

Order/Disorder Transitions Biological Molecules

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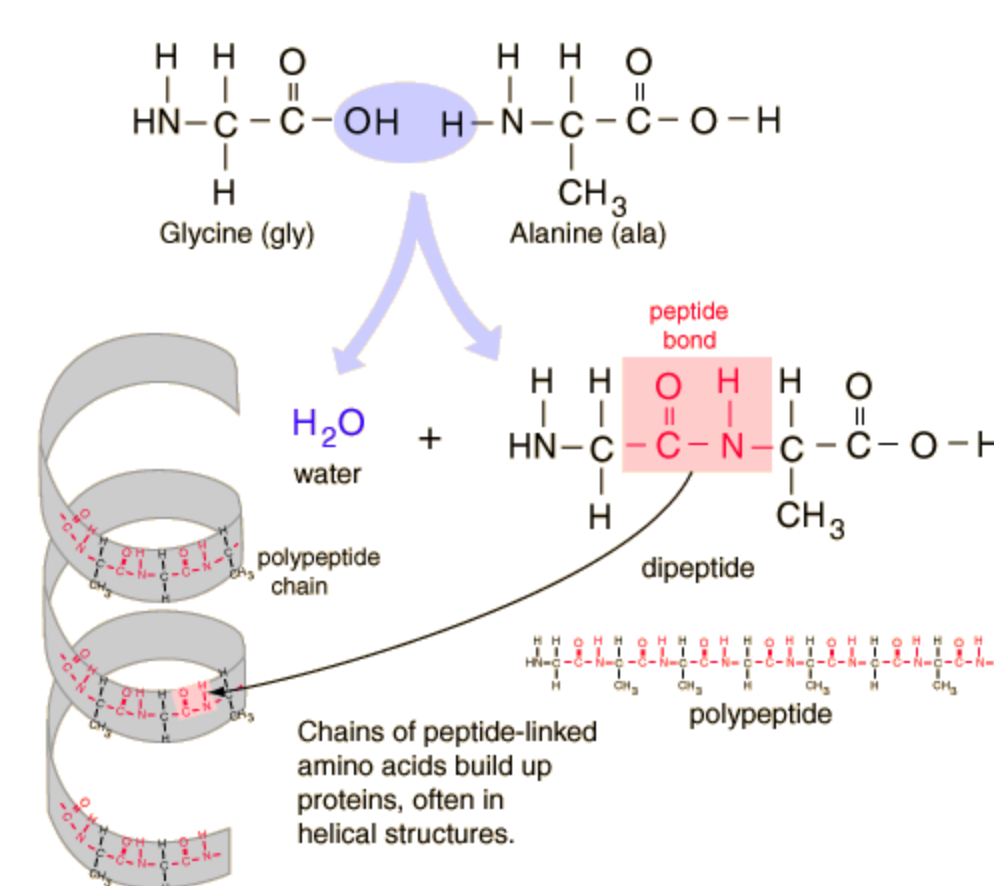
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Background

-What is amino acid

Peptides undergo an α -helix (hereafter referred to as helix) to coil transition with an increase in temperature. Experimentally, this yields a characteristic feature, a peak, in the specific heat. By using a model system to fit this experimental data, the strength of intra-peptide interactions and peptide-solvent interactions are measured. Understanding these fundamental interactions (e.g. knowing the free energies of the bonds) can lead to increased insight into peptide (and, to some degree, protein) stability and flexibility and is the subject of a large volume of prior work.



[1]

Model

Each amino acid can be in either the helix (h), coil (c) or helix nucleation (n) state
All helical segments begin and end with a nucleation state thus:

ccnhhhnccc is allowed whereas:
cchhhnccc is not allowed.

