

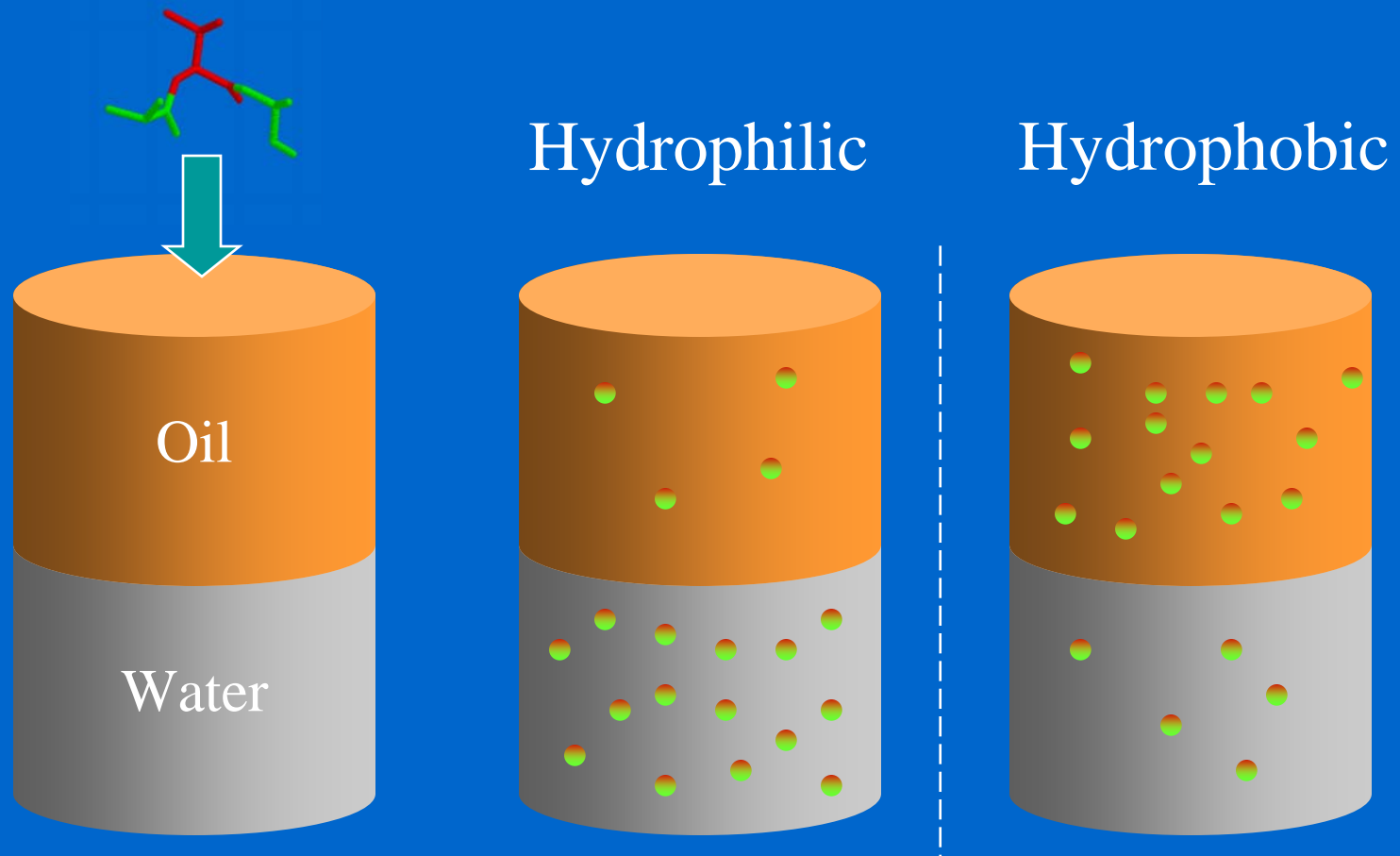
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Hydropathy Plot

Prediction hydrophobic and
hydrophilic regions in a protein

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Partition Coefficients



Hydrophobicity/Hydrophilicity Values

		Fauchere & Pliska	Kyte & Doolittle	Hopp & Woods	Eisenberg
↑ hydrophilic	R	-1.37	-4.50	3.00	-2.53
	K	-1.35	-3.90	3.00	-1.50
	D	-1.05	-3.50	3.00	-0.90
	Q	-0.78	-3.50	0.20	-0.85
	N	-0.85	-3.50	0.20	-0.78
	E	-0.87	-3.50	3.00	-0.74
	H	-0.40	-3.20	-0.50	-0.40
	S	-0.18	-0.80	0.30	-0.18
	T	-0.05	-0.70	-0.40	-0.05
	P	0.12	-1.60	0.00	0.12
↓ hydrophobic	Y	0.26	-1.30	-2.30	0.26
	C	0.29	2.50	-1.00	0.29
	G	0.48	-0.40	0.00	0.48
	A	0.62	1.80	-0.50	0.62
	M	0.64	1.90	-1.30	0.64
	W	0.81	-0.90	-3.40	0.81
	L	1.06	3.80	-1.80	1.06
	V	1.08	4.20	-1.50	1.08
	F	1.19	2.80	-2.50	1.19
	I	1.38	4.50	-1.80	1.38

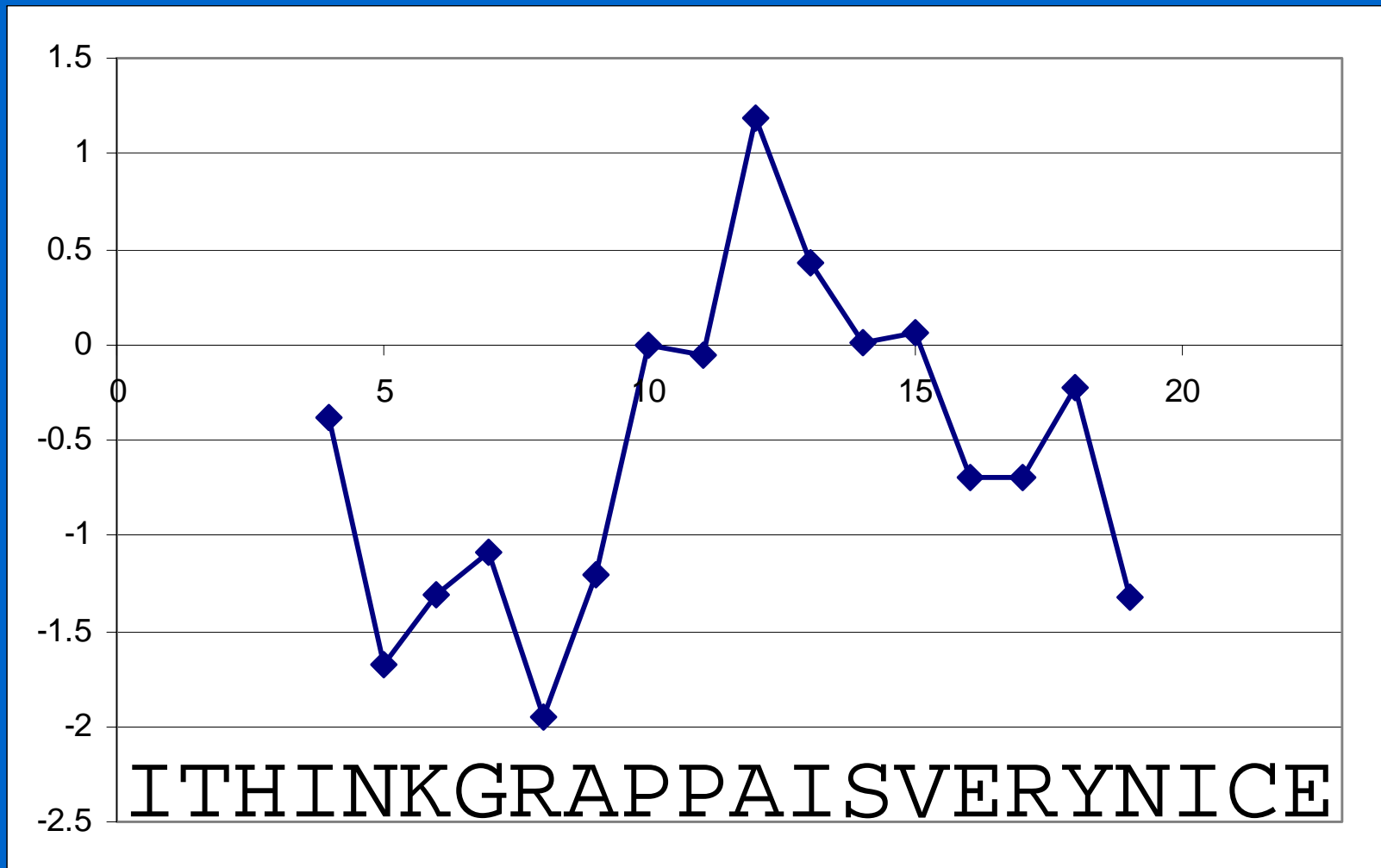
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Hydrophobicity Plot

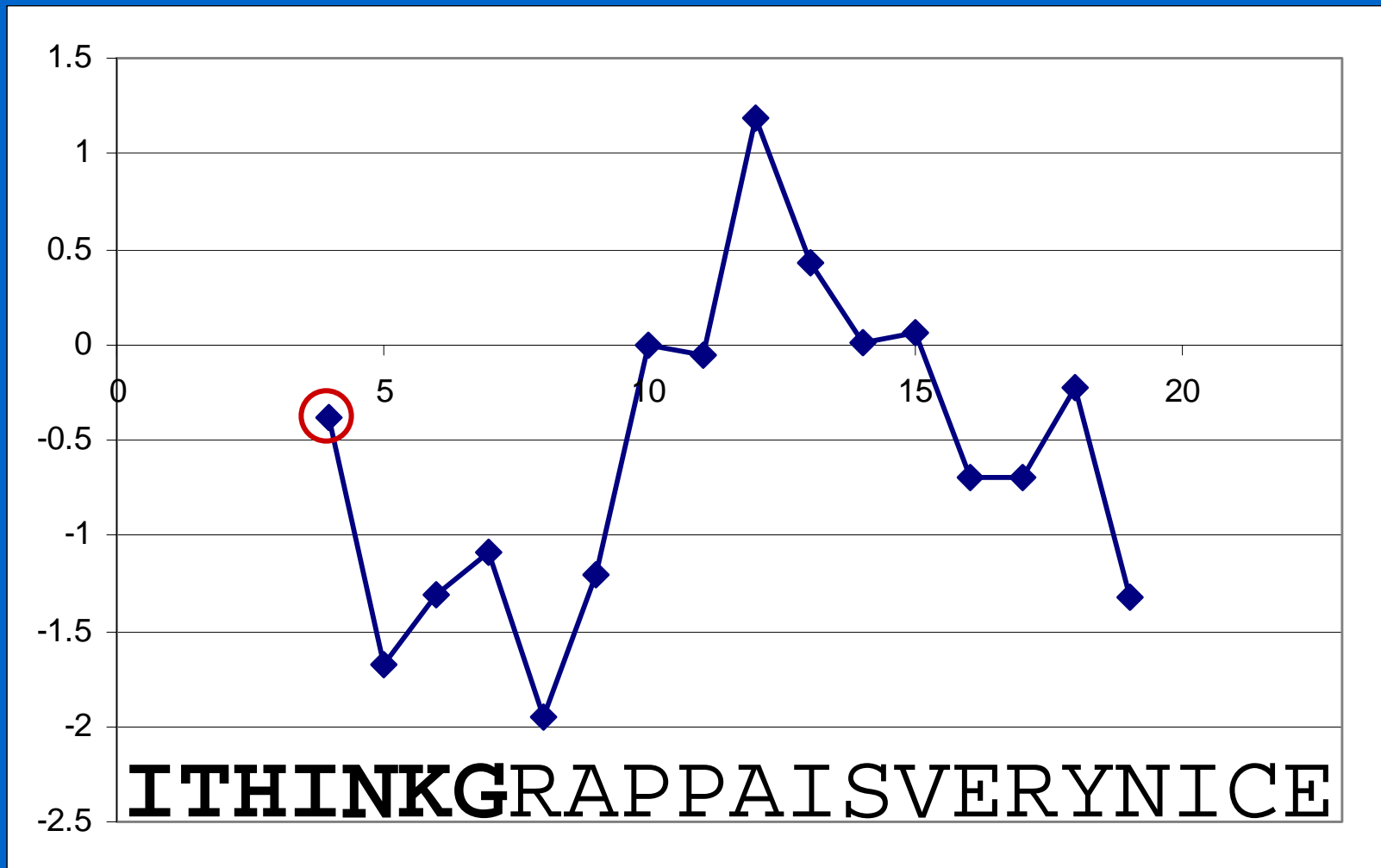
- Sum amino acid hydrophobicity values in a given window
- Plot the value in the middle of the window
- Shift the window one position

