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Protein Surface Characterization Using an Invariant Descriptor

Zainab Abu Deeb
West Virginia University

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Protein Surface Characterization Using an Invariant Descriptor

Zainab Abu Deeb

Thesis submitted to the
College of Engineering and Mineral Resources
at West Virginia University
in partial fulfillment of the requirements for the degree of

Master of Science
in
Computer Science

Donald Adjero, Ph.D., Chair
Arun Ross, Ph.D.
James Mooney, Ph.D.
Bojan Cukic, Ph.D.

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Abstract

Protein Surface Characterization Using an Invariant Descriptor

Zainab Abu Deeb

A novel descriptor to characterize protein surfaces, and hence classify functionally similar proteins into functional families is proposed. The descriptor exploits the protein tertiary structure surface, locally and globally, to identify intra-family proteins. By using only sparse data based on the C- α atoms on the protein surface, we characterize the surface using different invariant descriptors, namely, distance distributions, residue co-occurrences, and distance-residue co-occurrences between all atoms confined to a particular patch. Using the method, proteins with very low sequence similarity were successfully classified into their functional families with a high degree of accuracy.

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Mom, Dad, Fatima, Amal, Areej, Hussain, and Ahmad

This work is for you....

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Chapter1

1. Introduction

The function of a given protein is largely determined by its three-dimensional structure [2]. The specific shape and orientation of proteins in 3D space are key elements that determine how a given protein interacts with its environment, and hence the function of the protein. Although related proteins often have similar functions, it is well known that studying the functional similarity between proteins based only on the amino acid sequences does not always yield expected results [1]. The reason is general sequence and fold similarity do not always translate into protein function similarity [5]. While residues on the protein surface comprise a small percentage of the total residues that make up the protein, they often represent the most conserved functional elements of the protein [4]. Therefore, analyzing protein structures using information about their 3D surfaces is essential in the quest for protein functional annotation, especially in the study of functional similarities between non-homologous proteins.

1.1. Motivation and the Problem

There has been a growing interest in predicting protein functions based on their global similarities by comparing protein 3D structures [1]. The capability to extract information regarding protein function from the surface structure is a critical task in the structural genomic era [6]. Indeed, finding similarities between proteins using sequence alignments had received a great attention. The sequence is used to understand the relationship between sequence-structure-function paradigms. The paradigm is used to infer unknown protein functionality from a homologous protein that shares significant sequence similarity.

Although the one-to-one relationship rule postulates that similar sequence leads to similar structures and finally to similar functionality, this usually does not hold [15]. Some homologous proteins share significantly low sequence similarity and the sequence alignment approaches fail to identify them as homologs. This, problem can be solved using the protein structure which is more conserved over evolution than the sequence. As the number of protein structures with unknown functionality stored in the Protein Data Bank (PDB) increase rapidly, this poses a critical challenge for using the structural information to determine protein functionality.

A major difficulty in comparing protein surfaces locally is the problem of matching 3D structures, since structures need to undergo an exhaustive amount of rotation and translation in order to obtain an adequate structural alignment and to perform an accurate matching [5]. Several algorithms have been proposed to mitigate this problem, for example, Fourier Transform and Spherical Furrier Transform [20, 21]. Nevertheless, these methods are exhaustive and require a heavy computational overhead when it is been applied on large datasets, such as the PDB. The speed of any algorithm is an important factor to consider when implementing a tool to compare protein structures. Therefore, several methods make use of different descriptors to compute the profile of the protein and perform fast comparisons for local matching such as 3D Zernike and Spherical Harmonic [1,7]. Others make use of global geometric properties by capturing shape information in the form of probability distributions, thus reducing the shape-matching problem to that of histogram matching [5].

In this work we study the problem of classifying proteins into their functional families without considering the sequence similarity. This problem is a challenging one where many obstacles must be overcome.

1.2. General Approach

In this work, a novel descriptor for protein tertiary structure (chains) is introduced where the complexity of comparing protein structure is reduced to a problem of comparing their descriptors. The basic idea is to create a descriptor of the protein chain that captures the co-occurrence of specific residues on the protein surface and use this descriptor to determine functional similarity between proteins.

1.3. Main Contribution

We introduce a novel invariant global descriptor to characterize a protein surface by exploiting a sparse set of atoms (namely the C- α atoms) on the surface. This descriptor is extracted from local patches on the protein surface by averaging local descriptors acquired from patches with similar central residues. Applying such a method has the advantage of avoiding exhaustive alignment and transformations, and hence speeding up the process of similar protein surface retrieval. The method also avoids the time-consuming triangulation required to generate the protein surface graph, before scanning for patches. Our approach is unique in utilizing the residue co-occurrences on the surface of the protein. This way we preserve the key functional elements of the protein (the residues represented by the C- α atoms) and reduce the amount of information to be processed by more than half. Additionally, we avoid exhaustive matching between patches on the surface by averaging the local descriptors into one descriptor that can provide a faithful representation of the protein surface. This allowed us to perform fast classification and retrieval of functionally similar proteins based on our characterization of their surfaces.

1.4. Thesis Organization

The thesis is organized into four chapters. Chapter 2 describes the background to the problem we wish to address, and related work. Chapter 3 describes the proposed methodology used in this work. Chapter 4 provides our experimental results, while Chapter 5 concludes the thesis.

Chapter 2

2. Background and Related Work

In this chapter we provide a short description of the background of the problem we address and prior work that is closely related to our approach.

2.1. DNA, Protein, and Diseases

DNA is an important storage device for genetic materials. The information stored in the DNA is what can transform inactive molecules into functional cells and organisms, that can regulate the chemical composition of a protein as well as the their progression and reproduction of the molecule. It is what gives us the ability to inherit several traits from our predecessors [3,13].

Proteins are what alter the cell's chemistry by allowing specific chemical reaction to take place faster than it would be otherwise [13]. The process in which the sequence of genes is extracted and utilized to produce proteins is the same for all living creatures. This follows from the **Central Dogma** of molecular biology, in which, information from DNA is used to transcript into RNA and the information from RNA is used to translate to protein.

Proteins are the molecular kit to perform the work inside both prokaryotic and eukaryotic cells. Proteins have a huge and diverse list of functions, such as supporting bones, metabolizing food, and transporting small molecules through an organism etc. [13]. Each protein retains a specific 3D shape and is usually composed of 1000 to 50,000 atoms [14]. Indeed, proteins control our individualities in some sense, since the functional portion of any cell is determined by the amino-acid sequence of the protein. For instance, **immunoglobins**, which are a large group of proteins, control the functionality of our immune system, and hence, how we fight varying types of infections [14].

2.2. Protein Sequences, Structure, and Surface

Regardless of the tremendous amount of variation in functions and the 3D shape, all proteins share a mutual structure. Proteins are composed of 20-amino acids that are connected via peptide bounds [3]. Those amino acids are only different in the group **R** (see Figure 1), and consist of an amino group (NH) and carboxyl acid group (COOH). The constant part of the amino acid is referred to as a **backbone** while the group **R** is referred to as a **side chain** [13]. Each protein is composed of different number of the 20 amino acids organized in different order. The order of which these amino acids are connected is referred to as the Protein sequence, or the **primary structure** of the protein [13]. Table 1 shows the twenty amino acids.

Figure 1: The common structure of amino acid [17]

The protein does not remain in a stable form of simple chain, but rather it folds and collapses into more complex structures. The order of amino acids in the protein determines the fold structure of the protein. All proteins are composed of four common structural types: primary structure, secondary structure, tertiary structure, and quaternary structure. The primary structure is simply the amino acid sequence. The secondary structure is formed by patterns of intermolecular bonding of hydrogen, and is determined primarily by the location and the directions of these patterns [13]. The overall 3D shape of the secondary structures determines the tertiary structure of the protein. When two or more

chains combine to form a larger molecule, the whole structure is referred to as the quaternary structure. Figure 2, provides an example of the structures that comprise the protein (the sequence is not included). In order to predict the function of a protein, it is common that the function is inferred from a known homologous protein [16]. Functions of novel proteins can be determined by sequence comparisons. Nevertheless, when proteins evolve, the protein structure remains more highly conserved when compared to the sequence. Protein sequences change more easily during evolution due to residue mutations, substitution, for instance by substitution, insertion, or deletion [16]. Hence, proteins that belong to the same family (homologous proteins) may not be identified using sequences alone. Considerations of the protein structure become mandatory in such situations for further analysis of functional similarity between proteins.

Table 1: The 20-protein Residues type

Residue Type	Name
Ala	Alanine
Arg	Arginine
Asn	Asparagine
Asp	Aspartic acid
Cys	Cysteine
Glu	Glutamic acid
Gln	Glutamine
Gly	Glycine
His	Histidine
Ile	Isoleucine
Leu	Leucine
Lys	Lysine
Met	Methionine
Phe	Phenylalanine
Pro	Proline
Ser	Serine
Thr	Threonine
Trp	Tryptophan
Tyr	Tyrosine
Val	Valine

Figure 2: Protein 2UDI Structures
The components of the figure are produced using PMV[11]

Using structural analysis, Orengo et al, reported that proteins related to the same family could share fewer than 15% identical residues [16]. Table 2 shows some examples of related family proteins that share a very small percentage of sequence similarity. Appendix

C provides more detailed information on the sequence similarity within a functional group using **Smith-Waterman** alignment method.

Table 2: Text Representation of the Smith-Waterman Sequence Alignment
10.76 % similarity between the query protein 1ssp and 1UGI. (b) 7.79 % similarity between the query protein 1UDI chain E and the subject protein 2UGI chain A.

a)	
1SSP.E 15	EFGKPYFIK--LMGFVAERKHYTVYPPPHQVFTWTQMCDIKDVKVVLGQD-PYHGP 69
	
1UGI.A 11	ETGKQLVIQESILM--LPEEVVEEVIGNKPESDILVHTAYDESTDENVMMLLTSDAPEYKP 67
b)	
1UDI.E 57	QTEEVV--PPREDVFSWTRYCTPDEVVRVVIIGQD-PYHHP 93
	
2UGI.A 28	EVVEEVIGNKPESDILVHTAYDESTDENVMMLLTSDAPEYKP 67

In the other hand, the protein structure retains a significant portion of similarity even between distance homologs (see Figure 3). This contributes to more than half of the interior of protein surface. In general, the degree of the structural similarity and sequences similarity substantially varies between protein families, where some families can handle more changes than others. This degree of change is called **structural plasticity** [15]. This change can have a considerable impact on the functionality of some proteins, yet in some other families this change does not affect the protein function. Some proteins might share similar structures, yet are not homologues. Thus similarity in structure does not necessarily imply sequence, or functional similarity. Nevertheless, this case is not addressed in this work.

Biologists follow a classical method to derive the protein function, where they start by determining the 3D protein structure before inducing its function [15]. Indeed, the protein 3D structures provide information about the binding site, active sites, and how proteins interact with each other, as well as providing an insight to the protein function [15]. In fact, how proteins interact with each other and with other molecules (e.g. ligands) are determined by the amino acids on the protein surface [16]. The knowledge of the amino acids on the protein surface allows us to understand what molecules are binding together

and sometimes why they bind [16]. It also provides significant information on protein functions that cannot be detected in the absence of protein sequence similarity. Therefore, the analysis of protein surfaces is important in the study of the intermolecular interaction. This knowledge is invaluable to the design of drugs and in the fight against various diseases. Knowing the shape of proteins that are responsible of causing lethal diseases (such as cancer) could facilitate the design of the appropriate drugs, since the organism generates antibodies with specific shape (key) that can attack the lethal protein [16]. Advances in this area will surely advance the field of drug design.

Figure 3: The secondary structure and the Tertiary structures of the sequences provided
The components of the figure are produced using PMV[11]

2.3. Protein Surface Characterization Methods

Given the foregoing, it is not surprising that methods have been proposed to characterize the protein surface. A recent work [5] uses the idea of applying fingerprint matching on circular protein surface patches. These patches are obtained by generating the dot surface of the protein and constructing a graph to approximate the protein surface. Afterwards, the circular patches are generated as a continuous surface area from a center

point, where the radius of the patch is within a predetermined cutoff. Indeed, the patches are created for each single point in the surface. Afterward, a fingerprint for each patch is calculated from a center vertex as a geodesic distance-dependent distribution of directional curvature. The comparison between the fingerprints was performed using the Average Fingerprint Similarity Score (AFSS) and the Direct Fingerprint Similarity Score (DFSS). Final scores are computed after an alignment procedure based on AFSS. Seal et al. [1] introduced 3D Zernike to the area of protein structural similarity matching, in which the protein 3D structure is represented as a series expansion of 3D functions. In this approach, the triangulated Connolly surface of the protein is computed (using MSROLL version 3.9.3), where the protein is placed into a 3D cubic grid and voxelized. Each voxel has a value of 0 or 1 and the internal part of the protein is left empty. The 3D Zernike function is projected into the 3D protein shape to obtain the 3D Zernike descriptors. Therefore, the 3D comparison problem is reduced to comparing two vectors representing the 3D Zernike descriptors for each protein surface. Several distances were tried such as the Euclidean distance, Manhattan distance and a correlation-based distance that is defined as the complement of the correlation coefficient between two Zernike descriptors. In more recent similar work, Sael and Kihara [22] used the Zernike descriptor to study protein surfaces in low resolution data. Venkateraman et.al [7] focused on the use of the spherical harmonic and the 3D Zernike descriptors to retrieve functionally similar proteins by representing the proteins as a unique set of numbers. Jones and Thornton [19] analyzed protein-protein interaction by exploiting surface patches. In their work they extracted six parameters of solvation potential, residue interface propensity, hydrophobicity, planarity, protrusion, and accessible surface area for each surface patch in a protein. They used the notations of central surface accessible residue patch, and the solvent to define a patch. The patch is constructed by using the C- α atoms that have a predetermined accessible surface area, and adhere to the constraints on the solvent vectors. Then ranking among the patches was established using these parameters. Ferrè et. al [6] discovers locally similar structures by matching patches composed of subsets of amino acids. In their work, they reduce the dimensionality of the

atoms space through the creation of pseudo-residue for each residue as two points composed of C- α and the center of the side chain atoms. Then a legitimate match can be identified as the one that has decent residue similarity based on the substitution matrix and a low root mean square distance. Choi et. al. [18] identified similar protein structures through the use of finite local features from the distance matrices formed from the C- α positions. They encoded the C- α distance matrix for each protein by assigning its submatrices to the nearest local feature. The resulting protein structure is then represented using the frequency distribution of the local feature indices.

