Electronic Supporting Information for

Unusual binding mechanism of Cu(II) ions to the poly-histidyl domain of a peptide found in the venom of an african viper

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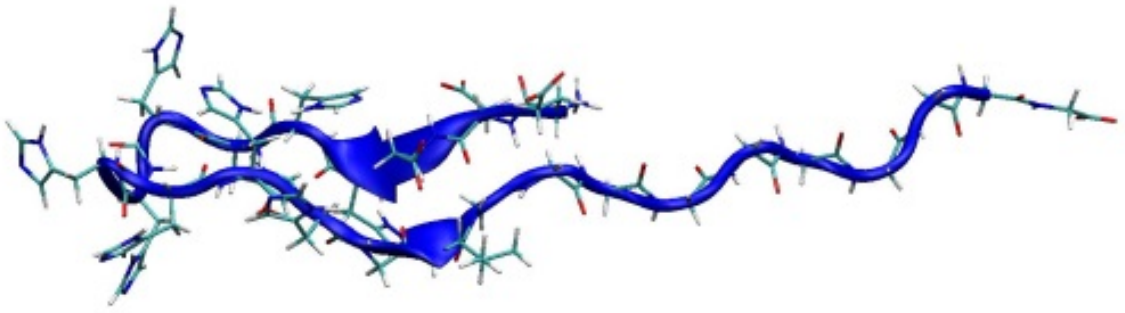

Fig. S1 Predicted model of folded EDD$(H)_9$GV$(G)_{10}$-NH_2 peptide obtained from Phyre 2.

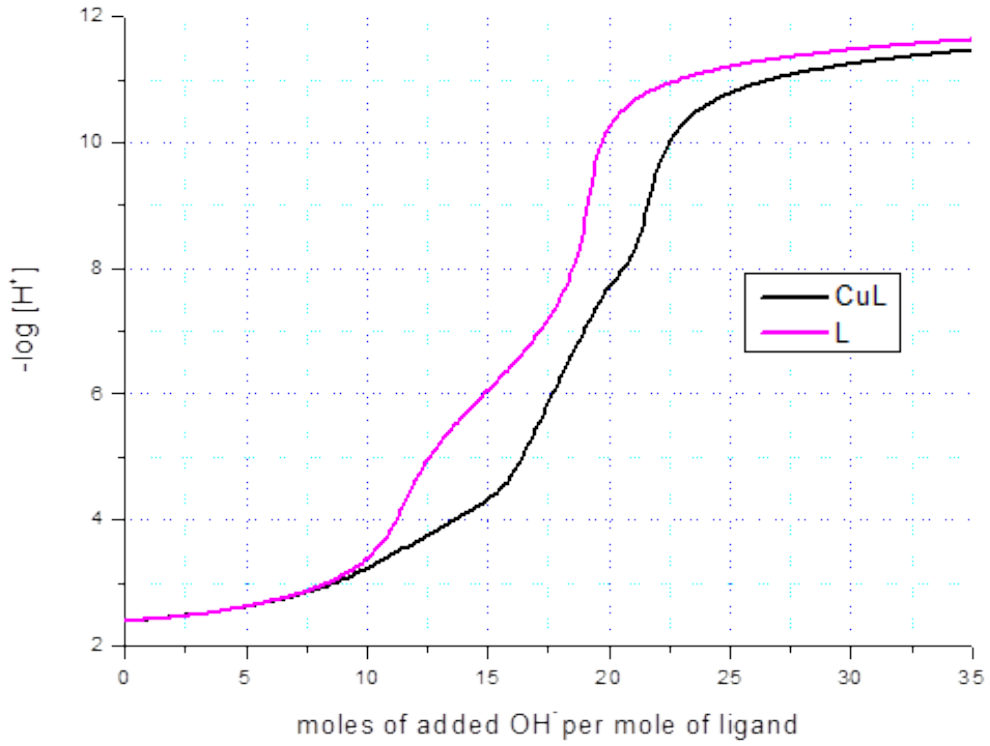

Fig. S2 Comparison between the experimental titration curve of pHpG in the absence/presence of Cu^{2+}, at 25°C and I = 0.1 M (KCl). $C°_M = 4 \cdot 10^{-4}$ M; M/L molar ratio = 1:1.2.

