Electronic Supplementary Material (ESI) for Dalton Transactions.

Metal coordination to solute binding proteins – exciting chemistry with potential biological meaning

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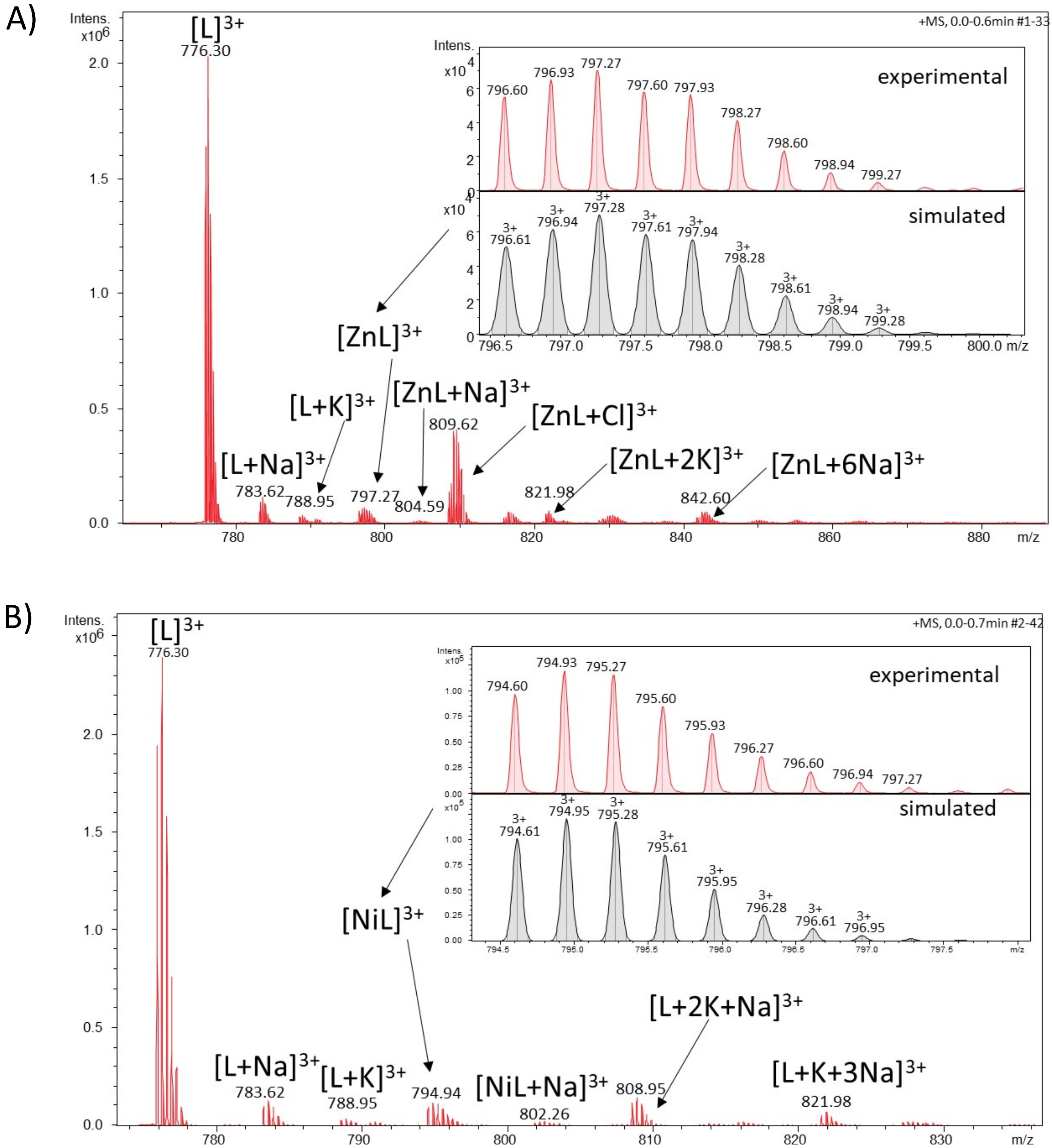
Mass spectrometry confirmed peptide purity and showed that they form mononuclear complexes with Zn(II) and Ni(II) (Fig. S1, Fig. S2 and Fig.S3, ESI†).
The signals: m/z = 776.30, z = 3+; m/z = 1131.92, z = 4+ and m/z = 914.44, z = 2+ correspond to the free ligand for the Ac-HEHEHEHEHEHEHEHEH-NH_2 - ZnuA-(120-136), Ac-GGEHEHEHEHEHEHEHEHEHEHDGHGHAEEQAHHDHDHSG-NH_2 - ZnuA-(117-133), and Ac-GGGHYHYIDGKAVFHAG-NH_2 - AztC-(117-133), respectively. The assignment peaks were compared to simulated isotopic patterns, which fit perfectly to experimental data (Fig. S1-3, ESI†). In all measured mass spectra, the signals corresponding to the sodium and potassium adducts of free ligands were observed.
In the mass spectra of Zn(II)-ZnuA-(120-136) (Fig. S1A, ESI†) beside the signals from the ligand and its sodium and potassium adducts, we observe a signals which comes from the zinc complex (m/z = 797.27, z = 3+) and its sodium (m/z = 804.59, z = 3+), chloride (m/z = 809.62, z = 3+), sodium and one chloride (m/z = 816.61, z = 3+), potassium (m/z =821.98 , z = 3+) and potassium and sodium (m/z = 842.60, z = 3+) adducts. In the case of Ni(II)-ZnuA-(120-136) (Fig. S1B, ESI†) the signal (m/z = 794.93, z = 3+) correspond to the equimolar Ni(II) complex. In these spectra also the sodium (m/z = 802.26, z = 3+); (m/z = 808.95, z = 3+) adducts of the nickel peptide are present and the signals correspond to adducts with one sodium atom and two potassium atoms.
In the Zn(II)-ZnuA-(117-133) spectra, aside from the signals which comes from the free ligand and its adducts, a equimolar Zn(II) complex (m/z = 1147.90, z = 4+),its different adducts can be observed (Fig. S2A, ESI†). In the spectra of the same ligand with Ni(II) (Fig. S2B, ESI†), the signals can be assigned to the nickel complex (m/z = 1146.16, z = 4+) and a nickel complex with a sodium adduct (m/z = 1151.91, z = 4+), potassium adduct (m/z = 1156.41, z = 4+) and sodium chloride adduct (m/z = 1166.18, z = 4+).
In the case of Zn(II)-AztC-(117-133) mass spectra (Fig. S3A, ESI†) the prevailing signals correspond to the Zn(II) complex (m/z = 945.90, z = 2+), its sodium adducts (m/z = 955.89, z = 2+) and its potassium adducts (m/z = 964.88, z = 2+). In the Ni(II)-AztC-(117-133) spectra (Fig. S3B, ESI†) the signals which come from Ni(II) complex (m/z = 942.40, z = 2+), its sodium adducts (m/z = 953.39, z = 2+) and potassium adducts (m/z = 961.38, z = 2+) are observed.