$$\langle H_i \rangle = \frac{1}{2k+1} \sum_{n=i-k}^{i+k} H_n$$

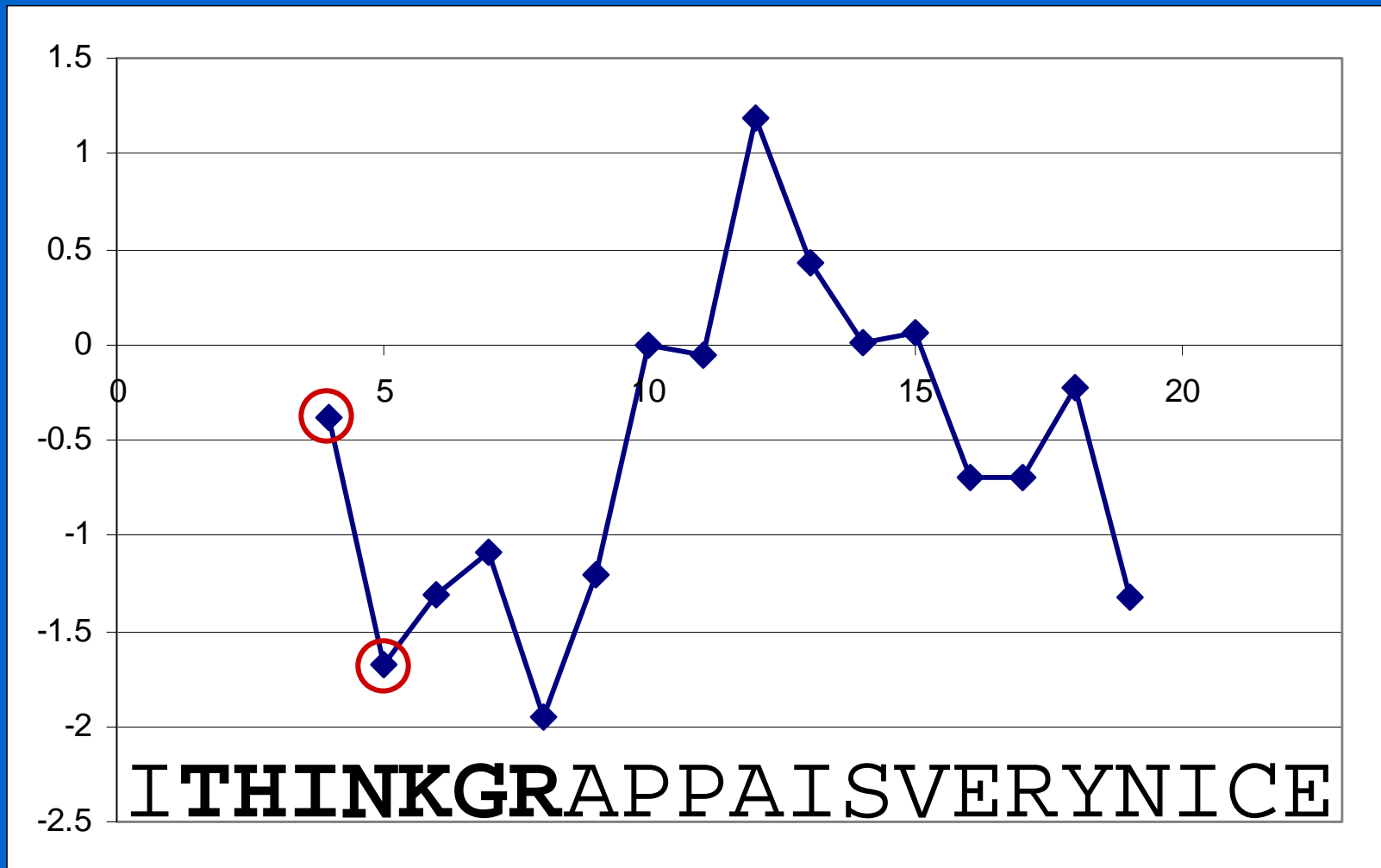
Hydrophobicity Plot



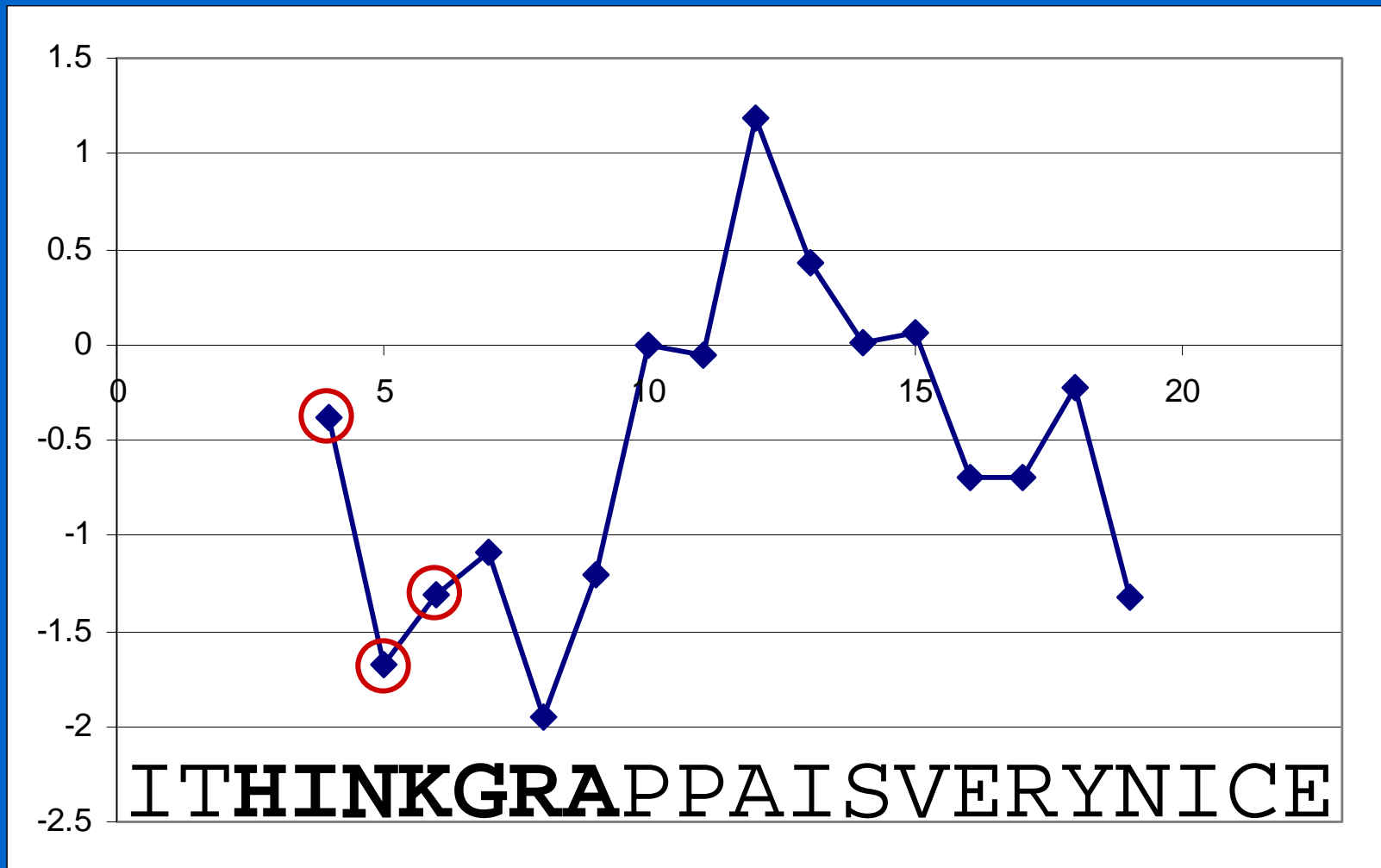
Hydrophobicity Plot



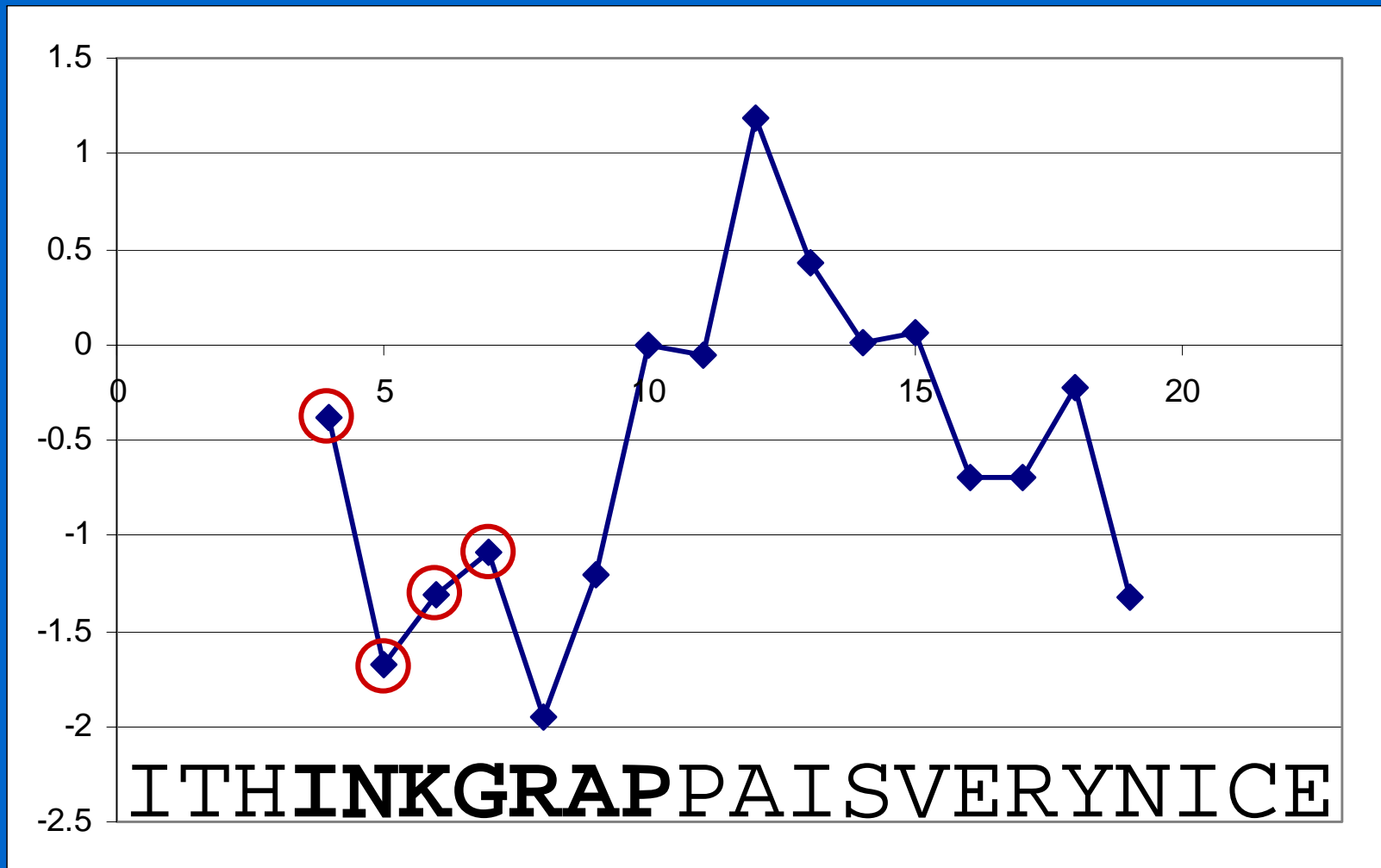
Hydrophobicity Plot



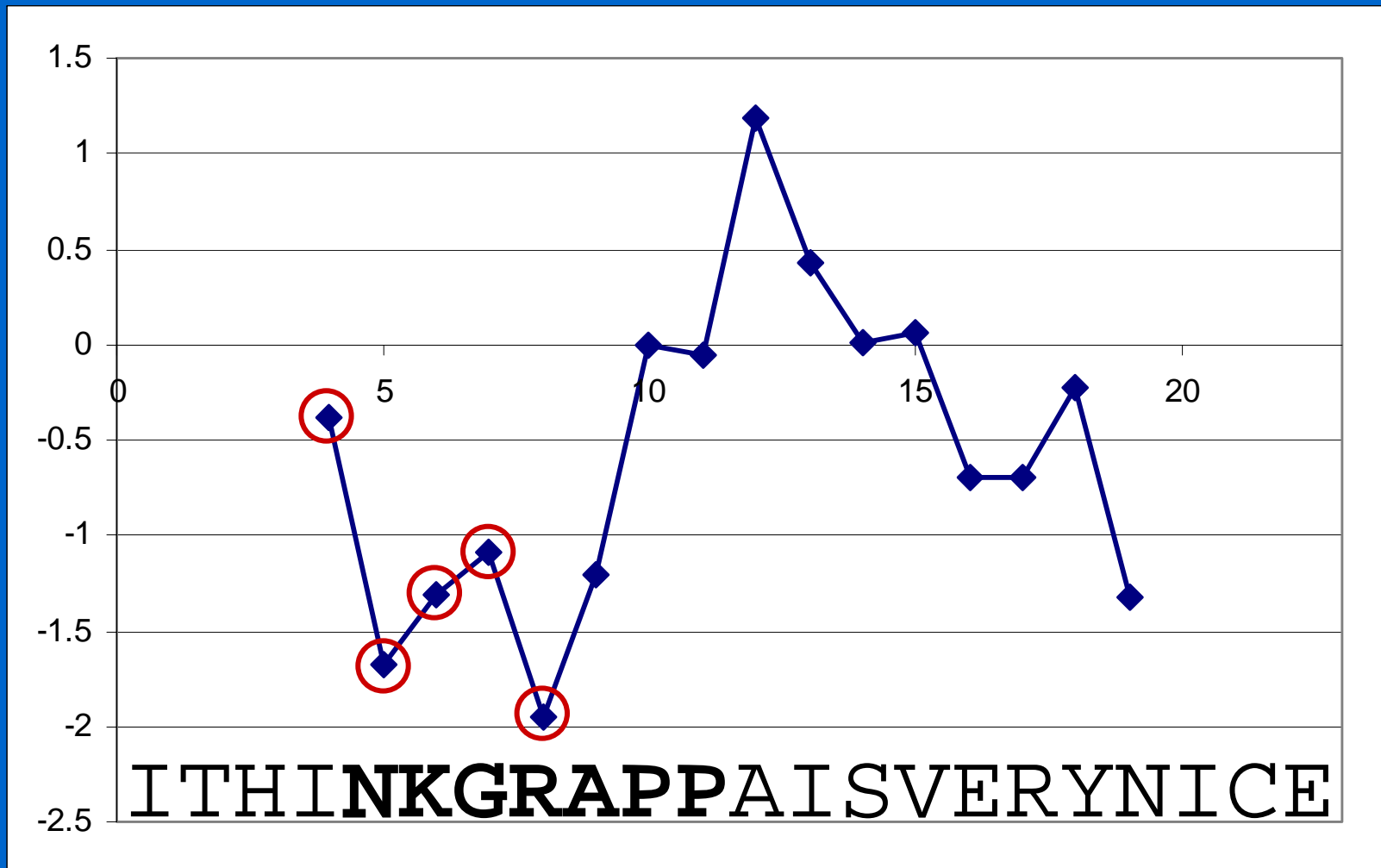
Hydrophobicity Plot



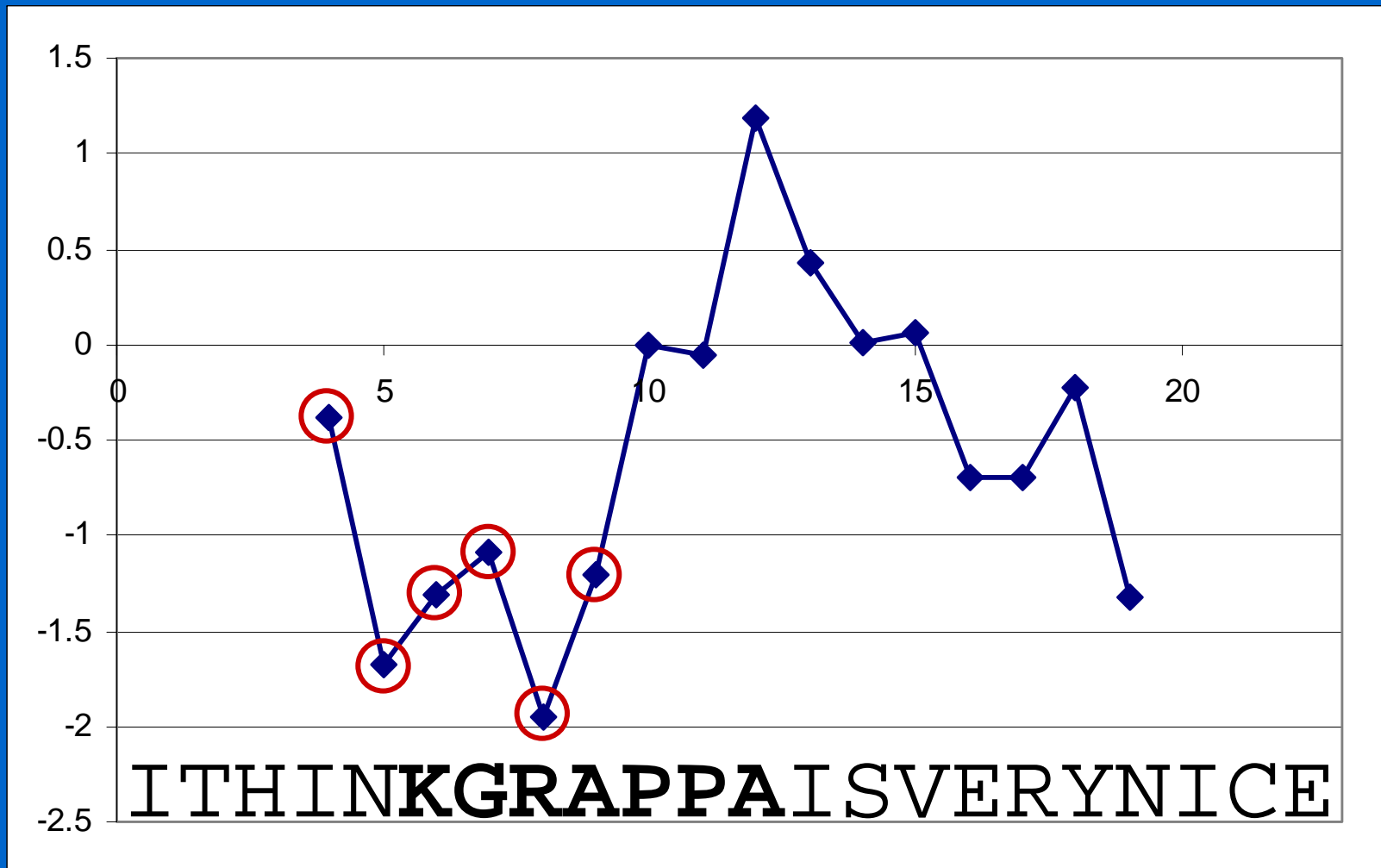
