Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Newly Synthesized Series of Oxoindole-Oxadiazole Conjugates as Potential Anti-SARS-CoV-2 Agents: *In Silico* and *In Vitro* Studies

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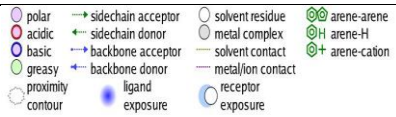
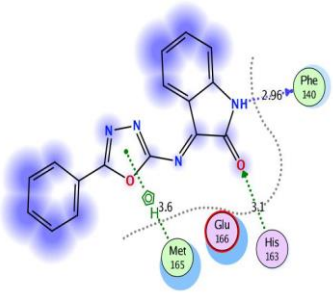
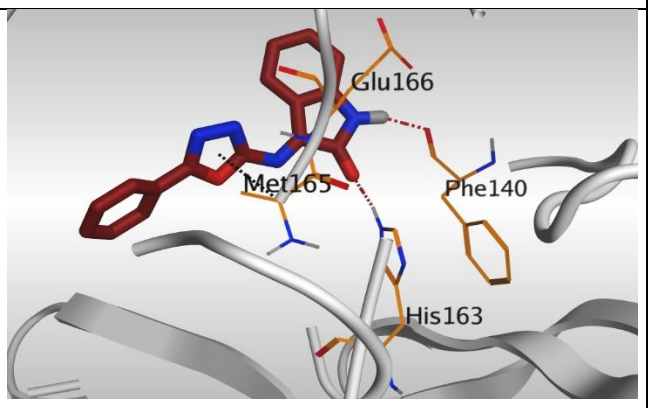
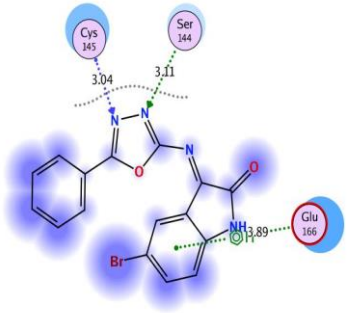
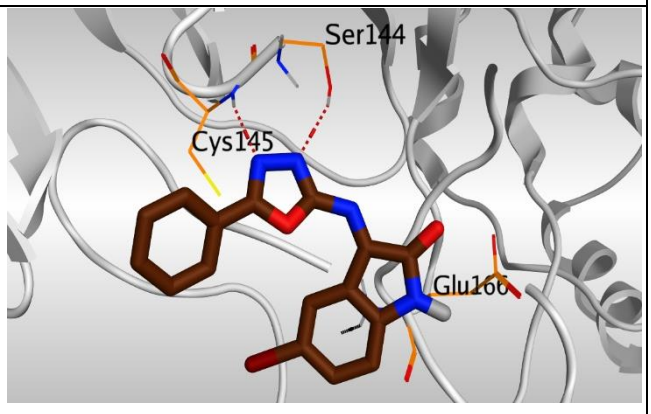
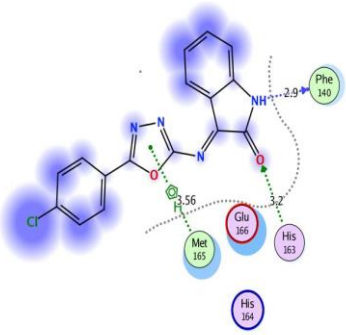
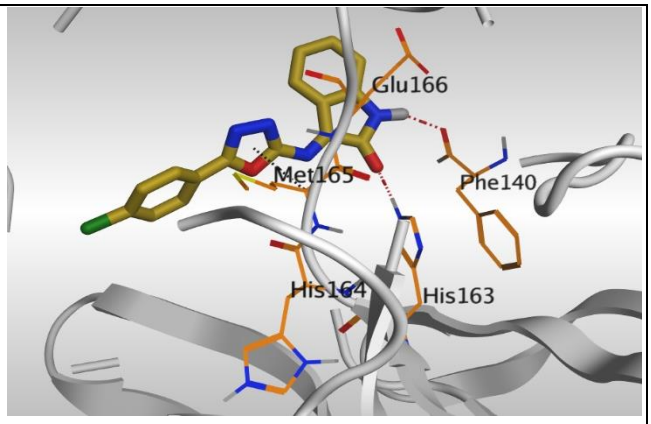
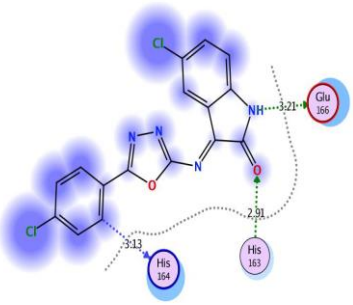
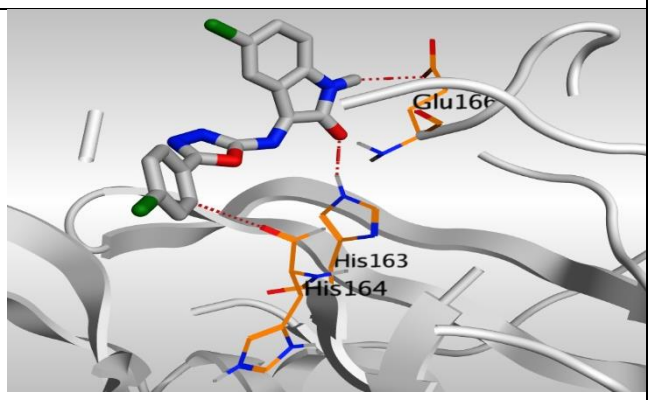
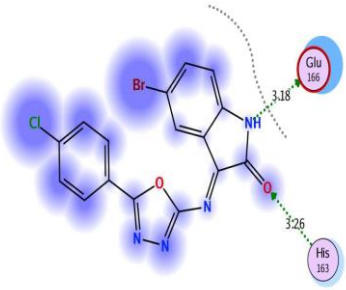
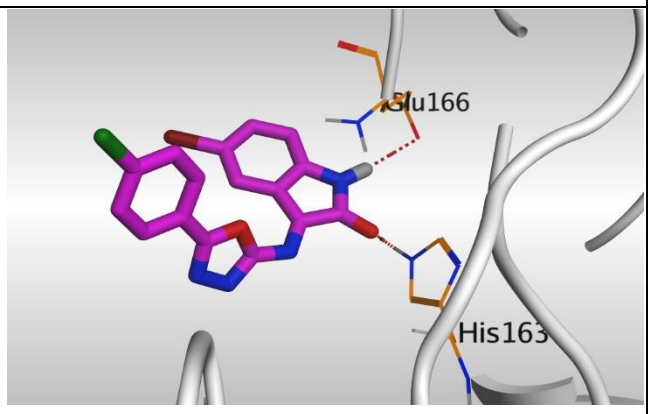
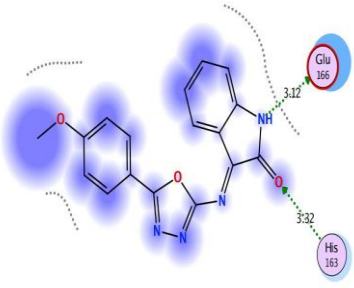
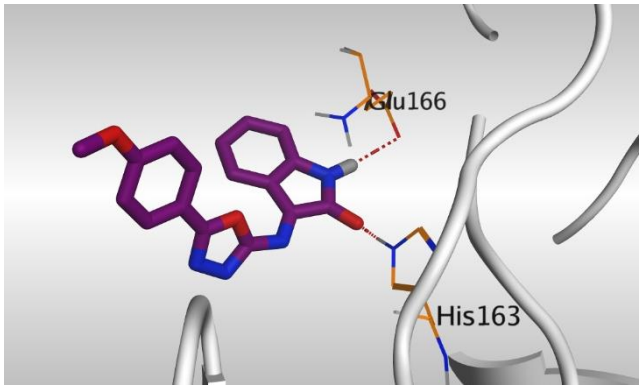
Figure SI1: 2D and 3D docking representations of the seven newly synthesized Oxoindole-Oxadiazole conjugates and the previously reported one (**I_a**) compared to the docked **N3** inhibitor against its binding site inside the COVID-19 main protease.

