Characterization of Protein-Protein Interactions in Chemokine Family using Sequence-derived Features

Julian Aileru, UNC Charlotte
Irina Nesmelova, Department of Physics and Optical Sciences, Department of Bioinformatics and Genomics

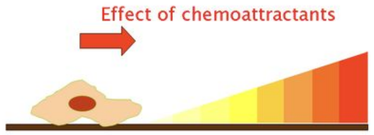
Introduction

Chemokines are a family of small proteins heavily involved in innate immune response and leukocyte migration.

These proteins,which normally exist in their monomeric or homooligomeric state, exhibit unique function in heteromeric states formed with other chemokines

Experimental evidence (reference) has revealed the identity of positive and negative interacting partners of proteins in the family.

With this information, further questions can be asked about the features important to binding

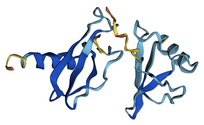


Methods

Principal Component Analysis was conducted to reduce high dimensional data (d=6-26) and observe natural groupings of individual and interacting proteins about orthogonal components.

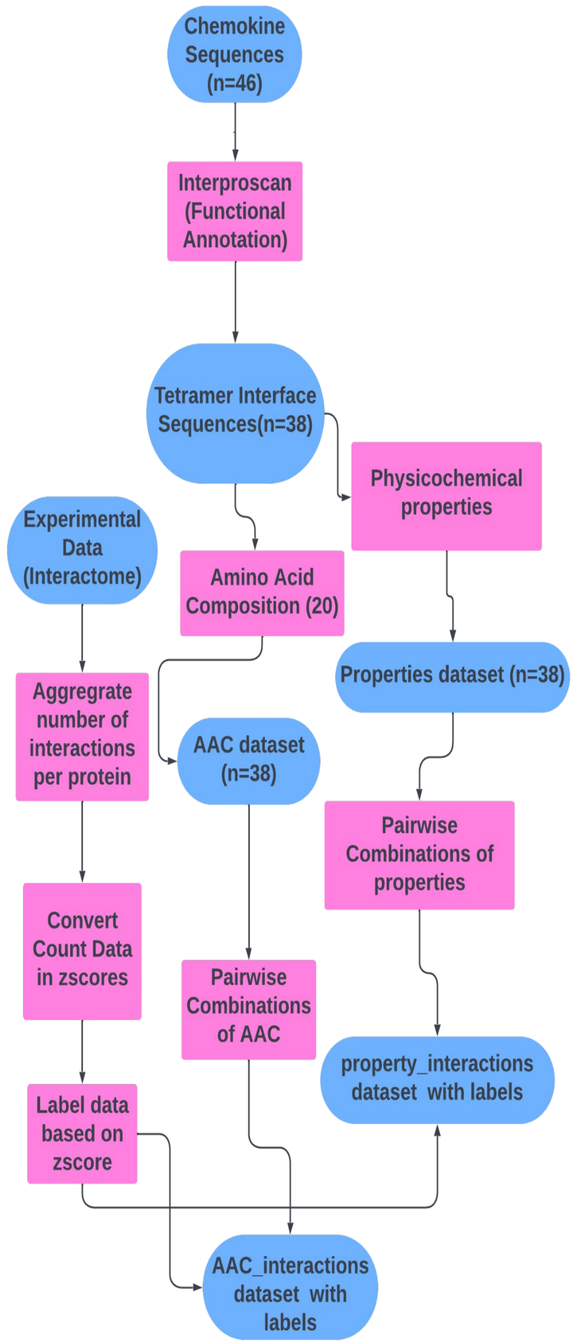
Element-wise vector addition was performed on protein vectors to represent the interacting nature of the two proteins.

Linear Discrimination Analysis was conducted using the features of individual proteins to classify according to CC and CXC type.



CXCL4_CCL20 Computed Structure

Workflow



Results

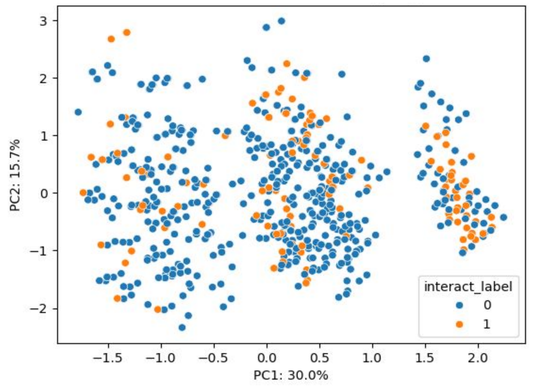


Figure 1.1 - PCA of Pairwise representation of amino acid composition of protein interactions

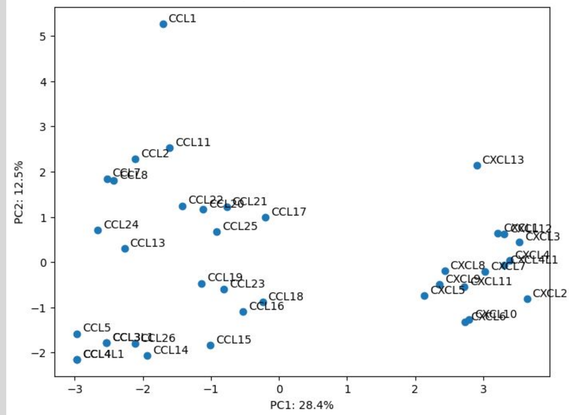


Figure 1.2 - PCA of individual tetramer interfaces using Amino Acid Composition

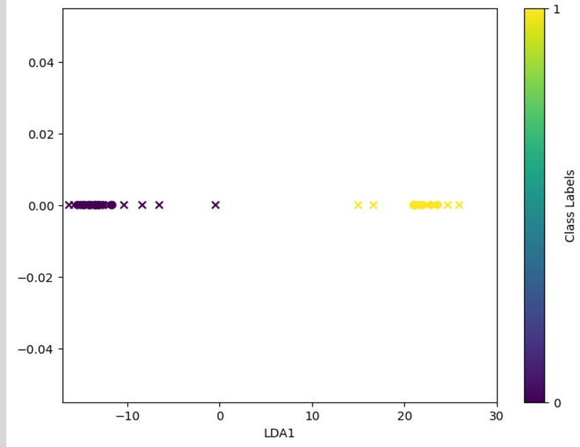


Figure 1.3 - Linear Discriminant Analysis of Amino Acid Composition of CC and CXC tetramer interfaces

Conclusions

Principal Component Analysis of Amino Acid Composition and Physicochemical properties of protein-protein interactions show vague groupings indiscriminate of interaction labels.

The low total variance explained by the two principal components along with the obscure groupings suggest that interacting/non interacting protein partners require a more detailed representation

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Further investigation is required to properly represent protein interactions for classification tasks

Tetramer interface of CXCL4 and CCL2 (positive interaction)

Principal component Analysis of the amino acid composition and the subsequent linear discrimination analysis reveal the ability to classify CC and CXC type chemokines based on the tetramer interface.

References

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