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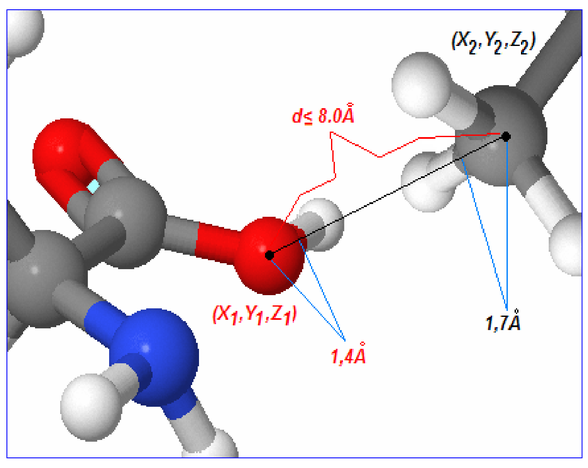
"Mean Packing Density" for each of the 20 common amino acid residues on a 30% non-redundant set of transmembrane proteins

Motivation:

While the functionality of a protein is a result of its 3D structure, and this structure is directly connected to the physicochemical properties, we considered valuable to focus on the calculation of packing parameters. An extensive work on this topic has already been done, with the calculation of "mean packing density" for each of the 20 common amino acid residues for a 25% non-redundant set of globular water-soluble proteins. The resulting matrix has been used for the prediction of amyloidogenic regions in protein chains with remarkable success. Our work has been focused on the same calculations for a 30% non-redundant set of transmembrane proteins. The aim was to compare the results of these two different groups of proteins in order to find similarities or identify unknown differences, which may be used in prediction methods beyond amyloidogenic propensity.

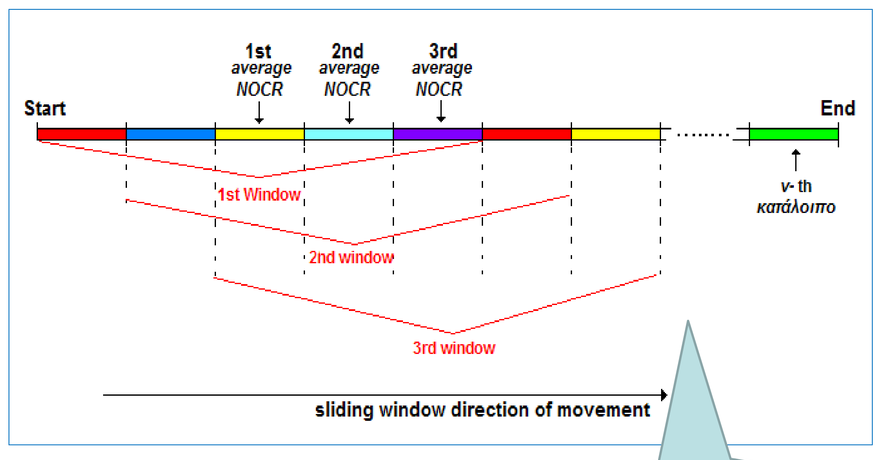
I. The Calculation Method:



- **"Mean Packing Density" (Average Number of Close Residues within a given distance).**
- **Two residues are "Close" Neighbors when:**

$$d = \sqrt{(X_2 - X_1)^2 + (Y_2 - Y_1)^2 + (Z_2 - Z_1)^2} \leq 8.0A$$

- **Covalently bonded residues (±1) are excluded .**
- **Only for heavy atoms (C, O, N, S, P).**



