Supplementary Material

Microsolvation of Histidine – A Theoretical Study of Intermolecular Interactions Based on AIM and SAPT Approaches

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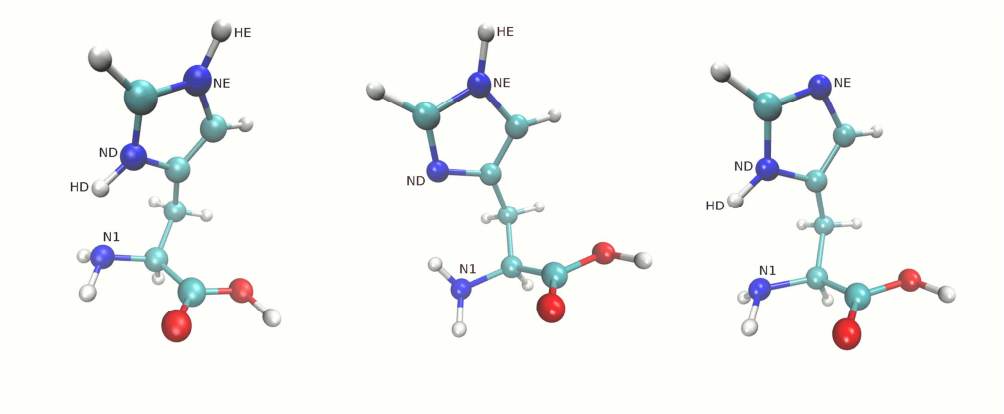

Figure S1I. Structures of the studied forms of histidine (**HIP**, **HIE** and **HID** forms respectively). Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

Table S1I. Metric parameters (interatomic distances are given in [Å]) of an intramolecular short contacts obtained as a result of DFT gas phase and with solvent reaction field (PCM with water as a solvent) simulations with various functionals and 6-311+G(d,p) basis set. For geometric details see Figure 1SI.

Metric parameters	Gas phase			PCM		
	B3LYP	**ωB97XD**	**PBE**	**B3LYP**	**ωB97XD**	**PBE**
HIP						
ND…N1	2.722	2.713	2.651	2.788	2.769	2.720
ND-HD	1.039	1.036	1.072	1.027	1.026	1.049
HD…N1	1.916	1.917	1.759	2.047	2.030	1.906
∠NHN [°]	131.8	131.2	137.6	127.0	126.9	131.8
HIE						
ND…N1	3.084	3.219	3.065	3.098	3.160	3.069
N1-H	1.017	1.012	1.027	1.017	1.017	1.028
H…ND	2.285	2.816	2.238	2.328	2.411	2.261
∠NHN [°]	134.5	104.2	136.4	131.5	129.8	134.4
HID						
ND…N1	2.933	2.905	2.899	2.902	2.872	2.859
ND-HD	1.012	1.011	1.024	1.016	1.014	1.028
HD…N1	2.275	2.247	2.205	2.228	2.197	2.142
∠NHN [°]	121.4	121.4	123.5	122.4	122.5	125.1

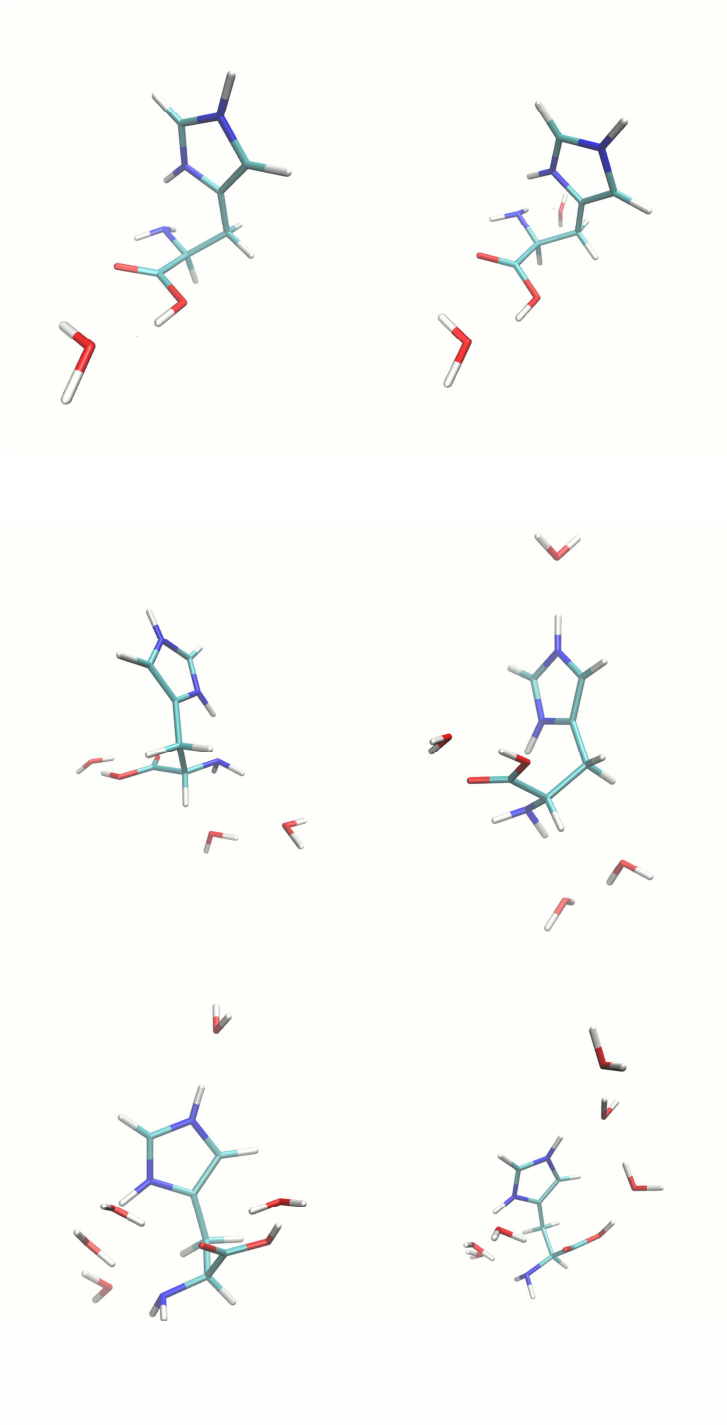

Figure S2I. Histidine HIP form microsolvation models (with 1-6 water molecules) used for the metric parameters and SAPT analyses. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

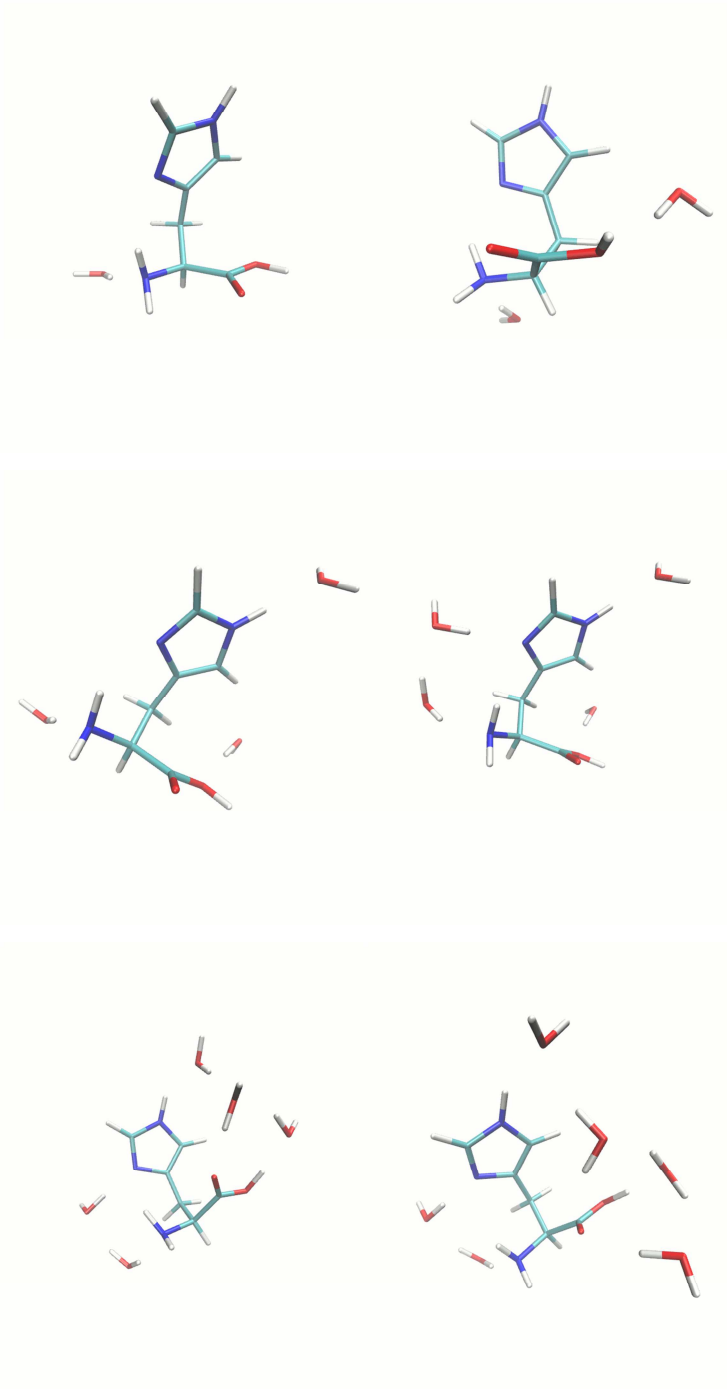

Figure S3I. Histidine HIE form microsolvation models (with 1-6 water molecules) used for the metric parameters and SAPT analyses. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

