Supporting Information Section

Revisiting Cu(II) Bound Amyloid-β40 and Amyloid-β42 Alloforms at The Atomic Level with Dynamics: Varying Coordination Chemistries

Orkid Coskuner-Weber*

National Institute of Standards and Technology, Biochemical Reference Data Division, 100 Bureau Drive, Gaithersburg, Maryland 20899 USA, Turkish-German University, Molecular Biotechnology, Şahinkaya Caddesi No. 86, Beykoz, Istanbul 34820 Turkey, The University of Texas at San Antonio, Department of Chemistry, One UTSA Drive, San Antonio, Texas

*Orkid Coskuner-Weber, E-mail: weber@tau.edu.tr

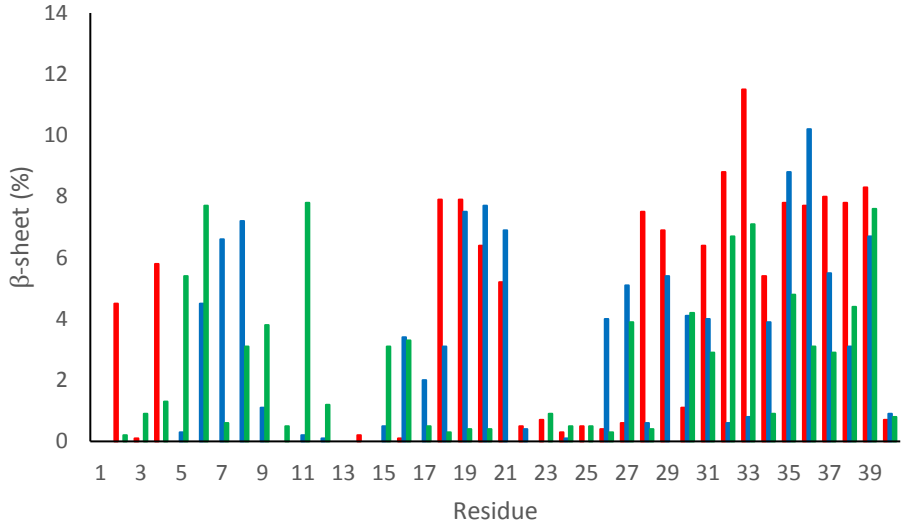


Figure S1A. The β-sheet abundance per residue of the Cu(II):His_3Asp1-Aβ40 (red), Cu(II):His_3Glu11-Aβ40 (blue), and Cu(II):His_3Tyr10-Aβ40 (green) structures in aqueous solution using Amber FF14SB parameters and the TIP5P model for water.

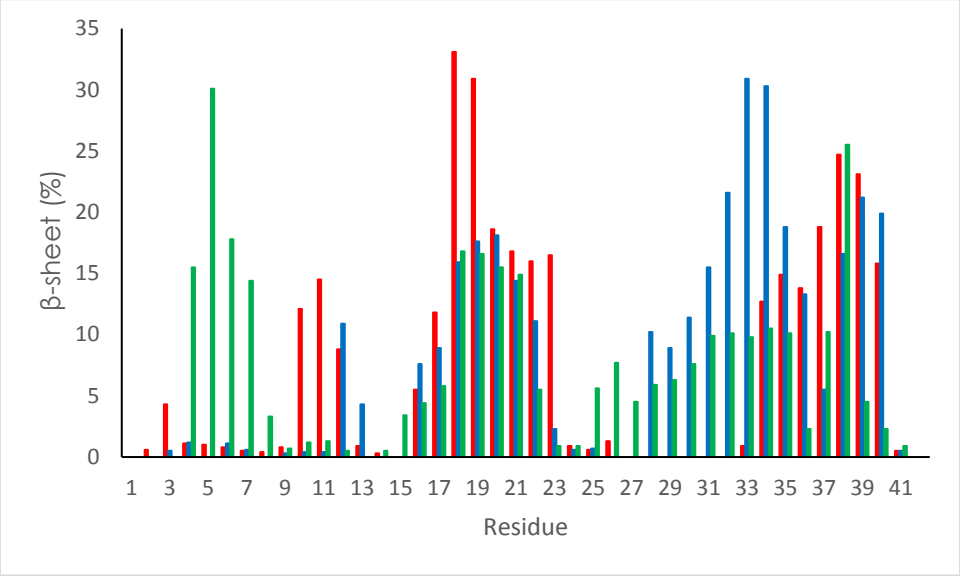


Figure S1B. The β-sheet abundance per residue of the Cu(II):His_3Asp1-Aβ42 (red), Cu(II):His_3Glu11-Aβ42 (blue), and Cu(II):His_3Tyr10-Aβ42 (green) structures in aqueous solution using Amber FF14SB parameters and the TIP5P model for water.

A comparison of residual secondary structure abundances of the Cu(II)-bound Aβ40 peptides using implicit and explicit water models reveals that the β-sheet structure formation in the C-terminal region of Cu(II):His_3Asp1-Aβ40 is more pronounced using an explicit water model. A similar trend is noticed for the N- and C-terminal regions of Cu(II):His_3Glu11-Aβ40. Furthermore, more abundant β-sheet structure is adopted in the N-terminal, mid-domain and C-terminal regions of Cu(II):His_3Tyr10-Aβ40 utilizing an explicit water model rather than an implicit model for water. More pronounced β-sheet formation is obtained in the mid-domian and C-terminal regions of Cu(II):His_3Tyr10-Aβ42 using the modified TIP5P model for water. Slightly more abundant β-sheet formation is detected in the N-terminal region of Cu(II):His_3Asp1-Aβ42 using the modified TIP5P model for water. The same trend is obtained fort he mid-domain and C-terminal regions of Cu(II):His_3Glu11-Aβ42.

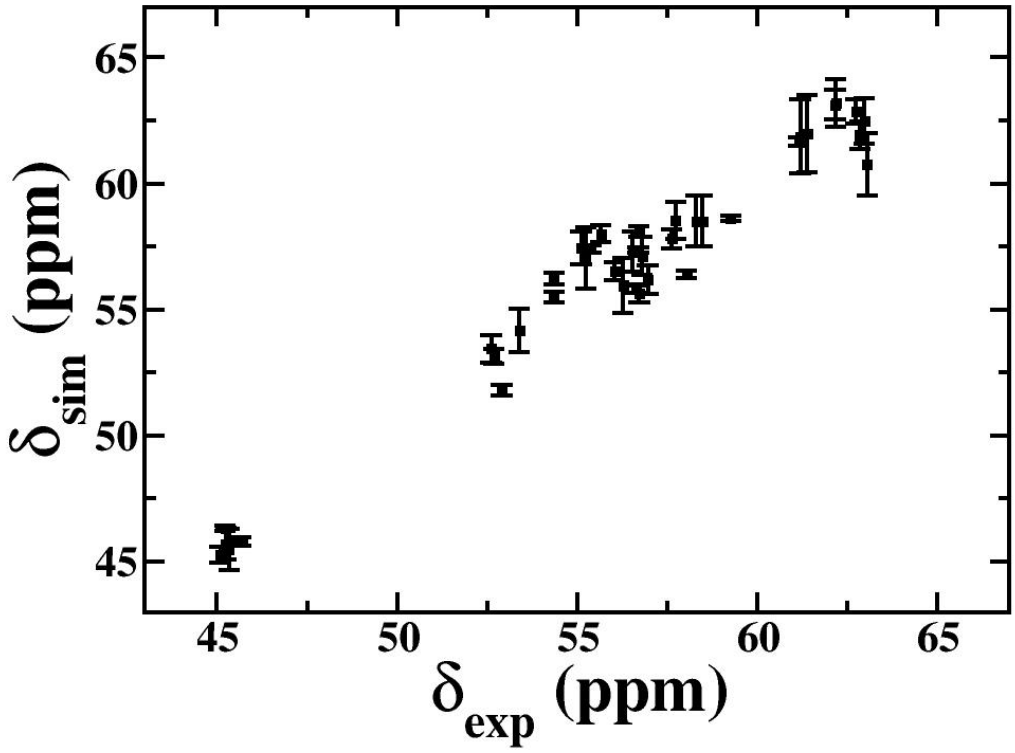


Figure S2A. Correlation between the Cα chemical shift values for Aβ42 at 280 K using the structures from our simulations (δsim.) and experimental (δexp.) chemical shift values provided by Dr. Michael Zagorski (CWRU). The computed Pearson correlation coefficient is 0.980.

