Molecular Simulations of Aromatase Reveal New Insights Into the Mechanism of Ligand Binding

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Supporting Information

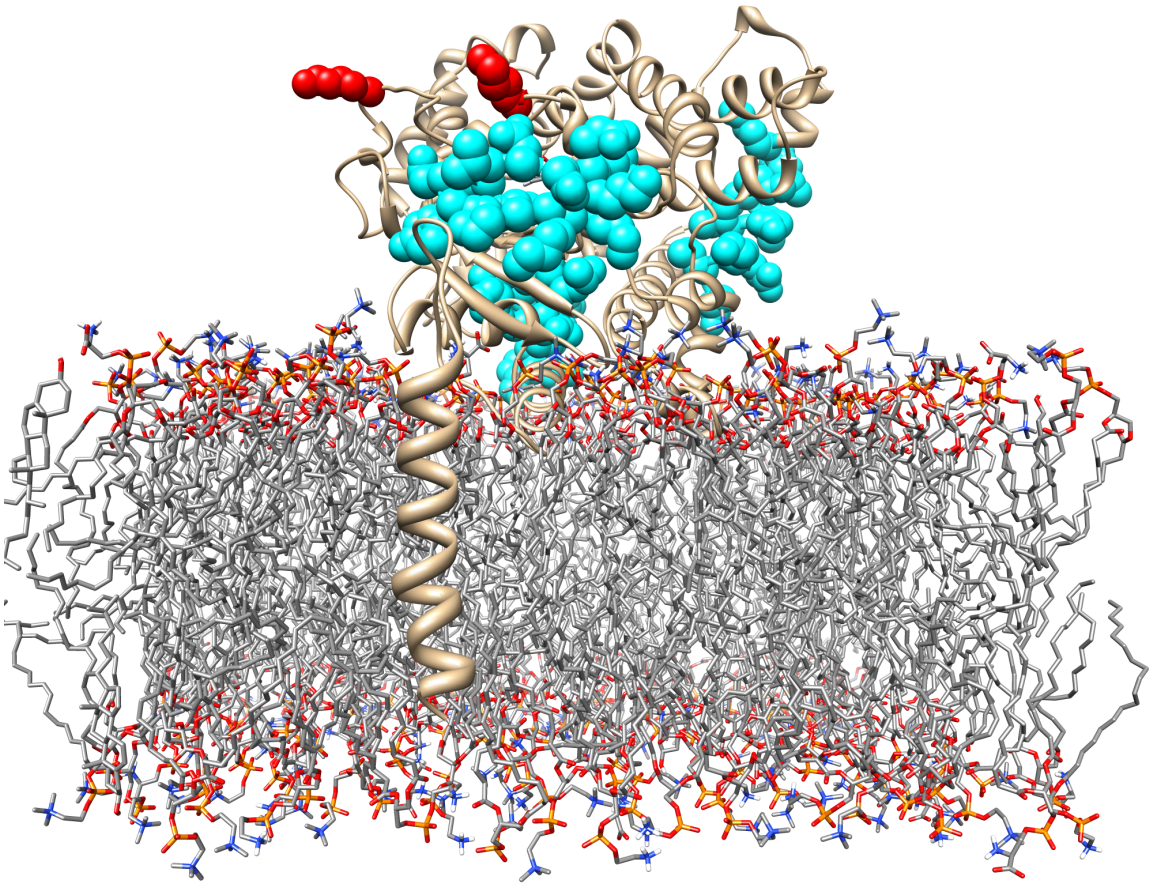

Figure S1: Illustration of the solvent-exposure of epitopes (cyan) and cytochrome P450 reductase binding residues (red) in the assembled model of membrane-bound aromatase.