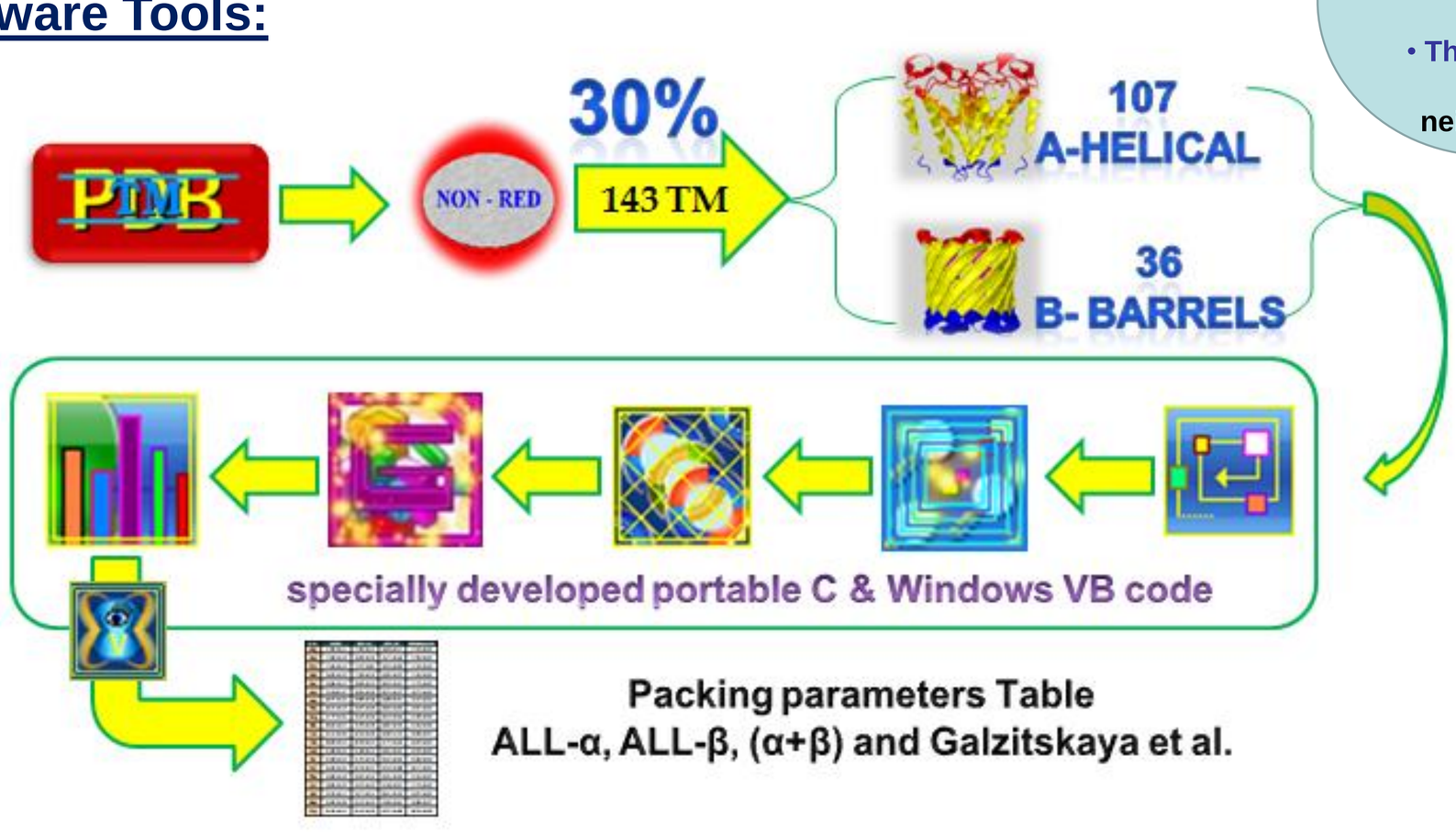
- **Window length: 5 residues**
- **Threshold: 21.4 neighbors**

II. The Protein Set & Software Tools:

1. **The protein set was obtained from PDB-TM (update of May 2009).**
2. **The 30% non-redundancy was achieved using the NON-RED on-line tool.**
3. **Transmembrane proteins: 143 (107 α-helical & 36 β-barrels).**
4. **Specially developed code for automation in:**

i) Multi-downloading from PDB protein database.

ii) Selected chains' separation & extraction from PDB files.



iii) Calculations of "Close packing parameters".

iv) Statistical process (Mean Packing Density per residue was calculated from the 3D structures as the sum of observed close neighbors of all residues - of the same type - divided by their total number in the set).

v) Verification for the proper participation of all chains in the calculations.