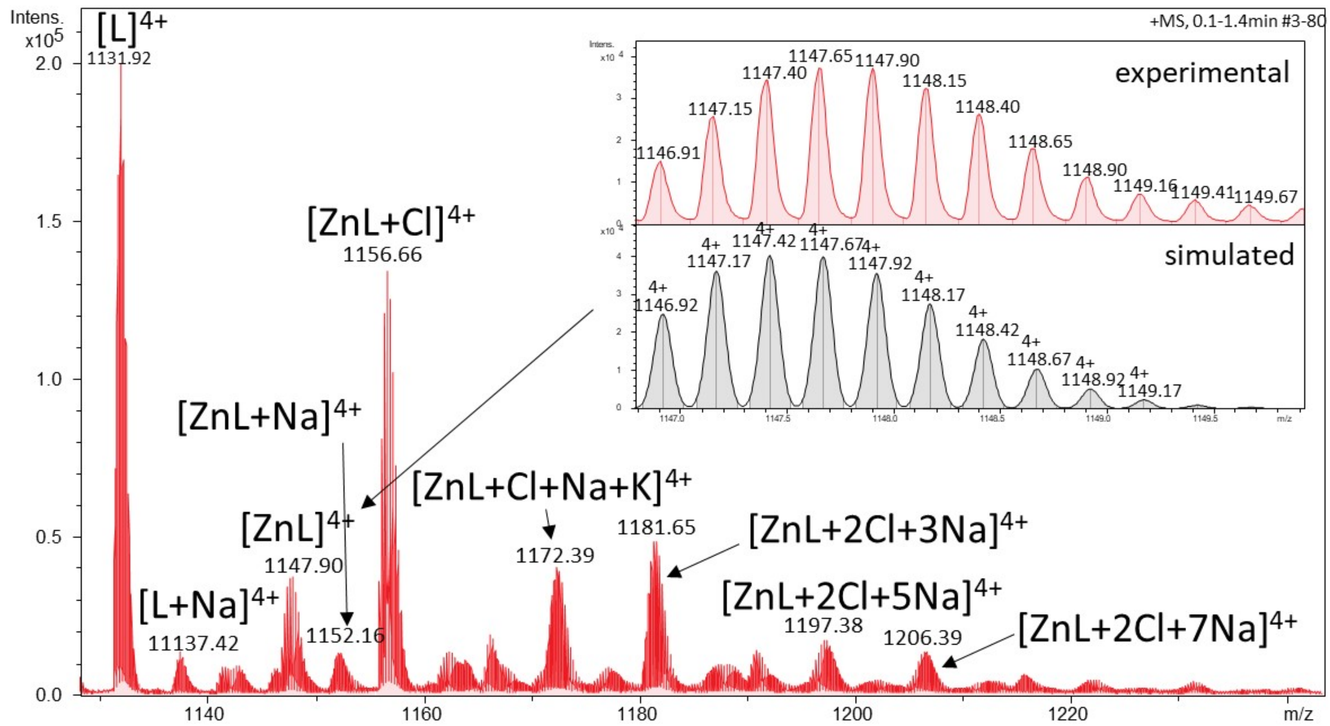
Figure 1. ESI-MS spectrum of A) Zn(II)-ZnuA-(120-136) - M(II)/L molar ratio= 0.5 : 1; B) Ni(II)-ZnuA-(120-136) -



M(II)/L molar ratio= 0.9 : 1.

Figure 2. ESI-MS spectrum of A) Zn(II)-ZnuA-(117-133) - M(II)/L molar ratio= 0.5 :1; B) Ni(II)-ZnuA-(117-133)- M(II)/L molar ratio= 0.9 : 1.