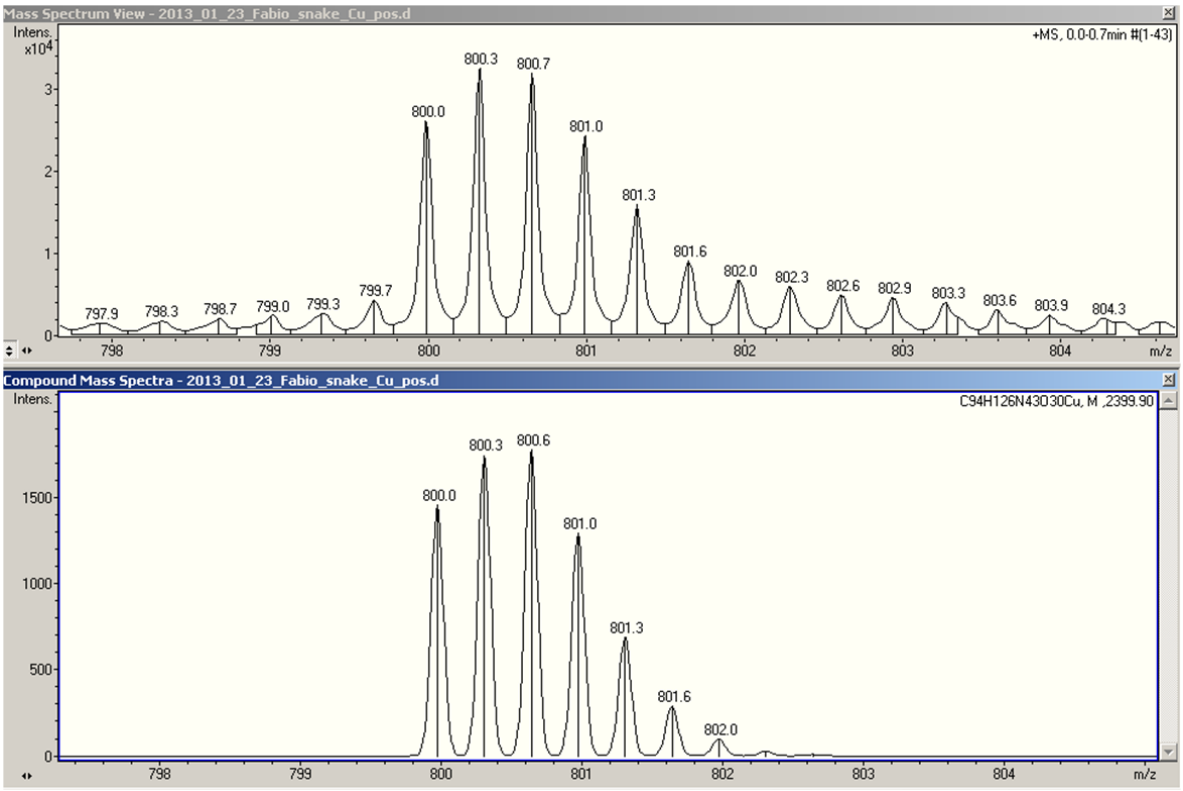

Fig. S3 Experimental (up) and simulated (down) ESI–MS spectrum for the complex $[CuH_4L]^{3+}$ (*m/z* = 800.3 D) in the Cu(II)/pHpG system, in aqueous solution, at pH 3.0.