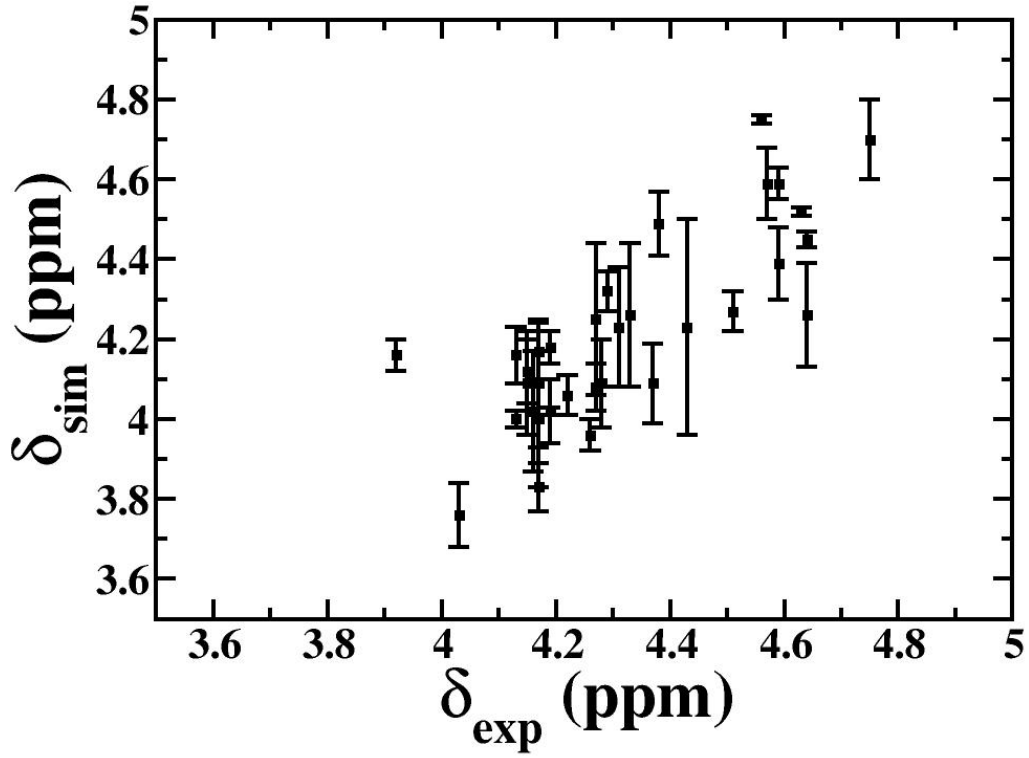
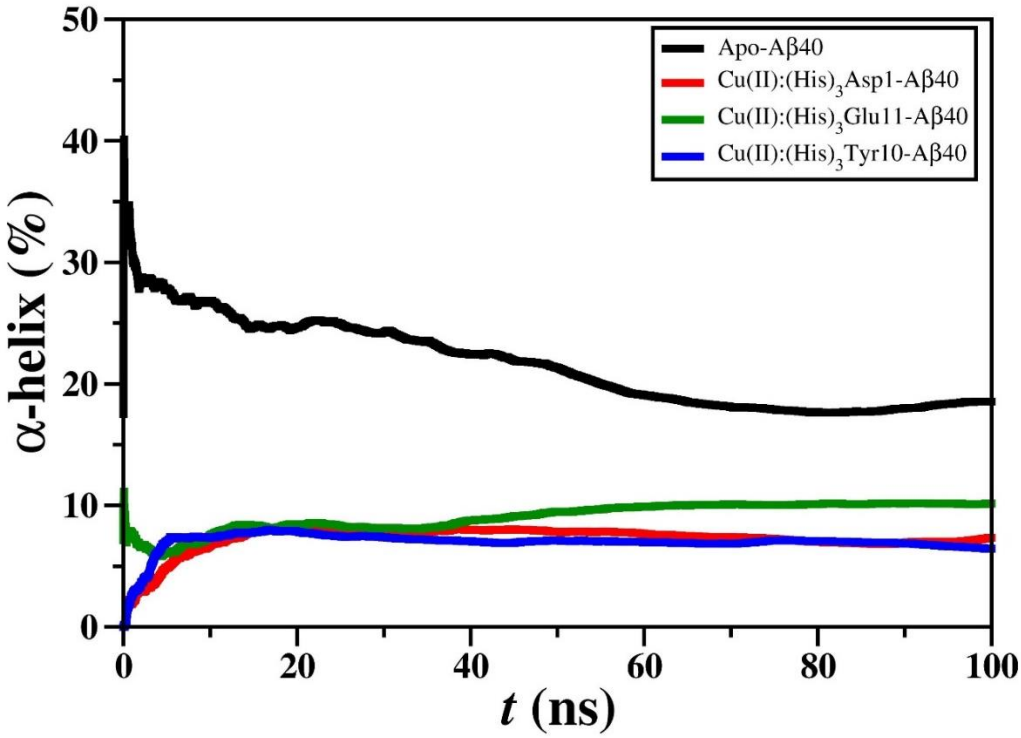
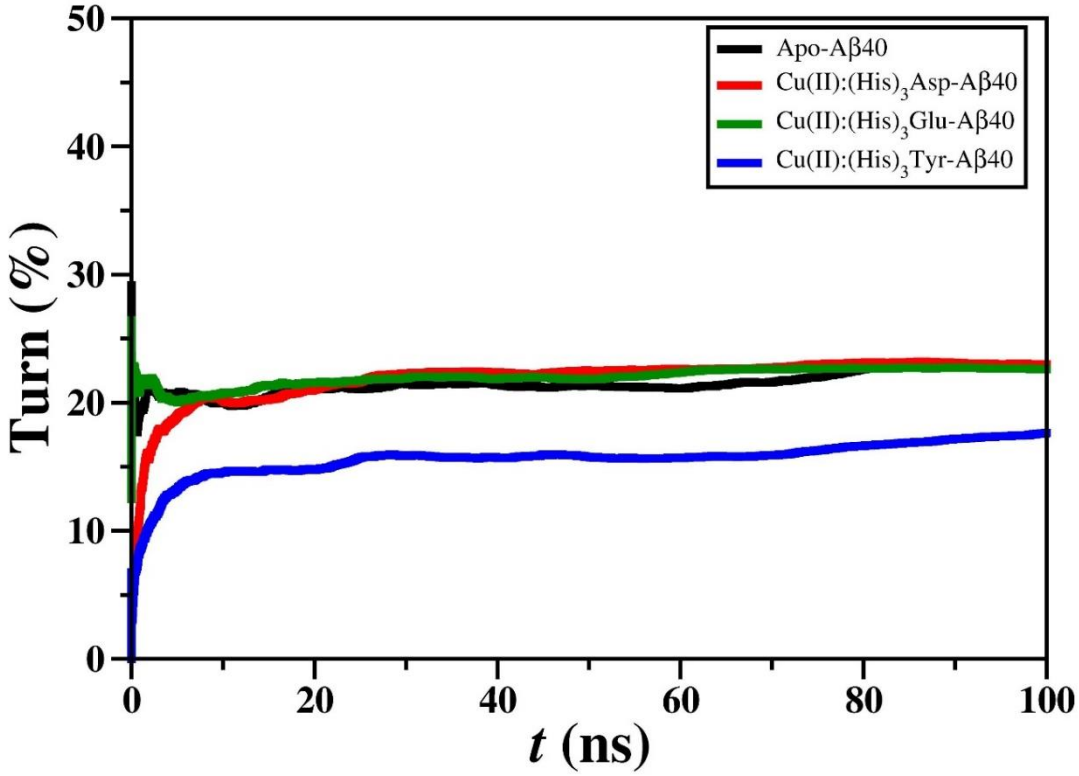


Figure S2B. Correlation between the Hα chemical shift values for Aβ42 at 280 K using the structures from our simulations (δsim.) and experimental (δexp.) chemical shift values provided by Dr. Michael Zagorski (CWRU). The computed Pearson correlation coefficient is 0.930.