Partition function is the sum over all possible sequences (ccnhhhnccc...)

$$Z = \sum \exp(-G/k_B T)$$

$$G = H - TS$$

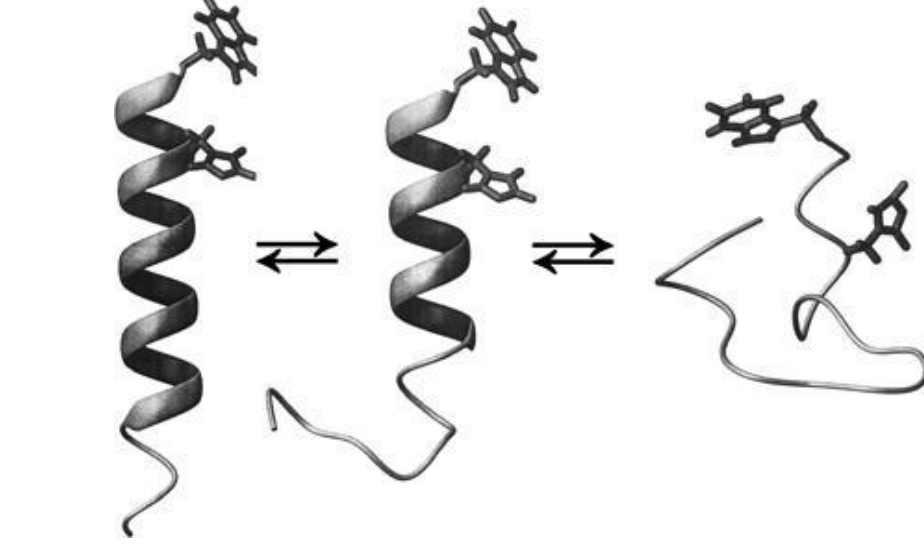
The helix content is the derivative of the free energy with respect to a small "ghost" parameter added to helix terms.

-Ordered (low entropy) helix state is favored at low temperature

-Disordered (high entropy) random coil state is favored at high temperature

[2]

Helix-Coil Transition



low T
mostly
helix
enthalpy
is more
important

high T
mostly
coil
entropy
is more
important

Motivation:

The alpha helix is one of the primary protein structures and understanding it can yield insight into protein folding, misfolding and kinetics.