No.	Tested comp.	2D	3D
			Red dashed lines refer to hydrogen bonds, while the black ones denote hydrophobic interactions.
1	**III_a**		
2	**III_b**		

3	**III_c**		
4	**III_d**		
5	**III_e**		
6	**III_f**		

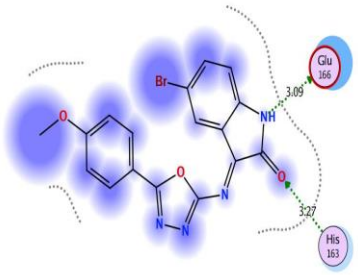
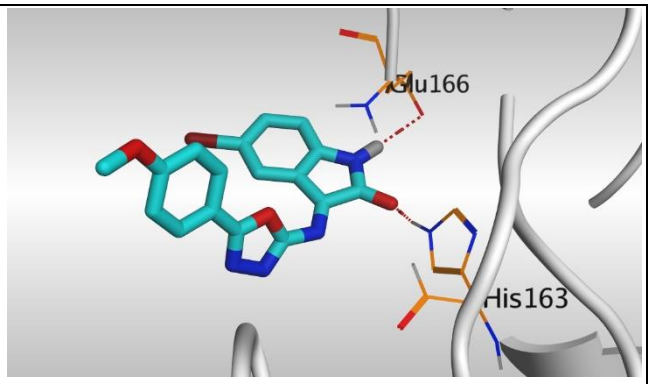
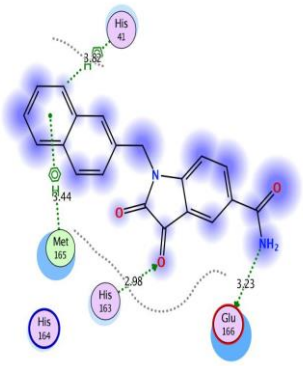
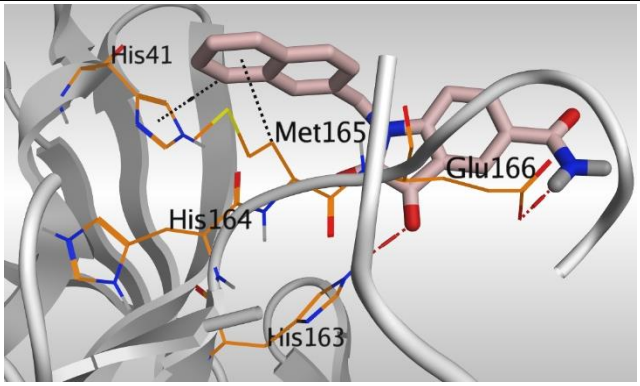
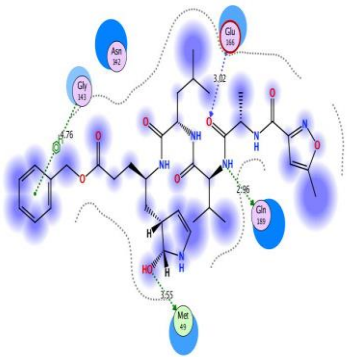
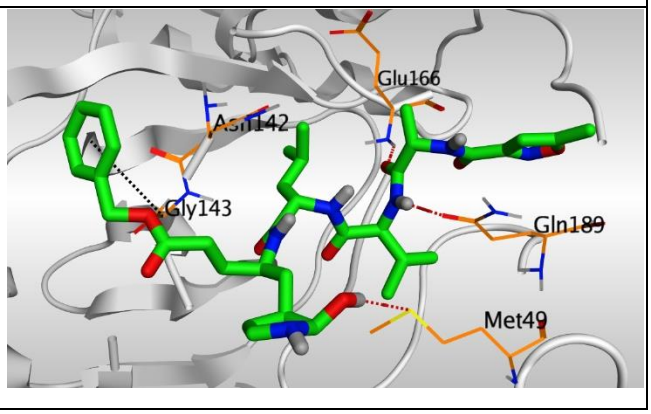
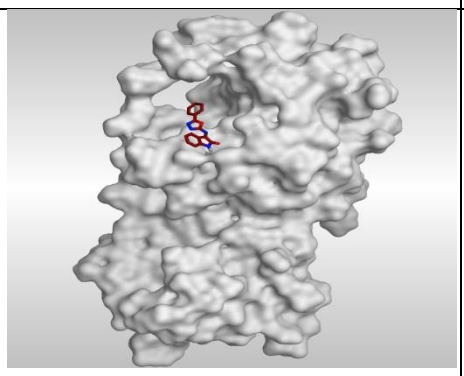
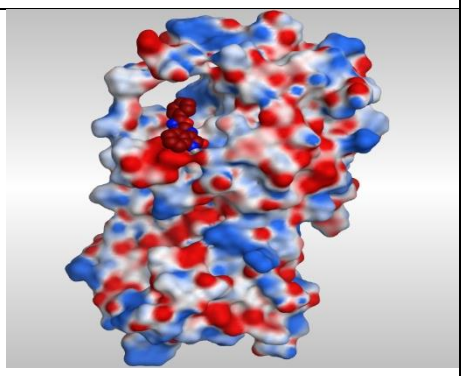
