and classes. This is achieved through finding efficient protein representations that able to predict whether a protein is DNA-binding protein and analyzing how well protein-derived representations predict each of DNA-binding protein classes. The protein features achieved accuracy improvement of about 7% on average for the prediction of DNA-binding proteins. The proposed representation when combined with other features achieved improvement in accuracy about 7% and 12% on average for the prediction of DNA-binding proteins and DNA-binding protein classes, respectively.

Table of Contents

Acknowledgement.....	ii
Abstract	iii
Summary	iv
Table of Contents	vi
List of Figures.....	ix
List of Tables.....	xi
List of Abbreviations	xiv
Chapter 1 Introduction	1
1.1 Overview.....	1
1.2 Motivation	1
1.3 Objective	2
1.4 Thesis Organization	2
Chapter 2 Background.....	4
2.1 Introduction	4
2.2 Bioinformatics	4
2.3 Proteins	5
2.4 Data Mining.....	16
2.4.1 Classification	17
2.4.2 Performance Measures.....	18

2.5 Summary	20
Chapter 3 Related Works	21
3.1 Introduction	21
3.2 Protein Representations.....	23
3.2.1 Sequence-Based Protein Representations	24
3.2.2 Structure-Based Protein Representations	26
3.3 Methodologies and Applications.....	28
3.3.1 Sequence-Based Function Prediction Methods	29
3.3.2 Structure-Based Function Prediction Methods.....	35
3.4 Protein Function Prediction Evaluation	38
3.5 Summary.....	39
Chapter 4 Proposed Protein Representations.....	41
4.1 Introduction	41
4.2 MCSM Representation	42
4.3 A Comparative Analysis of MCSM and CSM	48
4.3.1 Dataset.....	48
4.3.2 Experiments Setup	48
4.3.3 Results and Discussion	49
4.4 A New Protein Structure Representation	57
4.4.1 Protein Structure Matrix (PSM)	57
4.4.2 Protein Structure Matrix with Cutoff (PSM-C)	59
4.5 Evaluation of PSM and PSM-C	64
4.5.1 Datasets.....	64

4.5.2 Experiments Setup	64
4.5.3 Results and Discussion	65
4.6 Summary	73
Chapter 5 Enhanced Prediction of DNA-Binding Proteins and Classes	74
5.1 Introduction	74
5.2 Methodology	76
5.3 Datasets and Experiments Setup	77
5.4 Feature Selection.....	80
5.5 Prediction of DNA-Binding Proteins	83
5.6 Prediction of DNA-Binding Classes.....	98
5.7 Summary	107
Chapter 6 Conclusion and Future Work	108
6.1 MCSM Protein Representation.....	108
6.2 PSM and PSM-C Protein Representations.....	109
6.3 Enhanced Prediction of DNA-Binding Proteins and Classes.....	110
6.4 Future Work.....	111
List of Publications	113
References	114

List of Figures

Figure 2.1 The process of protein formation.....	6
Figure 2.2 Amino acid chemical structure.....	8
Figure 2.3 The protein structure levels [9].....	10
Figure 2.4 Dihedral Angles.....	14
Figure 3.1 Protein function prediction framework.	22
Figure 3.2 Protein representations approach.....	24
Figure 3.3 TOPS representation of bop2 protein.....	28
Figure 4.1 Protein Features Matrix.....	42
Figure 4.2 contact graph topology for protein PDB:2ZFG at different cutoff values: 6 Å, 9 Å and 12 Å [31].	43
Figure 4.3 CSM Algorithm.....	44
Figure 4.4 MCSM Algorithm.....	45
Figure 4.5 The flowchart of CSM representation.....	46
Figure 4.6 The flowchart of MCSM representation.....	47
Figure 4.7 Prediction Accuracy using Random Forest for (a) superfamily and (b) family level with non-zero minimum distance.	51
Figure 4.8 Prediction Accuracy using KNN for (a) superfamily and (b) family level with non-zero minimum distance.....	52
Figure 4.9 Prediction Accuracy using Random Forest for (a) superfamily and (b) family level with zero minimum distance.	55
Figure 4.10 Prediction Accuracy using KNN for (a) superfamily and (b) family level with zero minimum distance.....	56
Figure 4.11 The distance and angle between two residues [127].....	57
Figure 4.12 Protein Structure Matrix (PSM) for a set of proteins.	58

Figure 4.13 PSM Algorithm.....	60
Figure 4.14 The flowchart of PSM representation.....	61
Figure 4.15 PSM-C Algorithm.....	62
Figure 4.16 The flowchart of PSM-C representation.....	63
Figure 4.17 Recall comparison between CSM and PSM-C for different enzymes superfamilies.	71
Figure 4.18 Precision comparison between CSM and PSM-C for different enzymes superfamilies.	72
Figure 5.1 Sensitivity of each feature for P248 dataset.....	85
Figure 5.2 Sensitivity of each feature for P304 dataset.....	86
Figure 5.3 Sensitivity of each feature for P359 dataset.....	86