A)



B)

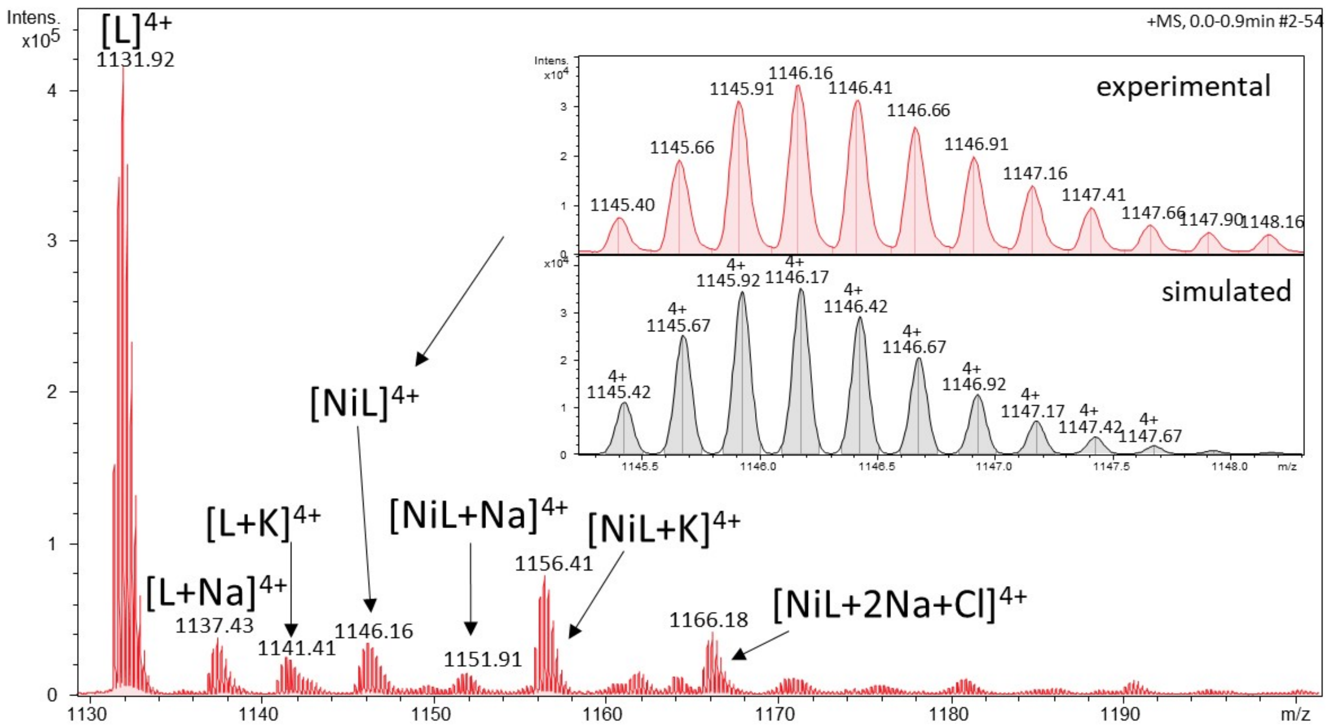


Figure 3. ESI-MS spectrum of A) Zn(II)-AztC-(117-133); B) Ni(II)-AztC-(117-133); M(II)/L molar ratio= 0.9 : 1.

