

Novel Index of Polar Amino Acids Characterizing End Region of Transmembrane Helices

Toshiyuki Hayashibe¹ Takatsugu Hirokawa² Shigeki Mitaku¹
 hayashibe@proteome.bio.tuat.ac.jp hiro@cubs.bio.rsi.co.jp mitaku@cc.tuat.ac.jp

¹ Department of Biotechnology, University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

² Ryoka Systems Co., Computational Science and Technology Division, Irifune, Urayasu, Chiba 279-0012, Japan

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1 Introduction

Index of amino acids is useful for extracting amino acid preference, which have large statistical noise [1]. Peaks of local average of appropriate index indicate clusters of preferable amino acids, because the statistical noise may be reduced by the averaging procedure. For example, hydrophobicity (hydropathy) index is very useful for visualizing hydrophobic segments in transmembrane helices [2]. However, characteristic preference of polar amino acids at the end regions of transmembrane helices has not been indexed for far. The propensity study of amino acids membrane proteins indicated that the polar residues, lysine, arginine and tryptophan, are preferable to the end region of transmembrane helices. Therefore, this preference of amino acids may become useful parameter for the prediction of transmembrane helical segments [3, 4].

In this work, a novel index of polar amino acids, which we call amphiphilicity index. The amphiphilicity index has finite values for larger polar residues (K, R, H, E, Q, W and Y), whereas the index was zero for small polar residues and hydrophobic residues. The value of amphiphilicity index showed good correlation with the propensity of amino acids at the end regions. When the local average of seven-residue window was plotted as a function of amino acid sequences, most peaks of the amphiphilicity index contained the end points of transmembrane helices, suggesting the possibility to improve the accuracy of transmembrane prediction.

2 Method and Results

We have calculated the transfer energy of stem part of a polar side chain that links a polar group to the main chain. First, the accessible surface area was calculated by Insight II of Molecular Simulation Inc. The transfer energy ΔG was evaluated from the accessible surface area ΔA : $\Delta G = \sigma \Delta A$, in which σ is the surface tension of 40 dyn/cm [5].

The dataset of membrane proteins for the analyses of amino acid propensity as well as amphiphilicity plots were taken from protein data bank (PDB), because exact polypeptide segments of transmembrane helices are necessary for the present work. The dataset contained 1A91, 1BGY, 1BRX, 1EUL, 1OCC, 1QLE, 1AR1, 1EHK, 1QLA,

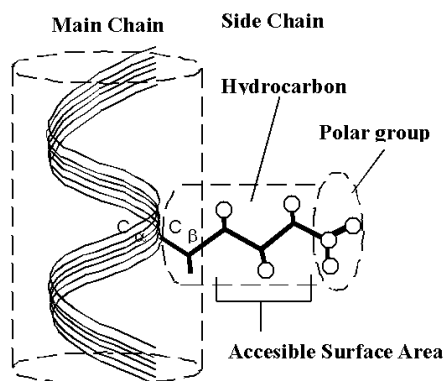


Figure 1: Schematic diagram of a polar side chain attached to a transmembrane helix.

1FUM, 1MSR, 1E12, 1BL8, 1KZU, 1LGH, 1MSL, 1PRC, 2RCR and 1F88. Some of data include several chains, and the total number of chains was 41. The number of helices was 15*.

3 Results and Discussions

Finite values of the amphiphilicity index were obtained for seven residues (K, R, H, E, Q, W and Y), because γ -carbon of other polar amino acids (D, N, S and T) is the member of polar groups. Table 1 shows the values of the amphiphilicity index for strongly polar residues A and those for weakly polar residues A' together with the hydrophathy index (Kyte & Doolittle, 1982). Positively charged residues, R, K and H, have high amphiphilicity and hydrophobicity indices, since they have a net elementary charge linked by a long hydrocarbon chain. On the other hand, a polar group is directly connected to the main chain in D and N, and the amphiphilicity index was zero. E and Q have intermediate properties, leading to the intermediate values of the amphiphilicity index.

Fig. 2 shows the propensity of polar residues at the central and the end regions, which to study the effect of amphiphilicity of side chains on the amino acid preference. The relative propensity was calculated by normalizing the propensity at the region in transmembrane segment with the corresponding value at loop segments. When three kinds of strongly polar residues were compared, the relative propensity showed good correlation with the values of the amphiphilicity. Namely, larger polar residues are preferable to the nonpolar-water interface of membrane, which is physically reasonable.

Finally, we analyzed by an amphiphilicity plot, which is very similar to the hydrophathy plot, The results showed that most peaks of local average amphiphilicity contained the end points of transmembrane helices. This fact suggests that this index may be useful for the improvement of the transmembrane region prediction.

References

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Table 1:

A.A.	A	A'	H	A.A.	A	A'	H
K	3.67	0	-3.9	T	0	0	-0.7
R	2.45	0	-4.5	P	0	0	-1.6
H	1.45	0	-3.2	G	0	0	-0.4
E	1.27	0	-3.5	A	0	0	1.8
Q	1.25	0	-3.5	M	0	0	1.9
D	0	0	-3.5	C	0	0	2.5
N	0	0	-3.5	F	0	0	2.8
W	0	6.93	-0.9	L	0	0	3.8
Y	0	5.06	-1.3	V	0	0	4.2
S	0	0	-0.8	I	0	0	4.5

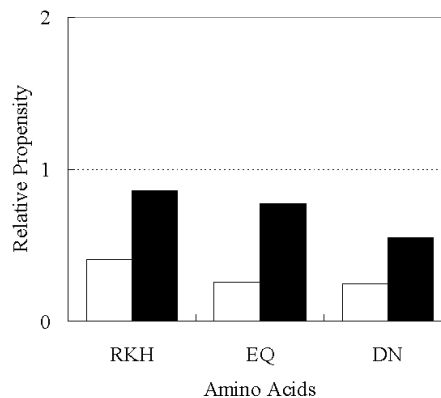


Figure 2: Relative propensities of polar residues at the central (open bar) and end (solid bar) regions of transmembrane helices.