Thermodynamic and spectroscopic study of Cu(II) and Zn(II) complexes with the (148-156) peptide fragment of C4YJH2, a putative metal transporter of *Candida albicans*

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Electronic Supplementary Information (ESI)

Table S1. Stoichiometry, molecular formula and average *m/z* value for the species shown in ESI-MS spectra of Cu(II) and Zn(II) complexes with **WT**, **D7A**,**S2A/S5A/S8A**, **HSGD** and **GSDH** ligands; L:M molar ratio = 1:0.8 in water/methanol 50:50 solution.

	Species	Formula	Average *m/z*
Cu(II)-WT	H_3L^+	C35H56N13O17	930.4
	$([H_2L] \cdot Na)^+$	C35H55N13O17Na	952.3
	$[CuHL]^+$	C35H54N13O17Cu	991.3
	$([CuL] \cdot Na)^+$	C35H53N13O17CuNa	1013.3
Zn(II)-WT	H_3L^+	C35H56N13O17	930.4
	$([H_2L] \cdot Na)^+$	C35H55N13O17Na	952.3
	$[ZnHL]^+$	C35H54N13O17Zn	992.3
	$([ZnL] \cdot Na)^+$	C35H53N13O17ZnNa	1014.3
Cu(II)-D7A	H_2L^+	C34H56N13O15	886.4
	$([HL] \cdot K)^+$	C34H55N13O15K	924.4
	$[CuL]^+$	C34H54N13O15Cu	947.3
	$([CuH_{-2}L] \cdot K_2)^+$	C34H52N13O15K2	1023.2
Zn(II)-D7A	H_2L^+	C34H56N13O15	886.4
	$([HL] \cdot Na)^+$	C34H55N13O15Na	908.4
	$([HL] \cdot K)^+$	C34H55N13O15K	924.4
	$[ZnL]^+$	C34H54N13O15Zn	948.3
	$([ZnH_{-2}L] \cdot K_2)^+$	C34H52N13O15ZnK2	1024.2
Cu(II)-S2A/S5A/S8A	H_3L^+	C35H56N13O14	882.4
	$([H_2L] \cdot Na)^+$	C35H55N13O14Na	904.3
	$([H_2L] \cdot K)^+$	C35H55N13O14K	920.4
	$([CuHL])^+$	C35H54N13O14Cu	943.3
Zn(II)-S2A/S5A/S8A	H_3L^+	C35H56N13O14	882.4
	$([H_2L] \cdot Na)^+$	C35H55N13O14Na	904.3
	$([H_2L] \cdot K)^+$	C35H55N13O14K	920.4
	$([ZnHL])^+$	C35H54N13O14Zn	944.3
	$([ZnH_{-1}L] \cdot KNa)^+$	C35H52N13O14ZnKNa	1004.3
	$([ZnH_{-1}L] \cdot K_2)^+$	C35H52N13O14ZnK2	1020.2
Cu(II)-HSGD	H_2L^+	C17H26N7O8	456.2
	$([HL] \cdot Na)^+$	C17H25N7O8Na	478.2
	$([HL] \cdot K)^+$	C17H25N7O8K	494.1
	$[CuL]^+$	C17H24N7O8Cu	517.1
	$([CuH_{-1}L] \cdot Na)^+$	C17H23N7O8CuNa	539.1
	$([CuH_{-1}L] \cdot K)^+$	C17H23N7O8CuK	555.1
Zn(II)-HSGD	H_2L^+	C17H26N7O8	456.2
	$([HL] \cdot Na)^+$	C17H25N7O8Na	478.2
	$([HL] \cdot K)^+$	C17H25N7O8K	494.1
	$[ZnL]^+$	C17H24N7O8Zn	518.1
	$([ZnH_{-1}L] \cdot Na)^+$	C17H23N7O8ZnNa	540.1
	$([ZnH_{-1}L] \cdot K)^+$	C17H23N7O8ZnK	556.1
Cu(II)-GSDH	H_2L^+	C17H26N7O8	456.2
	$([HL] \cdot Na)^+$	C17H25N7O8Na	478.2
	$([HL] \cdot K)^+$	C17H25N7O8K	494.1
	$[CuL]^+$	C17H24N7O8Cu	517.1
	$([CuH_{-1}L] \cdot Na)^+$	C17H23N7O8CuNa	539.1
	$([CuH_{-1}L] \cdot K)^+$	C17H23N7O8CuK	555.1
Zn(II)-GSDH	H_2L^+	C17H26N7O8	456.2
	$([HL] \cdot Na)^+$	C17H25N7O8Na	478.2
	$([HL] \cdot K)^+$	C17H25N7O8K	494.1
	$[ZnL]^+$	C17H24N7O8Zn	518.1
	$([ZnH_{-1}L] \cdot Na)^+$	C17H23N7O8ZnNa	540.1
	$([ZnH_{-1}L] \cdot K)^+$	C17H23N7O8ZnK	556.1

Table S2. Spectroscopic parameters at different pH values for the system Cu(II)-**WT**; M:L ratio = 0.8:1.

	UV-Vis			**CD**			**EPR**		
Species	***pH***	***λ (nm)***	***ε (M^{-1} cm^{-1})***	***pH***	***λ (nm)***	***Δε (M^{-1} cm^{-1})***	***pH***	***$A_{//}$ (G)***	***$g_{//}$***
-	**2.4**	800	16.40				**3.2**	119.5	2.41
-	**4.0**	800	14.10						
$[CuHL]^{+}$	**4.5**	795	16.40	**4.5**	230	-3.55	**4.8**	120.4	2.41
$[CuHL]^{+}$	**5.6**	726	25.45	**5.6**	230	-3.55	**5.7**	137.9	2.34
$[CuHL]^{+}$, $[CuH_{-1}L]^{-}$	**6.1**	615	35.62	**6.3**	613	-0.20	**6.2**	137.6	2.34
					328	0.39			
					296	-0.16			
					254	1.30			
					233	-2.06			
$[CuH_{-1}L]^{-}$	**7.1**	590	56.39	**7.1**	613	-0.37			
					512	0.06			
					329	0.76			
					296	-0.22			
					254	2.77			
					233	-0.97			
$[CuH_{-1}L]^{-}$, $[CuH_{-2}L]^{2-}$	**7.6**	583	59.01	**7.6**	613	-0.37	**7.4**	190.7	2.22
					512	0.06			
					329	0.76			
					296	-0.22			
					254	2.77			
					233	-0.97			
$[CuH_{-1}L]^{-}$, $[CuH_{-2}L]^{2-}$	**8.2**	573	59.93	**8.1**	602	-0.32	**8.5**	191.4	2.22
					511	0.08			
					326	0.71			
					297	0.02			
					257	2.42			
					233	-1.14			
$[CuH_{-2}L]^{2-}$	**9.3**	561	62.86	**9.5**	558	-0.47			
					495	0.15			
					307	0.85			
					268	2.11			
					235	-3.09			
$[CuH_{-2}L]^{2-}$	**10.0**	561	64.38	**10.1**	558	-0.47	**10.5**	195.8	2.21
					495	0.15			
					307	0.85			
					268	2.11			
					235	-3.09			
$[CuH_{-2}L]^{2-}$, $[CuH_{-3}L]^{3-}$	**11.2**	561	54.23	**11.4**	558	-0.32	**11.3**	199.5	2.20
					495	0.15			
					307	0.51			
					268	1.24			
					235	-3.09			
$[CuH_{-3}L]^{3-}$				**12.1**	558	-0.47			
					495	0.15			
					307	0.85			
					268	2.11			
					235	-2.33			

Table S3. Spectroscopic parameters at different pH values for the system Cu(II)-**S2A/S5A/S8A** ; M:L ratio = 0.8:1.

	UV-Vis			**CD**			**EPR**		
Species	***pH***	***λ (nm)***	***ε (M^{-1} cm^{-1})***	***pH***	***λ (nm)***	***Δε (M^{-1} cm^{-1})***	***pH***	***$A_{//}$ (G)***	***$g_{//}$***
-	**3.1**	800	16.26				**3.0**	116.9	2.43
-	**4.1**	800	18.67	**4.6**	230	-2.82	**4.6**	116.9	2.42
$[CuLH]^{+}$	**5.1**	740	26.98						
$[CuLH]^{+}$	**5.5**	735	29.67	**5.6**	230	-2.82	**5.7**	145.9	2.34
$[CuLH]^{+}$	**6.1**	710	33.74	**6.1**	230	-2.37			
$[CuL]$	**6.7**	610	49.34	**6.9**	612 329 298 255 234	-0.37 0.71 -0.23 2.79 -1.11	**7.0**	140.0	2.34
$[CuLH_{-1}]^{-}$	**7.6**	592	66.87	**7.5**	612 329 298 255 234	-0.37 0.71 -0.23 2.79 -1.11	**7.7**	166.8	2.23
$[CuLH_{-1}]^{2-}$	**8.3**	590	71.30	**8.3**	612 329 298 257 234	-0.37 0.71 -0.23 2.38 -1.11	**8.4**	167.0	2.23
$[CuLH_{-1}]^{-}$	**9.0**	574	75.02	**9.5**	652 494 323 253	0.48 -0.28 0.13 6.14	**9.4**	168.0	2.23
$[CuLH_{-2}]^{-}$	**10.3**	529	88.88	**10.4**	641 504 328 297 259	0.55 -0.74 0.36 -0.78 5.25	**10.6**	165.0	2.23
$[CuLH_{-3}]^{3-}$	**11.0**	522	73.89	**11.2**	641 504 328 297 259	0.55 -0.74 0.36 -0.78 5.25	**11.4**	190.7	2.19

Table S4. Spectroscopic parameters at different pH values for the system Cu(II)-**D7A**; M:L ratio = 0.8:1.