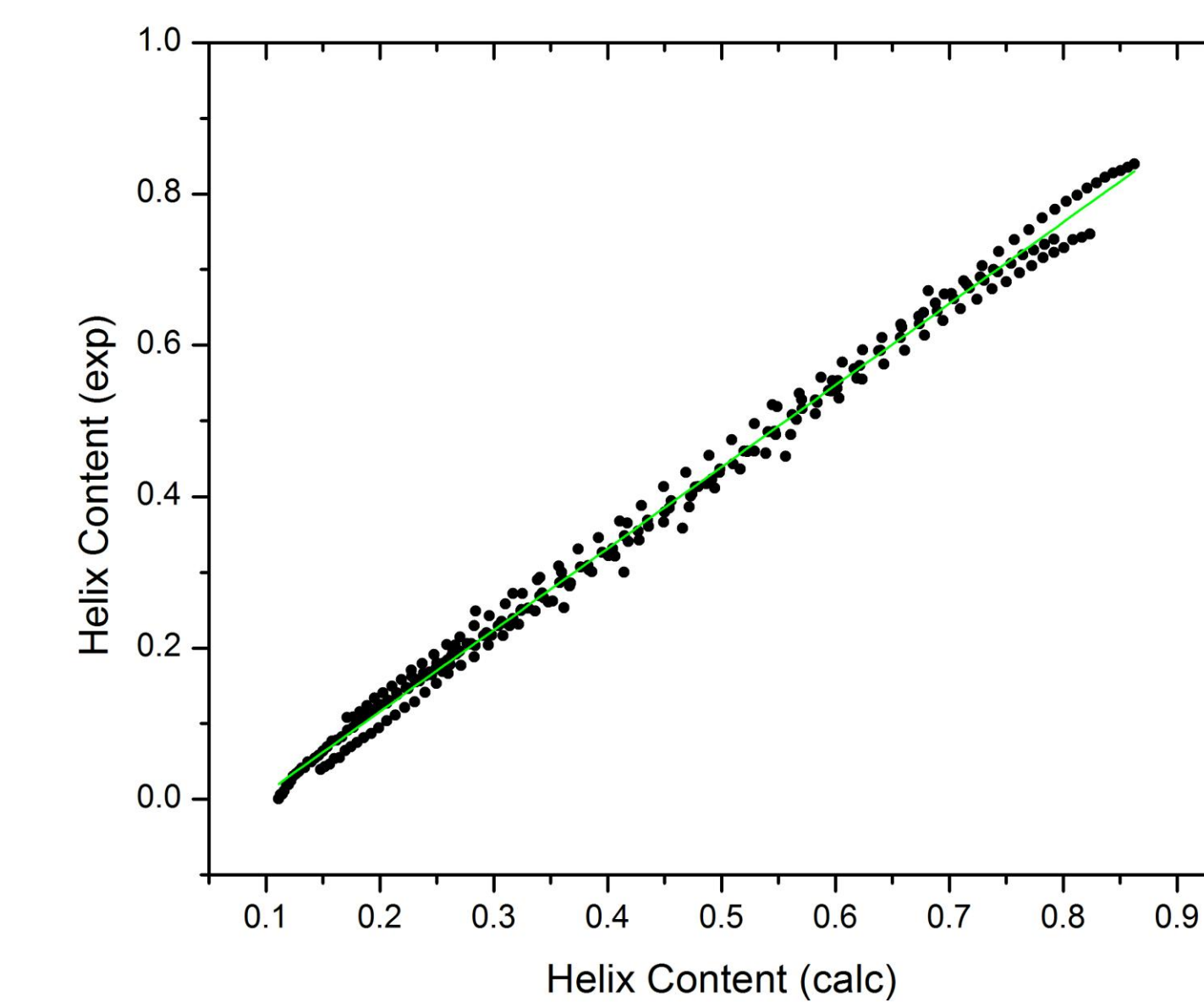
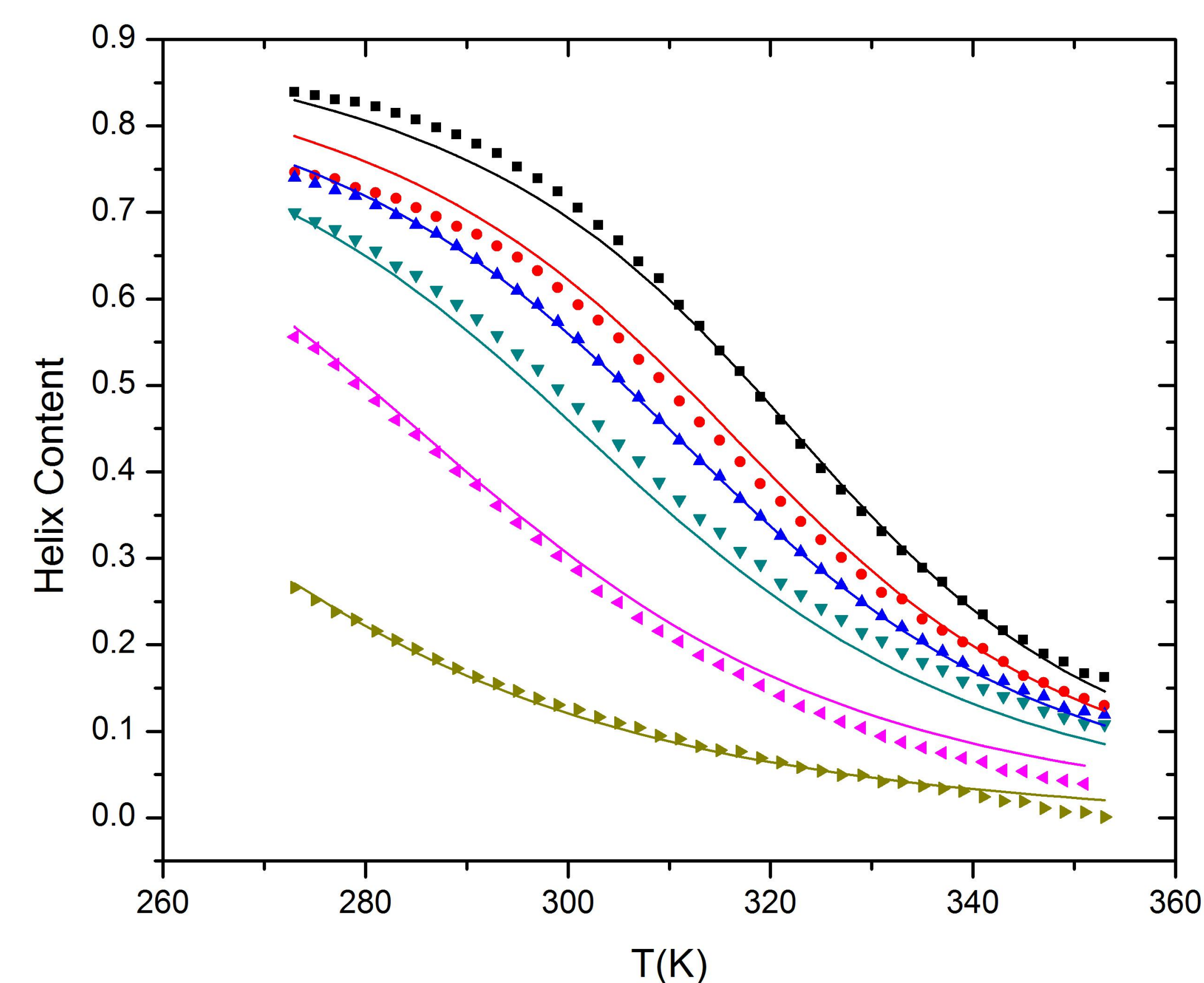
Sequences

