

## MEMBRANE AND NON-MEMBRANE PROTEINS - A COMPARISON

Rajneesh K. Gaur\*

Department of Biotechnology, Ministry of Science and Technology New Delhi-110003, INDIA

### ABSTRACT

Membrane and non-membrane proteins (MPs & nMPs) constitute the total cellular protein content. The correlation between the amino acid composition of these two classes of proteins within the same and different major class of organism is interesting to know. Amino acid composition analysis of two classes of proteins indicates that the prokaryotic and eukaryotic MPs and nMPs are unique. Furthermore, the composition analysis of essential amino acids in prokaryotic and eukaryotic MPs and nMPs shows the occurrence of high overall percentage frequency of essential amino acids in pkMPs. The high occurrence of essential amino acids in pkMPs may be exploited for medicinal purpose.

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#### KEY WORDS

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\*Corresponding author: Email: [meetgaur@gmail.com](mailto:meetgaur@gmail.com); Tel: +91-9990290384; Fax: +91-11-24360295

### [I] INTRODUCTION

Proteins are broadly classified as membrane (integral part of either cellular or organelle membrane i.e. MPs) and non-membrane (outside the membrane; nMPs) depending upon their cellular location [1]. Proteins are polymers of amino acids and all the organisms use limited repertoire of twenty amino acids for synthesis of MPs & nMPs. Simultaneously, MPs and nMPs of prokaryotes (pk) and eukaryotes (ek) work in a fundamentally different environment. The cellular working environment of MPs & nMPs may have an influence on the overall amino acid composition of these proteins e.g. the arrangement of hydrophobic amino acids helps in distinguishing MPs from nMPs [2]. The amino acid composition has been explored separately for different purposes such as determination of sequence length [3], identification of conserved sequences [4]; prediction of structural class [5], discrimination of intra- and extra cellular proteins [6], prediction of sub-cellular location [7]. To find out the contrasting features between MPs & nMPs of different as well as same class of organism, the overall amino acid composition analysis may be helpful.

The amino acids are classified as essential and non-essential depending upon whether they are absorbed or metabolically synthesized. It is also interesting to know the frequency distribution of essential amino acids between the two class of MPs & nMPs. The contrasting features of MPs and nMPs may be utilized to improve and develop prediction models or for either pharmaceutical or diagnostic purposes.

### [II] MATERIALS AND METHODS

Membrane protein sequences were taken from PDBTM [8] and OMP [9] databases. Mostly, the chosen sequences possess corresponding structures in PDB. The dataset for non-membrane proteins was curated manually from the sequences extracted from PSORT [10], eSLDB [11] and RefSeq [12] databases. Protein sequences flagged as putative, potential uncharacterized, hypothetical and similar to the predicted protein are deleted from the initially downloaded RefSeq sequences. For both dataset, the amino acid composition was calculated as reported by Gaur *et. al.* (2010) [13]. The calculated amino acid composition is compiled in Table-1.

### [III] RESULTS AND DISCUSSION

The amino acid composition of the prokaryotic and eukaryotic MPs and nMPs are shown in Table -1. The composition analysis shows that hydrophobic amino acids such as 'L', 'V', 'A', 'G' etc. occurs in higher proportion than hydrophilic amino acids as they are responsible for forming the core of proteins [14]. On broader scale, though many details are known about the proteins, there are still several questions remain unanswered such as what is the percentage of amino acid compositional similarity/difference in proteins of two major class of organism i.e. prokaryote and eukaryote as well as two major class of proteins i.e. MPs and nMPs.

Table: 1. Amino acid composition of prokaryotic and eukaryotic MPs and nMPs.

Amino acid residues	Amino acid composition (%)			
	Prokaryotes		Eukaryotes	
	MPs	nMPs	MPs	nMPs
F	5.59	3.60	5.23	3.78
I	6.57	5.26	6.12	4.98
W	2.28	1.35	1.68	1.14
L	10.39 <sup>A</sup>	10.40 <sup>A</sup>	11.13	9.01
V	7.63	7.05	7.19	6.34
M	<b>2.83</b>	2.44	<b>2.74</b>	2.36
Y	3.96	2.60	3.55	2.91
C	0.59	1.15	1.67	2.21
A	9.54	10.3	7.89	6.32
T	6.04	5.43	5.73 <sup>B</sup>	5.81 <sup>B</sup>
H	1.70	2.16	2.26	2.55
G	9.46	7.65	7.16	6.01
S	5.69	5.98	6.86	8.23
Q	<b>3.29</b>	4.10	<b>3.26</b>	4.42
R	4.12	6.83	4.92	5.41
K	3.56	4.07	4.59	6.38
N	3.94	3.33	3.48	4.65
E	4.32	5.98	5.03	6.76
P	4.12	4.87	5.37 <sup>B</sup>	5.37 <sup>B</sup>
D	4.38	<b>5.43</b>	4.15	<b>5.35</b>

The amino acids similar in their composition distribution between prokaryotic and eukaryotic MPs and nMPs are highlighted in bold. The superscript 'A' indicates the amino acids composition similarity between prokaryotic MPs and nMPs, while the superscript 'B' indicates the amino acids composition similarity between eukaryotic MPs and nMPs. The amino acids are arranged in decreasing order of hydrophobicity [19]. The total of the overall amino acid composition may not be 100% as the figures are rounded off to the second place of decimal.

