Amino Acid Properties

Elements of Biophysics

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Biomolecules
Folding and
Disease

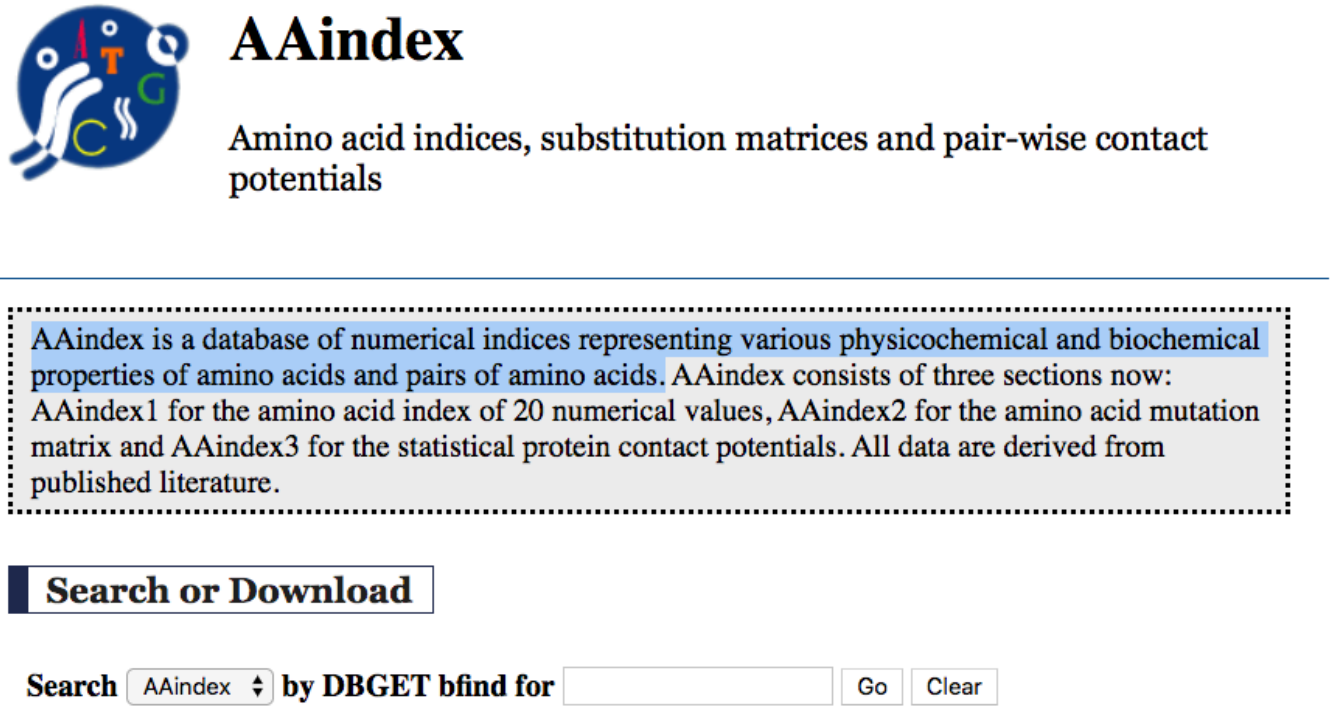
Amino Acid Properties

Physico-chemical and biochemical properties of amino acids are defined by indexes or propensity scales.

This properties can be used to perform simple protein structure predictions by associating each residue to different statistically evaluated features.

AAIndex Database

AAindex is a database of numerical indices representing various physicochemical and biochemical properties of amino acids and pairs of amino acids.



https://www.genome.jp/aaindex/

Amino Acid Volume

Some scales define the volume of the amino acids

```
H GRAR740103
D Volume (Grantham, 1974)
R PMID:4843792
A Grantham, R.
T Amino acid difference formula to help explain protein evolution
J Science 185, 862-864 (1974)
I    A/L     R/K     N/M     D/F     C/P     Q/S     E/T     G/W     H/Y     I/V
     31.    124.     56.     54.     55.     85.     83.      3.     96.    111.
    111.    119.    105.    132.    32.5     32.     61.    170.    136.     84.
//
```