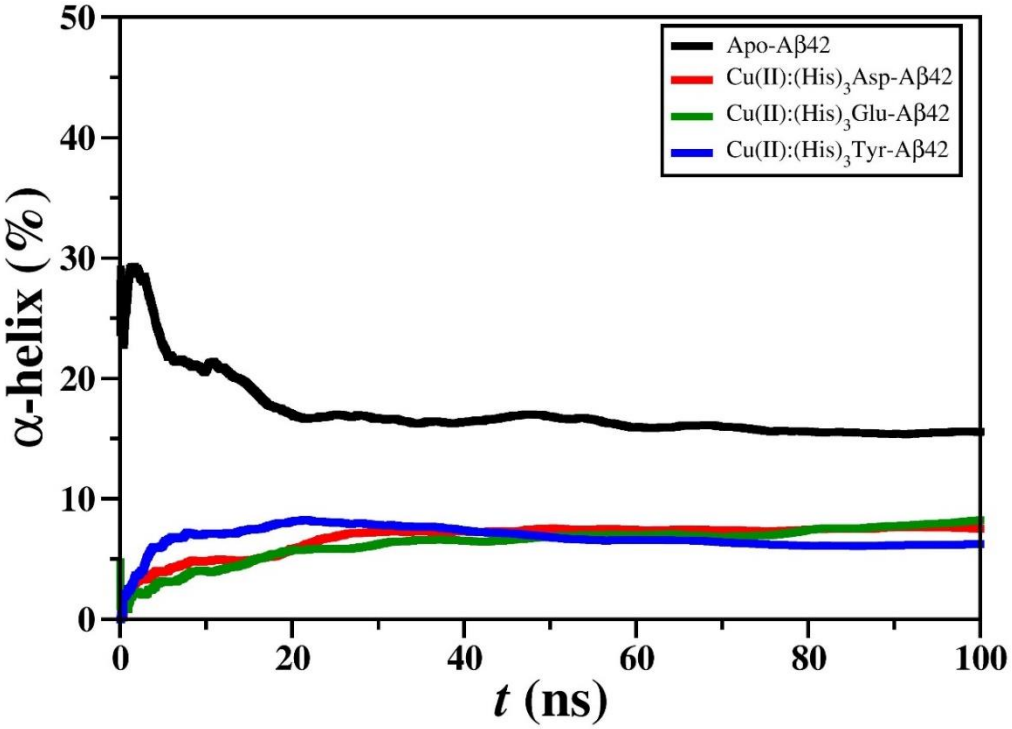


(a)

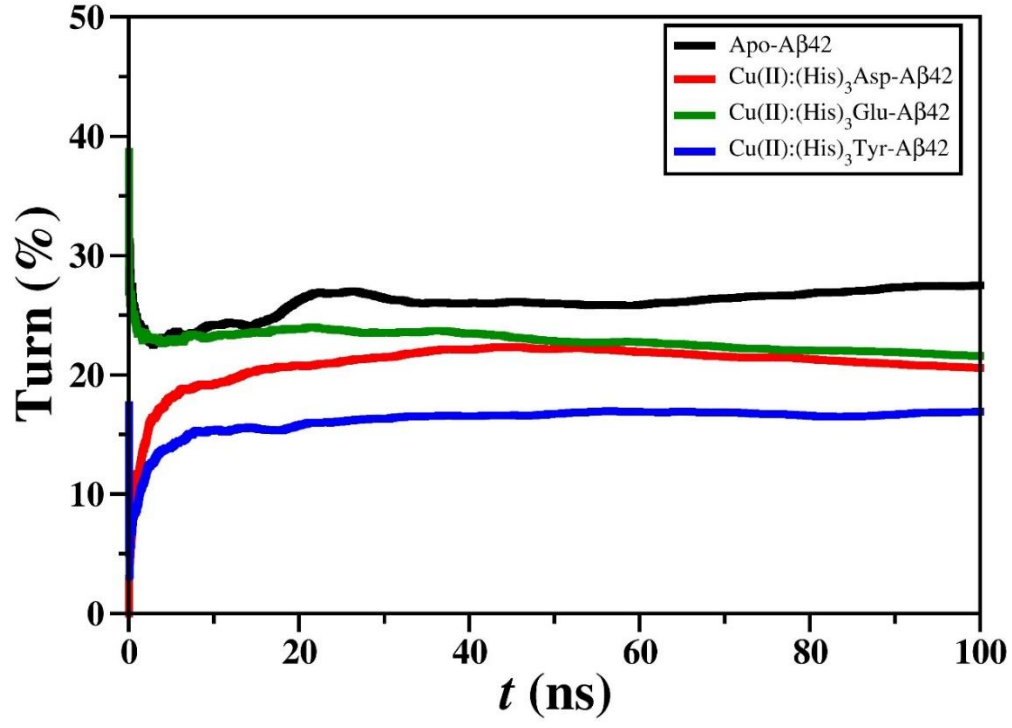


(b)

Figure S3A. The calculated α-helix (a) and turn (b) contents for Cu(II):His_3Asp1-Aβ40 (red), Cu(II):His_3Glu11-Aβ40 (blue) and Cu(II):His_3Tyr10-Aβ40 (green) in aqueous solution.



(a)



(b)

Figure S3B. The calculated α-helix (a) and turn (b) contents for Cu(II):His_3Asp1-Aβ42 (red), Cu(II):His_3Glu11-Aβ42 (blue) and Cu(II):His_3Tyr10-Aβ42 (green) in aqueous solution.