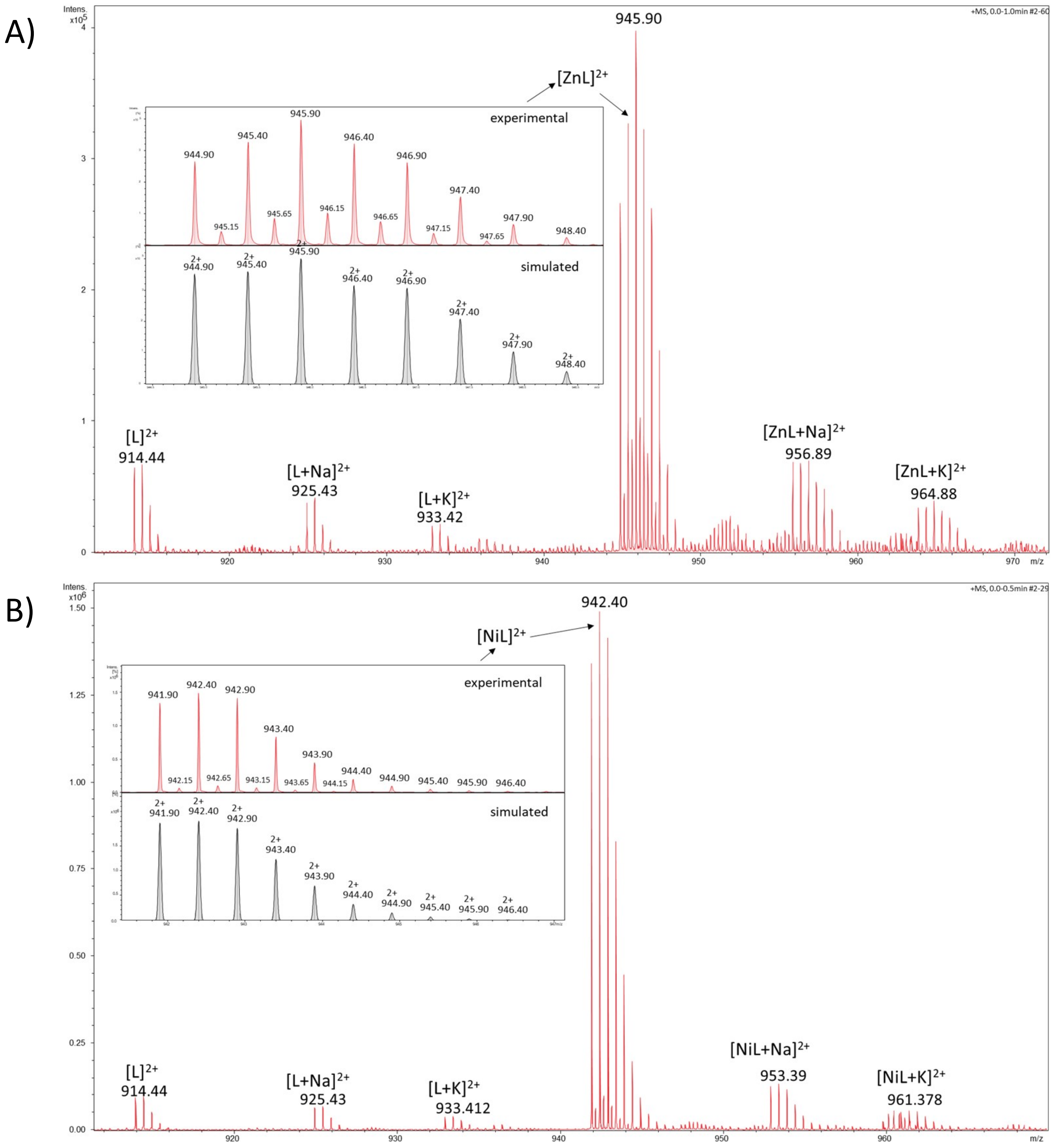


Figure 4. Species distribution diagrams for the formation of A) Zn(II) complexes with the ZnuA-(120-136) fragment; B) Zn(II) complexes with the ZnuA-(117-133) fragment, T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.5 : 1; C) Zn(II) complexes with the AztC-(117-133) fragment; T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.9 : 1.

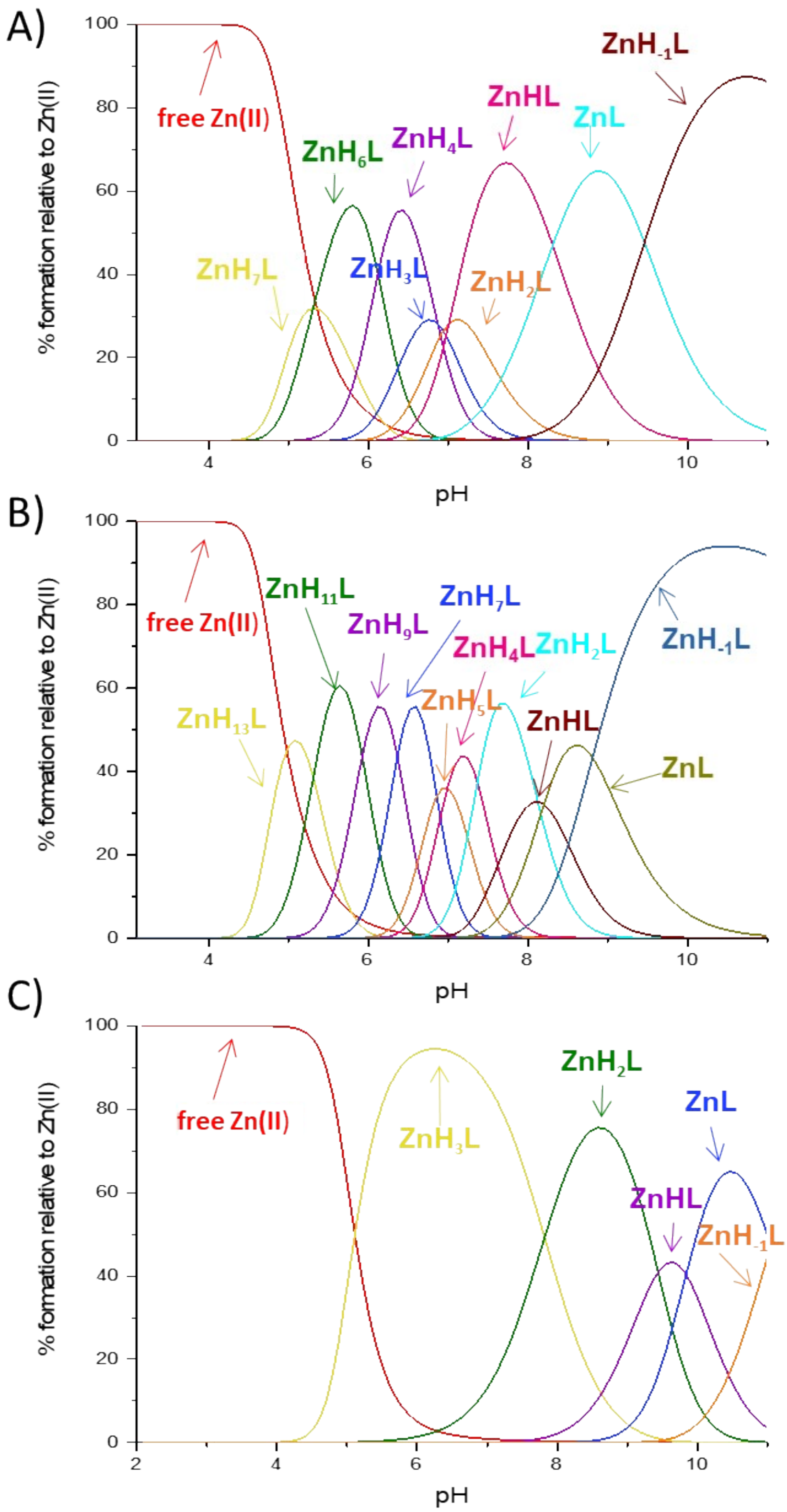
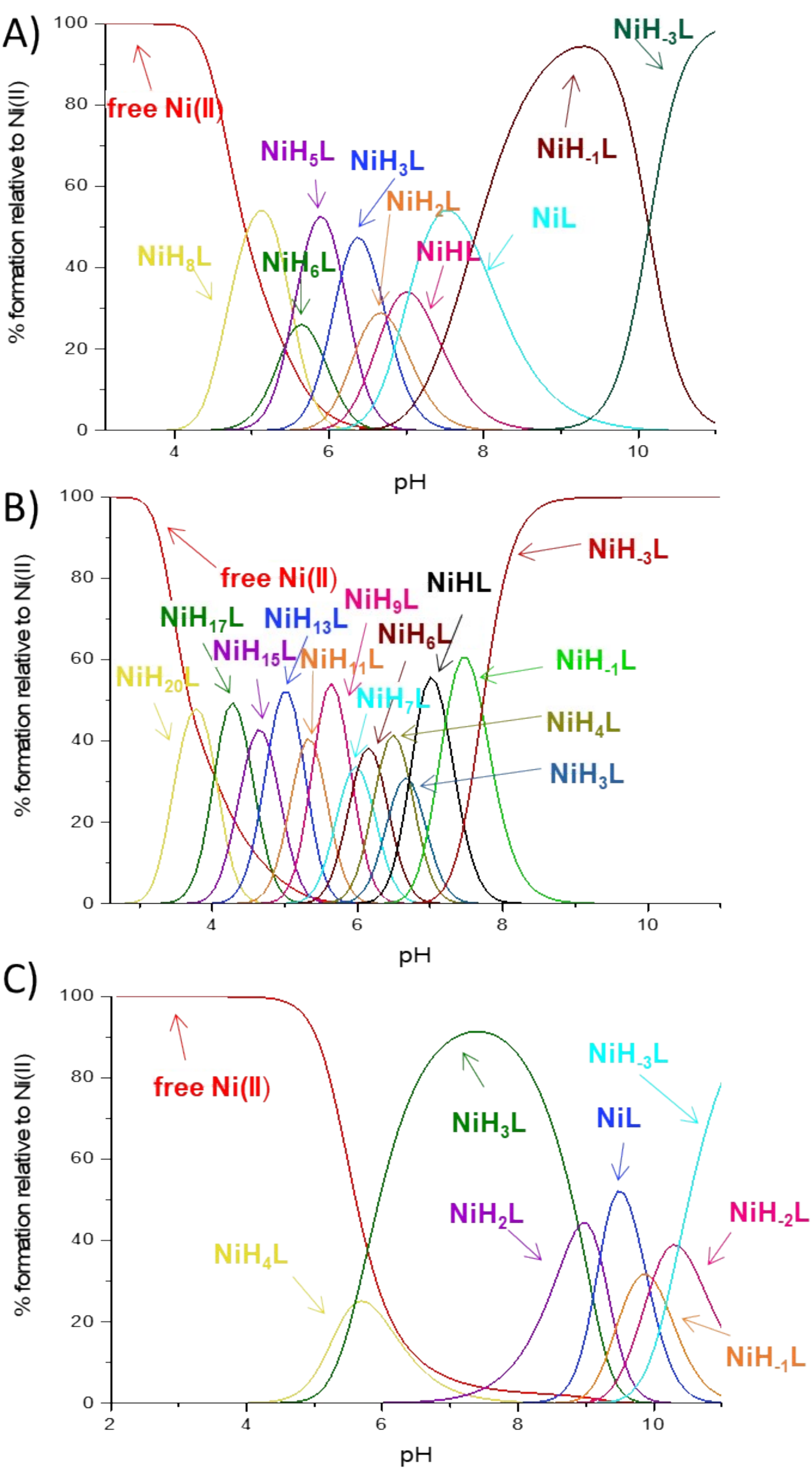