Amino Acid Surface

Some scales define the surface of the amino acids

```
H JANJ780101
D Average accessible surface area (Janin et al., 1978)
R PMID:731698
A Janin, J., Wodak, S., Levitt, M. and Maigret, B.
T Conformation of amino acid side-chains in proteins
J J. Mol. Biol. 125, 357-386 (1978)

I    A/L     R/K     N/M     D/F     C/P     Q/S     E/T     G/W     H/Y     I/V
    27.8    94.7    60.1    60.6    15.5    68.7    68.2    24.5    50.7    22.8
    27.6   103.0    33.5    25.5    51.5    42.0    45.0    34.7    55.2    23.7
//
```

```
H CHOC760101
D Residue accessible surface area in tripeptide (Chothia, 1976)
R PMID:994183
A Chothia, C.
T The nature of the accessible and buried surfaces in proteins
J J. Mol. Biol. 105, 1-14 (1976)
I    A/L     R/K     N/M     D/F     C/P     Q/S     E/T     G/W     H/Y     I/V
    115.    225.    160.    150.    135.    180.    190.     75.    195.    175.
    170.    200.    185.    210.    145.    115.    140.    255.    230.    155.
//
```

Amino Acid Energies

Some scales provides an estimation of the energies of transfer or contact

```
H JANJ790102
D Transfer free energy (Janin, 1979)
R PMID:763335
A Janin, J.
T Surface and inside volumes in globular proteins
J Nature 277, 491-492 (1979)
```

I	A/L	R/K	N/M	D/F	C/P	Q/S	E/T	G/W	H/Y	I/V
	0.3	-1.4	-0.5	-0.6	0.9	-0.7	-0.7	0.3	-0.1	0.7
	0.5	-1.8	0.4	0.5	-0.3	-0.1	-0.2	0.3	-0.4	0.6

```
//
```

```
H MIYS850101
D Effective partition energy (Miyazawa-Jernigan, 1985)
R
A Miyazawa, S. and Jernigan, R.L.
T Estimation of effective interresidue contact energies from protein crystal
  structures: Quasi-chemical approximation
J Macromolecules 18, 534-552 (1985)
```

I	A/L	R/K	N/M	D/F	C/P	Q/S	E/T	G/W	H/Y	I/V
	2.36	1.92	1.70	1.67	3.36	1.75	1.74	2.06	2.41	4.17
	3.93	1.23	4.22	4.37	1.89	1.81	2.04	3.82	2.91	3.49

```
//
```

Secondary Structure

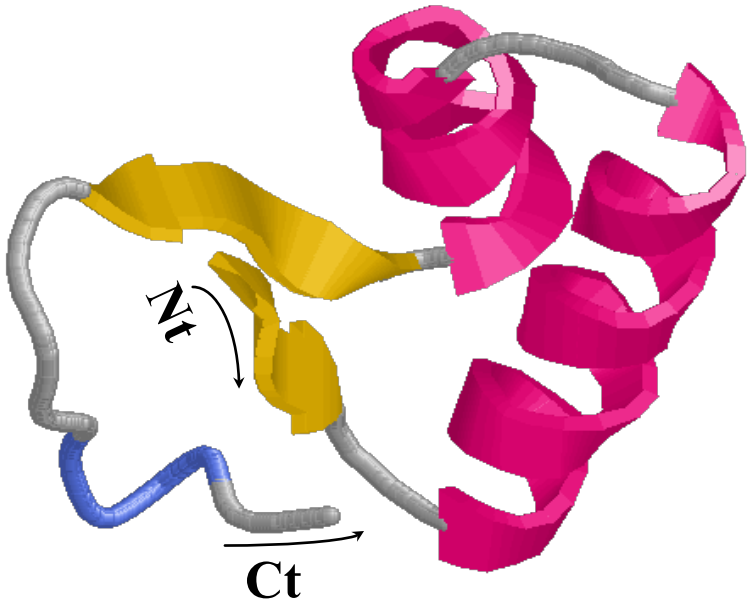
Covalent structure

TTCCPSIVARSNFNVCRLPGTPEAICATYTGCIIIPGATCPGDYAN

Secondary structure

EEEE..HHHHHHHHHHHH....HHHHHHHH.EEEE..........

