Supporting Information for

The effect of histidine, histamine, and imidazole on electrochemical properties of Cu(II) complexes of Aβ peptides containing His-2 and His-3 motifs

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Table S1. Electrochemical potential values related to the Cu(II) redox processes for 4N and 3N coordination modes of Cu(II)/Aβ complexes calculated based on DPV curves at 100 mM KNO_3

Cu(II) complexes	coordination	E (V) vs. Ag/AgCl	
		DPV	
		Cu(II)/Cu(I)	Cu(II)/Cu(III)
Cu(II)/Aβ$_{4-9}$	4N	n.d.	0.81(1)[a]
Cu(II)/Aβ$_{5-9}$	3N	-0.41(1)[a]	1.21(1)[a]
Cu(II)/Aβ$_{12-16}$	3N	-0.38(1)[ac]	1.25(1)[b]
	4N	n.d.	0.81(1)[a]

n.d. not detected

[a] based on the measurements at pH 7.4

[b] based on the measurements at pH 3.8-4.5

[c] based on the measurements at pH 4.5-5.0

Table S2 Species distribution for 0.45 mM Cu(II) and 0.50 mM $A\beta_{12-16}$ based on literature potentiometric data[1]

pH	Cu(II) molar fraction					
	Cu(II) not bound to $A\beta_{12-16}$	CuHL	CuL	$CuH_{-1}L$	$CuH_{-2}L$	$CuL+CuH_{-1}L+Cu_{H-2}L$
		3N	4N	4N	4N	4N total
3.6	**76.3%**	**23.0%**	0.8%	0.0%	0.0%	**0.8%**
3.8	**52.3%**	**45.3%**	2.4%	0.0%	0.0%	**2.4%**
4.0	**29.6%**	**65.0%**	5.4%	0.0%	0.0%	**5.4%**
4.5	**3.2%**	**76.5%**	20.3%	0.0%	0.0%	**20.3%**
5.0	**0.1%**	**54.3%**	45.4%	0.2%	0.0%	**45.6%**
6.0	**0.0%**	**10.3%**	86.4%	3.3%	0.0%	**89.7%**
7.4	**0.0%**	**0.2%**	51.0%	48.7%	0.1%	**99.8%**
8.0	**0.0%**	**0.0%**	20.7%	78.6%	0.7%	**100.0%**
10.0	**0.0%**	**0.0%**	0.1%	53.4%	46.5%	**100.0%**

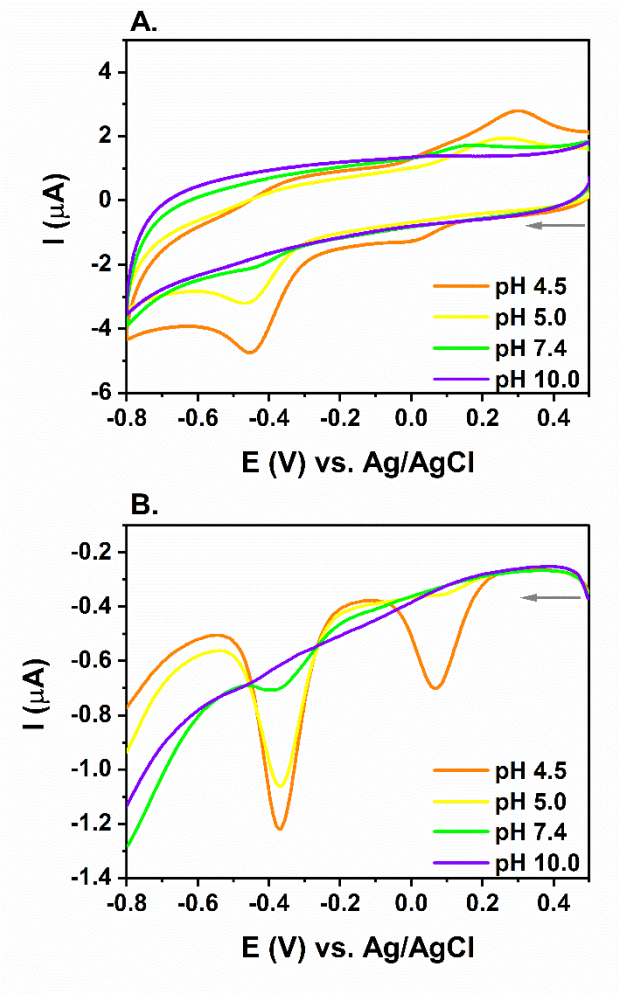

Fig. S1 CV (A) and DPV (B) curves recorded scanning towards more negative potential values for 0.45 mM Cu(II) and 0.50 mM $A\beta_{12-16}$ at selected pH values in 100 mM KNO_3.

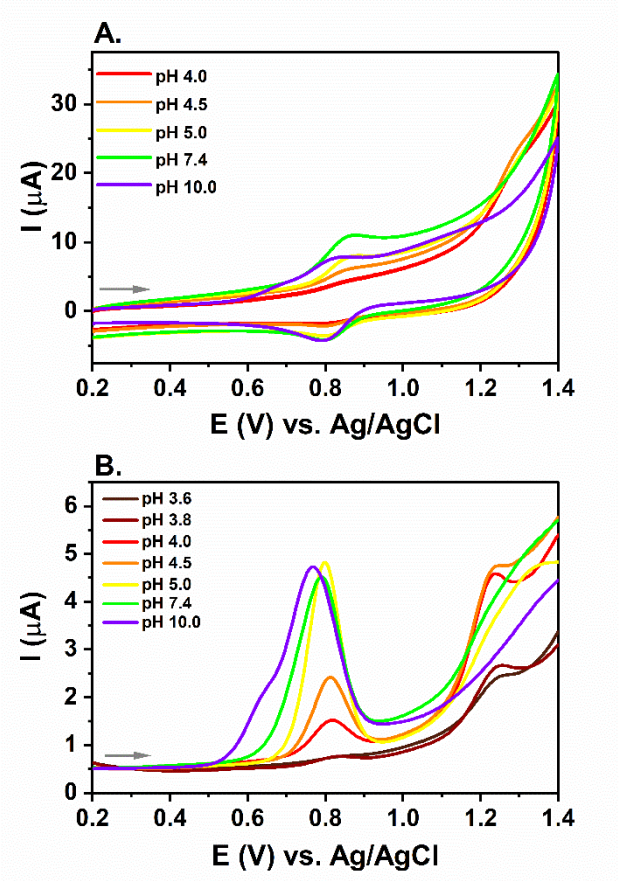

Fig. S2 CV (A) and DPV (B) curves recorded scanning towards more positive potential values for 0.45 mM Cu(II) and 0.50 mM $A\beta_{12\text{-}16}$ at selected pH values in 100 mM KNO_3.