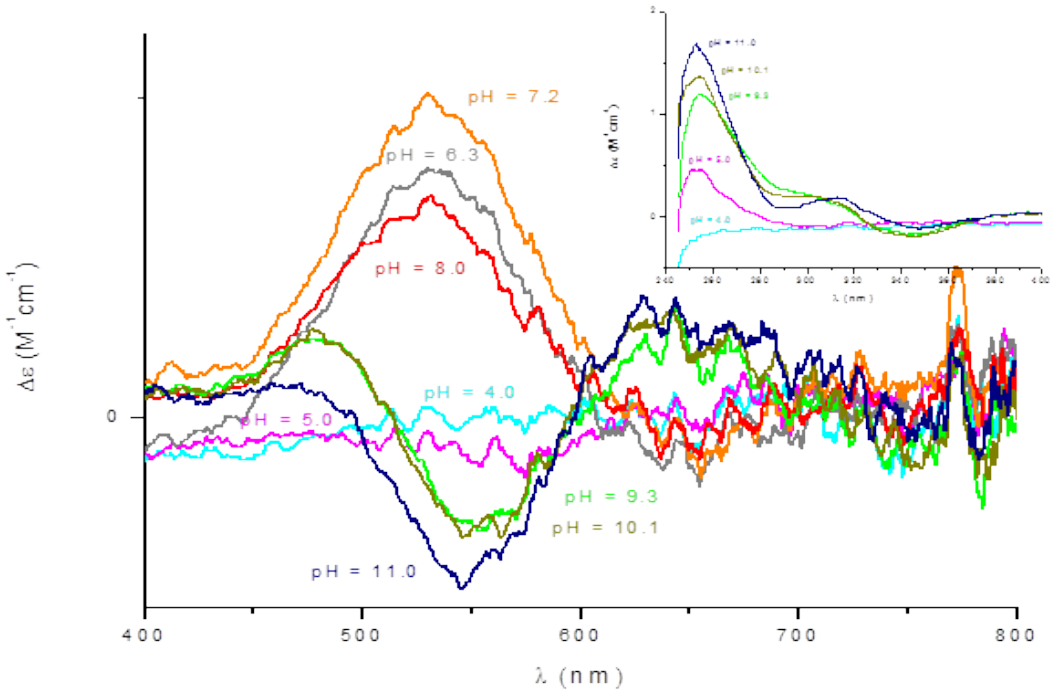

Fig. S4 CD spectra, at different pH values, for the system Cu(II)/pHpG. $C°_M = 4 \cdot 10^{-4}$ M; M/L molar ratio = 1:1.2.