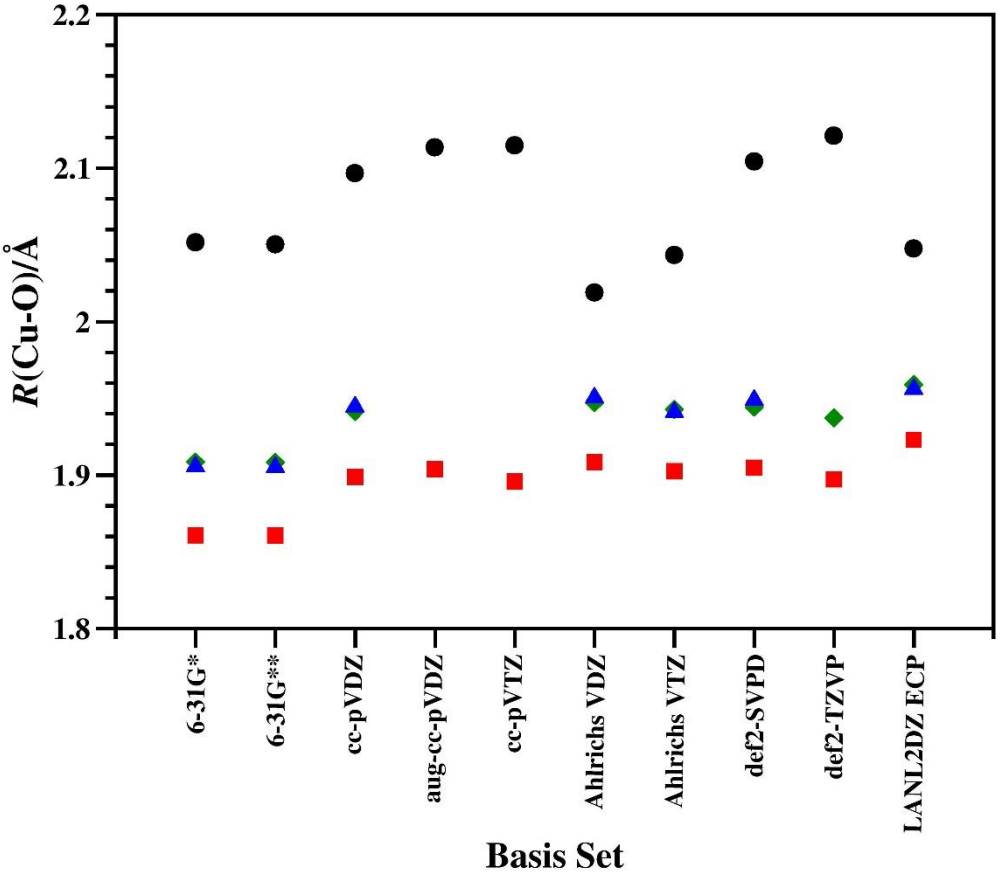
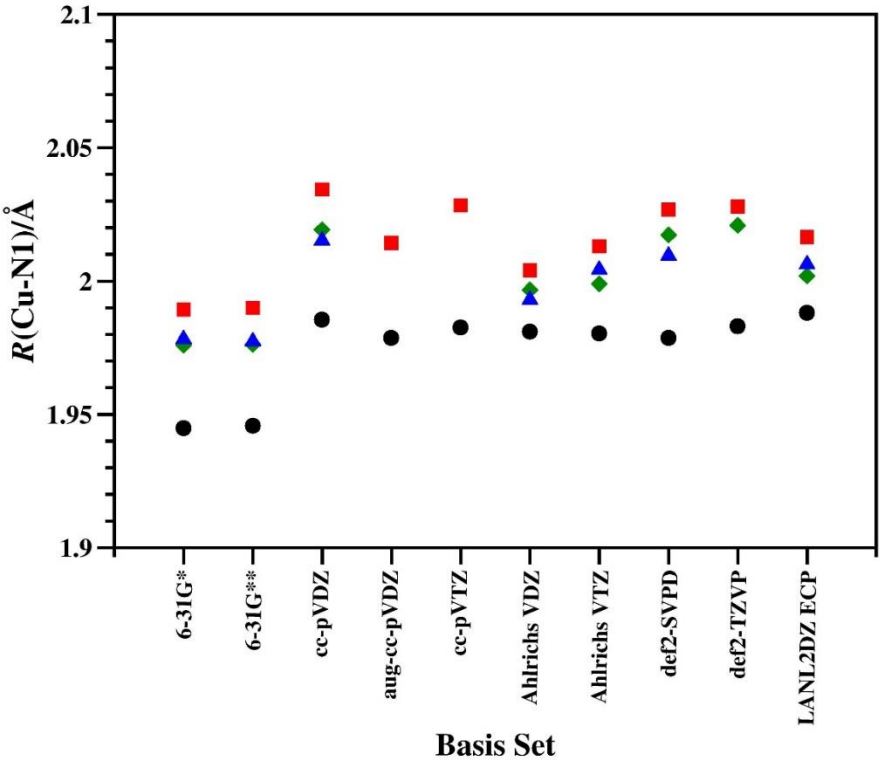
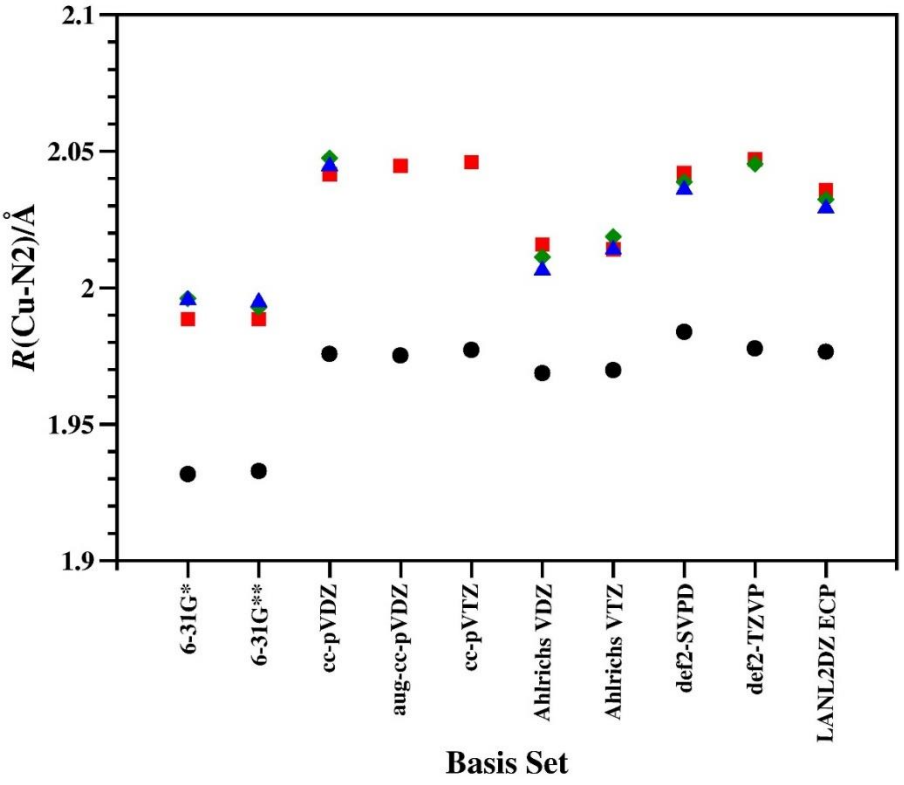


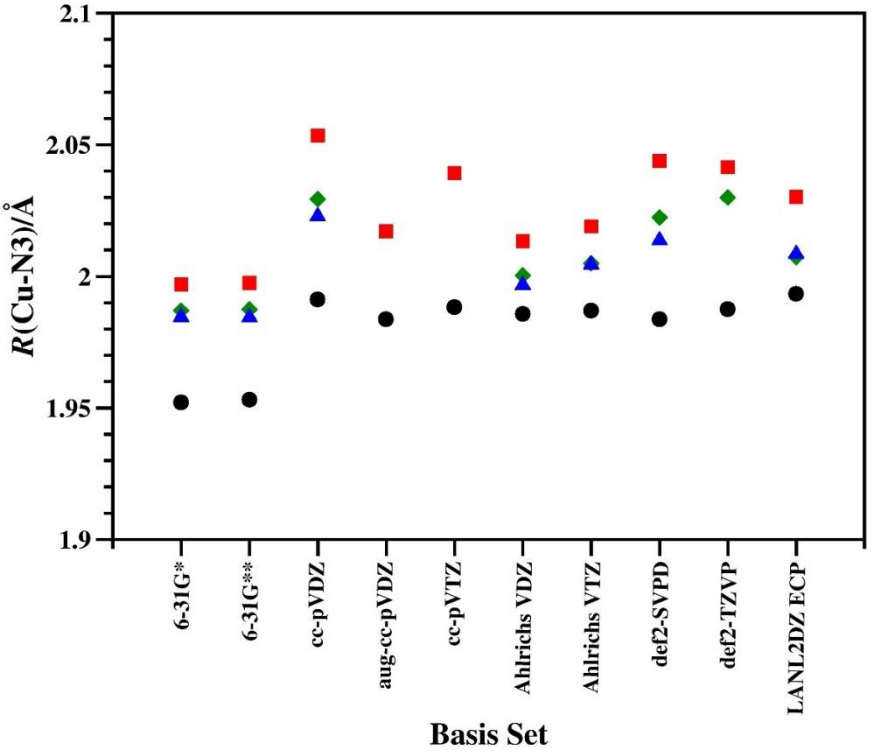
Figure S4. The calculated bond distances - using varying basis sets - between Cu(II) and coordinating O atom for Cu(II):$His_3(H_2O)$ (black), Cu(II):His_3Asp (green), Cu(II):His_3Glu (blue) and Cu(II):His_3Tyr (red).



(a)

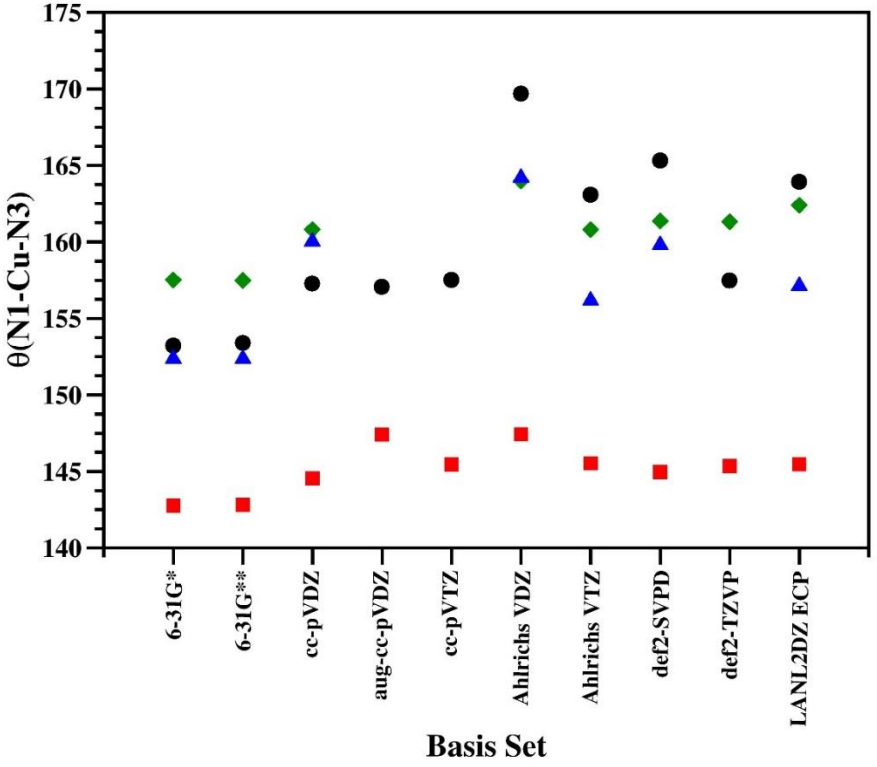


(b)

