International Journal of Natural and Engineering Sciences
E-ISSN: 2146-0086 13 (1): 15-18, 2019

In silico Designing of Biofilm-associated Protein (Bap) producing of *Acinetobacter baumannii*

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Received: 13 February 2019
Accepted: 15 October 2019

Abstract
Acinetobacter baumannii is a significant source of nosocomial infections worldwide. *A. baumannii* surface protein, commonly known as biofilm associated protein (Bap), is involved in biofilm formation. Several web servers have been used to facilitate the prediction and design of (Bap) for *A. baumannii.* The results that have been obtained from some servers that have been used in this study were gave a poor and good quality of prediction. SWISS MODEL server gave more promising results. Validation was done for the model study by using QMEAN score and ProSA server. 3D Refine and Mod Refiner were used for model refinement. Finally, ProSA server have been used in order to revalidate the model.

Keywords: *In silico*; Modeling; *Bap; Acinetobacter baumannii*

INTRODUCTION

Acinetobacter baumannii. are Gram-negative aerobic nonmotile coccobacilli, ubiquitous in nature and persistent in hospital environments cause a variety of nosocomial infections [1]. *A. baumannii* is associated with pneumonia, wound infections, meningitis and urinary tract infections. Infections caused by resistant strain of *Acinetobacter* leads to higher degree of morbidity, mortality and increased costs [2]. Biofilms with multiple drug resistance. Biofilm production in *A. baumannii* might promote increased colonization and persistence leading to higher rates of device related infections. Biofilms are highly structured communities of bacteria attached to a surface and are recognized as a common cause of human infection [3]. The discovery of innovative with potential interaction to specific targets is of central importance to the early-stage drug discovery [4]. The aim of this study was to Predict the 3D- Structure of *Bap* protein to *in silico* resolve the major obstacles in the control or in prevention of the diseases caused by *A. baumannii.*

MATERIALS AND METHODS

The amino acids sequence of *Bap* of *A. baumannii* with accession number SSU00145.Various physicochemical parameters of biofilm-associated four broad functional metabolism, cell VICMpred was classes viz.; virulence factor classify *Bap* into process and used to, information storage in the web site proteins and Topology prediction, Protein Data Bank (www.rcsb.org/pdb) was used to find PDB file of the protein,PSIPREDhttp://bioinf.cs.ucl.ac.uk/psipred/,[5] predict protein, Phyre2http://www.sbg.bio.ic.ac.uk/~phyre2/html/page.cgi?id=index, or[6] RaptXhttp://raptorx.uchicago.edu/andSOPMhttps://npsaprabi.ibcp.fr/cgibin/npsa_automat.pl?page=/NPSA/npsa_sopma.html [7,8,9] were used to predict the secondary structure calculations data. (helix, sheets, and coils) are of the default protein. First of all, the protein secondary structure was predicted by SOPMA server online [10]. It has been found that the alpha helix was the most predominant (46.50%), this result followed by random coil (35.31%) and extended strand (12.24%)., Beta turn was also found as (5.94%). Secondly, different results were obtained from the rest servers. Figure (2) represent *Bap* secondary structure obtained from SOPMA servers online.

RESULTS AND DISCUSSION

The primary sequence of the selected proteins from FASTA format of amino acids sequence of *Bap* with accession retrieved from NCBI as a target sequence which consists of 2271 amino acids. Analysis of the physicochemical characteristics of *Bap* revealed that the protein is acidic (estimated isoelectric point [pI] = 3.37) with a molecular weight of 220959.8 Da Table (1) and Figure (1).

Table (1): Shows Result of Physicochemical and Functional Characterization

Properties	Value
Sequence length	2271
Molecular weight (Da)	220959.8
Theoretical pI	3.37
Extinction coefficients (M-1 ·cm-1)	108525
Instability index	17.36
Aliphatic index	81.92
GRAVY index	0.020
Total number of positively charged residues (Arg + Lys)	210
Total number of negatively charged residues (Asp + Glu)	27

Characterization

Topological analysis was performed to predict the post-translation location of the proteins, analysis done at SRTpred indicated that all proteins had secretory Protein with score = 0.09524, which mean these proteins are exported outside the cell post-translation, secretory signal sequences that are located at the amino termini direct the translated proteins to the secretory (Sec) apparatus in the membrane and are

cleaved during secretion.

