1. Abstract

Alzheimer disease (AD) is the most common form of dementia contributing to about 60–70% of cases. B-Site amyloid precursor protein cleaving enzyme-1 (BACE1) plays an important role in the onset of AD and has become one of the important drug targets for AD. This approach has led to the development of promising inhibitors, many of which are going through different phases of clinical trials. Nonetheless, the high failure rate of lead drug candidates targeting brought to the forefront the need for finding new drugs to uncover the mystery behind AD. In Alzheimer's disease, brain cells that process, store and retrieve information degenerate and die. Although scientists do not yet know the underlying cause of this destruction, they have identified several possible culprits. Multiple ligands pharmacophore model was generated using phase to screen retrieved compounds against a four-site (ADDR) hypothesis. Based on binding affinity, the top eight compounds were chosen for further analysis. The compounds were filtered for drug-likeness using absorption, distribution, metabolism, excretion and toxicity to prediction. The insights obtained from this study could be employed to produce next-generation drug for AD.

2. Keyword

Alzheimer's disease, Beta-amyloid Protein, Uniprot, Swiss Model, Verify 3D, Protparam

3. Introduction

What is beta-amyloid?

Amyloid beta (Aβ or Abeta) denotes peptides of 36–43 amino acids that are crucially involved in Alzheimer's disease as the main component of the amyloid plaques found in the brains of Alzheimer patients Beta-amyloid is a small piece of a larger protein called “amyloid precursor protein” (APP). Although scientists have not yet determined APP’s normal function, they know a great deal about how it appears to work. In its complete form, APP extends from the inside of brain cells to the outside by passing through the fatty membrane around the cell. When APP is

“activated” to do its normal job, it is cut by other proteins into separate, smaller sections that stay inside and outside cells. There are several different ways APP can be cut; under some circumstances, one of the pieces produced is beta-amyloid.

Beta-amyloid and amyloid hypothesis

In Alzheimer’s disease, brain cells that process, store and retrieve information degenerate and die. Although scientists do not yet know the underlying cause of this destruction, they have identified several possible culprits. One prime suspect is a microscopic brain protein fragment called beta-amyloid, a sticky compound that accumulates in the brain, disrupting communication between brain cells and eventually killing them. Some researchers believe that flaws in the processes governing production, accumulation or disposal of beta-amyloid are the primary cause of Alzheimer’s. This theory is called “the amyloid hypothesis.” Although early studies suggested that amyloid plaques —large accumulations of beta-amyloid —were the cause of nerve cell toxicity in Alzheimer’s, researchers now believe that small, soluble aggregates of beta-amyloid may be more toxic.

Why beta-amyloid a prime suspect in Alzheimer’s disease?

It accumulates in stages into microscopic amyloid plaques that are considered a hallmark of a brain affected by Alzheimer’s. The pieces first form small clusters called oligomers, then chains of clusters called fibrils, then “mats” of fibrils called beta-sheets. The final stage is plaques, Which contain clumps of beta-sheets and other substances. According to the amyloid hypothesis, these stages of beta-amyloid aggregation disrupt cell-to-cell communication and activate immune cells. These immune cells trigger inflammation. Ultimately, the brain cells are destroyed.

 Protein structure prediction

Protein structure prediction is the inference of three dimensional structure of protein from its amino acid sequence. That is, the prediction of its folding and its secondary and tertiary structure from its primary structure. Protein structure prediction is one of the most important goals in bioinformatics.

It is highly important in medicine (for example, in drug design), a continuous evaluation of protein structure prediction web servers is performed by the community project CAMEO3D.

Methods for protein structure prediction.

1. Experimental methods.

2. Computational methods.

Experimental method –

X-RAY CRYSTALLOGRAPHY

X-Ray crystallography technique is most accurate In-vitro method but it is Time consuming and expensive technique. X-ray crystallography is a technique used for determining the atomic and molecular structure of a crystal, in which the crystalline atoms cause a beam of incident X- rays to diffract into many specific directions. By measuring the angles and intensities of these diffracted beams, a crystallographer can produce a three-dimensional picture of the density of electrons within the crystal. From this electron density, the mean positions of the atoms in the crystal can be determined, as well as their chemical bonds, their disorder, and various other information.

Since many materials can form crystals—such as salts, metals, minerals, semiconductors, as well as various inorganic, organic, and biological molecules—X-ray crystallography has been fundamental in the development of many scientific fields. In its first decades of use, this method determined the size of atoms, the lengths and types of chemical bonds, and the atomic-scale differences among various materials, especially minerals and alloys.

The method also revealed the structure and function of many biological molecules, including vitamins, drugs, proteins and nucleic acids such as DNA. X-ray crystallography is still the chief method for characterizing the atomic structure of new materials and in discerning materials that appear similar by other experiments.

X-ray crystal structures can also account for unusual electronic or elastic properties of a material, shed light on chemical interactions and processes, or serve as the basis for designing pharmaceuticals against diseases.

NMR

Over the past fifty years nuclear magnetic resonance spectroscopy, commonly referred to as NMR, has become the preeminent technique for determining the structure of organic compounds.

Of all the spectroscopic methods, it is the only one for which a complete analysis and interpretation of the entire spectrum is normally expected. Although larger amounts of sample are needed than for mass spectroscopy, NMR is non-destructive, and with modern instruments good data may be obtained from samples weighing less than a milligram. To be successful in using NMR as an analytical tool, it is necessary to understand the physical principles on which the methods are based.

Nuclear magnetic resonance spectroscopy, most commonly known as spectroscopy or magnetic resonance spectroscopy (MRS), is a spectroscopic technique to observe local magnetic fields around atomic nuclei. The sample is placed in a magnetic field and the NMR signal is produced by excitation of the nuclei sample with radio waves into nuclear magnetic resonance, which is detected with sensitive radio receivers. The intra-molecular magnetic field around an atom in a molecule changes the resonance frequency, thus giving access to details of the electronic structure of a molecule and its individual functional groups. As the fields are unique or highly characteristic to individual compounds, in modern organic chemistry practice, NMR

Spectroscopy is the definitive method to identify monomolecular organic compounds. Similarly, biochemists use NMR to identify proteins and other complex molecules. Besides identification, NMR spectroscopy provides detailed information about the structure, dynamics, reaction state, and chemical environment of molecules. The most common types of NMR are proton and carbon-13 NMR spectroscopy, but it is applicable to any kind of sample that contains nuclei possessing spin.

Electron Microscopy

The electron microscope is a type of microscope that uses a beam of electrons to create an image of the specimen. It is capable of much higher magnifications and has a greater resolving power than a light microscope, allowing it to see much smaller objects in finer detail. They are large, expensive pieces of equipment, generally standing alone in a small, specially designed room and requiring trained personnel to operate them. An electron microscope is a microscope that uses a beam of accelerated electrons as a source of illumination. As the wavelength of an electron can be up to 100,000 times shorter than that of visible light photons, electron microscopes have a higher resolving power than light microscopes and can reveal the structure of smaller objects. A scanning transmission electron microscope has achieved better than 50 pm resolution in annular dark-field imaging mode[1] and magnifications of up to about 10,000,000x whereas most light microscopes are limited by diffraction to about 200 nm resolution and useful magnifications below 2000x. Electron microscopes have electron optical lens systems that are analogous to the glass lenses of an optical light microscope.

Electron microscopes are used to investigate the ultrastructure of a wide range of biological and inorganic specimens including microorganisms, cells, large molecules, biopsy samples, metals, and crystals. Industrially, electron microscopes are often used for quality control and failure analysis. Modern electron microscopes produce electron micrographs using specialized digital cameras and frame grabbers to capture the image.

Computational Method

Protein structure prediction is the inference of the three-dimensional structure of a protein from its amino acid sequence that is, the prediction of its folding and its secondary and tertiary structure from its primary structure. Structure prediction is fundamentally different from the inverse problem of protein design. Protein structure prediction is one of the most important goals pursued by bioinformatics and theoretical chemistry; it is highly important in medicine (for example, in drug design) and biotechnology. Every two years, the performance of current methods is assessed in the CASP experiment (Critical Assessment of Techniques for Protein Structure Prediction). A continuous evaluation of protein structure prediction web servers is performed by the community project CAMEO3D.

The major techniques for three dimensional structure predictions are following

Structure Based

Homology Modelling

Threading

Sequence Based

1. Ab intio

1. Homology Modelling

Homology modeling, also known as comparative modeling of protein, refers to constructing an atomic-resolution model of the "target" protein from its amino acid sequence and an experimental three-dimensional structure of a related homologous protein (the "template"). Homology modeling relies on the identification of one or more known protein structures likely to resemble the structure of the query sequence, and on the production of an alignment that maps residues in the query sequence to residues in the template sequence. It has been shown that protein structures are more conserved than protein sequences amongst homologues, but sequences falling below a 20% sequence identity can have very different structure.

Homology modeling can produce high-quality structural models when the target and template are closely related, which has inspired the formation of a structural genomics consortium dedicated to the production of representative experimental structures for all classes of protein folds.[5] The chief inaccuracies in homology modeling, which worsen with lower sequence identity, derive from errors in the initial sequence alignment and from improper template selection.[6] Like other methods of structure prediction, current practice in homology modeling is assessed in a biennial large-scale experiment known as the Critical Assessment of Techniques for Protein Structure Prediction, or CASP.