2.4. The Problem

Categorizing proteins into families could provide invaluable information about protein functions. It could also help in a deeper understanding of the evolution of proteins and of the ability of the proteins to tolerate changes in both sequence and structure [16]. Consequently, the task of classifying proteins is non-trivial, since the protein is a multi-structural molecule that consists of primary, secondary, tertiary, and quaternary structures. The problem of classifying protein structure into families is different than that of protein sequence, since most of structural classification has been performed on the most evolutionary unit of the protein, which is the domain/ tertiary structure [15]. The problem of identifying protein function is a multi-faceted one. On the one hand, similar sequences could predict similar structure and similar structure can predict similar function, which is the desired outcome. On the other hand, similar protein sequences suggest similar structure, yet similar structure does not always correspond to a similar function. Additionally, similar fold may have similar functions, however, this is not always the case. Focusing on one part of the problem (for instance the surface) brings some more problems. For example, how do we represent the surface? What features to extract? Local or global? How do we define the features (e.g patch)? etc. Once that is solved, the next stage would be the computational complexity. How long would it take to extract these features? What

searching method to use? How do we define a patch? Therefore, the main task at hand is to classify a given functionally unknown protein to its homologous 3D structural family by exploiting the proteins' 3D structural surface, and that of its individual domains. Computationally efficient methods for this task are mandatory especially given the fast pace in which structures of unknown function are being stored in the PDB [22].

Chapter 3

3. Methodology

In this work, an invariant descriptor for each circular patch on the protein surface is defined, based on the residue distances from the center of the patch. The descriptor records the distance distribution between the residues within the patch and keeps track of the number of particular pair-wise residue co-occurrences in the patch. Lastly, a global descriptor is created to represent the whole protein tertiary structure by taking the average of the similar central descriptors. This will result in a standard descriptor for each protein tertiary structure with a fixed patch size. Thus, the standard descriptor can facilitate the matching of protein chains in an efficient manner and will eliminate the need for the exhaustive alignment of the protein 3D structures. This method has been applied on three proteins families: uracil-DNA glycosylase, estrogen receptor, and cell division protein kinase 2. These are the same protein families used in a recently published work [5]. The following steps summarize the methodology used:

- Obtain the protein data from the PDB database, generate the protein chain surfaces and keep track of the C- α atoms and their residue type.
- Generate the surface patches and the invariant descriptor for each patch.
- Perform matching and classify the proteins chains.

3.1. Surface Generation

To generate the protein surface, the protein file in the .pdb format is preprocessed using **Cygwin**, which is a Unix like environment for windows, to execute the **pdb_to_xyzr** and **atmtypenumbers** programs. The program **pdb_to_xyzr** produce the x, y, and z coordinates from the pdb file where the **r** represents the radius of the atoms. The program **pdb_to_xyzr** depends on the program **atmtypenumbers** to transform the pdb atom names into Connolly numeric codes and atomic radii [10]. This step is vital to the **MSMS** program version 2.6.1 from the Scripps Institute [11] to generate the dot surface (.vert files/ vertices files) for a given protein since **MSMS** expect .xyzr file as an input. During the stage of using **MSMS**, the probe radius parameter of the **MSMS** was tuned to be 1.4 Angstrom for generating the protein surface (dot surface). Next, **MATLAB Bioinformatics toolbox** was used to extract the proteins chains and to generate the surface for each chain. In this step, the chains are extracted while preserving the coordinates of C- α atoms and their type by extracting the information from the pdbs and the vertices files. Ultimately, the chains that are known to be a part of one of the families aforementioned are manually selected to create the dataset that is ready to be processed. Figure 4 shows the detailed process of surface generation.

3.2. The Invariant Descriptor

In order to capture protein structure similarities and to avoid the computational complexity and the time-consuming problem of aligning 3D protein structures, we propose the use of a global rotational invariant descriptor to describe overlapping circular patches on the surface. This descriptor is comprised of 20 distinct descriptors that represent each of the 20-protein residues types, which are listed in Table 1. For each residue on the surface (central residue), we consider its type and we look for all the residues within a certain distance threshold τ_p to obtain a circular patch. A descriptor for that patch is created by

calculating the distribution of all distances between the central residue and all other surface residues within the patch. Additionally, the residue co-occurrences within the patch are also recorded as a part of the local descriptor and a matrix D_A is created to represent this descriptor. The 2D Matrix D_A for each local descriptor is created where the size of D_A is $(20+1) \times (b+1)$. Here, $(20+1)$ represents the number of the rows in the matrix where the number 20 is used to represent each of the 20 distinct protein residues and the extra row is used to describe the general/ global distance distribution within the patch. The number of columns has been chosen to represent the number of bins b that was used to divide the distance distributions and the extra column is used to represent the residue co-occurrences.

Figure 4: Tertiary structure surface generation

This process is repeated for each residue on the surface, and therefore, the number of local invariant descriptors will be equal to the number of residues that compose the chain

surface. This number can vary from tens to hundreds and sometimes to thousands of residues that constitute one chain. However, using a huge number of local invariant descriptors for one chain to perform the matching requires an exhaustive search and would be very time-consuming. To overcome this problem, for a given chain the global rotation invariant descriptor is defined by combining the 20 distinct descriptors based on the 20 proteins residue types. Thus, all of the local descriptors for that particular chain have been reduced into one global descriptor by taking the average of all of the descriptors that belong to each given residue type and represent the result as a distinct part of the global descriptor to that chain. Figure 5 shows a schematic diagram for the procedure used in constructing the local and global descriptors.

3.2.1. Distance Distribution (DD2)

The basic idea of using the distance distribution is that similar functional proteins should have a similar distance distribution between the residues on their surfaces. The local patch descriptor captures the distribution in two forms. The first form is a detailed distance distribution between the central residue in the patch and each of other residues on the surface. To achieve this, a uniform distribution of the distances is assumed and the total number of bins b is used to estimate the probability distribution of finding a pair of residues at one of the b ranges. The second form is the global distance probability distribution. In this form we estimate the probability of observing any residue within a patch in a particular distance range from the central residue. Although the proposed descriptor captures the distance distribution in two forms, we investigate the importance of using the global distance distribution alone in identifying similar proteins surfaces and therefore protein with a similar function. Consequently, the question to be answered is, given a central residue, what is the distance distribution of the residues around the central residue? Basically, we try to find the probability of observing distance d_i between two

protein residues (as represented by their C- α atoms) on similar protein surfaces. According to the aforementioned assumption, we estimate that this probability should be similar for surface patches from functionally similar proteins.

Figure 5: Schematic diagram for the methodology used in creating the local and global descriptors. Some components of the figure are produced using PMV[11]

3.2.2. Residue Co-occurrence (RC)

Based on the assumption that functionally similar proteins have certain similar residues that cover their surfaces, the invariant descriptor is also designed to accommodate for residue co-occurrences on the protein surface patch. Using the distance distribution globally provide an idea of how the distances are distributed on the protein surface patch from the central residue. However, there is no constraint on or indication of which residues are involved in the formation of these distributions. The co-occurrence of given residues from the central residue is calculated by computing the number of times that residue occurs on the patch from the central residue. Thus, the main problem would be to find the probability of observing residue R_i , given a central residue R_c . Again, we expect that the probability $P(R_i|R_c)$ should be similar for protein surfaces from functionally similar proteins.

3.2.3 Distance-Residue Co-occurrences (DRC)

In this step, we investigate the significance of combining the general distance distribution (represented as a row vector **sumC**) and the residue co-occurrences (represented as a column vector from the global descriptor **sumR**) in identifying similar protein surfaces. The residue-distance co-occurrence vector (D_{RC}) is defined as in (1).

$$D_{RC} = (sumC \circ sumR^T) \quad (1)$$

where $\circ$ is the concatenation operator and x^T stands for the transpose of x

D_{RC} is used to calculate the conditional probability $P(d | R_i, R_j)$, that is, the probability of observing the distance d between residues R_i and R_j given that R_i is at the center of the patch. We expect that the residue co-occurrence (**sumR**) should carry more distinctive

functionally relevant information than the general distance distribution (**sumC**) since surface residue-co-occurrences are likely to be more conserved over evolution. By combining both vectors, we can account for both the geometry of the protein surface, and the distribution of specific residues within specific distances on the protein surface. Using both vectors brings in some biological relevance in the analysis and is likely to lead to improved performance in the identification of functionally similar protein surfaces.

3.3. Matching and Classification

Given two proteins, say Protein 1 and Protein 2 we represent them with their representative global descriptors, D_{g1} and D_{g2} respectively. In our work, the global descriptors could be the: Distance Distribution, Residue Co-occurrences, and Distance-Residue Co-occurrences.

3.3.1. Distance Distribution

For matching using the distance distribution we create a vector D_{g1d} that is composed of the 20 global distance distributions represented by all **sumC** vectors from each descriptor where D_{g1d} is defined as follows

$$D_{g1d} = (D_{d1} \circ D_{d2} \circ \dots \circ D_{d20}) \quad (2)$$

where $D_{d1}, D_{d2}, \dots, D_{d20}$ are the distance distribution from each distinct descriptor in the global descriptor for the chain of Protein 1. Repeat the same process for Protein 2 to create D_{g2d} . Then we perform the matching process by taking the simple Euclidean distance.

$$D_{12} = \left[\sum_{i=1}^n [D_{g1d}(i) - D_{g2d}(i)]^2 \right]^{\frac{1}{2}} \quad (3)$$

3.3.2. Residue Co-occurrences

For Protein 1 we create a vector D_{g1c} that combines the 20 residues co-occurrence vectors that are denoted by **sumR**, where D_{g1c} is defined as follows

$$D_{g1c} = (D_{c1}^T \circ D_{c2}^T \circ \dots \circ D_{c20}^T) \quad (4)$$

where $D_{c1}^T, D_{c2}^T, \dots, D_{c20}^T$ represents **sumR**₁^T, **SumR**₂^T, **sumR**₂₀^T. Similarly, we compute D_{g2c} . Matching is performed using the Euclidean distance between D_{g2c} and D_{g1c} .

3.3.3. Distance-Residue Co-occurrences

For matching two proteins using the Distance-Residue Co-occurrences we create a vector **DRC** that is comprised of all of the distance distributions as well as the residues co-occurrences. For Protein 1, we define the following

$$DRC_1 = (D_{d1} \circ D_{c1}^T \circ D_{d2} \circ D_{c2}^T \circ \dots \circ D_{d1} \circ D_{c1}^T) \quad (5)$$

Similarly we obtain DRC_2 for Protein 2. Again the matching can be performed using a simple Euclidean distance. Here we have used the Euclidean distance. Clearly, other distance measures could be used.

The classification is accomplished by applying several classification methods. The ones used include simple KNN classification and simple PCA classification using KNN. We also tried other classification schemes via the **WEKA** environment such as Simple Logistic classification, Complement Naïve Bayes, Naïve Bayes, Naïve Bayes Multinomial, Naïve Bayes updateable and J48 classifier.

Chapter 4

4. Results

This section describes detailed experimental results of applying the methodology proposed in Chapter 3, where we generate the local and global invariant descriptors.

4.1. Dataset

A dataset of three protein families: uracil-DNA glycosylase, cell division protein kinase 2, and estrogen receptor was created by scanning the PDB database and selecting the pdb files of those proteins that has chains belonging to one of the three families. The dataset used in the following experiments contains 416 chains that belong to 243 proteins. The dataset is distributed in the following fashion: 91 chains from 46 distinct proteins for **uracil-DNA glycosylase** (Group1), 186 chains from 95 distinct proteins for **estrogen receptor** family (Group2), and 139 chains from 102 distinct proteins from **cell division protein kinase 2** (Group3). The detailed dataset is provided in Appendix A.

4.2. Classification

In the classification part we divide the dataset into training and testing sets and we apply different classifiers on the different descriptors proposed and show the classification rate accordingly. For the following experiments we set the patch threshold $\tau_p = 10$. That is, we create the circular patch by searching for the nearby residues that fall within a distance threshold 10 Å. We also fixed the number of bins **b** for the distance distribution to 5. We used classification algorithms implemented in **WEKA** [23] version 3-6-4 to test the performance of our approach.

First, we explore the impact of the size of the testing set and of the training set on the classification rate using the proposed approach.

4.2.1. Impact of Training Set Size

We apply the Naïve Bayes, Logistic, and Simple Logistic classifiers on the dataset produced by the global invariant descriptor. In this experiment we divide the dataset into training and testing and we vary the training set size using a fix the testing set size. Consequently, we used fixed testing sets of size 100, 200, and 300. However, the training dataset was varying in size for each fixed testing set. Table 3 provides detailed information on the number of samples each group contributed to each training set or testing set.