Hydrophobicity Plot



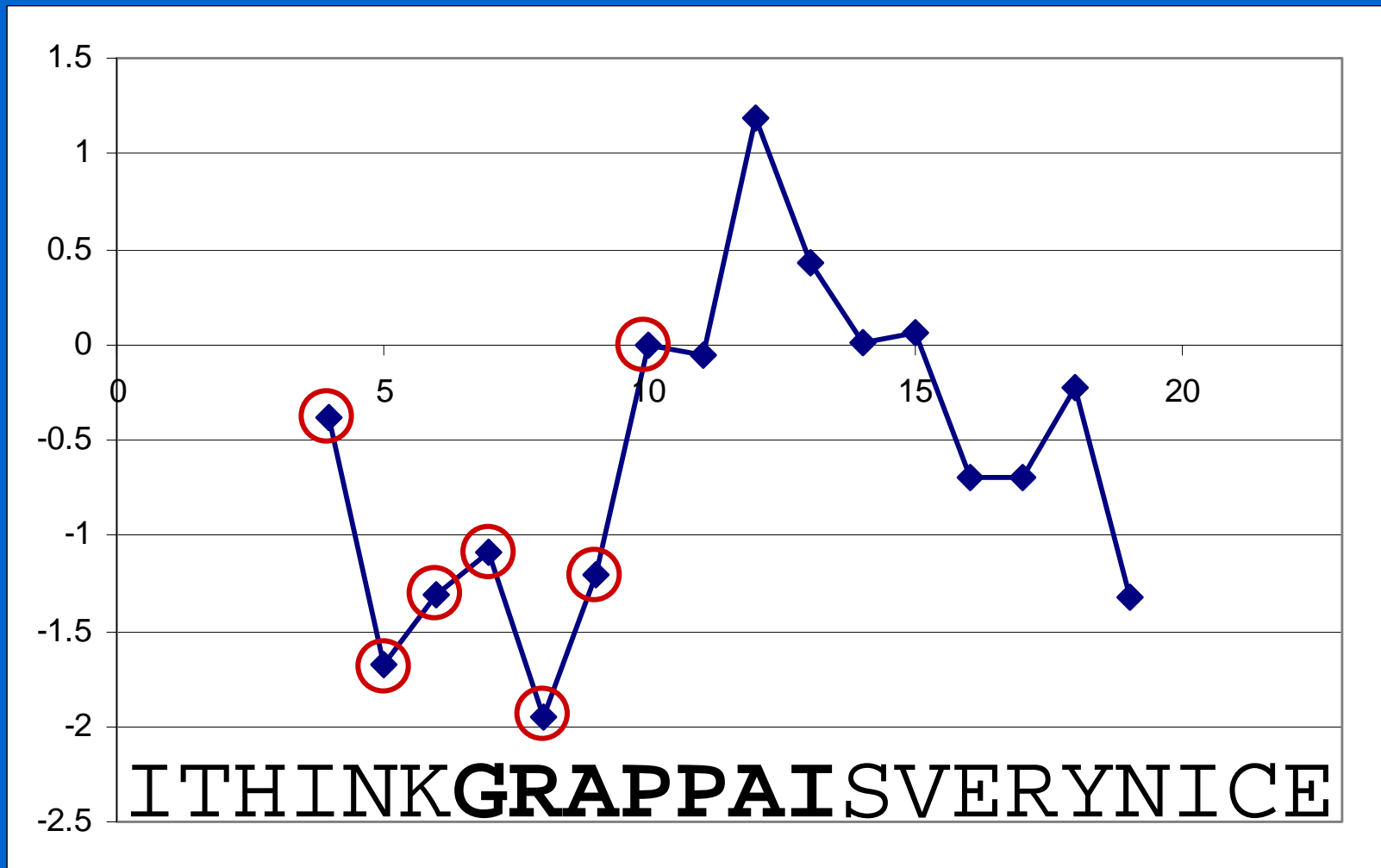
Hydrophobicity Plot



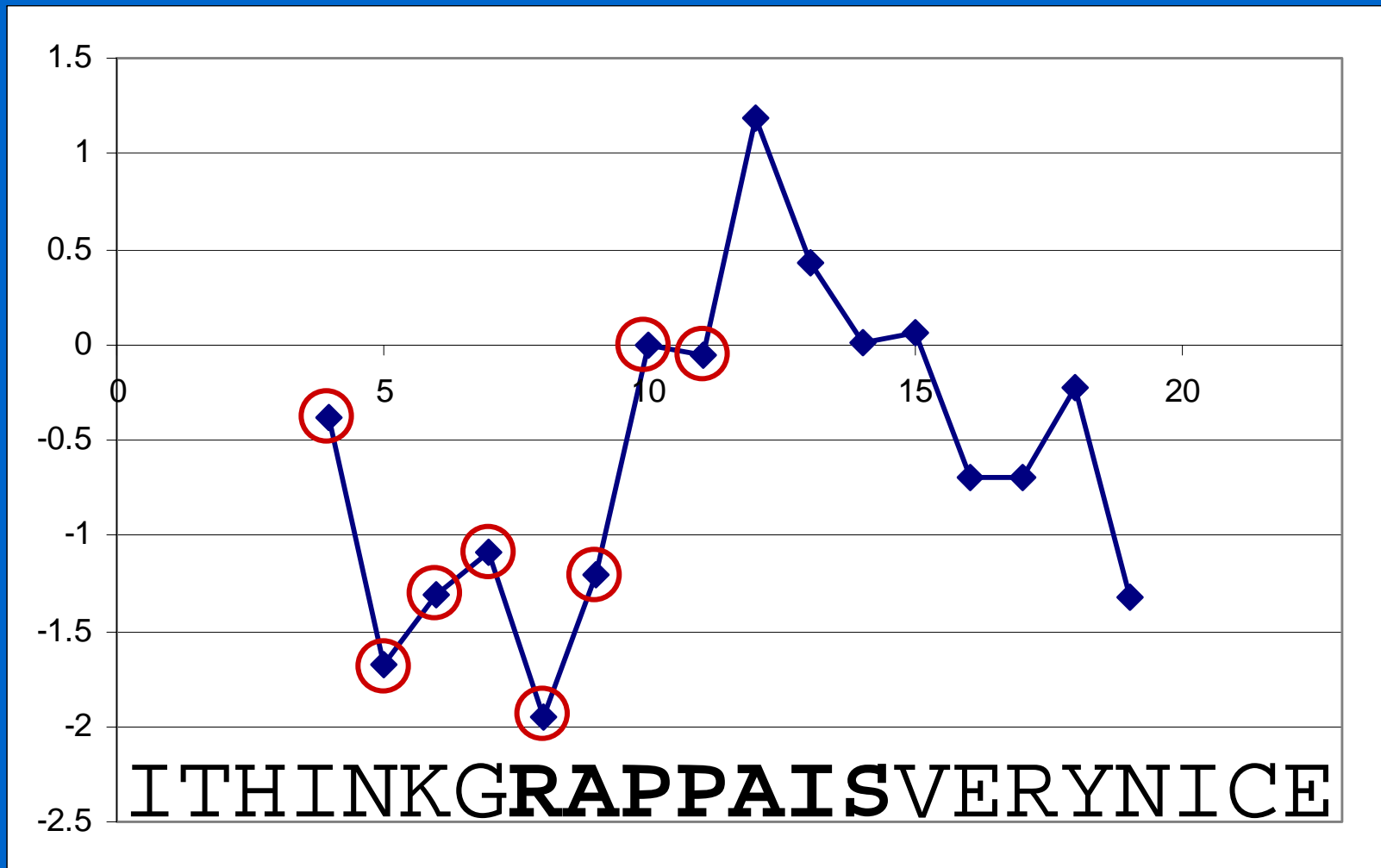
Hydrophobicity Plot



Hydrophobicity Plot

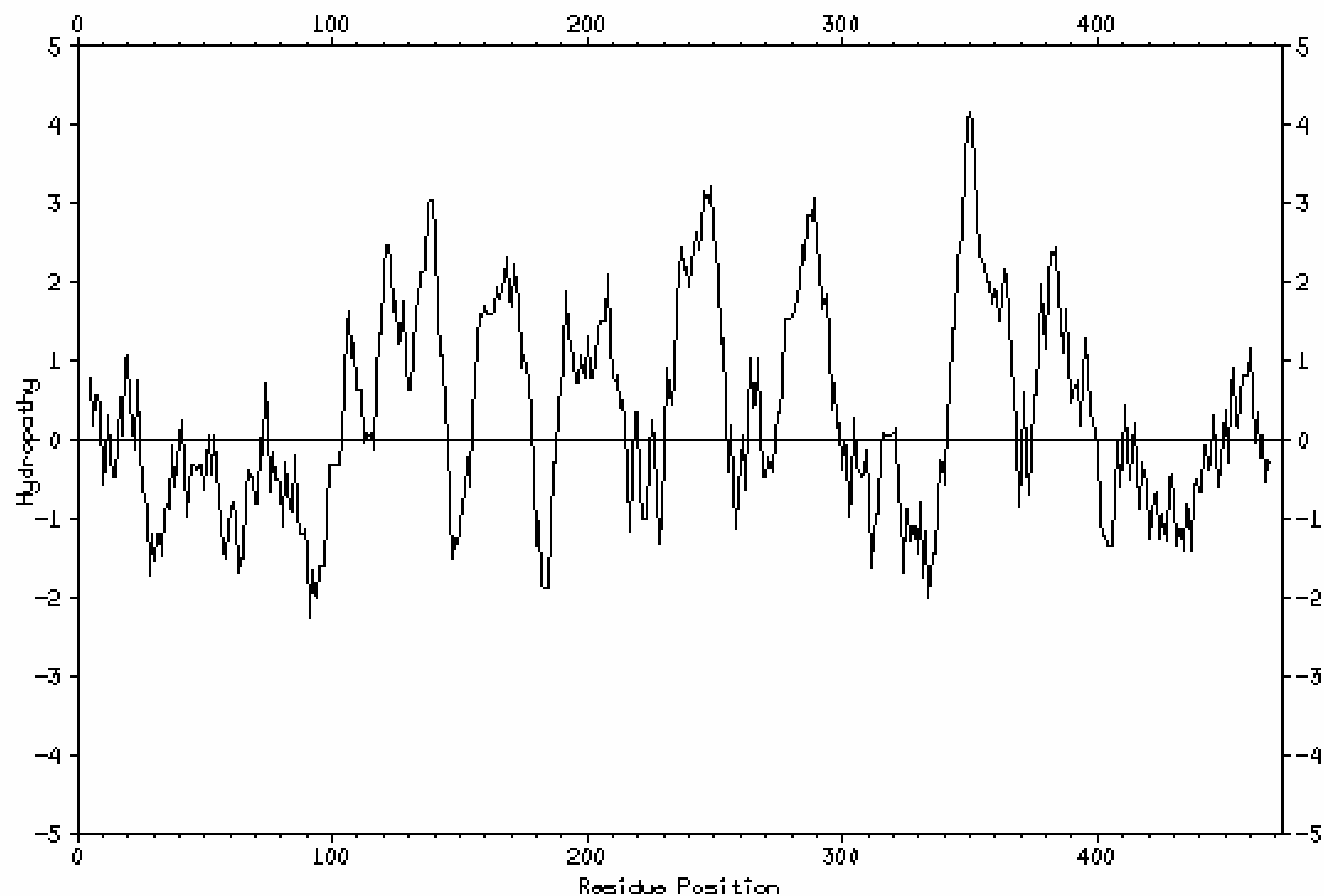


Hydrophobicity Plot

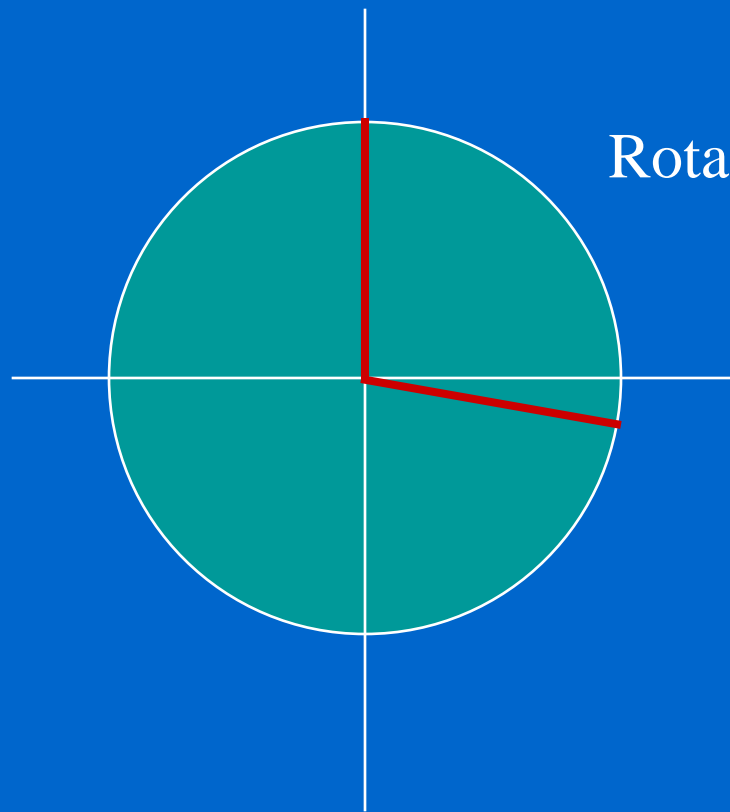


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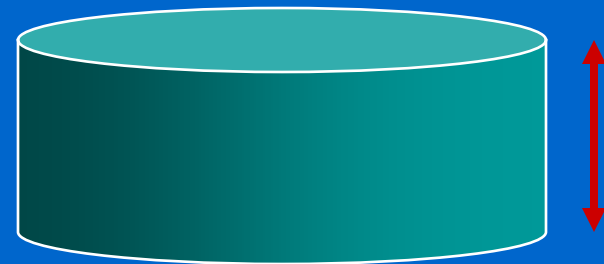
