MODELING ANALYSIS OF AMINO ACIDS HYDROPHOBICITY

Outline

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AMINO ACIDS - building blocks of proteins

- molecule that contains amine and carboxyl functional groups
- roles in biology:
  - synthesis of proteins
  - intermediates of metabolic pathways
  - neurotransmitters
  - antibiotics

AMINO ACIDS

- 20 essential amino acids (proteinogenic amino acids):
  - Encoded by the standard
- Non-protein amino acids
  - biological systems
  - biologically-important roles in humans:
    - Neurotransmitters
    - Used to synthesize other biological active molecules
- Abiotically synthesized
- Engineered by scientists : Fluorescent amino acid

AMINO ACIDS

- Quantitative investigations of the Structure-Activity Relationships of amino acids:
  - HLA-A*0201
  - Retention times
  - Peptides mobilities
  - Online resources:
    - National Center for Biotechnology Information
    - http://www.ncbi.nlm.nih.gov/Class/Structure/aa/aa_explorer.cgi
    - AA-QSPR Db = Amino Acid Quantitative Structure Property Relationships Database
    - AAindex

AMINO ACIDS HYDROPHOBICITY

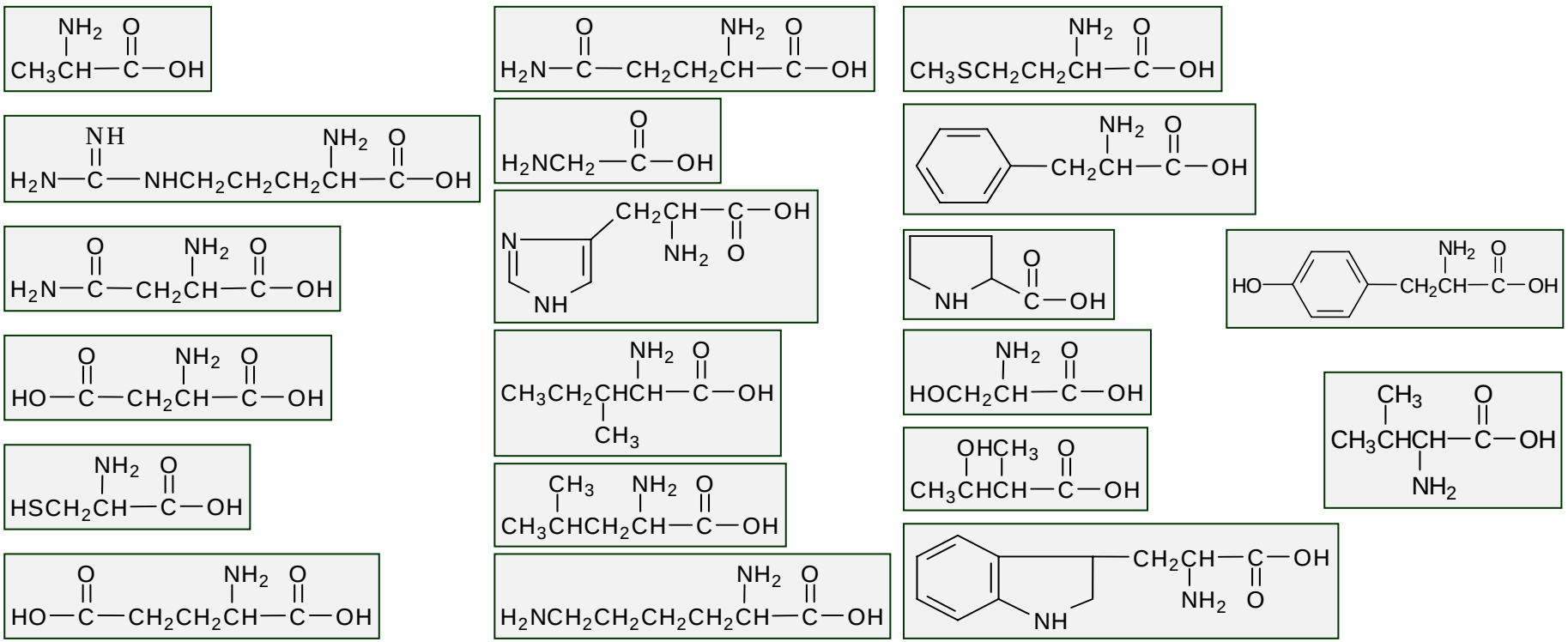
- Property important in protein structure and protein-protein interactions
- One of the most studied properties of amino-acids:
  - More than 37 scales
    - Kyle-Doolittle (1982) & Engelman (1986): predicting transmembrane regions in proteins
    - Hopp-Woods (1983): identification of potentially antigenic sites in proteins
    - Cornette et all (1987): optimized hydrophobicity scale based on 28 scales → suitable for prediction of alpha-helicesin proteins