Table 3: Detailed information on the dataset used for training and testing

Training =300				
	Group1	Group2	Group3	Total
Train	80	116	104	300
Test1	11	20	19	50
Test2	11	54	35	100
Training =200				
	Group1	Group2	Group3	Total
Train	60	70	70	200
Test1	12	20	18	50
Test2	25	40	35	100
Test3	31	69	50	150
Test4	31	100	69	200
Training =100				
	Group1	Group2	Group3	Total
Train	60	40	35	100
Test1	12	20	18	50
Test2	25	40	35	100
Test3	40	60	50	150
Test4	60	70	70	200
Test5	66	94	90	250
Test6	66	130	104	300

Figure 6 shows the effect of changing the training size on the classification rate as recorded by applying **WEKA** implementation of Naïve Bayes, Simple Logistic, and Logistic classifier using the invariant descriptors proposed.

Distance Distributions: The figure shows that applying the distance distribution (DD2) alone resulted on the lowest performance accuracy as compared to using the residue co-occurrences (RC) or the combination of distance-residue co-occurrences (DRC). Yet, our definition of the distance distribution shows encouraging results. Classification using Naïve Bayes on DD2 alone shows a degrading classification performance when the training size increases, however, we still achieved 70% classification accuracy. Indeed, a steady performance can be obtained when applying the simple logistic as well as logistic classifiers on the DD2 alone. One can observe that we achieved around 88% performance accuracy with a training size of 200 and the testing size of 100.

In fact, we are not unique in applying the distance information in protein structure analysis. Residue distances have been used in standard texture based analysis of 2D textures formed by the distances between residues in a protein structure [18]. Binkowski et al [4] introduced the *SurfaceShapeSignature* (SSS) metric, to describe protein global shape by exploiting the global shape geometrical properties to reduce the problem of matching between two 3D objects to that of a comparison of the probability distribution between the two objects. According to [4] this approach was used to perform a quick matching between complex 3D shape structures. In their approach the Euclidean distance was measured between each unique atoms pairs in the surface and then the distances were sorted before applying the Kolmogorov-Smirnov (KS) test. The use of the shape distribution has been proved to be an effective measure that is resilient to scale, rotation and mirroring. However, the key difference in our method is the use of the local patches as defined by the distance distribution between C- α atoms within each protein surface patch conditioned on the specific residue at the center of the patch and the particular residues found within the patch. The proposed method used the dot surface that was used in [5], to extract the C- α atoms that are on the surface of the protein. After that we compute the Euclidean distance distribution for each patch on the protein C- α surface by exploiting the base-1 index that holds the index of the nearest atom in the pdb file.

Therefore, our method is unique in computing the residue-specific distance distributions for the protein surface patches using the protein’s surface C- α atoms, while the C- α atoms of the interior protein residues are discarded.

Residue Co-occurrences on the protein surface: Because using the distance distribution of the local patches will increase the overall time complexity, we use the global distance distribution to soften the searching overhead, thus combining the ideas of using local and global protein information. This allows us to perform even faster comparison between proteins since these global descriptors will confine the local descriptors no matter how many they are to only one descriptor that represents the protein surface. We also avoided the time complexity of generating a graph representation of the surface before the surface can be scanned to generate the patches and then compute the distance distribution as in [5]. Indeed, The results shown below (see Figure 6 and Figure 7) prove that the use of surface residue co-occurrence is efficient and is resilient to model simplification according to [4].

Figure 6: Variation of Classification Rate with size of training set for Naive Bayes, Simple Logistic, and Logistic Regression on the proposed descriptors produced by DD, RC and DRC

Residue Co-occurrences: The distinctiveness of our approach is the use of residue co-occurrences on the protein surface. The results of classifying proteins to their corresponding families based on the residue co-occurrences (RC) provide a significant improvement in classification accuracy using all of the classifiers aforementioned. This approach assumes that functionally similar surface proteins have similar residue co-occurrences within a small local surface region. Thus, similar proportion of all possible predefined residues (20-residues) for each protein. This approach alone improved the classification performance to 98% classification accuracy rate using Naïve Bayes classifier using a testing set of 200 protein chains and training set of 200 chains. This can be compared to the 69% accuracy rate achieved using distance distribution on the same testing. It is interesting that our method can achieve an accuracy rate of 98% using a small training set, (50 samples) and six times larger testing set (300 chains) using the Naïve Bayes classifier. This shows the robustness of the residue co-occurrences, even when using a few training samples. It is important to mention that the DD2 performance using the simple logistic and logistic as well was not as robust as the performance of the RC. The performance was around 64% using DD2 with a small training set as opposed to using a larger training set. The performance using RC is improved steadily as we increase the size of the training set. It stabilized at about 95% as we increased the size of the training set to 300 using the three classifiers. However a better performance of 98% was obtained by performing the simple logistic classifier using 250 training sets on a 100-sample testing set.

Distance-Residue Co-occurrence: The use of distance-residue co-occurrence presents a steadier improvement in the classification rate. Using the DRC raised the accuracy rate to 99% using the simple logistic classifier on a training set of 150 and testing set of 100. The detailed confusion matrix is provided in Table 4. One can notice how effective this method is, that is out of 100 samples only one sample was misclassified. It is important to mention here that there is no overlap between the testing set and the training set.

Table 4: Confusion Matrix for DRC
Predicted Classes

Actual Classes	Predicted Classes			
		Group1	Group2	Group3
	Group1	25	0	0
	Group2	1	39	0
	Group3	0	0	35

4.2.2. Impact of Testing Set Size

Distance Distribution: Similarly to the previous experiments, we explore how the changing size of the testing set as opposed to a fixed training set size can affect the classification accuracy of the proposed method. Again, the Naïve Bayes classifier performed the worst on the training set of 200 protein chain samples when using the DD2, while the testing set changed up to 200 testing samples when the performance degrade to the lowest level of 61%. However, simple logistic and logistic classifiers showed more stable classification performance. Here the accuracy rate is at least 70% and the best performance achieved on the DD2 was 89% using the simple logistic.

Figure 7: Variation of Classification Rate with size of testing set for Naïve Bayes, Simple Logistic, and Logistic Regression on the proposed descriptors produced by DD, RC, and DRC

Residue Co-occurrence: Better performance was achieved when the RC is used where the Naïve Bayes Classifier performed well on these data. The lowest performance of Naïve Bayes when applied on RC was 84% when the training set is fixed to 300 samples using 50 testing samples. As we increase the number of samples in the testing sets, we can see that the classification rate shows significant improvement to 94% using Naïve Bayes. Applying Logistic classifier shows a stunning 99% accuracy when the training set is 300 samples and the testing set is 100. Similar classification rate on the same training and testing sets obtained when applying the simple logistic classifier where the classification rate is equal to 98%. Again, there was no overlap between the testing and training data sets. This shows how powerful and intuitive the technique of using the RC is, since it takes into account the co-occurrence of protein residues that are the backbone to the construction of any protein.

Distance-Residue Co-occurrence: The use of the DRC showed similar to better performance e.g. the logistic classifier in the DRC data performed better than RC since we can see stable increasing in the classification rate, yet the simple logistic and Naïve Bayes showed relatively poorer in the performance.

4.3. Ranking

In this section, we explore the efficacy of our approach on protein surface search and retrieval. We investigate if our approach has the robustness to retrieve most of the functionally similar protein in the top hits given a query protein. Here, a query protein from each of the three groups is used to screen the entire database (416 samples) and provide a ranking based on the similarity. In order to accomplish that, we used the k nearest neighbor search to find the k similar proteins in order of their similarity, where k is set to 416. That is the most similar will be the first one retrieved and so forth. Thus, the ranking is straightforward from 1 to 416. After that, we search over the retrieved proteins to find which rank the functionally similar proteins have achieved. We then measure the performance of our approach using the enrichment plot. We expect that most of the functionally similar proteins should be observed after a small percentage of screening. In other words, the top hits should all fit to functionally similar proteins. Figure 8 and Figure 9, shows two variations of the enrichment plot.

a) Query protein 1UDI chain I from Group1

b) Query protein 1QKN chain A from Group2

c) Query 1YKR chain A from Group 3

Figure 8: The enrichment plot for three query proteins

a) Query protein 1UDI chain I from Group1

b) Query protein 1QKN chain A from Group2

c) Query 1YKR chain A from Group 3
Figure 9: The enrichment plot (second variations)

Here, the enrichment plot shows that our proposed method provides better results as we screen the first few percentage of the dataset. In most of the cases, our method retrieved three times better than the expected random retrieval in the first 1% screened proteins for each of the 3 selected query proteins. As we increase the percent of the screening the retrieval degrades, as we are more likely to retrieve most if not all the proteins in the first few percentages of the screened dataset. Table 5, shows the rank of the retrieved proteins that belong to the same family of the query protein within the top 30 hits using DRC method. Detailed ranking using the other descriptors is provided in Appendix B.

We also provide the performance of DD1, which will be explained in the next section.

Table 5: Ranking the screened proteins according to their similarity to the query protein

RDC on query protein 1UDI chain I (Group 1)				RDC on query protein 1QKN chain A (Group 2)				RDC on query protein 1YKR chain A (Group 3)			
Protein ID	Chain	Rank	Distance	Protein ID	Chain	Rank	Distance	Protein ID	Chain	Rank	Distance
1UDI	I	1	0	1QKN	A	1	0	1YKR	A	1	0
2ZHX	B	2	2.1306	2J7X	A	2	1.3769	2UZO	A	2	1.0396
1LQM	B	3	2.3509	2J7Y	A	3	1.5753	2R3O	A	3	1.0810
1LQG	C	4	2.4589	1QKM	A	4	1.6793	3PXY	A	4	1.0846
2UUG	C	5	2.5353	1NDE	A	5	1.7368	3PY1	A	5	1.0940
1EUI	C	7	2.5920	2GIU	A	6	1.7371	2WMA	A	6	1.1389
2ZHX	L	8	2.6104	1L2I	A	7	1.7460	2IW6	A	7	1.1609
1UGH	I	10	2.6349	1U3R	B	8	1.7670	3NS9	A	8	1.2043
2UGI	A	15	2.6809	3ERD	A	9	1.7683	3IGG	A	9	1.2141
1UGI	E	16	2.6872	3OS9	A	10	1.7715	2WFE	A	10	1.2179
2ZHX	H	19	2.6969	2IOG	A	11	1.7738	2CSY	A	11	1.2270
2ZHX	D	21	2.7006	3LTX	C	12	1.7742	3DDP	A	12	1.2280
2ZHX	N	22	2.7017	1YIM	A	13	1.7854	2J9M	A	13	1.2284
2ZHX	J	23	2.7141	3ERT	A	14	1.7966	2R3J	A	14	1.2374
1UGI	G	25	2.7261	1U3Q	D	15	1.8009	2R3L	A	15	1.2402
				1YY4	A	16	1.8090	3PXR	A	16	1.2422
				2OUZ	A	17	1.8126	2DUV	A	17	1.2534
				1YIN	A	18	1.8152	1W8C	A	18	1.2586
				1XP6	A	19	1.8260	3DOG	A	19	1.2793
				2AYR	A	20	1.8269	2V22	A	20	1.2822
				3OS8	D	21	1.8311	2R3P	A	21	1.2883
				2QH6	A	22	1.8312	2V22	C	22	1.2963
				3OSA	A	23	1.8367	3IG7	A	23	1.3207
				1L2J	A	24	1.8385	2IGZ	A	24	1.3275
				2J3	A	25	1.8438	2R64	A	25	1.3303
				1G50	A	26	1.8490	2WHB	A	26	1.3381
				3OS8	A	27	1.8509	2VTN	A	27	1.3458
				2FSZ	A	28	1.8518	3LFN	A	28	1.3476
				2QGW	A	29	1.8604	2WIP	A	29	1.3514
				1UOM	A	30	1.8683	2BKZ	A	30	1.3580

4.4. Comparative Performance

In this section, the performance of the proposed method using the global descriptor in one of the three forms (DD2, RC, DRC) is compared with the performance of the regular definition of the distance distribution (DD1). An implementation of the DD1 based on what others have done before [18] in different contexts is used here. Here we extract DD1 by discarding any indication to residues information by collecting all the distributions DD2 and then taking the average distance as described in Figure 5 and equation (6). That is, for each bin position we compute:

$$DD1 = \frac{\sum_{i=1}^{20} SumC_i}{20} \quad (6)$$

The resulting vector is then used for surface analysis.

We tested the classification rate by using the three classifiers Naïve Bayes, Logistic, and Simple Logistic as we fixed the training set size and varied the testing set size. Another similar experiment is conducted as we varied the training set size and fixed the testing set size. Figure 10 shows the results.

Figure 10: Variation of Classification Rate with size of training set and testing set on DD1 for Naïve Bayes, Logistic, and Simple Logistic

One can notice that the highest performance of 76% is achieved when the training set is fixed to 300 and the testing set was 100 using simple logistic and logistic classifiers while Naïve Bayes achieved accuracy of 71% on the same dataset. Compared to our method by using the same training and testing sets, 89% is achieved using the simple logistic classifier, 85% using logistic, and 86% with Naïve Bayes on DD2. This shows that our definition of distance distribution DD2 is more distinctive than the regular definition of DD1. Using other forms of the descriptor (RC, and DRC) delivered further improvement on the accuracy (see Table 6)

Table 6: Classification Rate on 300 samples training set and 100 samples testing sets

Classifier \ Descriptor	DD1	DD2	RC	DRC
Naïve Bayes	71%	86%	94%	91%
Logistic	76%	85%	99%	97%
Simple Logistic	76%	89%	98%	91%

To further compare the performance of DD1 with our approach, we investigated the performance of DD1 on retrieving proteins from Group 3 and we observed the ranking. In this experiments, the search is applied using five different proteins from Group 3 and the final ranking was the average ranking. The enrichment plot in Figure 11 shows the ranking results of DD1 compared to our approach. Indeed, our approach showed

robustness in retrieving proteins two times better than DD1, and three times better than the random.