	UV-Vis			CD			EPR		
Species	***pH***	***λ (nm)***	***ε (M^{-1} cm^{-1})***	***pH***	***λ (nm)***	***Δε (M^{-1} cm^{-1})***	***pH***	***$A_{//}$ (G)***	***$g_{//}$***
-	**3.3**	800	17.70				**3.1**	119.6	2.41
$[CuHL]^{2+}$	**4.5**	795	20.35	**4.4**	230	-3.30	**4.7**	119.6	2.41
$[CuHL]^{2+}$	**5.5**	597/750	20.61	**5.4**	230	-3.01	**5.3**	119.6	2.41
$[CuL]^{+}$	**5.9**	593	44.34	**5.9**	622	-0.17	**6.1**	134.0	2.35
					330	0.35			
					294	-0.14			
					252	1.32			
					231	-2.20			
$[CuL]^{+}$				**6.5**	622	-0.37			
					330	0.71			
					296	-0.16			
					252	2.91			
					232	-0.79			
$[CuH_{-1}L]$	**7.1**	572	73.07	**7.3**	622	-0.37	**7.4**	186.0	2.22
					330	0.71			
					296	-0.16			
					256	2.74			
					233	-1.10			
$[CuH_{-1}L]$,$[CuH_{-2}L]^{-}$	**8.1**	572	71.40	**8.5**	565	-0.36	**8.7**	189.7	2.22
					316	0.64			
					266	2.01			
					235	-2.13			
$[CuH_{-3}L]^{2-}$	**9.3**	560	82.15	**9.4**	563	-0.47	**9.2**	191.0	2.21
					308	0.81			
					267	2.04			
					235	-3.14			
$[CuH_{-3}L]^{2-}$	**10.5**	556	76.70	**10.4**	563	-0.47	**10.6**	199.0	2.21
					308	0.81			
					267	2.04			
					235	-3.14			
$[CuH_{-3}L]^{2-}$	**11.5**	554	62.57	**11.2**	563	-0.47	**11.1**	199.0	2.21
					308	0.81			
					267	2.04			
					235	-3.14			

Table S5. Spectroscopic parameters at different pH values for the system Cu(II)-**HSGD**; M:L ratio = 0.8:1.

	UV-Vis			**CD**			**EPR**		
Species	***pH***	***λ (nm)***	***ε (M^{-1} cm^{-1})***	***pH***	***λ (nm)***	***Δε (M^{-1} cm^{-1})***	***pH***	***A_{II} (G)***	***g_{II}***
-	**3.0**	800	10.95				**3.1**	119.6	2.41
-	**4.1**	800	13.33	**4.3**	230	-0.99	**4.3**	119.6	2.41
					209	0.11			
$[CuL]^+$	**5.1**	755	18.49	**5.3**	230	-1.05	**5.1**	138.0	2.34
					210	0.27			
$[CuL]^+$, $[CuH_{-1}L]$	**6.0**	715	25.62	**6.1**	230	-1.45	**6.2**	142.0	2.33
$[CuL]^+$, $[CuH_{-1}L]$, $[CuH_{-2}L]^-$	**6.9**	636	45.31	**7.0**	618	-0.14	**7.2**	149.0	2.31
					349	0.88			
					298	-0.39			
					253	0.85			
					232	-1.13			
$[CuH_{-1}L]$, $[CuH_{-2}L]^-$	**7.6**	615	67.70	**7.6**	620	-0.31			
					349	0.19			
					301	-0.76			
					253	1.85			
					233	-0.31			
$[CuH_{-2}L]^-$	**8.1**	612	76.44	**8.3**	620	-0.31	**8.7**	145.9	2.24
					349	0.19			
					301	-0.65			
					253	1.98			
					233	-0.31			
$[CuH_{-2}L]^-$, $[CuH_{-3}L]^{2-}$	**9.0**	594	84.29	**9.3**	622	-0.07	**9.7**	173.0	2.23
					576	0.05			
					511	-0.10			
					322	0.32			
					292	-0.16			
					258	1.01			
					235	-0.41			
$[CuH_{-3}L]^{2-}$	**10.0**	582	97.67	**10.3**	579	0.14	**10.6**	190.7	2.217
					507	-0.13			
					315	0.55			
					287	-0.07			
					236	-0.55			
$[CuH_{-3}L]^{2-}$	**11.1**	575	96.01	**11.2**	579	0.11	**11.3**	190.7	2.217
					507	-0.27			
					312	0.48			
					285	-0.01			

Table S6. Spectroscopic parameters at different pH values for the system Cu(II)-**GSDH**; M:L ratio = 0.8:1.

	UV-Vis			**CD**			**EPR**		
Species	***pH***	***λ (nm)***	***ε (M^{-1} cm^{-1})***	***pH***	***λ (nm)***	***Δε (M^{-1} cm^{-1})***	***pH***	***$A_{//}$ (G)***	***$g_{//}$***
-	**3.1**	800	12.30	**3.1**	229	-2.61	**3.0**	119.5	2.41
-	**4.2**	800	13.72	**4.5**	229	-2.04	**4.2**	119.5	2.41
$[CuL]^+$	**5.3**	775	16.88	**5.3**	229	-1.89			
$[CuL]^+$	**5.5**	763	19.69				**5.7**	132.0	2.35
$[CuL]^+$,$[CuH_{-1}L]$, $[CuH_{-2}L]^-$	**6.0**	596	37.21	**6.0**	608 328 294 250 230	-0.19 0.34 -0.17 1.37 -1.31			
$[CuH_{-1}L]$,$[CuH_{-2}L]^-$	**6.9**	587	67.32	**6.93**	608 329 295 249	-0.44 0.75 -0.23 3.28	**6.6**	183.6	2.22
$[CuH_{-2}L]^-$	**7.1**	585	68.60	**7.3**	608 329 295 249	-0.44 0.75 -0.23 3.28			
$[CuH_{-2}L]^-$,$[CuH_{-3}L]^{2-}$	**8.1**	571	68.13	**8.4**	565 496 318 264 234	-0.52 0.13 0.64 2.19 -1.23	**8.6**	191.6	2.215
$[CuH_{-2}L]^-$,$[CuH_{-3}L]^{2-}$	**9.0**	560	73.15	**9.2**	560 489 305 267 235	-0.68 0.21 0.10 2.24 -2.19	**9.2**	191.6	2.215
$[CuH_{-3}L]^{2-}$	**10.1**	560	72.82	**10.4**	560 489 305 267 235	-0.68 0.21 0.10 2.24 -2.19	**10.1**	199.4	2.21
$[CuH_{-3}L]^{2-}$	**11.1**	560	72.08	**11.1**	560 489 305 267 235	-0.68 0.21 0.10 2.24 -2.19	**11.2**	199.4	2.205

Table S7. Hydrolysis constants for Cu(II)[1] and Zn(II).[2]

Species	log*β*
$[ZnH_{-1}]^{+}$	-8.96
$[ZnH_{-2}]$	-16.9
$[ZnH_{-3}]^{-}$	-28.4
$[ZnH_{-4}]^{2-}$	-41.2
$[CuH_{-1}]^{+}$	-7.7
$[Cu_2H_{-2}]^{2+}$	-10.75
$[Cu_3H_{-4}]^{2+}$	-21.36
$[CuH_{-4}]^{2-}$	-39.08

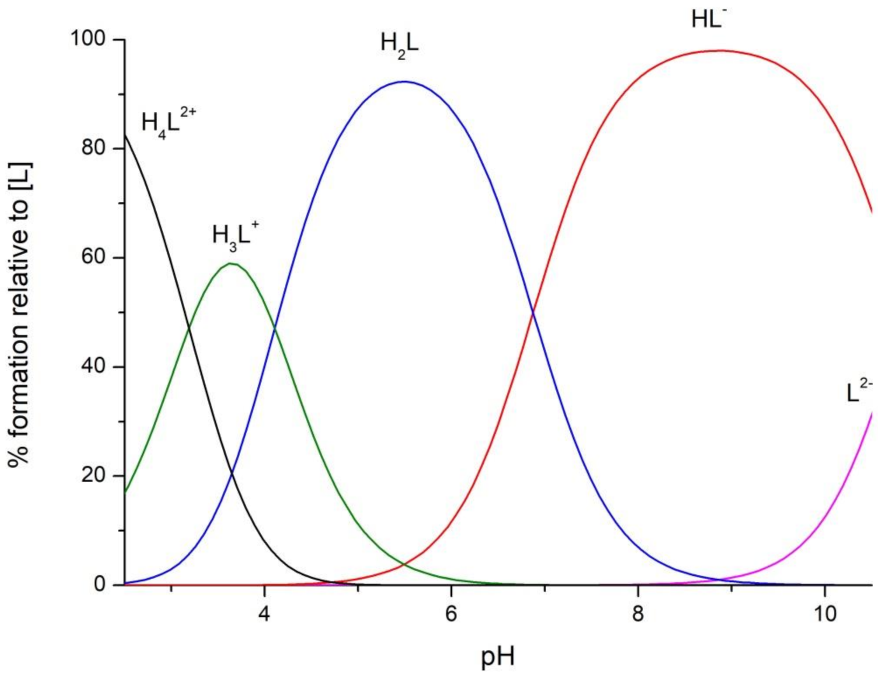


Figure S1. Species distribution diagram for protonation equilibria of ligand **WT**.