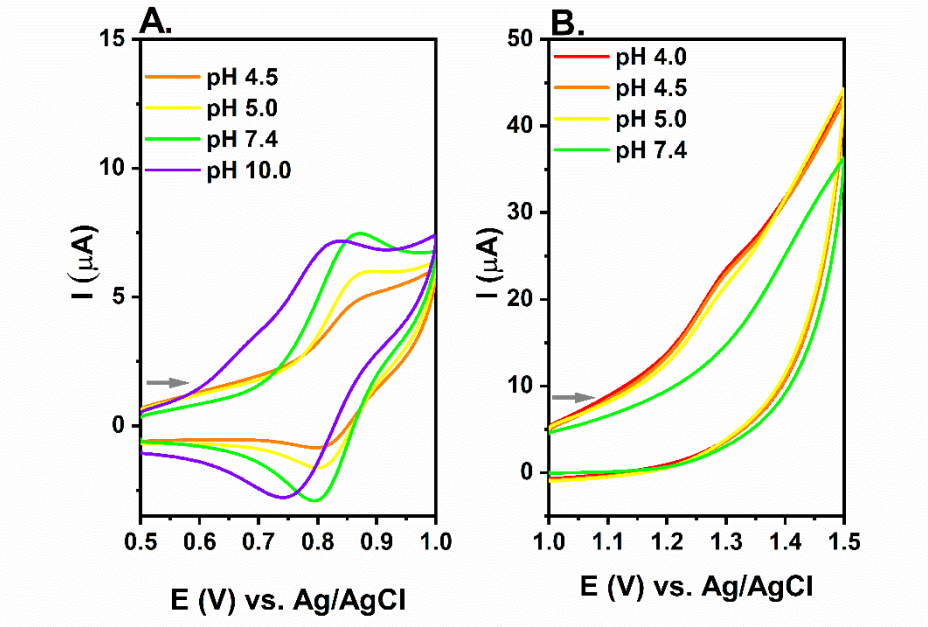

Fig. S3 CV curves recorded scanning towards more positive potential values in the range 0.5-1.0 V vs. Ag/AgCl (A) and 1.0-1.5 V vs. Ag/AgCl (B) for 0.45 mM Cu(II) and 0.50 mM $A\beta_{12\text{-}16}$ at selected pH values in 100 mM KNO_3.

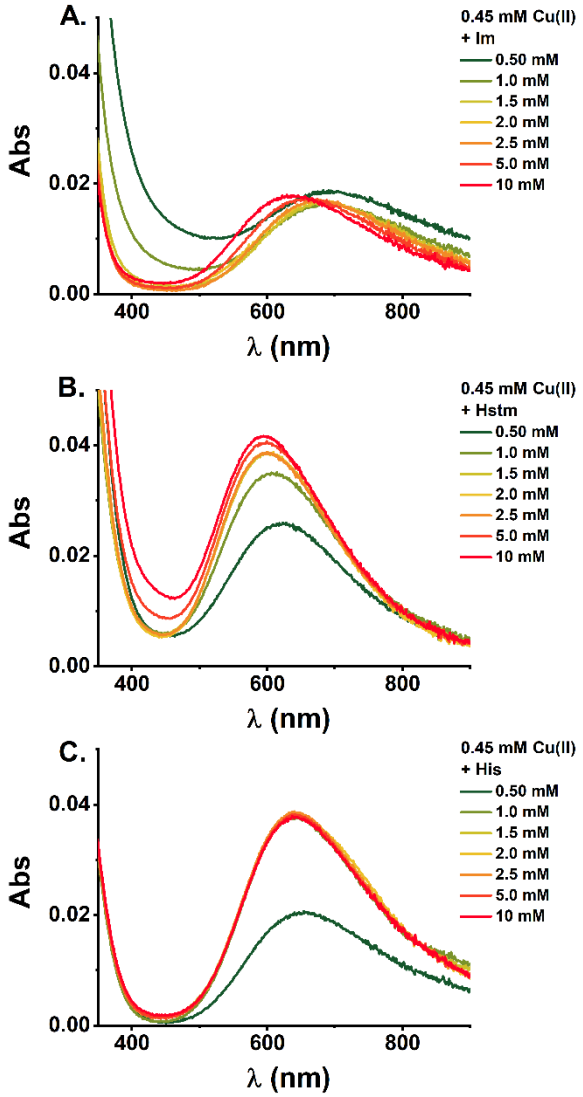

Fig. S4 UV-vis spectra of solutions containing 0.45 mM Cu(II) and various concentrations of imidazole (A), histamine (B), and histidine (C) in the range 0.50 mM – 10 mM coded with the color gradient from green (0.50 mM LMW) to red (10 mM LMW) and registered at pH 7.4. The total concentrations of LMW substances are given in the legend.

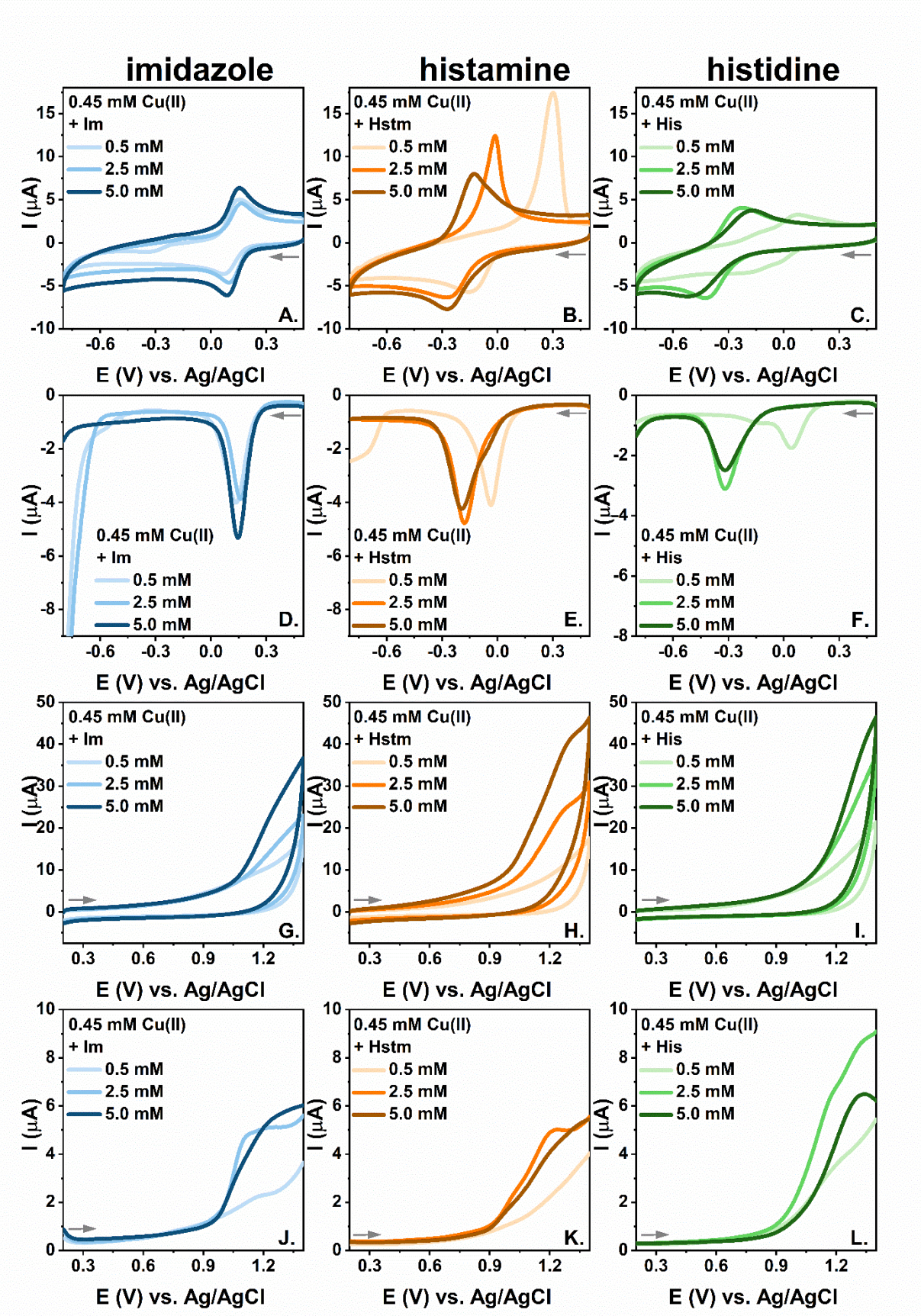

Fig. S5 CV (A-C, G-I) and DPV (D-F, J-L) curves recorded scanning towards more negative (A-F) or more positive (G-L) potential values for 0.45 mM Cu(II) and 0.50-5.0 mM imidazole (Im), histamine (Hstm), and histidine (His) in 100 mM KNO_3, pH 7.4.