Figure 11: Enrichment plot of DD1, DD2, RC, DRC, and random indicating the retrieval performance of DD1 and the proposed method

Thus, one can see that the global descriptor is a robust identifier of the protein surface similarity as well as the functional similarity in any form used and can provide higher performance accuracy.

Chapter 5

5. Conclusions

This chapter concludes the thesis by presenting some conclusions and possible future directions.

5.1. Conclusions

A novel approach to classify functionally similar proteins into families is introduced. This approach captures the surface structure of the protein by utilizing local patches not on the whole surface, but deliberately on the most informative, central part of the amino acid C- α , which is the main unit that comprises the protein. The novelty of this approach can be observed by the ease of handling both local and global variation on the surface (using local and global descriptors). Moving from local to global does not only reduce the complexity of the problem of matching 3D structure, it also facilitates direct comparison between proteins. By avoiding the construction of the complete 3D surface and retaining only the surface C- α atoms to do the analysis, the need for surface alignment of the 3D structure is eliminated. Further, we do not need to perform any geometrical transformation to insure reliable matching. This is very important for rapid analysis. By capturing the functionally relevant information on the surface of the protein using simple techniques, this will allow a real-time search.

We tested our approach in order to determine the impact of the testing set size and the training set size on the performance. The results are quite stunning that we achieved a stable classification rate of 95% using the simple logistic classifier on the Distance-Residue Co-occurrence. The method performed 94% when classifying 300 samples using only 50 training samples with the logistic classifier. These results are quite encouraging and require further investigation on a larger dataset (the whole PDB for example). All the

experimental results indicate that the global descriptor represented by either the Distance Distribution (DD2), Residue Co-occurrences (RC), or Distance-Residue Co-occurrences (DRC) is a robust descriptor that can perform excellently well in protein family classification. This new direction of avoiding the complete surface construction and using only the sparse data provided by the C- α positions shows that for protein surface characterization, we could apply the concept of “Less is more”. Perhaps more significantly, this provides an effective yet efficient method for the process of retrieving or identifying functionally similar proteins with little or no sequence similarity.

5.2. Future Work

Using the global surface descriptor and incorporating knowledge of the residues provides us with some biologically relevant information about the protein families. To further investigate this issue, we plan to use more functionally relevant information into the construction of the global descriptor. We propose the use of the 7-class functional grouping to expand the idea of using the global descriptor. We therefore, can reduce the feature space significantly and hopefully improve the results further. We also plan on testing this descriptor on the whole PDB to ensure its accuracy in providing reliable large scale searching at a considerable speed. We would like to explore the possibility of creating one representative descriptor for each protein family and then we can use the idea of bag of features to predict functionally similar proteins.

Appendix A

Detailed Information of The Dataset

Group 1: Uracil –DNA Glycosylase
46 proteins, 91 chains

Protein ID	chains
1SSP	E
2SSP	E
1UGI	A,B,C,D,E,F,G,H
2UGI	A,B
4SKN	E
1AKZ	A
1LAU	E
1UDH	A
1UDI	E,I
1UDG	A
2BOO	A
1YUO	A
1VK2	A
1OKB	A,B
1Q3F	A
1UI0	A
1UII	A
1LQJ	B
1LQM	A,B
1FLZ	A
1EMH	A
1EMJ	A
3A7N	A
2DP6	A
2DEM	A
2DDG	A
2HXM	A
2D3Y	A
2CS3	A
2CS6	A
3FCL	A
3FCI	A
3FCF	A
3CXM	A
2ZHX	A,B,C,D,E,F,G,H I,J,K,L,M,N
2OYT	A
2OXM	A
2OWR	A,B,C,D,E,F,G,H
2OWQ	A,B
2JHQ	A
3FCK	B
2UUG	A,B,C,D
1UGH	E,I
1LOG	A,B,C,D
2J8X	A,B,C,D
1EUI	A,B,C,D

Group 2: Estrogen Receptor
95 proteins, 186 chains

Protein ID	Chains
3OMO	A,B
3OMP	A,B
3OMQ	A,B
3LTX	A,B,C,D
3L03	A,B
3OLL	A,B
3OLS	A,B
3OS8	A,B,C,D
3OS9	A,B,C,D
3OSA	A,B,C,D
3HLV	A,B
3HM1	A,B
3DT3	A,B
2QXS	A,B
2QZO	A,B
3CBM	B
3CBO	B
3CBP	B
2R6W	A,B
2R6Y	A,B
2QA6	A,B
2QGT	A,B
2QGW	A,B
2QH6	A,B
2QR9	A,B
2QSE	A,B
2QXM	A,B
2OCF	A
2QTU	A,B
2IOG	A
2IOK	A,B
2POG	A,B
2QE4	A,B
2QE4	A,B
2NV7	A,B
2IJ3	A,B
2Q70	A,B
2Z4B	A,B
2Q6J	A,B
2OUZ	A
2P15	A,B
2G5O	A,B
2JF9	A,B,C
2JFA	A,B
2G44	A,B
2J7X	A
2J7Y	A
2IOG	A
2IOJ	A,B,C,D
2GIU	A
2B1Z	A,B
2B23	A,B
2FSZ	A,B
1ZKY	A,B
2B1V	A,B
2FAI	A,B
1ZAF	A,B
1YY4	A,B
1YYE	A,B

Group 3: Cell Division Protein
Kinase 2
102 proteins, 139 chains

Protein ID	chains
3PXF	A
3PXQ	A
3PXR	A
3PXY	A
3PXZ	A
3PY0	A
3PY1	A
3KF9	A
3NS9	A
3LE6	A
2XNB	A
3MY5	A,C
2WMB	A,C
2WMA	A,C
3LFN	A
3LFQ	A
3LFS	A
2WPA	A,C
2WXV	A,C
2X1N	A,C
3IG7	A
3IGG	A
2WIH	A,C
2WIP	A,C
2WEV	A,C
2WFY	A,C
2WHB	A,C
3FZ1	A
3EZV	A
3F5X	C
2W1H	A
2W17	A
3EOC	A,C
3EID	A,C
3EJ1	A,C
2W05	A
3DOG	A,C
2W06	A
2R64	A
2VTA	A
2VTH	A
2VTI	A
2VTJ	A
2VTL	A
2VTM	A
2VTN	A
2VTO	A
2VTP	A
2VTQ	A
2VTR	A
2VTS	A
2VTT	A
2VU3	A
2VV9	A
3DDP	A,C
3DDQ	A,C
3BHT	A,C
3BHU	A,C
3BHV	A,C

2AYR	A
1U3Q	A,B,C,D
1U3R	A,B
1U3S	A,B
1YIM	A
1YIN	A
1U9E	A,B
1X76	A,B
1X78	A,B
1X7E	A,B
1X7J	A,B
1X7R	A
2BJ4	A,B
1XQC	A,B,C,D
1XP1	A
1XP6	A
1XPC	A
1R5K	A,B,C
1SJ0	A
1PCG	A,B
1UOM	A
1NDE	A
1L2I	A,B
1L2J	A,B
1G50	A,B,C
1QKT	A
1QKU	A,B,C
1QKM	A
1QKN	A
3ERD	A,B
3ERT	A
1A52	A,B
1ERE	A,B,C,D,E,F
1ERR	A,B
1HCQ	B,E,F

2V22	A,C
2R3F	A
2R3G	A
2R3H	A
2R3I	A
2R3J	A
2R3K	A
2R3L	A
2R3M	A
2R3N	A
2R3O	A
2R3P	A
2R3Q	A
2R3R	A
2J9M	A
2UZB	A,C
2UZD	A,C
2UZE	C
2UZL	C
2UZN	A
2UZO	A
2DS1	A
2IGZ	A
2UUE	A,C
2DUV	A
2CLX	A
2FVD	A
2I40	A,C
2IW6	A,C
2IW8	A,C
2IW9	A,C
1W8C	A
2G9X	A,C
2CCH	A,C
2CCI	A,C
2CJM	A,C
2BKZ	A,C
2C5N	A,C
2C5O	A,C
2C5V	A,C
2C5Y	A
1YKR	A
2A0C	X

Appendix B

Detailed Ranking For Three Query Proteins Using DD2, RC, DRC

Ranking 416 proteins based on their similarities to the query 1UDI chain I using the global descriptors DD2, RC, and DRC and extract the rank of the Group1 proteins

DD2				RC				DRC			
Protein ID	Chain	Rank	Distance	Protein ID	Chain	Rank	Distance	Protein ID	Chain	Rank	Distance
1UDI	I	1	0	1UDI	I	1	0	1UDI	I	1	0
2ZHX	B	2	1.5742	2ZHX	B	2	1.4359	2ZHX	B	2	2.1307
1LQG	C	3	1.8300	1LQM	B	3	1.4431	1LQM	B	3	2.3509
2UGI	A	4	1.8500	2UUG	C	4	1.6287	1LQG	C	4	2.4590
1LQM	B	5	1.8600	1LQG	C	5	1.6466	2UUG	C	5	2.5354
1UGI	E	6	1.9100	2ZHX	L	6	1.6629	1EUI	C	7	2.5920
2UUG	C	7	1.9400	1EUI	C	7	1.6769	2ZHX	L	8	2.6105
2ZHX	H	8	1.9575	2ZHX	J	8	1.7105	1UGH	I	10	2.6350
1UGH	I	11	1.9700	1UGH	I	11	1.7499	2UGI	A	15	2.6809
1EUI	C	14	1.9765	2ZHX	N	14	1.7803	1UGI	E	16	2.6873
1LQJ	B	18	1.9892	1UGI	G	18	1.8072	2ZHX	H	19	2.6969
2ZHX	D	19	1.9938	2OWR	C	19	1.8125	2ZHX	D	21	2.7006
1EMJ	A	22	1.9966	2ZHX	D	22	1.8215	2ZHX	N	22	2.7017
2BOO	A	23	2.0122	1UGI	A	23	1.8286	2ZHX	J	23	2.7142
2ZHX	L	31	2.0123	2ZHX	H	31	1.8551	1UGI	G	25	2.7262
2ZHX	N	39	2.0322	2J8X	D	39	1.8715	1EMJ	A	42	2.7758
1UGI	G	43	2.0411	1UGI	D	43	1.8852	2BOO	A	45	2.7808
1SSP	E	45	2.0453	1UGI	E	45	1.8876	1UGI	D	47	2.7868
1UGI	D	52	2.0525	2OWR	B	52	1.8935	2OWR	B	50	2.7952
2OWR	B	67	2.0561	2UUG	D	67	1.9107	2J8X	D	61	2.8129
1UGI	C	74	2.0561	1LQG	D	74	1.9160	1LQG	D	70	2.8263
2ZHX	A	80	2.0641	2BOO	A	80	1.9194	1Q3F	A	90	2.8533
3CXM	A	91	2.0677	2OWR	D	91	1.9260	2UUG	D	99	2.8675
1LQG	D	96	2.0778	1EMJ	A	96	1.9285	1UGI	A	101	2.8689
1Q3F	A	99	2.0929	2OWR	A	99	1.9303	2OWR	C	110	2.8749
2J8X	D	102	2.1000	2OWR	E	102	1.9317	2ZHX	F	116	2.8850
2UUG	B	116	2.1002	1UII	A	116	1.9388	2OWQ	B	129	2.8977
2ZHX	J	117	2.1074	1Q3F	A	117	1.9394	1SSP	E	141	2.9115
2C56	A	119	2.1125	2UGI	A	119	1.9408	1UGI	C	142	2.9117
2J8X	C	138	2.1126	2ZHX	F	138	1.9540	2ZHX	A	147	2.9150
1UI0	A	139	2.1137	2OWR	H	139	1.9555	2OWR	E	151	2.9164
2ZHX	C	153	2.1176	2OWQ	B	153	1.9646	4SKN	E	160	2.9220
1EMH	A	167	2.1219	2OWR	F	167	1.9785	1UI0	A	170	2.9294
2ZHX	F	171	2.1225	1EUI	D	171	1.9818	1EUI	D	179	2.9337
2OWQ	B	187	2.1300	4SKN	E	187	1.9932	2OWR	A	183	2.9363
2C53	A	195	2.1321	2OWQ	A	195	1.9974	1UDI	E	184	2.9376
4SKN	E	197	2.1366	2UGI	B	197	1.9989	1EMH	A	200	2.9485
2UUG	D	211	2.1382	1UDI	E	211	2.0111	2UGI	B	201	2.9489
3FCF	A	214	2.1387	2ZHX	K	214	2.0129	2ZHX	K	208	2.9560
1UDI	E	217	2.1413	1EUI	A	217	2.0157	2J8X	C	216	2.9648
2J8X	A	220	2.1449	1UDH	A	220	2.0176	1UDH	A	219	2.9689
1AKZ	A	223	2.1494	2OXM	A	223	2.0195	3FCF	A	222	2.9699
1EUI	D	225	2.1631	1YUO	A	225	2.0216	2C53	A	223	2.9702
1UDG	A	230	2.1645	1UI0	A	230	2.0282	2OWQ	A	229	2.9720
2ZHX	K	232	2.1648	1LQM	A	232	2.0299	1LQJ	B	231	2.9733
2UGI	B	234	2.1680	1LQG	A	234	2.0350	3CXM	A	232	2.9763
1UDH	A	241	2.1780	1VK2	A	241	2.0397	2C56	A	233	2.9779
2OWR	E	249	2.1849	1EMH	A	249	2.0473	2OWR	D	235	2.9783
1LQG	B	256	2.1995	1FLZ	A	256	2.0583	2OWR	F	237	2.9823
2OWQ	A	257	2.2008	2ZHX	A	257	2.0583	2ZHX	C	247	2.9908
1VK2	A	259	2.2013	3FCF	A	259	2.0607	1UDG	A	251	2.9946
3FCK	B	262	2.2102	1UGI	C	262	2.0616	1VK2	A	255	3.0010
1UGI	A	265	2.2106	1OKB	A	265	2.0640	2UUG	B	264	3.0135
2OWR	A	267	2.2126	2C53	A	267	2.0678	1YUO	A	276	3.0310
2OWR	F	272	2.2314	1UDG	A	272	2.0695	2OWR	H	279	3.0353
2OWR	C	275	2.2315	1SSP	E	275	2.0722	1UII	A	280	3.0354
1FLZ	A	280	2.2462	2J8X	C	280	2.0801	1FLZ	A	282	3.0466
2ZHX	E	285	2.2496	2SSP	E	285	2.0841	2OXM	A	285	3.0515
1UGI	F	288	2.2546	2ZHX	M	288	2.0877	1AKZ	A	292	3.0583
1YUO	A	297	2.2584	2C56	A	297	2.0989	1LQG	B	296	3.0600
1OKB	A	301	2.2613	2OWR	G	301	2.1106	1OKB	A	299	3.0616
3A7N	A	302	2.2636	2ZHX	C	302	2.1120	1EUI	A	303	3.0675