III. Results:

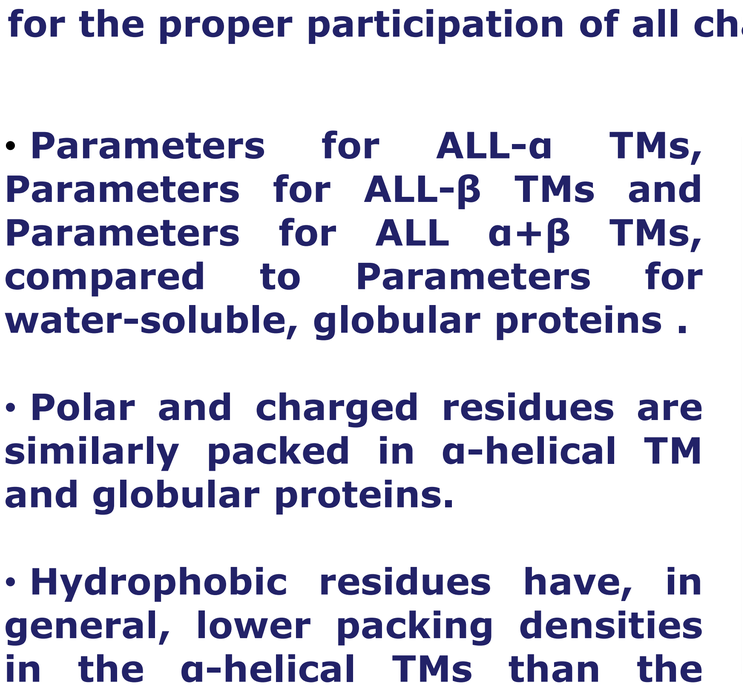
Packing Parameters					
AA:	alpha & beta:	ALL alpha:	ALL beta:	Galzitskaya et al:	ID:
Ser(S)	19.09 ±0.15	18.36 ±0.19	20.35 ±0.21	17.72 ±0.03	POLAR
Asn(N)	19.42±0.19	18.34 ±0.26	20.72 ±0.27	18.57 ±0.04	
Gln(Q)	20.47 ±0.22	18.90 ±0.28	22.88 ±0.31	19.19 ±0.04	
Thr(T)	20.13 ±0.16	19.67 ±0.20	20.94 ±0.23	19.91 ±0.04	
Pro(P)	17.64 ±0.14	17.37 ±021	18.52 ±0.39	17.53 ±0.04	HYDROPHOBIC
Val(V)	20.99 ±0.14	20.76 ±0.16	21.77 ±0.24	24.05 ±0.03	
Leu(L)	21.60 ±0.12	21.29 ±0.14	22.61 ±0.21	25.53 ±0.03	
Ile(I)	21.90 ±0.16	21.55 ±0.18	23.45 ±0.34	25.96 ±0.04	
Phe(F)	22.86 ±0.18	22.81 ±0.22	23.01 ±0.34	27.42 ±0.05	
Ala(A)	19.54 ±0.11	19.17 ±0.14	20.41 ±0.18	19.97 ±0.03	
Met(M)	22.99 ±0.29	22.55 ±0.33	25.09 ±0.61	24.80 ±0.07	
Trp(W)	23.24 ±0.31	23.19 ±0.39	23.37 ±0.49	28.53 ±0.09	
Gly(G)	17.93 ±0.11	17.73 ±0.15	18.28 ±0.17	17.18 ±0.03	
Cys(C)	23.12 ±0.39	23.10 ±0.40	23.69 ±1.19	23.99 ±0.07	
Tyr(Y)	24.36 ±0.22	23.74 ±0.31	25.25 ±0.28	26.17 ±0.05	
Asp(D)	17.96 ±0.18	16.93 ±0.23	19.17 ±0.24	17.39 ±0.03	(-)
Glu(E)	18.63 ±0.19	17.26 ±0.22	22.03 ±0.35	17.43 ±0.03	
Lys(K)	18.03 ±0.19	16.55 ±0.22	21.28 ±0.31	17.72 ±0.03	(+)
Arg(R)	21.75 ±0.22	19.25 ±0.26	26.19 ±0.34	21.03 ±0.04	
His(H)	20.02 ±0.31	19.70 ±0.38	20.85 ±0.53	21.64 ±0.06	

Table 1: Mean Observed Packing Densities for the 20 AA Residues

- **Parameters for ALL-α TMs, Parameters for ALL-β TMs and Parameters for ALL α+β TMs, compared to Parameters for water-soluble, globular proteins .**
- **Polar and charged residues are similarly packed in α-helical TM and globular proteins.**
- **Hydrophobic residues have, in general, lower packing densities in the α-helical TMs than the globular, water-soluble proteins.**
- **Residues in ALL-β pack well.**

Distribution of the 20 AA Residues in the 30% non-redundant set

IV. Additional 3D Visualization Software:



- **Creates 3D models by PDB type files transformed by amyl_G.**
- **Marks the high packing areas on model.**
- **Fully controlled parameters' set (ALL-α, ALL-β, (α+β) and Galzitskaya et al.) and window length and threshold in sliding window method.**
- **Reads and visualizes AmylPRED output files.**