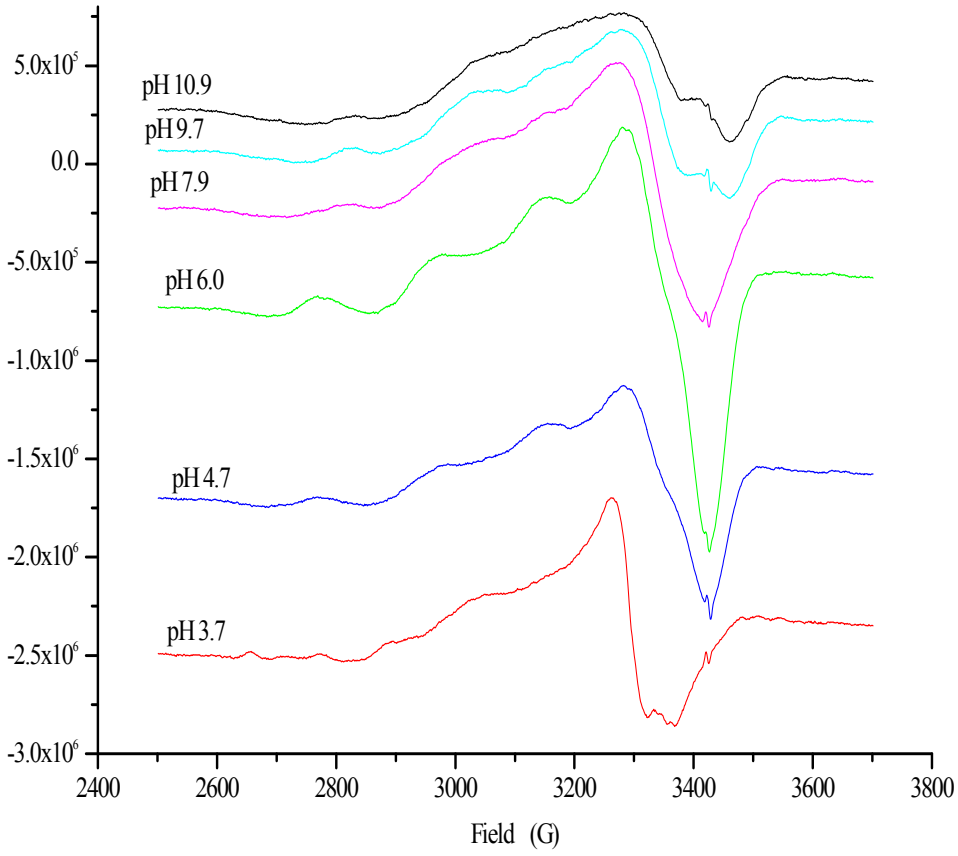

Fig. S5 EPR spectra, at different pH values, for the system Cu(II)/pHpG.$C°_M$ = $1 \cdot 10^{-3}$ M; M/L molar ratio = 1:1.2.

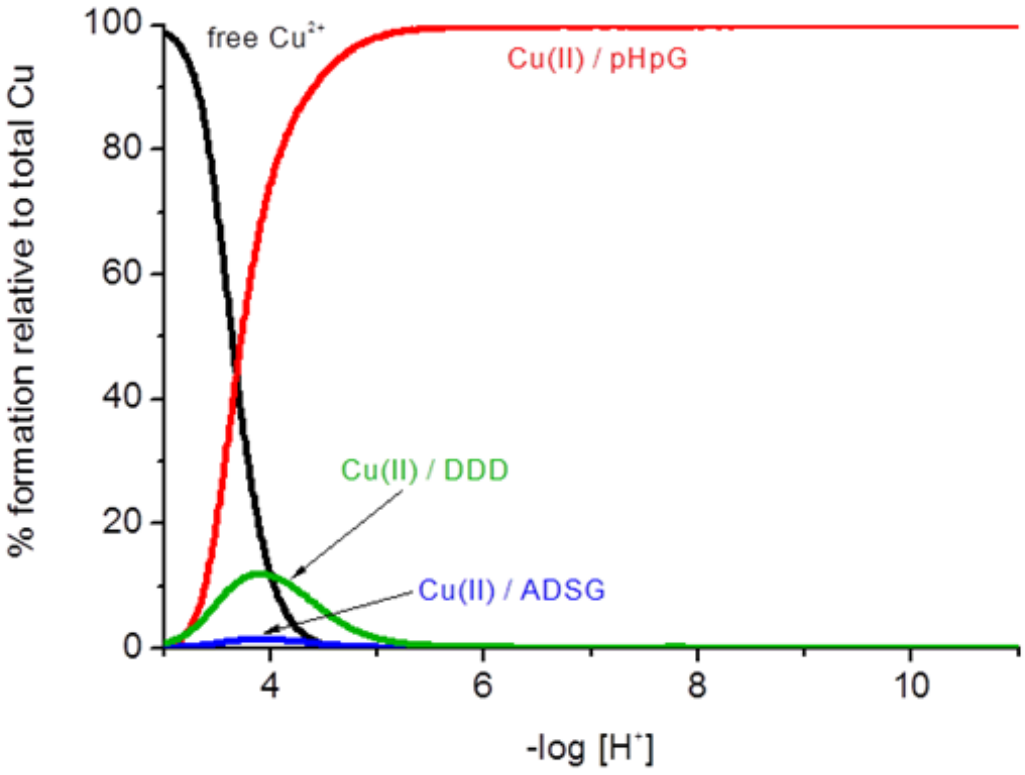

Fig. S6 Calculated competition diagram for a solution containing Cu(II), pHpG-1 and two peptides having Asp as second residue at their unprotected amino-terminus. The total concentration of each component is $1 \cdot 10^{-3}$ mol·dm^{-3}. Data from: L. D. Pettit and H. K. J. Powell, The IUPAC Stability Constants Database, Royal Society of Chemistry, London, 1992-2000.