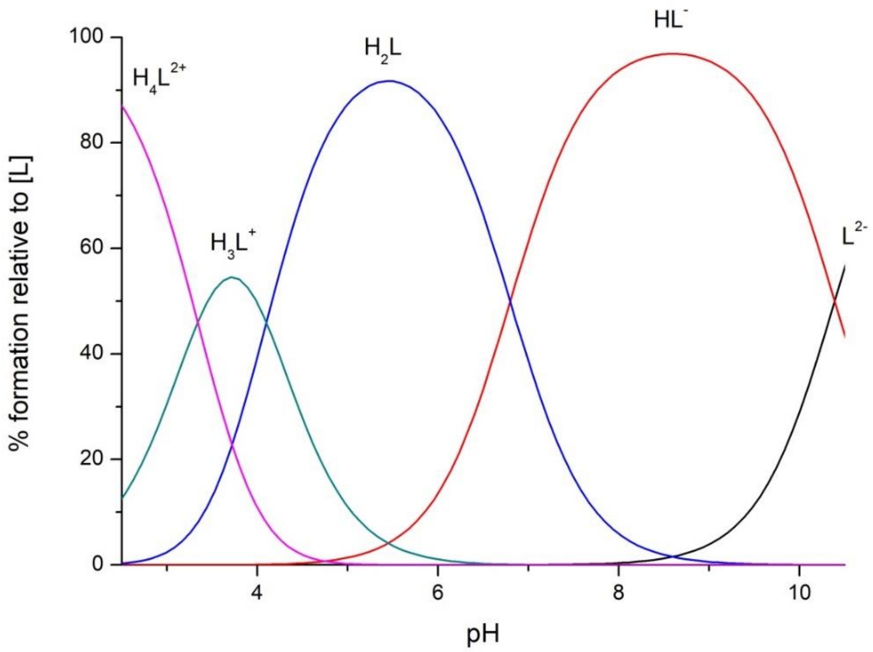


Figure S2. Species distribution diagram for protonation equilibria of ligand **S2A/S5A/S8A**.

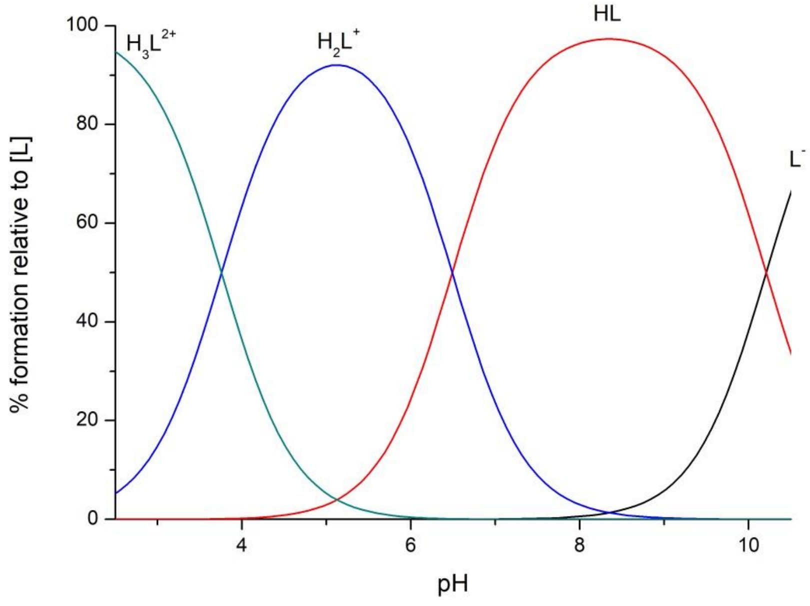


Figure S3. Species distribution diagram for protonation equilibria of ligand **D7A**.

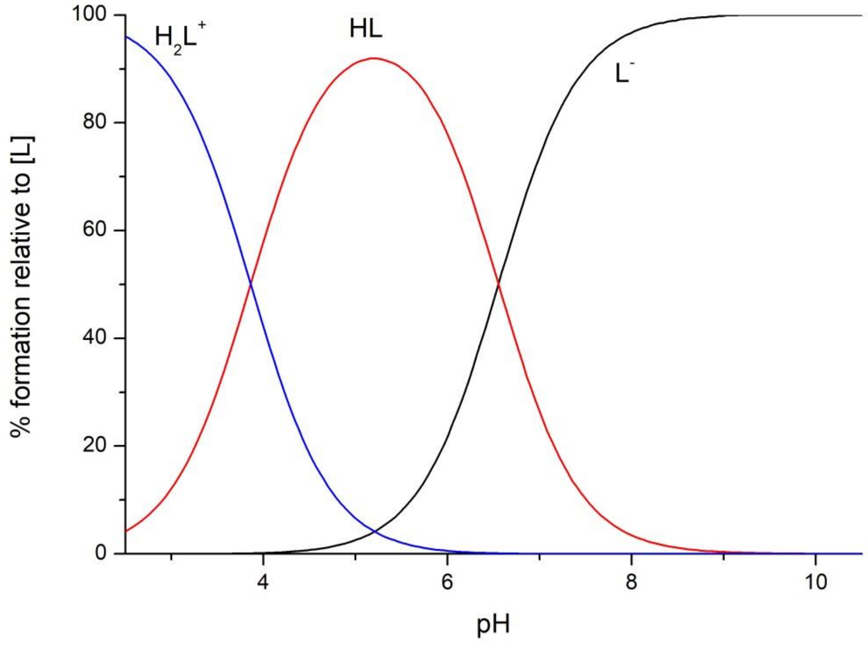


Figure S4. Species distribution diagram for protonation equilibria of ligand **HSGD**.

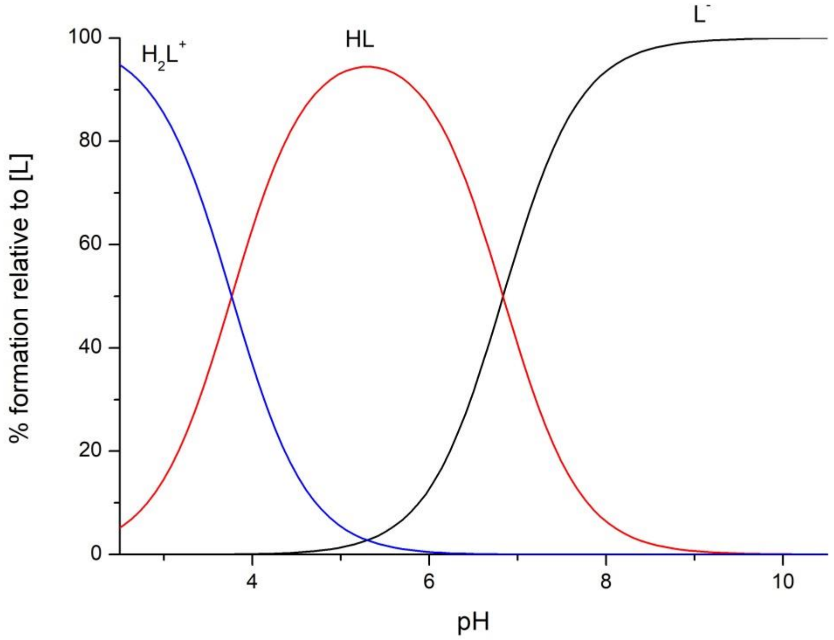


Figure S5. Species distribution diagram for protonation equilibria of ligand **GSDH**.

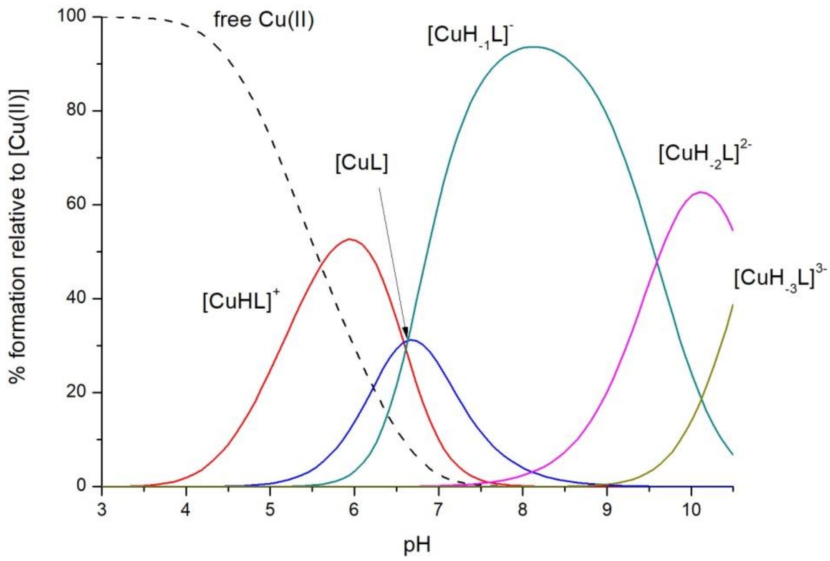


Figure S6. Exemplificative species distribution diagram relative to Cu(II)-**S2A/S5A/S8A** complexes; M:L molar ratio = 0.8:1.