3D structure



Chou-Fasman (I)

Given a set of known structures we can count how many times a residue is associated to a structure.

Example:

AL**A**KSL**A**KPSDTL**A**KSDFREKWEWLKLLK**A**L**A**CCKLS**AA**L
hh**h**hhhh**h**hcccccc**c**cccccchhhhhhhh**h**h**h**hhhhhh**hh**h

N(A,h) = 7, N(A,c) =1, N= 40

P(A,h) = 7/40, P(A,c) = 1/40

Is that enough for estimating a propensity?

Chou-Fasman (II)

We need to estimate how much independent the residue-to-structure association is.

$$P(h) = 27/40,\ P(c) = 13/40,\ P(A) = 8/40$$

If the structure is independent of the residue:

$$P(A,h) = P(A) \times P(h)$$

The propensity is:

$$\frac{P(A,h)}{P(A) \times P(h)}$$

The prediction method

The Chou-Fasman method was published in 1974 and the propensity scales were calculated on a set of 19 proteins.

Helical Residues[b]	P_α		β-Sheet Residues[c]	P_β	
$Glu^{(-)}$	1.53		Met	1.67	
Ala	1.45	H_α	Val	1.65	H_β
Leu	1.34		Ile	1.60	
$His^{(+)}$	1.24		Cys	1.30	
Met	1.20		Tyr	1.29	
Gln	1.17		Phe	1.28	
Trp	1.14	h_α	Gln	1.23	h_β
Val	1.14		Leu	1.22	
Phe	1.12		Thr	1.20	
$Lys^{(+)}$	1.07		Trp	1.19	
Ile	1.00	I_α	Ala	0.97	I_β
$Asp^{(-)}$	0.98		$Arg^{(+)}$	0.90	
Thr	0.82		Gly	0.81	i_β
Ser	0.79	i_α	$Asp^{(-)}$	0.80	
$Arg^{(+)}$	0.79		$Lys^{(+)}$	0.74	
Cys	0.77		Ser	0.72	
Asn	0.73		$His^{(+)}$	0.71	b_β
Tyr	0.61	b_α	Asn	0.65	
Pro	0.59		Pro	0.62	
Gly	0.53	B_α	$Glu^{(-)}$	0.26	B_β

[a] Chou and Fasman (1974). [b] Helical assignments: H_α, strong α former; h_α, α former; I_α, weak α former; i_α, α indifferent; b_α, α breaker; B_α, strong α breaker. I_α assignments are also given to Pro and Asp (near the N-terminal helix) as well as Arg (near the C-terminal helix). [c] β-sheet assignments: H_β, strong β former; h_β, β former; I_β, weak β former; i_β, β indifferent; b_β, β breaker; B_β, strong β breaker. b_β assignment is also given to Trp (near the C-terminal β region).

Chou and Fasman Biochemistry 1974

Updated Chou-Fasman

An update version of the Chou-Fasman propensity scales are available at the AAIndex database.