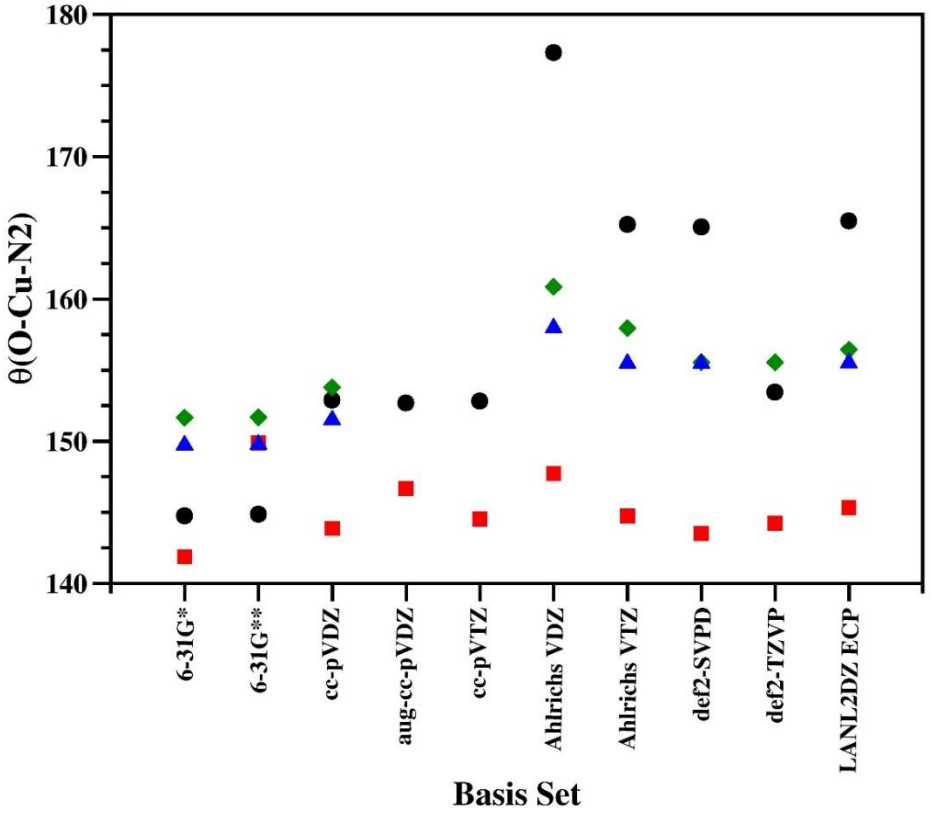


(c)

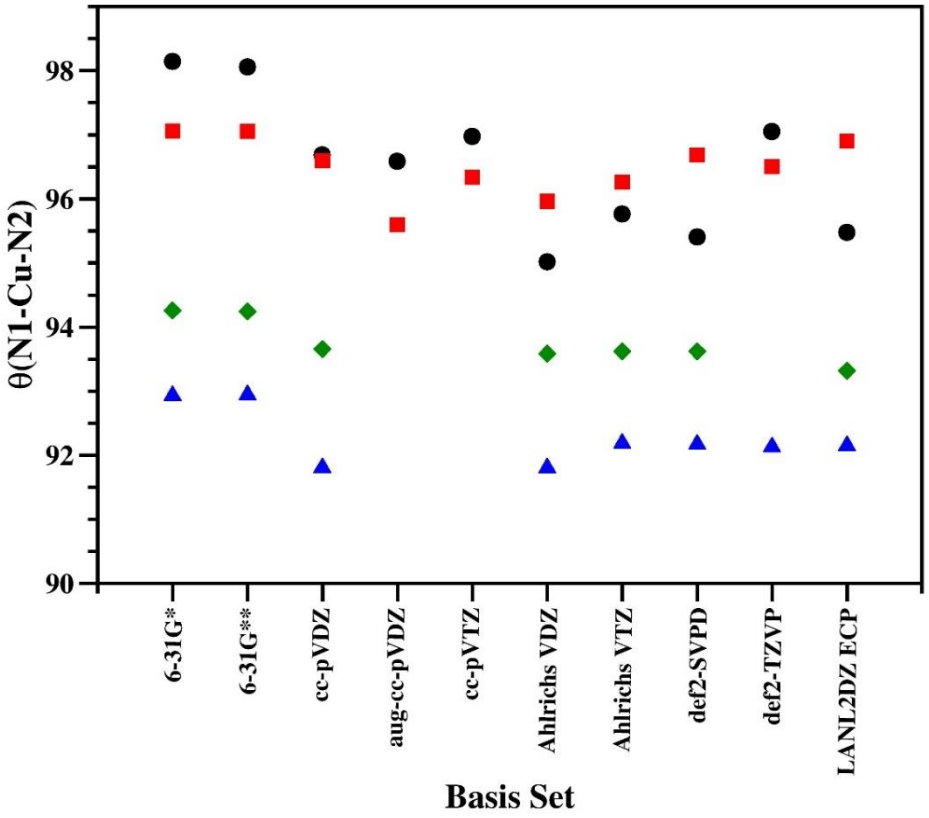
Figure S5. The calculated bond distances - using varying basis sets - between Cu(II) and coordinating (a) N1, (b) N2 and (c) N3 atoms for Cu(II):His3(H2O) (black), Cu(II):His3Asp (green), Cu(II):His3Glu (blue) and Cu(II):His3Tyr (red).


θ(N1-Cu-N3)
175
170
165
160
155
150
145
140
6-31G*
6-31G**
cc-pVDZ
aug-cc-pVDZ
cc-pVTZ
Ahlrichs VDZ
Ahlrichs VTZ
def2-SVPD
def2-TZVP
LANL2DZ ECP
Basis Set

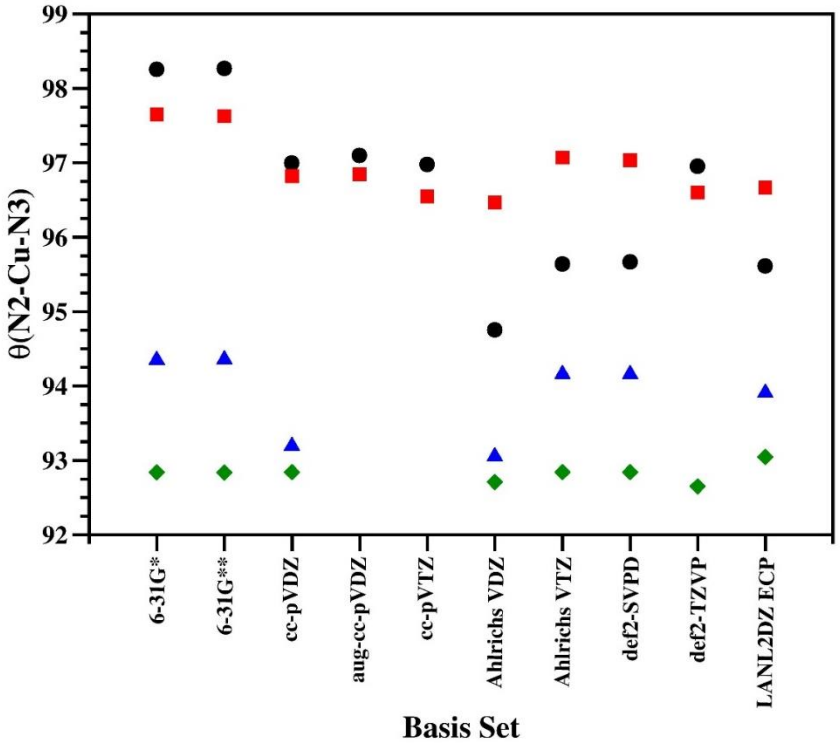
(a)