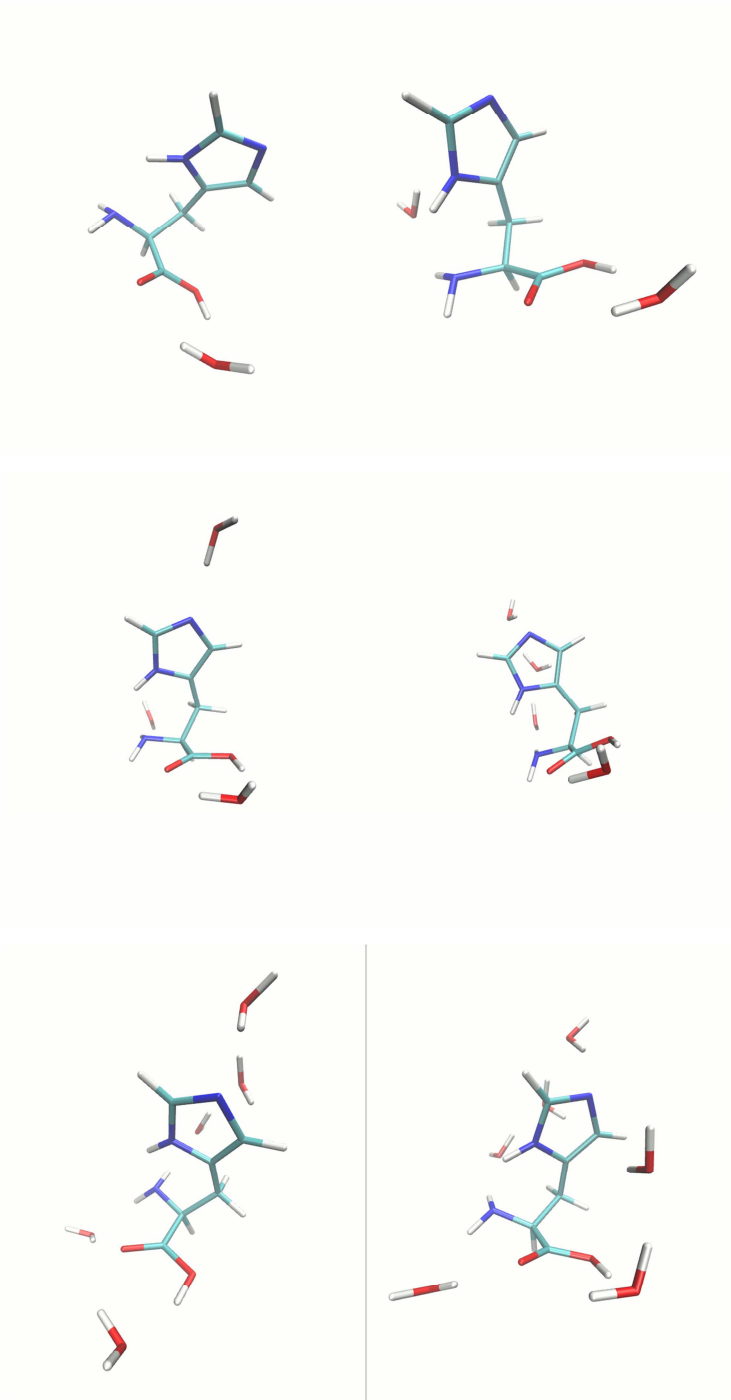

Figure S4I. Histidine HID form microsolvation models (with 1-6 water molecules) used for the metric parameters and SAPT analyses. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

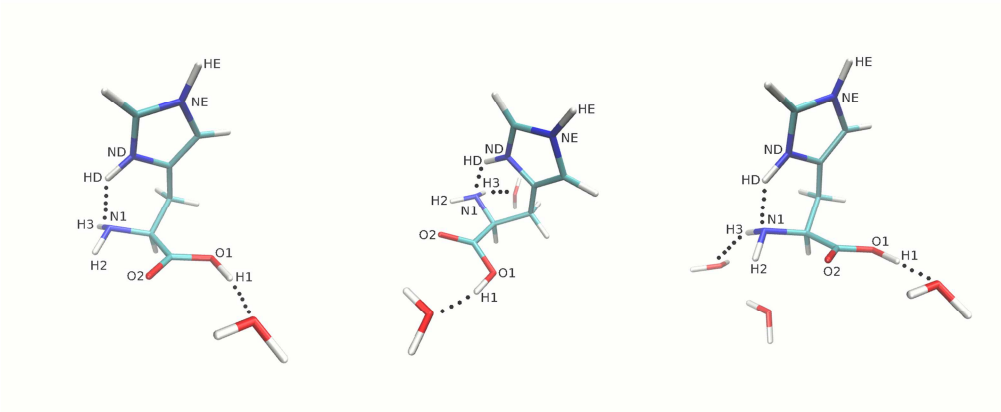

Figure S5I. Schematic presentation of microsolvation models for histidine HIP form. Only three water molecules are presented in the Figure for clarity. The dotted lines indicate the presence of selected intra- and intermolecular short contacts. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

Table S2I. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIP form are presented. Interatomic distances are given in [Å].

Metric parameters	B3LYP	ωB97XD	M06-2X	B3LYP	ωB97XD	M06-2X
	HIP with 1-6 water molecules			HIP with 1-6 water molecules and with PCM		
Histidine HIP form						
One water molecule (HIP-1)						
Intramolecular HB						
ND...N1	2.716	2.706	2.721	2.773	2.763	2.777
ND-HD	1.041	1.038	1.036	1.029	1.027	1.026
HD...N1	1.905	1.901	1.932	2.020	2.015	2.051
∠NHN [°]	132.2	131.9	130.4	127.9	127.5	125.7
Intermolecular HB						
O1...O	2.644	2.644	2.631	2.673	2.671	2.655
O1-H1	0.998	0.992	0.993	0.996	0.992	0.992
H1...O	1.672	1.671	1.671	1.695	1.679	1.688
∠O1H1O [°]	163.5	165.7	161.1	166.1	178.0	163.6
Two water molecules (HIP-2)						
Intramolecular HB						
ND...N1 [A]	2.678	2.668	2.678	2.747	2.737	2.758
ND-HD	1.051	1.048	1.047	1.033	1.030	1.028
HD...N1	1.830	1.824	1.848	1.971	1.966	2.011
∠NHN [°]	134.9	134.7	133.5	129.6	129.3	127.3
Intermolecular HB						
O1...O	2.654	2.651	2.641	2.680	2.676	2.664
O1-H1	0.996	0.991	0.991	0.995	0.991	0.991
H1...O	1.687	1.685	1.688	1.707	1.686	1.701
∠O1H1O [°]	162.5	163.6	160.1	165.1	178.1	162.8
N1...O	3.016	2.996	2.990	3.017	3.005	2.986
N1-H3	1.019	1.018	1.018	1.019	1.018	1.018
H3...O	2.103	2.067	2.112	2.074	2.052	2.102
∠N1H3O [°]	148.1	150.5	143.1	152.9	154.9	144.0

Table S2I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIP form are presented. Interatomic distances are given in [Å].