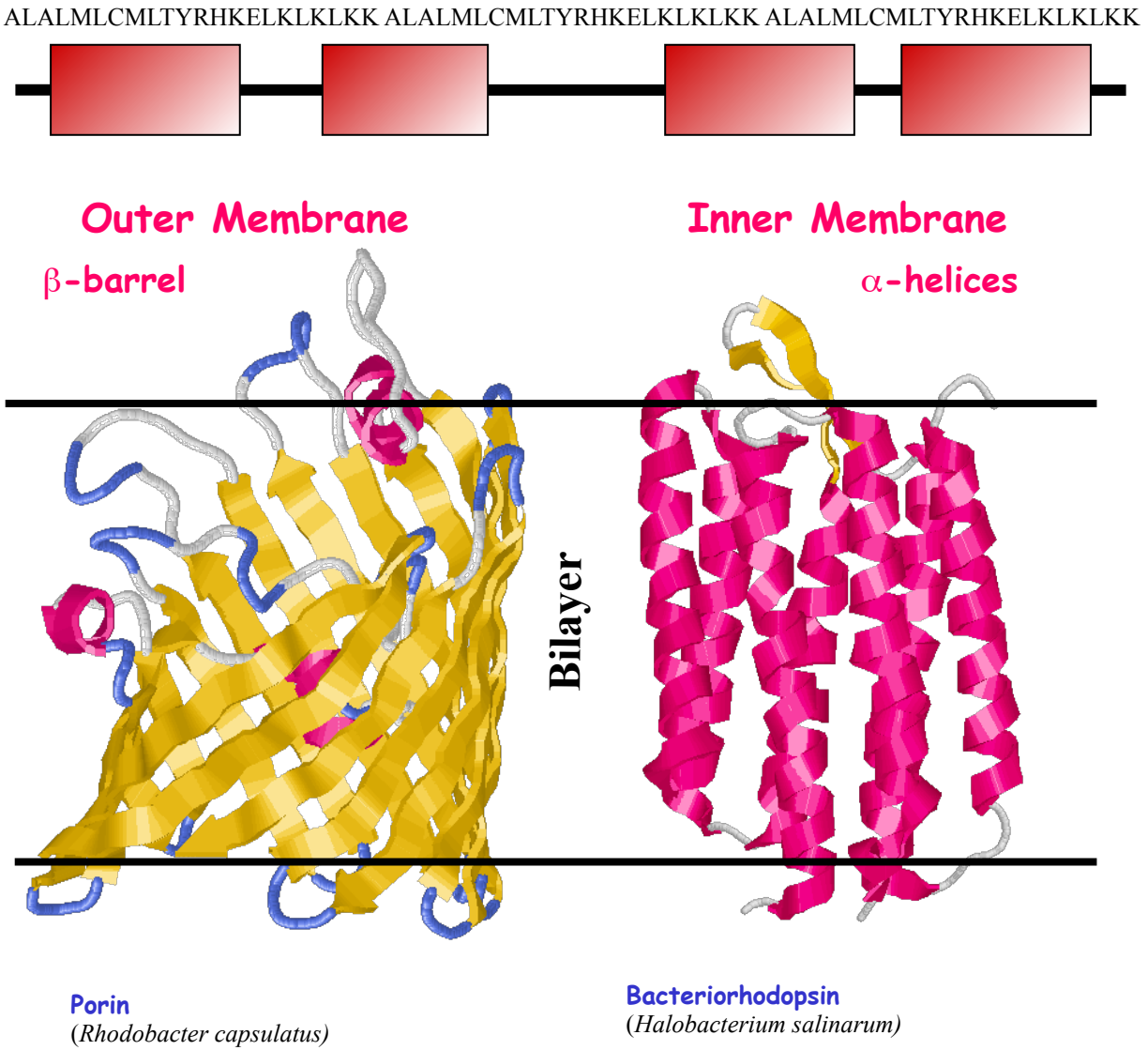
```
H CHOP780201
D Normalized frequency of alpha-helix (Chou-Fasman, 1978b)
R PMID:364941
A Chou, P.Y. and Fasman, G.D.
T Prediction of the secondary structure of proteins from their amino acid
  sequence
J Adv. Enzymol. 47, 45-148 (1978)
I     A/L     R/K     N/M     D/F     C/P     Q/S     E/T     G/W     H/Y     I/V
     1.42    0.98    0.67    1.01    0.70    1.11    1.51    0.57    1.00    1.08
     1.21    1.16    1.45    1.13    0.57    0.77    0.83    1.08    0.69    1.06
//

H CHOP780202
D Normalized frequency of beta-sheet (Chou-Fasman, 1978b)
R PMID:364941
A Chou, P.Y. and Fasman, G.D.
T Prediction of the secondary structure of proteins from their amino acid
  sequence
J Adv. Enzymol. 47, 45-148 (1978)
I     A/L     R/K     N/M     D/F     C/P     Q/S     E/T     G/W     H/Y     I/V
     0.83    0.93    0.89    0.54    1.19    1.10    0.37    0.75    0.87    1.60
     1.30    0.74    1.05    1.38    0.55    0.75    1.19    1.37    1.47    1.70
//
```