RESEARCH AIM

- **Structural modeling analysis**
- **Amino acids**
- **Hydrophobicity**
  - To identify and characterize if there exists a relationship between the structure and the property
  - To quantifying the interrelation when exits

MATERIAL: STANDARD AMINO ACIDS

- 20 standard amino acids (directly encoded for protein synthesis by the standard genetic code)



MATERIAL: NON-STANDARD AMINO ACIDS

- 11 nonstandard amino acids:

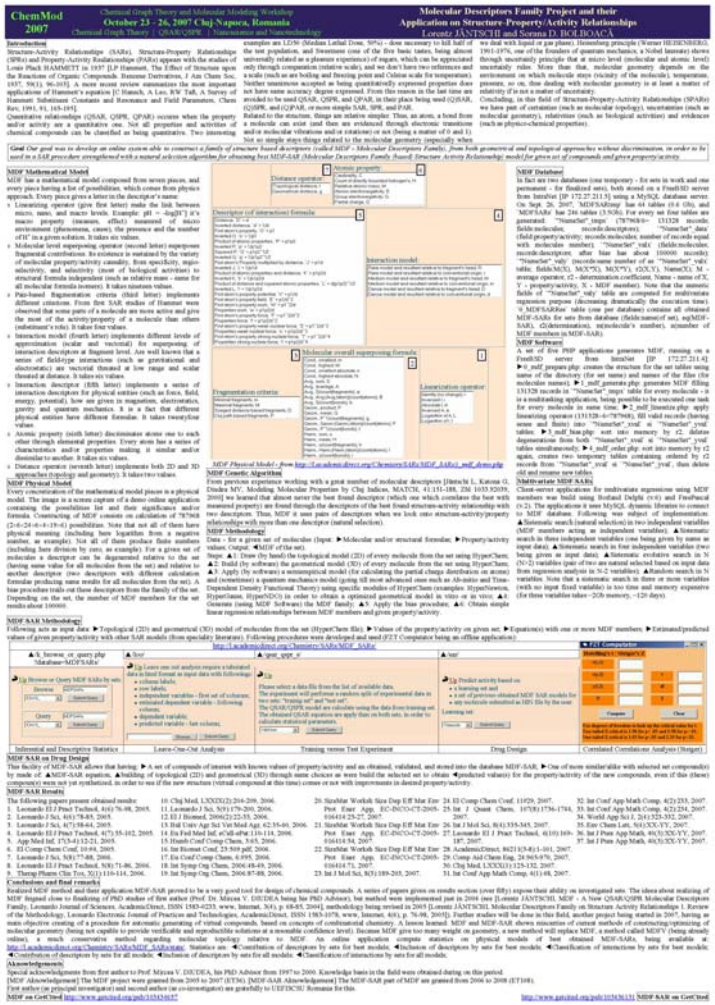
2-Aminoisobutyric Acid (Aib)	**Hydroxyproline (Hyp)**
Citrulline (Ciu)	**Lanthionine (Lth)**
Dehydroalanine (Dhd)	**Ornithine (Oth)**
Dopamine (Dop)	**Pyrrolysine (Pyl)**
Gamma-Aminobutyric Acid (Gab)	**Seleno-L-Cysteine (Sec)**
Homocysteine (Hcy)	