Three water molecules (HIP-3)						
Intramolecular HB						
ND...N1	2.650	2.644	2.663	2.748	2.739	2.764
ND-HD	1.061	1.055	1.050	1.033	1.030	1.028
HD...N1	1.775	1.780	1.823	1.971	1.968	2.021
∠NDHDN [°]	136.7	136.2	134.2	129.7	129.3	127.0
Intermolecular HB						
O1...O	2.664	2.661	2.642	2.681	2.677	2.665
O1-H1	0.994	0.989	0.991	0.995	0.991	0.991
H1...O	1.704	1.703	1.687	1.707	1.686	1.702
∠O1H1O [°]	161.2	161.7	160.4	165.3	178.2	163.0
N1...O	3.246	3.225	2.900	3.105	3.081	3.083
N1-H3	1.018	1.017	1.020	1.019	1.018	1.017
H3...O	2.326	2.300	2.116	2.112	2.091	2.224
∠N1H3O [°]	149.7	150.6	132.1	164.5	163.6	141.2
Four water molecules (HIP-4)						
Intramolecular HB						
ND...N1 [A]	2.709	2.699	2.709	2.861	2.750	2.776
ND-HD	1.042	1.039	1.038	1.021	1.028	1.026
HD...N1	1.888	1.881	1.906	2.218	1.990	2.040
∠NDHDN1 [°]	133.1	133.0	131.6	119.4	128.5	126.5
Intermolecular HB						
O1...O	2.668	2.664	2.658	2.798	2.676	2.668
O1-H1	0.993	0.989	0.988	0.983	0.991	0.990
H1...O	1.708	1.707	1.712	1.896	1.686	1.708
∠O1H1O [°]	161.2	161.6	158.9	151.1	177.3	162.5
N1...O	3.321	3.281	3.312	3.113	3.092	3.182
N1-H3	1.016	1.016	1.017	1.018	1.018	1.018
H3...O	2.334	2.291	2.352	2.127	2.074	2.187
∠N1H3O [°]	163.3	164.6	157.0	162.5	180.0	165.5
NE...O	2.792	2.781	2.793	2.757	2.773	2.777
NE-HE	1.030	1.029	1.029	1.022	1.033	1.033
HE...O	1.763	1.753	1.765	1.969	1.741	1.745
∠NEHEO [°]	178.1	178.2	177.8	131.8	177.8	177.1

Table S2I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIP form are presented. Interatomic distances are given in [Å].

Five water molecules (HIP-5)						
No intramolecular HB						
Intermolecular HB						
O1...O	2.661	2.664	2.648	2.662	2.655	2.643
O1-H1	0.995	0.990	0.991	0.998	0.995	0.995
H1...O	1.689	1.687	1.690	1.679	1.661	1.668
∠O1H1O [°]	164.4	168.1	161.5	167.1	177.7	165.6
N1...O	2.747	2.751	2.780	2.721	2.764	2.762
O-H	0.995	0.988	0.986	1.002	0.991	0.990
H...N1	1.774	1.789	1.835	1.730	1.785	1.791
∠N1HO [°]	164.9	163.5	159.5	169.6	169.0	166.1
NE...O	2.796	2.785	2.799	2.785	2.769	2.775
NE-HE	1.029	1.029	1.028	1.034	1.033	1.033
HE...O	1.767	1.756	1.772	1.752	1.736	1.742
∠NEHEO [°]	178.3	178.1	177.1	177.5	178.1	177.0
ND...O	2.668	2.676	2.701	2.724	2.742	2.762
ND-HD	1.057	1.051	1.048	1.045	1.039	1.038
HD...O	1.627	1.640	1.666	1.698	1.721	1.750
∠NDHDO [°]	167.5	167.6	168.3	166.3	166.7	163.9
O...O2	2.883	2.869	2.896	2.855	2.816	2.846
O-H	0.973	0.970	0.970	0.974	0.971	0.971
H...O2	1.924	1.910	1.936	1.885	1.851	1.881
∠OHO2 [°]	168.3	169.5	169.3	172.9	171.7	172.6

Table S2I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIP form are presented. Interatomic distances are given in [Å].

Six water molecules (HIP-6)						
No intramolecular HB						
Intermolecular HB						
O1...O	2.704	2.696	2.701	2.653	2.643	2.634
O1-H1	0.991	0.986	0.986	1.002	0.998	0.999
H1...O	1.745	1.741	1.753	1.664	1.659	1.658
∠O1H1O [°]	162.1	161.7	160.1	168.4	168.1	164.3
N1...O	2.751	2.754	2.766	2.732	2.780	2.762
O-H	0.997	0.990	0.990	1.002	0.990	0.991
H...N1	1.776	1.789	1.804	1.738	1.801	1.788
∠N1HO [°]	164.7	163.8	162.9	171.0	169.3	166.7
NE...O	2.828	2.811	2.822	2.792	2.773	2.787
NE-HE	1.023	1.023	1.023	1.023	1.022	1.021
HE...O	1.901	1.884	1.895	1.925	1.910	1.962
∠NEHEO [°]	149.0	149.2	149.2	140.5	140.1	135.9
ND...O	2.669	2.673	2.672	2.727	2.743	2.747
ND-HD	1.055	1.051	1.053	1.043	1.037	1.038
HD...O	1.641	1.652	1.643	1.722	1.746	1.747
∠NDHDO [°]	163.4	162.6	163.9	160.4	156.0	160.3
O...O2	2.847	2.837	2.856	2.855	2.819	2.856
O-H	0.974	0.971	0.972	0.975	0.971	0.971
H...O2	1.889	1.880	1.898	1.886	1.855	1.891
∠OHO2 [°]	167.2	168.0	168.2	172.3	171.7	172.1

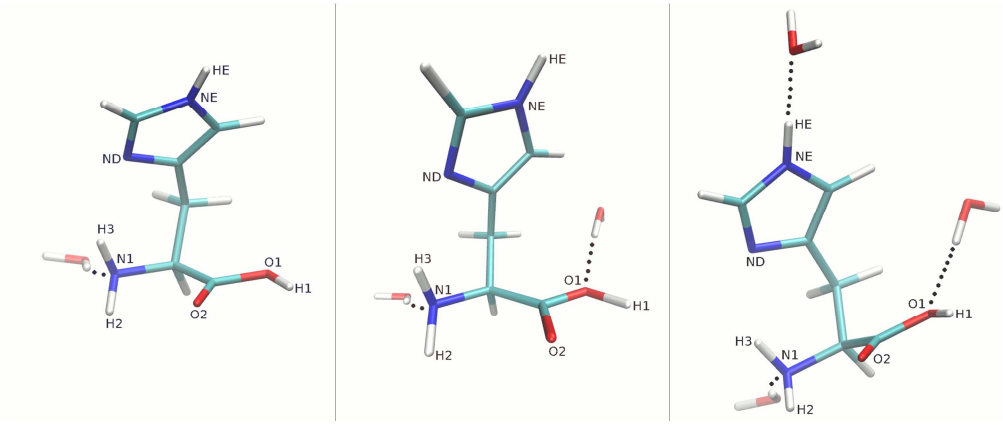

Figure S6I. Schematic presentation of microsolvation models for histidine HIE form. Only three water molecules are presented in the Figure for clarity. The dotted lines indicate the presence of selected intra- and intermolecular short contacts. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

Table S3I. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIE form are presented. Interatomic distances are given in [Å].

Metric parameters	B3LYP	ωB97XD	M06-2X	B3LYP	ωB97XD	M06-2X
	HIE with 1-6 water molecules			HIE with 1-6 water molecules and with PCM		
Histidine HIE form						
One water molecule (HIE-1)						
Intermolecular HB						
O...N1	2.827	2.837	2.815	2.821	2.829	2.828
O-H	0.983	0.978	0.976	0.990	0.984	0.983
H...N1	1.881	1.889	1.906	1.831	1.846	1.852
∠OHN1 [º]	160.8	162.6	153.7	177.4	178.3	171.4
Two water molecules (HIE-2)						
Intermolecular HB						
O...O1	2.931	2.921	2.909	2.967	2.956	2.950
O-H	0.968	0.964	0.965	0.968	0.964	0.965
H...O1	1.981	1.973	1.967	2.013	2.004	2.005
∠OHO1 [º]	166.7	167.1	164.6	168.1	169.0	165.7
O...N1	2.826	2.834	2.814	2.823	2.830	2.835
O-H	0.982	0.977	0.976	0.990	0.987	0.982
H...N1	1.884	1.891	1.910	1.834	1.847	1.856
∠OHN1 [º]	159.7	161.2	152.8	177.7	177.4	173.7
Three water molecules (HIE-3)						
Intermolecular HB						
O...O1	2.935	2.924	2.912	2.967	2.958	2.950
O-H	0.968	0.964	0.965	0.968	0.964	0.965
H...O1	1.980	1.972	1.961	2.011	2.004	2.003
∠OHO1 [º]	168.6	169.0	168.0	169.1	170.0	166.2
O...N1	2.827	2.836	2.813	2.822	2.828	2.834
O-H	0.983	0.978	0.976	0.990	0.984	0.982
H...N1	1.878	1.886	1.902	1.832	1.845	1.855
∠OHN1 [º]	161.4	163.2	154.1	177.8	177.7	174.0
NE…O	2.935	2.921	2.938	2.883	2.866	2.881
NE-HE	1.016	1.016	1.015	1.023	1.022	1.021
HE...O	1.919	1.906	1.923	1.861	1.844	1.860
∠NEHEO [º]	179.0	178.0	178.7	178.3	178.5	177.6

Table S3I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIE form are presented. Interatomic distances are given in [Å].