Steps: Template recognition and initial alignment

The sequence of similarity can be searched using BLAST or Psi blast or fold recognition methods and align with the known structures in PDB. PDB which is the largest database contains only experimentally resolved structure. BLAST allows comparing a query sequence with a database such as PDB and identifying the best sequence which shares a high degree of similarity.

Backbone generation

The backbone generation from the aligned regions can be done using modelling tools such as Modeller or CASP. The actual experimentally determined structures contain Manual errors due to poor electron density in the map. Therefore a good model has to be chosen with less number of errors.

Loop Modelling

There are two main ways to overcome this and model the loop region:

Knowledge based:

User can search PDB for known loops with endpoints that match the residues between loops that have to be inserted and simply copy the loop conformation.

Energy based:

The quality of a loop is determined with energy function and minimizes the function using Monte Carlo or molecular dynamics to find the best loop conformation.

Side Chain Modelling

Proteins that are structurally similar, have similar torsion angle about Ca-Cb bond (psi angle) when comparing with side chain conformations. In such cases, copying conserved residues entirely from the template to the model will result in higher accuracy than copying the backbone or re-predicting side chains. Side chain conformations are partially knowledge based which uses libraries of roamers extracted from high resolution x-ray structures.

Model Optimization

Sometimes the roamers are predicted based on incorrect backbone or incorrect prediction. Such cases modeling programs either restrain the atom positions and/or apply only a few hundred steps of energy minimization to get an accurate value. This accuracy can be achieved by 2 ways.

Quantum force field

Self-parameterizing force fields

Model Validation

If the value is > 90% then accuracy can be compared to crystallography, except for a few individual side chains. If its value ranges between 50-90 % r.m.s.d. error can be as large as

1.5 Å, with considerably more errors. If the value is <25% the alignment turns out to be difficult for homology modeling, often leading to quite larger errors.

2. Threading

Protein threading, also known as fold recognition, is a method of protein modelling which is used to model those proteins which have the same fold as proteins of known structures, but do not have homologous proteins with known structure. It differs from the homology modelling method of structure prediction as it (protein threading) is used for proteins which do not have their homologous protein structures deposited in the Protein Data Bank (PDB), whereas homology modelling is used for those proteins which do. Threading works by using statistical knowledge of the relationship between the structures deposited in the PDB and the sequence of the protein which one wishes to model.

The prediction is made by "threading" (i.e. placing, aligning) each amino acid in the target sequence to a position in the template structure, and evaluating how well the target fits the template. After the best-fit template is selected, the structural model of the sequence is built based on the alignment with the chosen template. Protein threading is based on two basic observations: that the number of different folds in nature is fairly small (approximately 1300); and that 90% of the new structures submitted to the PDB in the past three years have similar structural folds to ones already in the PDB.

3. Ab initio

Protein modelling methods seek to build three-dimensional protein models "from scratch", i.e., based on physical principles rather than on previously solved structures. There are many possible procedures that either attempt to mimic protein folding or apply some stochastic method to search possible solutions (i.e., global optimization of a suitable energy function). These procedures tend to require vast computational resources, and have thus only

Been carried out for tiny proteins. To predict protein structure de novo for larger proteins will require better algorithms and larger computational resources like those afforded by either powerful supercomputers (such as Blue Gene or MDGRAPE-3) or distributed computing. Although these computational barriers are vast, the potential benefits of structural genomics (by predicted or experimental methods) make ab initio structure prediction an active research field.

4. Technological Aspect

Uniprot

UniProt is a freely accessible database of protein sequence and functional information, many entries being derived from genome sequencing projects. It contains a large amount of information about the biological function of proteins derived from the research literature.

The Universal Protein Resource (UniProt) is a comprehensive resource for protein sequence and annotation data. The UniProt databases are the UniProt Knowledgebase (UniProtKB), the UniProt Reference Clusters (UniRef), and the UniProt Archive (UniParc). UniProt is a collaboration between the European Bioinformatics Institute (EMBL-EBI), the SIB Swiss Institute of Bioinformatics and the Protein Information Resource (PIR). Across the three institutes more than 100 people are involved through different tasks such as database curation, software development and support.

Swiss Model

SWISS-MODEL is a structural bioinformatics web-server dedicated to homology modeling of protein 3D structures. Homology modeling is currently the most accurate method to generate reliable three-dimensional protein structure models and is routinely used in many practical applications. Homology (or comparative) modelling methods make use of experimental protein structures ("templates") to build models for evolutionary related proteins ("targets").

Today, SWISS-MODEL consists of three tightly integrated components: (1) The SWISS-MODEL pipeline – a suite of software tools and databases for automated protein structure modelling, (2) The SWISS-MODEL Workspace – a web-based graphical user workbench, (3) The SWISS-MODEL Repository – a continuously updated database of homology models for a set of model organism proteomes of high biomedical interest.

SWISS-MODEL pipeline comprises the four main steps that are involved in building a homology model of a given protein structure:

Identification of structural template(s). BLAST and HHblits are used to identify Templates. The templates are stored in the SWISS-MODEL Template Library (SMTL), which is derived from PDB.

Alignment of target sequence and template structure(s).

Model building and energy minimization. SWISS-MODEL implements a rigid fragment assembly approach for modelling.

Assessment of the model's quality using QMEAN, a statistical potential of mean force.

Verify 3D

Macromolecular structure validation is the process of evaluating reliability for 3-dimensional atomic models of large biological molecules such as proteins and nucleic acids. These models, which provide 3D coordinates for each atom in the molecule (see example in the image), come from structural biology experiments such as x-ray crystallography or nuclear magnetic resonance (NMR). The validation has three aspects:

Checking on the validity of the thousands to millions of measurements in the experiment;

Checking how consistent the atomic model is with those experimental data; and

Checking consistency of the model with known physical and chemical properties.

ProtParam

ProtParam computes various physico-chemical properties that can be deduced from a protein sequence. No additional information is required about the protein under consideration. The protein can either be specified as a Swiss-Prot/TrEMBL accession number or ID, or in form of a raw sequence. White space and numbers are ignored. If you provide the accession number of a Swiss-Prot/TrEMBL entry, you will be prompted with an intermediary page that allows you to select the portion of the sequence on which you would like to perform the analysis. The choice includes a selection of mature chains or peptides and domains from the Swiss-Prot feature table (which can be chosen by clicking on the positions), as well as the possibility to enter start and end position in two boxes. By

Thomas J. Paul, Zachary Hoffmann, and Rajeev Prabhakar et.al.2016, 7 In this combined experimental (deep ultraviolet resonance Raman (DUVRR) spectroscopy and atomic force microscopy (AFM)) and theoretical (molecular dynamics (MD) simulations and stress–strain (SS)) study, the structural and mechanical properties of amyloid beta (Aβ40) fibrils have been investigated. The DUVRR spectroscopy and AFM experiments confirmed the formation of linear, unbranched and β-sheet rich fibrils. The fibrils (Aβ40), formed using monomers, were equilibrated using all-atom MD simulations. The structural properties such as β-sheet character, twist, interstrand distance, and periodicity of these fibrils were found to be in agreement with experimental measurements. Furthermore, Young's modulus = 4.2 GPa computed using SS calculations was supported by measured values of 1.79 ± 0.41 and 3.2 ± 0.8 GPa provided by two separate AFM experiments. These results revealed size dependence of structural and material properties of amyloid fibrils and show the utility of such combined experimental and theoretical studies in the design of precisely engineered biomaterials.

D Tripathi, et.al, December 17, 2017 Alzheimer's Disease (AD) is a progressive neurodegenerative disease that affects memory and other mental functions due to the accumulation of Amyloid-Beta (Aβ) plaques. The functions carried out by the Aβ protein leads to abnormalities in the suffering patient. If a molecule binds to the Aβ protein, it could lead to potential treatment. To propose new treatments for AD, novel molecules were identified that

bind to the active site of Aβ. First, a correlation between reported. he results of this study can be used as a tool to finding novel, medically relevant new molecules for other neurodegenerative diseases and assist researchers in developing new drugs to treat Alzheimer's Disease.

Ga Yeon Lee, et.al, December 15, 2017. Amyloidosis is caused by the extracellular deposition of insoluble fibrils and results in multiple organ dysfunctions. Shotgun proteomics analysis obligatorily requires not only expensive instruments but also highly-experienced specialists to interpret the analysis. Thus, they developed a method of LMD combined with multiple reaction monitoring mass spectrometry (MRM-MS) that can detect three most common types of amyloidosis. They tested this diagnostic method in 16 Congo red-positive tissues and 10 Congo Red-negative control tissues. The results showed better performance in amyloidosis typing than other analytical techniques. This novel diagnostic approach can achieve successful amyloidosis typing with high specificity and sensitivity and be implemented more easily in general clinical laboratories.

Wei-Dong Chen, et.al, 30 September 2015**.** The amyloid β peptide (Aβ) is a critical initiator that triggers the progression of Alzheimer's disease (AD) via accumulation and aggregation, of which the process may be caused by Aβ overproduction or perturbation clearance. Aβ is generated from amyloid precursor protein through sequential cleavage of β- and γ-secretes while

Aβ removal is dependent on the proteolysis and lysosome degradation system. Here, we overviewed the biogenesis and toxicity of Aβ as well as the regulation of Aβ production and clearance. Moreover, we also summarized the animal models correlated with Aβ that are essential in AD research. In addition, we discussed current immunotherapeutic approaches targeting Aβ to give some clues for exploring the more potentially efficient drugs for treatment of AD.

