



Let's do the Twist - Chiral Information Transfer in Supramolecular Peptide Complexes

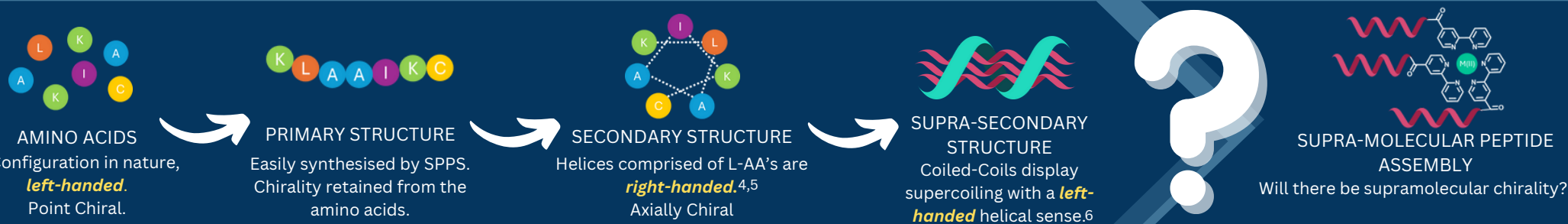
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<https://doi.org/10.17952/37EPS.2024.P1303>

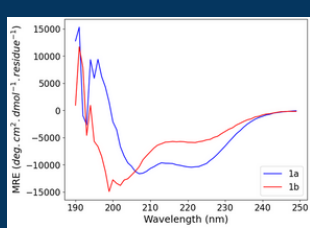
INTRODUCTION

Chirality is inherent in nature from molecular to macroscales.^{1,2} How this information is transferred is still poorly understood.³ A model system using the well documented inbuilt chirality of peptides is being used to investigate this phenomena.



PEPTIDE SEQUENCES

All peptides are designed **3-heptad homotrimeric coiled-coils** and have been synthesised by microwave assisted **SPPS** and further functionalised on resin with a bipyridine (bpy, X) group at the N-terminus. All sequences have been tabulated below, except **1b** all other **b** control sequences have been omitted.



bpy at the N-term stabilises the secondary structure

1a	X-GQ EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	5a	X- α Q EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	9a	X- IAAIKKE IAAIKKEIAAIKKEYG-NH2 <i>g-abcdefg</i>
1b	Ac-GQ EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	6a	X-PQ EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	10a	X- AAIKKE IAAIKKEIAAIKKEIYG-NH2 <i>a-bcdefga</i>
2a	X-AQ EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	7a	X-Q EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>e-fgabcdef</i>	11a	X- AIKKE IAAIKKEIAAIKKEIAYG-NH2 <i>b-cdefgab</i>
3a	X-GG EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>d-efgabcdef</i>	8a	X- EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>f-gabcdef</i>	12a	X- IKKE IAAIKKEIAAIKKEIAYG-NH2 <i>c-defgabc</i>
4a	X-PEG- EIAAIKKE IAAIKKEIAAIKYG-NH2 <i>gabcdef</i>			13a	X- QKE IAAIKKEIAAIKKEIAYG-NH2 <i>d-efgabcd</i>

EFFECT OF METAL AND COUNTERION ON THE FORMATION OF CHIRAL PEPTIDE-BPY COMPLEXES

To investigate the relationship between the chirality of the secondary structure and the supramolecular bpy-peptide complex, peptide **1a** was titrated against a series of 1st row TMs.

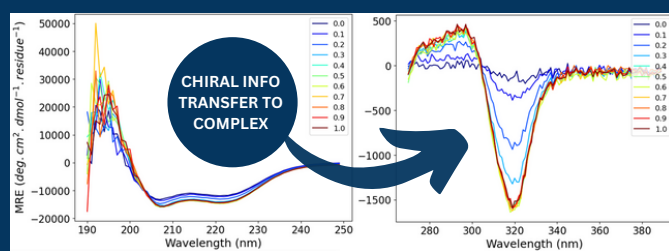
EFFECT OF ACHIRAL LINKER ON THE FORMATION OF CHIRAL PEPTIDE-BPY COMPLEXES

To investigate the limits of the chiral effect of the peptide on the bpy-peptide complex peptides **1a-6a** with differing lengths of achiral spacer were titrated against **Zn(II)**.

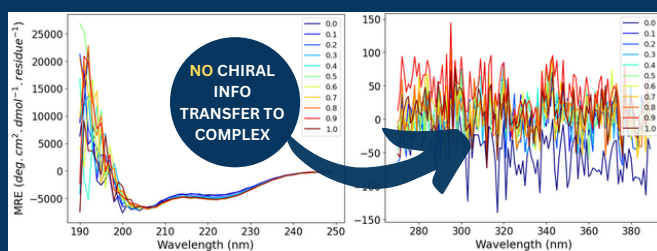
EFFECT OF N-TERMINAL REGISTER POSITION ON THE FORMATION OF CHIRAL PEPTIDE-BPY COMPLEXES

To investigate the spacial requirements for the formation of the chiral bpy-peptide complex peptides **7a-13a** with systematically varied N-terminal register position were titrated against **Zn(II)**.