Kyte & Doolittle Plot of: swissprot:cb1r_human cki: 0, 1 to 472 July 2, 1999 18:34
CANNABINOID RECEPTOR 1 (CB1) (CB-R) (CANNB). Window = 9



Transmembrane Regions

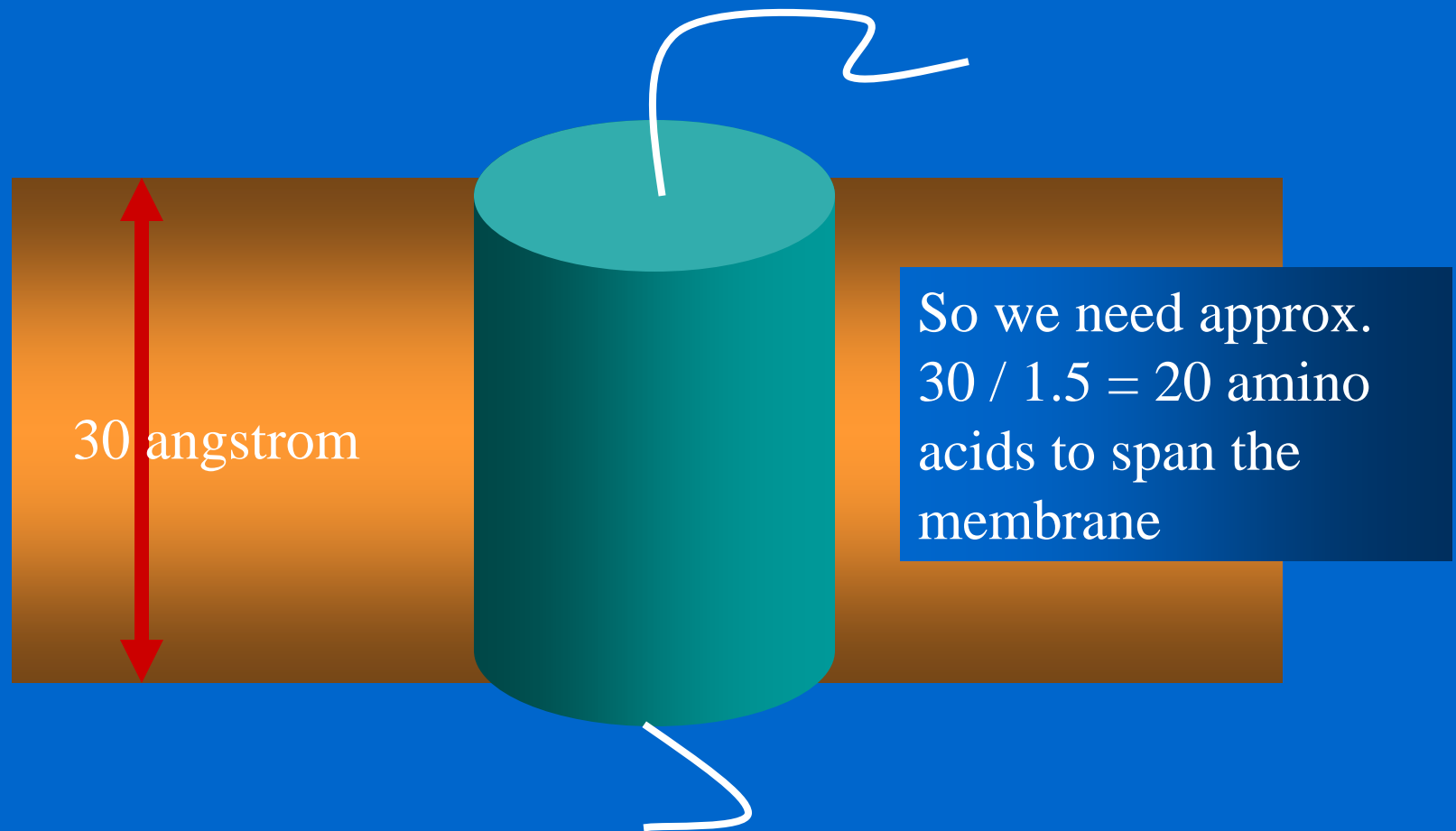


Rotation is 100 degrees per amino acid



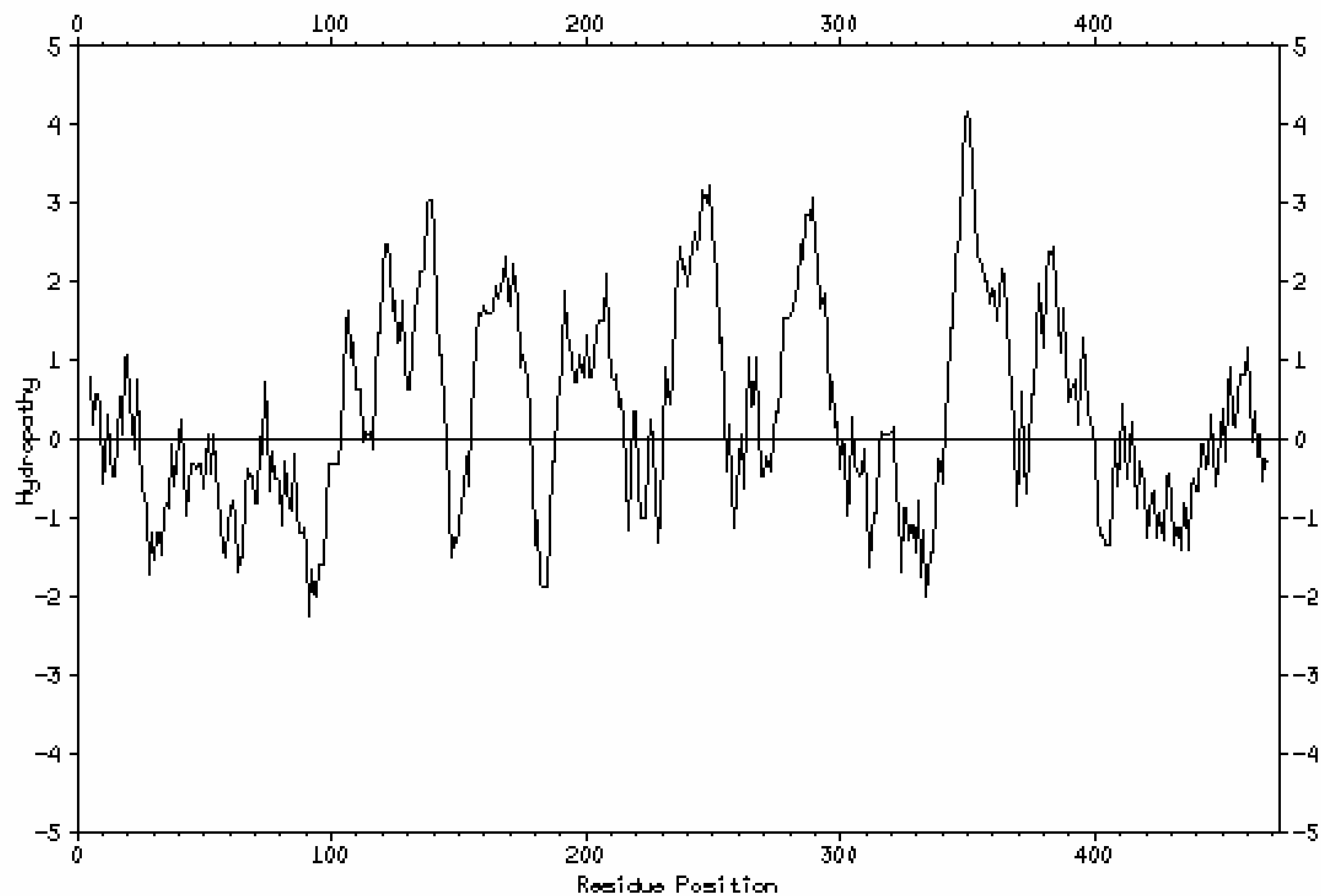
Climbing 1.5 Angstrom
per amino acid residue