5. Objectives

Modelling of the 3D protein structure of available protein sequence of beta amyloid using Swiss model.

Estimation of Structure Quality by Verify 3D.

Finding the Physiochemical properties of structure.

6. METHODOLOGY-

UNIPROT –

Uniprot is a freely accessible database of protein sequence and functional information.

It contains a large amount of information about the biological function of proteins derived from the research literature.

STEP 1 - Open the UniProt database.

STEP 2 - Search Beta-amyloid protein.

STEP 3 - Download fasta sequence.

SWISS-MODEL -

Swiss-model is a structural bioinformatics web-server, which is used for homology

Modeling of protein 3D structures.

Homology modeling is most accurate method to generate for 3 Dimensional protein structures.

STEP 1 - Open the Swiss-model software.

STEP 2 - Paste the fasta sequence. STEP 3 - Upload the fasta sequence file. STEP 4 - Build the model.

VERIFY 3D –

Verify 3D is a software use for the Quality estimation and structure validation.

It used to obtain a score for each of 20 amino acid in this structural class. The vertical axis in the plot represent the averages 3D and 1D profile score for each residues sliding windows .The scores ranges from -1 bad score to + 1 good score

Graphs of Verify _3d result for template structures and the model showing the average environmental propensity score for each residue.

STEP 1 - Open the verify_3d tool.

STEP 2 - Upload a file in browser.

STEP 3 - Run verify_3d after complete procedure we got a graph as result.

ProtParam -

ProtParam is a tool which allows the computation of various physical and chemical parameters for a given protein stored in swiss-prot.

ProtParam computes various physio-chemical properties that can be deduced from a protein sequence.

STEP 1 - Open a ProtParam tool

STEP 2 – Enter a Swiss prot accession number (AC) or a sequence identifier (ID)

STEP 3 – or paste a protein sequence

STEP 4 – After these process Compute the parameters

STEP 5 - Get a complete sequence of amino acid

STEP 6 – finally get a CSV (Comma Separated Value) format

Procedure

STEP 1 - Open the Unipart database and search protein beta amyloid.

STEP 2 - Download a fasta sequence of this protein

STEP 3 - Open the Swiss model software and paste the protein fasta sequence

STEP 4 - Upload the fasta sequence & Build a model

STEP 5 - Open the verify_3d tool.

STEP 6 - Upload a file in browser.

STEP 7 - Run verify_3d after complete procedure we got a graph as result

STEP 8 - Open a protparam tool

STEP 9 - Enter a Swiss port accession number (AC) or A sequence identifier (ID)

STEP 10 - OR paste a protein sequence

STEP 11 - After these process Compute the parameters

STEP 12 - Get a complete sequence of amino acid

STEP 13 - Finally get a CSV (Comma Separated Value) format.

7. Results and Discussion

1. A0A3Q1MGE4

Fig1. Structure of A0A3Q1MGE4

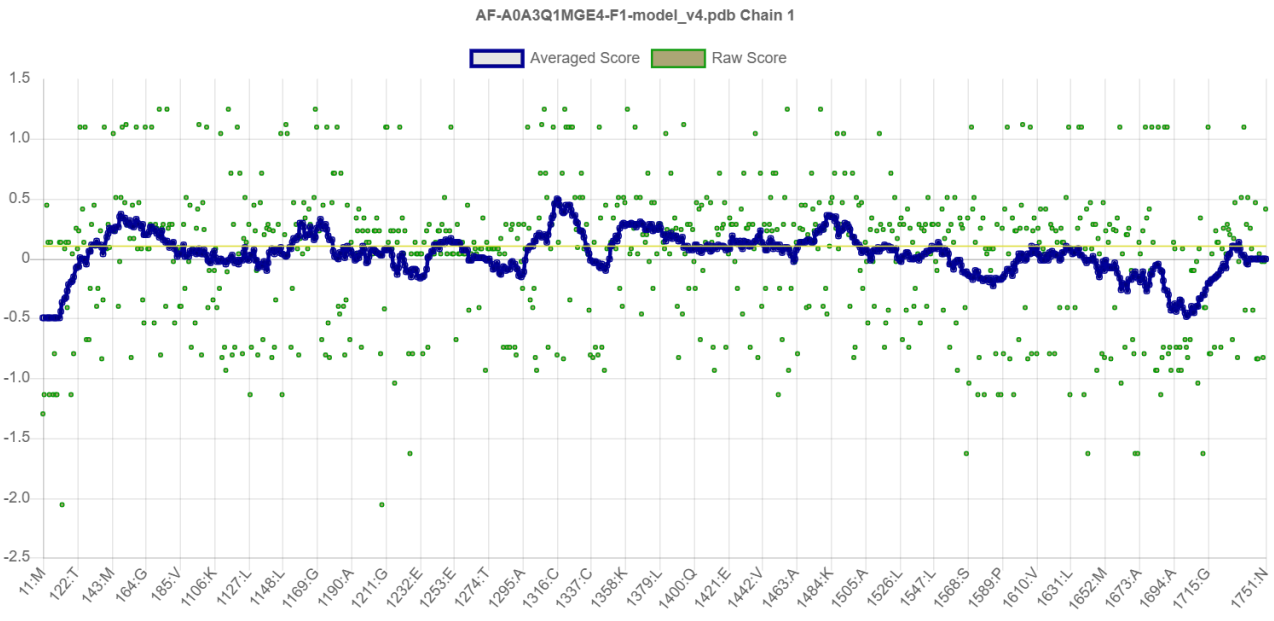

Fig2.Varify_3D

Expasy ProtParam Home | Contact

ProtParam

Selection of endpoints on the sequence

A0A3Q1MGE4_BOVIN (A0A3Q1MGE4)

Amyloid-beta A4 protein
Bos taurus (Bovine)

Please select one of the following features by clicking on a pair of endpoints, and the computation will be carried out for the corresponding sequence fragment. By default, the complete sequence is used.
Note: Only the features corresponding to subsequences of at least 5 residues are highlighted.

FT	SIGNAL	1-17	
FT	CHAIN	18-751	Amyloid-beta A4 protein
FT	TRANSMEM	682-704	Helical
FT	DOMAIN	28-189	E1
FT	DOMAIN	291-341	BPTI/Kunitz inhibitor
FT	DOMAIN	355-546	E2
FT	REGION	28-123	GFLD subdomain
FT	REGION	131-189	CuBD subdomain
FT	REGION	194-284	Disordered
FT	COILED	380-440	
FT	COMPBIAS	195-210	Acidic residues
FT	COMPBIAS	225-263	Acidic residues
FT	COMPBIAS	267-284	Polar residues

Or, if you wish to select a different sequence fragment (at least 5 amino acids long), you can enter the desired endpoints on the sequence here (by default, the computation will be carried out for the complete sequence).
N-terminal:

Fig3.

ProtParam

A,62,8.25565912117177
B,0,0
C,18,2.39680426098535
D,46,6.12516644474035
E,93,12.3834886817577
F,20,2.66311584553928
G,38,5.05992010652463
H,25,3.3288948069241
I,26,3.46205059920106
K,40,5.32623169107856
L,52,6.92410119840213
M,23,3.06258322237017
N,31,4.12782956058589
O,0,0
P,33,4.39414114513981
Q,34,4.52729693741678
R,35,4.66045272969374
S,32,4.26098535286285
T,48,6.39147802929427
U,0,0
V,66,8.78828229027963
W,9,1.19840213049268
X,0,0
Y,20,2.66311584553928
Z,0,0