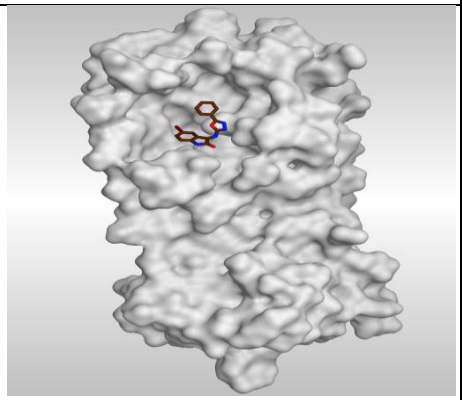
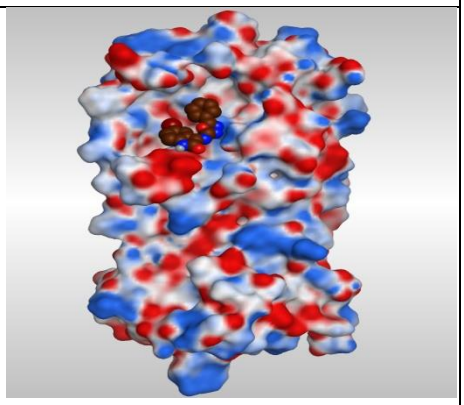
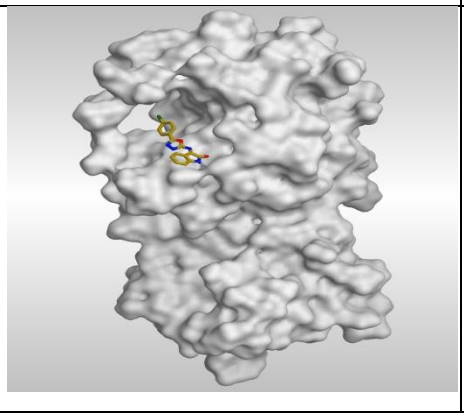
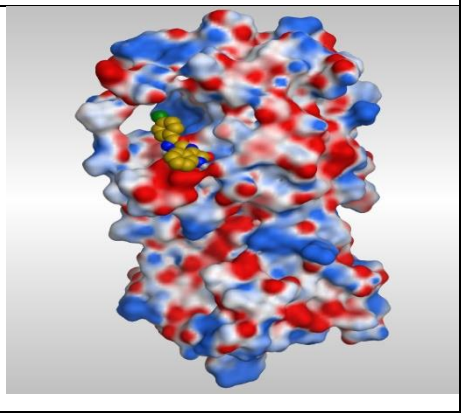
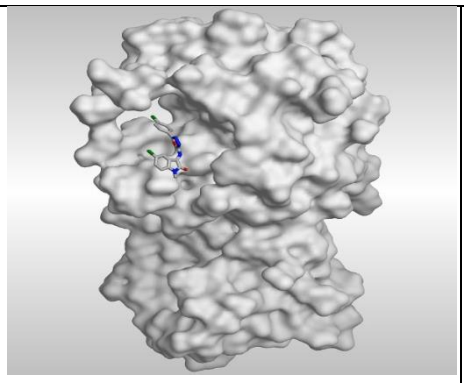
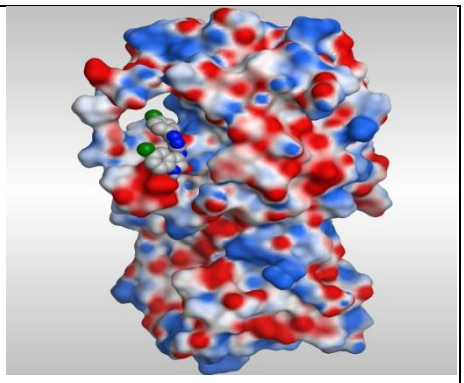
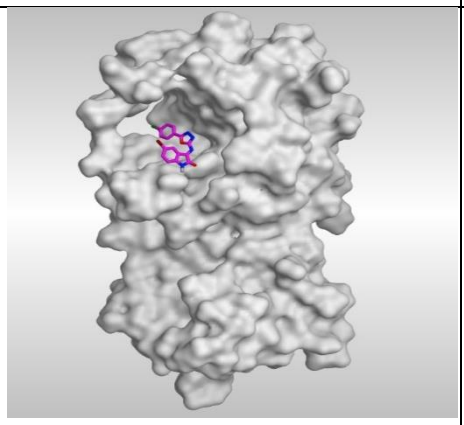
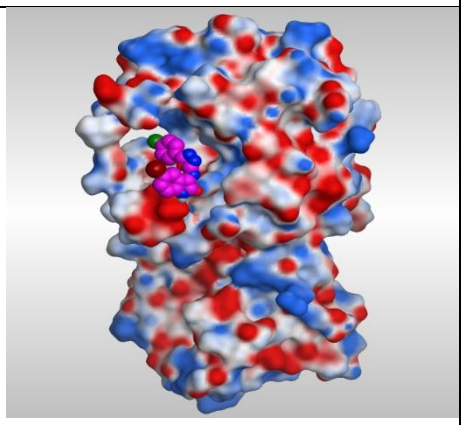
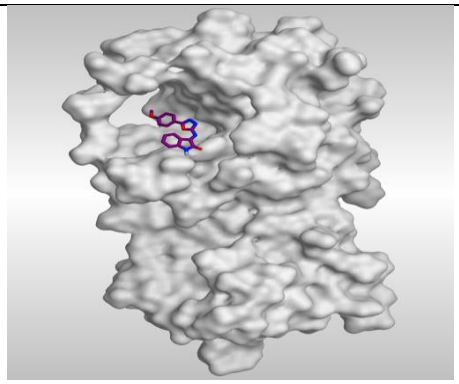
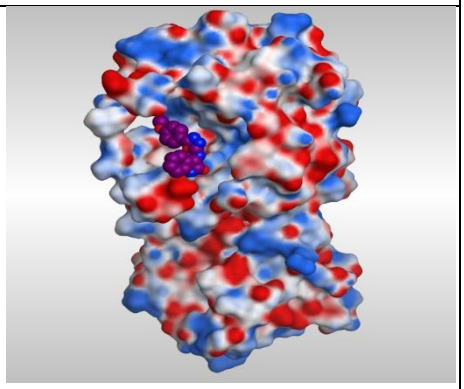
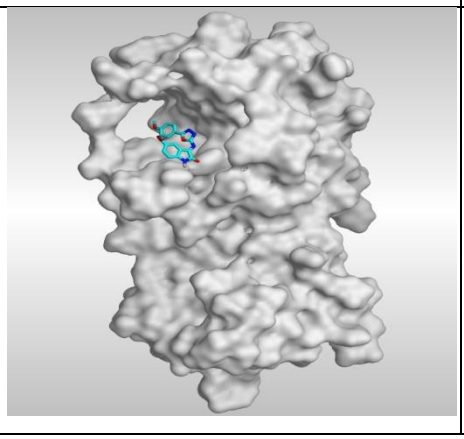
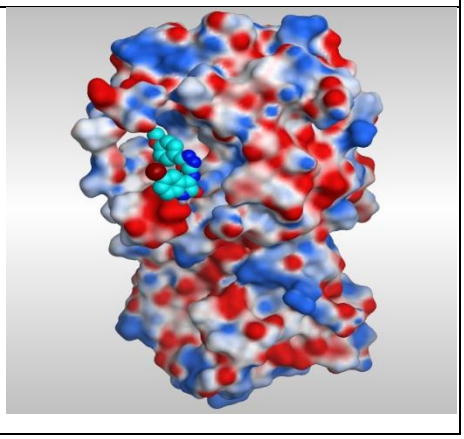
7	**III_g**		
8	**I_a**		
9	**N3**		