Transmembrane Regions



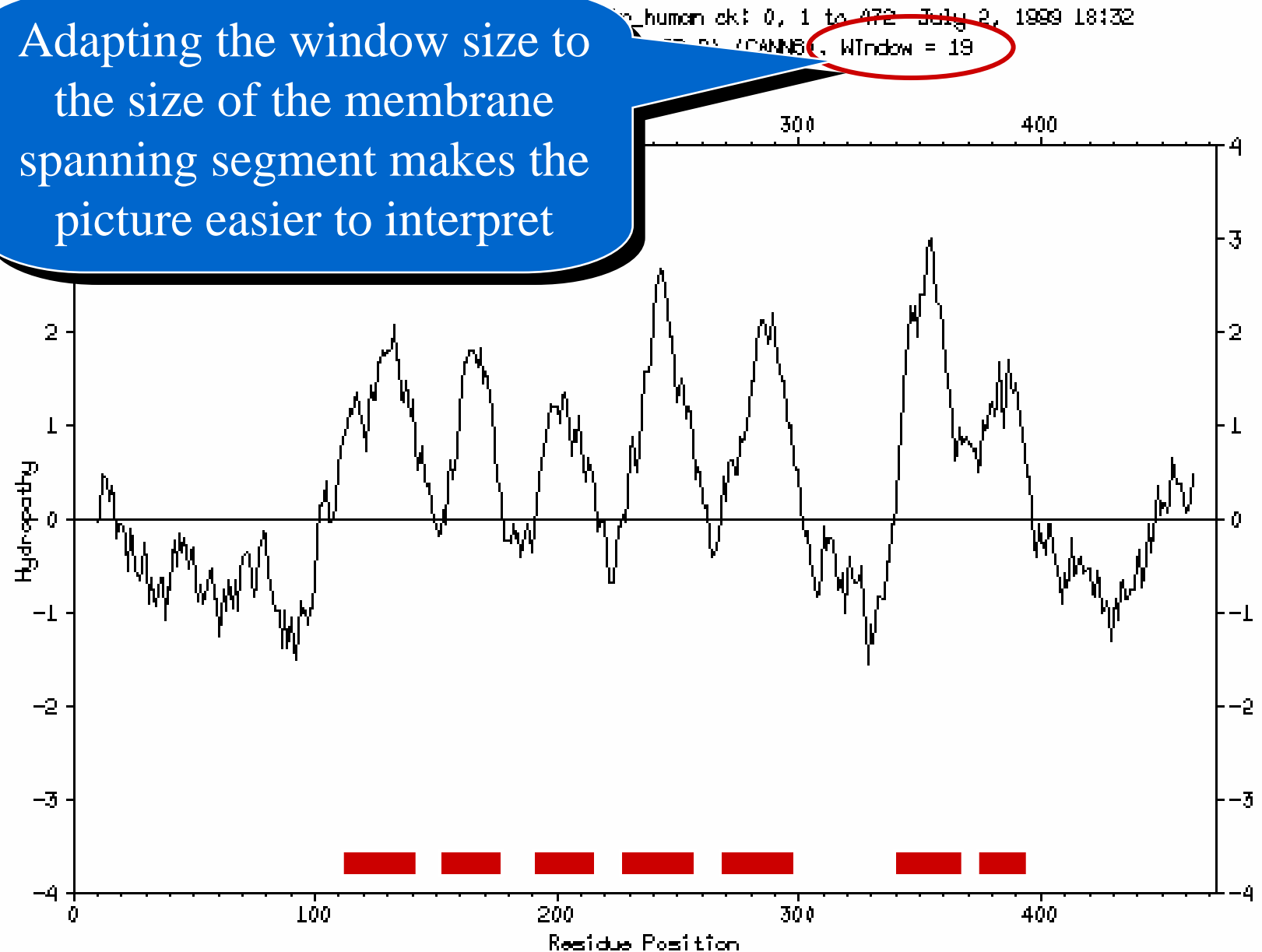
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Kyte & Doolittle Plot of: swissprot:cb1r_human cki: 0, 1 to 472 July 2, 1999 18:34
CANNABINOID RECEPTOR 1 (CB1) (CB-R) (CANNB). Window = 9



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Adapting the window size to the size of the membrane spanning segment makes the picture easier to interpret





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Secondary Structure Prediction

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Secondary Structure Prediction

- Traditional methods
 - Chou & Fasman
 - Statistical & rule-based method
 - Lim
 - Stereochemical rules
 - Garnier, Osguthorpe & Robson
 - Statistical method
- Accuracy ~ 60%

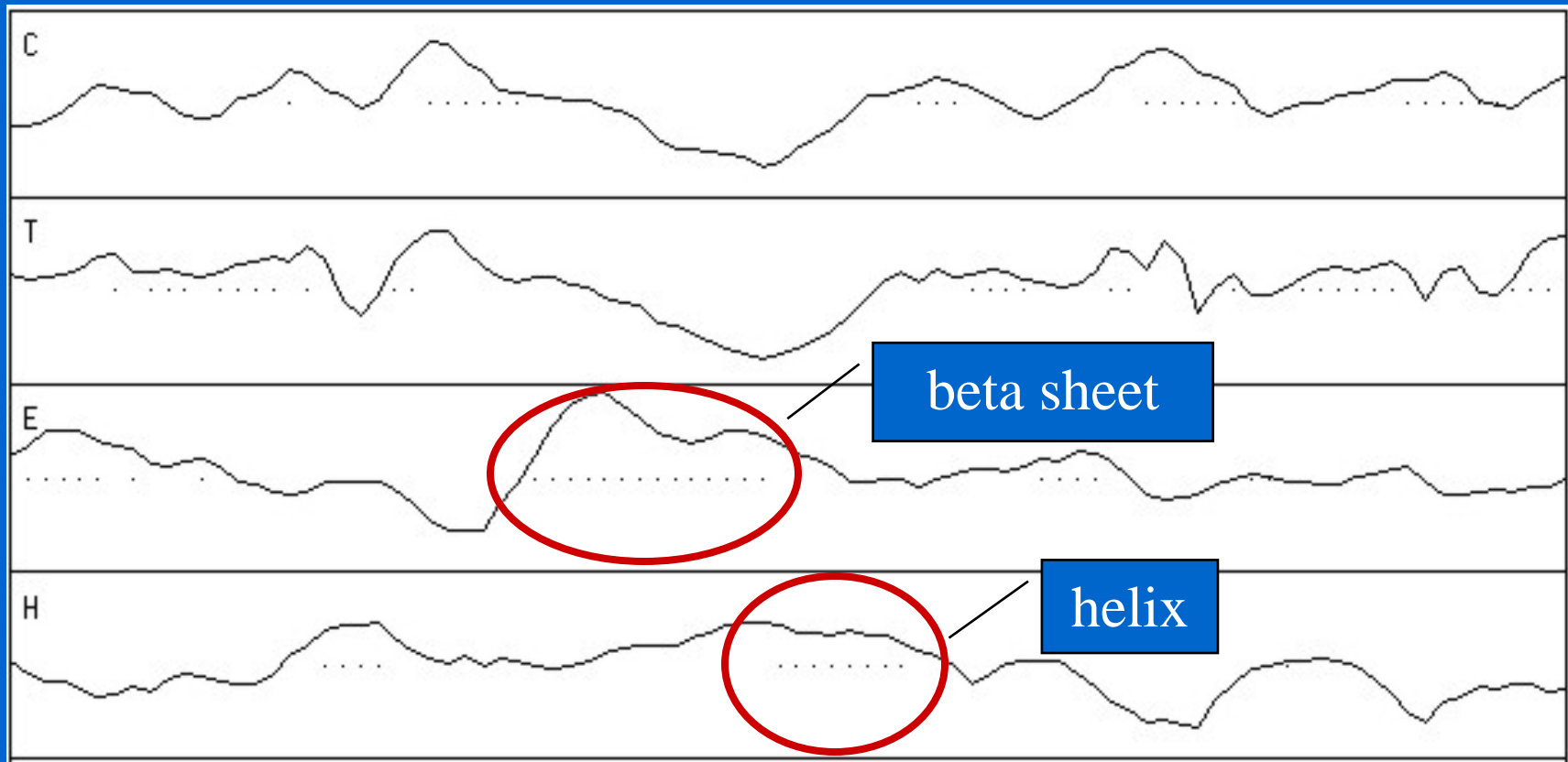
GOR Helix Parameters

	$i-8$	$i-6$	$i-4$	$i-2$	i	$i+2$	$i+4$	$i+6$	$i+8$								
Gly	-5	-10	-15	-20	-30	-40	-50	-60	-86	-60	-50	-40	-30	-20	-15	-10	-5
ala	5	10	15	20	30	40	50	60	65	60	50	40	30	20	15	10	5
val	0	0	0	0	0	0	5	10	14	10	5	0	0	0	0	0	0
leu	0	5	10	15	20	25	28	30	32	30	28	25	20	15	10	5	0
ile	5	10	15	20	25	20	15	10	6	0	-10	-15	-20	-25	-20	-10	-5
ser	0	-5	-10	-15	-20	-25	-30	-35	-39	-35	-30	-25	-20	-15	-10	-5	0
thr	0	0	0	-5	-10	-15	-20	-25	-26	-25	-20	-15	-10	-5	0	0	0
asp	0	-5	-10	-15	-20	-15	-10	0	5	10	15	20	20	20	15	10	5
glu	0	0	0	0	10	20	60	70	78	78	78	78	78	70	60	40	20
asn	0	0	0	0	-10	-20	-30	-40	-51	-40	-30	-20	-10	0	0	0	0
gln	0	0	0	0	5	10	20	20	10	-10	-20	-20	-10	-5	0	0	0
lys	20	40	50	55	60	60	50	30	23	10	5	0	0	0	0	0	0
his	10	20	30	40	50	50	50	30	12	-20	-10	0	0	0	0	0	0
arg	0	0	0	0	0	0	0	0	-9	-15	-20	-30	-40	-50	-50	-30	-10
phe	0	0	0	0	0	5	10	15	16	15	10	5	0	0	0	0	0
tyr	-5	-10	-15	-20	-25	-30	-35	-40	-45	-40	-35	-30	-25	-20	-15	-10	-5
trp	-10	-20	-40	-50	-50	-10	0	10	12	10	0	-10	-50	-50	-40	-20	-10
cys	0	0	0	0	0	0	-5	-10	-13	-10	-5	0	0	0	0	0	0
met	10	20	25	30	35	40	45	50	53	50	45	40	35	30	25	20	10
pro	-10	-20	-40	-60	-80	-100	-120	-140	-77	-60	-30	-20	-10	0	0	0	0

I S **G A R N I E R H E** L I X P R E D I C T

	$i-8$	$i-6$	$i-4$	$i-2$	i	$i+2$	$i+4$	$i+6$	$i+8$								
Gly	-5	-10	-15	-20	-30	-40	-50	-60	-86	-60	-50	-40	-30	-20	-15	-10	-5
ala	5	10	15	20	30	40	50	60	65	60	50	40	30	20	15	10	5
val	0	0	0	0	0	0	5	10	14	10	5	0	0	0	0	0	0
leu	0	5	10	15	20	25	28	30	32	30	28	25	20	15	10	5	0
ile	5	10	15	20	25	20	15	10	6	0	-10	-15	-20	-25	-20	-10	-5
ser	0	-5	-10	-15	-20	-25	-30	-35	-39	-35	-30	-25	-20	-15	-10	-5	0
thr	0	0	0	-5	-10	-15	-20	-25	-26	-25	-20	-15	-10	-5	0	0	0
asp	0	-5	-10	-15	-20	-15	-10	0	5	10	15	20	20	20	15	10	5
glu	0	0	0	0	10	20	60	70	78	78	78	78	78	70	60	40	20
asn	0	0	0	0	-10	-20	-30	-40	-51	-40	-30	-20	-10	0	0	0	0
gln	0	0	0	0	5	10	20	20	10	-10	-20	-20	-10	-5	0	0	0
lys	20	40	50	55	60	60	50	30	23	10	5	0	0	0	0	0	0
his	10	20	30	40	50	50	50	30	12	-20	-10	0	0	0	0	0	0
arg	0	0	0	0	0	0	0	0	-9	-15	-20	-30	-40	-50	-50	-30	-10
phe	0	0	0	0	0	5	10	15	16	15	10	5	0	0	0	0	0
tyr	-5	-10	-15	-20	-25	-30	-35	-40	-45	-40	-35	-30	-25	-20	-15	-10	-5
trp	-10	-20	-40	-50	-50	-10	0	10	12	10	0	-10	-50	-50	-40	-20	-10
cys	0	0	0	0	0	0	-5	-10	-13	-10	-5	0	0	0	0	0	0
met	10	20	25	30	35	40	45	50	53	50	45	40	35	30	25	20	10
pro	-10	-20	-40	-60	-80	-100	-120	-140	-77	-60	-30	-20	-10	0	0	0	0