Fig4. CSV Format

2. A0A140VJC8

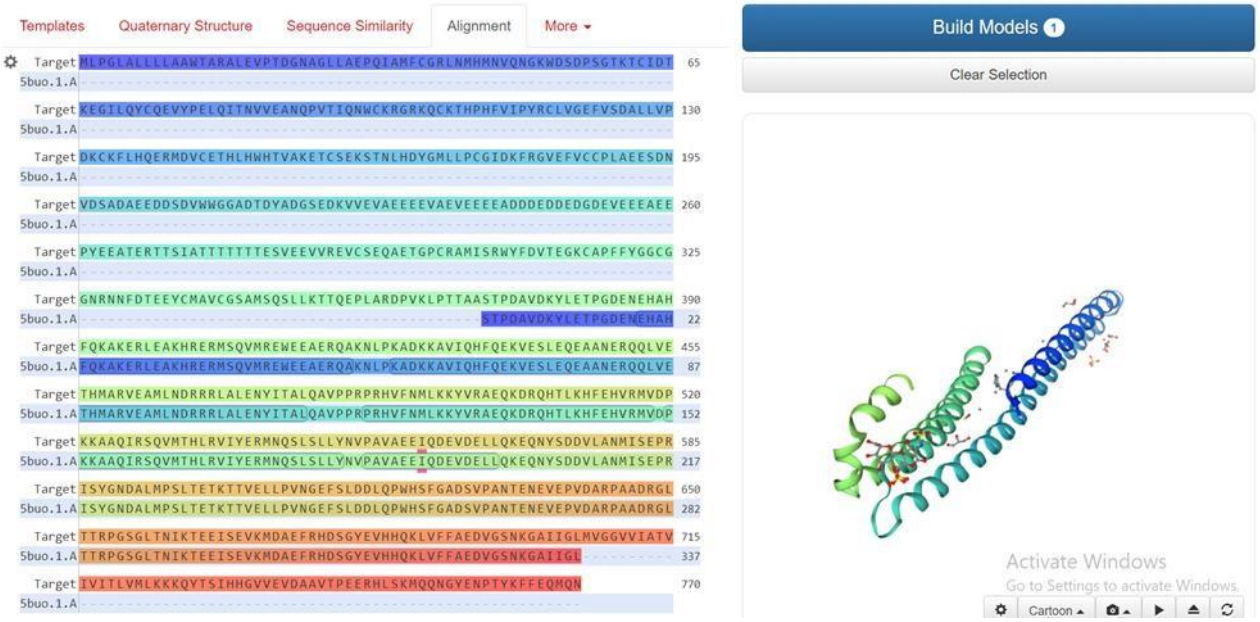

Fig1.
Structure of A0A140VJC8

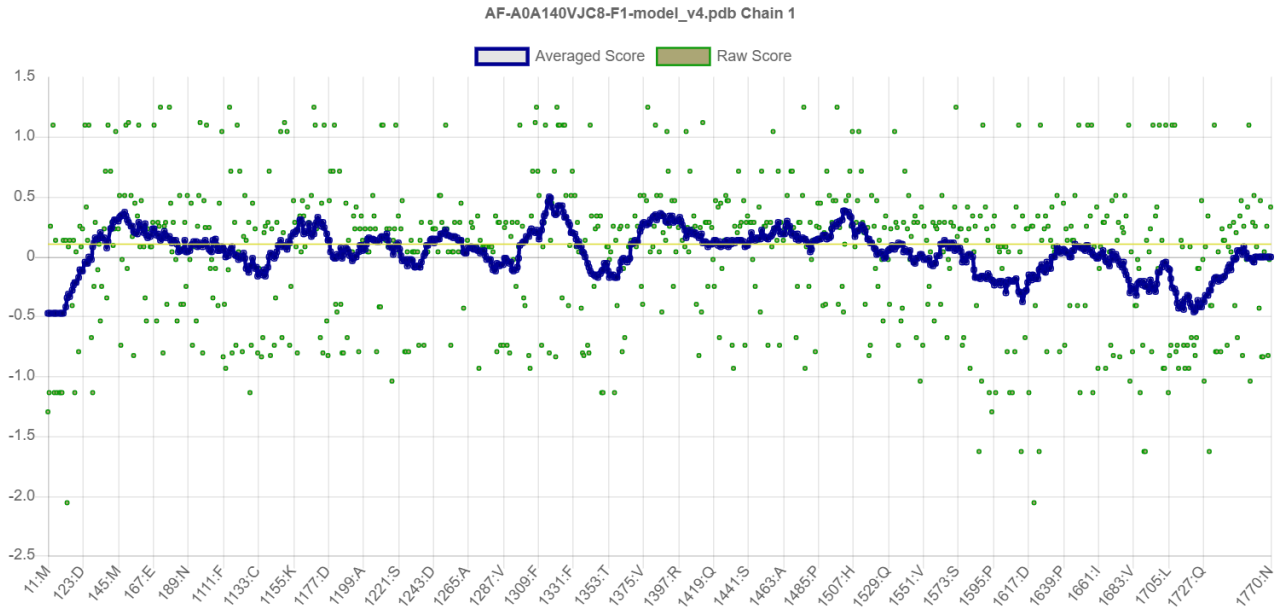

Fig2.veify3

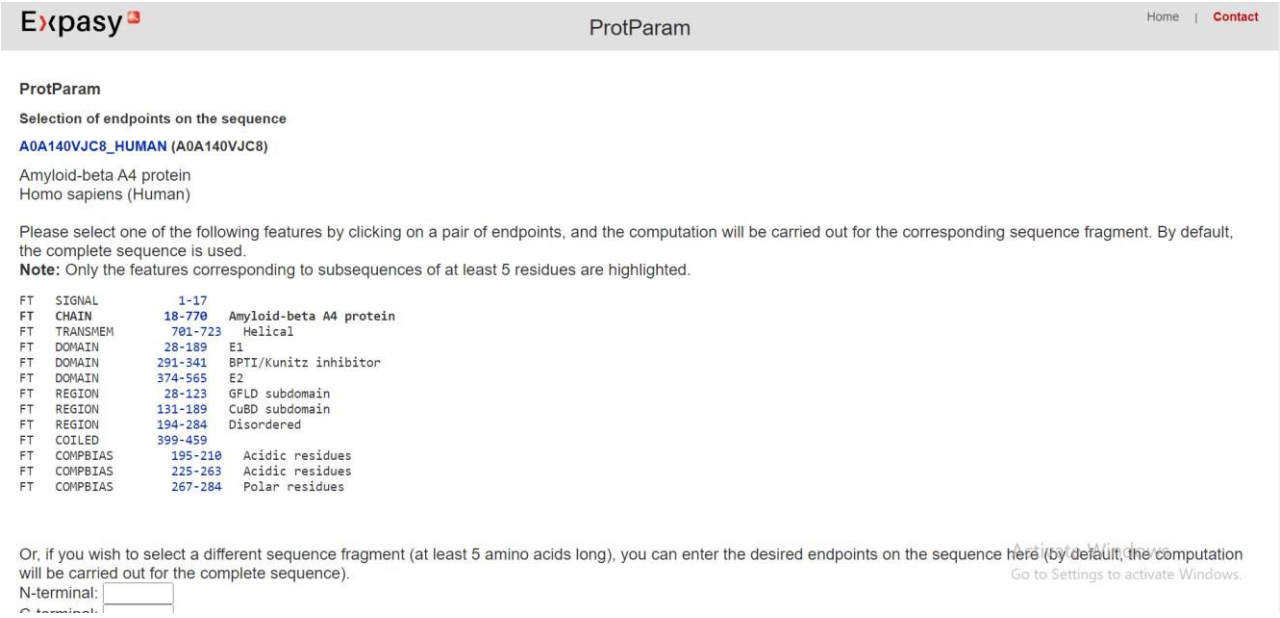

Fig 3. ProtParam

A,63,8.18181818181818
B,0,0
C,18,2.33766233766234
D,50,6.49350649350649
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F,21,2.72727272727273
G,38,4.93506493506494
H,25,3.24675324675325
I,24,3.11688311688312
K,41,5.32467532467532
L,56,7.27272727272727
M,24,3.11688311688312
N,31,4.02597402597403
O,0,0
P,35,4.54545454545455
Q,36,4.67532467532468
R,37,4.80519480519481
S,35,4.54545454545455
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V,65,8.44155844155844
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Fig4. CSV Format