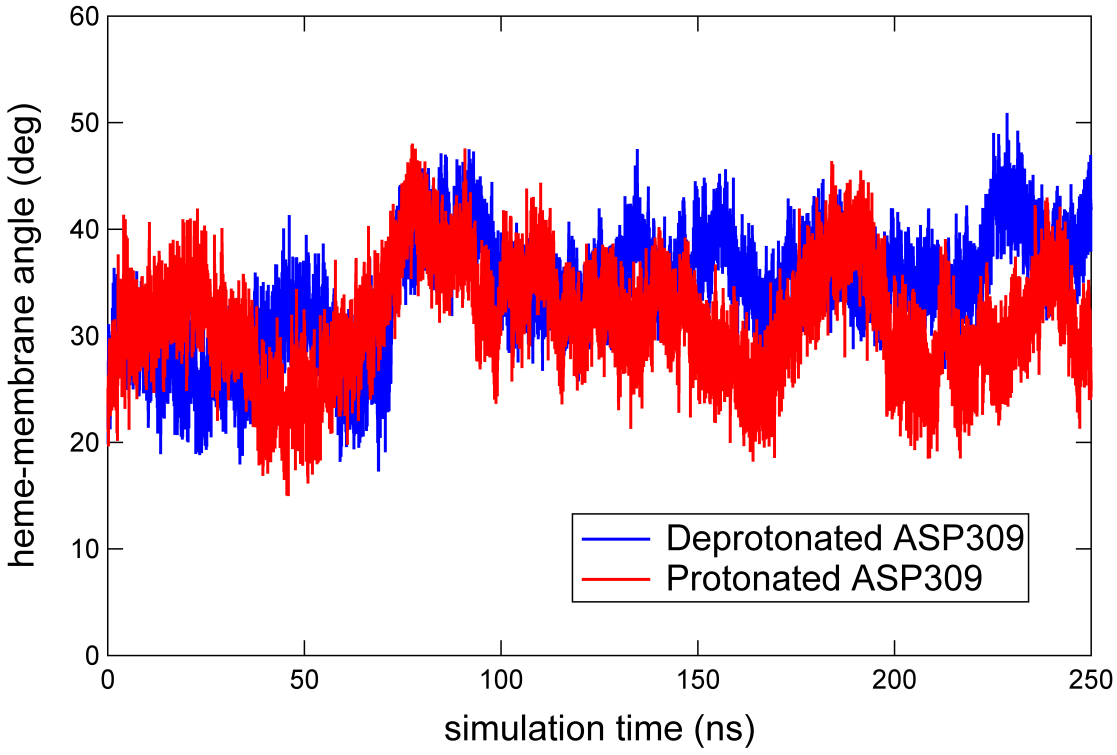

Figure S2: Illustration of the angle between the normal to the plane of the heme and the normal to the plane of the membrane (the z-axis) in both trajectories.