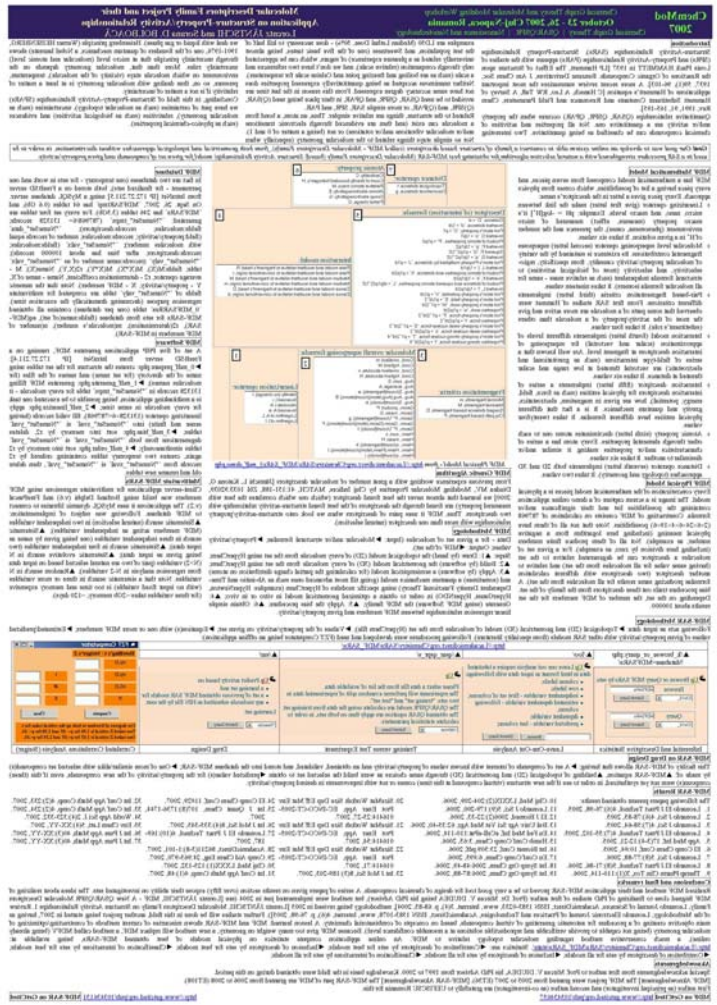
MATERIAL: HOYDROPHOBICITY

Scale - Set abb.
Black et all., 1991 - Hyd_01
Kyte-Doolittle, 1982 - Hyd_02
Wimley-White, 1996 - Hyd_03
Hessa et all., 2005 - Hyd_04
Sereda et all., 1994 - Hyd_05
Hopp-Woods, 1981 - Hyd_06
Cornette et all., 1987 - Hyd_07
Eisenberg et all., 1984 - Hyd_08
Janin, 1979 - Hyd_09
Rose et all., 1985 - Hyd_10
Engelman et all., 1986 - Hyd_11
Sweet-Eisenberg, 1983 - Hyd_12

Scale - Set abb.
Bull-Breese, 1974 - Hyd_13
Roseman, 1988 - Hyd_14
Welling et all., 1985 - Hyd_15
Parker et all., 1986 - Hyd_16
Cowan-Whittaker, 1990 - Hyd_17
Manavalan-Ponnuswamy, 1978 - Hyd_18
Fauchere-Pliska, 1983 - Hyd_19
Rao-Argos, 1986 - Hyd_20
Wilson et all., 1981 - Hyd_21
Cowan-Whittaker, 1990 - Hyd_22
Urry, 2004 - Hyd_23
Monera et all., 1995 - Hyd_24

MODELLING METHOD





HYDROPHOBICITY MODELS

Amino acid property	Welling et all., 1985	Wilson et all., 1981
MDF SPR Equation	$\hat{y} = -1.23 + x \cdot 0.39$	$\hat{y} = 6.55 + x \cdot (-27.79)$
SPR Determination (%)	44	66
MDF Descriptor (x)	amMRLQt	immRoQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Bonds (topology)	Space (geometry)
Interaction Model	Q·d	Q^{-1}
Structure on Property Scale	Inversed	Inversed

n = 20
r = 0.6649; F = 14*; s = 1.21
r_{loo} = 0.5961; F_{loo}=7 *; sloo = 1.37

n = 20
r = 0.8163; F = 36*; s = 2.19
r_{loo} = 0.7740 ; F_{loo} = 27*; s_{loo} = 2.41

HYDROPHOBICITY MODELS

Amino acid property	Cornette et all., 1987	Wimley-White, 1996
MDF SPR Equation	$\hat{y} = -2.88 + x \cdot (-1.73)$	$\hat{y} = -3.37 + x \cdot 7.35$
SPR Determination (%)	69	71
MDF Descriptor (x)	LmDROQg	iBmrWQt
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Bonds (topology)
Interaction Model	Q	Q^2/d
Structure on Property Scale	Logarithmic	Inversed

n = 20
r = 0.8309; F = 40*; s = 1.70
r_{loo} = 0.7936; F_{loo} = 30*; sloo = 1.87

n = 20
r = 0.8434; F = 44*; s = 0.48
r_{loo} = 0.8009 ; F_{loo} = 32*; s_{loo} = 0.54