3. B0V0E5

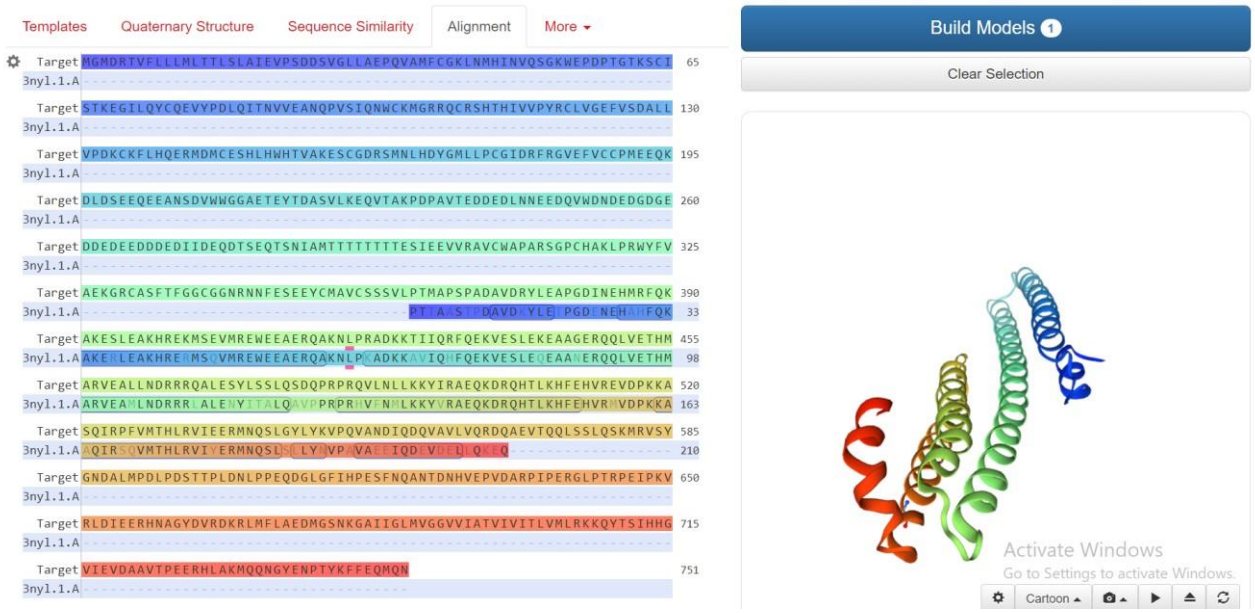

Fig1.N Structure of B0V0E5

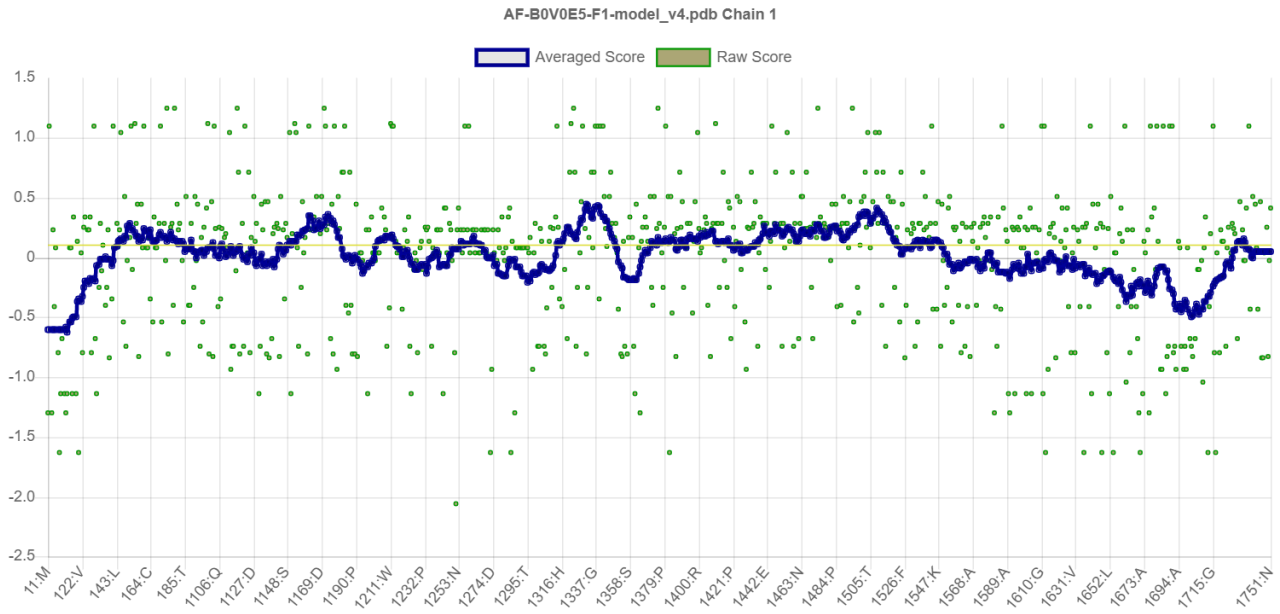

Fig2. Verify 3D

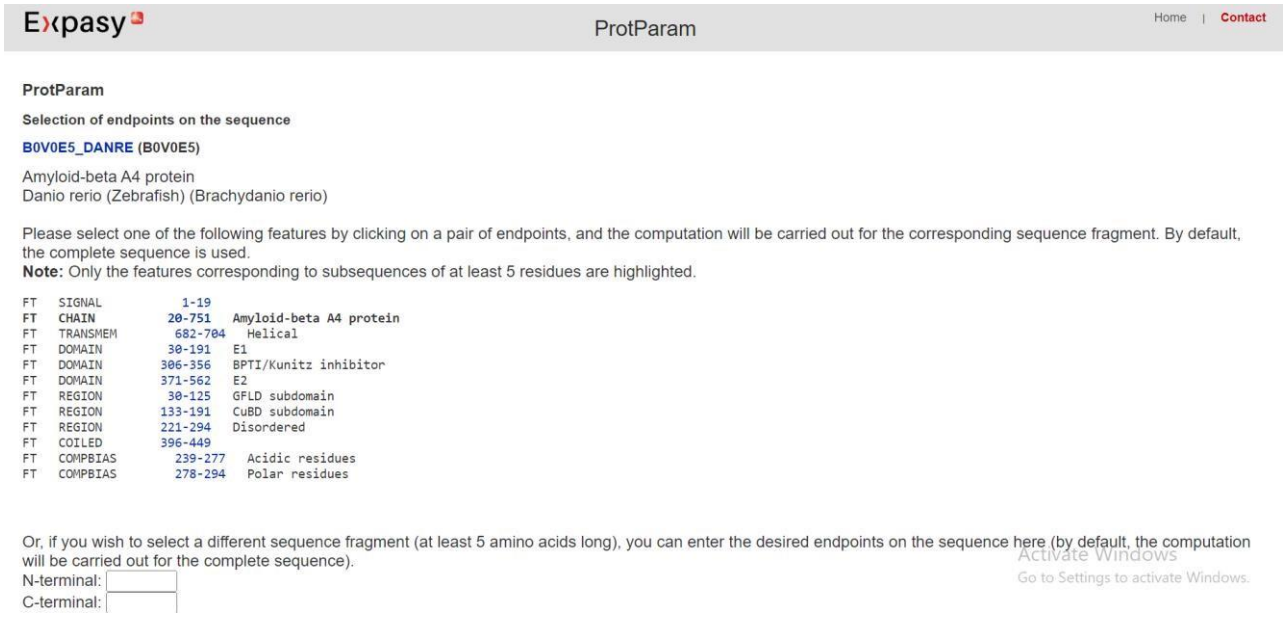

Fig3. Protparam

A,48,6.39147802929427
B,0,0
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D,56,7.45672436750999
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F,19,2.52996005326232
G,37,4.92676431424767
H,22,2.92942743009321
I,30,3.99467376830892
K,37,4.92676431424767
L,57,7.58988015978695
M,28,3.72836218375499
N,30,3.99467376830892
O,0,0
P,39,5.1930758988016
Q,44,5.85885486018642
R,45,5.99201065246338
S,42,5.59254327563249
T,39,5.1930758988016
U,0,0
V,58,7.72303595206391
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Z,0,0

Fig4. CSV Format

4. B4DGD0

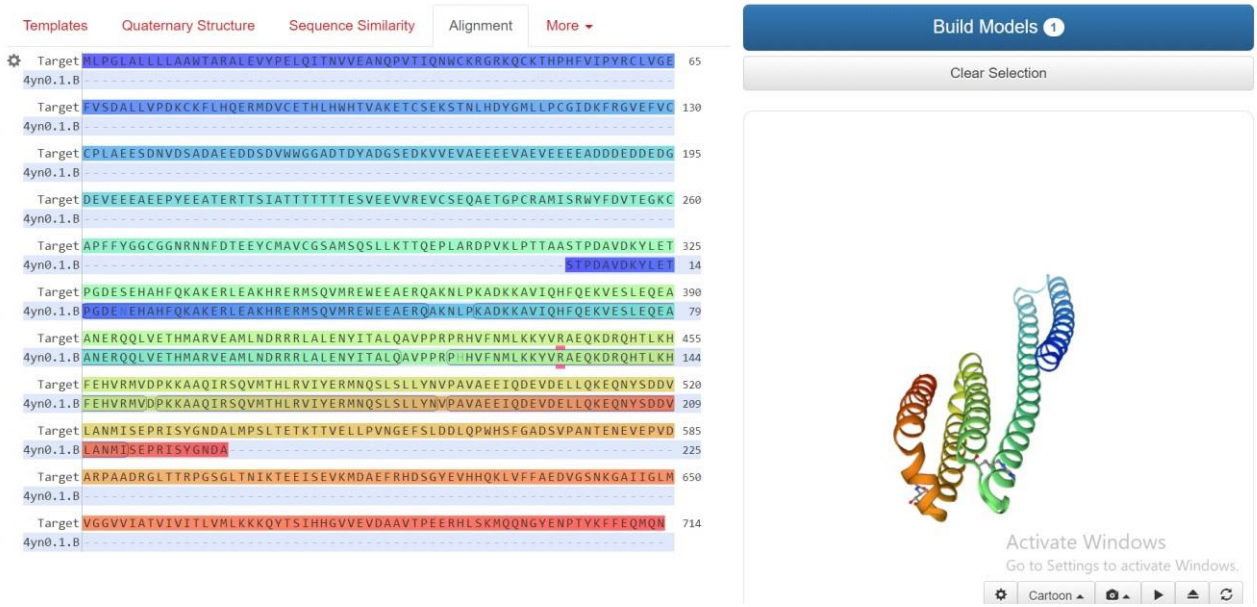

Fig. 1 Structure of B4DGD0

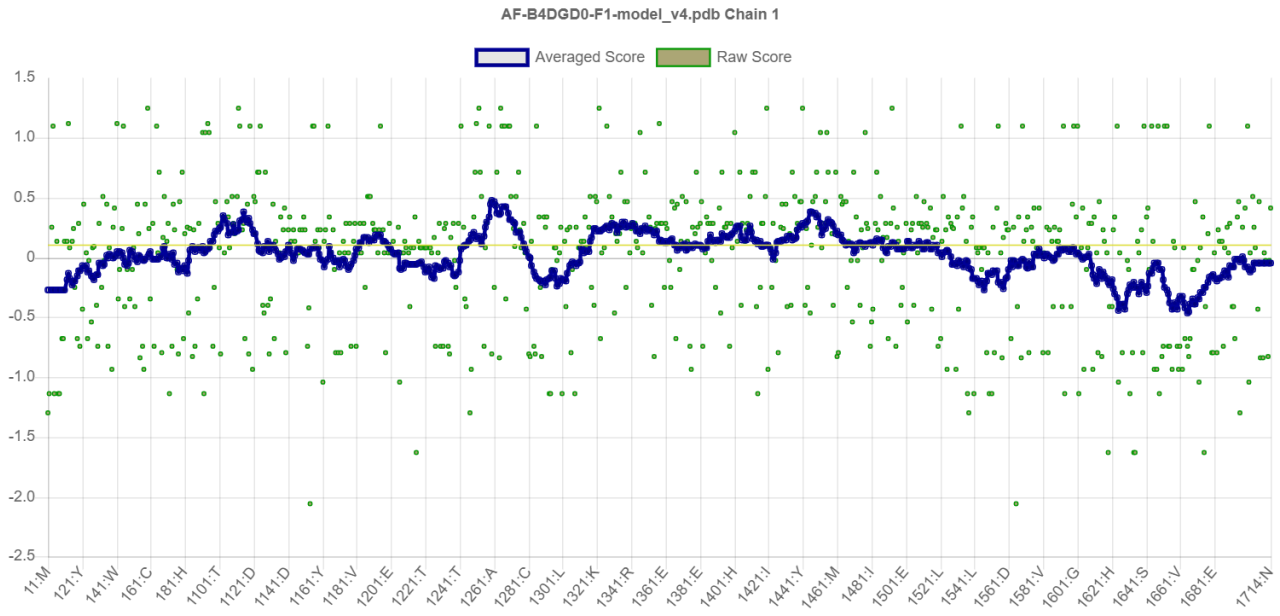

Fig2.