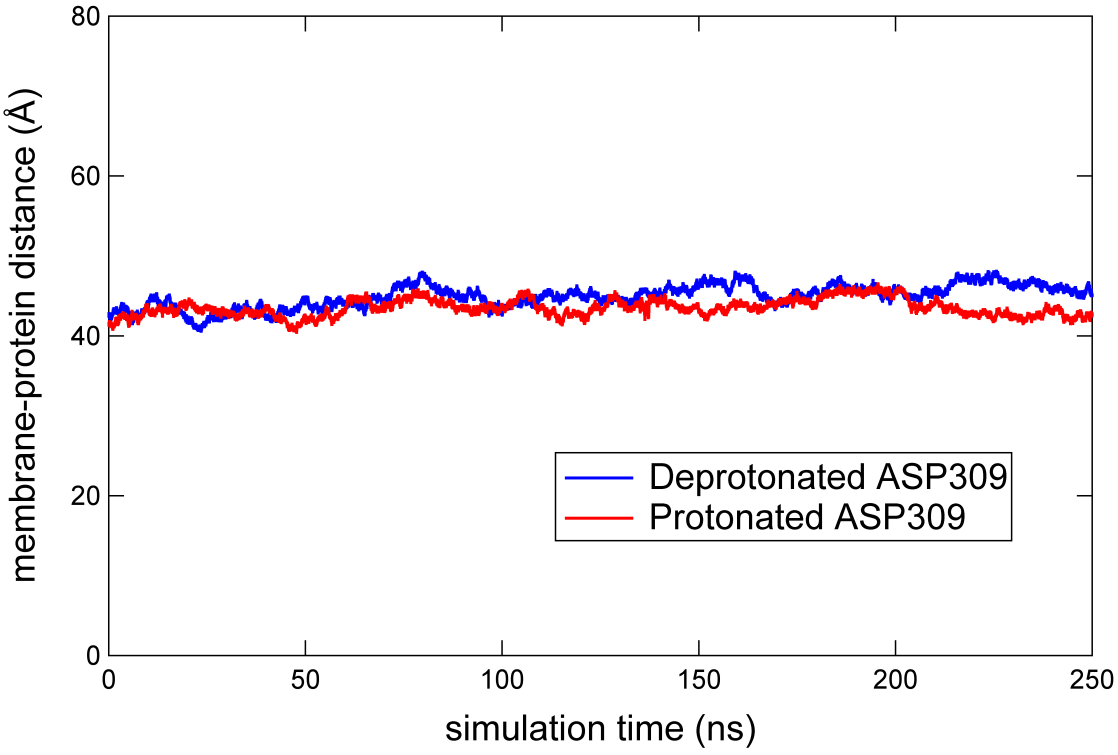

Figure S3: Illustration of the vertical distance between aromatase and the center of the membrane in both trajectories. The center of mass of the non-hydrogen atoms of protein that are present in the crystal structure (PDB accession code 3EQM) is used as the position of the protein.

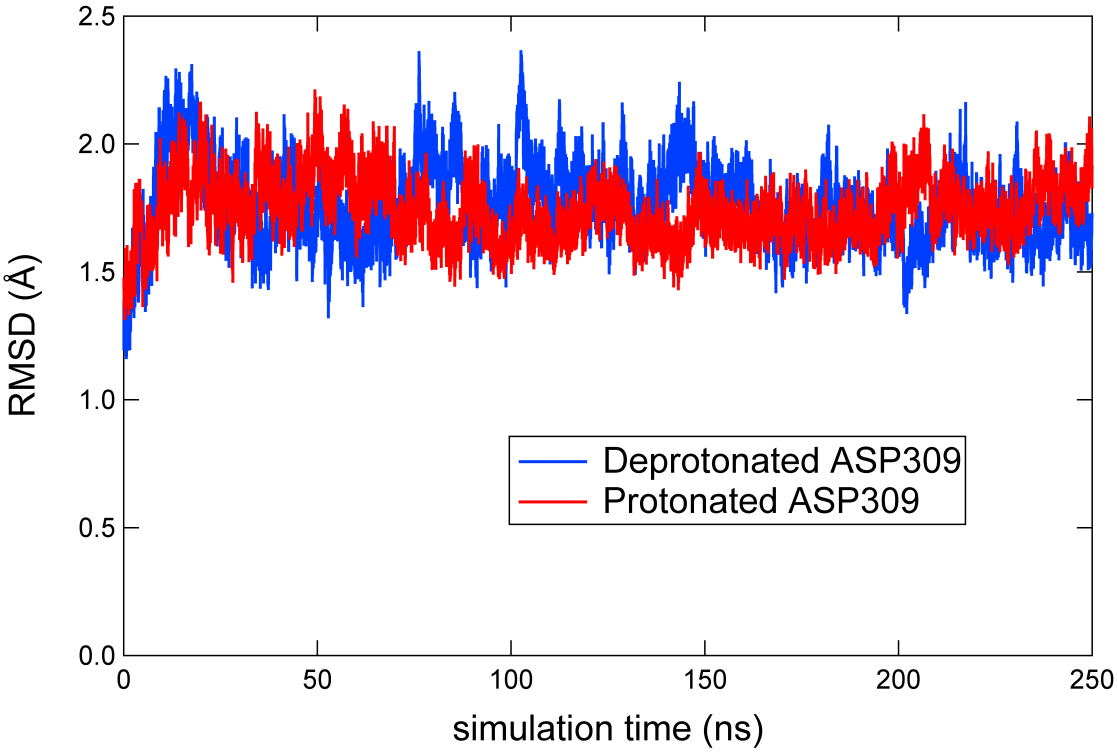

Figure S4: Illustration of the relative RMSD for simulated trajectories of aromatase with both a protonated and deprotonated Asp-309 residue. The relative RMSD of protein non-hydrogen atoms of residues 45-496 are reported by aligning the structures from the trajectories to the original crystal structure (PDB accession code 3EQM).