2SSP	E	306	2.2690
1UGH	E	308	2.2701
1UGI	B	311	2.2713
2OWR	D	320	2.2718
2JHQ	A	322	2.2819
2OXM	A	324	2.2876
1EUI	B	328	2.2885
2ZHX	M	329	2.2918
1UGI	H	331	2.2943
2UUG	A	336	2.3042
1EUI	A	340	2.3123
1LAU	E	345	2.3166
2DDG	A	349	2.3175
1LQM	A	350	2.3181
2OWR	H	353	2.3215
2D3Y	A	355	2.3234
2ZHX	I	357	2.3272
2ZHX	G	373	2.3318
1LQG	A	374	2.3334
1UUI	A	377	2.3355
2DP6	A	379	2.3358
2OWR	G	382	2.3484
2DEM	A	386	2.3746
2HXM	A	388	2.3847
3FCL	A	389	2.3929
2J8X	B	395	2.4235
1OKB	B	397	2.5705
3FCI	A	408	2.6351
2OYT	A	416	2.6615

2UUG	A	306	2.1175
2ZHX	E	308	2.1210
1LQG	B	311	2.1273
3CXM	A	320	2.1408
2D3Y	A	322	2.1455
1UGI	H	324	2.1505
2UUG	B	328	2.1612
1UGH	E	329	2.1624
2ZHX	I	331	2.1647
1AKZ	A	336	2.1757
2J8X	B	340	2.1869
2J8X	A	345	2.1947
1UGI	B	349	2.2020
2HXM	A	350	2.2037
2DP6	A	353	2.2094
1LQJ	B	355	2.2099
3FCL	A	357	2.2185
2JHQ	A	373	2.2510
2ZHX	G	374	2.2570
1EUI	B	377	2.2631
1UGI	F	379	2.2706
3FCK	B	382	2.2751
3FCI	A	386	2.3049
2DDG	A	388	2.3063
3A7N	A	389	2.3167
2DEM	A	395	2.3603
1LAU	E	397	2.3667
2OYT	A	408	2.4565
1OKB	B	416	2.6335

2J8X	A	305	3.0688
2SSP	E	308	3.0808
1LQM	A	309	3.0812
2ZHX	E	317	3.0918
1LQG	A	319	3.0961
2ZHX	M	321	3.1001
2UUG	A	332	3.1294
1UGH	E	337	3.1351
1UGI	H	343	3.1446
2OWR	G	347	3.1574
2D3Y	A	350	3.1625
1UGI	B	351	3.1635
3FCK	B	355	3.1720
2ZHX	I	359	3.1783
1UGI	F	368	3.1998
2JHQ	A	370	3.2053
2DP6	A	372	3.2152
1EUI	B	374	3.2185
3A7N	A	376	3.2390
2ZHX	G	378	3.2453
2HXM	A	379	3.2470
3FCL	A	381	3.2631
2J8X	B	383	3.2643
2DDG	A	384	3.2695
1LAU	E	389	3.3118
2DEM	A	393	3.3481
3FCI	A	408	3.5009
2OYT	A	413	3.6219
1OKB	B	415	3.6801

Ranking 416 proteins based on their similarities to the query 1QKN chain A using the global descriptors DD2, RC, and DRC and extract the rank of the Group2 proteins

DD2

Protein ID	Chain	Rank	Distance
1QKN	A	1	0.0000
2J7X	A	2	0.9521
1U3R	B	3	1.0687
3OS9	A	4	1.0773
1L2I	A	5	1.0796
1U3S	B	6	1.0953
2QA6	A	7	1.0981
3ERD	A	8	1.0999
3LTX	C	9	1.1038
2J7Y	A	10	1.1116
1X7R	A	11	1.1365
1YIM	A	12	1.1382
1YY4	A	13	1.1455
3OS8	D	15	1.1519
2QR9	A	16	1.1533
1QKM	A	17	1.1585
2OUZ	A	18	1.1601
2IOG	A	19	1.1608
2QGW	A	20	1.1643
2QH6	A	21	1.1658
1ERE	A	22	1.1727
INDE	A	23	1.1809
1YIN	A	24	1.1826
3LTX	A	25	1.1843
1X7J	A	27	1.1931
2QE4	A	28	1.2049
2IOK	A	29	1.2050
3ERT	A	30	1.2059
3DT3	A	31	1.2081
1QKU	A	32	1.2094
1G50	A	33	1.2153
2GIU	A	35	1.2322
1UOM	A	36	1.2357
2QXM	A	38	1.2430
1R5K	A	39	1.2463
1A52	A	40	1.2487
2B1V	A	41	1.2495
1L2J	A	42	1.2522
2Q70	A	45	1.2579
3OS8	A	46	1.2589
1XP6	A	49	1.2622
3OSA	A	50	1.2666
3HLV	A	51	1.2678
1X7E	A	52	1.2687
2QZO	A	53	1.2689
1U3S	A	55	1.2701
1L2J	B	56	1.2701
2IOJ	A	58	1.2709
1XPC	A	60	1.2733
2AYR	A	61	1.2743
2QGT	A	63	1.2760
2JFA	A	64	1.2783
2R6Y	A	65	1.2804
1XP9	A	67	1.2840
2B1Z	A	68	1.2842
1U3Q	D	73	1.2904
1G50	C	79	1.2992
3LTX	D	80	1.3038
2BJ4	A	83	1.3072
2JJ3	A	84	1.3100
2JF9	A	91	1.3175
2FSZ	A	92	1.3180
1U3Q	A	98	1.3289
2POG	A	102	1.3334
1X76	A	111	1.3442
1U3R	A	112	1.3472
2OCF	A	115	1.3543
2Z4B	A	116	1.3582
1SJ0	A	119	1.3606
1PCG	A	121	1.3623
3OS9	D	128	1.3730
1ERE	C	132	1.3782

RC

Protein ID	Chain	Rank	Distance
1QKN	A	1	0.0000
2J7X	A	2	0.9521
1U3R	B	3	1.0687
3OS9	A	4	1.0773
1L2I	A	5	1.0796
1U3S	B	6	1.0953
2QA6	A	7	1.0981
3ERD	A	8	1.0999
3LTX	C	9	1.1038
2J7Y	A	10	1.1116
1X7R	A	11	1.1365
1YIM	A	12	1.1382
1YY4	A	13	1.1455
3OS8	D	15	1.1519
2QR9	A	16	1.1533
1QKM	A	17	1.1585
2OUZ	A	18	1.1601
2IOG	A	19	1.1608
2QGW	A	20	1.1643
2QH6	A	21	1.1658
1ERE	A	22	1.1727
INDE	A	23	1.1809
1YIN	A	24	1.1826
3LTX	A	25	1.1843
1X7J	A	27	1.1931
2QE4	A	28	1.2049
2IOK	A	29	1.2050
3ERT	A	30	1.2059
3DT3	A	31	1.2081
1QKU	A	32	1.2094
1G50	A	33	1.2153
2GIU	A	35	1.2322
1UOM	A	36	1.2357
2QXM	A	38	1.2430
1R5K	A	39	1.2463
1A52	A	40	1.2487
2B1V	A	41	1.2495
1L2J	A	42	1.2522
2Q70	A	45	1.2579
3OS8	A	46	1.2589
1XP6	A	49	1.2622
3OSA	A	50	1.2666
3HLV	A	51	1.2678
1X7E	A	52	1.2687
2QZO	A	53	1.2689
1U3S	A	55	1.2701
1L2J	B	56	1.2701
2IOJ	A	58	1.2709
1XPC	A	60	1.2733
2AYR	A	61	1.2743
2QGT	A	63	1.2760
2JFA	A	64	1.2783
2R6Y	A	65	1.2804
1XP9	A	67	1.2840
2B1Z	A	68	1.2842
1U3Q	D	73	1.2904
1G50	C	79	1.2992
3LTX	D	80	1.3038
2BJ4	A	83	1.3072
2JJ3	A	84	1.3100
2JF9	A	91	1.3175
2FSZ	A	92	1.3180
1U3Q	A	98	1.3289
2POG	A	102	1.3334
1X76	A	111	1.3442
1U3R	A	112	1.3472
2OCF	A	115	1.3543
2Z4B	A	116	1.3582
1SJ0	A	119	1.3606
1PCG	A	121	1.3623
3OS9	D	128	1.3730
1ERE	C	132	1.3782

DRC

Protein ID	Chain	Rank	Distance
1QKN	A	1	0.0000
2J7X	A	2	1.3769
2J7Y	A	3	1.5753
1QKM	A	4	1.6794
1NDE	A	5	1.7369
2GIU	A	6	1.7371
1L2I	A	7	1.7461
1U3R	B	8	1.7671
3ERD	A	9	1.7684
3OS9	A	10	1.7716
2IOG	A	11	1.7738
3LTX	C	12	1.7742
1YIM	A	13	1.7854
3ERT	A	14	1.7967
1U3Q	D	15	1.8009
1YY4	A	16	1.8090
2OUZ	A	17	1.8127
1YIN	A	18	1.8152
1XP6	A	19	1.8260
2AYR	A	20	1.8270
3OS8	D	21	1.8311
2QH6	A	22	1.8312
3OSA	A	23	1.8367
1L2J	A	24	1.8385
2IJ3	A	25	1.8439
1G50	A	26	1.8490
3OS8	A	27	1.8510
2FSZ	A	28	1.8519
2QGW	A	29	1.8605
1UOM	A	30	1.8683
3LTX	A	31	1.8692
1X7J	A	32	1.8721
1U3Q	A	33	1.8734
1XPC	A	34	1.8736
1U3S	B	35	1.8786
1XP9	A	36	1.8817
1QKU	A	37	1.8840
2B1Z	A	38	1.8848
3DT3	A	39	1.8859
2QZO	A	41	1.8914
1X7R	A	42	1.8924
2R6Y	A	46	1.9022
2QTU	A	51	1.9134
2IOG	A	56	1.9183
2Z4B	A	57	1.9199
2POG	A	63	1.9287
1ERE	A	68	1.9339
2OGT	A	70	1.9363
2Q70	A	71	1.9380
2QA6	A	72	1.9406
1U3S	A	73	1.9409
2QR9	A	75	1.9421
2B1V	A	77	1.9436
1L2J	B	78	1.9461
3LTX	D	79	1.9464
2QE4	A	80	1.9500
2IOJ	A	85	1.9601
2IOK	A	88	1.9664
1U9E	A	95	1.9786
3HLV	A	96	1.9796
2R6W	A	100	1.9845
1R5K	A	103	1.9905
1X78	A	104	1.9920
2JFA	A	108	1.9928
1U3R	A	110	1.9980
2OCF	A	113	2.0007
1PCG	A	115	2.0062
1X7E	A	116	2.0068
1ERE	D	123	2.0162
1X76	A	126	2.0184
1A52	A	129	2.0205
2BJ4	A	131	2.0236

2I0G	A	133	1.3785
1ERE	F	134	1.3795
1U9E	A	139	1.3874
3HM1	A	140	1.3875
1X78	A	141	1.3883
2QTU	A	142	1.3899
1R5K	C	143	1.3923
1X1P	A	144	1.3954
3OS8	C	145	1.3959
2R6W	A	146	1.3974
1ZAF	A	152	1.4049
1ERE	D	154	1.4061
2Q6J	A	160	1.4188
2JF9	C	164	1.4228
3LTX	B	167	1.4273
1A52	B	169	1.4297
2B23	A	175	1.4424
1XQC	C	177	1.4444
3OLS	A	178	1.4451
2QXS	A	180	1.4456
1XQC	A	182	1.4469
3L03	A	184	1.4514
1ERE	E	186	1.4528
1X7B	A	189	1.4552
1R5K	B	194	1.4627
1XQC	D	196	1.4642
2QR9	B	200	1.4731
2NV7	A	201	1.4748
2G5O	A	212	1.4969
2G44	A	213	1.4976
2QGT	B	214	1.4977
1ERR	A	217	1.5086
1ZKY	A	221	1.5121
2QA6	B	227	1.5280
1U3Q	C	230	1.5342
2FSZ	B	239	1.5603
3OMO	A	240	1.5623
1PCG	B	244	1.5668
2B23	B	245	1.5701
2FAI	B	247	1.5722
3DT3	B	248	1.5768
2FAI	A	249	1.5778
1YYE	A	255	1.5918
3OSA	C	260	1.5966
3OSA	D	266	1.6020
2Q6J	B	270	1.6082
2QSE	A	277	1.6308
3OS9	C	283	1.6394
3OMP	A	285	1.6402
2B1V	B	286	1.6408
2G5O	B	287	1.6482
1HCQ	E	290	1.6533
3OSA	B	293	1.6643
3HLV	B	297	1.6801
1QKT	A	302	1.6924
3ERD	B	303	1.6928
3OMQ	A	304	1.6948
2QXM	B	305	1.6974
1QKU	C	306	1.7030
2JFA	B	308	1.7041
1ERR	B	309	1.7043
2B1Z	B	312	1.7083
2QTU	B	313	1.7102
2JJ3	B	314	1.7105
2Q70	B	316	1.7196
3L03	B	330	1.7587
2I0J	B	333	1.7704
2R6Y	B	334	1.7716
2QXS	B	336	1.7832
2QGW	B	338	1.7937
2I0K	B	339	1.7942
2Z4B	B	340	1.7970
2QE4	B	344	1.8075
1L2I	B	346	1.8239
2G44	B	348	1.8331
3HM1	B	351	1.8405
1G50	B	352	1.8424
2QSE	B	353	1.8428

