Position separation of discriminative sequence motifs with protein domains of unknown functions

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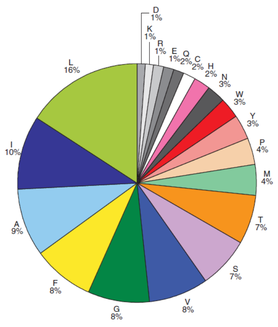
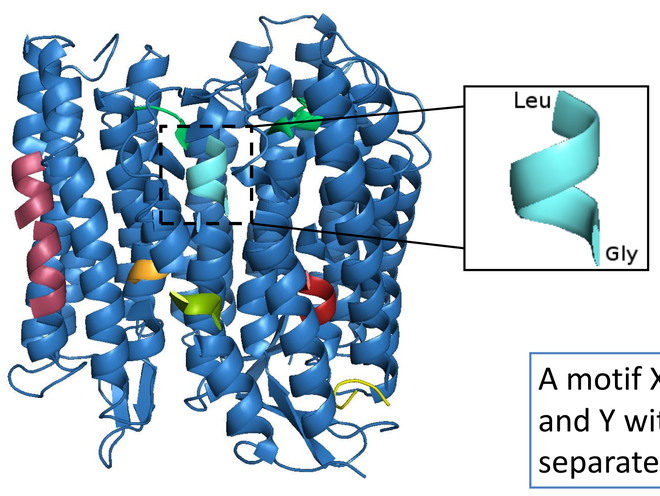
Background and Motivation

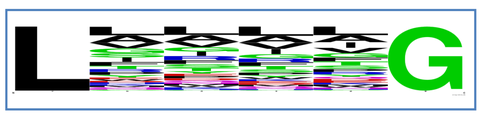
Protein sequence motifs support the understanding of the features that are important for the folded protein in the membrane environment. The protein sequence motif analysis is helpful for target mutagens studies, for investigations of diseases and further studies.

The amino acid composition in the TM-helical regions





e.g. LG5 = LXXXXG



A motif XYn corresponds to amino acid X and Y with X,Y ε 20 canonical amino acids separated by (n-1) variable residues.

Methods

Pfam

32 membrane protein families with domains of unknown functions

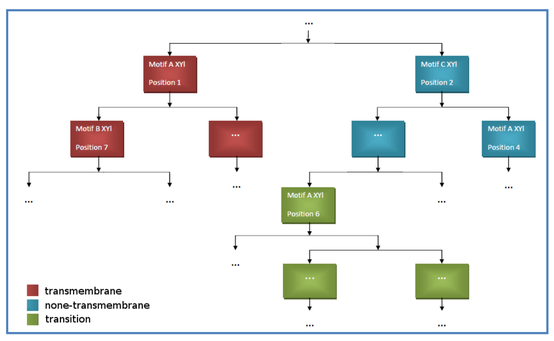
50 protein sequence motifs

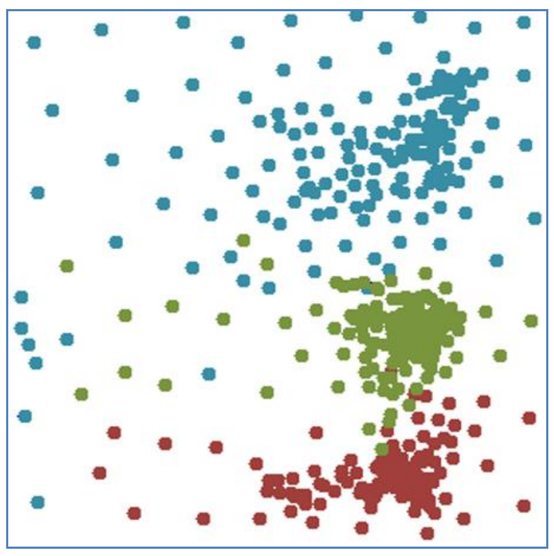
Statistical analysis

$$P(a|pos_i|M) = \frac{\sum_{j=1}^{k} g\,(pos_i)}{k}$$

$$g\,(pos_i, a) = \begin{cases} 1 & pos_i \text{ equals } a \\ 0 & else \end{cases},$$