HYDROPHOBICITY MODELS

Amino acid property	Hopp-Woods, 1981	Cowan-Whittaker, 1990
MDF SPR Equation	$\hat{y} = -1.99 + x \cdot 10.63$	$\hat{y} = 1.47 + x \cdot (-6.57)$
SPR Determination (%)	74	75
MDF Descriptor (x)	iMPRoQg	AmDROQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	Q^{-1}	Q
Structure on Property Scale	Inversed	Absolute

n = 20
r = 0.8608; F = 52*; s = 1.01
r_{loo} = 0.8288; F_{loo} = 39*; sloo = 1.11

n = 20
r = 0.8661; F = 54*; s = 0.66
r_{loo} = 0.8344; F_{loo} = 41*; s_{loo} = 0.73

HYDROPHOBICITY MODELS

Amino acid property	Manavalan-Ponnuswamy, 1978	Fauchere-Pliska, 1983
MDF SPR Equation	$\hat{y} = 14.55 + x \cdot 23.43$	$\hat{y} = -4.36 + x \cdot 5.94$
SPR Determination (%)	78	78
MDF Descriptor (x)	inMrpQg	ibDRPQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	Q^{-2}	Q^{2}
Structure on Property Scale	Inversed	Inversed

n = 20
r = 0.8814; F = 63*; s = 0.76
r_{loo} = 0.8546; F_{loo} = 49*; sloo = 0.84

n = 20
r = 0.8832; F = 65*; s = 0.50
r_{loo} = 0.8611; F_{loo} = 51*; s_{loo} = 0.54

HYDROPHOBICITY MODELS

Amino acid property	Rao-Argos, 1986	Janin, 1979
MDF SPR Equation	$\hat{y} = 1.43 + x \cdot (-2.73)$	$\hat{y} = 0.86 + x \cdot 1.74$
SPR Determination (%)	79	81
MDF Descriptor (x)	AmDROQg	inMrpQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	Q	Q^{-2}
Structure on Property Scale	Proportional	Inversed

n = 20
r = 0.8901; F = 69*; s = 0.24
r_{loo}= 0.8545; F_{loo}= 48*; sloo = 0.28

n = 20
r = 0.8974; F = 74*; s = 0.05
r_{loo}= 0.8744; F_{loo}= 58*; s_{loo} = 0.06

HYDROPHOBICITY MODELS

Amino acid property	Roseman, 1988	Rose et all., 1985
MDF SPR Equation	$\hat{y} = -3.36 + x \cdot 3.76$	$\hat{y} = 0.48 + x \cdot (-137.72)$
SPR Determination (%)	81	81
MDF Descriptor (x)	iBDdwQg	IHPrFQt
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Bonds (topology)
Interaction Model	Q^2/d	Q^2/d^2
Structure on Property Scale	Inversed	Logarithmic

n = 20
r = 0.8986; F = 75*; s = 0.45
r_{loo} = 0.8812; F_{loo} = 62*; sloo = 0.48

n = 20
r = 0.8997; F = 76*; s = 0.32
r_{loo} = 0.8599; F_{loo} = 56*; s_{loo} = 0.36

HYDROPHOBICITY MODELS

Amino acid property	Urry, 2004	Engelman et all., 1986
MDF SPR Equation	$\hat{y} = -29.73 + x \cdot (-11.96)$	$\hat{y} = 1.85 + x \cdot (-753.09)$
SPR Determination (%)	82	83
MDF Descriptor (x)	iBDMkEt	INPrWQg
Dominant Atomic Property	Electronegativity (E)	Charge (Q)
Interaction via	Bonds (topology)	Space (geometry)
Interaction Model	$Q^{-2} \cdot d^{-1}$	Q^2/d
Structure on Property Scale	Inversed	Logarithmic

n = 20
r = 0.9047; F = 81*; s = 1.07
r_{loo} = 0.8819; F_{loo} = 63*; s_{loo} = 1.18

n = 20
r = 0.9116; F = 89*; s = 2.07
r_{loo} = 0.8731; F_{loo} = 51*; s_{loo} = 2.56