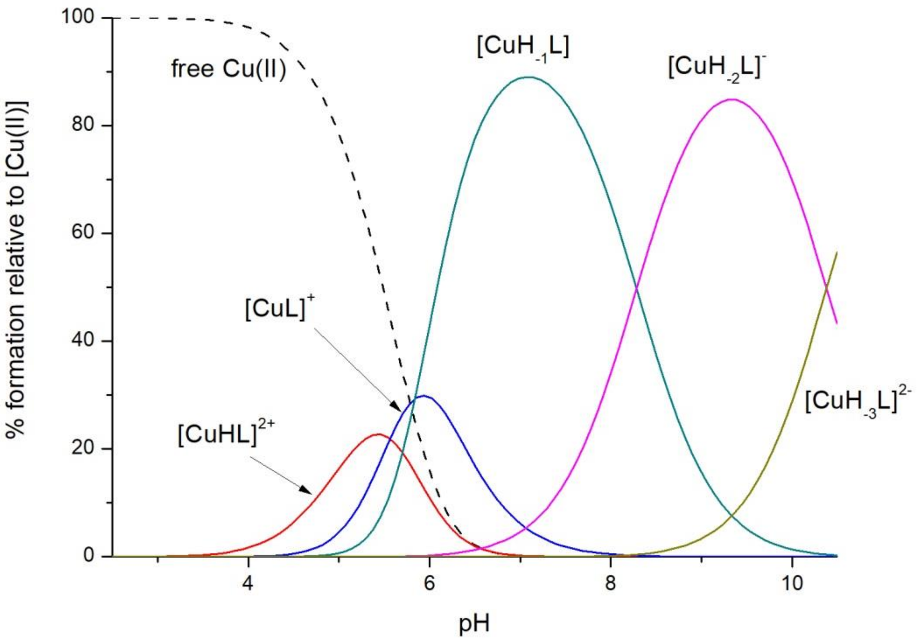


Figure S7. Exemplificative species distribution diagram relative to Cu(II)-**D7A** complexes; M:L molar ratio = 0.8:1.

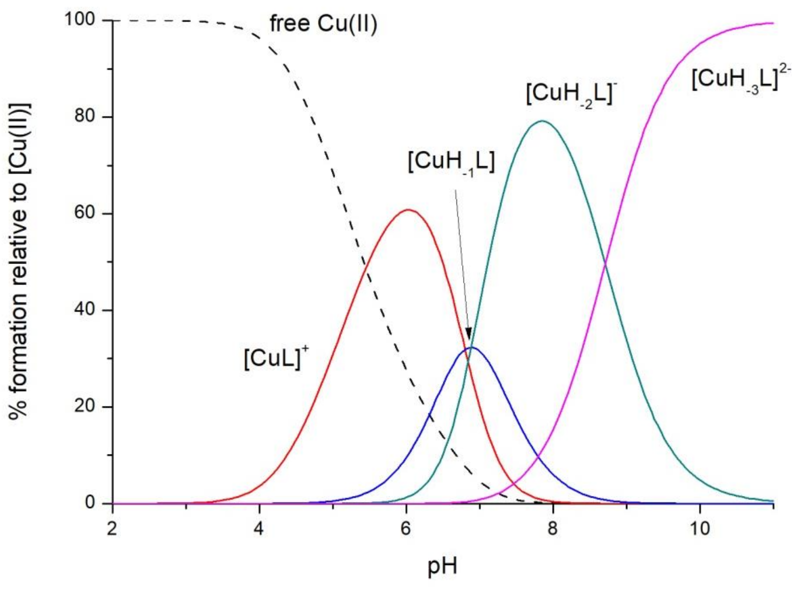


Figure S8. Exemplificative species distribution diagram relative to Cu(II)-**HSGD** complexes; M:L molar ratio = 0.8:1.

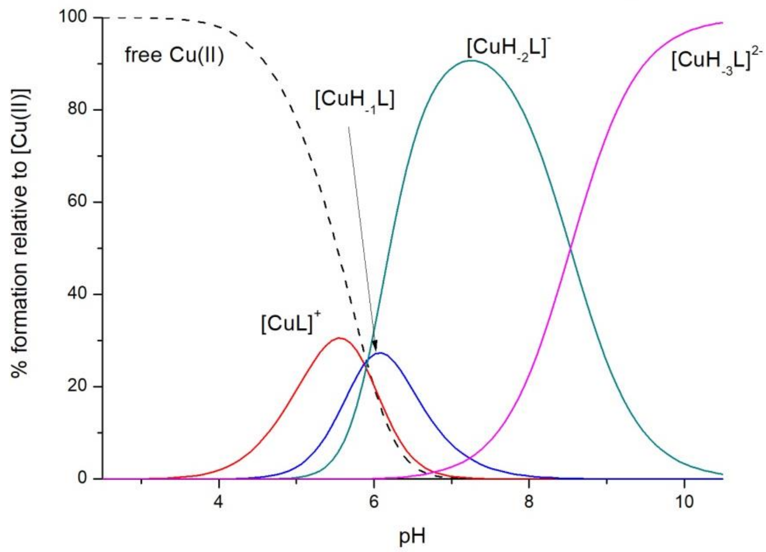


Figure S9. Exemplificative species distribution diagram relative to Cu(II)-**GSDH** complexes; M:L molar ratio = 0.8:1.

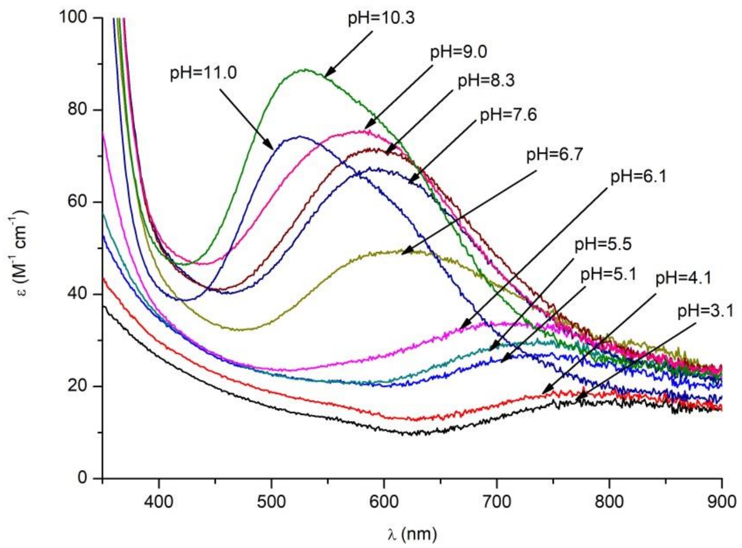


Figure S10. Vis absorption spectra [350–900 nm; optical path 1 cm] for Cu(II) complexes with **S2A/S5A/S8A**; M:L ratio = 0.8:1.

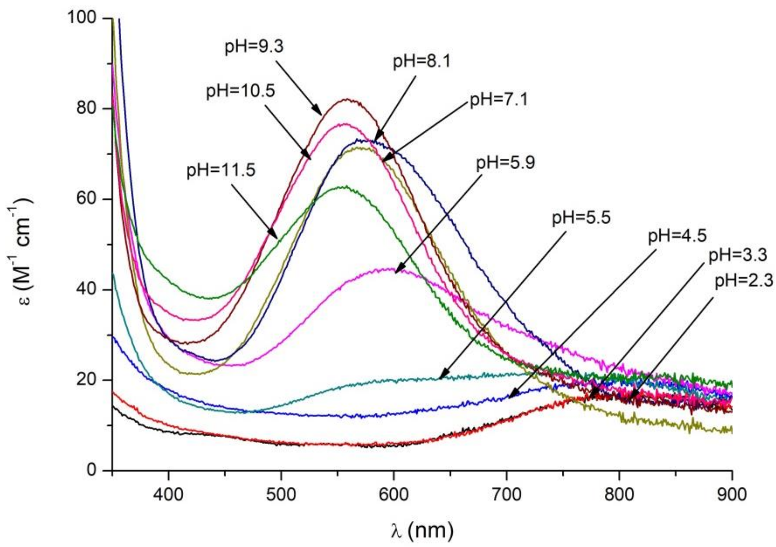


Figure S11. Vis absorption spectra [350–900 nm; optical path 1 cm] for Cu(II) complexes with **D7A**; M:L ratio = 0.8:1.

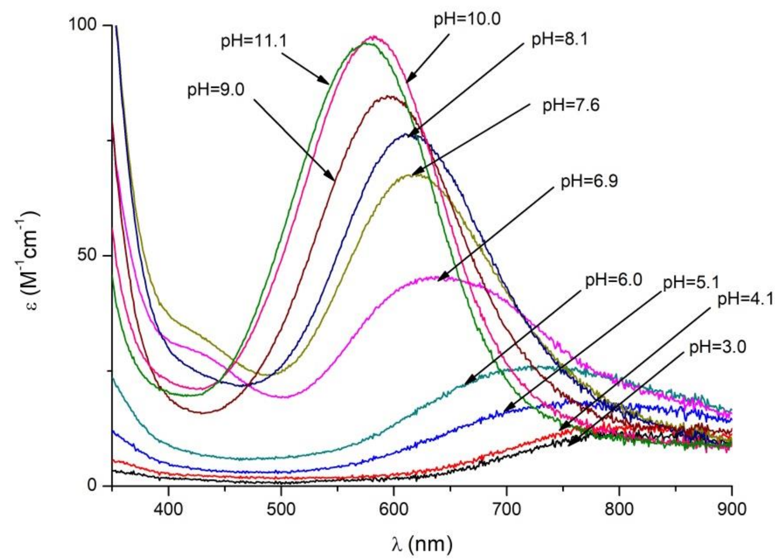


Figure S12. Vis absorption spectra [350–900 nm; optical path 1 cm] for Cu(II) complexes with **HSGD**; M:L ratio = 0.8:1.