Figure SI2: A) Surface of the COVID-19 main protease pocket showing the positioning and fitting of the tested compounds, **B)** surface and maps of the tested compounds and the previously reported one (Ia) compared to the docked N3 inhibitor against its binding site inside the COVID-19 main protease.

No.	Tested comp.	A	B
1	III_a		
2	III_b		
3	III_c		

4	**III_d**		
5	**III_e**		
6	**III_f**		
7	**III_g**		

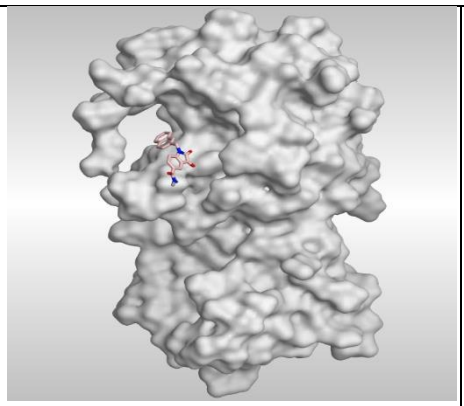
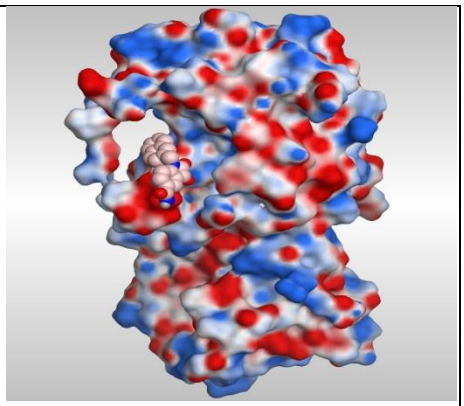
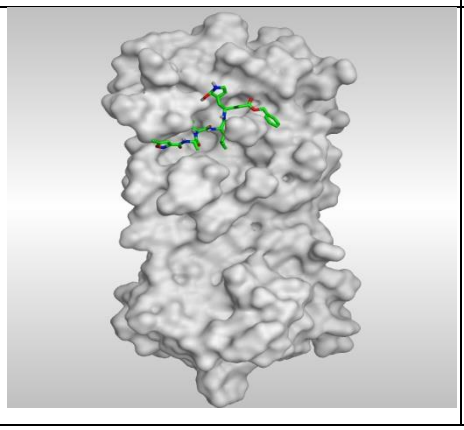
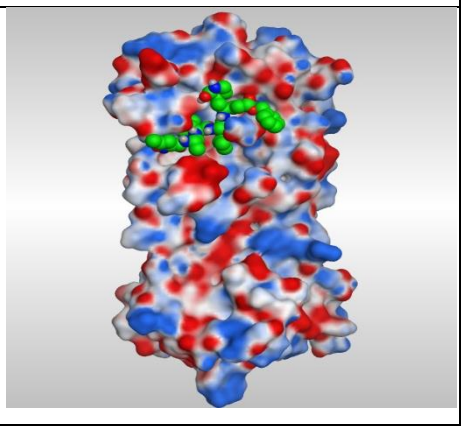
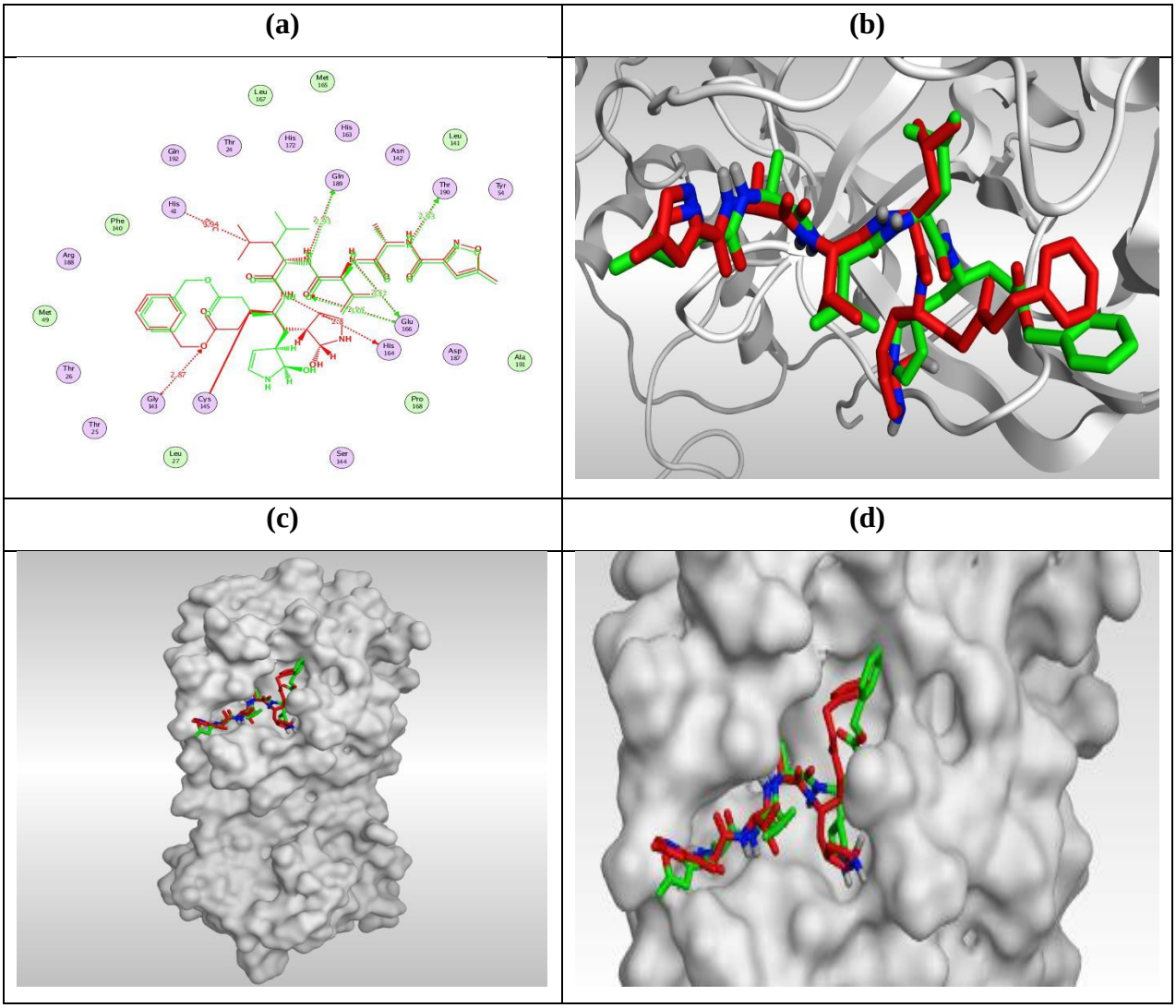
8	**I_a**		
9	**N3**		

Figure SI3: 2 D diagram (a), 3 D representation (b), and protein positioning (c and d) of the superimposition of the co-crystallized (red) and the docked pose (green), respectively, of N3 inhibitor inside the COVID-19 main protease binding site with RMSD of 1.46 Å.