Figure 5. Distribution diagrams for the formation of A) Ni(II) complexes with the ZnuA-(120-136) fragment; B) Ni(II) complexes with the ZnuA-(117-133) fragment, T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.5 : 1; C) Ni(II) complexes with the AztC-(117-133)fragment; T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.9 : 1.



A)
free Ni(II)
NiH_8L
NiH_6L
NiH_5L
NiH_3L
NiH_2L
$NiHL$
NiL
$NiH_{-1}L$
$NiH_{-3}L$
% formation relative to Ni(II)
pH
B)
free Ni(II)
$NiH_{20}L$
$NiH_{17}L$
$NiH_{15}L$
$NiH_{13}L$
$NiH_{11}L$
NiH_9L
NiH_7L
NiH_6L
$NiHL$
NiH_4L
NiH_3L
$NiH_{-1}L$
$NiH_{-3}L$
% formation relative to Ni(II)
pH
C)
free Ni(II)
NiH_4L
NiH_3L
NiH_2L
NiL
$NiH_{-1}L$
$NiH_{-2}L$
$NiH_{-3}L$
% formation relative to Ni(II)
pH

Figure 6. UV-Vis spectra of Ni(II) complexes with A) the ZnuA-(120-136) fragment; B) the ZnuA-(117-133) fragment, T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.5 : 1; C) the AztC-(117-133) fragment in the range 300-700 nm and pH range 3.0-11.0; T=298 K; optical path=1 cm; [L]=0.0005 M; M(II)/L=0.9 : 1.