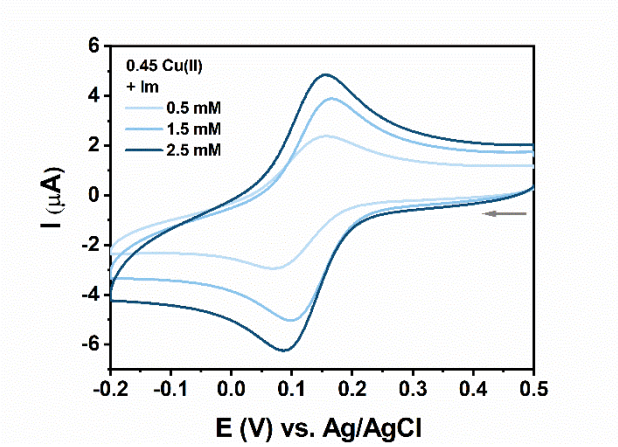

Fig. S6 CV curves recorded scanning towards more negative (potential values for 0.45 mM Cu(II) and 0.50-5.0 mM imidazole (Im) in 100 mM KNO_3, pH 7.4 in the narrowed potential range 0.5-(-0.2) V vs. Ag/AgCl, v= 100 mV/s.

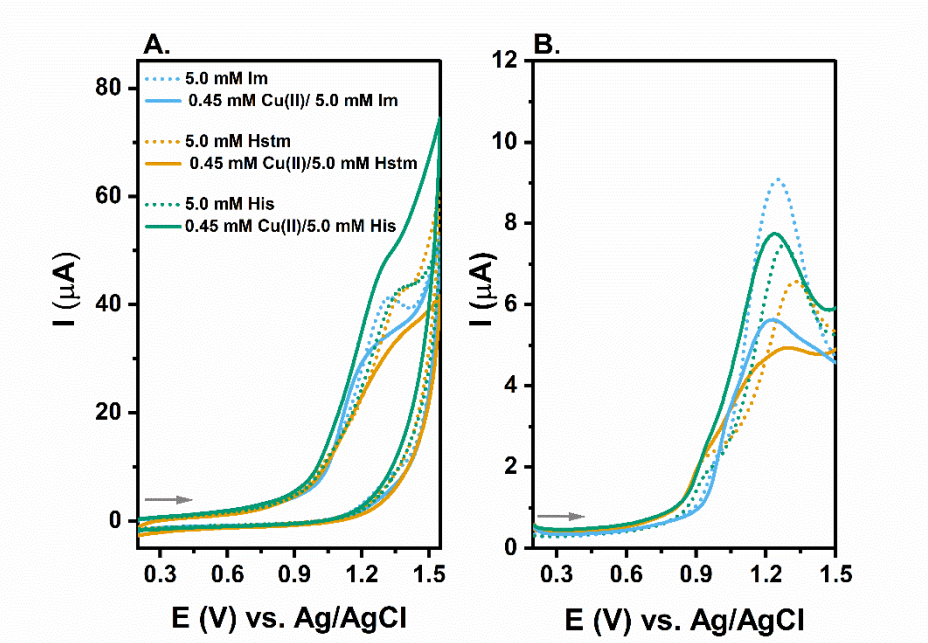

Fig. S7 CV (A) and DPV (B) curves recorded scanning towards more positive potential values for 5.0 mM histidine (His), histamine (Hstm), and imidazole (Im) with (solid lines) or without (dotted lines) 0.45 mM Cu(II) in 100 mM KNO_3, pH 7.4.

Table S3 Theoretical distribution of Cu(II) ions in the ternary systems Cu(II)/Aβ/low molecular weight (LMW) substances assuming exclusively the formation of binary complexes Cu(II)/Aβ and Cu(II)/LMW for the concentrations given in the table calculated based on the potentiometric complex formation constants given in literature for Cu(II)/$A\beta_{4-9}$,[1] Cu(II)/$A\beta_{5-9}$,[2] Cu(II)/$A\beta_{12-16}$,[1] Cu(II)/imidazole (Im),[3] Cu(II)/histamine (Hstm),[4] and Cu(II)/histidine (His).[5]

$C_{Cu(II)}$	$C_{A\beta}$	C_{LMW}	$x_{Cu(II)}$ (%)	
			Cu(II)/Aβ	Cu(II)/LMW
0.45 mM	0.50 mM $A\beta_{4-9}$	0.50 mM Im	>99.9%	<0.1%
		2.5 mM Im	>99.9%	<0.1%
		5.0 mM Im	**>99.9%**	**<0.1%**
		30.0 mM Im	>99.9%	<0.1%
		0.50 mM Hstm	>99.9%	<0.1%
		2.5 mM Hstm	>99.9%	<0.1%
		5.0 mM Hstm	**99.9%**	**0.1%**
		30 mM Hstm	98.3%	1,7%
		0.50 mM His	98.8%	1.2%
		2.5 mM His	87.1%	12.9%
		5.0 mM His	**72.9%**	**27.1%**
		30 mM His	15.2%	84.8%
	0.50 mM $A\beta_{5-9}$	0.50 mM Im	>99.9%	<0.1%
		2.5 mM Im	>99.9%	<0.1%
		5.0 mM Im	**>99.9%**	**<0.1%**
		30 mM Im	**>99.9%**	**<0.1%**
		0.50 mM Hstm	>99.9%	<0.1%
		2.5 mM Hstm	99.6%	0.4%
		5.0 mM Hstm	**98.7%**	**1.3%**
		30 mM Hstm	83.3%	16.7%
		0.50 mM His	89.2%	10.8%
		2.5 mM His	48.2%	51.8%
		5.0 mM His	**22.7%**	**77.3%**
		30 mM His	0.8%	99.2%
	0.50 mM $A\beta_{12-16}$	0.50 mM Im	>99.9%	<0.1%
		2.5 mM Im	>99.9%	<0.1%
		5.0 mM Im	**>99.9%**	**<0.1%**
		30 mM Im	>99.9%	<0.1%
		0.50 mM Hstm	>99.9%	<0.1%
		2.5 mM Hstm	>99.9%	<0.1%
		5.0 mM Hstm	**99.9%**	**0.1%**
		30 mM Hstm	97.7%	2.3%
		0.50 mM His	98.4%	1.6%
		2.5 mM His	84.2%	15.8%
		5.0 mM His	**68.1%**	**31.8%**
		30 mM His	11.5%	88.5%