List of Tables

Table 2.1 Conversion between single and three-letter amino acid codes and RNA codon.....	7
Table 2.2 Hydrophobic values of amino acids.	13
Table 3.1 Comparison of protein subcellular localization prediction methods based on different sequence features using Reinhardt's dataset [72].	33
Table 3.2 Comparison of protein subcellular localization prediction methods using different sequence features on different datasets.	34
Table 4.1 Superfamily prediction accuracy using Random Forest and KNN with non-zero minimum distance.....	50
Table 4.2 Family prediction accuracy using Random Forest and KNN with non-zero minimum distance.	50
Table 4.3 Superfamily prediction accuracy using Random Forest and KNN with zero minimum distance.....	54
Table 4.4 Family prediction accuracy using Random Forest and KNN with zero minimum distance.....	54
Table 4.5 Superfamily prediction accuracy using different classification algorithms.	65
Table 4.6 Family prediction accuracy comparison using different classification algorithms.	66
Table 4.7 Enzyme prediction accuracy comparison using different classification algorithms.	67
Table 4.8 Comparison of superfamily prediction accuracy for PSM-C and CSM with and without SVD.....	68

Table 4.9 Superfamily classification comparison of CSM and PSM-C using Naive Bayes.....	69
Table 4.10 Superfamily classification comparison of CSM and PSM-C using KNN.	69
Table 4.11 Superfamily classification comparison of CSM and PSM-C using Random Forest.....	70
Table 5.1 Summary of proteins datasets.....	78
Table 5.2 Class distribution of DNA-binding proteins datasets	79
Table 5.3 Prediction accuracy using differnt feature selection methods using benchmark datasets.....	81
Table 5.4 Number of correctly classified proteins using each feature for P248 dataset.....	84
Table 5.5 Number of correctly classified proteins using each feature for P304 dataset.....	84
Table 5.6 Number of correctly classified proteins using each feature for P359 dataset.....	85
Table 5.7 Feature representations achieving maximum MCC for P248.....	87
Table 5.8 Feature representations achieving maximum MCC for P304.....	88
Table 5.9 Feature representations achieving maximum MCC for P359.....	89
Table 5.10 Prediction results comparison using P248 dataset.....	91
Table 5.11 Prediction results comparison using P304 dataset.....	92
Table 5.12 Prediction results comparison using P359 dataset.....	93
Table 5.13 DNA-binding proteins prediction results using PSM-C.....	94
Table 5.14 Number of correctly classified proteins using PSM-C.....	94
Table 5.15 Improvements achieved after adding PSM-C.....	95

Table 5.16 DNA-binding proteins prediction results with and without PSM-C using Random Forest.....	97
Table 5.17 DNA-binding proteins prediction results with and without PSM-C using SVM.	97
Table 5.18 The sensitivity and the number of correctly classified proteins using SVM.	98
Table 5.19 Correctly classified proteins using Random Forest for DB54 dataset.....	99
Table 5.20 The sensitivity of each feature using Random Forest for DB54 dataset.....	99
Table 5.21 Comparison of correctly classified proteins using DB54 dataset.	100
Table 5.22 Correctly classified proteins using PSM-C and Random Forest.	101
Table 5.23 Improvement indication after using PSM-C for RDB53 dataset.	103
Table 5.24 Improvement indication after using PSM-C for R239 dataset. ..	103
Table 5.25 Sensitivity comparison of each feature with and without PSM-C for RDB53 dataset.....	104
Table 5.26 Sensitivity comparison of each feature with and without PSM-C for RDB239 dataset.	105
Table 5.27 DNA-binding protein classes prediction results with and without PSM-C.	106

List of Abbreviations

2SAAC	Two-segment Amino Acid Composition
AAC	Amino Acid Composition
AACD	Amino Acid Composition Distribution
ANN	Artificial Neural Network
APGM	Approximate Graph Mining
BLAST	Basic Local Alignment Search Tool
CAFA	Critical Assessment of protein Function Annotation
CDF	Cumulative Distribution Function
CE	Combinatorial Extension
CFS	Correlation-based Featured Subset
CSM	Cutoff Scanning Matrix
DALI	Distance-matrix ALIgnment
DC	Dipeptide Composition
DNA	Deoxyribonucleic Acid
DWT	Discrete Wavelet Transform
EC	Enzyme Commission
ETA	Evolutionary Trace Annotation
FAIR	Finding All Internal Repeats
FASTA	Fast-All
FN	False Negative
FP	False Positive
GAAP	Gapped Amino Acid Pair Composition
GO	Gene Ontology
GRAVY	Grand Average of Hydropathicity Index
KNN	K-Nearest Neighbor
MCC	Mathew Correlation Coefficient
MCSM	Modified Cutoff Scanning Matrix
MD	Moment Descriptor

MIPS	Munich Information Center for Protein Sequences
mRNA	messenger Ribonucleic Acid
MSE	Multi-Scale Energy
NMR	Nuclear Magnetic Resonance
OIT	Optimal and Information Theoretic
PCA	Principle Components Analysis
PcAA	Pair-coupled Amino Acid Composition
PDB	Protein Data Bank
PDF	Probability Distribution Function
PPI	Protein-protein Interactions
PSAS	Pairwise Sequence Alignments Scores
PseAAC	Pseudo Amino Acid Composition
PSI-BLAST	Position-Specific Iterative Basic Local Alignment Search Tool
PSM	Protein Structure Matrix
PSM-C	Protein Structure Matrix using Cutoff
RBF	Radial Basis Function
ROC	Receiver Operating Characteristics
SALSA	Structurally Aligned Local Sites of Activity
SCOP	Structural Classification of Proteins
SSAP	Sequence Structure Alignment Program
SSMBS	Sequentially Separated Motifs in Biological Sequences
SVD	Singular Value Decomposition
SVM	Support Vector Machine
TN	True Negative
TOPS	Topology-based Protein Structure
TP	True Positive