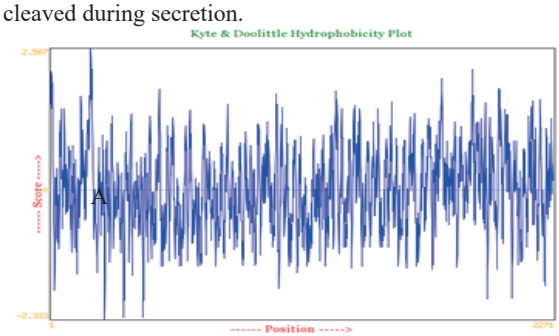


Figure (1): Hydrophobicity Plot of Bap protein

The secondary structure analysis PSIPRED, SOPMA and Phyre2 were applied for secondary structure calculations (helix, sheets, and coils) of the hypothetical protein. First, the secondary structure of the protein remained predicted by SOPMA server. The alpha helix was found to be the most predominant (0.14%), followed by random coil (48.38%) and extended strand (51.49%).as shown in figure (2).

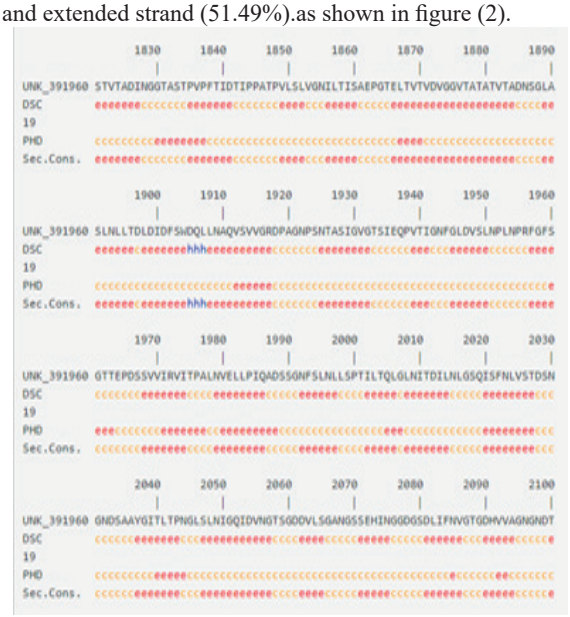


Figure (2): Predication of the *Bap* Secondary Structure

Homology Modeling

The hypothetical protein sequence 3D structure predicted by using homology modeling and this 3D structure an assumed protein sequence built principally by respect of its alignments to one or more proteins of known structureSWISSMODELhttps://swissmodel.expasy.org/ [11],RaptorX[12,13],Phyre2http://www.sbg.bio.ic.ac.uk/ phyre2/html/page.cgi?id=index[14], was used to perform the homology modeling. The model was obtained visualized under UCSF Chimera software [15] and then submitted to 3D-Structure validation and refinement. The 3D-Structure of Phyre2 is given in Figure (3).

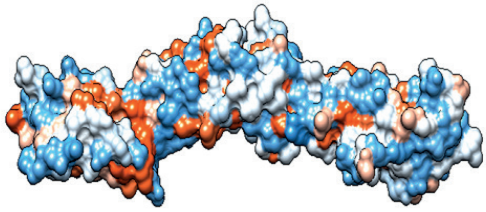


Figure (3): 3D-Structure of Phyre2 [15]

Model refinement and validation

The protein model created needs to be evaluated for quality. PROSAweb [16] has been used for checking Z-score of the query model, and in order to estimate the quality of model using structured solved proteins as reference, (Z-score was used to increase the quality of these models. Higher QMEAN Z-score value means better acceptation with the detected features. QMEANS value was (2.22) for phyre2 and (-3,94) for Swiss Model by QMEAN server [17] Z-score value as shown in Figure (4).

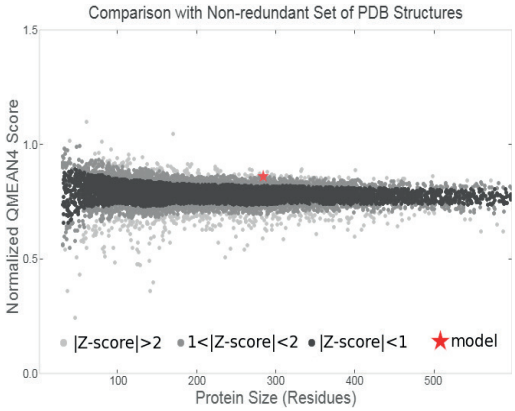
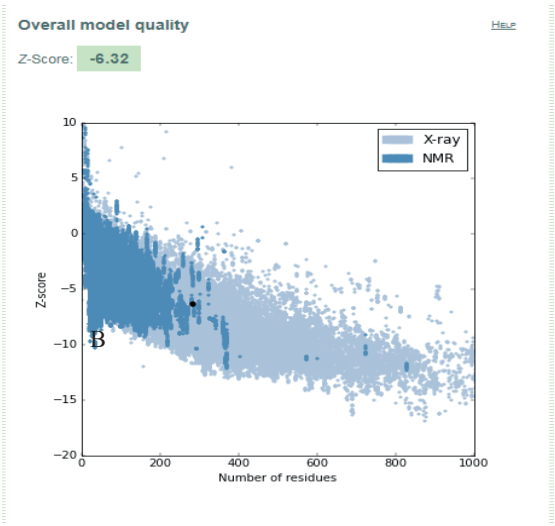


Figure (4): Statistical Potentials of Z-score for the reliable Bap protein model [17].