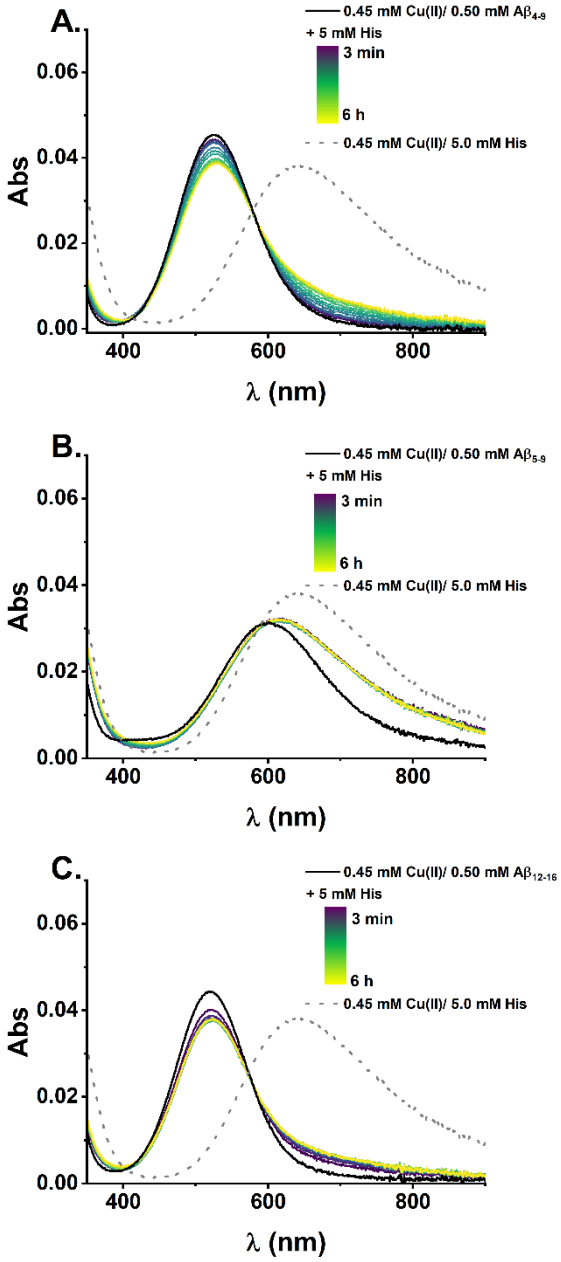

Fig. S8 UV-vis spectra registered upon the addition of histidine to 0.45 mM Cu(II)/0.50 mM $A\beta_{4-9}$ (A), $A\beta_{5-9}$ (B), or $A\beta_{12-16}$ (C), reaching the final histidine concentration of the histidine in the cuvette of 5 mM and pH 7.4. The spectra are codded in the gradient colors from violet (3 min after the His addition) to yellow (6 h after the His addition). The black line refers to the initial spectrum of 0.45 mM Cu(II)/0.50 mM Aβ peptides, whereas the dashed grey line refers to the control spectrum of 0.45 mM Cu(II)/5.0 mM His.

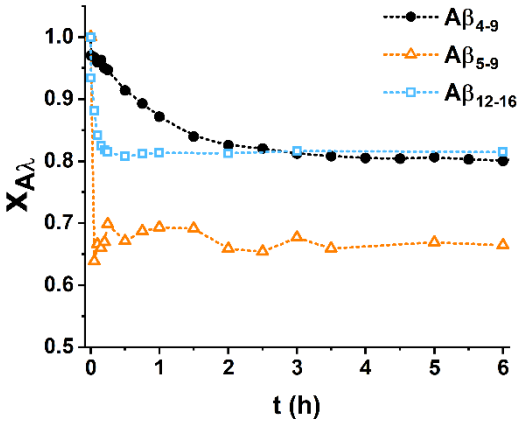

Fig. S9 The normalized changes of absorbance at 525 nm ($A\beta_{4-9}$), at 640 nm ($A\beta_{5-9}$), and at 520 nm ($A\beta_{12-16}$) upon the addition of histidine to 0.45 mM Cu(II)/0.50 mM Aβ reaching the final histidine concentration of the histidine in the cuvette of 5 mM and pH 7.4. The initial absorbance values at the given wavelength for 0.45 mM Cu(II)/0.50 mM Aβ and the control sample of 0.45 mM Cu(II)/5.0 mM His were used as the reference points.

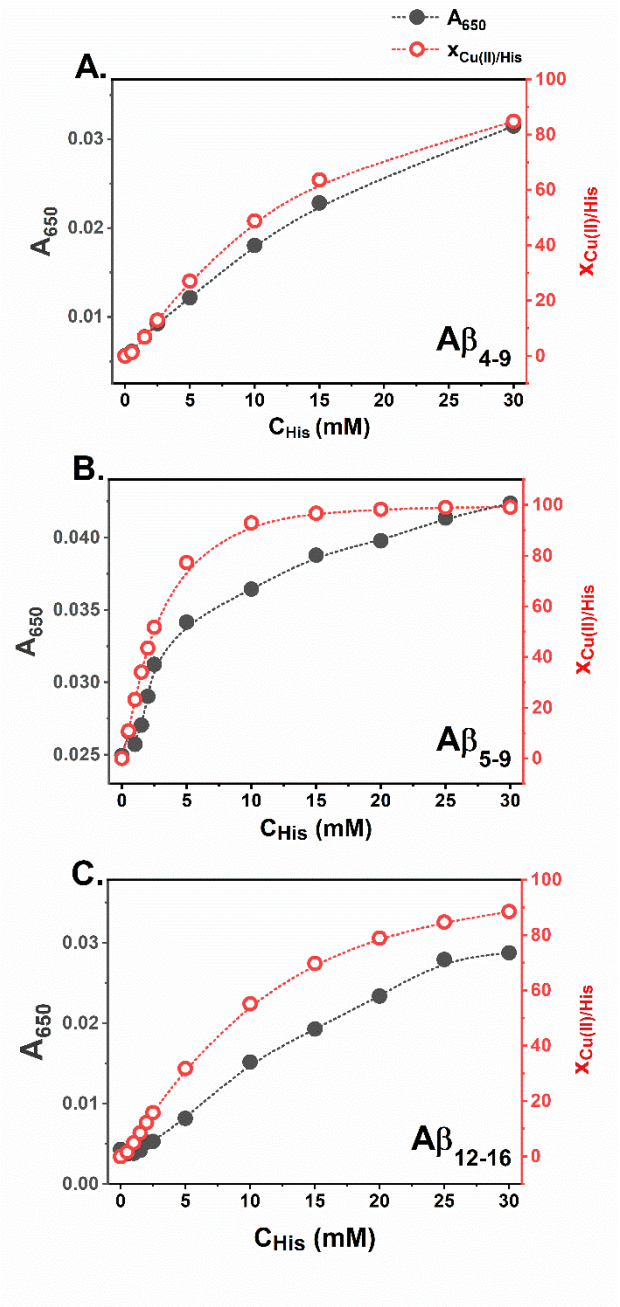

Fig. S10 The comparison of changes of absorbance at 650 nm and the theoretical molar fraction of Cu(II)/His complexes during the titration of 0.45 mM Cu(II)/0.50 mM Aβ peptides, $A\beta_{4-9}$ (A), $A\beta_{5-9}$ (B), $A\beta_{12-16}$ (C), with histidine at pH 7.4 based on the UV-vis spectra in Fig. 3. The A_{650} values at the level of 100% $x_{Cu(II)/His}$ refer to the absorbance at 650 nm expected for the binding of 100% Cu(II) ions by histidine, considering the baseline signal in the respective experiment.