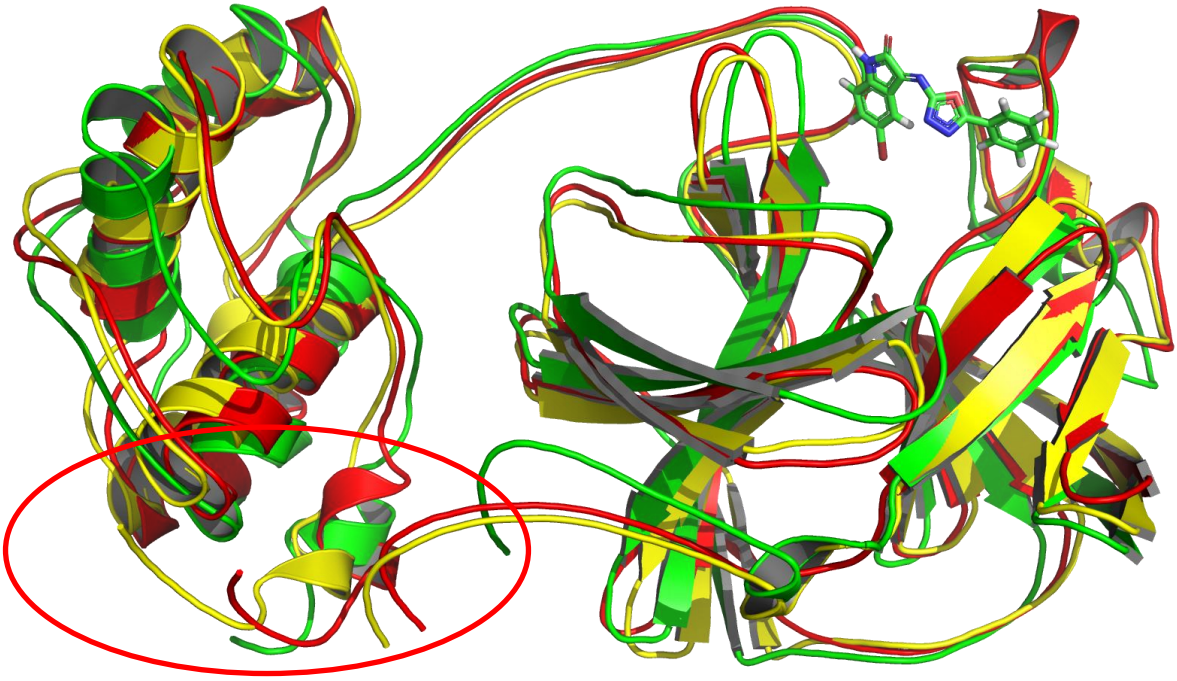


Figure SI4: The aligned structures of IVe_4-6LU7 during simulation; green 0ns, yellow 50ns, red 100 ns.

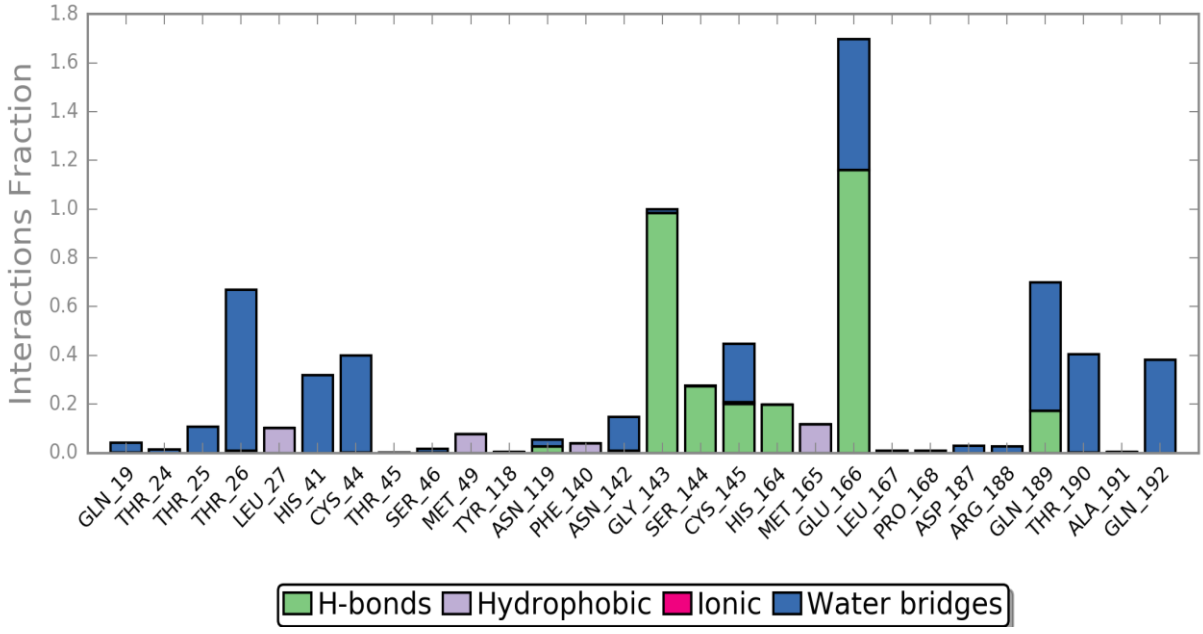


Figure SI5: The histogram of N3 – 6LU7 contact throughout the trajectory.

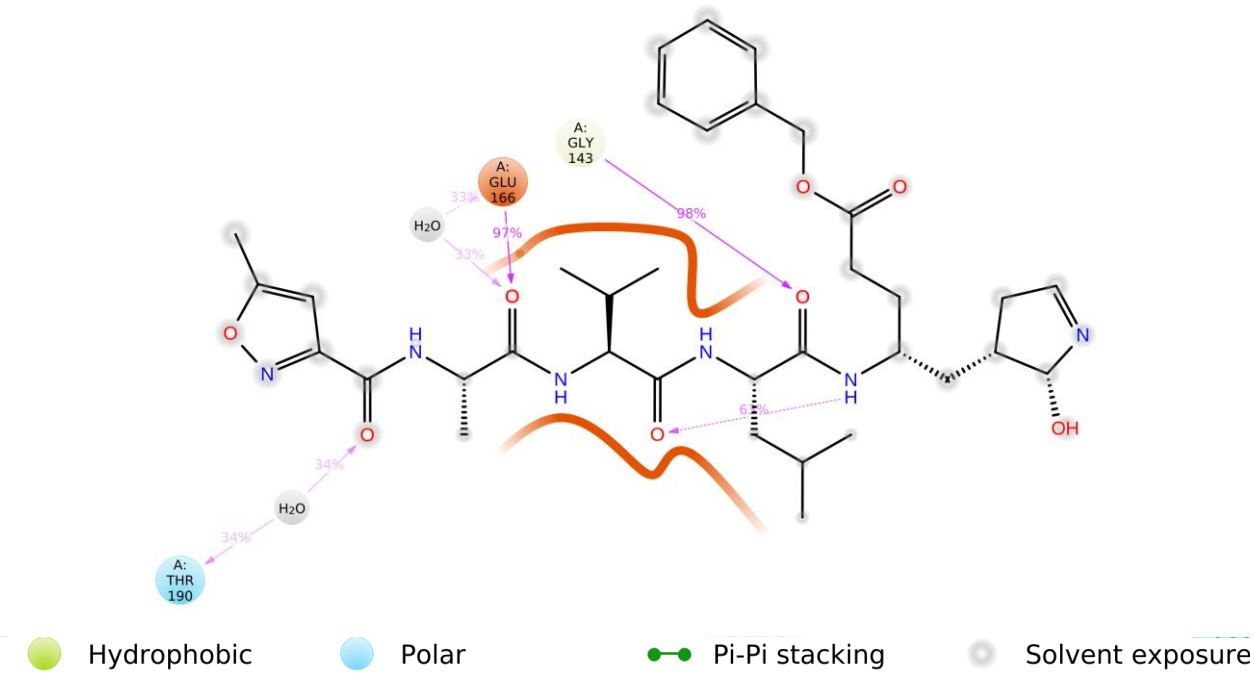


Figure SI6: The N3 – 6LU7 Interactions that occur more than 30.0% of the simulation time.