Six Sequences of the form: Y(AKAAKA)ⁿF where n=2,3,4,5,6 and 8
Resulting in lengths of: 14, 20, 26, 32, 38 and 50, with helix content data via circular dichroism measurements from T=273K up to T=355K.

Additionally, the following 21 sequences were added but only at T=273K. [3,4,5]

YKAAAAKAAAAKAAAAK YKAAAAKAAAAKAAAAK
YKGAATAKAAAAKAAAAK YKAAAAKAAAAKAAAAK
YKAGAAKAAAAKAAAAK YGKAAAAKAAAAKAAAAK
YKAAGAKAAAAKAAAAK YGGKAAAAKAAAAKAAAAK
YKAAAGKAAAAKAAAAK YGGGKAAAAKAAAAKAAAAK
YKAAAAKGAATAKAAAAK YGGKAAGAKAAAAKAAAAK
YKAAAAKAGAAKAAAAK YGGKAAAAKAAAGAKAAAAK
YKAAAAKAAAGAKAAAAK YGGKAAAAKAAAAKAAAGK
YKAAAAKAAAAKGAATAK YGGKAAAAKAAAAKAAAGK
YKAAAAKAAAAKAGAAK YGGKAAAAKAAAAKAAAGK
YKAAAAKAAAAKAAAGK YGGKAAAAKAAAAKAAAGK
YKAAAAKAAAAKAAAGK

Results



Parameters:

	ALA	GLY	LYS	Cap
ΔH	-0.90	-0.65	-0.88	
ΔS	-1.2	-3.4	-1.5	
ΔG				
σ	3.6E-3	3.6E-3	4.4E-3	1.1E-1

Conclusion

-Helix content versus temperature for six sequences and helix content (at 273 K) for 23 other sequences is fit with a minimal model.

-R2 value of 0.995 (compared with 0.90 from prior work[6]).

- Future work: incorporate more amino acid types

References:

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- [3] A. Chakrabarty, J. A. Schellman, R.L. Baldwin, Large differences in the helix propensities of alanine and glycine, *Nature* 351, (1991) 586-588
- [4] A. Chakrabarty, R. Kortemme, S. Padmanabhan, R.L. Baldwin, Aromatic Side-Chain Contribution to Far-Ultraviolet Circular Dichroism of Helical Peptides and Its Effect on Measurement of Helix Propensities, *Biochemistry*, 32, (1993), 5560-5565
- [5] J. Scholtz, H. Qian, E. York, *et. al.* Parameters of the Helix-Coil Theory for Alanine Based Peptides of Varying Chain Lengths, *Biopolymers* 31 (1991), 1463-1470.
- [6] V. Munoz, L. Serrano, Elucidating the folding problem of helical peptides using empirical parameters. *Nature*, 1 (1994) 399-409