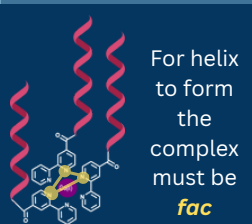
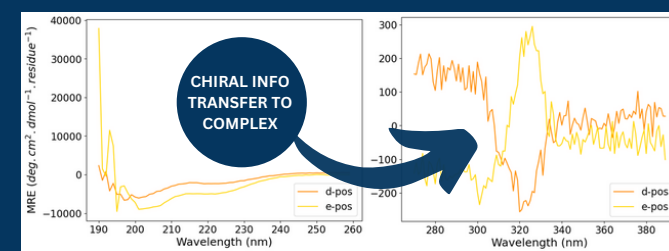
1a CD Titration with Co(II)



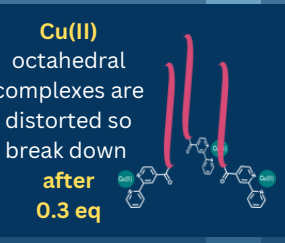
4a CD Titration with Zn(II)



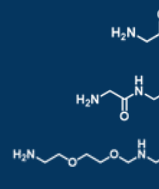
7a and 13a CD Titrations with Zn(II)



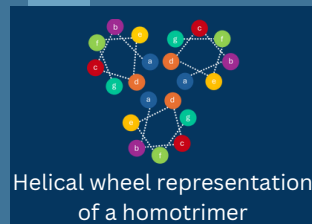
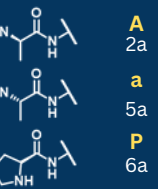
Signal at 222 nm intact except Co(II) and Cu(II) Co(II) **stabilised** Cu(II) **destabilised**



ACHIRAL

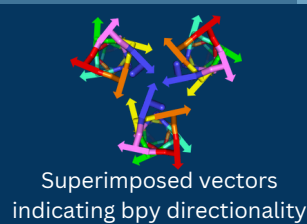


CHIRAL



Helical wheel representation of a homotrimer

a, d, e **bpy** pointed inward
b, c, f, g **bpy** pointed outward



Superimposed vectors indicating bpy directionality

Octahedral - 320 nm signal increases rapidly until 0.3 eq (Zn(II), Co(II) Cu(II) and Ni(II))

Favours Right-handed - Signal has a negative Cotton-Effect^{7,8}

Signal at 320 nm - G > A > GG > a > P > PEG

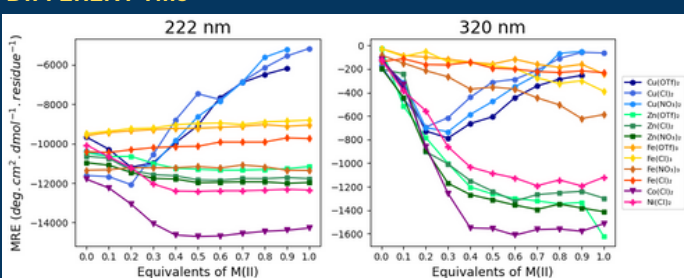
Signal at 222 nm - A > G > GG > a > P > PEG

Only d and e positions formed bpy-peptide complex with chiral preference.

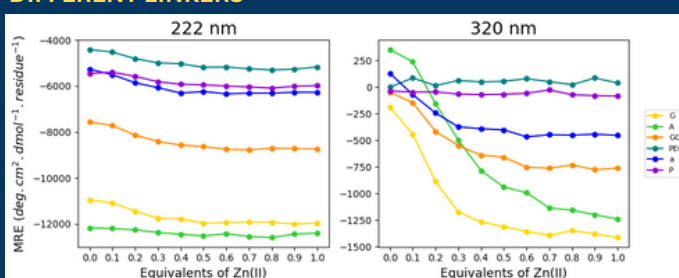
d position - **right-handed** e position - **left-handed**

Plots of the CD signals at 222 nm and 320 nm for all peptides allows the relationship between the bpy-complex and the helicity of the peptide to be observed.

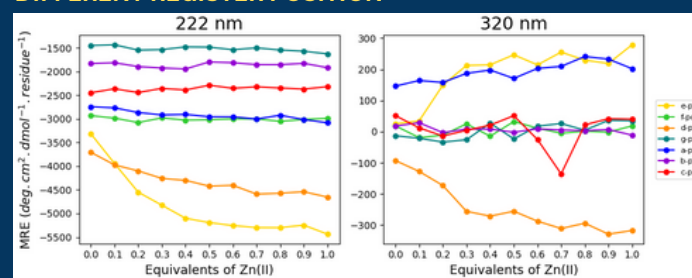
DIFFERENT TMs



DIFFERENT LINKERS



DIFFERENT REGISTER POSITION



CONCLUSION

Zn(II), Ni(II) or Co(II) appear to have the strongest preferences for forming octahedral complexes.

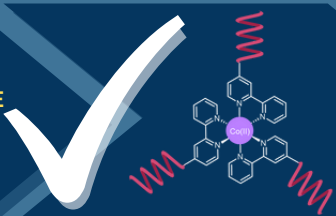
CONCLUSION

Distance from chiral centre should be no more than 7 atoms.

CONCLUSION

d or e position preferred for attachment BUT will give preference for opposite handedness.

CHIRAL PREFERENCE CAN BE INDUCED



FUTURE WORK

NMR studies to determine ratios of isomers
Titration with a 2nd row TM

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ACKNOWLEDGEMENTS

I would like to thank the Thomson Group, our collaborators in the Forgan Group, the Chemical Biology Laboratory, Captain, Skipper and Matthew.

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