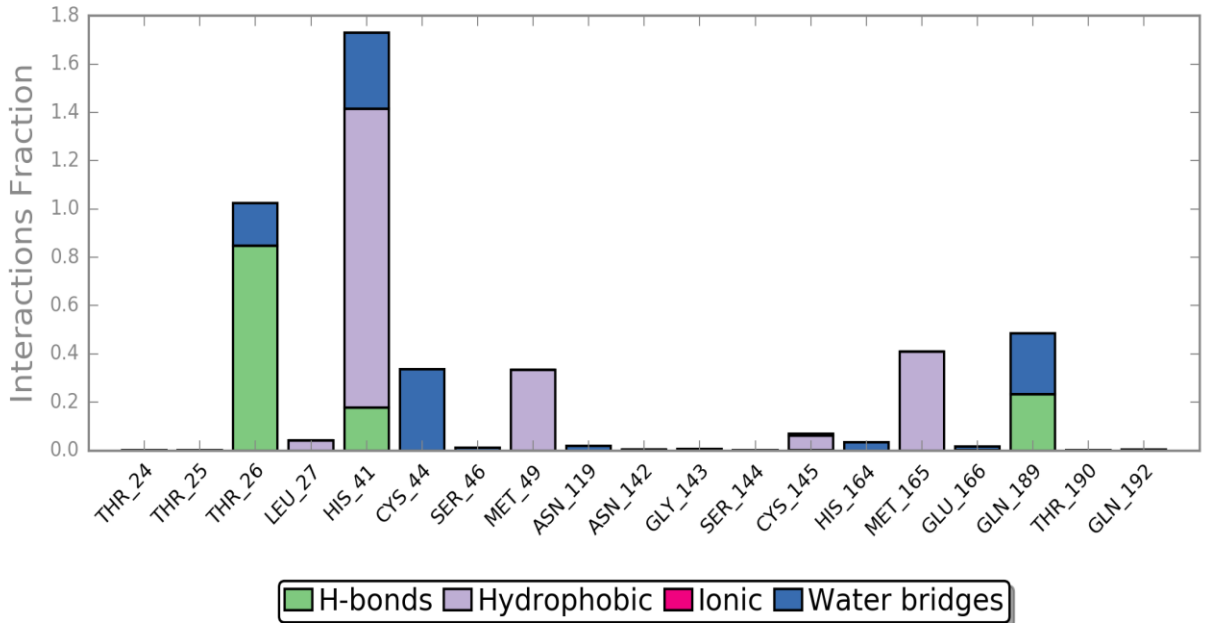


Figure SI7: The histogram of IVa – 6LU7 contact throughout the trajectory.

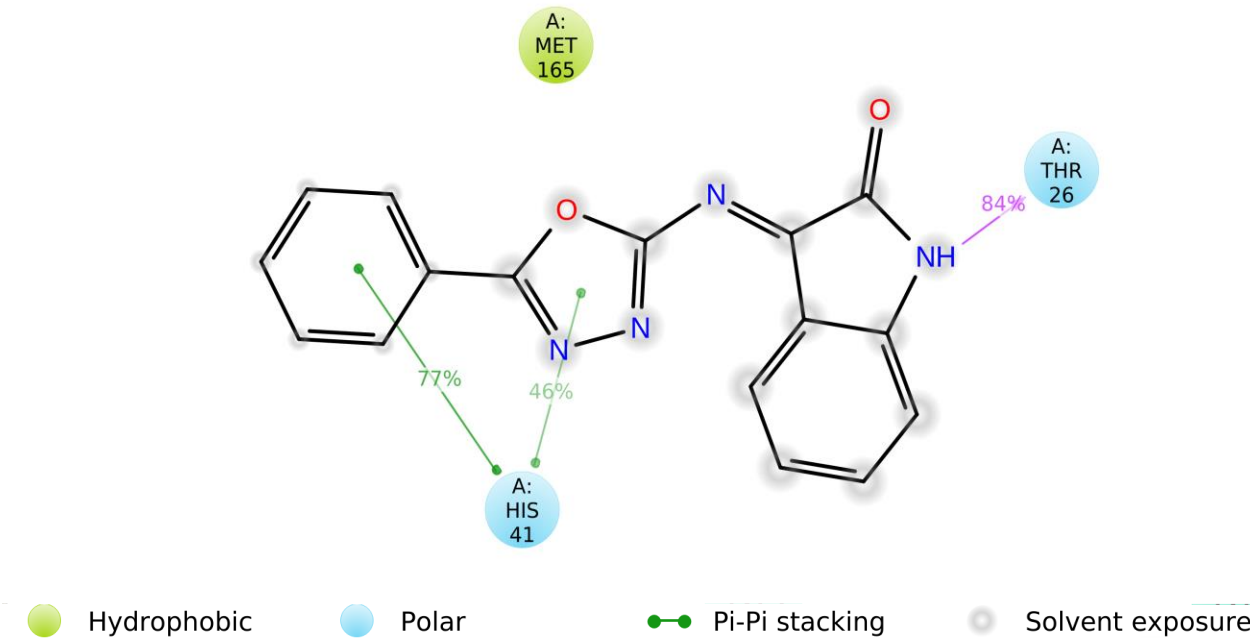


Figure SI8: The IVa – 6LU7 Interactions that occur more than 30.0% of the simulation time.

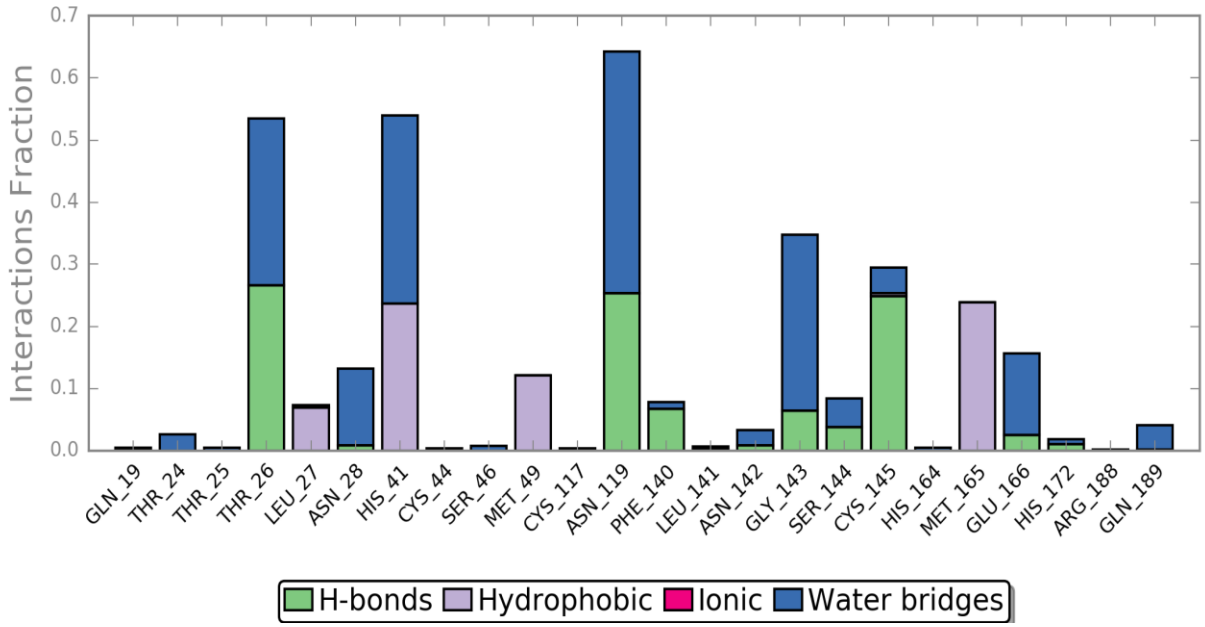


Figure SI9: The histogram of IVb – 6LU7 contact throughout the trajectory.