2I0G	A	133	1.3785
1ERE	F	134	1.3795
1U9E	A	139	1.3874
3HM1	A	140	1.3875
1X78	A	141	1.3883
2QTU	A	142	1.3899
1R5K	C	143	1.3923
1X1P	A	144	1.3954
3OS8	C	145	1.3959
2R6W	A	146	1.3974
1ZAF	A	152	1.4049
1ERE	D	154	1.4061
2Q6J	A	160	1.4188
2JF9	C	164	1.4228
3LTX	B	167	1.4273
1A52	B	169	1.4297
2B23	A	175	1.4424
1XQC	C	177	1.4444
3OLS	A	178	1.4451
2QXS	A	180	1.4456
1XQC	A	182	1.4469
3L03	A	184	1.4514
1ERE	E	186	1.4528
1X7B	A	189	1.4552
1R5K	B	194	1.4627
1XQC	D	196	1.4642
2QR9	B	200	1.4731
2NV7	A	201	1.4748
2G5O	A	212	1.4969
2G44	A	213	1.4976
2QGT	B	214	1.4977
1ERR	A	217	1.5086
1ZKY	A	221	1.5121
2QA6	B	227	1.5280
1U3Q	C	230	1.5342
2FSZ	B	239	1.5603
3OMO	A	240	1.5623
1PCG	B	244	1.5668
2B23	B	245	1.5701
2FAI	B	247	1.5722
3DT3	B	248	1.5768
2FAI	A	249	1.5778
1YYE	A	255	1.5918
3OSA	C	260	1.5966
3OSA	D	266	1.6020
2Q6J	B	270	1.6082
2QSE	A	277	1.6308
3OS9	C	283	1.6394
3OMP	A	285	1.6402
2B1V	B	286	1.6408
2G5O	B	287	1.6482
1HCQ	E	290	1.6533
3OSA	B	293	1.6643
3HLV	B	297	1.6801
1QKT	A	302	1.6924
3ERD	B	303	1.6928
3OMQ	A	304	1.6948
2QXM	B	305	1.6974
1QKU	C	306	1.7030
2JFA	B	308	1.7041
1ERR	B	309	1.7043
2B1Z	B	312	1.7083
2QTU	B	313	1.7102
2JJ3	B	314	1.7105
2Q70	B	316	1.7196
3L03	B	330	1.7587
2I0J	B	333	1.7704
2R6Y	B	334	1.7716
2QXS	B	336	1.7832
2QGW	B	338	1.7937
2I0K	B	339	1.7942
2Z4B	B	340	1.7970
2QE4	B	344	1.8075
1L2I	B	346	1.8239
2G44	B	348	1.8331
3HM1	B	351	1.8405
1G50	B	352	1.8424
2QSE	B	353	1.8428

3OLS	A	135	2.0300
1SJO	A	136	2.0323
2JF9	A	139	2.0365
3HM1	A	142	2.0414
2QXM	A	144	2.0489
1ZAF	A	152	2.0569
3LTX	B	158	2.0647
3OS9	D	160	2.0708
1X7B	A	163	2.0771
1R5K	C	165	2.0843
1X1P	A	166	2.0890
1XQC	C	169	2.0970
1ERE	E	172	2.1050
1ERR	A	175	2.1084
1G50	C	178	2.1118
2Q6J	A	181	2.1182
1ZKY	A	190	2.1353
1R5K	B	194	2.1418
2FSZ	B	196	2.1435
2G5O	A	199	2.1453
1ERE	C	203	2.1551
1XQC	D	204	2.1556
2QXS	A	205	2.1564
1ERE	F	206	2.1586
1XQC	A	208	2.1625
3L03	A	209	2.1637
2JF9	C	211	2.1699
2B23	A	212	2.1701
2NV7	A	213	2.1702
3OMO	A	216	2.1718
1U3Q	C	217	2.1755
3OS8	C	218	2.1760
3OSA	D	226	2.1845
1A52	B	235	2.2051
2B23	B	249	2.2280
2G44	A	250	2.2286
2QGT	B	252	2.2316
2JJ3	B	255	2.2354
2FAI	A	257	2.2377
1HCQ	E	262	2.2571
2QA6	B	263	2.2610
3OMP	A	267	2.2707
3DT3	B	271	2.2918
3OMQ	A	274	2.3015
3OSA	B	275	2.3077
2QR9	B	276	2.3130
1PCG	B	277	2.3149
1YYE	A	280	2.3186
2FAI	B	283	2.3263
2QTU	B	285	2.3340
2Q6J	B	287	2.3372
2Z4B	B	289	2.3467
3OSA	C	290	2.3493
1ERR	B	291	2.3535
2G5O	B	300	2.3935
2Q70	B	301	2.4050
2B1V	B	304	2.4158
2QXM	B	305	2.4201
3ERD	B	307	2.4237
3OS9	C	310	2.4444
1QKT	A	311	2.4460
2B1Z	B	312	2.4488
3HLV	B	313	2.4524
2QSE	A	314	2.4536
2JFA	B	316	2.4610
2QXS	B	321	2.4813
2I0J	B	322	2.4828
2G44	B	328	2.5098
2R6Y	B	333	2.5223
3HM1	B	340	2.5403
3L03	B	341	2.5433
2I0K	B	342	2.5455
2QGW	B	344	2.5542
1QKU	C	346	2.5620
1HCQ	F	352	2.6212
2QSE	B	353	2.6232
3OS9	B	354	2.6254
3OS8	B	356	2.6434

1ZAF	B	354	1.8528
1HCQ	F	355	1.8570
3OS9	B	356	1.8571
2P15	A	357	1.8571
1ERE	B	359	1.8592
2QH6	B	362	1.8785
2R6W	B	364	1.8959
1X7J	B	365	1.9199
3OLL	A	368	1.9297
2JF9	B	369	1.9308
3OS8	B	370	1.9361
1YY4	B	372	1.9472
1X7B	B	374	1.9605
2POG	B	376	1.9723
3OMP	B	377	1.9734
2P15	B	378	1.9839
1X7E	B	379	1.9875
1XQC	B	383	2.0065
3OMO	B	385	2.0406
1U9E	B	386	2.0597
1U3Q	B	387	2.0611
2BJ4	B	389	2.0984
1YYE	B	391	2.1176
3OLS	B	392	2.1290
2NV7	B	395	2.1510
3OMQ	B	397	2.1746
1X76	B	400	2.2412
1ZKY	B	401	2.2448
3OLL	B	403	2.2624
1HCQ	B	406	2.4074
3CBO	B	407	2.4074
1X78	B	408	2.4144
2QZO	B	409	2.4212
3CBP	B	412	2.4828
1QKU	B	413	2.4839
3CBM	B	416	2.5903

1ZAF	B	354	1.8528
1HCQ	F	355	1.8570
3OS9	B	356	1.8571
2P15	A	357	1.8571
1ERE	B	359	1.8592
2QH6	B	362	1.8785
2R6W	B	364	1.8959
1X7J	B	365	1.9199
3OLL	A	368	1.9297
2JF9	B	369	1.9308
3OS8	B	370	1.9361
1YY4	B	372	1.9472
1X7B	B	374	1.9605
2POG	B	376	1.9723
3OMP	B	377	1.9734
2P15	B	378	1.9839
1X7E	B	379	1.9875
1XQC	B	383	2.0065
3OMO	B	385	2.0406
1U9E	B	386	2.0597
1U3Q	B	387	2.0611
2BJ4	B	389	2.0984
1YYE	B	391	2.1176
3OLS	B	392	2.1290
2NV7	B	395	2.1510
3OMQ	B	397	2.1746
1X76	B	400	2.2412
1ZKY	B	401	2.2448
3OLL	B	403	2.2624
1HCQ	B	406	2.4074
3CBO	B	407	2.4074
1X78	B	408	2.4144
2QZO	B	409	2.4212
3CBP	B	412	2.4828
1QKU	B	413	2.4839
3CBM	B	416	2.5903

2QE4	B	358	2.6566
3OLL	A	361	2.6637
1L2I	B	362	2.6642
2R6W	B	363	2.6656
2P15	A	366	2.6859
1G50	B	368	2.6948
1U3Q	B	369	2.6969
1YY4	B	370	2.6972
1X7B	B	371	2.7035
3OMO	B	372	2.7132
1ZAF	B	373	2.7193
1ERE	B	374	2.7293
2POG	B	376	2.7429
2JF9	B	377	2.7700
3OMP	B	378	2.7792
1X7J	B	379	2.8011
1XQC	B	380	2.8102
2P15	B	382	2.8267
2QH6	B	384	2.8345
1U9E	B	385	2.8421
1X7E	B	388	2.8984
2BJ4	B	389	2.9397
3OMQ	B	390	2.9535
1YYE	B	391	2.9604
1HCQ	B	396	3.0334
3CBO	B	397	3.0334
2NV7	B	399	3.0658
1ZKY	B	402	3.0833
3CBP	B	403	3.0935
3OLL	B	404	3.0961
3OLS	B	405	3.0976
1X76	B	406	3.1256
3CBM	B	410	3.2651
2QZO	B	412	3.3277
1X78	B	413	3.3625
1QKU	B	414	3.4456

Ranking 416 proteins based on their similarities to the query 1YKR chain A using the global descriptors DD2, RC, and DRC and extract the rank of the Group3 protein

DD2

Protein ID	Chain	Rank	Distance
1YKR	A	1	0
3PY1	A	2	0.7436
2R3O	A	3	0.7449
3NS9	A	4	0.7490
2C5Y	A	5	0.7590
2UZO	A	6	0.7761
3PXY	A	7	0.7896
2WMA	A	8	0.7996
3DDP	A	9	0.8082
2V22	C	10	0.8257
2IW6	A	11	0.8316
2WFY	A	12	0.8346
2R3L	A	13	0.8554
2DUV	A	14	0.8582
3LFN	A	15	0.8740
2R3J	A	16	0.8774
2J9M	A	17	0.8810
3DOG	A	18	0.8837
1W8C	A	19	0.8839
2WIP	A	20	0.8993
2R3P	A	21	0.9028
2R3M	A	22	0.9130
2VTN	A	23	0.9131
2W05	A	24	0.9140
3DDP	C	25	0.9163
3PXR	A	26	0.9226
2C5N	C	27	0.9230
3EZR	A	28	0.9268
2R64	A	29	0.9270
2VTP	A	30	0.9378
3IGG	A	31	0.9389
2WEV	C	32	0.9407
2UZD	C	33	0.9443
2WXV	A	34	0.9459
2WIP	C	35	0.9475
2WIH	C	37	0.9570
2JGZ	A	38	0.9575
2W06	A	39	0.9596
2V22	A	40	0.9625
2BKZ	C	41	0.9628
3EID	C	42	0.9629
2WXV	C	43	0.9656
2WHB	C	44	0.9659
2I40	C	45	0.9671
2UZE	C	46	0.9680
2C5V	C	47	0.9690
2I40	A	49	0.9709
2C5V	A	50	0.9793
2UZL	C	51	0.9811
3LFQ	A	52	0.9827
2BKZ	A	53	0.9853
3EJ1	A	54	0.9876
3EOC	A	55	0.9891
2WHB	A	56	0.9898
3IG7	A	57	0.9909
2WPA	C	58	0.9914
3PY0	A	59	0.9919
2UUE	C	60	0.9930
2VV9	A	61	0.9931
2X1N	C	62	0.9933
2R3K	A	63	0.9955
2R3H	A	64	0.9963
2VTA	A	65	0.9979
2WIH	A	66	1.0016
2IW8	A	67	1.0030
3EOC	C	68	1.0032
2WPA	A	70	1.0120
3F5X	C	71	1.0137
3PXZ	A	72	1.0186
2UUE	A	75	1.0266
3EJ1	C	76	1.0277
2CCH	C	77	1.0306
2WMA	C	78	1.0323
3FZ1	A	79	1.0327