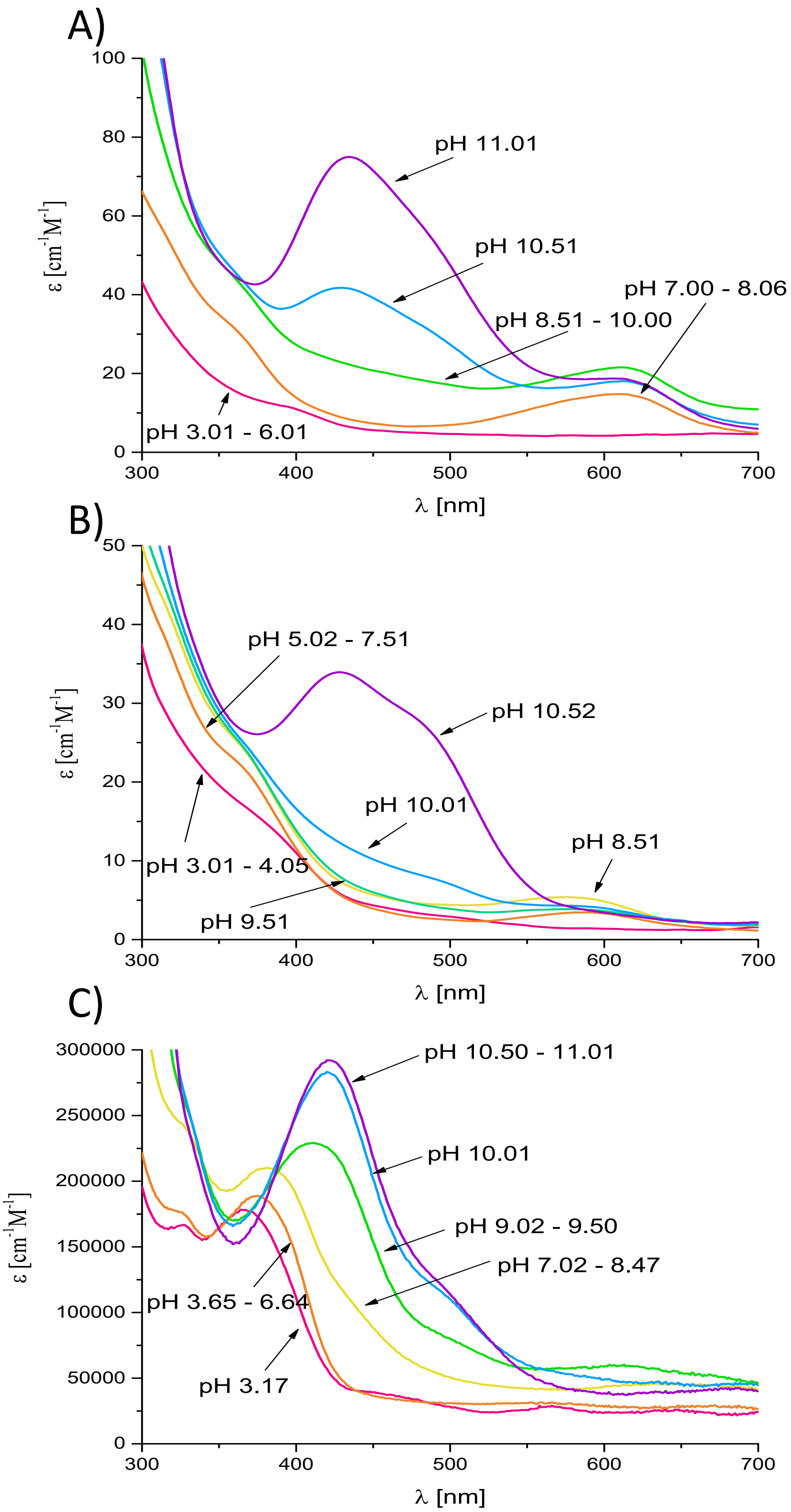


Figure 7. CD spectra of Ni(II) complexes with A) the ZnuA-(120-136) fragment; B) the ZnuA-(117-133) fragment, T=298 K; I=0.1 M; [L]=0.0005 M; M(II)/L molar ratio=0.5 : 1; C) the AztC-(117-133) fragment in the range 250-650 nm and pH range 3.5-11.0; T=298 K; optical path=1 cm; [L]=0.0005 M; M(II)/L=0.9 : 1.