GOR Prediction



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Secondary Structure Prediction

- Recent methods
 - Neural networks = flexible statistics
 - Multiple alignments = variability
 - Heuristics = common sense
 - Or a combination of the above
- Accuracy ~ 70%

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Heuristics

- Conserved parts are structurally and/or functionally important
- Segments with many gaps must be in loop regions

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Secondary Structure Prediction

- Strategy
 - Use as many methods as possible
 - Use homologous sequences
 - Combine predictions into consensus prediction

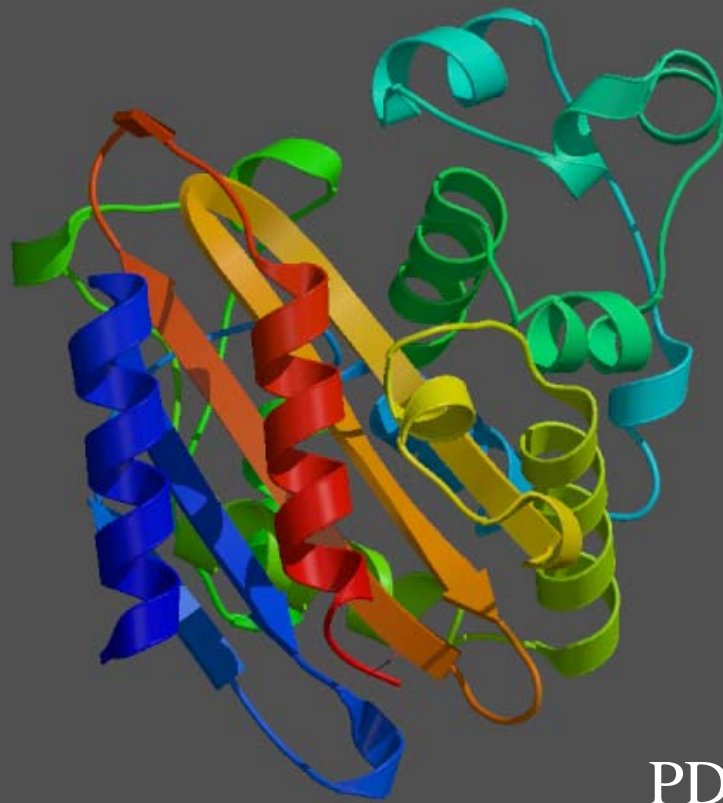
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Why can't it be 100% correct?

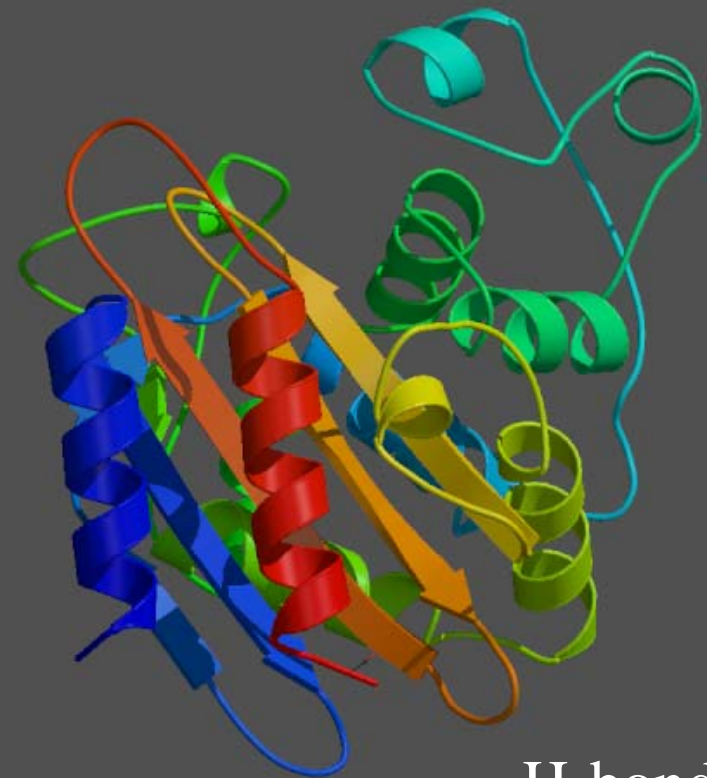
- All current 2D prediction schemes are based upon observation of occurrence of 2D elements in 3D structures
- Deduction of 2D elements from structures is ambiguous!

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Hydrolase



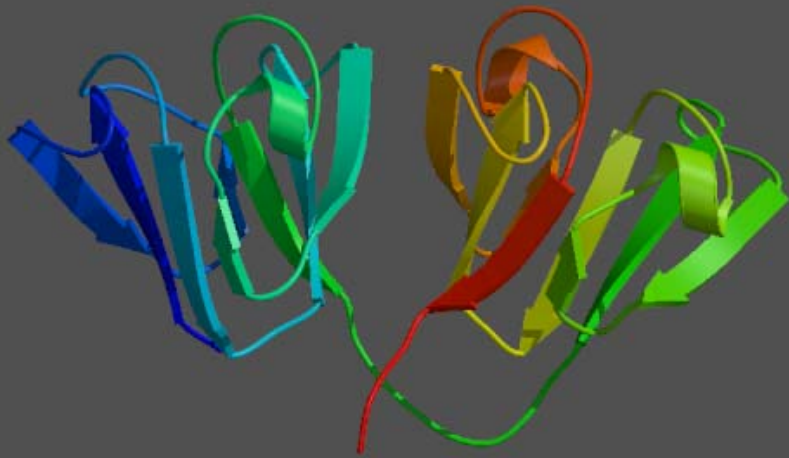
PDB



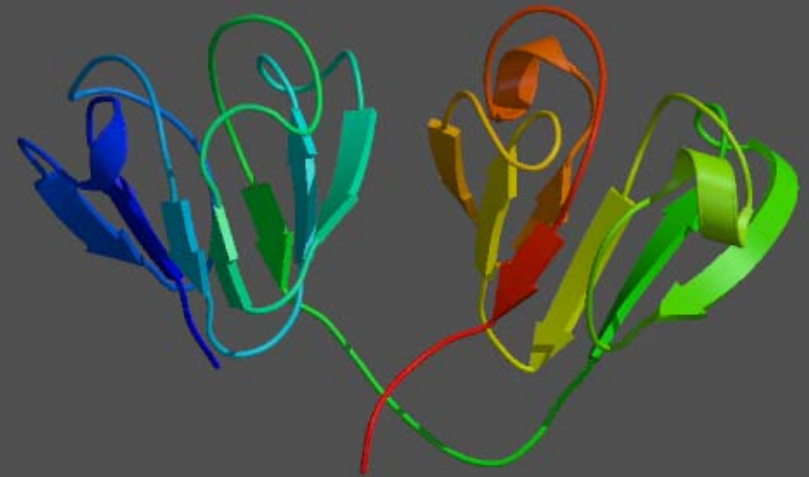
H-bonds

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Gamma4 Crystallin



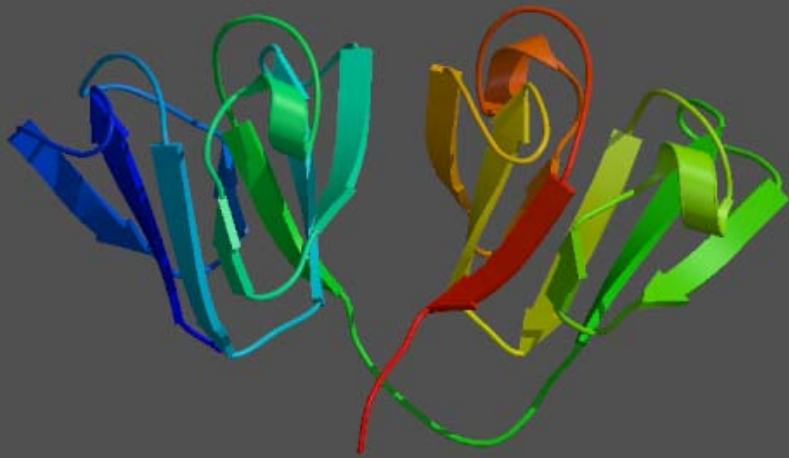
PDB



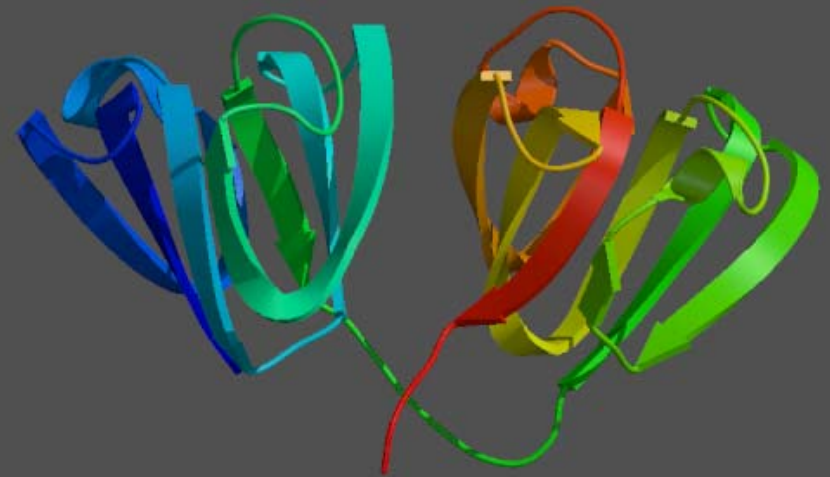
H-bonds

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Gamma4 Crystallin

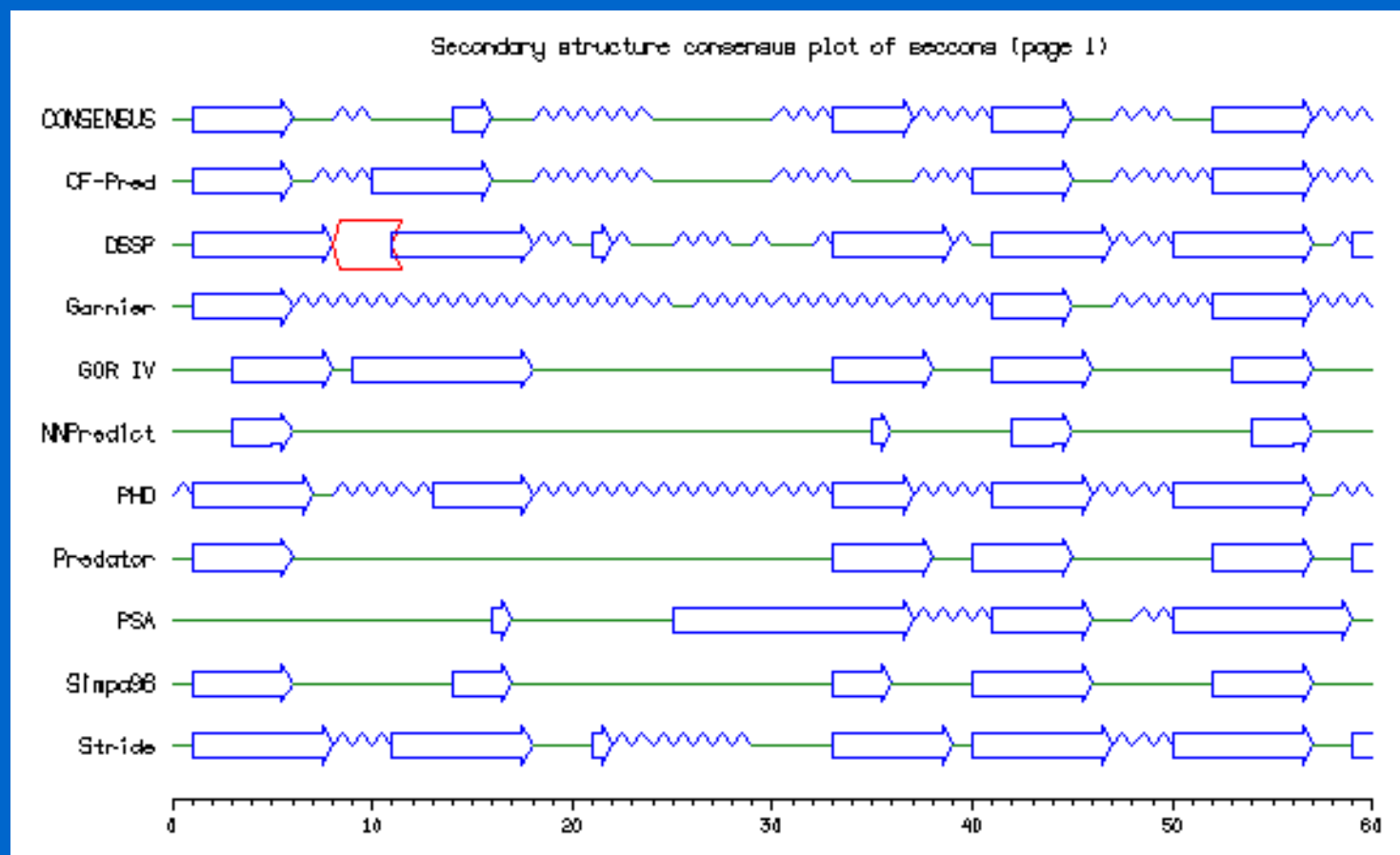


PDB



C-alpha

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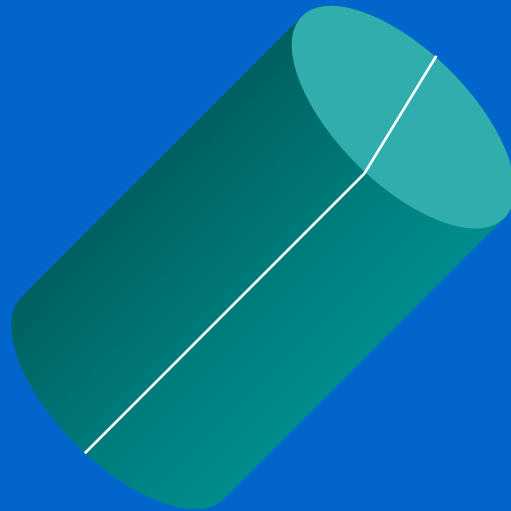
Hydrophobic Moment

