Aromatic Interactions and Metal Binding in β-hairpin Peptides

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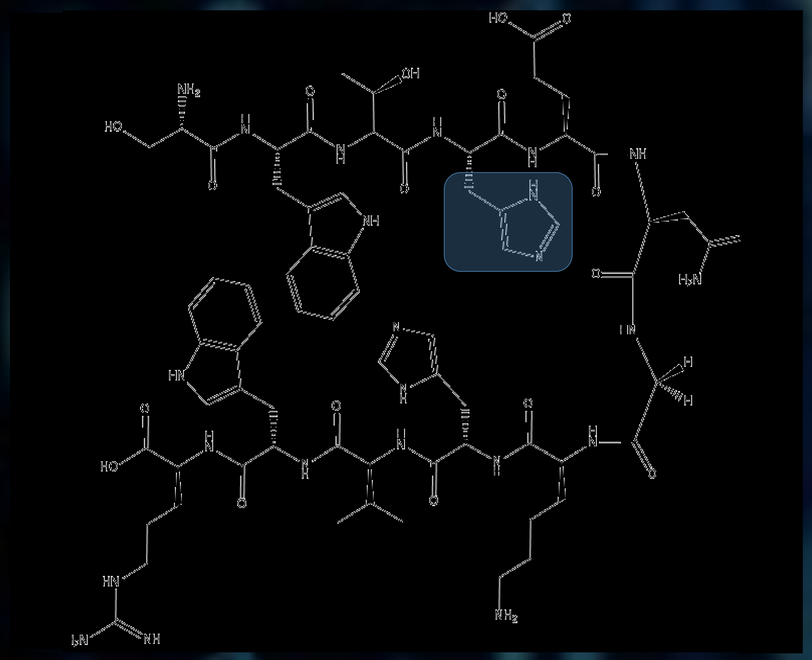
Abstract

Biomolecular folding is a type of molecular self-assembly in which self-interaction drives a molecule to its native conformation. We synthesized six 12-amino acid β-hairpin peptides stabilized by π-π interactions between the indole groups of two tryptophan residues. Histidine binding pockets of varying stability are incorporated closer to the β-turn. Folding stability and binding affinity were tracked via NMR, MALDI and UV-Vis spectroscopy and the data modeled using factor analysis methods. Comparative thermodynamic details of the binding events are presented, including binding constants and spectroscopic signatures for intermediate peptide:metal complexes. Future work will include further analysis of folding by NMR and CD spectroscopy.

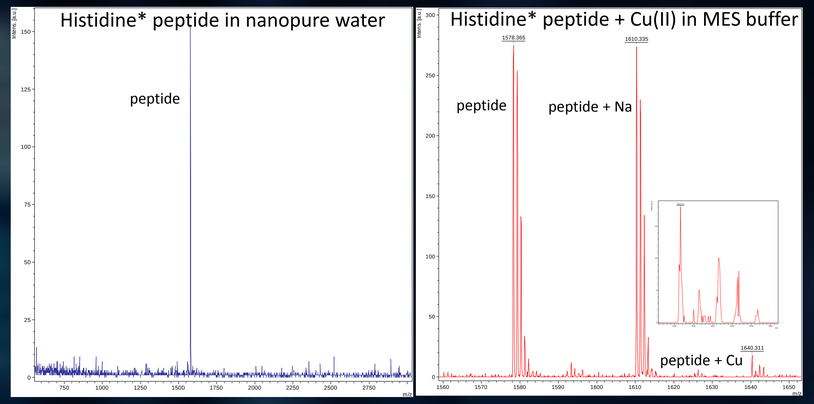
Peptide Sequence & Structure

Ser	Trp	Thr	His	Glu	Asn	Gly	Lys	His	Val	Trp	Arg
Ser	Trp	Thr	**Asn**	Glu	Asn	Gly	Lys	His	Val	Trp	Arg
Ser	Trp	Thr	**Cys**	Glu	Asn	Gly	Lys	His	Val	Trp	Arg
Ser	Trp	Thr	**Tyr**	Glu	Asn	Gly	Lys	His	Val	Trp	Arg
Ser	Trp	Thr	**Val**	Glu	Asn	Gly	Lys	His	Val	Trp	Arg
Ser	Trp	Thr	**Ile**	Glu	Asn	Gly	Lys	His	Val	Trp	Arg

