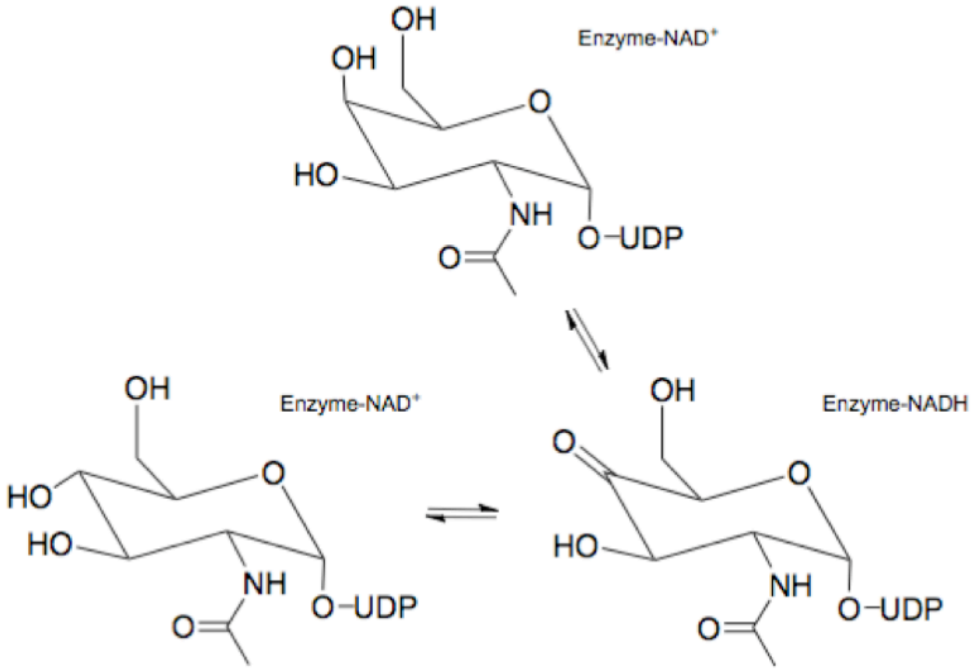
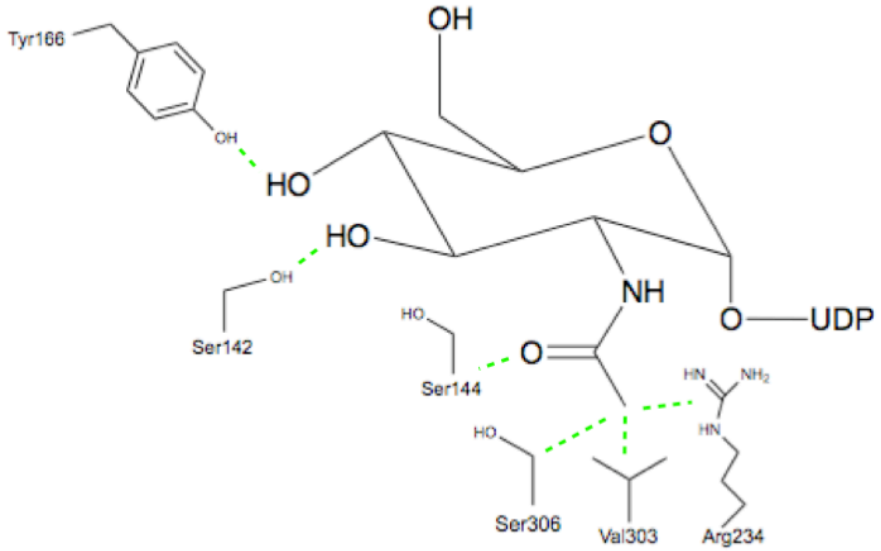
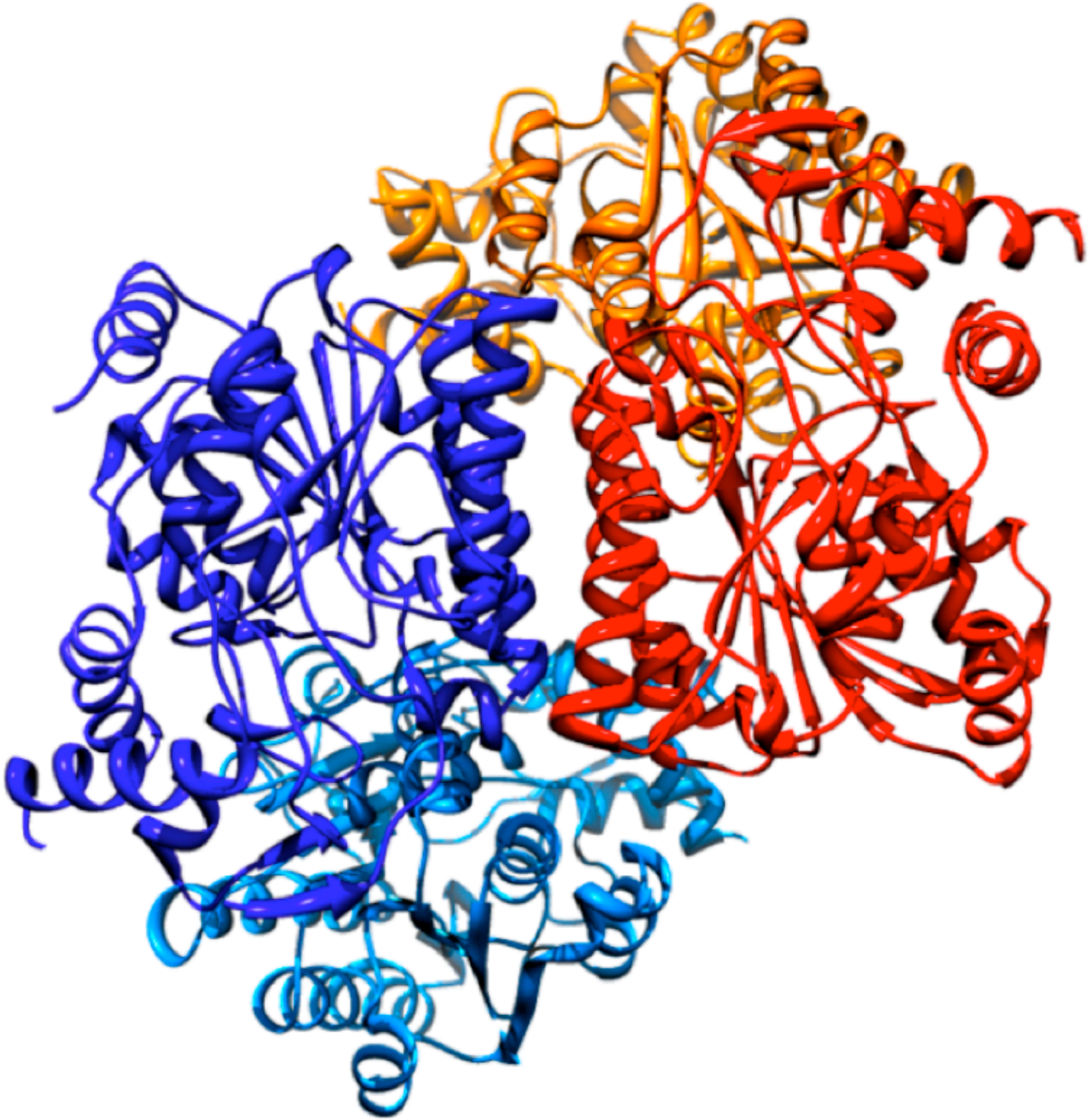