Four water molecules (HIE-4)						
Intermolecular HB						
O...O1	2.900	2.887	2.867	2.960	2.942	2.931
O-H	0.967	0.964	0.964	0.968	0.964	0.965
H...O1	1.985	1.972	1.973	2.014	1.997	2.002
∠OHO1 [º]	157.0	157.7	153.0	165.3	165.9	160.8
O...N1	2.944	2.948	2.945	2.873	2.874	2.889
O-H	0.973	0.968	0.969	0.982	0.977	0.976
H-N1	2.018	2.028	2.038	1.902	1.910	1.930
∠OHN1 [º]	158.3	157.9	155.1	169.3	168.5	167.0
NE...O	2.914	2.903	2.920	2.867	2.852	2.867
NE-HE	1.017	1.017	1.016	1.024	1.023	1.023
HE...O	1.897	1.886	1.904	1.844	1.829	1.845
∠NEHEO [º]	178.9	178.9	178.4	177.6	178.0	176.9
O...ND	2.840	2.852	2.871	2.782	2.792	2.807
O-H	0.984	0.978	0.976	0.993	0.986	0.984
H...ND	1.858	1.877	1.906	1.789	1.807	1.825
∠OHND [º]	176.2	174.7	169.5	178.0	177.1	176.2

Table S3I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIE form are presented. Interatomic distances are given in [Å].

Five water molecules (HIE-5)						
Intermolecular HB						
O1...O	2.701	2.697	2.694	2.661	2.656	2.634
O1-H1	0.994	0.989	0.988	1.003	0.997	1.000
H1...O	1.711	1.712	1.711	1.660	1.661	1.635
∠O1H1O [º]	174.0	173.3	172.1	175.4	175.1	176.1
O...N1	2.952	2.956	2.957	2.874	2.875	2.888
O-H	0.972	0.968	0.968	0.983	0.978	0.976
H...N1	2.021	2.030	2.046	1.898	1.906	1.922
∠OHN1 [º]	159.6	159.3	156.0	171.5	170.8	169.9
NE...O	2.817	2.799	2.787	2.830	2.814	2.782
NE-HE	1.017	1.016	1.016	1.021	1.020	1.018
HE...O	1.955	1.934	1.951	1.932	1.914	1.940
∠NEHEO [º]	140.8	141.1	137.7	145.1	145.3	138.0
O...ND	2.831	2.842	2.858	2.771	2.781	2.792
O-H	0.984	0.979	0.977	0.994	0.987	0.986
H...ND	1.847	1.865	1.887	1.777	1.794	1.808
∠OHND [º]	177.3	176.9	172.4	178.1	177.5	175.5
O...O2	2.699	2.700	2.713	2.784	2.783	2.791
O-H	0.989	0.983	0.982	0.980	0.976	0.975
H...O2	1.717	1.724	1.741	1.822	1.828	1.845
∠OHO2 [º]	171.5	170.8	169.6	166.3	165.4	163.0

Table S3I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HIE form are presented. Interatomic distances are given in [Å].

Six water molecules (HIE-6)						
Intermolecular HB						
O1...O	2.603	2.606	2.566	2.623	2.629	2.578
O1-H1	1.019	1.011	1.021	1.015	1.007	1.018
H1...O	1.584	1.596	1.546	1.610	1.623	1.562
∠O1H1O [º]	176.3	176.1	175.7	175.9	176.0	175.9
O...N1	2.945	2.950	2.951	2.864	2.873	2.886
O-H	0.973	0.969	0.968	0.983	0.978	0.977
H...N1	2.012	2.022	2.039	1.887	1.904	1.921
∠OHN1 [º]	160.0	159.7	156.2	171.6	170.3	169.0
NE...O	2.961	2.940	2.955	2.895	2.875	2.883
NE-HE	1.013	1.012	1.013	1.018	1.017	1.017
HE...O	2.044	2.022	2.034	1.971	1.946	1.963
∠NEHEO [º]	149.2	149.7	149.9	149.6	150.4	149.0
O...ND	2.841	2.853	2.871	2.776	2.787	2.803
O-H	0.983	0.977	0.976	0.994	0.986	0.984
H...ND	1.859	1.876	1.901	1.783	1.801	1.821
∠OHND [º]	178.0	177.4	172.6	178.2	177.4	175.4
O...O2	2.960	2.944	2.90	2.841	2.843	2.848
O-H	0.969	0.966	0.967	0.975	0.971	0.970
H...O2	2.077	2.063	2.024	1.895	1.901	1.918
∠OHO2 [º]	150.6	150.7	149.5	162.9	163.0	159.7
O...O2	2.841	2.838	2.825	-	-	-
O-H	0.974	0.970	0.970	-	-	-
H...O2	1.903	1.904	1.899	-	-	-
∠OHO2 [º]	160.8	160.8	158.8	-	-	-

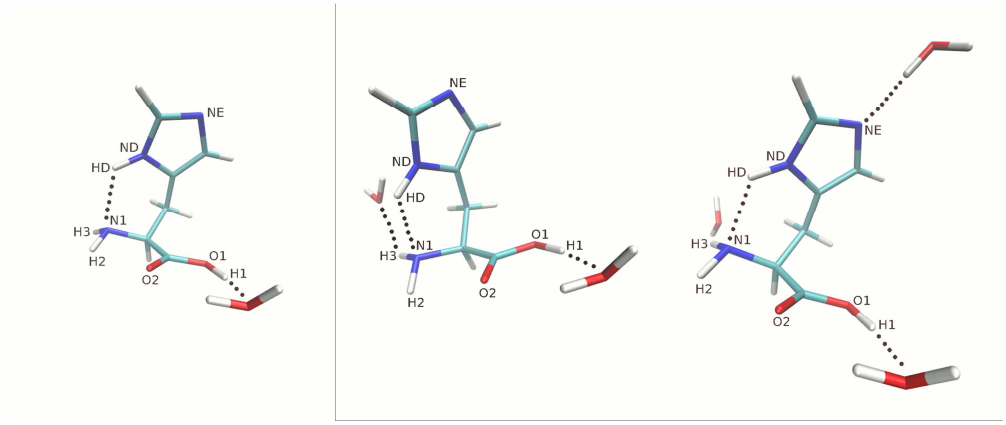

Figure S7I. Schematic presentation of microsolvation models for histidine HID form. Only three water molecules are present in the Figure for clarity. The dotted lines indicate the presence of selected intra- and intermolecular short contacs. Color coding: carbon, cyan; nitrogen, dark blue; oxygen, red; hydrogen, white.

Table S4I. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HID form are presented. Interatomic distances are given in [Å].

Metric parameters	B3LYP	ωB97XD	M06-2X	B3LYP	ωB97XD	M06-2X
	HID with 1-6 water molecules			HID with 1-6 water molecules and with PCM		
Histidine HID form						
One water molecule (HID-1)						
Intramolecular HB						
ND...N1	2.920	2.909	2.904	2.888	2.875	2.878
ND-HD	1.013	1.011	1.012	1.016	1.015	1.015
HD...N1	2.260	2.258	2.260	2.209	2.20	2.215
∠NDHN1 [°]	121.5	120.8	120.2	122.8	122.5	121.4
Intermolecular HB						
O1...O	2.705	2.698	2.696	2.690	2.683	2.675
O1-H1	0.990	0.986	0.985	0.993	0.990	0.989
H1...O	1.761	1.756	1.759	1.718	1.704	1.716
∠O1H1O [°]	158.3	158.6	157.4	164.7	169.3	162.3
Two water molecules (HID-2)						
Intramolecular HB						
ND...N1	2.818	2.803	2.80	2.872	2.860	2.869
ND-HD	1.020	1.018	1.019	1.018	1.016	1.016
HD...N1	2.094	2.083	2.089	2.175	2.169	2.196
∠NDHN1 [°]	126.2	125.8	125.0	124.1	123.6	122.2
Intermolecular HB						
O1...O	2.713	2.707	2.705	2.697	2.690	2.683
O1-H1	0.989	0.984	0.984	0.992	0.988	0.988
H1...O	1.773	1.769	1.774	1.730	1.720	1.726
∠O1H1O [°]	157.5	157.9	156.7	163.8	166.2	161.7
N1...O	3.100	3.090	3.027	3.055	3.040	3.013
N1-H3	1.015	1.014	1.016	1.018	1.018	1.017
H3...O	2.394	2.378	2.328	2.093	2.058	2.118
∠N1H3O [°]	125.9	126.4	124.7	156.8	161.3	145.6

Table S4I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HID form are presented. Interatomic distances are given in [Å].