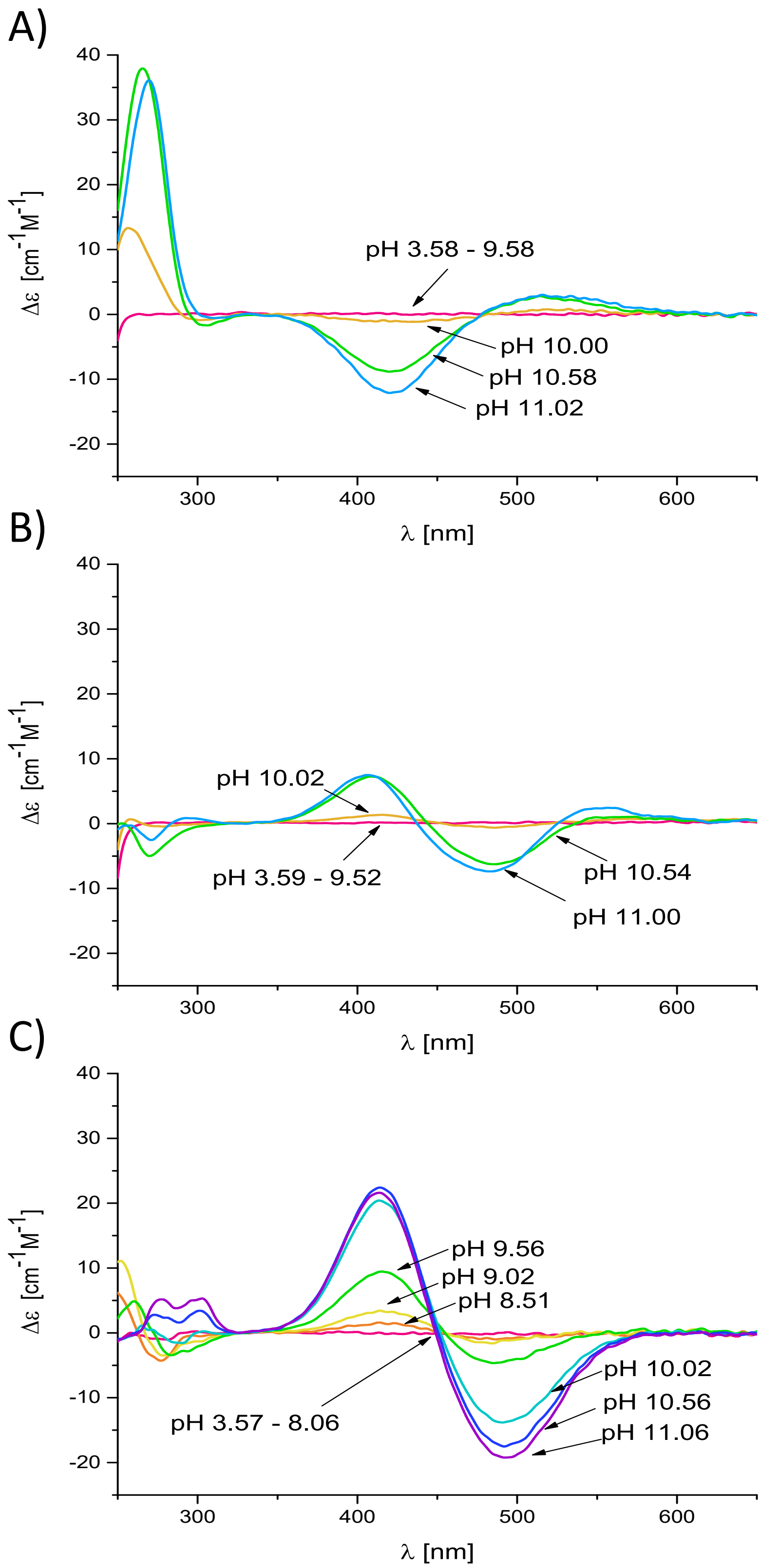


Figure 8. Proposed binding mode for A) Zn(II)-AztC-(117-133) and B) Ni(II)-AztC-(117-133) at physiological pH, pH 7.4, generated by PyMOL [1].