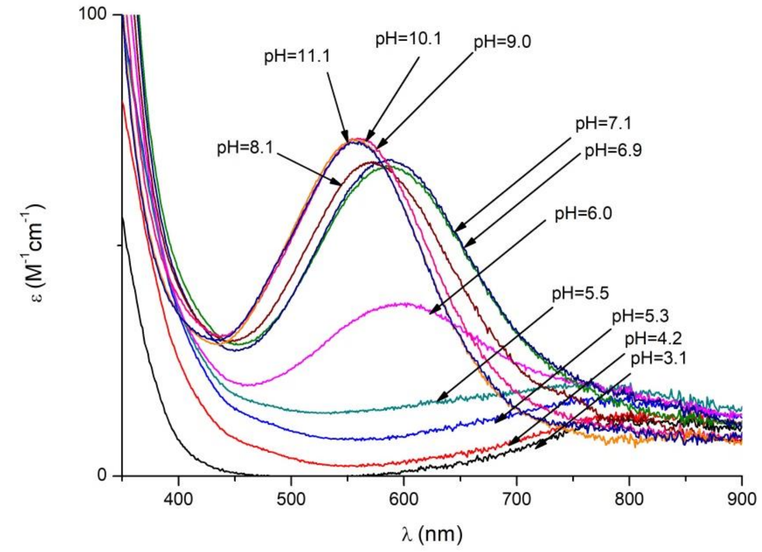


Figure S13. Vis absorption spectra [350–900 nm; optical path 1 cm] for Cu(II) complexes with **GSDH**; M:L ratio = 0.8:1.

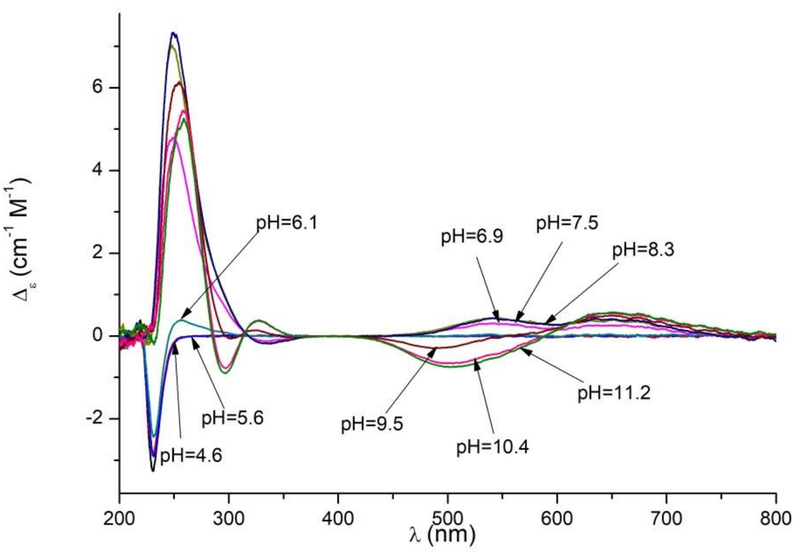


Figure S14. CD spectra [200–800 nm; optical path 1 cm] for Cu(II) complexes with **S2A/S5A/S8A**; M:L ratio = 0.8:1.

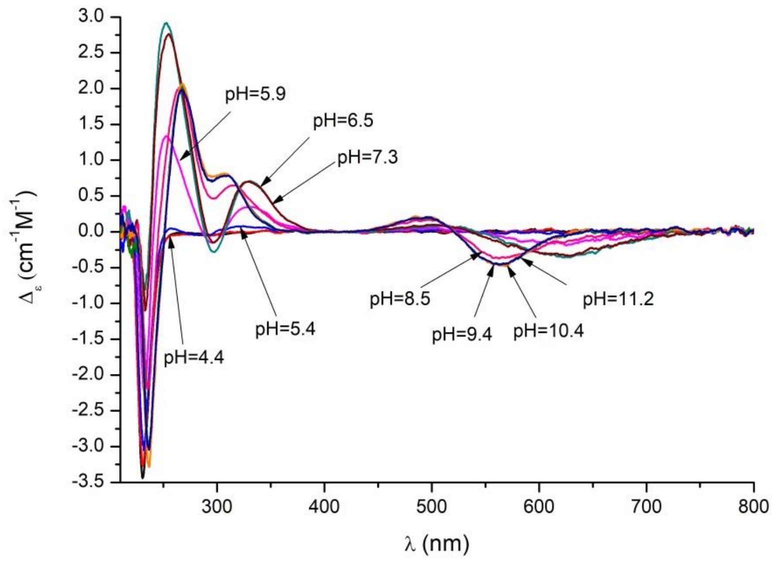


Figure S15. CD spectra [200–800 nm; optical path 1 cm] for Cu(II) complexes with **D7A**; M:L ratio = 0.9:1.

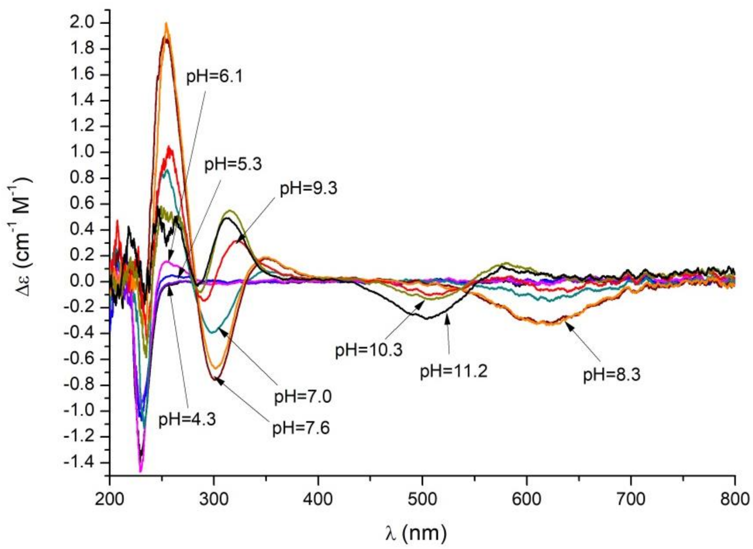


Figure S16. CD spectra [200–800 nm; optical path 1 cm] for Cu(II) complexes with **HSGD**; M:L ratio = 0.8:1.

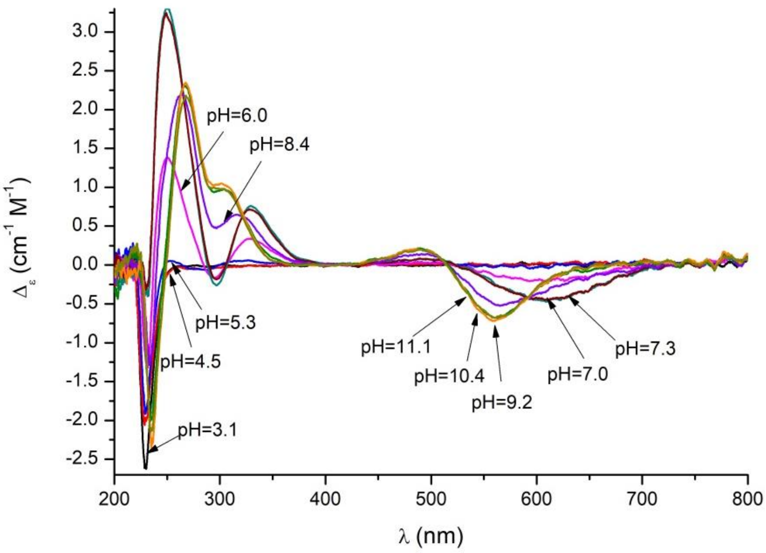


Figure S17. CD spectra [200–800 nm; optical path 1 cm] for Cu(II) complexes with **GSDH**; M:L ratio = 0.8:1.

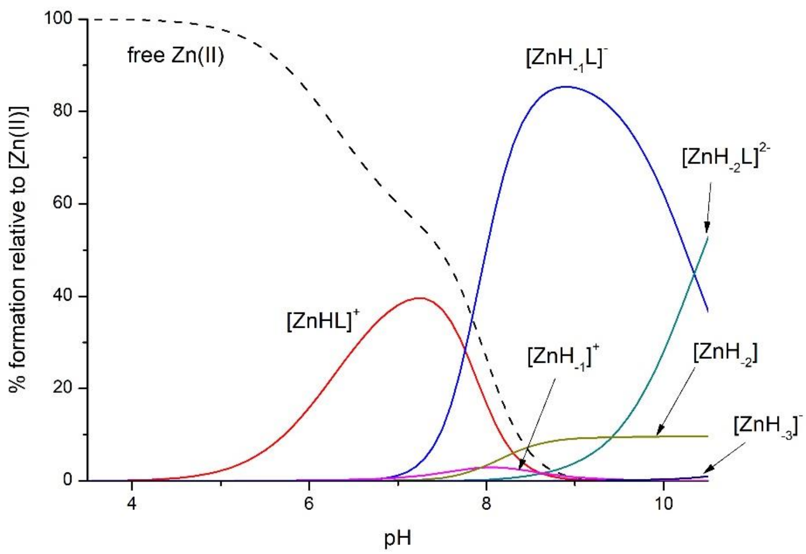


Figure S18. Exemplificative species distribution diagram relative to Zn(II)-**S2A/S5A/S8A** complexes; M:L molar ratio = 0.8:1.