RC

Protein ID	Chain	Rank	Distance
1YKR	A	1	0
2UZO	A	2	0.6917
3PXY	A	3	0.7436
3IGG	A	4	0.7699
2R3O	A	5	0.7834
3PY1	A	6	0.8025
2IW6	A	7	0.8101
2WMA	A	8	0.8110
3PXR	A	9	0.8318
2V22	A	10	0.8473
2J9M	A	11	0.8561
2R3J	A	12	0.8726
3IG7	A	13	0.8733
2WFY	A	14	0.8871
1W8C	A	15	0.8960
2R3L	A	16	0.8980
2WHB	A	17	0.9005
2X1N	A	18	0.9017
2CCI	A	19	0.9091
2UUE	A	20	0.9097
2UZD	A	21	0.9124
2DUV	A	22	0.9136
2R3P	A	23	0.9191
2JGZ	A	24	0.9196
3DDP	A	25	0.9245
3DOG	A	26	0.9251
2BKZ	A	27	0.9346
3PXZ	A	28	0.9413
3NS9	A	29	0.9431
3PY0	A	30	0.9487
2WMB	A	31	0.9499
2VU3	A	32	0.9538
2R64	A	33	0.9542
2R3N	A	34	0.9600
2C5Y	A	35	0.9642
3LFQ	A	36	0.9655
2WPA	A	37	0.9690
2R3K	A	38	0.9704
3EOC	A	39	0.9718
2WIH	A	40	0.9732
2VTT	A	41	0.9865
2W06	A	42	0.9878
2VTN	A	43	0.9887
2VTR	A	44	0.9892
3EID	A	45	0.9903
2C5V	A	46	0.9903
3EJ1	A	47	0.9914
3EZV	A	48	0.9970
3EZR	A	49	0.9978
2V22	C	50	0.9994
2IW8	A	51	1.0000
2WXV	A	52	1.0021
2I40	A	53	1.0049
2W05	A	54	1.0067
2WIP	A	55	1.0088
2R3M	A	56	1.0126
3EJ1	C	57	1.0128
2UZN	A	58	1.0143
2R3H	A	59	1.0174
2VTO	A	60	1.0238
3EID	C	61	1.0258
3LFN	A	62	1.0258
2WIH	A	63	1.0276
3EOC	C	64	1.0280
3F5X	C	65	1.0321
2VTM	A	66	1.0325
2WIH	C	67	1.0352
3FZ1	A	68	1.0356
2VTP	A	69	1.0356
3LE6	A	70	1.0361
2BKZ	C	71	1.0371
2I40	C	72	1.0374
2W17	A	73	1.0388
3LFS	A	74	1.0427

DRC

Protein ID	Chain	Rank	Distance
1YKR	A	1	0
2UZO	A	2	1.0396
2R3O	A	3	1.0810
3PXY	A	4	1.0847
3PY1	A	5	1.0940
2WMA	A	6	1.1389
2IW6	A	7	1.1610
3NS9	A	8	1.2043
3IGG	A	9	1.2142
2WFY	A	10	1.2179
2C5Y	A	11	1.2270
3DDP	A	12	1.2280
2J9M	A	13	1.2284
2R3J	A	14	1.2375
2R3L	A	15	1.2402
3PXR	A	16	1.2422
2DUV	A	17	1.2534
1W8C	A	18	1.2587
3DOG	A	19	1.2794
2V22	A	20	1.2823
2R3P	A	21	1.2884
2V22	C	22	1.2964
3IG7	A	23	1.3208
2JGZ	A	24	1.3276
2R64	A	25	1.3303
2WHB	A	26	1.3382
2VTN	A	27	1.3458
3LFN	A	28	1.3476
2WIP	A	29	1.3515
2BKZ	A	30	1.3580
2W05	A	31	1.3597
3EZR	A	32	1.3619
2R3M	A	33	1.3634
2UUE	A	34	1.3717
2X1N	A	35	1.3720
3PY0	A	36	1.3726
2W06	A	37	1.3772
3LFQ	A	38	1.3777
2WXV	A	39	1.3780
2UZD	A	40	1.3799
3EOC	A	41	1.3866
3PXZ	A	42	1.3870
2R3K	A	43	1.3902
2C5V	A	44	1.3927
2WIH	A	45	1.3966
2VTP	A	46	1.3972
2I40	A	47	1.3973
3EJ1	A	48	1.3994
2CCI	A	49	1.4003
2WPA	A	50	1.4011
3EID	C	51	1.4069
2WIH	C	52	1.4098
3DDP	C	53	1.4115
2VU3	A	54	1.4149
2WEV	C	55	1.4150
2BKZ	C	56	1.4151
2IW8	A	57	1.4163
2I40	C	58	1.4182
2R3H	A	59	1.4240
2C5N	C	60	1.4285
2WIP	C	61	1.4298
2UZD	C	62	1.4306
2WHB	C	63	1.4329
2R3N	A	64	1.4339
2VTR	A	65	1.4346
3EOC	C	66	1.4364
2WXV	C	67	1.4382
3EID	A	68	1.4406
3EJ1	C	69	1.4429
2C5V	C	70	1.4456
2VV9	A	71	1.4459
2UZE	C	72	1.4465
3F5X	C	73	1.4467
2VTT	A	74	1.4495

2X1N	A	80	1.0340
2UZD	A	81	1.0352
2FVD	A	82	1.0352
2VTR	A	83	1.0390
2W1H	A	84	1.0400
3LFS	A	85	1.0410
2DS1	A	86	1.0415
2UZN	A	87	1.0444
2VU3	A	88	1.0450
2UZB	C	89	1.0462
3E1D	A	90	1.0463
2VTM	A	91	1.0499
2VTS	A	92	1.0508
2W17	A	93	1.0555
2VTQ	A	94	1.0598
2VTT	A	97	1.0620
2CCI	A	98	1.0651
2R3N	A	99	1.0652
2WFY	C	100	1.0697
2G9X	C	101	1.0729
2VTJ	A	102	1.0736
2R3F	A	103	1.0778
2IW6	C	104	1.0829
3LE6	A	107	1.1022
2VTO	A	110	1.1139
2WMB	C	111	1.1142
2WEV	A	112	1.1160
2CCI	C	113	1.1174
3EZV	A	115	1.1216
3DOG	C	121	1.1337
2VTL	A	122	1.1344
2R3Q	A	124	1.1372
2VTI	A	126	1.1392
2UZB	A	129	1.1520
2C5O	C	134	1.1635
2CLX	A	135	1.1650
2IW8	C	138	1.1677
2G9X	A	141	1.1696
2C5O	A	149	1.1878
2XNB	A	152	1.1905
2R3R	A	159	1.1985
2CJM	C	164	1.2057
2WMB	A	166	1.2088
2R3G	A	168	1.2148
2R3I	A	170	1.2183
2IW9	A	171	1.2197
3BHU	C	191	1.2548
3PXF	A	197	1.2709
3BHV	C	199	1.2755
2C5N	A	219	1.3128
3PXQ	A	224	1.3218
2IW9	C	236	1.3490
3DDQ	A	237	1.3511
3MY5	A	238	1.3556
3BHU	A	240	1.3606
3DDQ	C	245	1.3730
3BHV	A	251	1.3815
2VTH	A	260	1.4077
3MY5	C	265	1.4188
3BHT	C	271	1.4385
2A0C	X	276	1.4508
3KF9	A	282	1.4648
3BHT	A	292	1.5033
2CJM	A	300	1.5297
2CCH	A	400	2.1933

2IW6	C	75	1.0427
2DS1	A	76	1.0429
2FVD	A	77	1.0439
2VTI	A	78	1.0490
2VV9	A	79	1.0509
2UZB	A	80	1.0532
2WEV	C	81	1.0570
2CCH	C	82	1.0580
2WHB	C	83	1.0585
2WFY	C	84	1.0596
2R3F	A	85	1.0637
2VTS	A	86	1.0641
2WXV	C	87	1.0658
2X1N	C	88	1.0682
2UZL	C	89	1.0702
2UZB	C	90	1.0706
2WIP	C	91	1.0708
2G9X	A	92	1.0723
2C5V	C	93	1.0727
3DDP	C	94	1.0736
2UZD	C	95	1.0746
2UZE	C	96	1.0748
2WEV	A	97	1.0759
2CCI	C	98	1.0761
2R3G	A	99	1.0797
2WPA	C	100	1.0799
2UUE	C	101	1.0811
2R3Q	A	102	1.0829
2WMA	C	103	1.0898
2C5N	C	104	1.0903
2XNB	A	105	1.0989
2CJM	C	106	1.0997
3PXQ	A	107	1.1008
2VTA	A	108	1.1043
2VTJ	A	109	1.1131
2CLX	A	110	1.1198
2C5O	A	111	1.1312
3PXF	A	112	1.1374
2R3I	A	113	1.1434
2R3R	A	114	1.1437
2VTO	A	116	1.1553
2VTL	A	117	1.1555
2IW9	A	118	1.1783
2IW8	C	119	1.1872
2WMB	C	120	1.1957
2G9X	C	122	1.2144
3DOG	C	124	1.2520
2C5N	A	125	1.2524
3BHU	C	126	1.2531
2A0C	X	127	1.2597
3DDQ	A	128	1.2718
2VTH	A	129	1.2803
2IW9	C	130	1.2804
3MY5	A	133	1.2910
2C5O	C	134	1.3023
3BHV	A	136	1.3057
3MY5	C	145	1.3470
3BHT	C	178	1.4156
3BHU	A	199	1.4560
3BHV	C	201	1.4568
3DDQ	C	208	1.4660
2CJM	A	218	1.4801
3BHT	A	251	1.5478
3KF9	A	288	1.6310
2CCH	A	397	2.0451

2UZL	C	75	1.4518
2UZN	A	76	1.4558
2X1N	C	77	1.4586
2W1H	A	78	1.4620
3FZ1	A	79	1.4625
2WPA	C	80	1.4660
2UUE	C	81	1.4679
2FVD	A	82	1.4702
2VTM	A	83	1.4726
3LFS	A	84	1.4734
2DS1	A	85	1.4738
2CCH	C	86	1.4770
2W17	A	87	1.4810
2VTA	A	88	1.4884
2VTS	A	89	1.4955
2UZB	C	90	1.4969
3EZV	A	91	1.5007
2WMA	C	92	1.5011
2IW6	C	93	1.5033
2WFY	C	94	1.5057
3LE6	A	95	1.5127
2VTO	A	96	1.5129
2R3F	A	97	1.5143
2WMB	A	98	1.5374
2VTJ	A	99	1.5465
2VTI	A	100	1.5486
2WEV	A	101	1.5502
2CCI	C	102	1.5513
2UZB	A	103	1.5609
2VTQ	A	105	1.5678
2R3Q	A	106	1.5703
2G9X	A	107	1.5868
2CLX	A	108	1.6159
2VTL	A	109	1.6193
2XNB	A	110	1.6202
2G9X	C	111	1.6204
2R3G	A	112	1.6253
2CJM	C	113	1.6318
2WMB	C	114	1.6343
2C5O	A	115	1.6403
2R3R	A	118	1.6566
2IW8	C	119	1.6653
2R3I	A	121	1.6708
3DOG	C	123	1.6890
2IW9	A	124	1.6959
3PXF	A	125	1.7056
3PXQ	A	127	1.7202
2C5O	C	130	1.7463
3BHU	C	133	1.7734
2C5N	A	142	1.8144
3DDQ	A	161	1.8555
2IW9	C	165	1.8599
3MY5	A	172	1.8720
3BHV	A	184	1.9009
2VTH	A	186	1.9028
2A0C	X	190	1.9214
3BHV	C	204	1.9363
3MY5	C	214	1.9564
3BHU	A	225	1.9928
3DDQ	C	233	2.0086
3BHT	C	236	2.0182
2CJM	A	271	2.1286
3BHT	A	277	2.1576
3KF9	A	284	2.1922
2CCH	A	398	2.9989

Appendix C

Intra-Family Sequence Similarities for randomly selected family members.

(a) Group 1

Protein 1	Chain	Protein 2	Chain	Identities	Similarities
1SSP	E	2SSP	E	99.55	99.55
1SSP	E	1UGI	A	7.17 % (query) and 19.05 % (subject)	10.76 % (query) and 28.57 % (subject)
1SSP	E	1UGI	B	7.17 % (query) and 19.05 % (subject)	10.76 % (query) and 28.57 % (subject)
2SSP	E	1UGI	A	7.17 % (query) and 19.05 % (subject)	10.76 % (query) and 28.57 %
1UGI	A	2UGI	A	100%	100%
2SSP	E	2UGI	A	4.93 % (query) and 5.67 % (subject)	7.62 % (query) and 8.76 % (subject)
1SSP	E	2UGI	A	4.93 % (query) and 5.67 % (subject)	7.62 % (query) and 8.76 % (subject)
1SSP	E	4SKN	E	99.10	99.55
2SSP	E	4SKN	E	99.10	99.55
1UGI	E	4SKN	E	17.86 % (query) and 6.73 % (subject)	28.57 % (query) and 10.76 % (subject)
2UGI	E	4SKN	E	17.86 % (query) and 6.73 % (subject)	28.57 % (query) and 10.76 % (subject)
1SSP	E	1AKZ	A	100%	100%
2SSP	E	1AKZ	A	99.55 %	99.55%
1UGI	A	1AKZ	A	7.17 % (query) and 19.05 % (subject)	10.76 % (query) and 28.57 % (subject)
2UGI	A	1AKZ	A	7.17 % (query) and 19.05 % (subject)	10.76 % (query) and 28.57 % (subject)
4SKN	E	1AKZ	A	99.10 %	99.55 %
1LAU	E	1SSP	E	43.95 % (query) and 40.16 % (subject)	56.95 % (query) and 52.05 % (subject)
1LAU	E	2SSP	E	43.50 % (query) and 39.75 % (subject)	56.50 % (query) and 51.64 % (subject)
1LAU	E	1UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1LAU	E	2UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1LAU	E	4SKN	E	39.34 % (query) and 43.05 % (subject)	52.05 % (query) and 56.95 % (subject)
1LAU	E	1AKZ	A	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1SSP	E	1UDH	A	43.95 % (query) and 40.16 % (subject)	56.95 % (query) and 52.05 % (subject)
1UDH	A	2SSP	E	39.75 % (query) and 43.50 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDH	A	1UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 %
1UDH	A	2UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1UDH	A	4SKN	E	39.34 % (query) and 43.05 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDH	A	1AKZ	A	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1UDH	A	1LAU	E	100%	100%
1UDI	E	1SSP	E	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1UDI	E	2SSP	E	39.75 % (query) and 43.50 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDI	E	1UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1UDI	E	2UGI	A	5.74 % (query) and 7.22 % (subject)	9.02 % (query) and 11.34 % (subject)
1UDI	E	4SKN	E	39.34 % (query) and 43.05 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDI	E	1AKZ	A	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1UDI	E	1LAU	E	100%	100%
1UDI	E	1UDH	A	100%	100%
1UDG	A	1SSP	E	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1UDG	A	2SSP	E	39.75 % (query) and 43.50 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDG	A	1UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1UDG	A	2UGI	A	4.51 % (query) and 13.10 % (subject)	7.79 % (query) and 22.62 % (subject)
1UDG	A	4SKN	E	39.34 % (query) and 43.05 % (subject)	52.05 % (query) and 56.95 % (subject)
1UDG	A	1AKZ	A	40.16 % (query) and 43.95 % (subject)	52.46 % (query) and 57.40 % (subject)
1UDG	A	1LAU	E	100%	100%
1UDG	A	1UDH	A	100%	100%
1UDG	A	1UDI	E	100%	100%