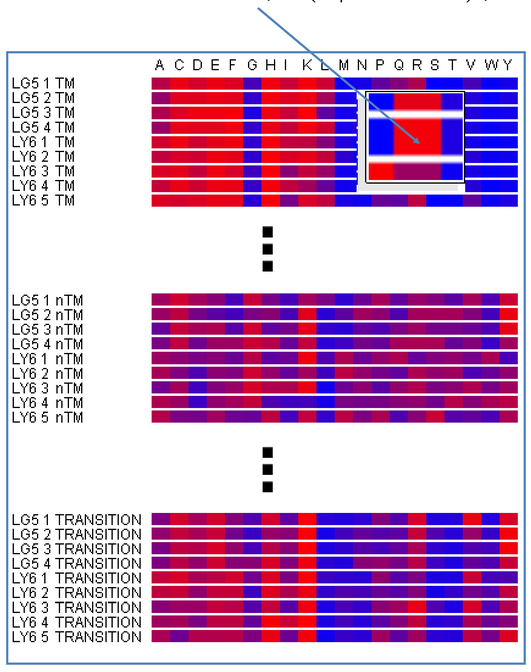
Clustering methods





Naturally occurring

$$f(x) = 1 - \log\left(\frac{P(a|pos_i|M)}{P(a|Nature)}\right)$$

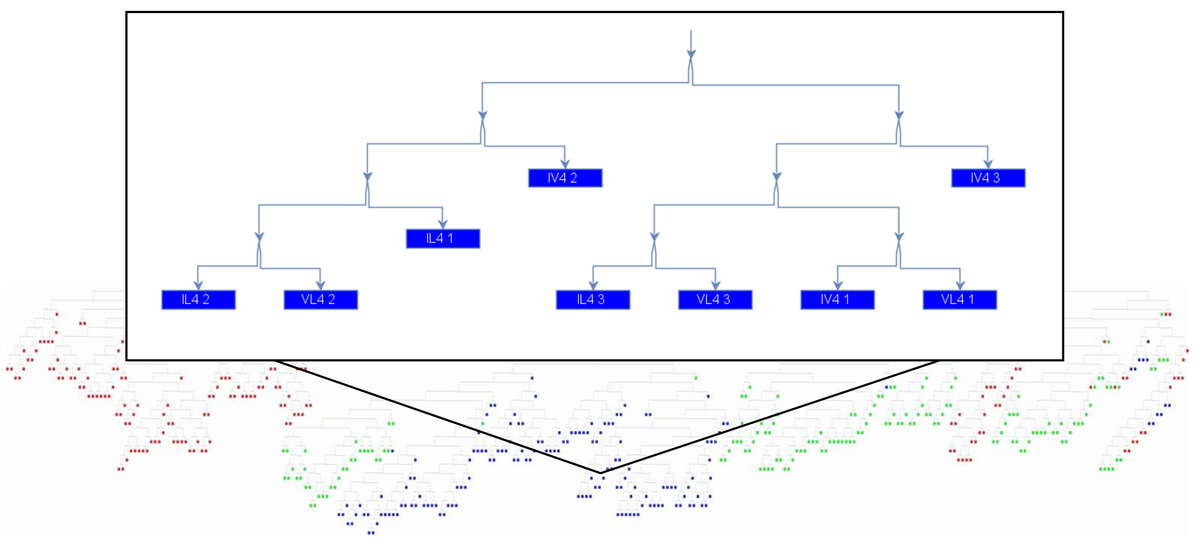


Spearman´s rank to each position

Position specific separation and clustering

Results and Application

- Position specific separation and clustering
- Clustering into transmembrane, non-transmembrane and transition regrions
- Motifpositions with great similarity as a direct leaf neighbors

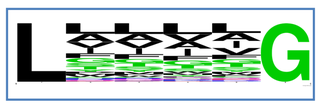


- Motif tendency to region distribution

$$tendency = \sum f(x)$$

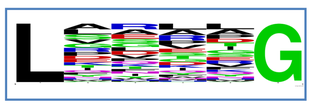
- Separation of motifs by a residue specific distribution.

transmembrane



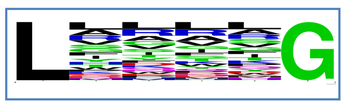
L-[LAY]-[LAY]-[LVA]-[LAI]-G

non-transmembrane



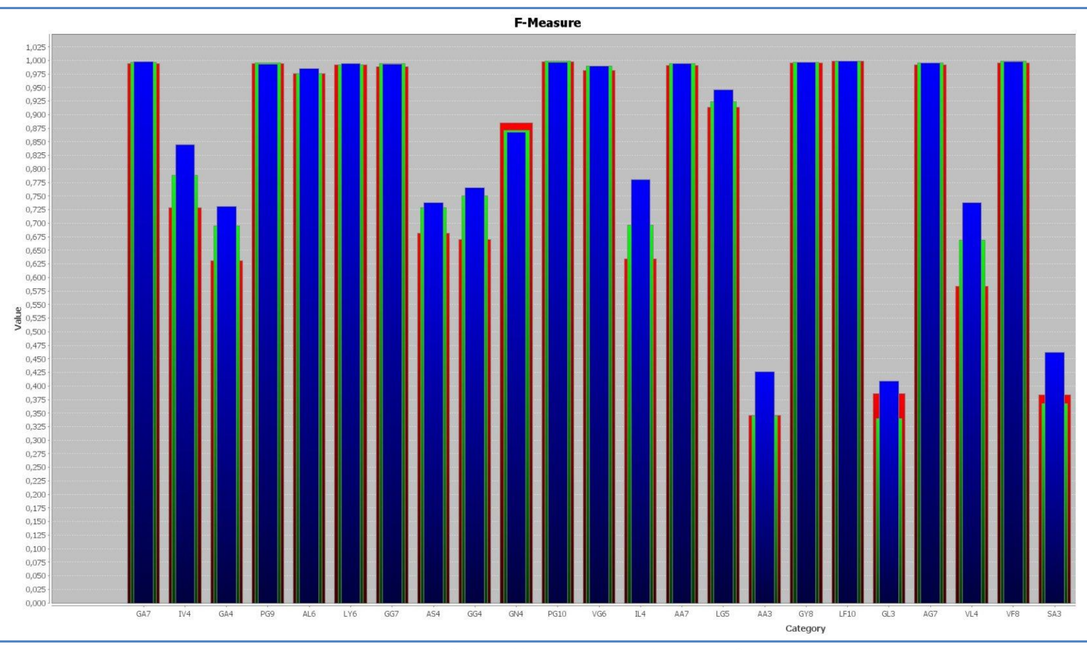
L-[ALS]-[RAE]-[LAR]-[LAP]-G

transition



L-[LAR]-[LRA]-[LRA]-[LAR]-G

- F-measure up to over 90% within all derived protein families
- Prediction of location inside of the protein's topology for the majority of identified motifs.
- Functional relevance and diverse specificity of motifs with rather small F-measure.



F-measure histogram for all analyzed motifs XYn with n>2

References

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