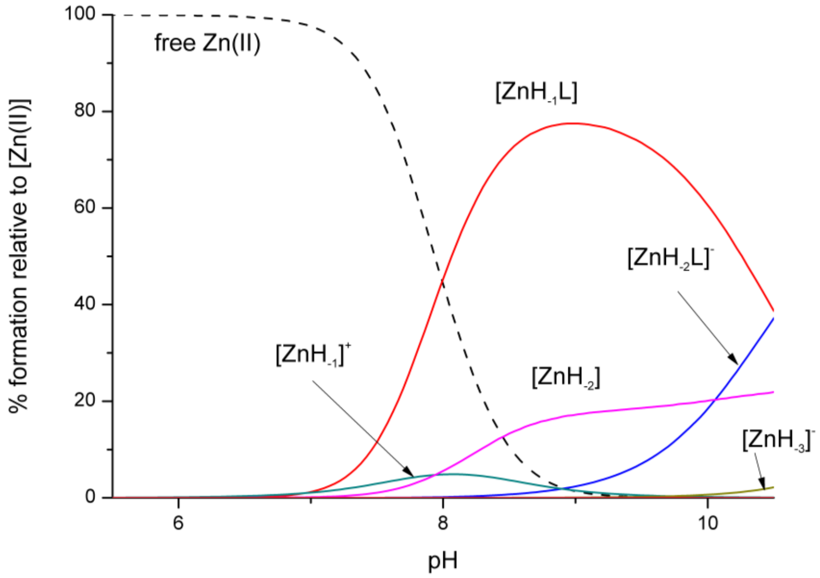


Figure S19. Exemplificative species distribution diagram relative to Zn(II)-**D7A** complexes; M:L molar ratio = 0.8:1.

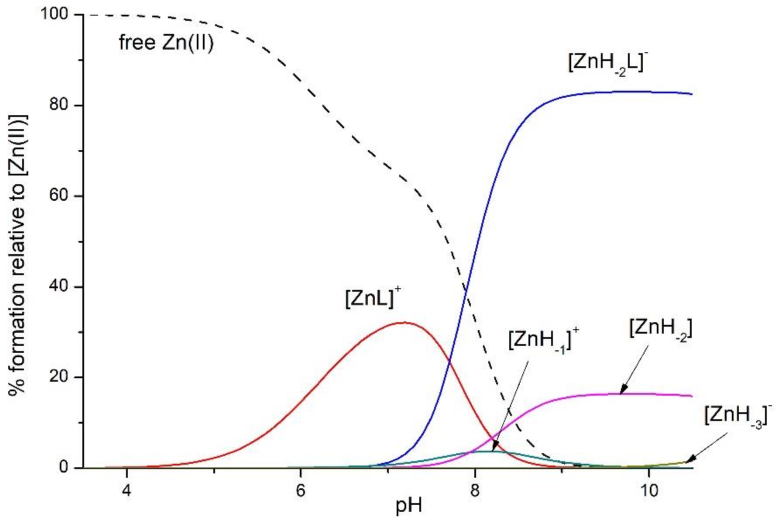


Figure S20. Exemplificative species distribution diagram relative to Zn(II)-**HSGD** complexes; M:L molar ratio = 0.8:1.

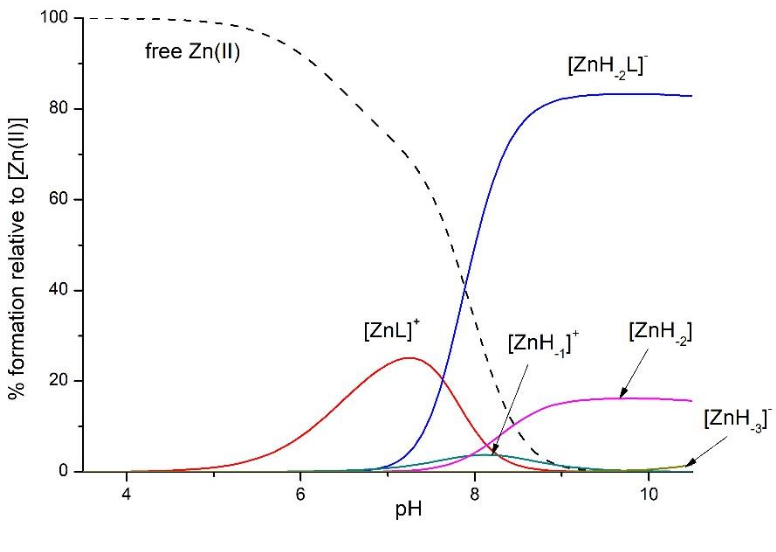
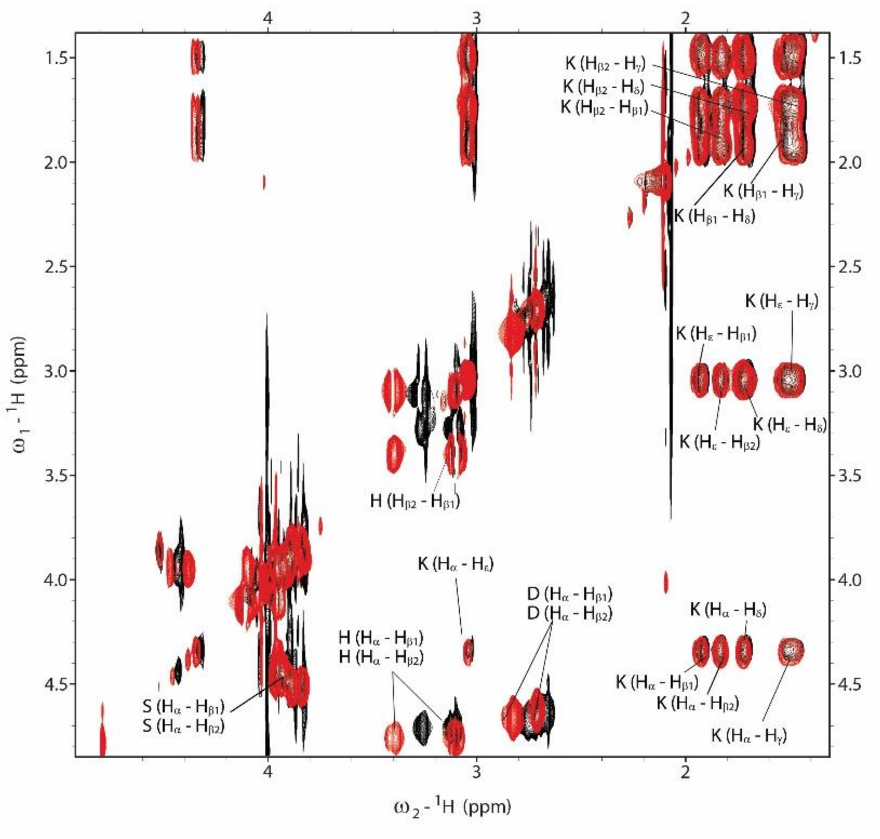


Figure S21. Exemplificative species distribution diagram relative to Zn(II)-**GSDH** complexes; M:L molar ratio = 0.8:1.

a)



b)

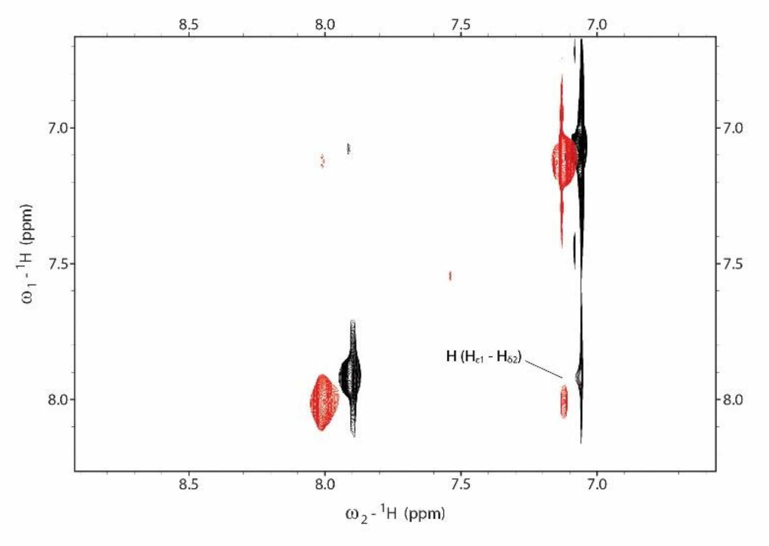
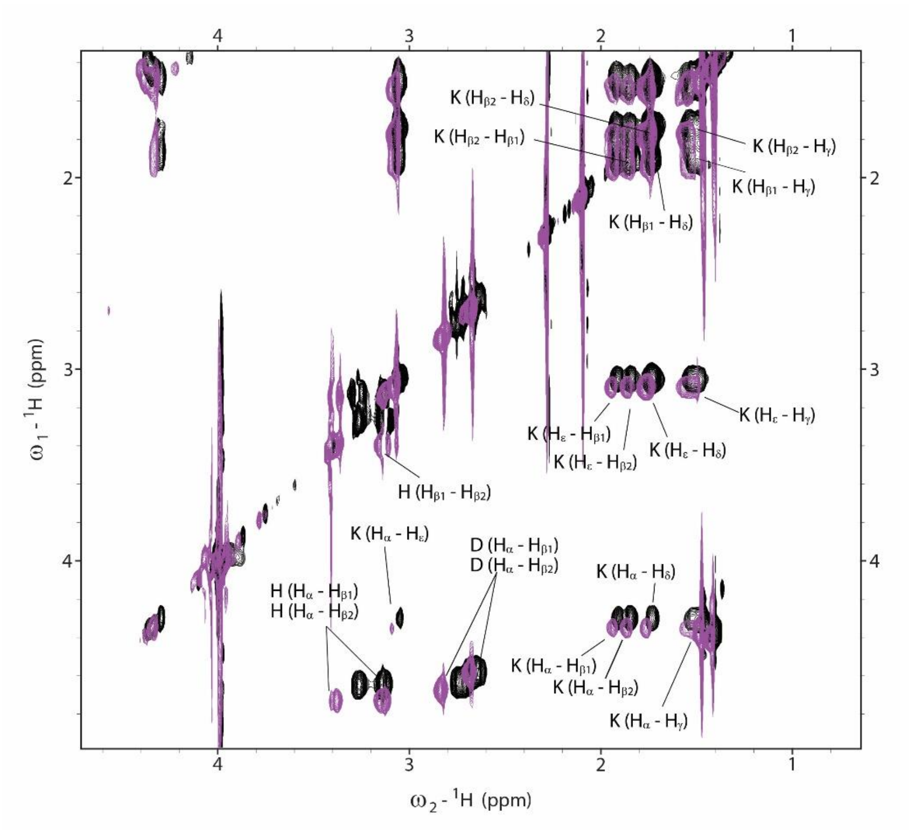