http://www.genome.jp/aaindex/

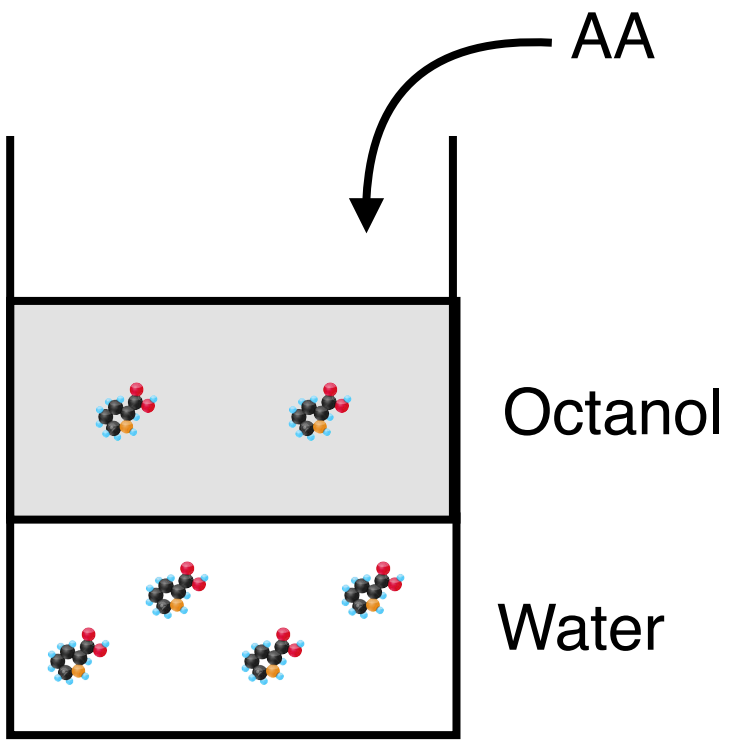
Trans Membrane Regions

Predicting the position of Trans Membrane Segments along the sequence



Partition coefficient

The partition coefficient (P) is the ratio of concentrations of a compound in a mixture of two immiscible solvents at equilibrium.