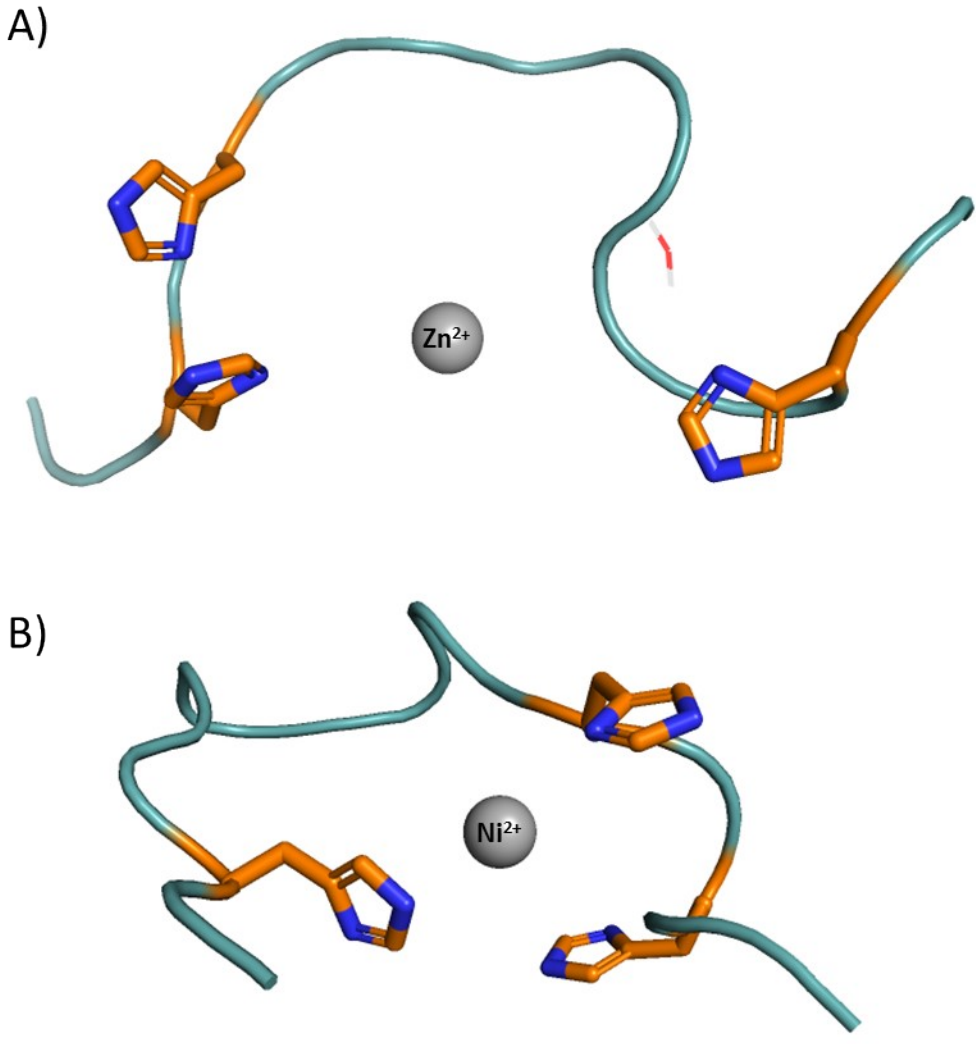
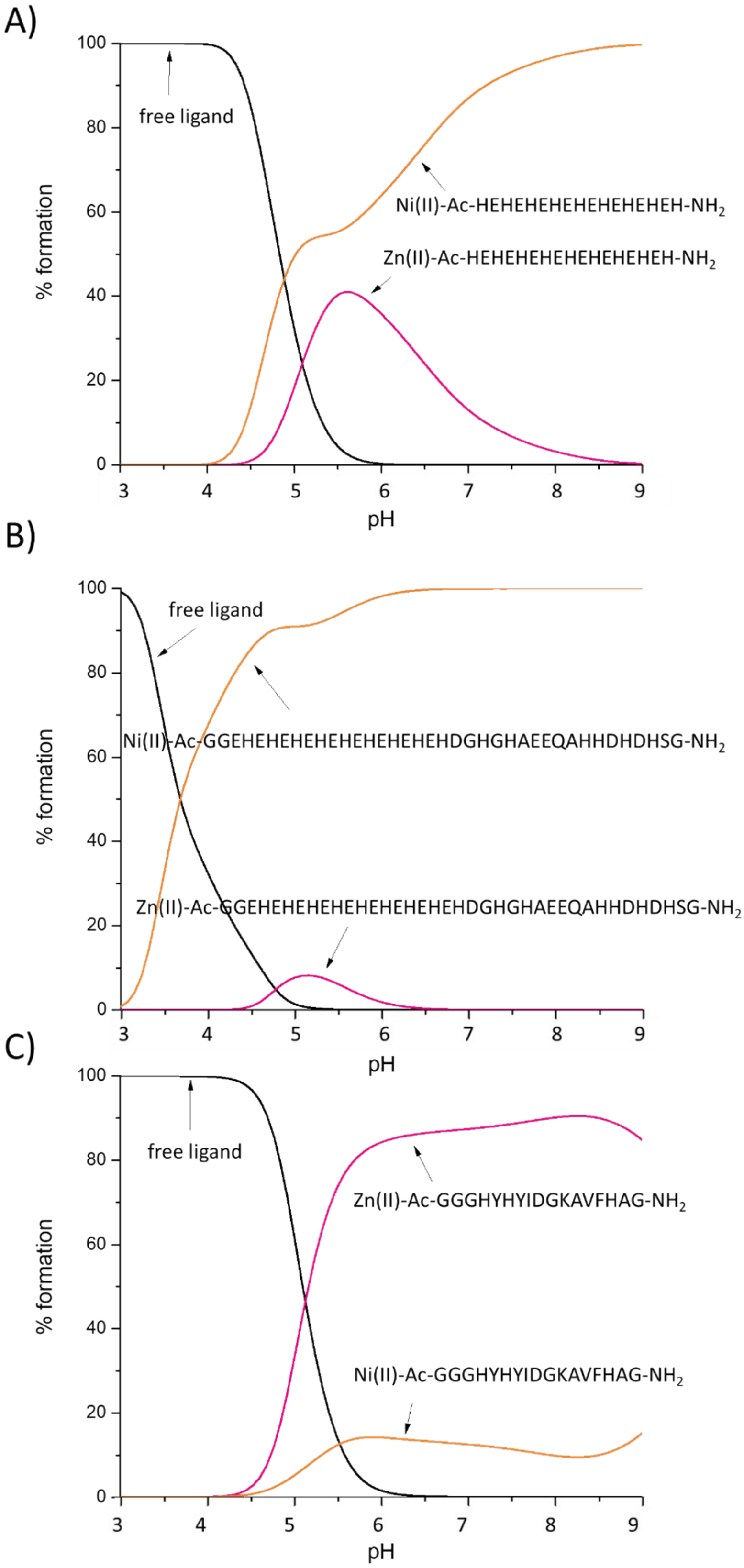


Figure 9. Competition plot between A) ZnuA-(120-136), B) ZnuA-(117-133), C) AztC-(117-133), Zn(II) and Ni(II), describes complex formation at different pH values in a hypothetical situation in which equimolar amounts of the three reagents are mixed. Calculations are based on binding constants from Table 1.


A)
100
80
60
40
20
0
% formation
3
4
5
6
7
8
9
pH
free ligand
Ni(II)-Ac-HEHEHEHEHEHEHEHEHEH-NH2
Zn(II)-Ac-HEHEHEHEHEHEHEHEHEH-NH2
B)
100
80
60
40
20
0
% formation
3
4
5
6
7
8
9
pH
free ligand
Ni(II)-Ac-GGEHEHEHEHEHEHEHEHEHEHDGHGHAEEQAHHDHDHSG-NH2
Zn(II)-Ac-GGEHEHEHEHEHEHEHEHEHEHDGHGHAEEQAHHDHDHSG-NH2
C)
100
80
60
40
20
0
% formation
3
4
5
6
7
8
9
pH
free ligand
Zn(II)-Ac-GGGHYHYIDGKAVFHAG-NH2
Ni(II)-Ac-GGGHYHYIDGKAVFHAG-NH2

References:

[1] L. Alderighi, P. Gans, A. Ienco, d. Peters, A. Sabatini and A. Vacca.*Coordination Chemistry Reviews 1999; 184:311-318*