HYDROPHOBICITY MODELS

Amino acid property	Eisenberg et all., 1984	Cowan-Whittaker, 1990
MDF SPR Equation	$\hat{y} = 1.68 + x \cdot (-0.92)$	$\hat{y} = 4.64 + x \cdot (-2.16)$
SPR Determination (%)	83	84
MDF Descriptor (x)	IAMdKQg	lbmdKQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	$Q^2 \cdot d$	$Q^2 \cdot d$
Structure on Property Scale	Logarithmic	Logarithmic

n = 20
r = 0.9128; F = 90*; s = 0.42
r_{loo} = 0.8935; F_{loo} = 70*; s_{loo} = 0.46

n = 20
r = 0.9182; F = 97*; s =0.52
r_{loo} = 0.8984; F_{loo} = 75*; s_{loo} = 0.58

HYDROPHOBICITY MODELS

Amino acid property	Roseman, 1988	Sereda et all., 1994
MDF SPR Equation	$\hat{y} = 5.30 + x \cdot (-3.78)$	$\hat{y} = 81.72 + x \cdot 817.95$
SPR Determination (%)	85	85
MDF Descriptor (x)	IAmrLQg	inMrpQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	Q·d	Q^{-2}
Structure on Property Scale	Logarithmic	Inversed

n = 20
r = 0.9208; F = 100*; s = 0.80
r_{loo} = 0.9073; F_{loo} = 84*; s_{loo} = 0.86

n = 20
r = 0.9232; F = 104*; s =20.73
r_{loo} = 0.9082; F_{loo} = 85*; s_{loo} = 22.58

HYDROPHOBICITY MODELS

Amino acid property	Hessa et all., 2005	Bull-Breese, 1974
MDF SPR Equation	$\hat{y} = -0.41 + x \cdot 7.18$	$\hat{y} = 1.36 + x \cdot (-0.20)$
SPR Determination (%)	85	85
MDF Descriptor (x)	AmDROQg	iIPmLQt
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Bonds (topology)
Interaction Model	Q	Q·d
Structure on Property Scale	Proportional	Inversed

n = 20
r = 0.9238; F = 105*; s = 0.32
r_{loo} = 0.9018; F_{loo} = 78*; s_{loo} = 0.58

n = 20
r = 0.9252; F = 107*; s =0.36
r_{loo} = 0.9003; F_{loo} = 75*; s_{loo} = 0.42

HYDROPHOBICITY MODELS

Amino acid property	Parker et all., 1986	Kyte-Doolittle, 1982
MDF SPR Equation	$\hat{y} = 11.05 + x \cdot 1.85$	$\hat{y} = -7.60 + x \cdot 19.17$
SPR Determination (%)	86	87
MDF Descriptor (x)	lfPROQg	iGPdLQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	Q	$d \cdot \sqrt{Q}$
Structure on Property Scale	Logarithmic	Inversed

n = 20
r = 0.9259; F = 108*; s = 2.46
r_{loo} = 0.8935; F_{loo} = 69*; sloo = 2.97

n = 20
r = 0.9327; F = 120*; s = 1.11
r_{loo} = 0.9226; F_{loo} = 103*; s_{loo} = 1.18

HYDROPHOBICITY MODELS

Amino acid property	Black et all., 1991	Monera et all., 1995
MDF SPR Equation	$\hat{y} = 0.86 + x \cdot (-0.96)$	$\hat{y} = 86.05 + x \cdot 843.88$
SPR Determination (%)	88	90
MDF Descriptor (x)	lAmrLQg	inMrpQg
Dominant Atomic Property	Charge (Q)	Charge (Q)
Interaction via	Space (geometry)	Space (geometry)
Interaction Model	$d \cdot \sqrt{Q}$	Q^{-2}
Structure on Property Scale	Proportional	Inversed

n = 20
r = 0.9376; F = 131*; s = 0.12
r_{loo}= 0.9263; F_{loo}= 109*; sloo = 0.13

n = 19 (- Prolina)
r = 0.9504; F = 159*; s = 16.49
r_{loo}= 0.9382; F_{loo}= 125*; s_{loo} = 18.37