Verify 3D

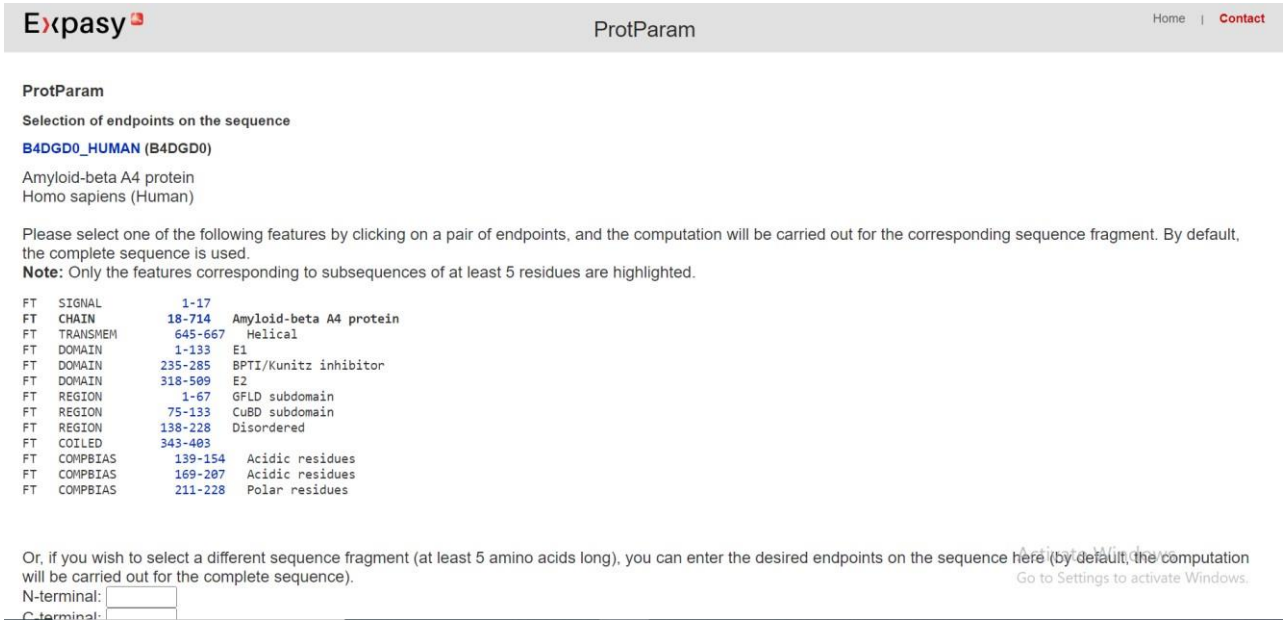

Fig3.

Protparam

A,60,8.40336134453782
B,0,0
C,15,2.10084033613445
D,46,6.44257703081232
E,89,12.4649859943978
F,20,2.80112044817927
G,32,4.48179271708683
H,24,3.36134453781513
I,21,2.94117647058824
K,38,5.32212885154062
L,52,7.28291316526611
M,21,2.94117647058824
N,26,3.64145658263305
O,0,0
P,32,4.48179271708683
Q,32,4.48179271708683
R,36,5.04201680672269
S,34,4.76190476190476
T,46,6.44257703081232
U,0,0
V,63,8.82352941176471
W,8,1.12044817927171
X,0,0
Y,19,2.66106442577031
Z,0,0

Fig4. CSV Format

5. **Q6P6Q5**

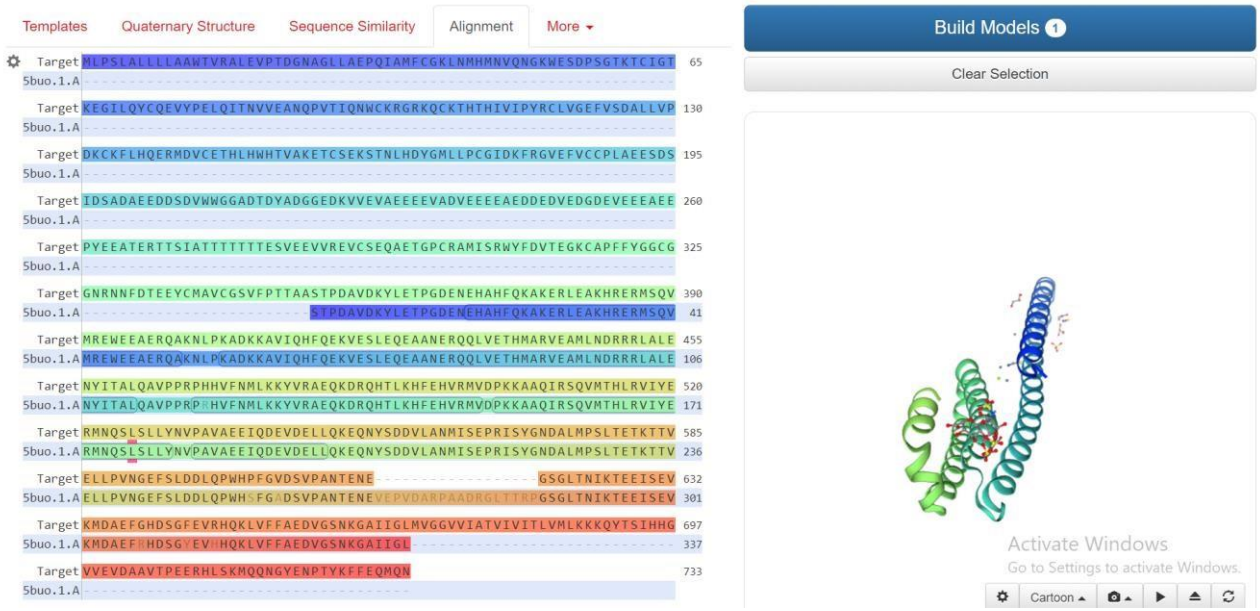

Fig1.
Structure of Q6P6Q5

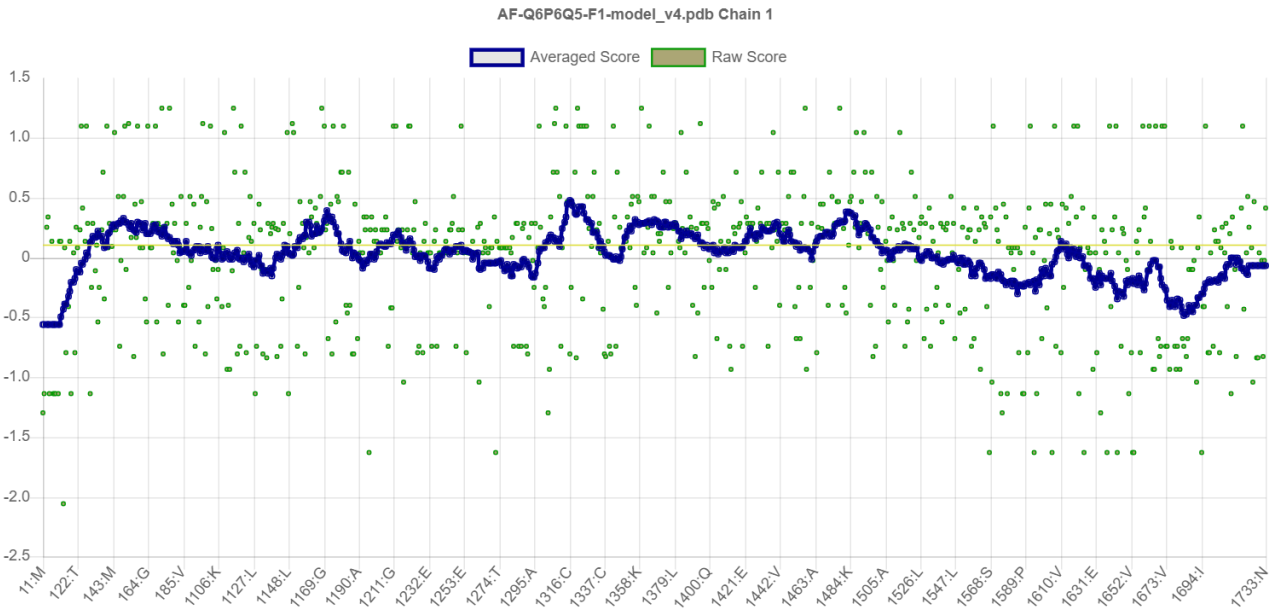

Fig2.Verify 3D

Expasy ProtParam Home | Contact

ProtParam

Selection of endpoints on the sequence

Q6P6Q5_RAT (Q6P6Q5)

Amyloid-beta A4 protein
Rattus norvegicus (Rat)

Please select one of the following features by clicking on a pair of endpoints, and the computation will be carried out for the corresponding sequence fragment. By default, the complete sequence is used.
Note: Only the features corresponding to subsequences of at least 5 residues are highlighted.

