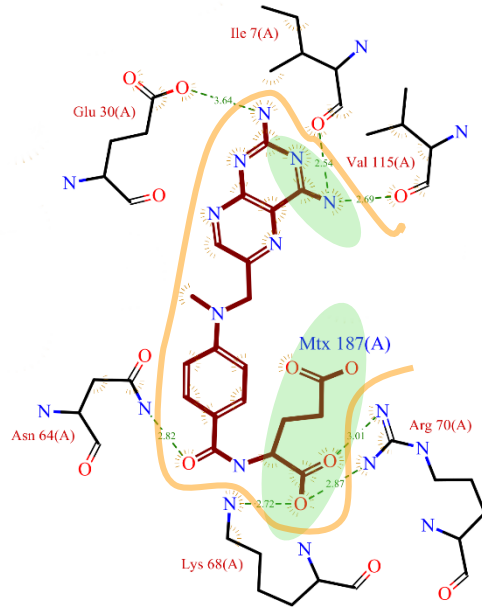
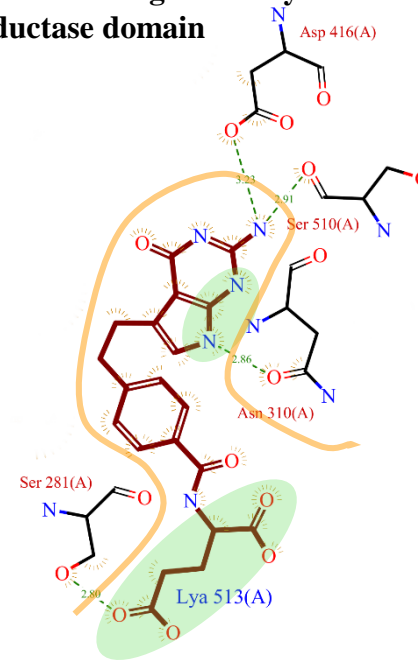


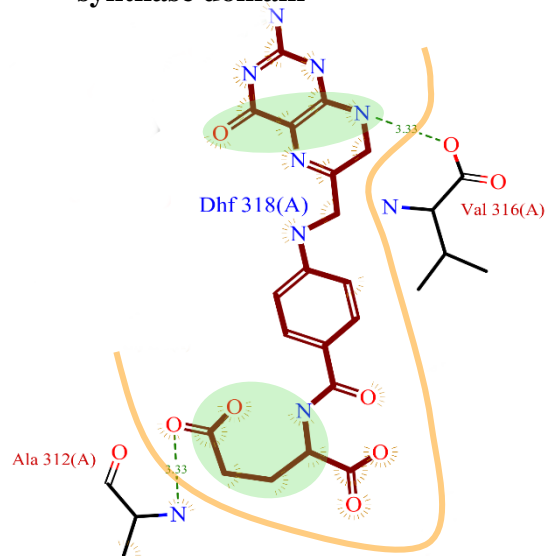
**A. Methotrexate against dihydrofolate reductase domain**



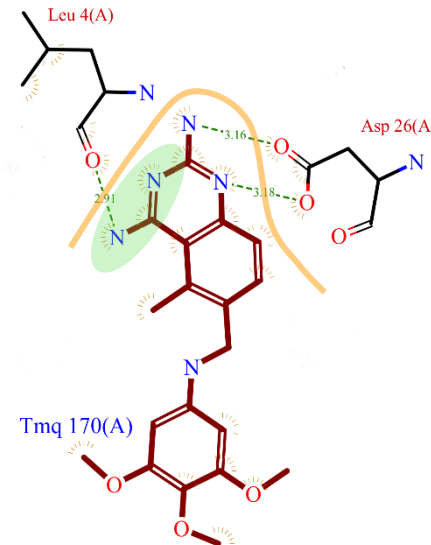
**B. Pemetrexed against dihydrofolate reductase domain**








**C. DHF against thymidylate synthase domain**



**D. Trimetrexate against dihydrofolate reductase domain**



-  Predicted substructures targeting the domains
-  Hydrogen bond and its length
-  Hydrophobic contact
-  Compound bond
-  Non-compound bond