Look for amphipathic helices or beta sheets

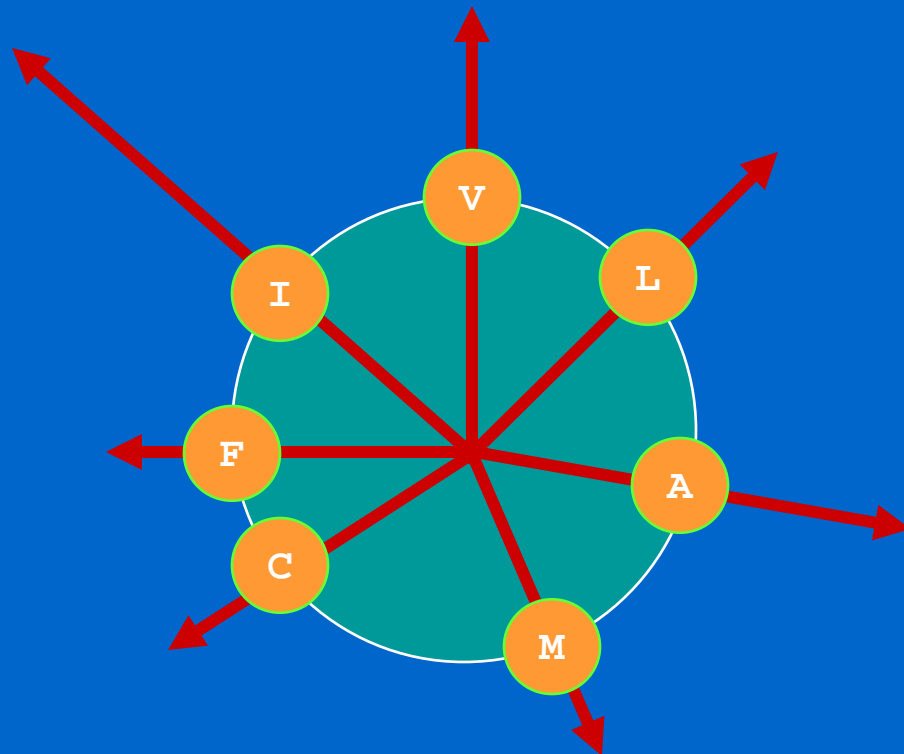
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Amphipathic Helices

- An amphipathic helix is a helix in which there is a distinct difference in distribution of hydrophobic and hydrophilic residues

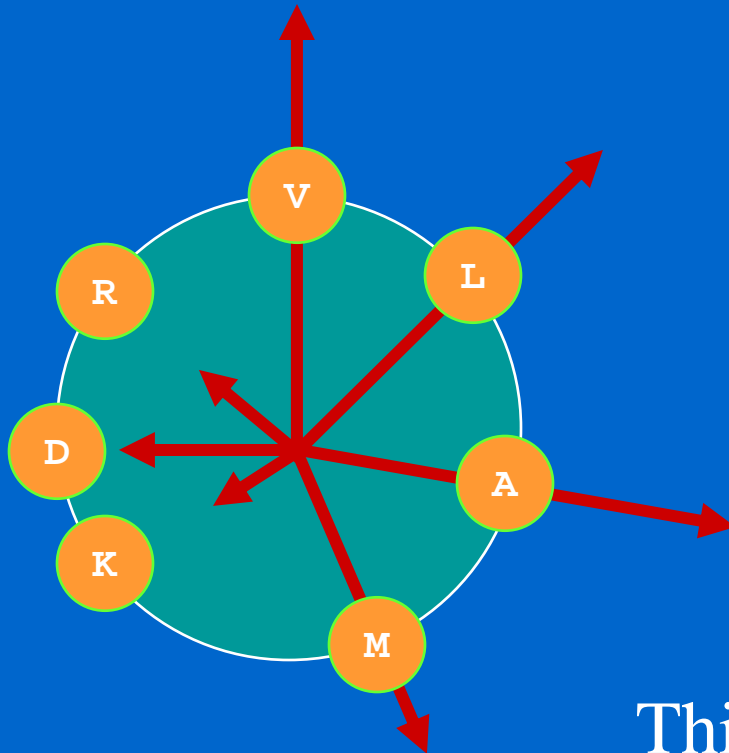


Hydrophobic Moment



Hydropathy vectors are distributed more or less equally in all directions, hence resultant vector has small or zero size

Hydrophobic Moment



Hydropathy vectors are distributed unequally over all directions, hence resultant vector has a greater than zero size.

This helix is amphipathic!

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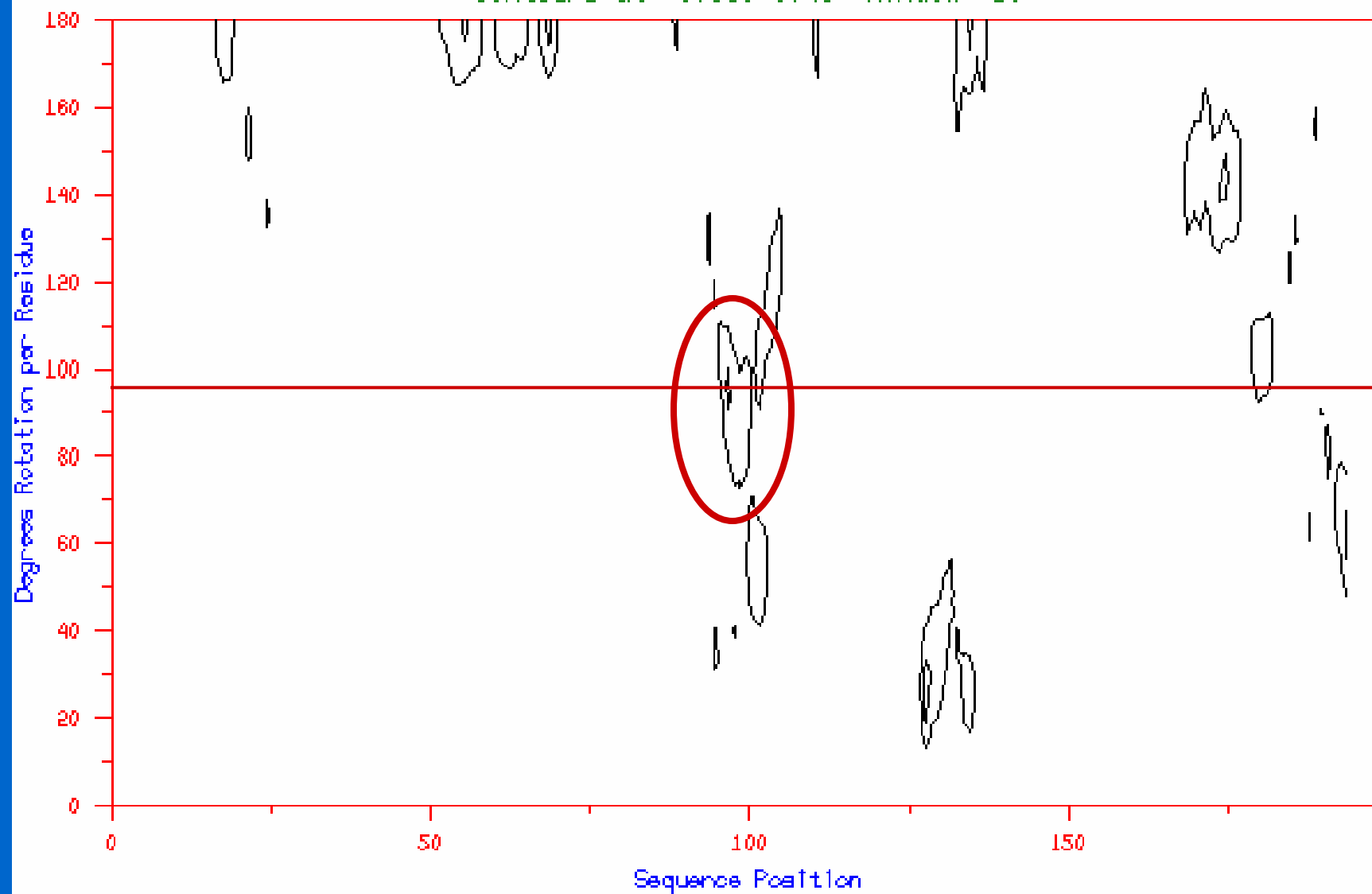
Hydrophobic Moment Plot

$$\mu_{H_i} = \sqrt{\left(\sum H_n \cdot \sin \delta_n\right)^2 + \left(\sum H_n \cdot \cos \delta_n\right)^2}$$

In text: the hydrophobic moment is the sum the vectors of the hydrophobicity values of all amino acids in a window, while imposing a certain secondary structure element to it.

Alpha-helix: delta = 100, beta-sheet: delta = ~ 160

MOMENT of: 1abm.pdb Ck: 2532. 1 to 198 July 2, 1999 18:23
Contours at: 0.35, 0.45 Window: 10