θ(O-Cu-N2)
180
170
160
150
140
6-31G*
6-31G**
cc-pVDZ
aug-cc-pVDZ
cc-pVTZ
Ahlrichs VDZ
Ahlrichs VTZ
def2-SVPD
def2-TZVP
LANL2DZ ECP
Basis Set

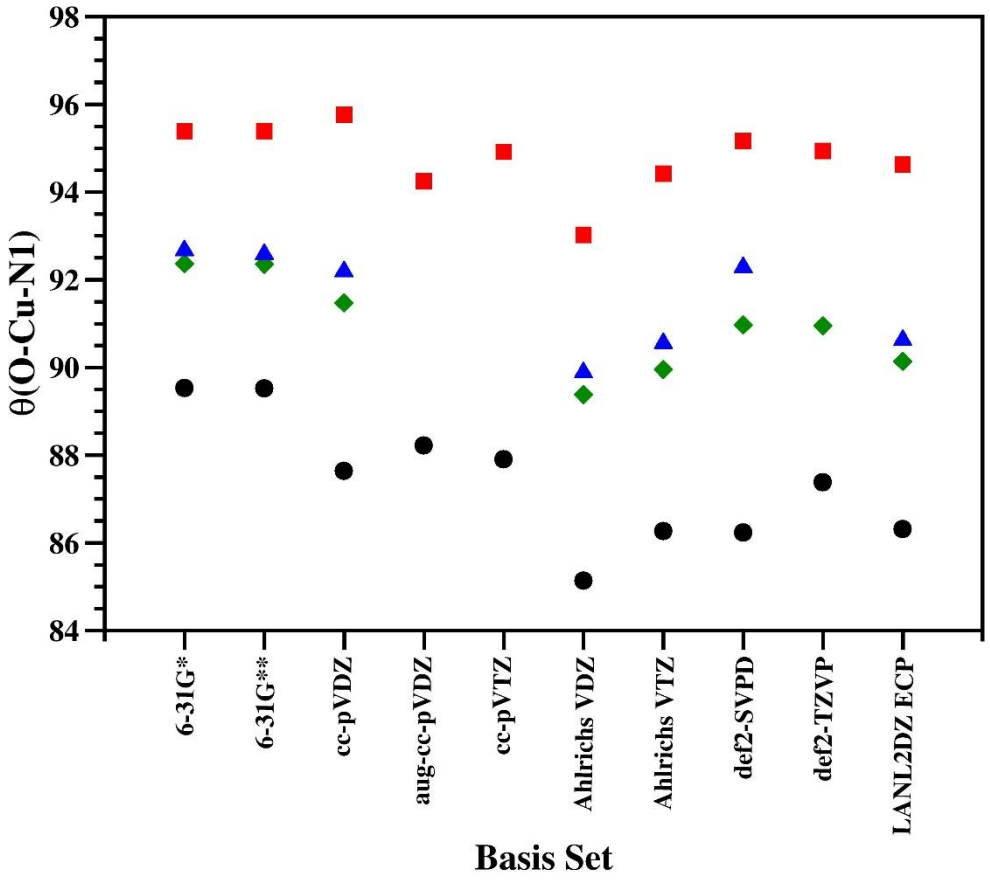
(b)


θ(N1-Cu-N2)
98
96
94
92
90
6-31G*
6-31G**
cc-pVDZ
aug-cc-pVDZ
cc-pVTZ
Ahlrichs VDZ
Ahlrichs VTZ
def2-SVPD
def2-TZVP
LANL2DZ ECP
Basis Set

(c)

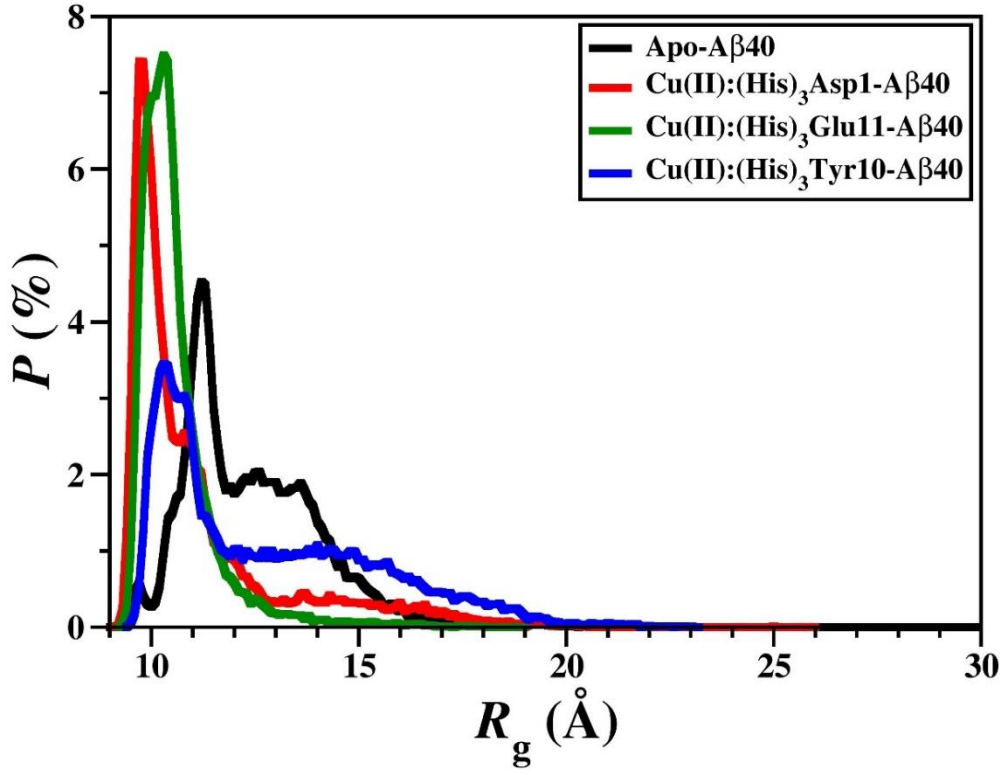

θ(N2-Cu-N3)
99
98
97
96
95
94
93
92
6-31G*
6-31G**
cc-pVDZ
aug-cc-pVDZ
cc-pVTZ
Ahlrichs VDZ
Ahlrichs VTZ
def2-SVPD
def2-TZVP
LANL2DZ ECP
Basis Set

(d)

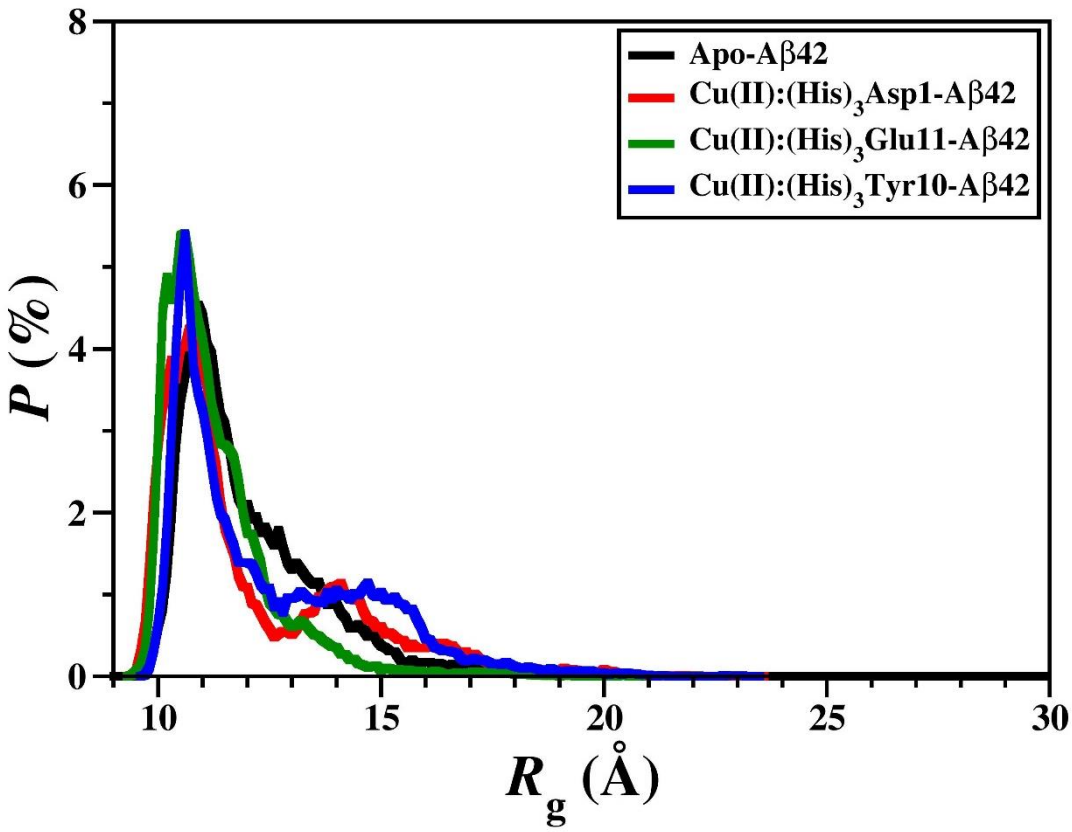


(e)

Figure S6. The optimized bond angles for (a) N1-Cu-N3, (b) O-Cu-N2, (c) N1-Cu-N2, (d) N2-Cu-N3, (e) O-Cu-N1 in the structures of Cu(II):His3(H2O) (black), Cu(II):His3Asp (green), Cu(II):His3Glu (blue) and Cu(II):His3Tyr (red).