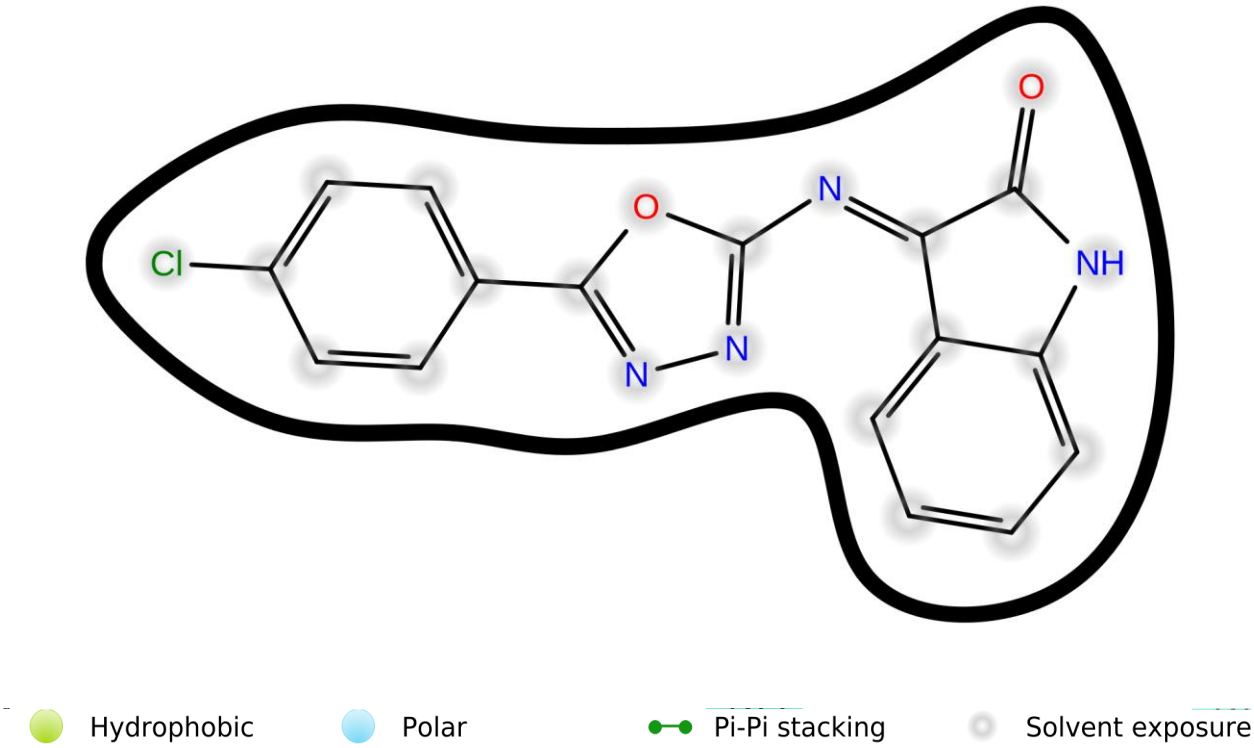


Figure SI10: The IV_b – 6LU7 Interactions that occur more than 30.0% of the simulation time.

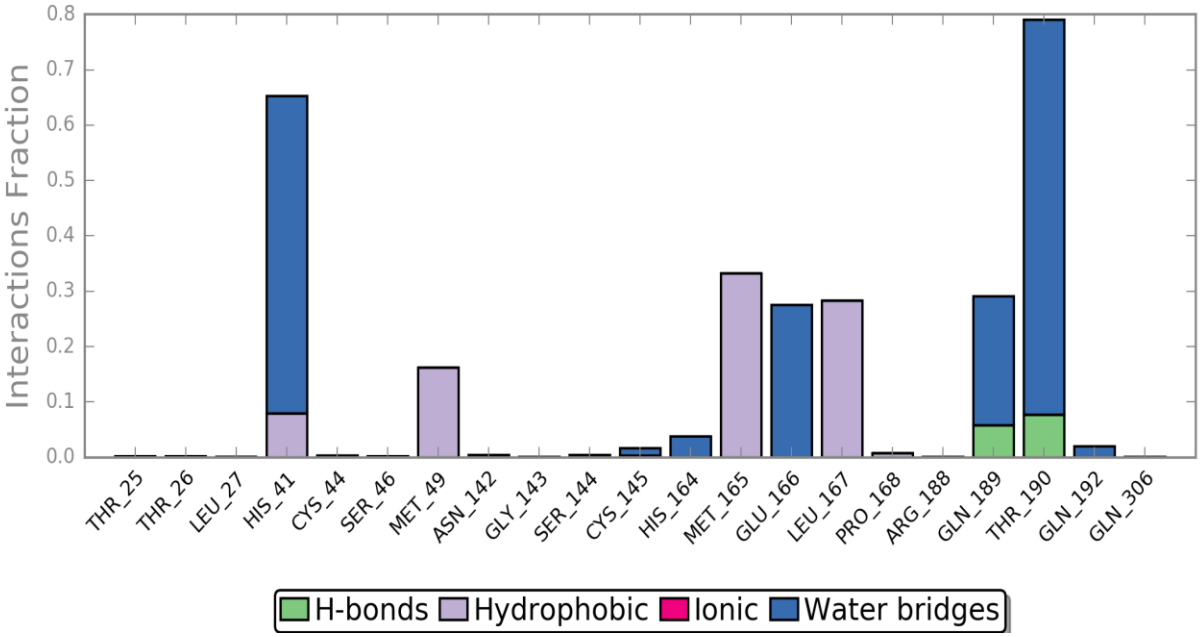


Figure SI11: The histogram of IV_e – 6LU7 contact throughout the trajectory.