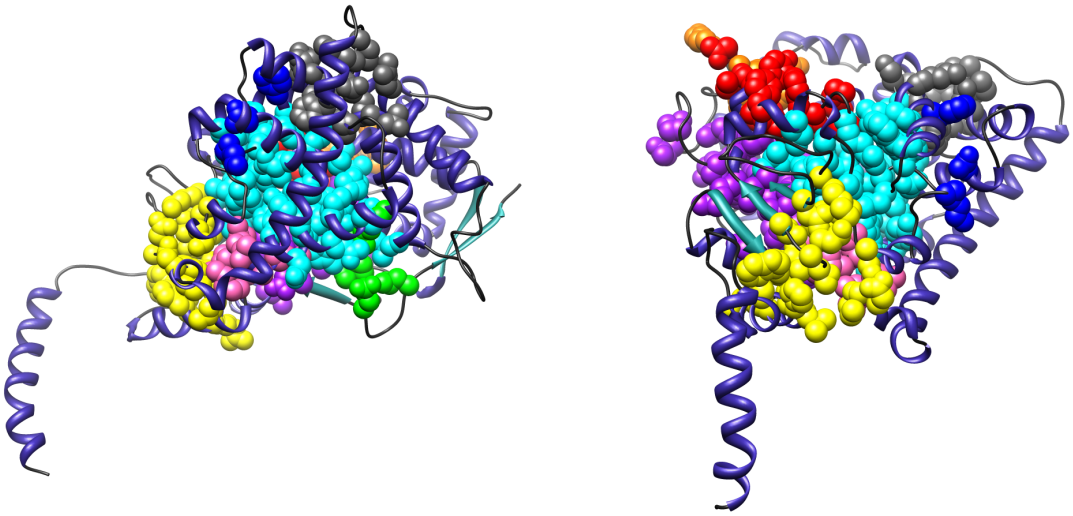

Figure S5: Depiction of the nine consensus sites identified by FTprod after computational solvent mapping calculations. Color Key: CS1 – Cyan, CS2 – Red, CS3 – Gray, CS4 – Orange, CS5 – Yellow, CS6 – Pink, CS7 – Purple, CS8 – Green, CS9 – Blue

Table S1: Results of the GROMOS++ clustering of trajectory ensembles in the deprotonated and protonated trajectories.

Protonated Asp-309 Trajectory Clustering

Cluster Number	Number of Frames	Percentage of Trajectory
1	6149	61.49
2	1426	14.26
3	983	9.83
4	577	5.77
5	441	4.41
6	133	1.33
7	87	0.87
8	70	0.70
9	44	0.44
10	33	0.33
11	14	0.14
12	11	0.11
13	10	0.10
14	9	0.09
15	6	0.06
16	5	0.05
17	1	0.01
18	1	0.01

Deprotonated Asp-309 Trajectory Clustering

Cluster Number	Number of Frames	Percentage of Trajectory
1	6687	66.88
2	1092	10.92
3	564	5.64
4	420	4.20
5	384	3.84
6	320	3.20
7	138	1.38
8	83	0.83
9	58	0.58
10	53	0.53
11	39	0.39
12	36	0.36
13	22	0.22
14	22	0.22
15	18	0.18

16	16	0.16
17	13	0.13
18	11	0.11
19	5	0.05
20	5	0.05
21	3	0.03
22	3	0.03
23	2	0.02
24	1	0.01
25	1	0.01
26	1	0.01
27	1	0.01