FT	SIGNAL	1-17	
FT	CHAIN	18-733	Amyloid-beta A4 protein
FT	TRANSMEM	664-686	Helical
FT	REGION	28-123	GFLD subdomain
FT	REGION	131-189	CuBD subdomain
FT	REGION	196-283	Disordered
FT	COILED	380-440	
FT	COMPBIAS	196-210	Acidic residues
FT	COMPBIAS	225-263	Acidic residues
FT	COMPBIAS	267-283	Polar residues

Or, if you wish to select a different sequence fragment (at least 5 amino acids long), you can enter the desired endpoints on the sequence here (by default, the computation will be carried out for the complete sequence).
N-terminal:
C-terminal:

The sequence Q6P6Q5_RAT consists of 733 amino acids.

Fig3. Protparam

A,56,7.63983628922237
B,0,0
C,18,2.45566166439291
D,44,6.00272851296044
E,91,12.4147339699864
F,22,3.00136425648022
G,39,5.3206002728513
H,25,3.4106412005457
I,26,3.54706684856753
K,40,5.45702592087312
L,51,6.95770804911323
M,23,3.13778990450205
N,30,4.09276944065484
O,0,0
P,30,4.09276944065484
Q,34,4.63847203274215
R,31,4.22919508867667
S,33,4.50204638472033
T,47,6.41200545702592
U,0,0
V,65,8.86766712141883
W,9,1.22783083219645
X,0,0
Y,19,2.59208731241473
Z,0,0

Fig4. CSV Format

6. A0A218KGR2

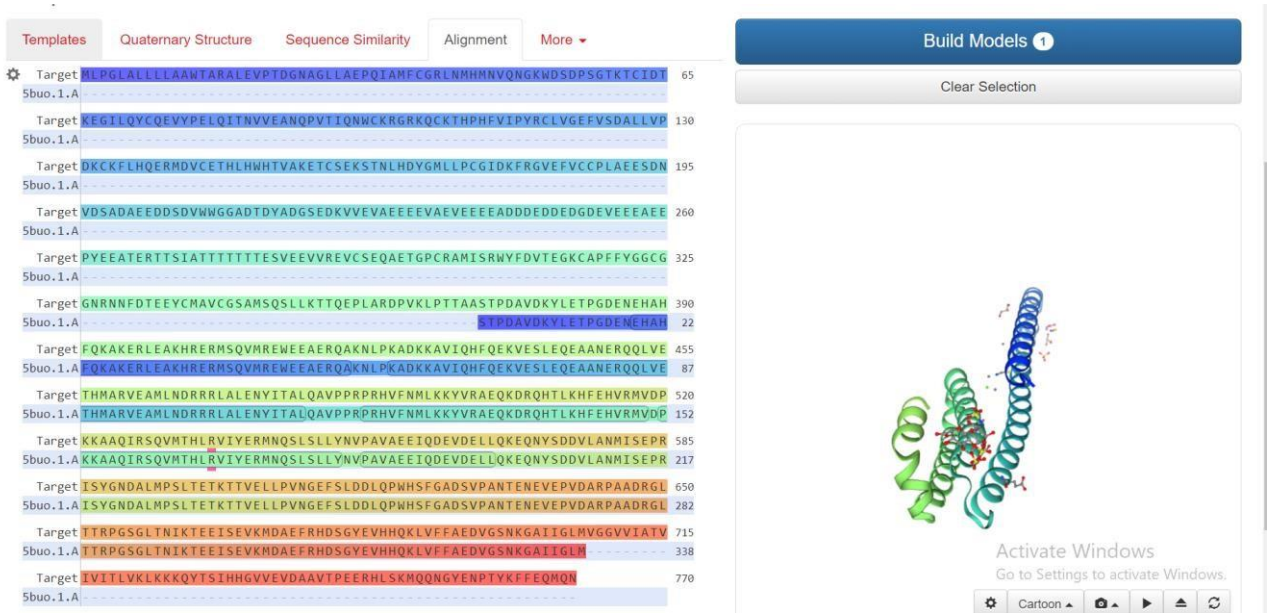

Fig.1 Structure of A0A218KGR2

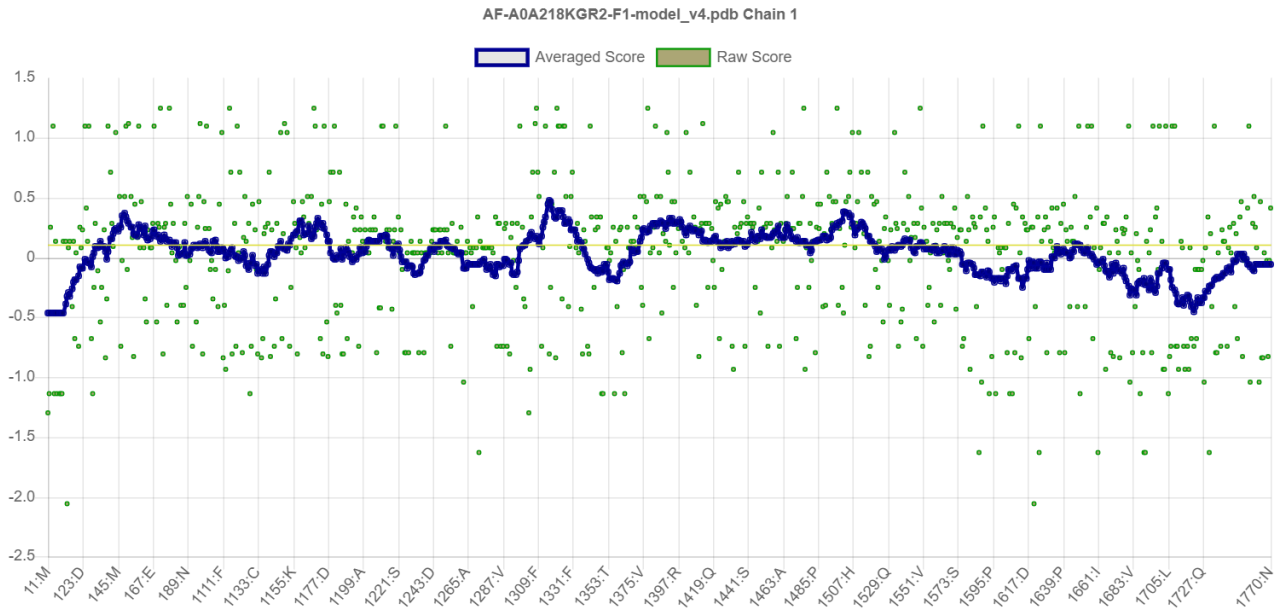

Fig 2. Verify 3D

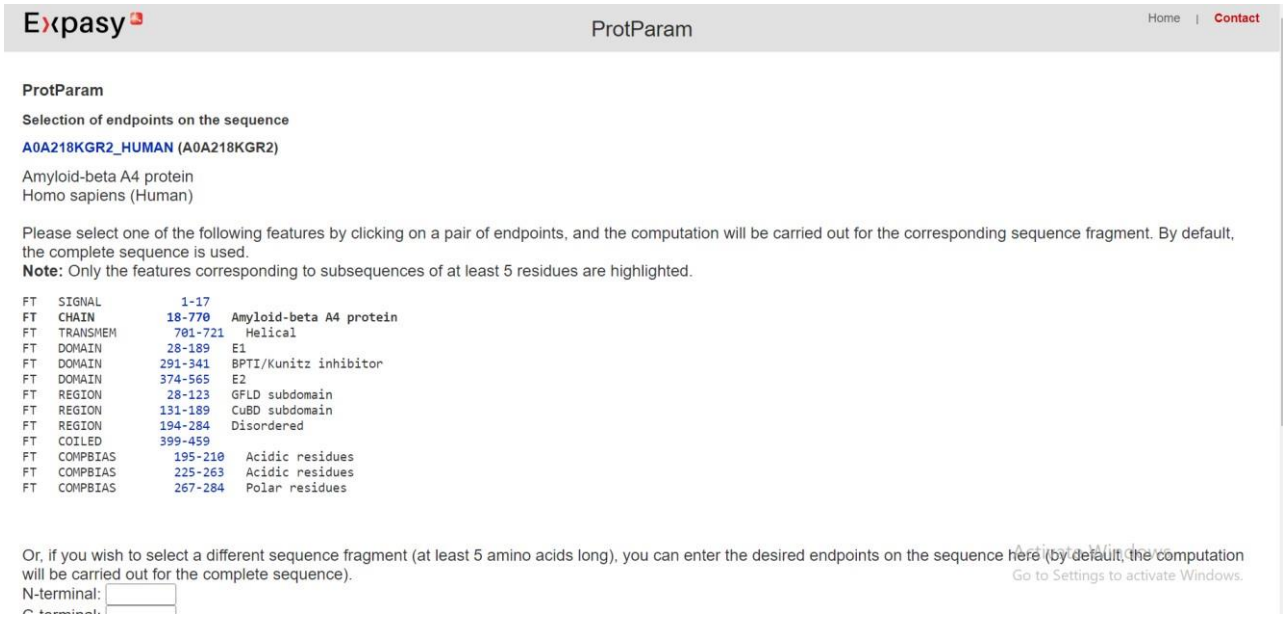

Fig3.