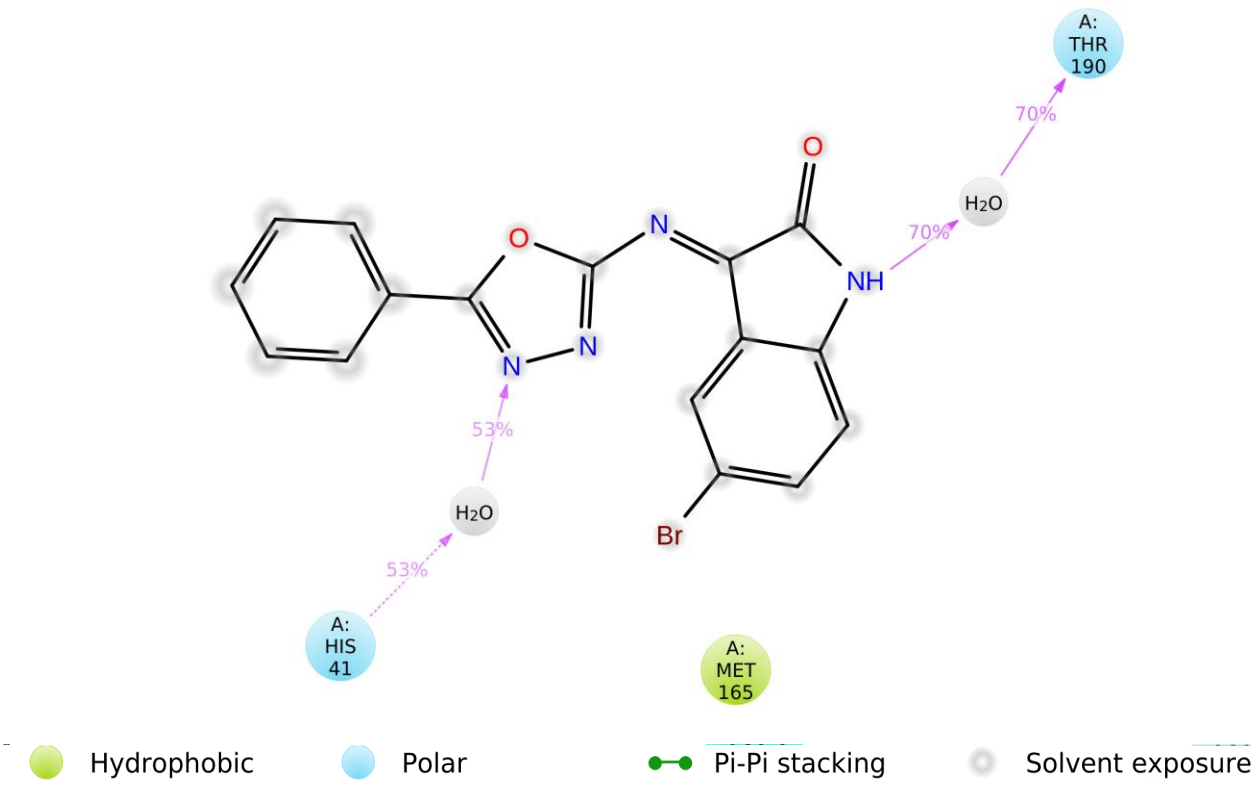


Figure SI12: The IV_e – 6LU7 Interactions that occur more than 30.0% of the simulation time.

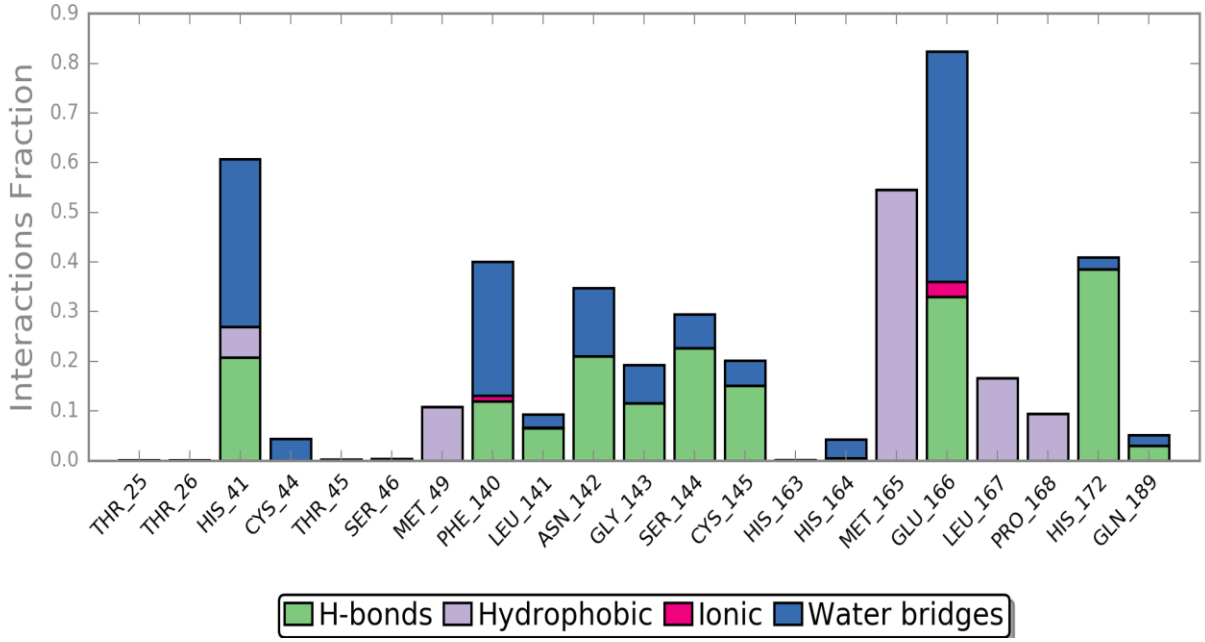


Figure SI13: The histogram of I_a – 6LU7 contact throughout the trajectory.

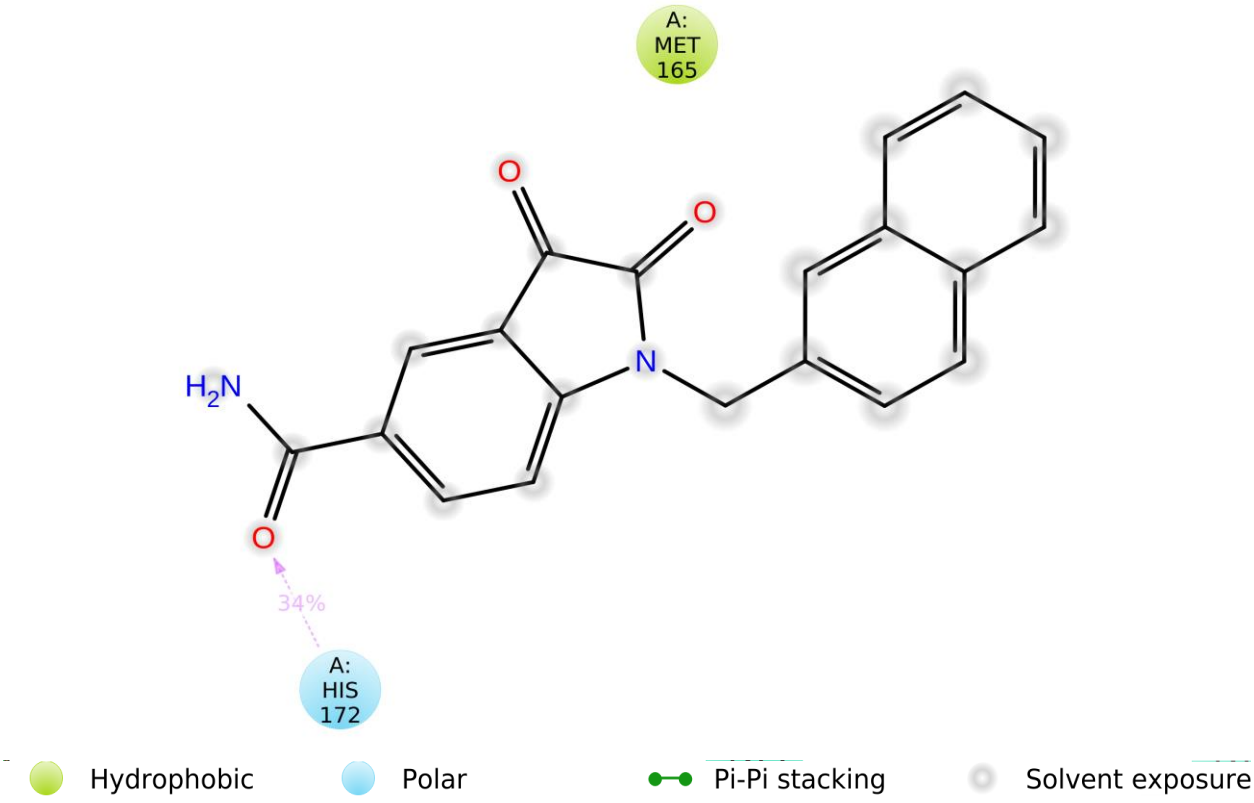


Figure SI14: The I_a – 6LU7 Interactions that occur more than 30.0% of the simulation time.