Firstly, we compare the amino acid composition MPs and nMPs between two separate class of organism i.e. prokaryotes and eukaryotes [Table-1]. Amino acid composition of MPs of prokaryotes and eukaryotes revealed that out of 20 amino acids, only two amino acids i.e. 'M' (Hydrophobic; ~ 2.8% of total amino acid composition) & 'Q' (Hydrophilic; ~3.3% of total amino acid composition) is similar between each other. The MPs have similar cellular environment in prokaryotes and eukaryotes but they are unique in their amino acid composition distribution. The existing difference may be attributed towards cellular functional requirement [15]. In contrast to MPs, amino acid composition analysis of prokaryotic and eukaryotic nMPs indicates the existence of only one residue similarity i.e. 'D' (Hydrophilic; ~5.4% of total amino acid composition). The observed similarity for the 'D' residue may be explained due to the role of this residue in the stability of the protein's active site as well as their structure as a whole [16]. The analysis shows that nMPs of prokaryotes and eukaryotes are also unique in their distribution of amino acids.

Secondly, we compare the amino acid composition MPs and nMPs with in each class of organism i.e. prokaryotes and eukaryotes [Table-1]. The compositional analysis between pkMPs and pknMPs shows the similar compositional distribution of only single amino acid i.e. 'L' (Hydrophobic; ~10.4% of total amino acid composition), while comparison of

ekMPs and eknMPs indicate the similar distribution of 'T' (hydrophilic; ~5.8% of total amino acid composition) and 'P' (Hydrophobic; ~5.3% of total amino acid composition). Therefore, the MPs and nMPs are different from each other even within the same class of organism in their amino acid composition.

Thirdly, since both prokaryotes and eukaryotes are dependent on an external supply of essential amino acids (i.e. F, I, W, L, V, M, T, H, K), it is interesting to compare their overall composition between MPs and nMPs. The overall essential amino acid comparison shows that pkMPs & ekMPs possess 46.59% & 43.93%, while pknMPs and eknMPs possess 41.07% & 42.35% of essential amino acids content respectively [Table-1]. The slightly high percentage of essential amino acids in pkMPs may be explained as a result of difference in evolution of metabolic pathways [17]. The high percentage of essential amino acids in pkMPs may be utilized for pharmaceutical advantages. pkMPs & ekMPs have relatively high percentage of 'I' in comparison to respective nMPs. The compositional percentage of 'H' & 'K' is low in pkMPs with respect to remaining types of proteins under consideration, while eknMPs is rich in 'K' in comparison to pkMPs, pknMPs & ekMPs [Figure-1]. 'K' residue more often involved in post-translational modifications of proteins, which explain its slightly high frequency distribution in eknMPs [18].

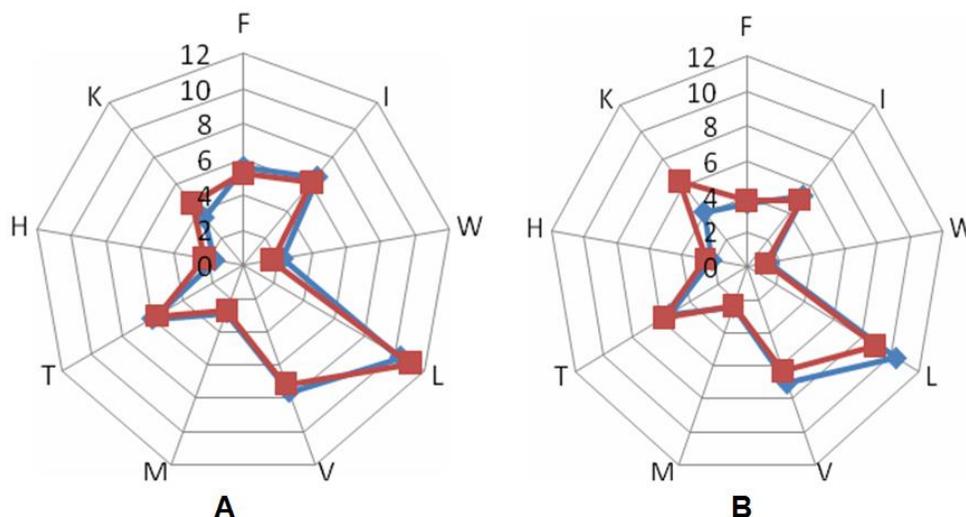


Fig. 1. Radar diagram presents the comparison of essential amino acids distribution between (A) prokaryotic and eukaryotic MPs. (B) prokaryotic and eukaryotic nMPs.

#### [IV] CONCLUSION

In conclusion, depending upon the amino acid composition, MPs and nMPs are unique to prokaryotes and eukaryotes as well as significantly different within the same class of organism. Furthermore, the comparison of essential amino acid content shows the occurrence of high percentage of these amino acids in pkMPs.

**ABBREVIATIONS:** MPs - Membrane Proteins, nMPs - non-Membrane Proteins, pknMPs – Prokaryotic non-Membrane Proteins, eknMPs – Eukaryotic non-Membrane Proteins, pkMPs – Prokaryotic Membrane Proteins, ekMPs – Eukaryotic Membrane Proteins

#### CONFLICT OF INTEREST

The author declares having no competing interests.

#### FINANCIAL DISCLOSURE

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## ABOUT AUTHOR

**Dr. Rajneesh Kumar Gaur** is currently associated with Department of Biotechnology, Ministry of Science and Technology, New Delhi, India. He is interested in analyzing the biological data available as Structural Biology and Bioinformatics based databases.