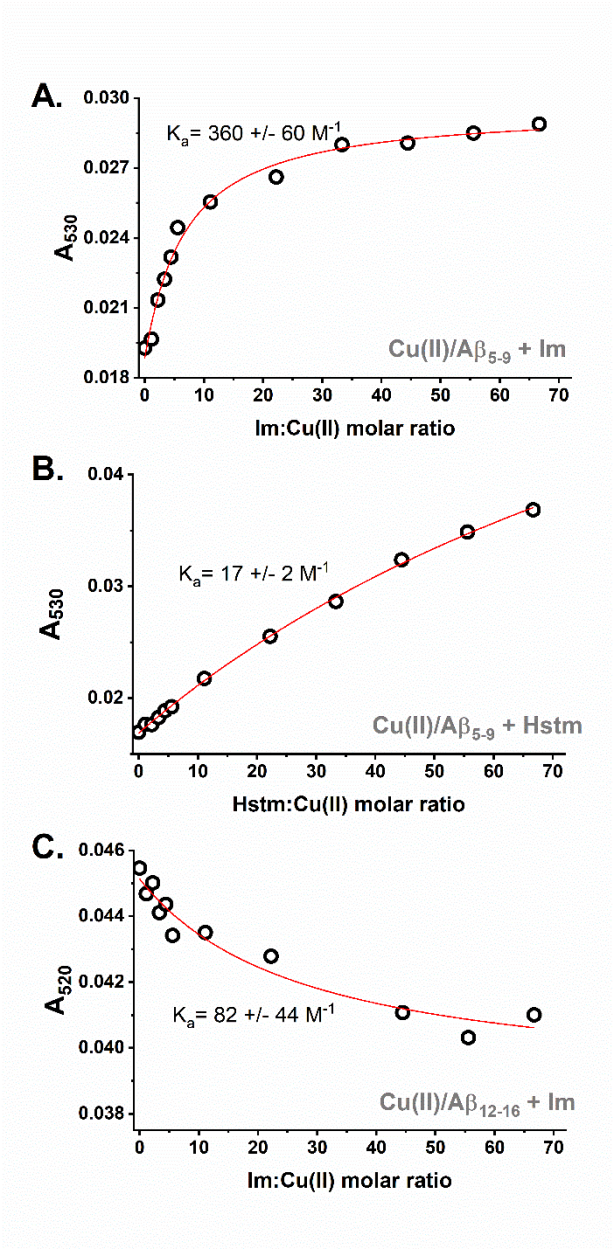

Fig. S11 The changes of d-d band absorbance at wavelengths characteristic for the formation of ternary complexes during the titrations of Cu(II)/Aβ_{5-9} with imidazole (A), Cu(II)/Aβ_{5-9} with histamine (B), and Cu(II)/Aβ_{12-16} with imidazole (C). The experiments were performed for 0.45 mM Cu(II)/0.50 mM Aβ at pH 7.4.

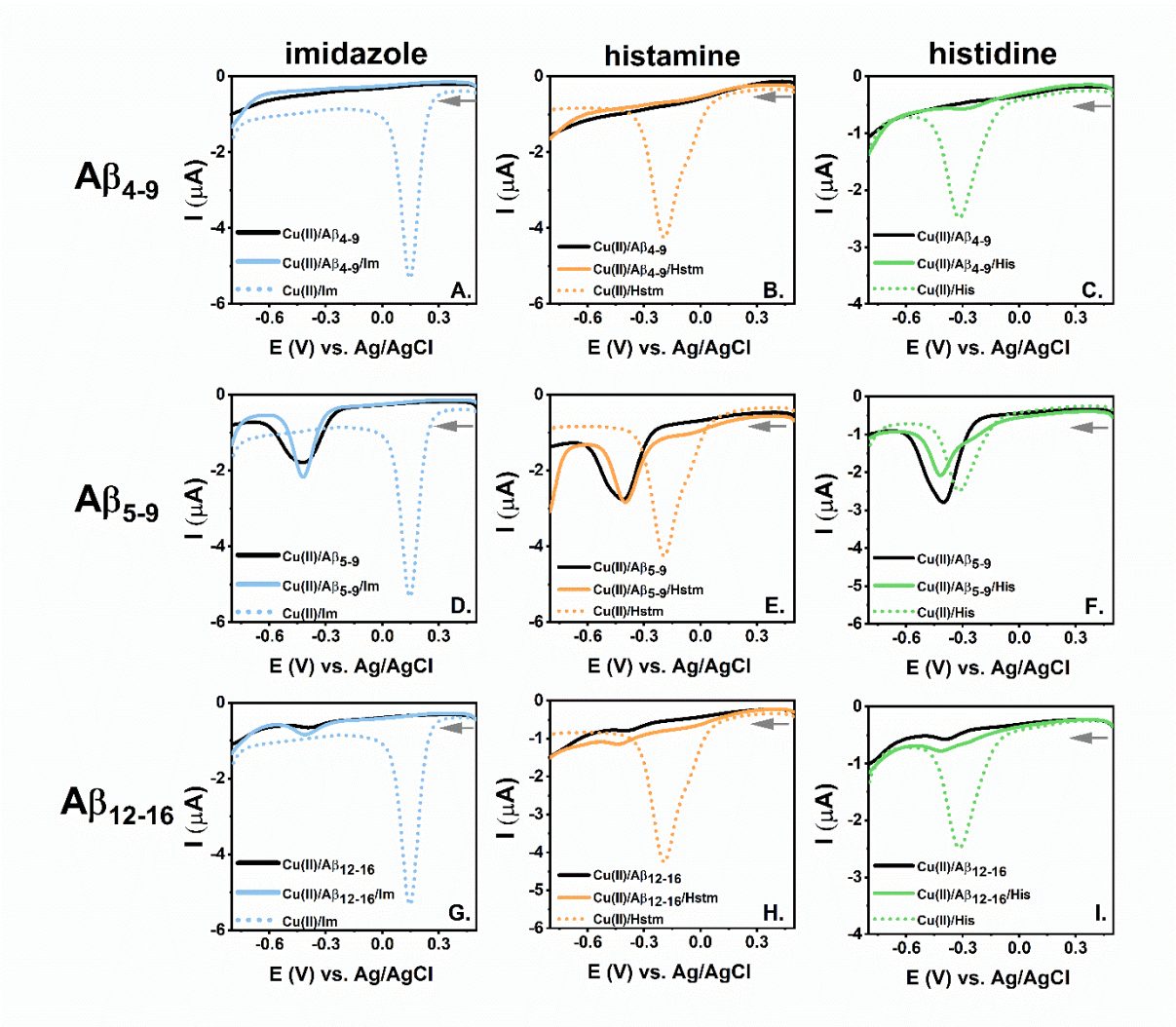

Fig. S12 DPV curves recorded scanning towards more negative potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), with 5.0 mM LMW substances, imidazole (A, D, G), histamine (B, E, H), and histidine (C, F, I) (blue, orange or green solid lines, respectively). For comparison, the curves for the corresponding binary systems containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) and 0.45 mM Cu(II)/ 5.00 imidazole (Im), histamine (Hstm), and histidine (His) (blue, orange or green dotted lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