Three water molecules (HID-3)						
Intramolecular HB						
ND...N1	2.856	2.848	2.868	2.857	2.848	2.868
ND-HD	1.017	1.015	1.015	1.019	1.015	1.015
HD...N1	2.143	2.144	2.191	2.153	2.144	2.191
∠NDHDN1 [°]	125.4	124.8	122.7	124.6	124.8	122.7
Intermolecular HB						
O1...O	2.708	2.707	2.706	2.695	2.707	2.705
O1-H1	0.989	0.984	0.984	0.993	0.984	0.984
H1...O	1.768	1.769	1.773	1.727	1.769	1.772
∠O1H1O [°]	157.4	157.9	156.9	163.9	157.9	156.9
N1...O	3.051	3.051	3.029	3.053	3.052	-
N1-H3	1.016	1.015	1.015	1.018	1.015	-
H3...O	2.119	2.110	2.159	2.092	2.110	-
∠N1H3O [°]	151.6	153.3	142.7	156.4	153.3	-
O…NE	2.860	2.878	2.846	2.788	2.872	2.845
O-H	0.981	0.976	0.973	0.991	0.976	0.973
H...NE	1.879	1.897	1.914	1.797	1.898	1.913
∠OHNE [°]	180.0	176.2	159.4	178.6	176.2	159.4

Table S4I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HID form are presented. Interatomic distances are given in [Å].

Four water molecules (HID-4)						
Intramolecular HB						
ND...N1	2.769	2.757	2.776	2.793	2.777	2.817
ND-HD	1.022	1.020	1.019	1.021	1.020	1.018
HD...N1	2.021	2.015	2.054	2.061	2.050	2.123
∠NDHDN1 [°]	127.8	127.4	125.8	126.6	126.2	123.6
Intermolecular HB						
O1...O	2.716	2.711	2.710	2.695	2.689	2.683
O1-H1	0.988	0.984	0.983	0.993	0.989	0.988
H1...O	1.777	1.775	1.780	1.725	1.716	1.727
∠O1H1O [°]	157.3	157.6	156.4	164.3	167.2	161.7
N1...O	3.026	3.001	2.998	3.118	3.077	-
N1-H3	1.018	1.018	1.016	1.018	1.018	-
H3...O	2.116	2.085	2.180	2.222	2.163	-
∠N1H3O [°]	147.8	148.5	136.3	146.0	148.4	-
O...NE	2.832	2.838	2.810	2.845	2.859	2.839
O-H	0.980	0.975	0.974	0.981	0.975	0.975
H...NE	1.925	1.939	1.938	1.922	1.946	1.950
∠OHNE [°]	152.7	152.3	147.6	155.7	154.8	150.5

Table S4I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HID form are presented. Interatomic distances are given in [Å].

Five water molecules (HID-5)						
Intramolecular HB						
ND...N1	2.767	2.756	2.783	2.861	2.839	2.875
ND-HD	1.024	1.021	1.020	1.017	1.016	1.017
HD...N1	2.018	2.014	2.064	2.186	2.161	2.221
∠NDHDN1 [°]	127.9	127.4	125.4	122.3	122.5	120.6
Intermolecular HB						
O1...O	2.705	2.699	2.702	2.677	2.672	2.663
O1-H1	0.989	0.985	0.984	0.996	0.992	0.991
H1...O	1.758	1.754	1.765	1.699	1.680	1.698
∠O1H1O [°]	158.9	159.4	157.6	166.1	178.8	163.3
N1...O	3.068	3.049	3.005	3.153	3.052	-
N1-H2	1.016	1.016	1.016	1.014	1.019	-
H2...O	2.133	2.118	2.085	3.233	2.101	-
∠N1H2O [°]	152.1	151.5	149.5	153.6	154.5	-
N1...O	3.055	3.028	3.023	-	-	-
N1-H3	1.018	1.018	1.017	-	-	-
H3...O	2.127	2.100	2.169	-	-	-
∠N1H3O [°]	150.4	150.6	140.4	-	-	-
O...NE	2.821	2.828	2.805	2.832	2.846	2.837
O-H	0.981	0.975	0.975	0.981	0.976	0.975
H...NE	1.914	1.928	1.932	1.908	1.933	1.950
∠OHNE [°]	152.7	152.2	147.8	155.8	154.7	150.2
O2...O	2.830	2.825	2.814	2.844	2.836	2.873
O-H	0.971	0.967	0.967	0.975	0.972	0.972
H...O2	1.926	1.919	1.937	1.872	1.867	1.909
∠OHO2 [°]	153.9	154.9	149.5	175.1	174.5	171.7

Table S4I Continuation. The metric parameters values obtained for the microsolvation models. The simulations were performed in the gas phase with 1-6 water molecules and with the continuum PCM model (water as a solvent) at the DFT level of theory and 6-311+G(d,p) basis set. Only selected interactions with histidine HID form are presented. Interatomic distances are given in [Å].

Six water molecules (HID-6)						
Intramolecular HB						
ND...N1	2.753	2.738	2.759	2.876	2.862	3.180
ND-HD	1.027	1.026	1.024	1.017	1.016	1.019
HD...N1	1.987	1.976	2.017	2.201	2.190	2.843
∠NDHDN1 [°]	129.1	128.8	127.2	122.4	122.0	99.8
Intermolecular HB						
O1...O	2.638	2.642	2.622	2.637	2.635	2.646
O1-H1	1.004	0.997	1.002	1.003	0.997	0.997
H1...O	1.666	1.673	1.653	1.656	1.659	1.660
∠O1H1O [°]	161.5	162.5	161.5	164.8	164.9	169.5
N1...O	3.052	3.034	3.008	3.095	3.057	-
N1-H2	1.017	1.016	1.017	1.018	1.018	-
H2...O	2.104	2.087	2.060	2.175	2.126	-
∠N1H2O [°]	154.3	154.1	154.2	149.5	151.1	-
N1...O	3.080	3.042	3.020	-	-	-
N1-H3	1.018	1.017	1.017	-	-	-
H3...O	2.186	2.138	2.169	-	-	-
∠N1H3O [°]	145.7	147.0	140.0	-	-	-
O...N1	-	-	-	-	-	2.872
O-H	-	-	-	-	-	0.981
H...N1	-	-	-	-	-	1.892
∠OHN1 [°]	-	-	-	-	-	177.0
O...NE	2.826	2.833	2.810	2.829	2.840	2.813
O-H	0.979	0.974	0.973	0.981	0.975	0.978
H...NE	1.931	1.945	1.953	1.909	1.930	1.881
∠OHNE [°]	150.8	150.3	145.6	155.0	154.1	158.2
O...NE	-	-	-	-	-	3.141
O-H	-	-	-	-	-	0.967
H...NE	-	-	-	-	-	2.239
∠OHNE [°]	-	-	-	-	-	154.8
O2...O	2.811	2.806	2.795	2.835	2.832	-
O-H	0.972	0.968	0.968	0.976	0.972	-
H...O2	1.905	1.900	1.913	1.861	1.863	-
∠OHO2 [°]	154.0	154.8	150.2	175.4	174.6	-