(a)



(b)

Figure S7. The density distribution of radius of gyration for (a) Aβ40 (black), Cu(II):His_3Asp1-Aβ40 (red), Cu(II):His3Tyr10-Aβ40 (blue) and Cu(II):His_3Glu11-Aβ40 (green) and for (b) Aβ42 (black), Cu(II):His_3Asp1-Aβ42 (red), Cu(II):His3Tyr10-Aβ42 (blue) and Cu(II):His_3Glu11-Aβ42 (green).

Table S1. P_{agg} and Z_{agg} scores for apo and Cu(II)-bound Aβ40

AB40			
Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.7750336
2	Ala	0.7761	0.92810857
3	Glu	-5.7220325	-0.3960412
4	Phe	3.9434975	1.57354149
5	Arg	-2.548855	0.25056955
6	His	-1.931145	0.37644272
7	Asp	-8.2984175	-0.9210412
8	Ser	-3.6107375	0.03418562
9	Gly	-1.1156475	0.54261982
10	Tyr	1.66366	1.10897013
11	Glu	-7.55907	-0.7703815
12	Val	1.57642	1.09119289
13	His	-2.9741525	0.16390502
14	His	-2.9257825	0.17376156
15	Gln	-4.0165875	-0.048516
16	Lys	-6.98695	-0.6537983
17	Leu	1.254195	1.02553185

18	Val	0.51222	0.87433672
19	Phe	2.59576	1.29890777
20	Phe	1.5447825	1.084746
21	Ala	-1.0797575	0.54993326
22	Glu	-7.7556325	-0.8104358
23	Asp	-9.62189	-1.1907303
24	Val	2.0740175	1.19259027
25	Gly	-0.2004875	0.72910553
26	Ser	-2.6401375	0.23196856
27	Asn	-3.69081	0.01786893
28	Lys	-5.528465	-0.3565972
29	Gly	0.155325	0.80161083
30	Ala	0.9801275	0.96968405
31	Ile	3.8187175	1.54811458
32	Ile	3.6641575	1.51661929
33	Gly	-0.5845375	0.65084617
34	Leu	2.8115375	1.34287759
35	Met	1.20381	1.0152647
36	Val	1.8712225	1.15126595
37	Gly	-0.1583125	0.7376997
38	Gly	0.0000425	0.76996831
39	Val	2.5941075	1.29857104
40	Val	2.68525	1.3171435

Cu:His3Asp1-AB40

Residue	Type	Pagg	Zagg
1	Asp	-7.58566176	-0.775800171
2	Ala	0.9743857	0.96851402
3	Glu	-5.70604285	-0.392782909
4	Phe	4.83672855	1.755558656
5	Arg	-2.0899	0.344092595
6	His	-1.27750408	0.509637674
7	Asp	-7.501345699	-0.758618759
8	Ser	-2.47087715	0.266459398
9	Gly	-0.00342	0.769262746
10	Tyr	2.92373715	1.365740952
11	Glu	-5.711077148	-0.393808768
12	Val	2.587	1.297122713
13	His	-1.987072627	0.365046129
14	His	-2.00938408	0.360499637
15	Gln	-3.31845145	0.093745884
16	Lys	-5.940048547	-0.440467161
17	Leu	3.142817153	1.410383737
18	Val	2.37765715	1.254464105

19	Phe	4.225811397	1.63106969
20	Phe	3.8129343	1.546936117
21	Ala	-0.005762848	0.768785335
22	Glu	-6.5548457	-0.56574677
23	Asp	-8.390082847	-0.939720187
24	Val	1.949688603	1.167255289
25	Gly	-0.608188547	0.646026705
26	Ser	-2.904125697	0.178174655
27	Asn	-4.122397203	-0.070077272
28	Lys	-5.669759997	-0.385389411
29	Gly	0.085054302	0.787291499
30	Ala	0.6362286	0.899606431
31	Ile	3.665728553	1.516939429
32	Ile	3.571105703	1.497657762
33	Gly	-0.214094299	0.726332824
34	Leu	3.643282852	1.512365581
35	Met	1.432731397	1.061912906
36	Val	2.453545697	1.26992821
37	Gly	0.134674248	0.797402749
38	Gly	0.222925697	0.81538609
39	Val	2.8407143	1.348823063
40	Val	2.6757143	1.315200371

Cu:His3Glu11-AB40

Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.775033623
2	Ala	0.7606075	0.924951604
3	Glu	-5.6975175	-0.391045666
4	Phe	4.129175	1.611377715
5	Arg	-2.3939825	0.28212852
6	His	-1.4732939	0.46974082
7	Asp	-7.94419	-0.848858866
8	Ser	-2.47505	0.26560908
9	Gly	0.060875	0.782364388
10	Tyr	2.931425	1.367307536
11	Glu	-5.53165472	-0.357247161
12	Val	2.1217375	1.202314362
13	His	-1.8062689	0.401889208
14	His	-1.8031239	0.402530077
15	Gln	-3.0439425	0.149683641
16	Lys	-5.6819125	-0.387865774
17	Leu	2.8568825	1.35211772
18	Val	1.442415	1.063886172
19	Phe	3.2854625	1.439451135
20	Phe	3.38484	1.459701675
21	Ala	-0.41773	0.684837185

22	Glu	-6.49992	-0.554554346
23	Asp	-8.142925	-0.889355871
24	Val	1.39953	1.055147329
25	Gly	-1.4222525	0.480141725
26	Ser	-3.9286275	-0.030592065
27	Asn	-5.22046	-0.293833802
28	Lys	-6.70165	-0.595661654
29	Gly	-0.24925	0.71916901
30	Ala	0.6476475	0.901933305
31	Ile	3.330095	1.448546073
32	Ile	3.3983875	1.462462302
33	Gly	-0.7254275	0.622136467
34	Leu	2.5146975	1.282389351
35	Met	0.9375575	0.961009394
36	Val	1.7767225	1.132009312
37	Gly	-0.0761375	0.754444818
38	Gly	0.12089	0.794593879
39	Val	2.8497125	1.350656661
40	Val	2.68175	1.316430289

Cu:His3Tyr10-AB40

Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.775033623
2	Ala	0.779725	0.928847251
3	Glu	-5.709275	-0.393441537
4	Phe	4.5173	1.690467457
5	Arg	-2.088525	0.344372784
6	His	-1.1822874	0.529040347
7	Asp	-7.3299	-0.723682602
8	Ser	-2.229225	0.315701797
9	Gly	0.0005	0.77006154
10	Tyr	2.95696212	1.372511334
11	Glu	-5.69365	-0.39025757
12	Val	2.587	1.297122713
13	His	-1.2904124	0.507007295
14	His	-1.5574574	0.452590496
15	Gln	-2.853295	0.188532624
16	Lys	-5.7975625	-0.411432225
17	Leu	3.29058	1.440493948
18	Val	2.1588225	1.209871317
19	Phe	4.1750925	1.620734503
20	Phe	3.774575	1.539119493