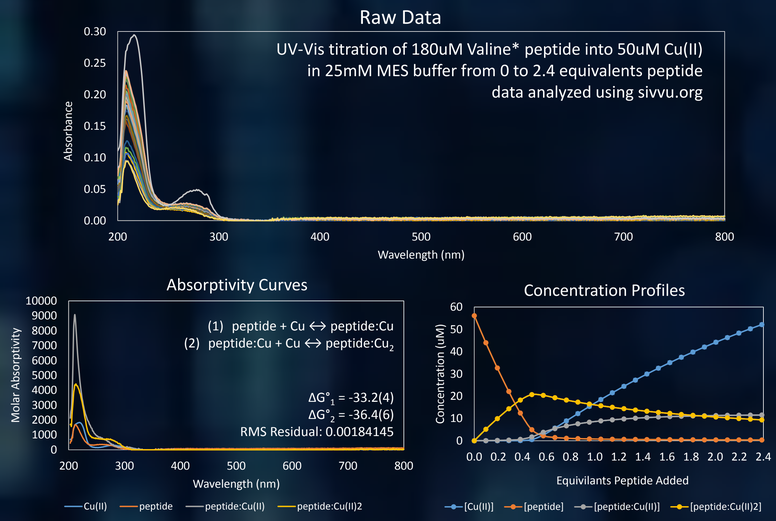


Metal Binding

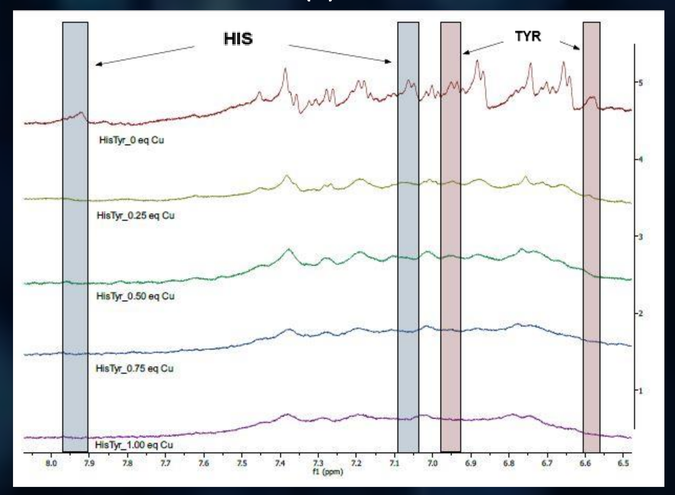
MALDI MASS SPECTROSCOPY



EQUILIBRIUM RESTRICTED FACTOR ANALYSIS OF UV-VIS TITRATION USING SIVVU.ORG

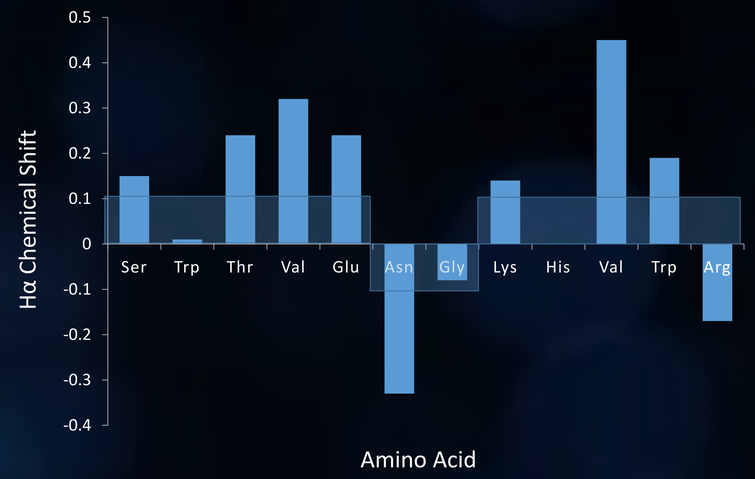


NMR TITRATION OF CU(II) INTO TYROSINE* PEPTIDE



Folding Stability

TOCSY NMR OF VALINE* PEPTIDE



Conclusions

- All six peptides adopt β-hairpin structure, stabilized by aromatic-aromatic interactions
- Copper and Nickel complex to peptide as shown by MALDI mass spectroscopy
- NMR titration of copper suggests that binding occurs between residues 4 & 9 in histidine “binding pocket”
- Factor analysis of UV-Vis data shows 1:1 metal to peptide complexation to be most significant
- The size, polarity, and charge of the amino acid across from histidine (residue 4) affect binding affinity.

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NOTE: Amino acids named with a star (*) refer to the peptide with that amino acid as residue 4 of the sequence