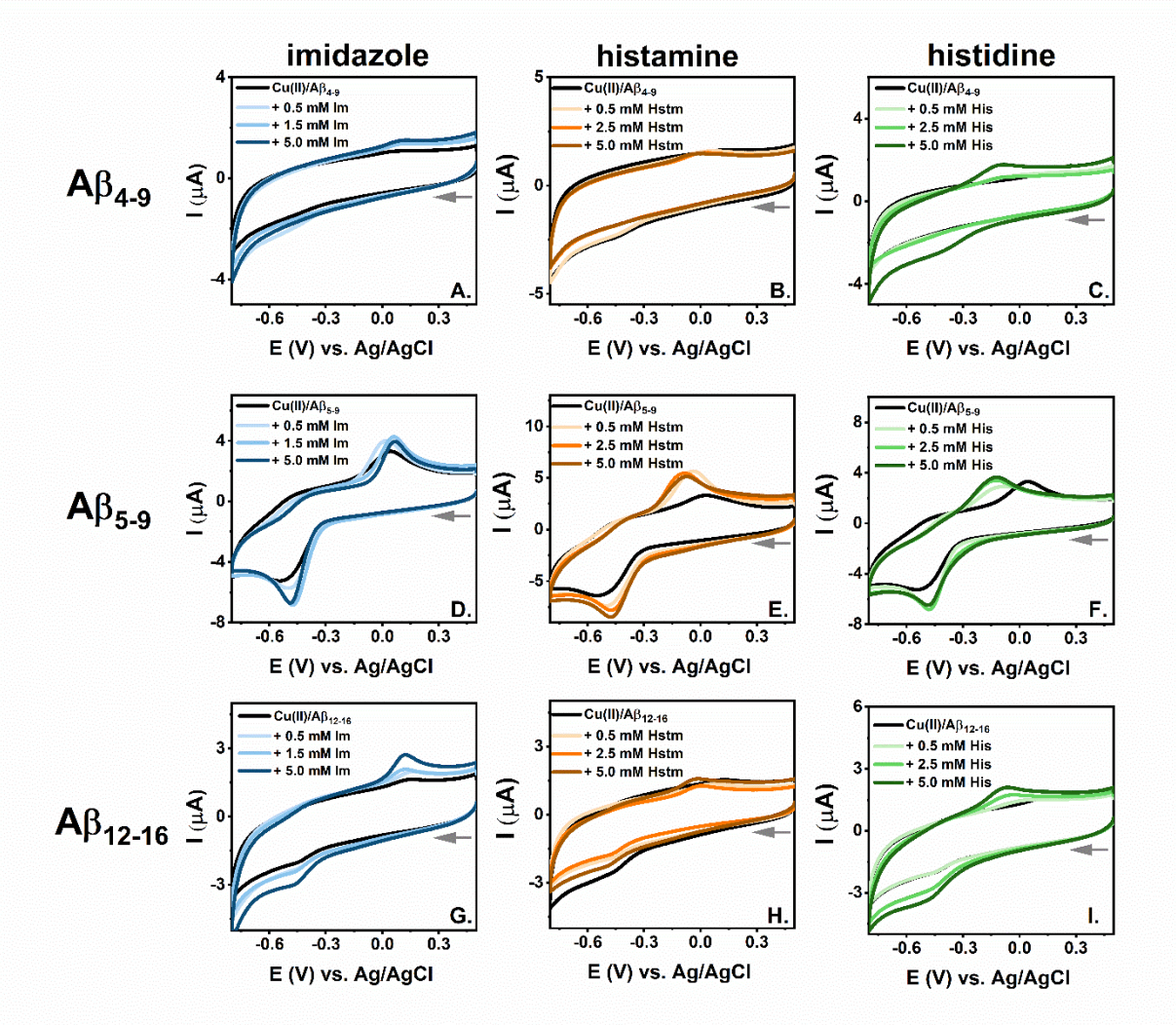

Fig. S13 CV curves recorded scanning towards more negative potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), and 0.5, 1.5, 5.0 mM imidazole (Im) (A, D, G) or 0.5, 2.5, 5.0 mM histamine (Hstm) (B, E, H), and histidine (His) (C, F, I). For comparison, the curves for the corresponding binary system containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

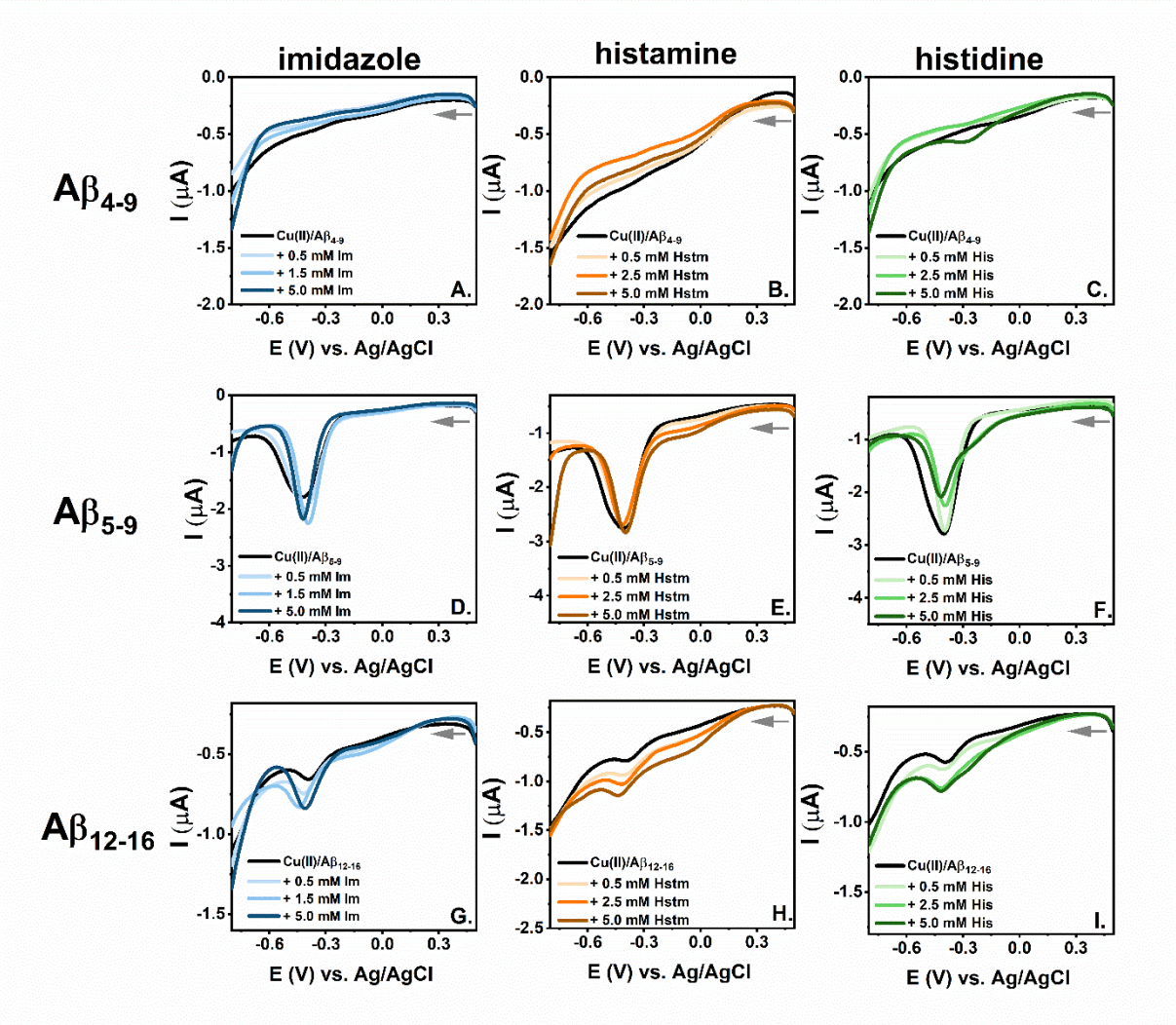

Fig. S14 DPV curves recorded scanning towards more negative potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), and 0.5, 1.5, 5.0 mM imidazole (Im) (A, D, G) or 0.5, 2.5, 5.0 mM histamine (Hstm) (B, E, H), and histidine (His) (C, F, I). For comparison, the curves for the corresponding binary system containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