21	Ala	0.10205	0.790754778
22	Glu	-6.7160725	-0.598600583
23	Asp	-8.4484725	-0.951618474
24	Val	2.17398	1.21296002
25	Gly	-0.40572	0.687284509
26	Ser	-2.683565	0.223119167
27	Asn	-3.96729	-0.038470473
28	Lys	-6.0306575	-0.4589309
29	Gly	-0.11582	0.746358561
30	Ala	0.46631	0.864981457
31	Ile	3.235255	1.429220157
32	Ile	3.0645175	1.394428312
33	Gly	-0.6171	0.644210784
34	Leu	3.0342175	1.388253963
35	Met	1.583225	1.092579574
36	Val	2.596305	1.299018829
37	Gly	-0.0442625	0.760940111
38	Gly	0.0293775	0.77594602
39	Val	2.8383825	1.348347903
40	Val	2.690125	1.318136895

Table S2. P_{agg} and Z_{agg} scores for apo and Cu(II)-bound Aβ42

AB42			
Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.775033623
2	Ala	0.7759575	0.928079533
3	Glu	-5.8706425	-0.426324021
4	Phe	3.2677175	1.435835167
5	Arg	-3.6429625	0.027619004
6	His	-3.10915	0.136396055
7	Asp	-9.404455	-1.146422749
8	Ser	-3.2596575	0.105726556
9	Gly	-0.3059325	0.707618596
10	Tyr	2.479455	1.275207849
11	Glu	-6.529195	-0.560519827
12	Val	1.7196875	1.120387069
13	His	-2.0029675	0.361807169
14	His	-2.4781725	0.264972796
15	Gln	-4.226605	-0.0913121
16	Lys	-7.2351825	-0.704381648
17	Leu	1.6306875	1.102251192
18	Val	0.8393675	0.941000835
19	Phe	3.62363	1.508360843
20	Phe	4.647095	1.71691629
21	Ala	1.2781175	1.030406631
22	Glu	-6.57876	-0.57061988
23	Asp	-8.2712725	-0.91550974
24	Val	1.767715	1.130173819

25	Gly	-0.043215	0.761153564
26	Ser	-1.96717	0.369101765
27	Asn	-4.0517575	-0.055682744
28	Lys	-6.1423825	-0.481697538
29	Gly	-0.732205	0.62075539
30	Ala	-0.08999	0.75162204
31	Ile	2.575355	1.294749766
32	Ile	2.6539825	1.310771997
33	Gly	-1.171485	0.531241594
34	Leu	2.1703425	1.212218792
35	Met	0.73323	0.919372784
36	Val	2.24561	1.227556343
37	Gly	-0.112155	0.747105392
38	Gly	-0.0397375	0.761862188
39	Val	2.5854825	1.296813486
40	Val	2.7881875	1.338119473
41	Ile	3.77861	1.539941721
42	Ala	0.856225	0.944435954

Cu:His3Asp1-AB42

Residue	Type	Pagg	Zagg
1	Asp	-7.58566176	-0.775800171
2	Ala	0.784725	0.929866121
3	Glu	-5.507025	-0.352228268
4	Phe	4.603175	1.70796654
5	Arg	-2.0484	0.352549211
6	His	-1.23462908	0.518374479
7	Asp	-7.4929175	-0.756901312
8	Ser	-2.477925	0.26502323
9	Gly	0.0431575	0.778754025
10	Tyr	3.3959575	1.461967131
11	Glu	-5.1289575	-0.275187981
12	Val	2.891125	1.359095448
13	His	-2.42163658	0.276493341
14	His	-2.44244158	0.272253825
15	Gln	-3.7450625	0.00681369
16	Lys	-5.6124475	-0.373710621
17	Leu	4.04693	1.594618331
18	Val	3.5363325	1.490571891
19	Phe	5.2075025	1.831112707
20	Phe	4.30908	1.648037657
21	Ala	0.54992	0.882018992
22	Glu	-6.073095	-0.467578555
23	Asp	-7.9688625	-0.853886478
24	Val	1.9296175	1.163165322
25	Gly	-0.5728675	0.653224212
26	Ser	-2.80287	0.198807923

27	Asn	-4.09699	-0.064899947
28	Lys	-6.11591	-0.476303134
29	Gly	-0.3642325	0.695738578
30	Ala	0.2814175	0.827305192
31	Ile	2.8793775	1.356701614
32	Ile	2.7491875	1.330172291
33	Gly	-1.126065	0.540497005
34	Leu	2.3179	1.242287158
35	Met	1.21277	1.017090516
36	Val	2.56143	1.291912214
37	Gly	0.34301	0.839856136
38	Gly	0.677285	0.907972654
39	Val	3.588295	1.501160492
40	Val	3.5052775	1.484243693
41	Ile	4.1661225	1.618906651
42	Ala	0.78335	0.929585931

Cu:His3Glu11-AB42

Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.775033623
2	Ala	0.77616	0.928120797
3	Glu	-5.689035	-0.389317154
4	Phe	4.985905	1.785956922
5	Arg	-1.0034975	0.565473061
6	His	-0.8336039	0.600092941
7	Asp	-7.26845	-0.711160696
8	Ser	-2.5125225	0.257973163
9	Gly	0.055125	0.781192689
10	Tyr	2.959175	1.372962261
11	Glu	-5.60627972	-0.372453788
12	Val	2.220775	1.222495619
13	His	-1.7227689	0.418904328
14	His	-1.6936964	0.424828545
15	Gln	-3.0221675	0.154120818
16	Lys	-5.617965	-0.374834943
17	Leu	2.776185	1.335673676
18	Val	1.33472	1.041940743
19	Phe	3.6617125	1.516121062
20	Phe	3.6275075	1.509150976
21	Ala	0.51911	0.875740718
22	Glu	-7.17518	-0.692154705
23	Asp	-8.8433675	-1.032087765
24	Val	1.1409425	1.002453947
25	Gly	-1.469755	0.470461955

26	Ser	-3.6251325	0.031252292
27	Asn	-4.690965	-0.185936545
28	Lys	-6.3767925	-0.529464177
29	Gly	-0.254245	0.718151159
30	Ala	0.632905	0.898929168
31	Ile	3.211885	1.424457961
32	Ile	3.186885	1.419363614
33	Gly	-0.4133175	0.685736337
34	Leu	2.98358	1.377935363
35	Met	1.5465525	1.085106676
36	Val	2.6184575	1.30353293
37	Gly	0.33031	0.837268207
38	Gly	0.01701	0.773425847
39	Val	2.978035	1.376805437
40	Val	3.5609975	1.495597974
41	Ile	4.5418625	1.695472654
42	Ala	0.8786	0.948995395

Cu:His3Tyr10-AB42

Residue	Type	Pagg	Zagg
1	Asp	-7.5819	-0.775033623
2	Ala	0.7846	0.929840649
3	Glu	-5.69165	-0.389850022
4	Phe	4.57905	1.703050495
5	Arg	-2.086775	0.344729388
6	His	-1.2534124	0.514546929
7	Asp	-7.4969	-0.757712842
8	Ser	-2.4671	0.267229083
9	Gly	0.038375	0.777779476
10	Tyr	2.95146212	1.371390577
11	Glu	-5.7084	-0.393263235
12	Val	3.009	1.383115295
13	His	-1.3201949	0.500938399
14	His	-1.5121424	0.46182451
15	Gln	-2.793105	0.200797775
16	Lys	-5.639195	-0.379161063
17	Leu	3.6254475	1.508731202
18	Val	2.77548	1.335530016
19	Phe	4.64051	1.715574439
20	Phe	4.073825	1.60009883
21	Ala	0.30391	0.831888576
22	Glu	-6.590695	-0.573051922
23	Asp	-8.6926125	-1.001367832
24	Val	1.783115	1.133311937

25	Gly	-0.7921875	0.608532522
26	Ser	-2.939535	0.170959164
27	Asn	-4.19287	-0.084437788
28	Lys	-5.7939975	-0.410705771
29	Gly	0.2825975	0.827545645
30	Ala	0.74756	0.922292864
31	Ile	3.761495	1.53645413
32	Ile	3.966175	1.578162571
33	Gly	0.4667125	0.865063476
34	Leu	4.274405	1.640971798
35	Met	2.4706325	1.273410054
36	Val	2.6425725	1.308446937
37	Gly	0.07305	0.784845336
38	Gly	-0.03097	0.763648775
39	Val	3.30522	1.443477198
40	Val	3.551655	1.493694217
41	Ile	4.375235	1.661518319
42	Ala	0.900975	0.953554836