The best model for *Bap* protein was phyre2 because it has the higher z-score (-6.32), and best local model quality with 99.5% covering of the protein sequence as shown in Figure (5A, B) meanwhile with Swiss Model it has the lower z-score (-6.24) as shown in Figure (6A, B).

Results of validation after refinement appeared in table (2) and the best predicted protein structure was selected according to the rules Refinement (8480.64) This is the potential energy of the refined model according to $3D^{refine}$ force filed. Lower score generally indicates better quality model, Z-score (-6.5) and Qmean4 (2.98), but in comparison with the lower predicted protein structure was selected according to the rules Refinement (11514.3), Z-score (-6.30) and Qmean4 (2.93).



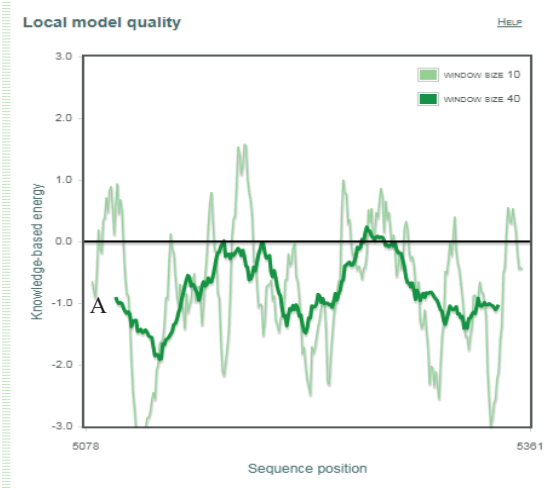


Figure (5 A&B): Validation result A- overall model quality; B- local model quality [16].

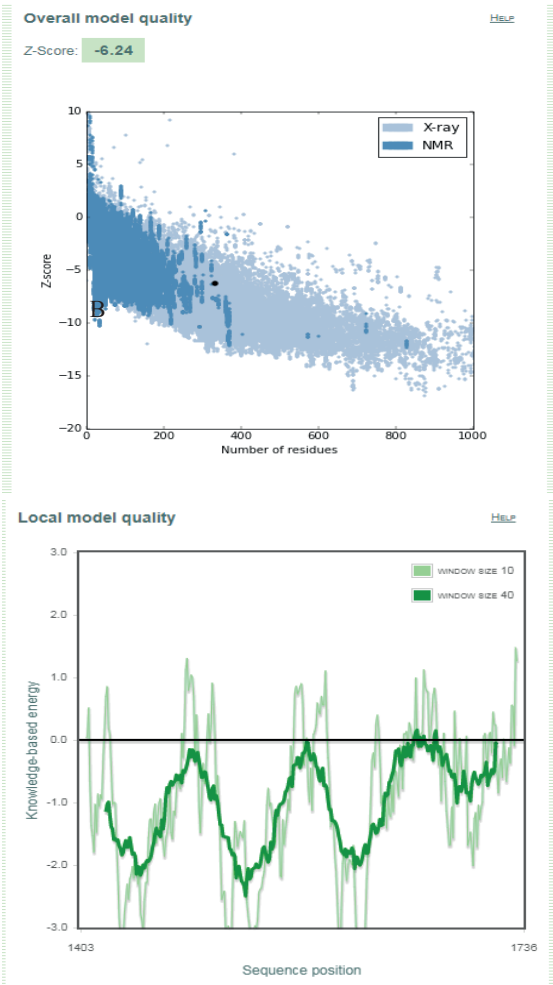


Figure (6A&B): Validation result, overall model and local quality from [16].

Table (2): Result of validation of *Bap* after refinement.

Model	3D^{refine} Score	Z-Score	Qmean 4
1	11514.3	-6.3	2.93
2	9039.68	-6.45	3.04
3	8739.37	-6.48	2.98
4	8587.85	-6.39	2.94
5	8480.64	-6.5	2.98

CONCLUSION

The purpose of this study was to minimize the gap between *In Silico* and wet lab prediction of 3D-Structure of a protein by molecular modeling. The 3D-Structure model of *Bap* protein was stable proved reliable using the ProSA server and the QMEAN server the overall results provided the evidences that the predicted 3D-Structure of *Bap* by Phrye2 is acceptable and of good quality. The predicted structure for *Bap* will give an idea of its active site and the active site residues which can be farther analyzed for designing inhibitors to inactive one of the most important virulence factor of *Acinetobacter baumannii* (result have not been published yet).

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