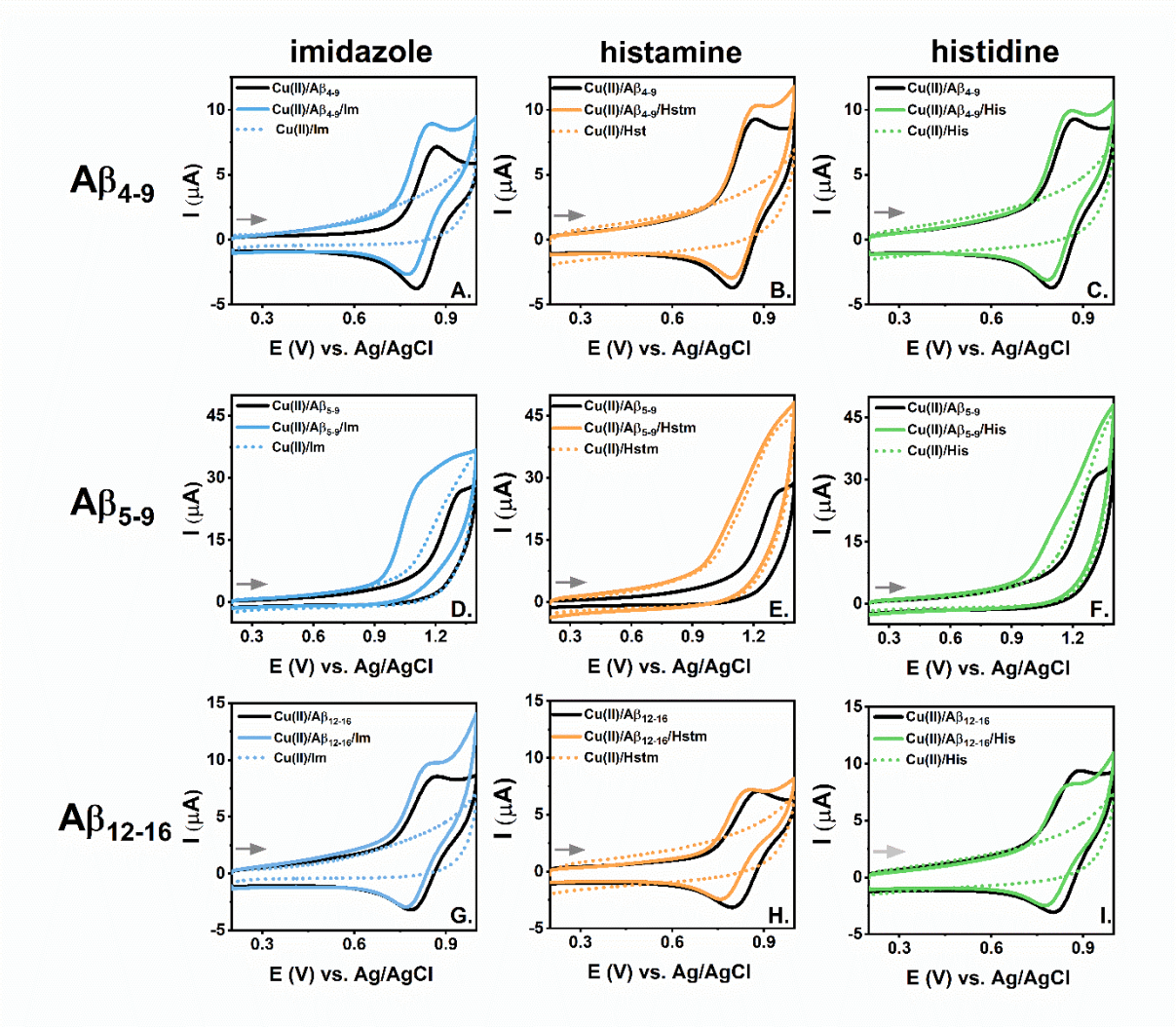

Fig. S15 CV curves recorded scanning towards more positive potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), with 5.0 mM LMW substances, imidazole (A, D, G), histamine (B, E, H), and histidine (C, F, I) (blue, orange or green solid lines, respectively). For comparison, the curves for the corresponding binary systems containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) and 0.45 mM Cu(II)/5.00 mM imidazole (Im), histamine (Hstm), and histidine (His) (blue, orange or green dotted lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

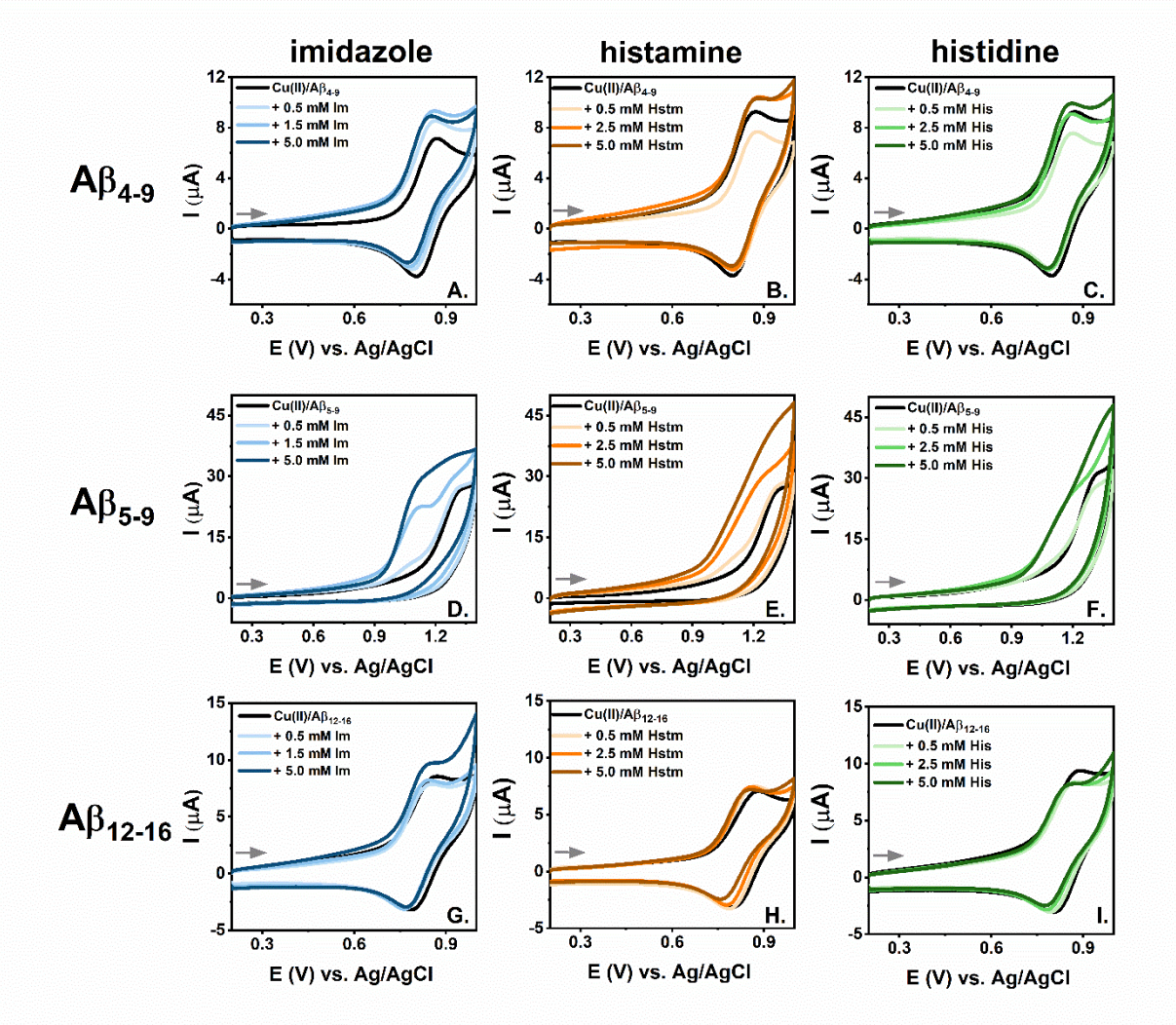

Fig. S16 CV curves recorded scanning towards more positive potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), and 0.5, 1.5, 5.0 mM imidazole (Im) (A, D, G) or 0.5, 2.5, 5.0 mM histamine (Hstm) (B, E, H), and histidine (His) (C, F, I). For comparison, the curves for the corresponding binary system containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