(b) Group 2

Protein 1	Chain	Protein 2	Chain	Identities	Similarities
3OMO	A	3HM1	A	60.00 % (query) and 56.92 % (subject)	83.33 % (query) and 79.05 % (subject)
3OMO	B	3DT3	B	60.42 % (query) and 56.86 % (subject)	83.75 % (query) and 78.82 % (subject)
3OMO	B	2QXS	A	60.42 % (query) and 56.20 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2QZO	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	3CBM	B	1.25 % (query) and 30.00 % (subject)	1.67 % (query) and 40.00 % (subject)
3OMO	A	3CBO	B	1.25 % (query) and 30.00 % (subject)	1.67 % (query) and 40.00 % (subject)
3OMO	A	3CBP	B	12.92 % (query) and 12.11 % (subject)	22.50 % (query) and 21.09 % (subject)
3OMO	A	2R6W	A	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	A	2R6Y	A	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	B	2QA6	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	B	2QGT	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	B	2QGW	B	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2QH6	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2QR9	B	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2QSE	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2QXM	A	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	B	2OCF	A	60.00 % (query) and 48.32 % (subject)	83.33 % (query) and 67.11 % (subject)
3OMO	B	2QTU	B	100.00 % (query) and 93.39 % (subject)	100.00 % (query) and 93.39 % (subject)
3OMO	B	2IOG	A	60.42 % (query) and 58.94 % (subject)	83.75 % (query) and 81.71 % (subject)
3OMO	A	2IOK	A	60.42 % (query) and 57.09 % (subject)	83.75 % (query) and 79.13 % (subject)
3OMO	A	2POG	B	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	A	2QE4	B	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	B	2NV7	A	99.17 % (query) and 100.00 % (subject)	99.17 % (query) and 100.00 % (subject)
3OMO	A	2JJ3	A	100.00 % (query) and 93.39 % (subject)	100.00 % (query) and 93.39 % (subject)
3OMO	A	2Q70	B	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	A	2Z4B	A	100.00 % (query) and 93.39 % (subject)	100.00 % (query) and 93.39 % (subject)
3OMO	B	2Q6J	B	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	B	2OUZ	A	60.42 % (query) and 57.31 % (subject)	83.75 % (query) and 79.45 % (subject)
3OMO	A	2P15	B	60.00 % (query) and 55.81 % (subject)	83.33 % (query) and 77.52 % (subject)
3OMO	A	2G5O	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	B	2JF9	C	55.00 % (query) and 52.38 % (subject)	77.50 % (query) and 73.81 % (subject)
3OMO	A	2JFA	B	55.00 % (query) and 52.38 % (subject)	77.50 % (query) and 73.81 % (subject)
3OMO	A	2G44	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	B	2J7X	A	92.50 % (query) and 87.06 % (subject)	95.83 % (query) and 90.20 % (subject)
3OMO	A	2J7Y	A	92.50 % (query) and 87.06 % (subject)	95.83 % (query) and 90.20 % (subject)
3OMO	A	2IOG	A	100.00 % (query) and 93.39 % (subject)	100.00 % (query) and 93.39 % (subject)
3OMO	A	2IOJ	D	59.58 % (query) and 58.61 % (subject)	82.92 % (query) and 81.56 % (subject)
3OMO	B	2GIU	A	100.00 % (query) and 99.59 % (subject)	100.00 % (query) and 99.59 % (subject)
3OMO	A	2BIZ	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	B	2B23	B	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	A	2FSZ	B	98.75 % (query) and 96.34 % (subject)	98.75 % (query) and 96.34 % (subject)
3OMO	A	1ZKY	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	B	2BIV	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	A	2FAI	A	60.00 % (query) and 56.03 % (subject)	83.33 % (query) and 77.82 % (subject)
3OMO	A	1ZAF	B	98.75 % (query) and 99.58 % (subject)	99.17 % (query) and 100.00 % (subject)
3OMO	B	1YY4	A	99.17 % (query) and 88.81 % (subject)	99.17 % (query) and 88.81 % (subject)
3OMO	A	1YYE	B	99.17 % (query) and 88.81 % (subject)	99.17 % (query) and 88.81 % (subject)
3OMO	B	2AYR	A	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	A	1U3Q	C	100.00 %	100.00 %
3OMO	B	1U3R	B	100.00 % (query) and 99.59 % (subject)	100.00 % (query) and 99.59 % (subject)
3OMO	B	1U3S	B	100.00 %	100.00 %
3OMO	A	1YIM	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	A	1YIN	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	B	1U9E	B	100.00 % (query) and 99.59 % (subject)	100.00 % (query) and 99.59 % (subject)
3OMO	A	1X76	A	100.00 % (query) and 99.59 % (subject)	100.00 % (query) and 99.59 % (subject)
3OMO	A	1X78	A	100.00 %	100.00 %
3OMO	A	1X7J	B	100.00 %	100.00 %
3OMO	B	1X7R	A	60.00 % (query) and 58.78 % (subject)	83.33 % (query) and 81.63 % (subject)
3OMO	B	2BJ4	B	55.00 % (query) and 52.38 % (subject)	77.50 % (query) and 73.81 % (subject)
3OMO	B	1XQC	D	60.00 % (query) and 56.69 % (subject)	83.33 % (query) and 78.74 % (subject)
3OMO	A	1XP1	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	A	1XP6	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	A	1XPC	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	A	1R5K	C	60.42 % (query) and 55.56 % (subject)	83.75 % (query) and 77.01 % (subject)
3OMO	B	1SJ0	A	60.42 % (query) and 58.47 % (subject)	83.75 % (query) and 81.05 % (subject)
3OMO	A	1PCG	B	59.58 % (query) and 58.61 % (subject)	82.92 % (query) and 81.56 % (subject)
3OMO	A	1UOM	A	60.00 % (query) and 56.69 % (subject)	83.33 % (query) and 78.74 % (subject)
3OMO	B	1NDE	A	100.00 % (query) and 94.12 % (subject)	100.00 % (query) and 94.12 % (subject)
3OMO	A	1L2I	A	60.42 % (query) and 55.56 % (subject)	83.75 % (query) and 77.01 % (subject)
3OMO	B	1L2J	B	100.00 % (query) and 88.56 % (subject)	100.00 % (query) and 88.56 % (subject)
3OMO	B	1G50	C	60.42 % (query) and 58.70 % (subject)	83.75 % (query) and 81.38 % (subject)
3OMO	B	1QKT	A	60.00 % (query) and 58.06 % (subject)	83.33 % (query) and 80.65 % (subject)
3OMO	A	1QKU	C	60.42 % (query) and 58.00 % (subject)	83.75 % (query) and 80.40 % (subject)
3OMO	A	1QKM	A	100.00 % (query) and 94.12 % (subject)	100.00 % (query) and 94.12 % (subject)

3OMO	A	1QKN	A	92.08 % (query) and 86.67 % (subject)	95.83 % (query) and 90.20 % (subject)
3OMO	A	3ERD	B	60.42 % (query) and 55.56 % (subject)	83.75 % (query) and 77.01 % (subject)
3OMO	A	3ERT	A	60.42 % (query) and 55.56 % (subject)	83.75 % (query) and 77.01 % (subject)
3OMO	B	1A52	B	60.42 % (query) and 56.20 % (subject)	83.75 % (query) and 77.91 % (subject)
3OMO	B	1ERE	F	60.42 % (query) and 57.31 % (subject)	83.75 % (query) and 79.45 % (subject)
3OMO	B	1ERR	A	60.42 % (query) and 57.31 % (subject)	83.75 % (query) and 79.45 % (subject)
3OMO	A	1HCQ	E	2.08 % (query) and 5.95 % (subject)	3.75 % (query) and 10.71 % (subject)
3OMP	A	3OMQ	A	100.00 %	100.00 %
3OMP	A	3LTX	D	36.25 % (query) and 35.80 % (subject)	58.33 % (query) and 57.61 % (subject)
3OMP	A	3L03	B	60.00 % (query) and 56.92 % (subject)	83.33 % (query) and 79.05 % (subject)
3OMP	B	3OLL	A	100.00 %	100.00 %
3OMP	B	3OLS	B	100.00 %	100.00 %
3OMP	A	3OS8	C	60.00 % (query) and 55.81 % (subject)	82.92 % (query) and 77.13 % (subject)
3OMP	A	3OS9	D	60.00 % (query) and 55.81 % (subject)	82.92 % (query) and 77.13 % (subject)
3OMP	B	3OSA	C	60.00 % (query) and 55.81 % (subject)	82.92 % (query) and 77.13 % (subject)
3OMP	B	3HLV	A	60.00 % (query) and 56.92 % (subject)	83.33 % (query) and 79.05 % (subject)

c) Group 3

Protein 1	Chain	Protein 2	Chain	Similarities	Identities
3PXF	A	2CCI	I	1.63 % (query) and 16.67 % (subject)	1.96 % (query) and 20.00 % (subject)
3PXF	A	2WEV	F	0.65 % (query) and 33.33 % (subject)	0.65 % (query) and 33.33 % (subject)
3PXF	A	2WFY	E	0.65 % (query) and 33.33 % (subject)	0.65 % (query) and 33.33 % (subject)
3PXF	A	3KF9	A	6.86 % (query) and 14.09 % (subject)	12.42 % (query) and 25.50 % (subject)
3PXF	A	2WPA	B	10.78 % (query) and 12.45 % (subject)	18.63 % (query) and 21.51 % (subject)
3PXF	A	2WIH	D	10.78 % (query) and 12.45 % (subject)	18.63 % (query) and 21.51 % (subject)
3PXF	A	2WIP	B	10.78 % (query) and 12.45 % (subject)	18.63 % (query) and 21.51 % (subject)
3PXF	A	2WHB	D	10.78 % (query) and 12.69 % (subject)	18.63 % (query) and 21.92 % (subject)
3PXF	A	3EJI	B	10.78 % (query) and 12.69 % (subject)	18.63 % (query) and 21.92 % (subject)
3PXF	A	3F5X	B	10.78 % (query) and 12.89 % (subject)	18.63 % (query) and 22.27 % (subject)
3PXF	A	3BHU	D	11.76 % (query) and 13.74 % (subject)	18.95 % (query) and 22.14 % (subject)
3PXF	A	2CCH	E	1.63 % (query) and 41.67 % (subject)	1.96 % (query) and 50.00 % (subject)
3PXF	A	3PXQ	A	100.00 %	100.00 %
3PXF	A	3PXR	A	100.00 %	100.00 %
3PXF	A	3PXV	A	100.00 %	100.00 %
3PXF	A	3PXZ	A	100.00 %	100.00 %
3PXF	A	3PY0	A	100.00 %	100.00 %
3PXF	A	3PY1	A	100.00 %	100.00 %
3PXF	A	2JGZ	A	94.12 % (query) and 99.65 % (subject)	94.12 % (query) and 99.65 % (subject)
3PXF	A	2WXV	A	98.37 % (query) and 97.41 % (subject)	98.37 % (query) and 97.41 % (subject)
3PXF	A	2BKZ	A	98.37 % (query) and 97.41 % (subject)	98.37 % (query) and 97.41 % (subject)
3PXF	A	2DS1	A	96.41 % (query) and 98.99 % (subject)	96.73 % (query) and 99.33 % (subject)
3PXF	A	3MY5	A	97.39 % (query) and 99.33 % (subject)	97.39 % (query) and 99.33 % (subject)
3PXF	A	3EZV	A	97.39 % (query) and 99.33 % (subject)	97.39 % (query) and 99.33 % (subject)
3PXF	A	3BHT	C	97.39 % (query) and 99.33 % (subject)	97.39 % (query) and 99.33 % (subject)
3PXF	A	3BHV	C	97.39 % (query) and 99.33 % (subject)	97.39 % (query) and 99.33 % (subject)
3PXF	A	2IW8	C	97.71 % (query) and 99.01 % (subject)	97.71 % (query) and 99.01 % (subject)
3PXF	A	3IG7	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	3IGG	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2W17	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	3D0G	C	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2W06	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2VV9	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	3DDP	C	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	3DDQ	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3F	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3G	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3H	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3I	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3J	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3K	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3L	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3M	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3N	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3O	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3P	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2R3R	A	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	1WSC	C	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	2G9X	C	97.39 % (query) and 99.67 % (subject)	97.39 % (query) and 99.67 % (subject)
3PXF	A	3NS9	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3LE6	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2XNB	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3LFN	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3LFQ	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3LFS	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2XIN	C	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3FZ1	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2WIH	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3EOC	C	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	3EID	C	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2W05	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2R64	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTA	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTH	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTI	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTJ	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VT	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTM	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTN	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTO	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)
3PXF	A	2VTP	A	97.39 % (query) and 100.00 % (subject)	97.39 % (query) and 100.00 % (subject)

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