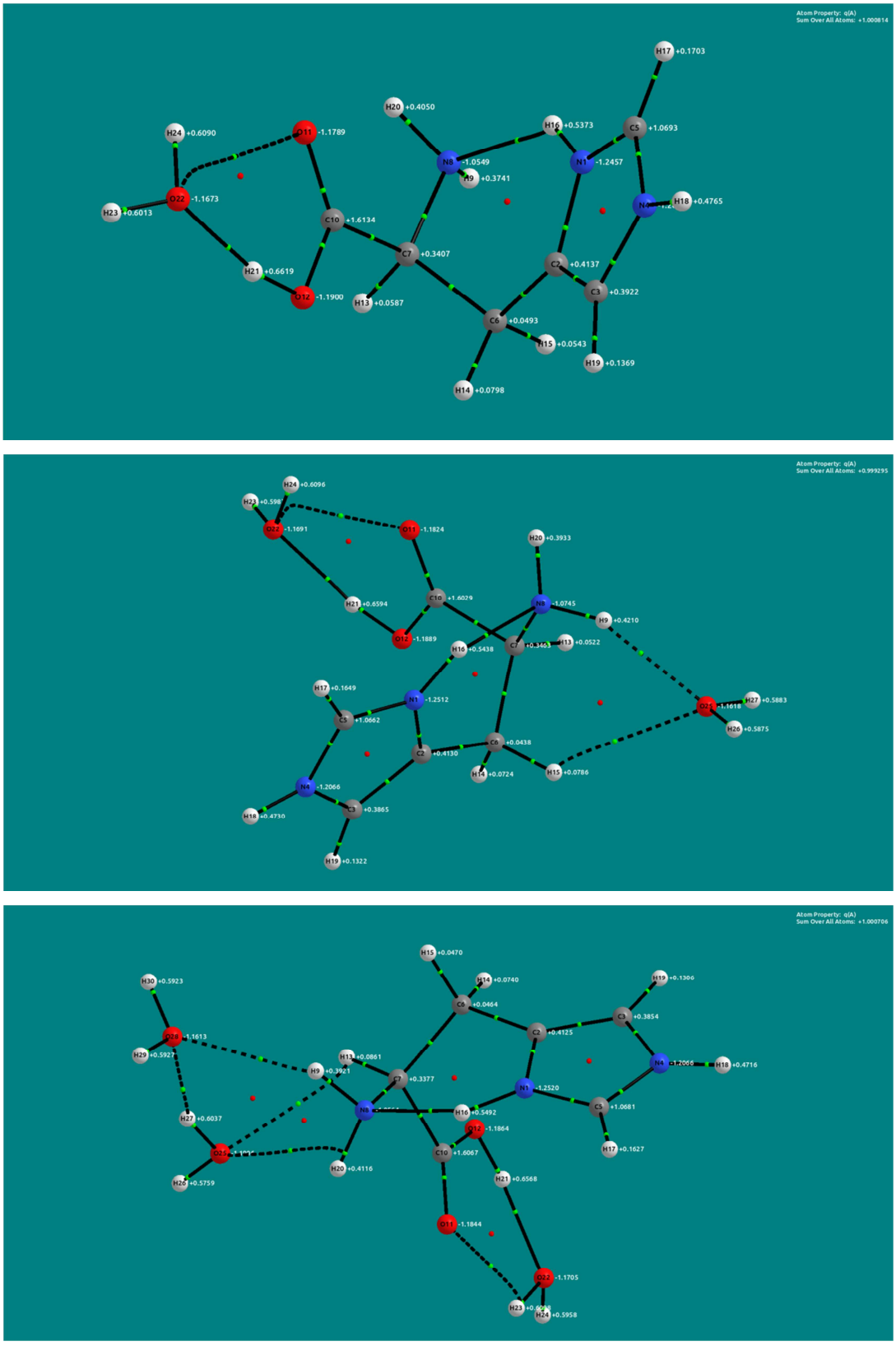

Figure S8I. The topological maps of histidine HIP microsolvation model (1-3 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

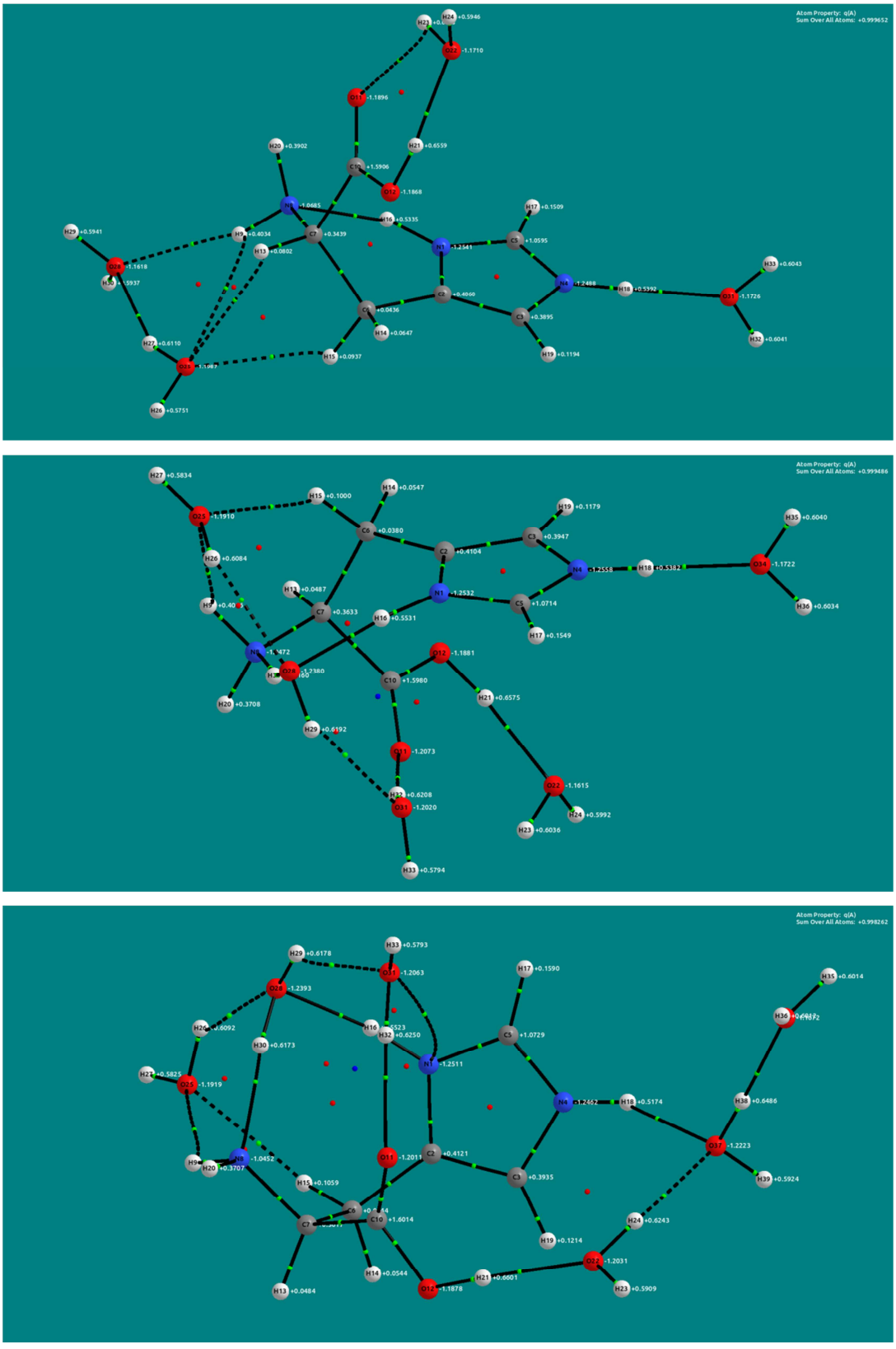

Figure S8I Continuation. The topological maps of histidine HIP microsolvation model (4-6 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