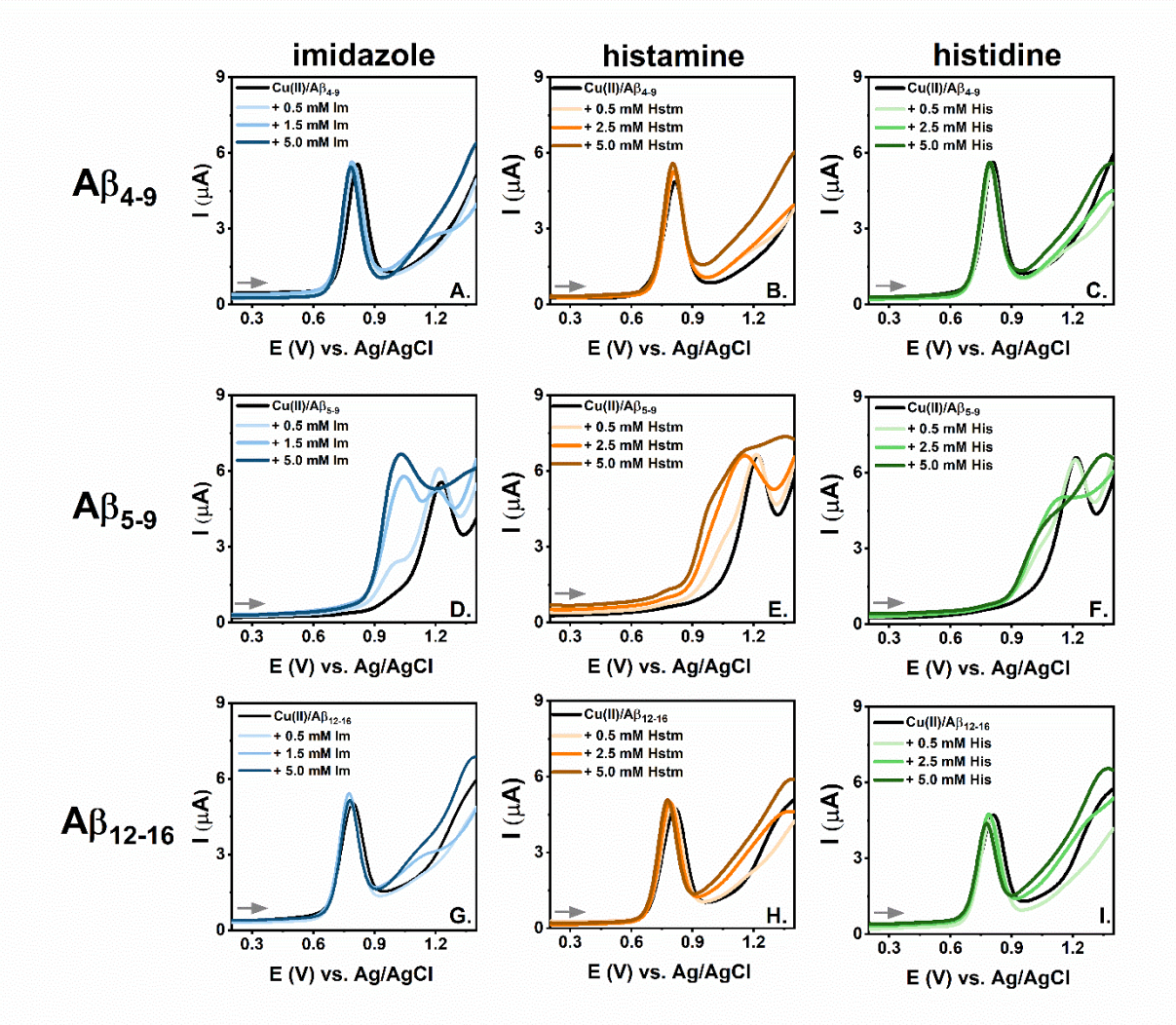

Fig. S17 DPV curves recorded scanning towards more positive potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM Aβ peptides, $A\beta_{4-9}$ (A-C), $A\beta_{5-9}$ (D-F), and $A\beta_{12-16}$ (G-I), and 0.5, 1.5, 5.0 mM imidazole (Im) (A, D, G) or 0.5, 2.5, 5.0 mM histamine (Hstm) (B, E, H), and histidine (His) (C, F, I). For comparison, the curves for the corresponding binary system containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

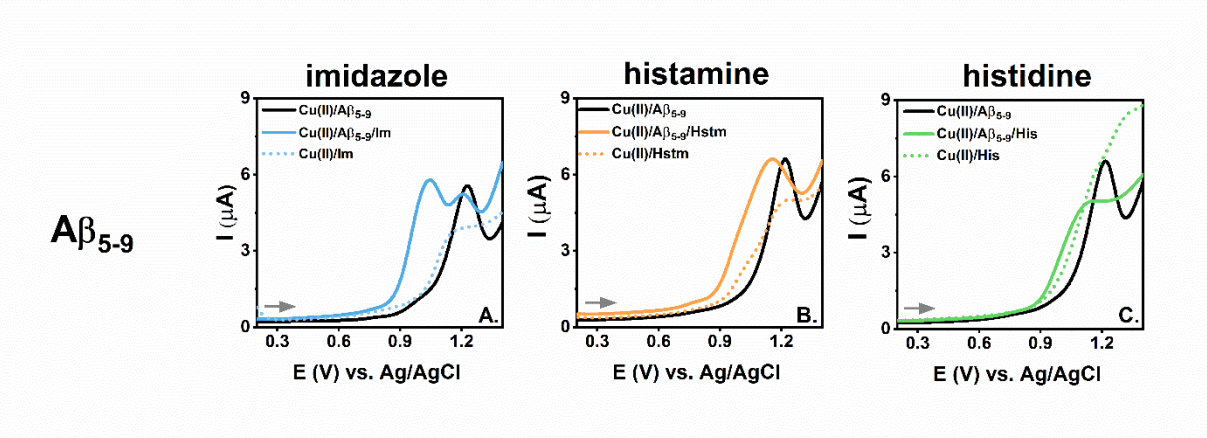

Fig. S18 DPV curves recorded scanning towards more positive potential values for ternary systems containing 0.45 mM Cu(II), 0.50 mM $A\beta_{5-9}$ peptide and (A) 1.5 mM imidazole (Im), (B) 2.5 mM histamine (Hstm) or (C) 2.5 mM histidine (His) (blue, orange or green solid lines, respectively). For comparison, the curves for the corresponding binary systems containing 0.45 mM Cu(II)/0.50 mM Aβ peptides (black lines) and 0.45 mM Cu(II)/ 1.5 mM imidazole (Im), 2.5 mM histamine (Hstm), and 2.5 mM histidine (His) (blue, orange or green dotted lines) are shown. The measurements were performed in 100 mM KNO_3, pH 7.4.

References

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