Figure S22. (a) Aliphatic and (b) aromatic regions of ^{1}H-^{1}H TOCSY NMR spectra for ligand **WT**, 3.0 mM, pH 7.4, T = 298 K, in the absence (black) and in the presence (red) of 1 equivalent of Zn(II), pH 7.4.

a)



b)

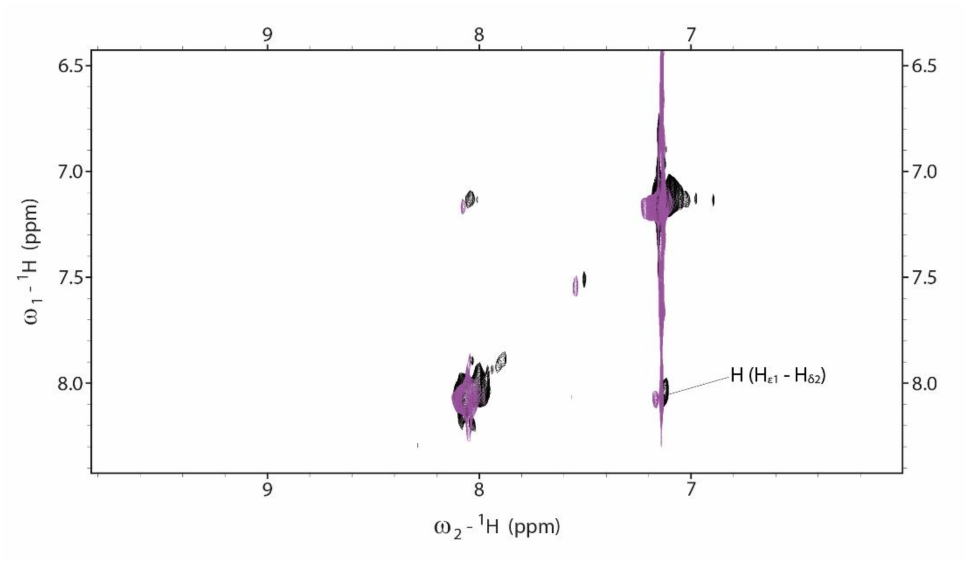
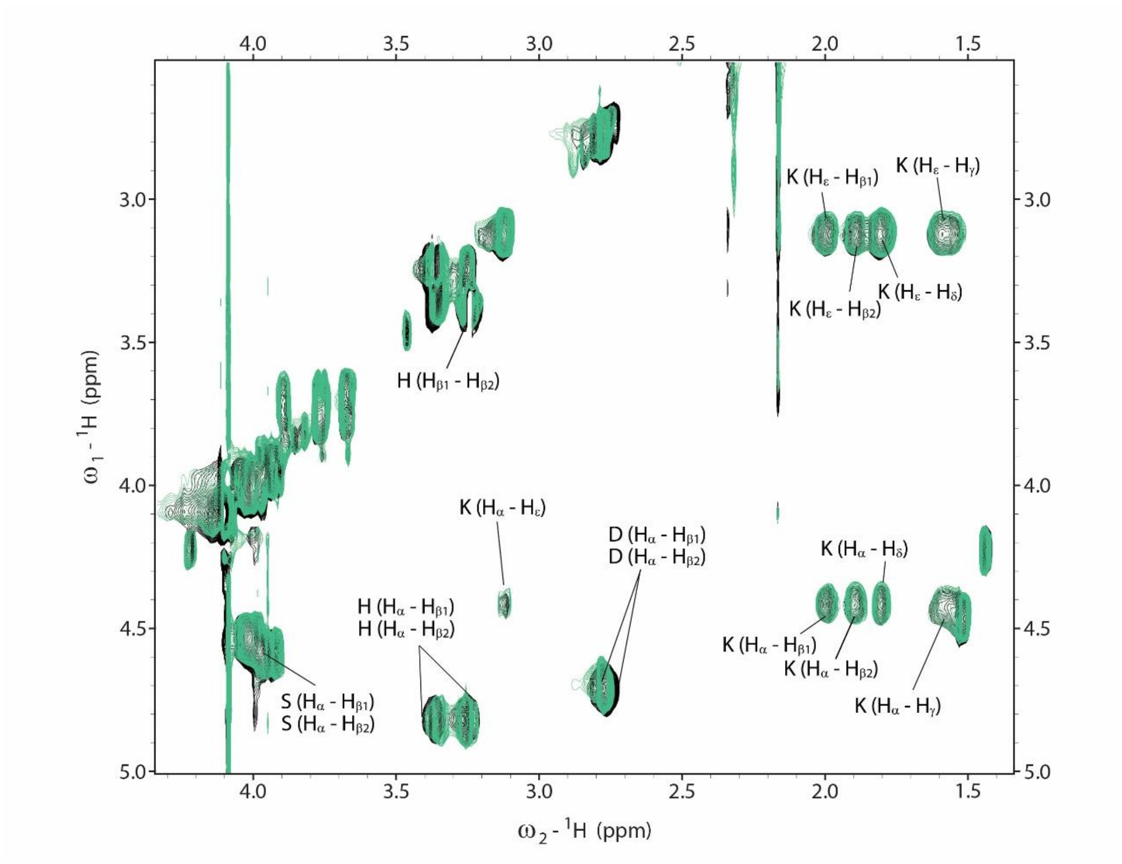


Figure S23. (a) Aliphatic and (b) aromatic regions of ^1H-^1H TOCSY NMR spectra for ligand **S2A/S5A/S8A**, 3.0 mM, pH 7.4, T = 298 K, in the absence (black) and in the presence (purple) of 1 equivalent of Zn(II), pH 7.4.

a)



b)

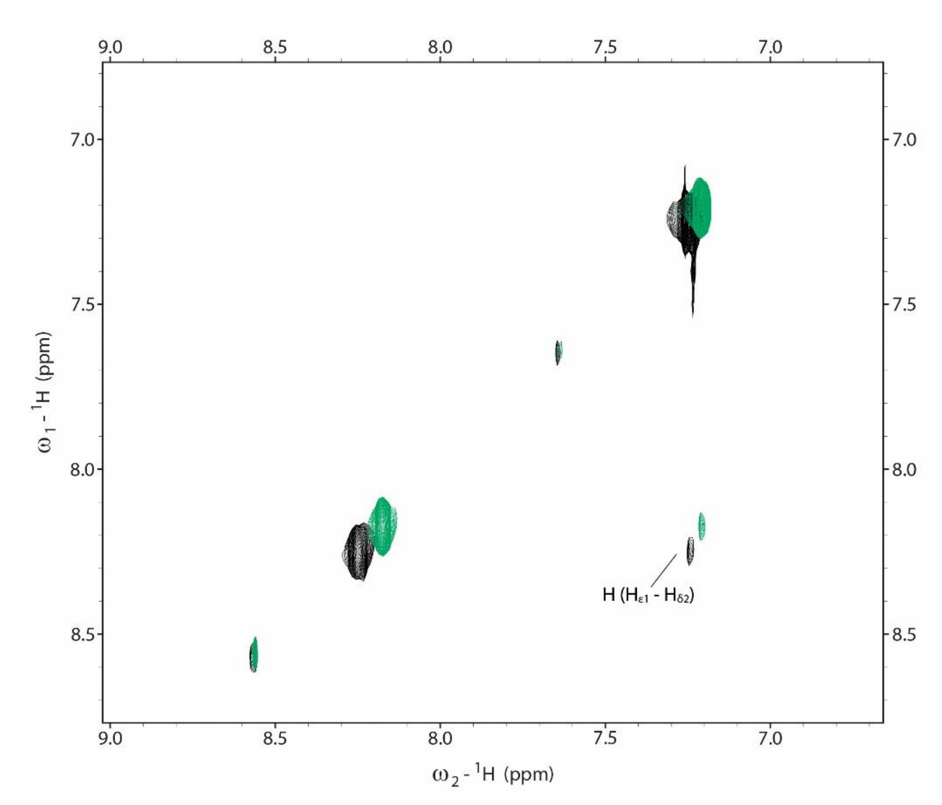
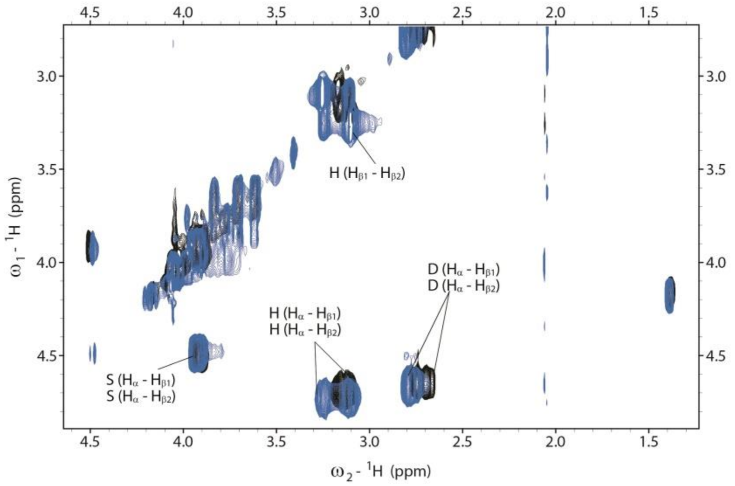