MOMENT of: labm.pdb Ck: 2532. 1 to 198 July 2, 1999 18:23

Contours at: 0.35, 0.45 Window: 10

180

Contour level 2

Contour level 1

0

0

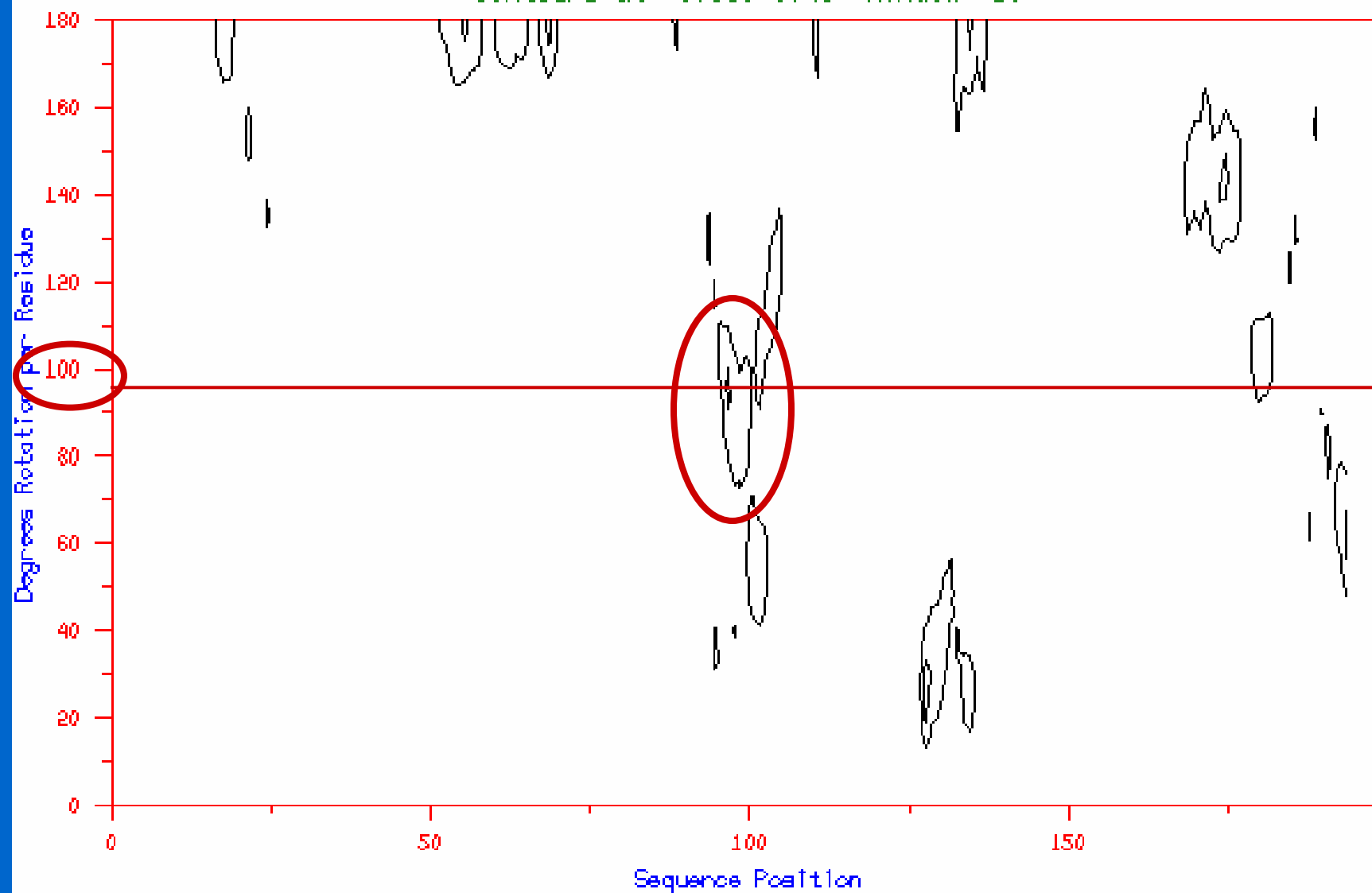
50

100

150

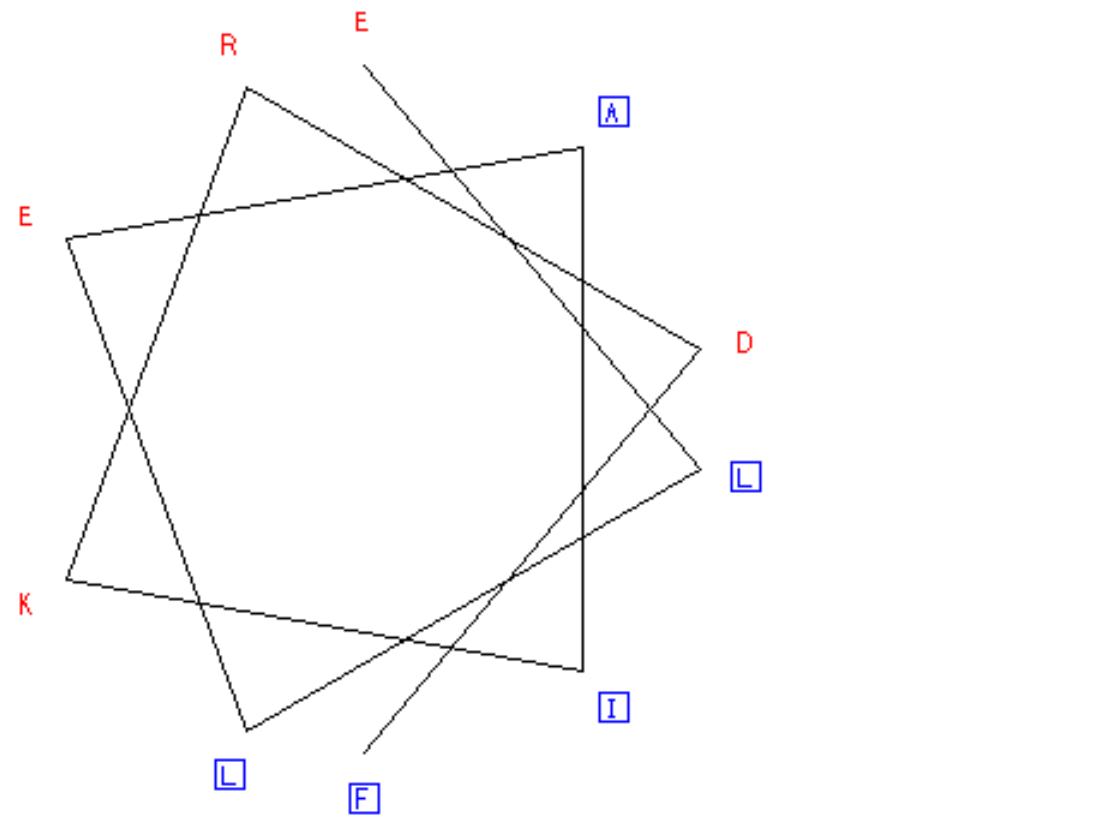
Sequence Position

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Contours at: 0.35, 0.45 Window: 10



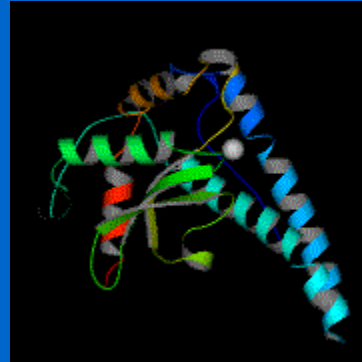
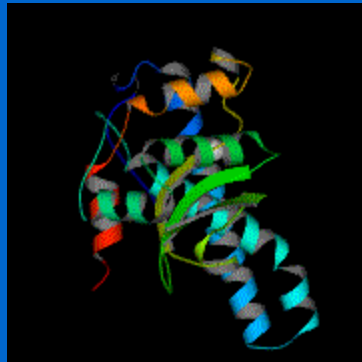
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Helical Wheel Plot

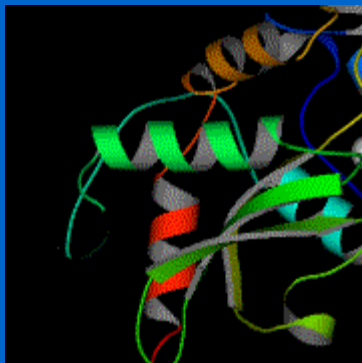


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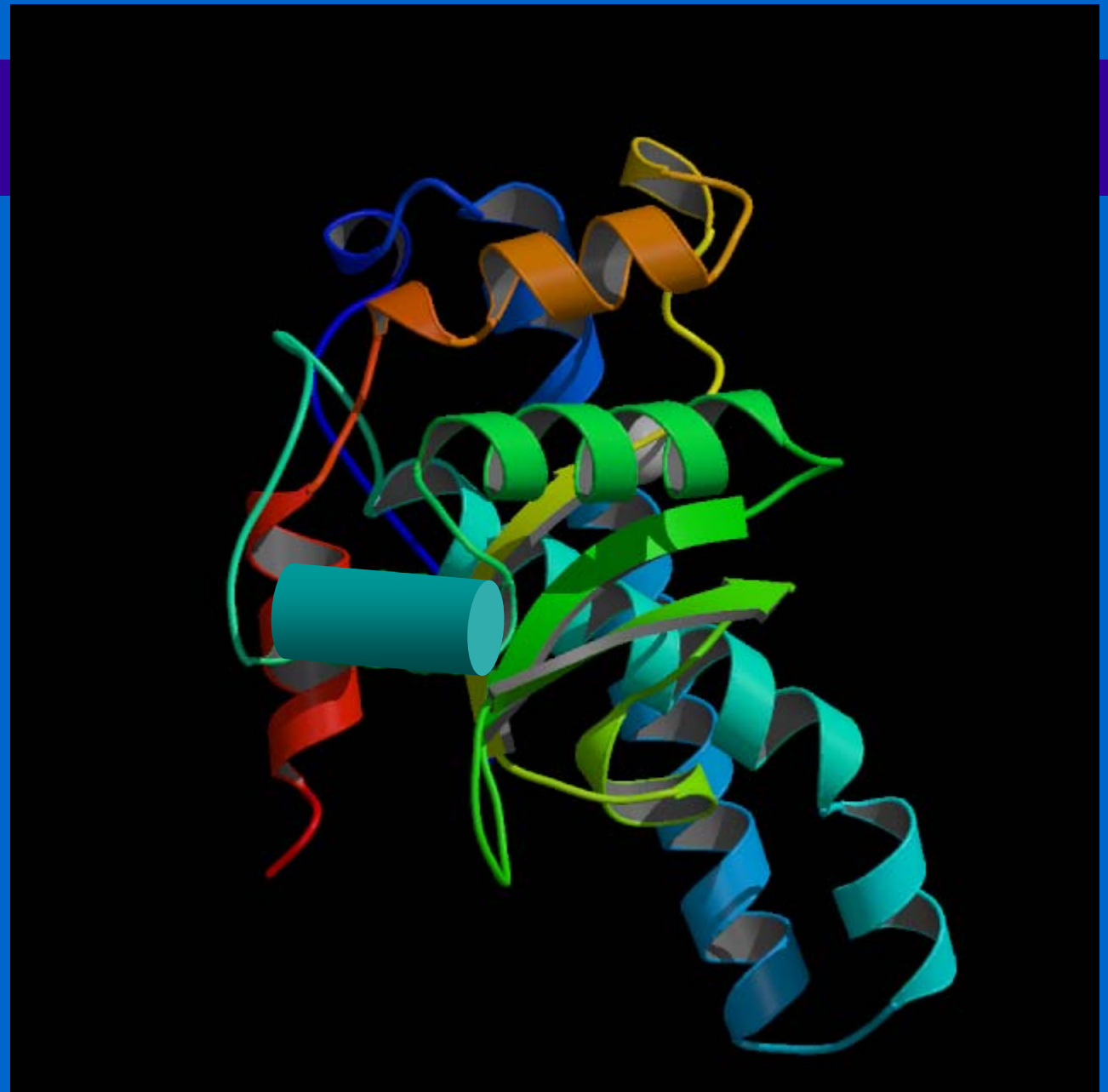
Amphipathic Helices



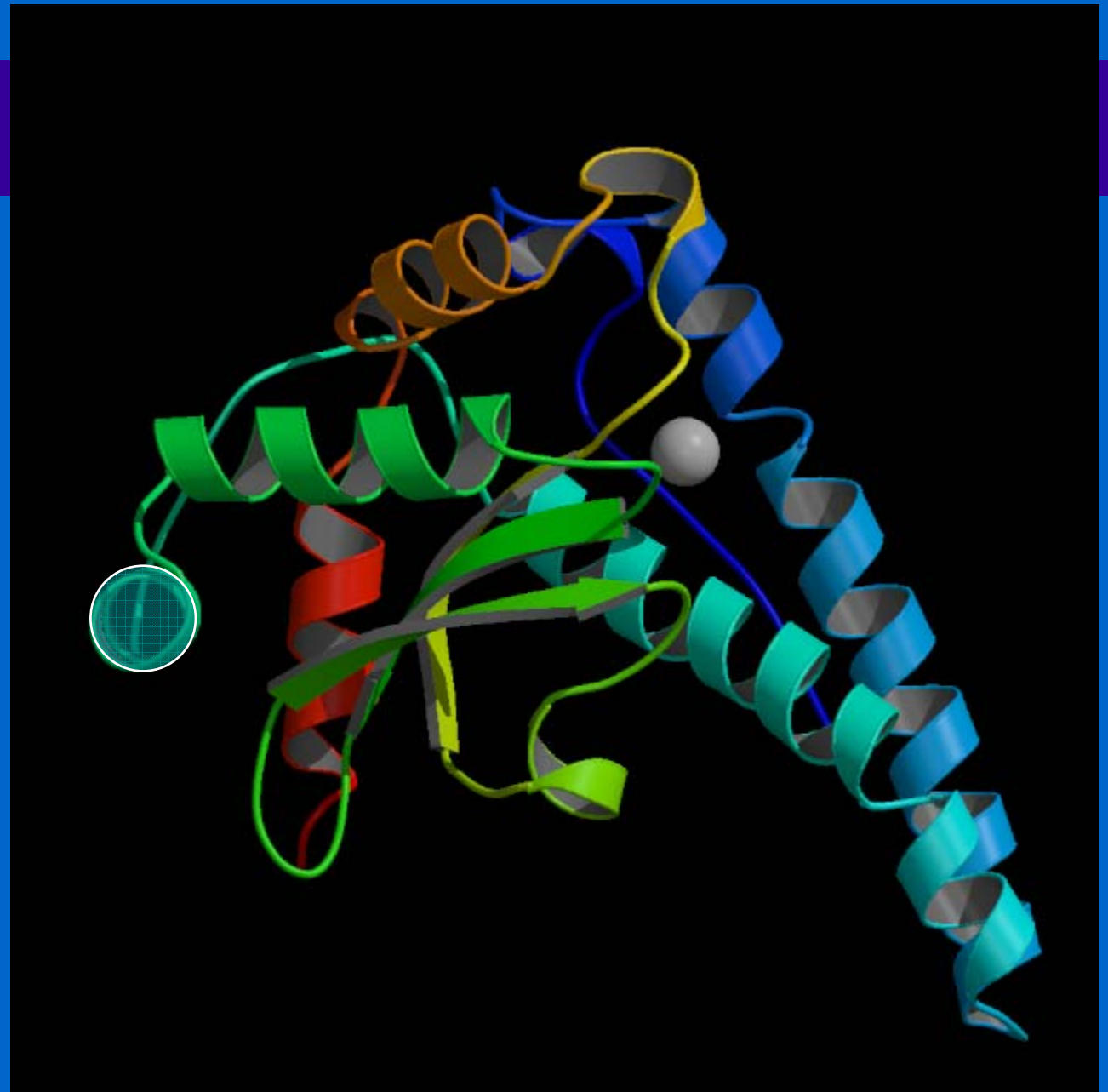
Manganese superoxide
dismutase (PDB:1ABM)



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