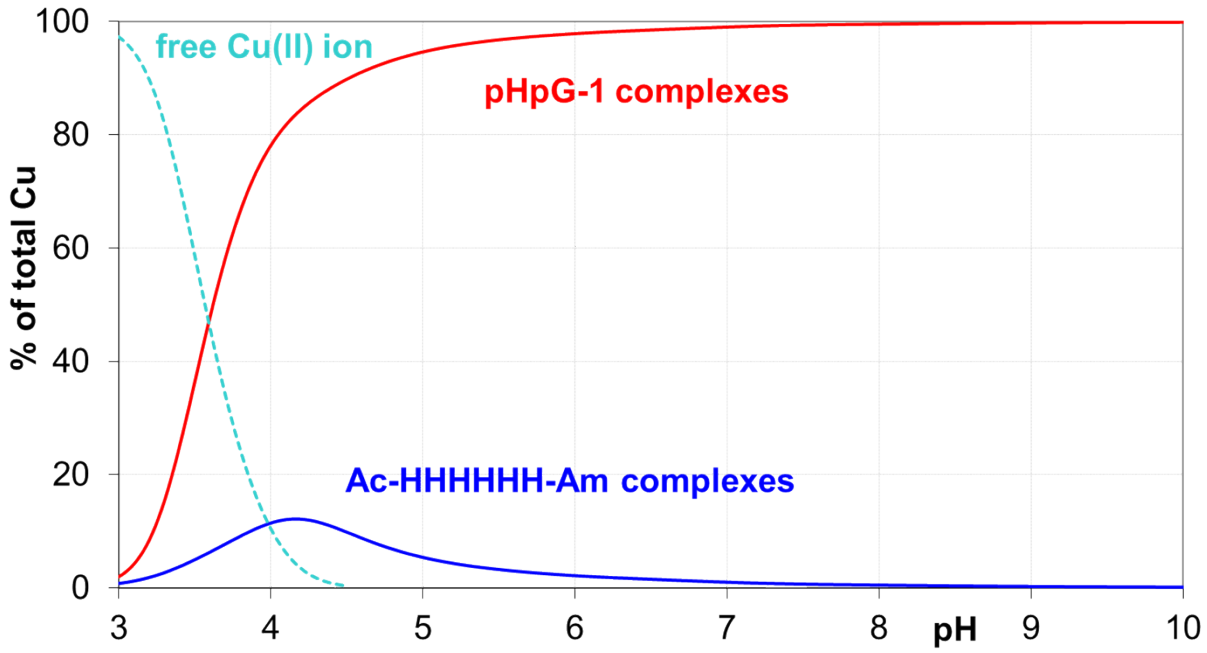

Fig. S7 Calculated competition diagram for a ternary solution containing the Cu(II), pHpG-1 and the protected peptide Ac-HHHHHH-Am. The total concentration of each component is $1 \cdot 10^{-3}$ mol·dm^{-3}. The equilibrium constants for the system Cu(II)/Ac-HHHHHH-Am are taken from J. Watly, E. Simonovsky, R. Wieczorek, N. Barbosa, Y. Miller, H. Kozlowski, Inorg. Chem. 2014, 53, 6675−6683.

Table S1 The conformational energies (computed using the GBMV calculations[1,2]) for the ten simulated constructed models for Cu^{2+}-$EDD(H)_9GV(G)_{10}$-Am complex.

Model	Conformational energy (kcal/mol)	Standard deviation (kcal/mol)
M1	-1021.74	0.69
M2	-986.10	1.25
M3	-1000.61	1.49
M4	-989.42	0.76
M5	-981.94	0.89
M6	-980.53	3.28
M7	-961.68	1.08
M8	-988.15	0.44
M9	-972.20	2.89
M10	-955.18	0.97

Lee, M. S.; Feig, M.; Salsbury, F. R.; Brooks, C. L., *J. Comp. Chem*., **2003**, 24, 1348.

[2] Lee, M. S.; Salsbury, F. R.; Brooks, C. L., *J. Chem. Phys*., **2002**, 116, 10606.