$$P = \frac{[AA]_{Octanol}}{[AA]_{water}}$$

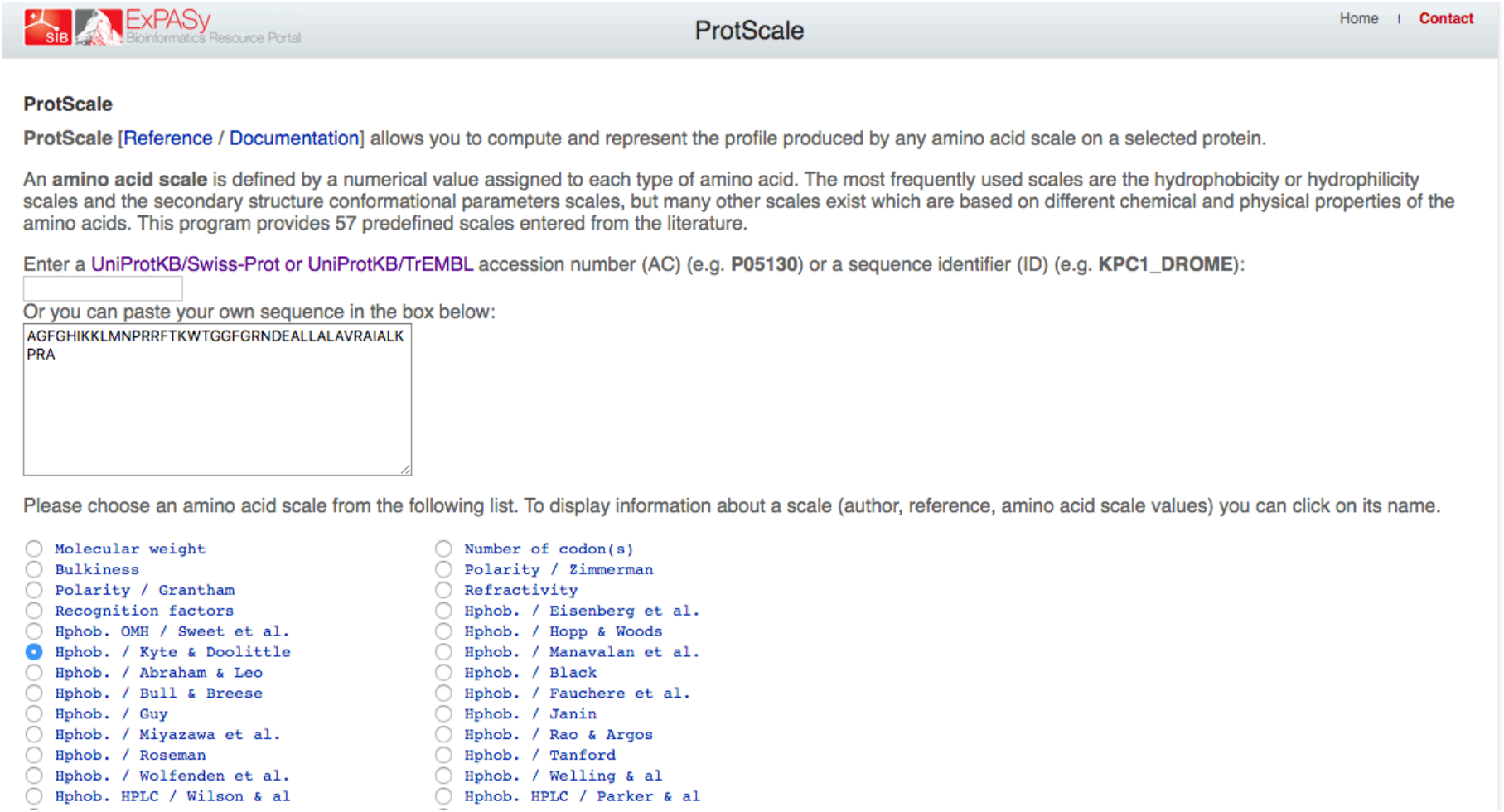
Kyte-Doolittle scale

It is computed taking into consideration the octanol-water partition coefficient, combined with the propensity of the residues to be found in known transmembrane helices

```
H KYTJ820101
D Hydropathy index (Kyte-Doolittle, 1982)
R PMID:7108955
A Kyte, J. and Doolittle, R.F.
T A simple method for displaying the hydropathic character of a protein
J J. Mol. Biol. 157, 105-132 (1982)
I     A/L      R/K      N/M      D/F      C/P      Q/S      E/T      G/W      H/Y      I/V
      1.8     -4.5     -3.5     -3.5      2.5     -3.5     -3.5     -0.4     -3.2      4.5
      3.8     -3.9      1.9      2.8     -1.6     -0.8     -0.7     -0.9     -1.3      4.2
//
```

ProtScale at ExPASy

ExPASy webserver plots protein plots based on different scales



https://web.expasy.org/protscale/

Exercise 1

Extract data from the average accessible surface (JANJ780101), the effective partition energy (MIYS850101) and the hydrophobicity (KYTJ820101) scales.

Calculate the correlation coefficient for all the possible pairs.

Which pair of scales are the most correlated ones?

Suggestion: Parse the text files and import the data in excel.

Exercise 2

Consider the Bacterial Rhodopsin structure 1FBB extract the chain A and calculate the secondary structure using dssp-web.

Identify the regions corresponding to the seven alpha helices.

Use the scale of Kyte-Doolittle and Chou-Fasman to verify that helical regions correspond to high level of helical propensity and hydrophobicity.

Suggestion: In the dssp file generated from the PDB ,the residue type and the secondary structure are reported in columns 14 and 17 respectively. Replace blank secondary structure with C (coil). A single residue in turn conformation (T) in the middle of long stretch of helical residues should be considered as helical.