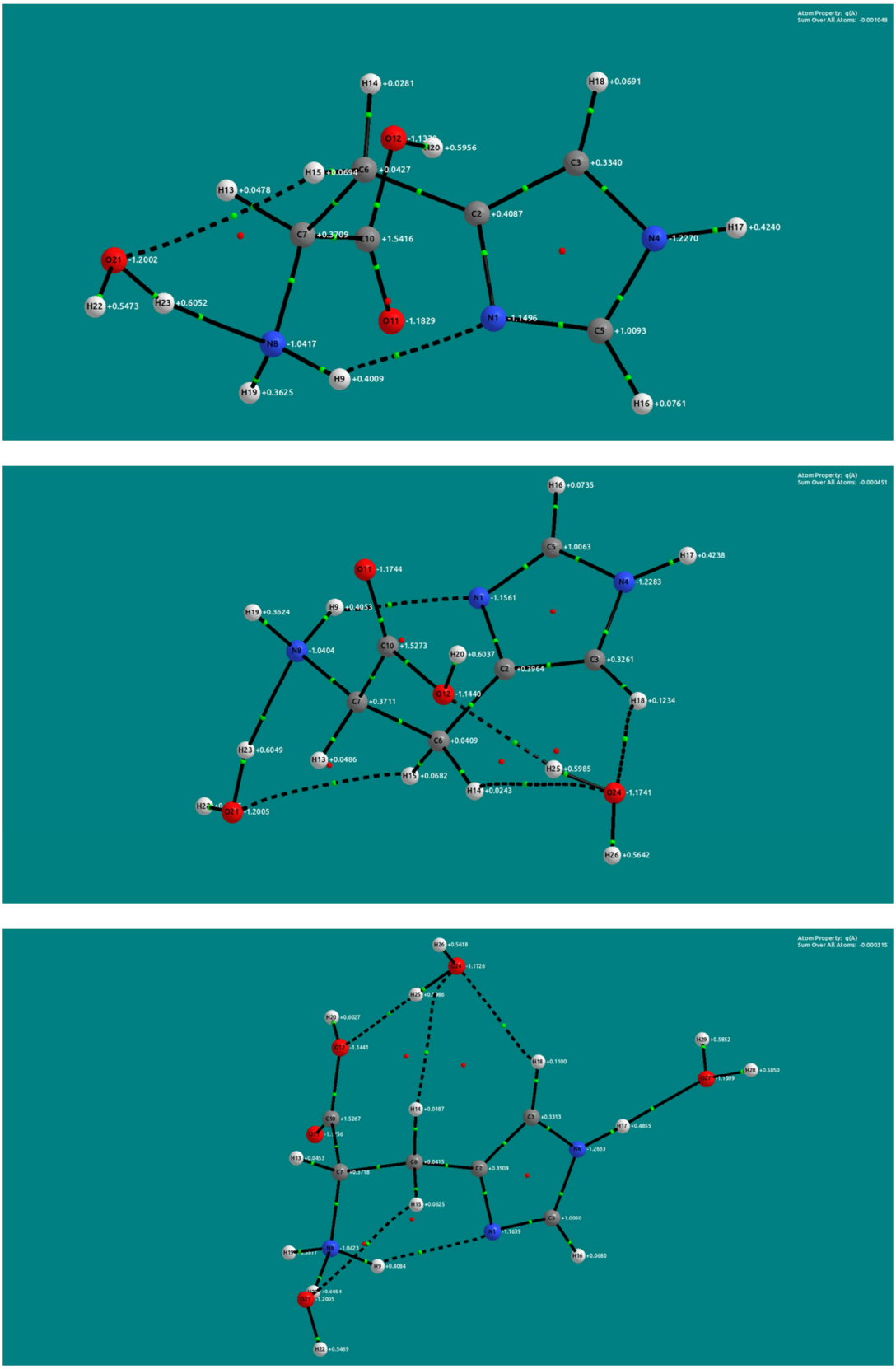

Figure S9I. The topological maps of histidine HIE microsolvation model (1-3 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

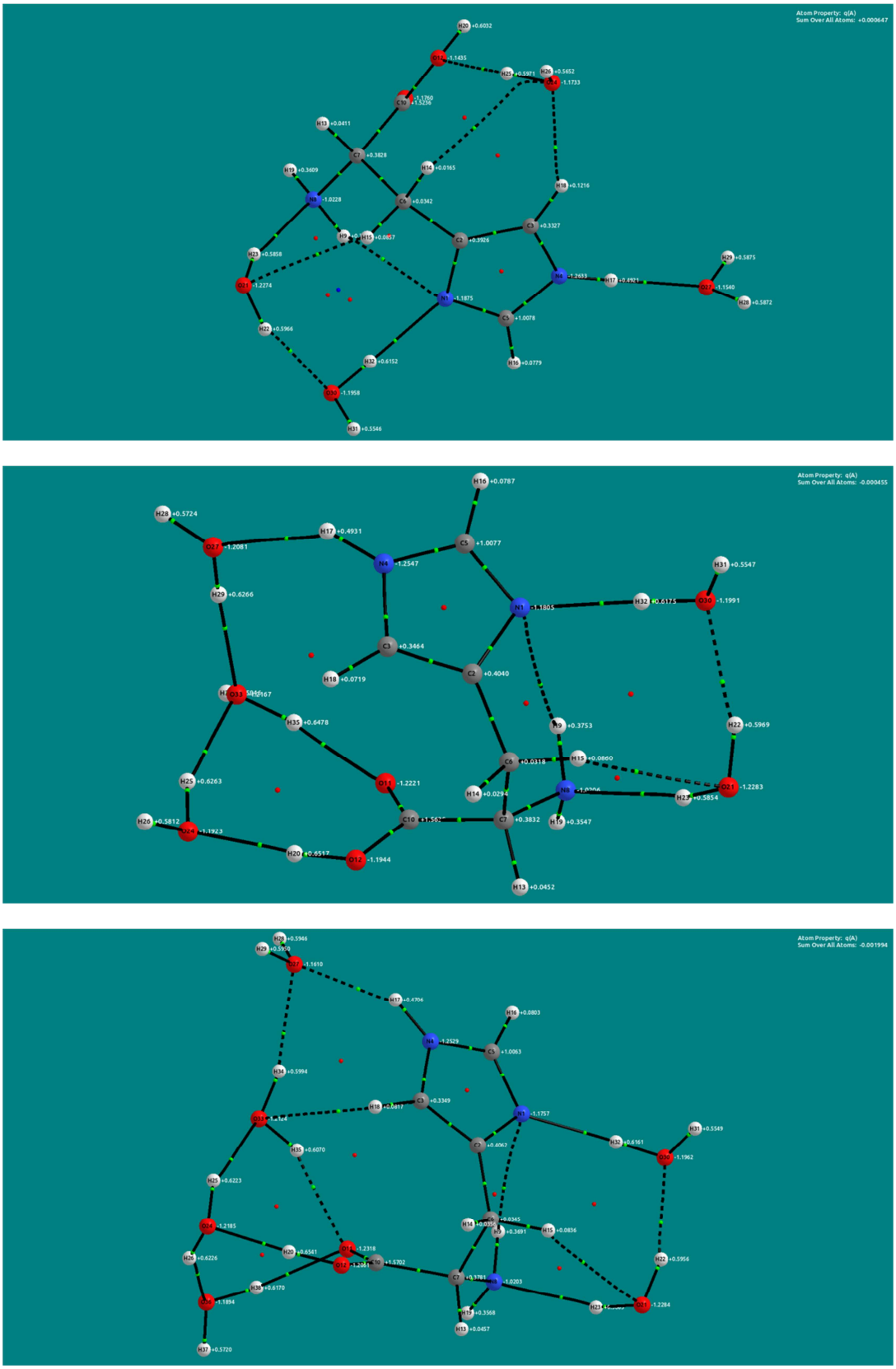

Figure S9I Continuation. The topological maps of histidine HIE microsolvation model (4-6 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