PREDICTIONS

aa	Hyd_01	Hyd_02	Hyd_03	Hyd_04	Hyd_05	Hyd_06	Hyd_07	Hyd_08	Hyd_09	Hyd_10
Aib	0.71	-9.91	-0.22	0.14	143.07	-1.20	1.56	0.68	0.99	0.45
Ciu	-0.07	-19.45	-0.81	2.95	105.51	2.98	-1.57	-2.50	0.91	-0.83
Dhd	0.51	-11.39	-0.16	0.78	232.95	-0.23	0.22	0.72	1.18	-0.07
Dop	0.79	-14.31	5.04	1.09	98.01	-0.99	-0.18	0.15	0.90	0.17
Gab	0.50	-10.67	0.14	0.22	93.32	-1.07	1.33	0.16	0.89	0.46
Hcy	0.54	-11.47	0.06	-0.29	96.35	-1.83	4.30	0.39	0.89	0.49
Hyp	0.33	-11.88	-0.42	0.20	159.64	-1.66	1.38	-0.07	1.03	0.49
Lth	-0.21	-23.87	-1.04	3.19	353.92	3.33	-1.69	-3.54	1.44	-1.32
Oth	0.38	-13.92	0.07	2.35	98.86	2.09	-1.23	-0.61	0.90	-1.33
Pyl	0.25	-33.21	-0.78	2.98	119.29	0.63	-1.59	-4.71	0.94	-0.72
Sec	0.18	-12.87	-1.14	10.97	145.69	5.19	-3.68	-2.03	1.00	-13.33

PREDICTIONS

aa	Hyd_11	Hyd_12	Hyd_13	Hyd_14	Hyd_15	Hyd_16	Hyd_17	Hyd_18	Hyd_19	Hyd_20
Aib	1.69	0.46	-0.27	0.90	3.58	-1.77	0.94	16.31	0.63	1.22
Ciu	-8.25	-0.73	0.56	-4.59	-1.02	6.16	-2.38	15.23	-0.74	0.15
Dhd	-0.30	0.21	0.64	-0.13	-0.80	4.04	0.73	18.89	0.38	0.98
Dop	1.38	3.94	0.07	1.25	-0.97	1.36	1.19	15.02	2.23	0.86
Gab	1.67	0.85	0.41	-0.18	3.27	4.53	0.33	14.89	0.46	1.19
Hcy	1.85	0.84	0.22	0.03	-1.20	1.12	0.44	14.97	1.10	1.39
Hyp	1.84	-0.09	0.70	-1.23	-1.10	1.63	-0.37	16.79	1.63	1.20
Lth	-15.63	-1.31	0.60	-6.18	-1.14	7.63	-2.89	22.35	-0.57	0.06
Oth	-5.84	0.31	0.40	-0.92	-0.53	5.57	-0.35	15.04	0.34	0.38
Pyl	-5.70	-2.42	0.53	-1.78	-1.17	17.39	-2.05	15.63	-3.58	0.14
Sec	-67.94	-1.32	0.58	-2.37	-0.59	10.79	-0.87	16.39	-2.86	-2.90

PREDICTIONS

aa	Hyd_21	Hyd_22	Hyd_23	Hyd_24
Aib	-2.82	0.96	-1.87	149.34
Ciu	0.38	-1.61	0.88	110.59
Dhd	-2.76	0.38	-1.33	242.07
Dop	5.66	0.09	-5.41	102.85
Gab	0.14	0.89	0.00	98.02
Hcy	5.78	1.36	-1.48	101.15
Hyp	0.53	0.91	-3.27	166.44
Lth	4.56	-1.83	-0.17	366.88
Oth	0.11	-1.06	-0.96	103.74
Pyl	1.25	-1.64	-2.66	124.81
Sec	5.18	-8.96	-0.39	152.04
Pro				96.57

SUMMARY

1st letter		2nd letter		3rd letter		4th letter		5th letter		6th letter		7th letter	
Cha.	f_a	Cha.	f_a	Cha.	f_a	Cha.	f_a	Cha.	f_a	Cha.	f_a	Cha.	f_a
A	4	A	3	D	7	d	4	F	1	E	1	g	19
i	16	B	5	m	11	m	2	K	3	Q	23	t	5
l	4	f	1	P	6	r	18	L	5				
		G	1					O	7				
		H	1					p	5				
		I	1					W	3				
		m	7										
		n	5										

Cha. = character: f_a = absolute frequency

FUTURE WORKS

- How reliable the predicted values are?
- Is it possible to rescale the hydrophobicity scales?
  - QSPR models
  - Confidence intervals for intercept and slope

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- **Thank you for your attention!**