Figure S24. (a) Aliphatic and (b) aromatic regions of ^{1}H-^{1}H TOCSY NMR spectra for ligand **D7A**, 3.0 mM, pH 7.2, *T* = 298 K, in the absence (black) and in the presence (green) of 1 equivalent of Zn(II), pH 7.4.

a)



b)

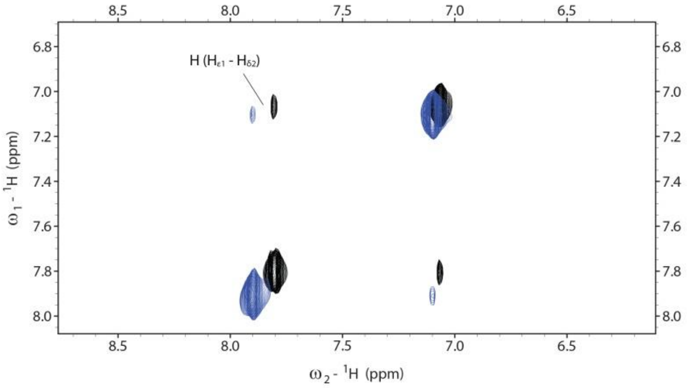


Figure S25. (a) Aliphatic and (b) aromatic regions of ^{1}H-^{1}H TOCSY NMR spectra for ligand **HSGD**, 3.0 mM, pH 7.1, T = 298 K, in the absence (black) and in the presence (blue) of 1 equivalent of Zn(II), pH 7.4.

a)

b)

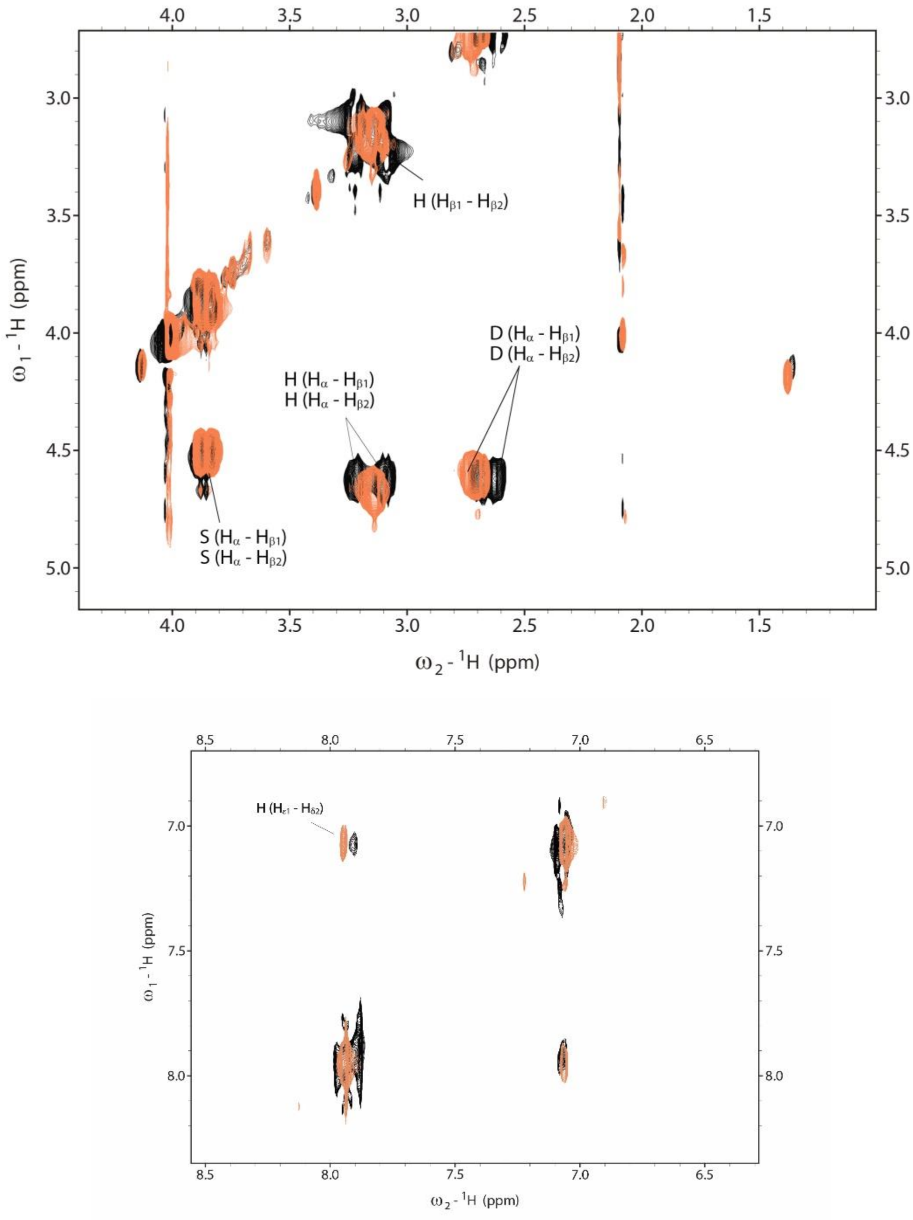


Figure S26. (a) Aliphatic and (b) aromatic regions of ^{1}H-^{1}H TOCSY NMR spectra for ligand **GSDH**, 3.0 mM, pH 7.1, T = 298 K, in the absence (black) and in the presence (orange) of 1 equivalent of Zn(II), pH 7.4.

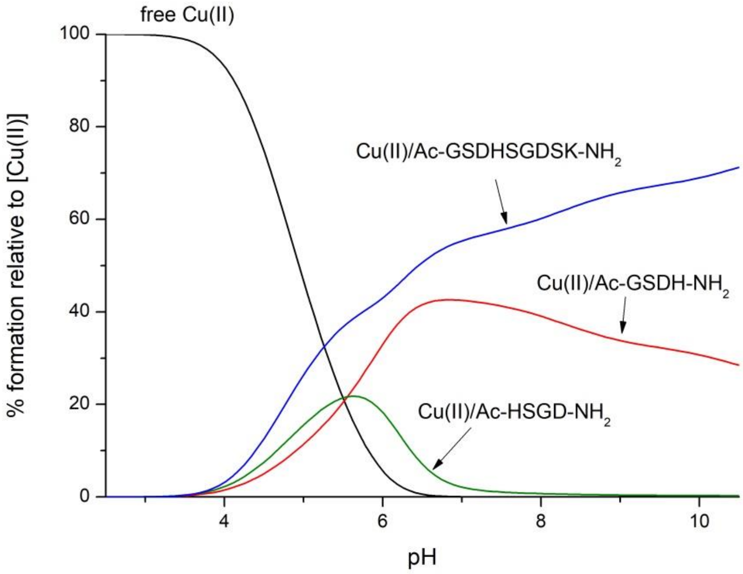


Figure S27. Competition plots for solutions containing equimolar concentrations of Cu(II), **WT**, **GSDH** and **HSGD**.

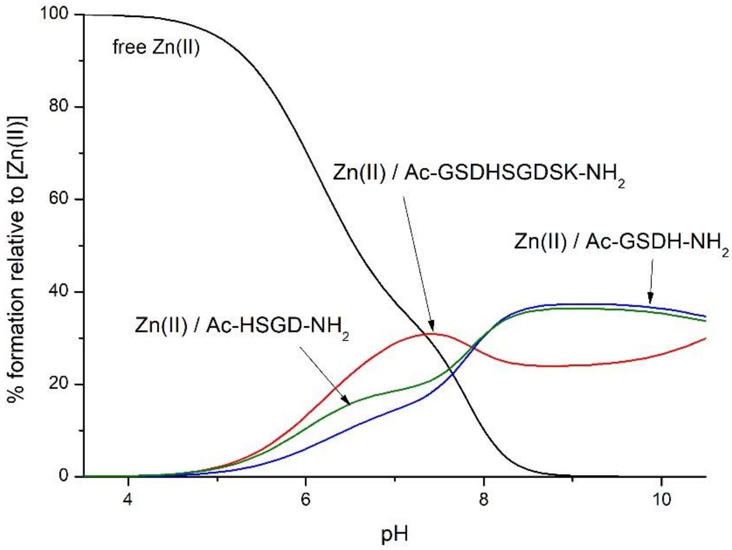


Figure S28. Competition plots for solutions containing equimolar concentrations of Zn(II), **WT**, **GSDH** and **HSGD**.

References

[1] G. Arena, R. Cali, E. Rizzarelli, S. Sammartano, *Therm. Acta* **1976**, *16*, 315-321.

[2] L. D. Pettit, H. K. J. Powell, *The IUPAC Stability Constants Database*, Royal Society of Chemistry, London, **1992-2000**.