Protparam

A,63,8.18181818181818
B,0,0
C,18,2.33766233766234
D,50,6.49350649350649
E,92,11.9480519480519
F,21,2.72727272727273
G,38,4.93506493506494
H,25,3.24675324675325
I,24,3.11688311688312
K,42,5.45454545454545
L,56,7.27272727272727
M,23,2.98701298701299
N,31,4.02597402597403
O,0,0
P,35,4.54545454545455
Q,36,4.67532467532468
R,37,4.80519480519481
S,35,4.54545454545455
T,50,6.49350649350649
U,0,0
V,65,8.44155844155844
W,9,1.16883116883117
X,0,0
Y,20,2.5974025974026
Z,0,0

Fig.4 CSV Format

7. Q53ZT3

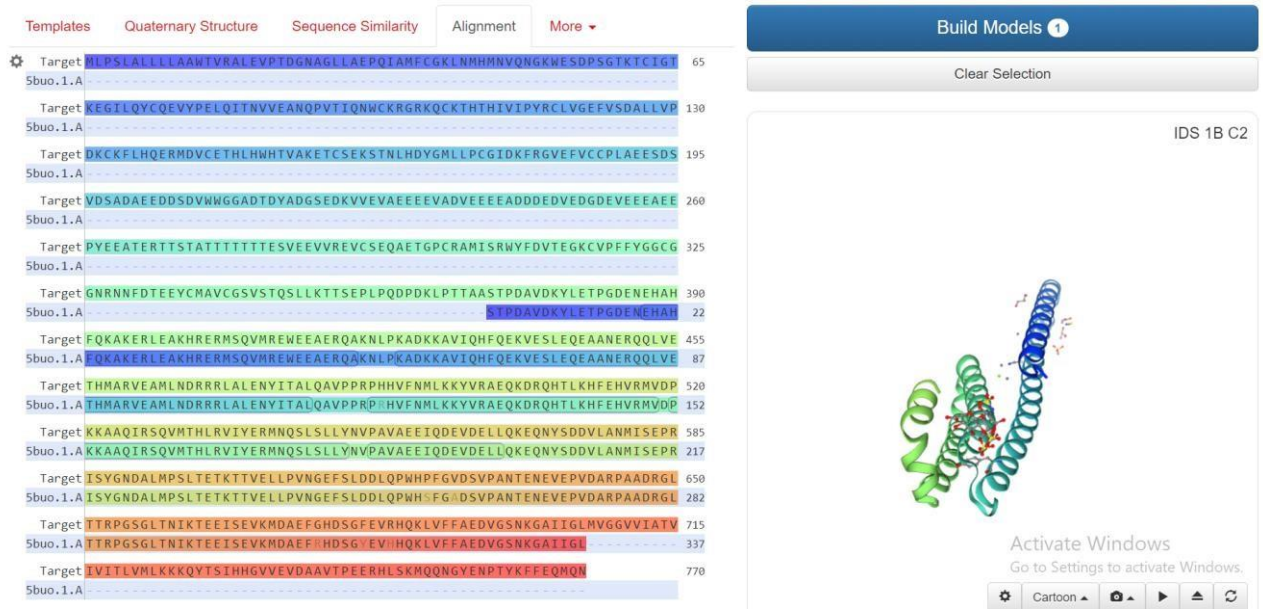

Fig .1

Structure of Q53ZT3

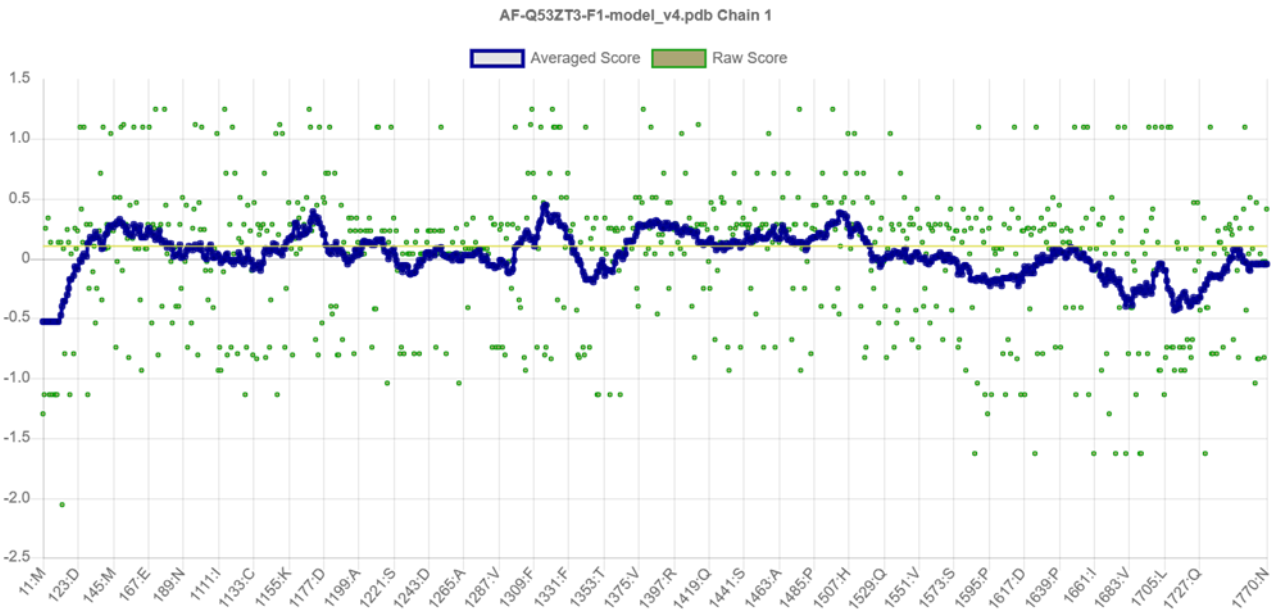

Fig.3 Verify 3D

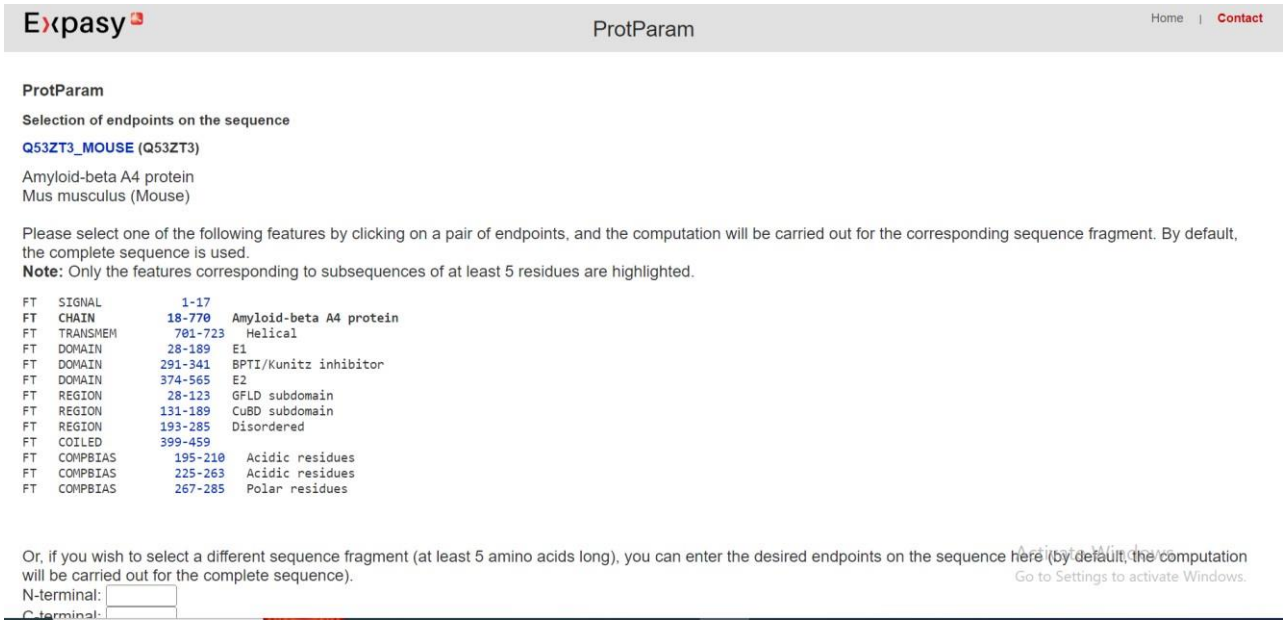

Fig. 4

Protparam

A,58,7.53246753246753
B,0,0
C,18,2.33766233766234
D,49,6.36363636363636
E,92,11.9480519480519
F,21,2.72727272727273
G,39,5.06493506493507
H,25,3.24675324675325
I,24,3.11688311688312
K,42,5.45454545454545
L,56,7.27272727272727
M,23,2.98701298701299
N,30,3.8961038961039
O,0,0
P,36,4.67532467532468
Q,36,4.67532467532468
R,34,4.41558441558442
S,37,4.80519480519481
T,53,6.88311688311688
U,0,0
V,69,8.96103896103896
W,9,1.16883116883117
X,0,0
Y,19,2.46753246753247
Z,0,0

Fig.5 CS Format

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