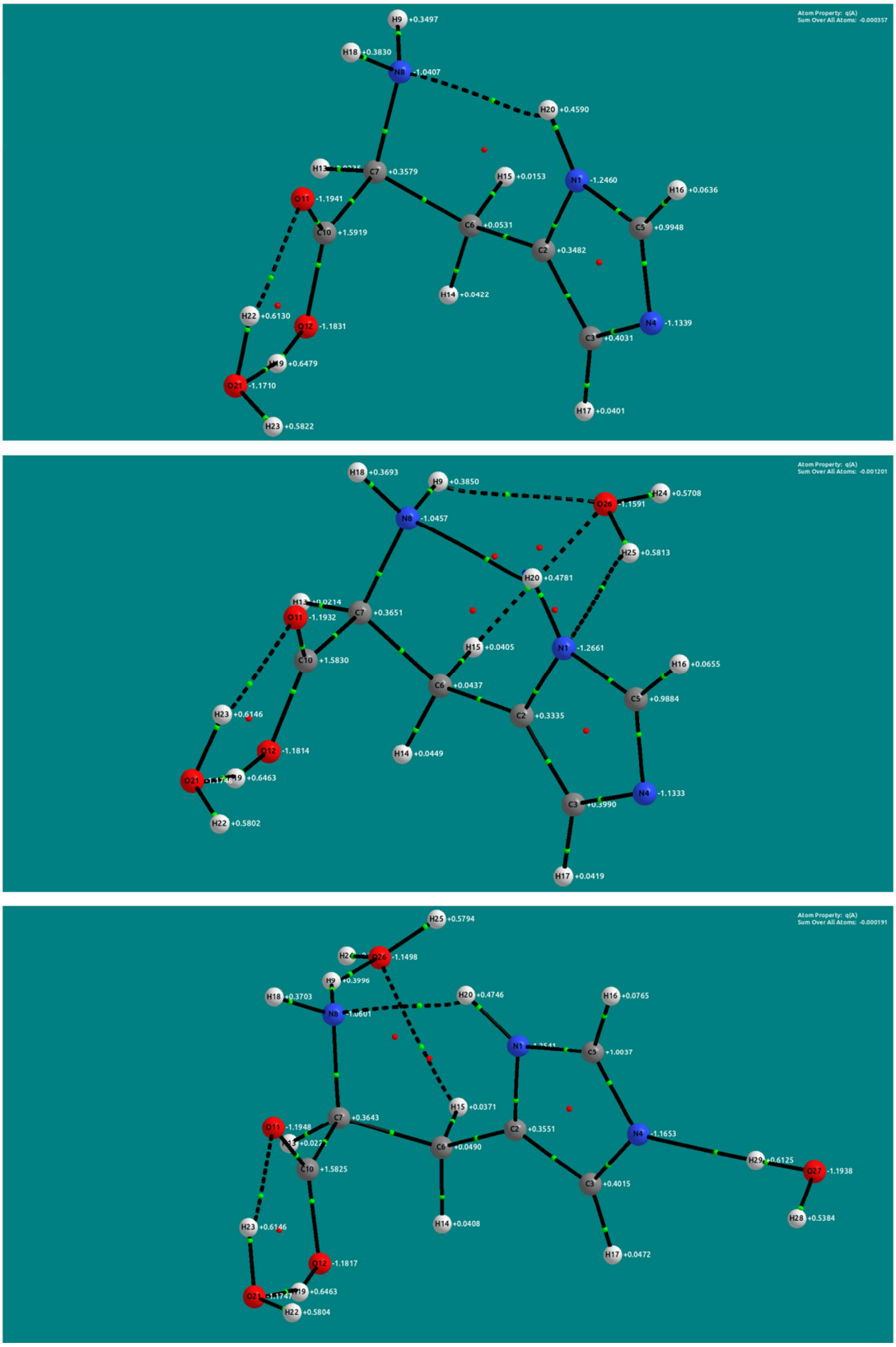

Figure S10I. The topological maps of histidine HID microsolvation model (1-3 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

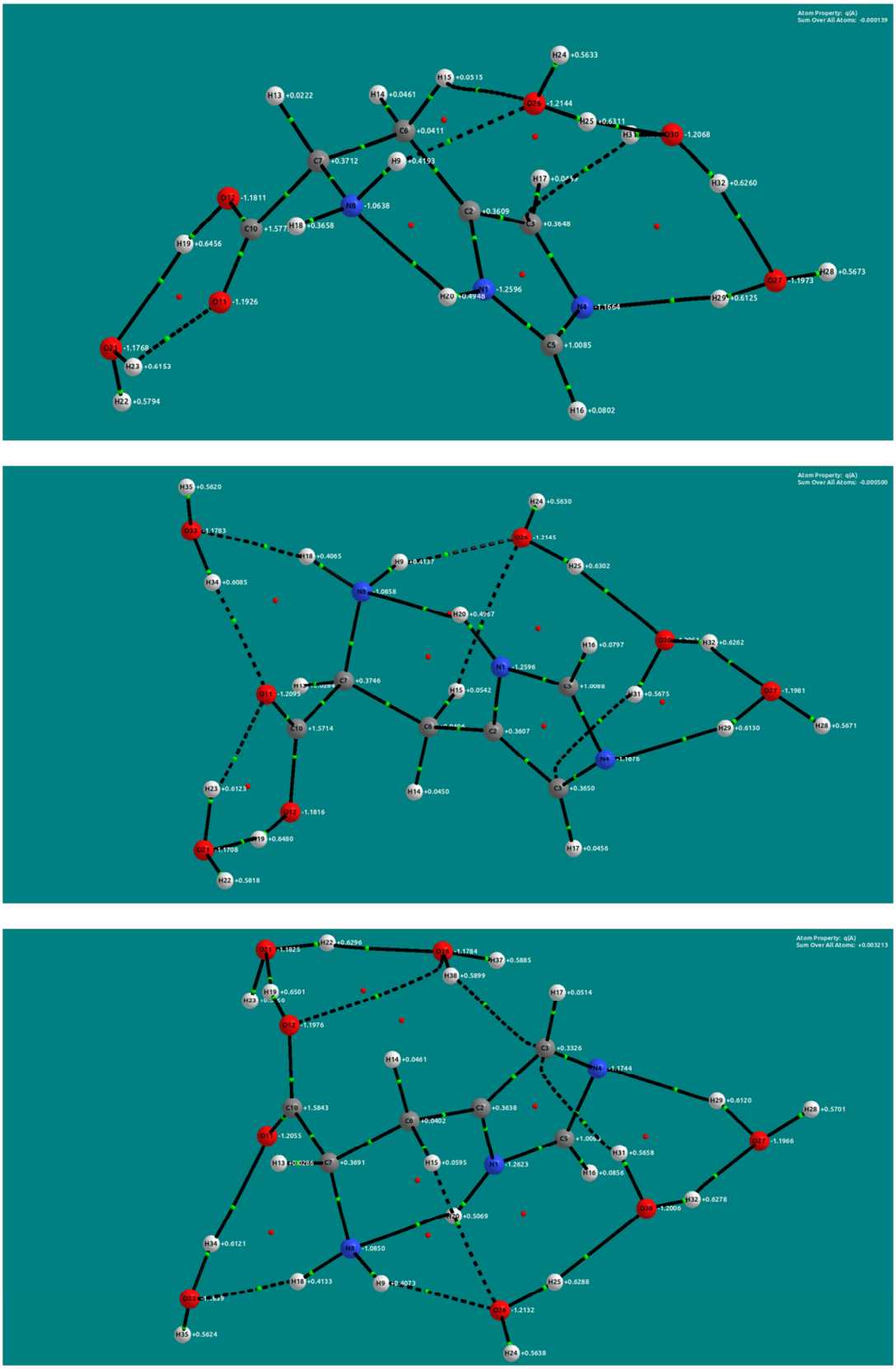

Figure S10I Continuation. The topological maps of histidine HID microsolvation model (4-6 water molecules) obtained as a result of AIM theory. The values of partial atomic charges are shown as well as bond critical points (BCPs) and ring critical points (RCPs) are indicated.

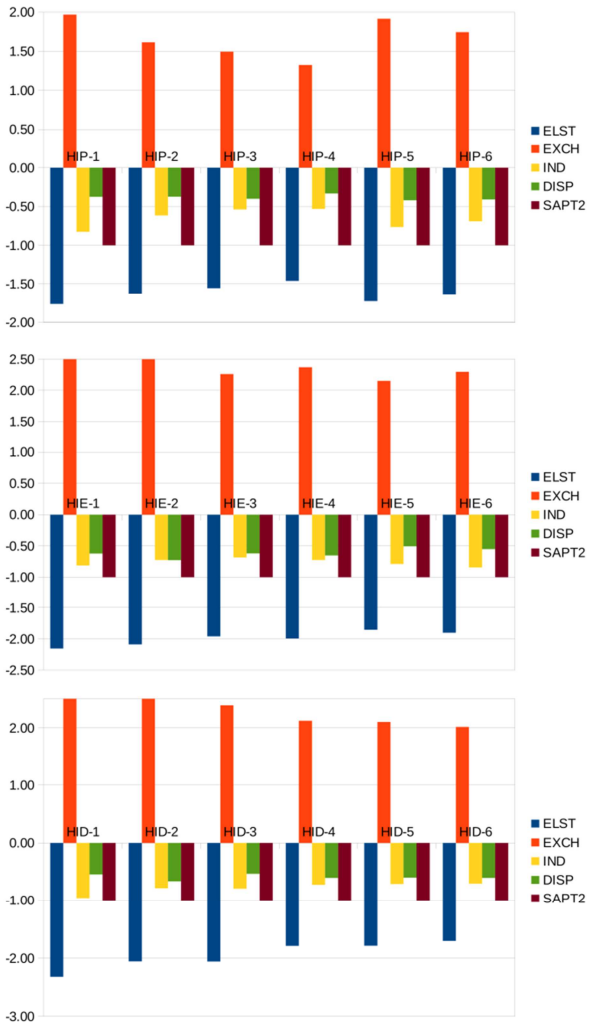

Figure S11I. Ratios of the interaction energy components relative to the total SAPT2 interaction energy (SAPT2 – scaled to be -1.00 in order to follow the convention of assigning negative values to the stabilizing terms). ELST – electrostatic interaction of frozen monomer electron densities, EXCH – Pauli repulsion of the frozen monomer densities, IND – the effect of mutual polarization and relaxation of monomer electron densities, DISP – dispersion contribution.