Supplementary Scheme 1

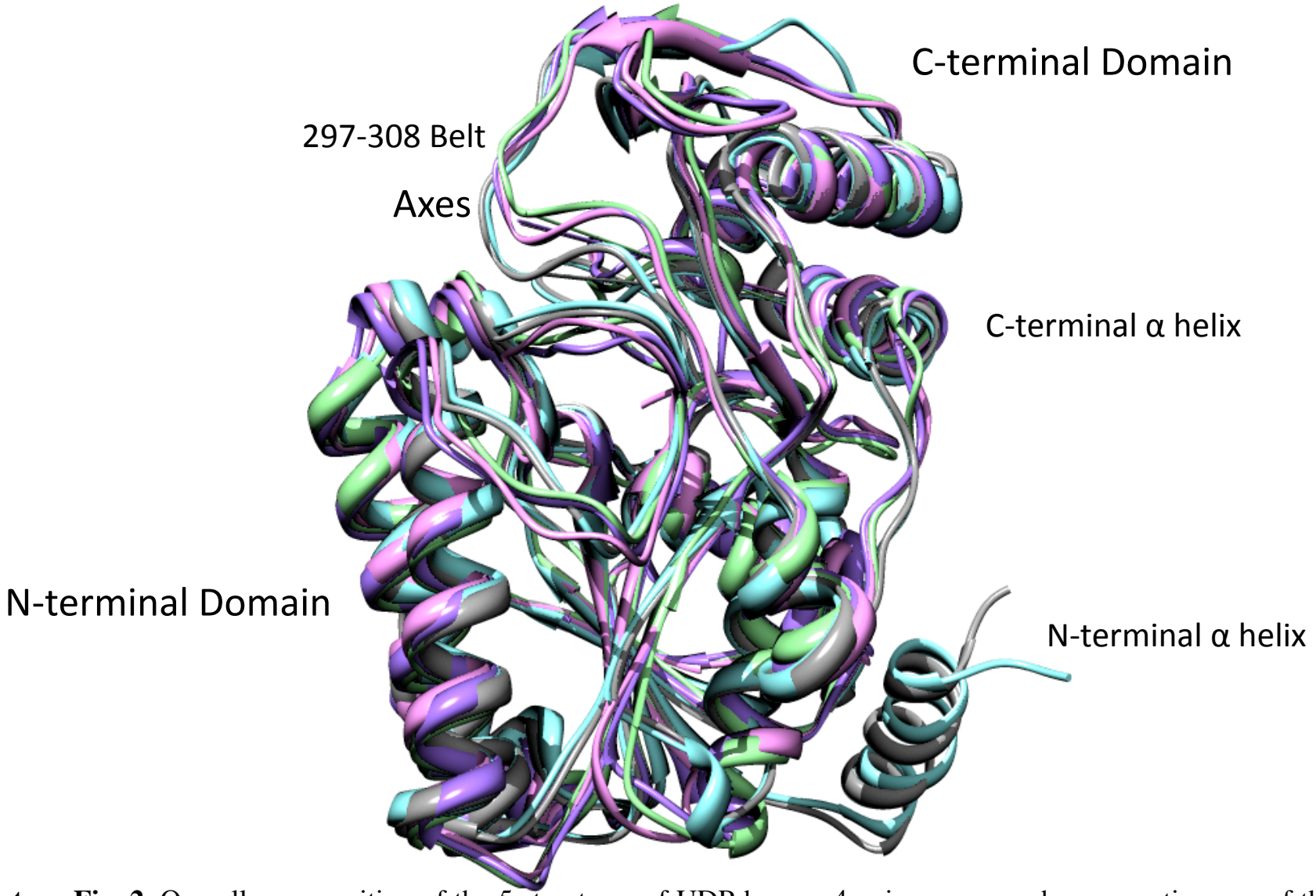
SCHEME 1: On the right is the reaction mechanism. On the left is a schematic depicting some critical interactions with the N-acetyl group and with 3' and 4' hydroxyl groups



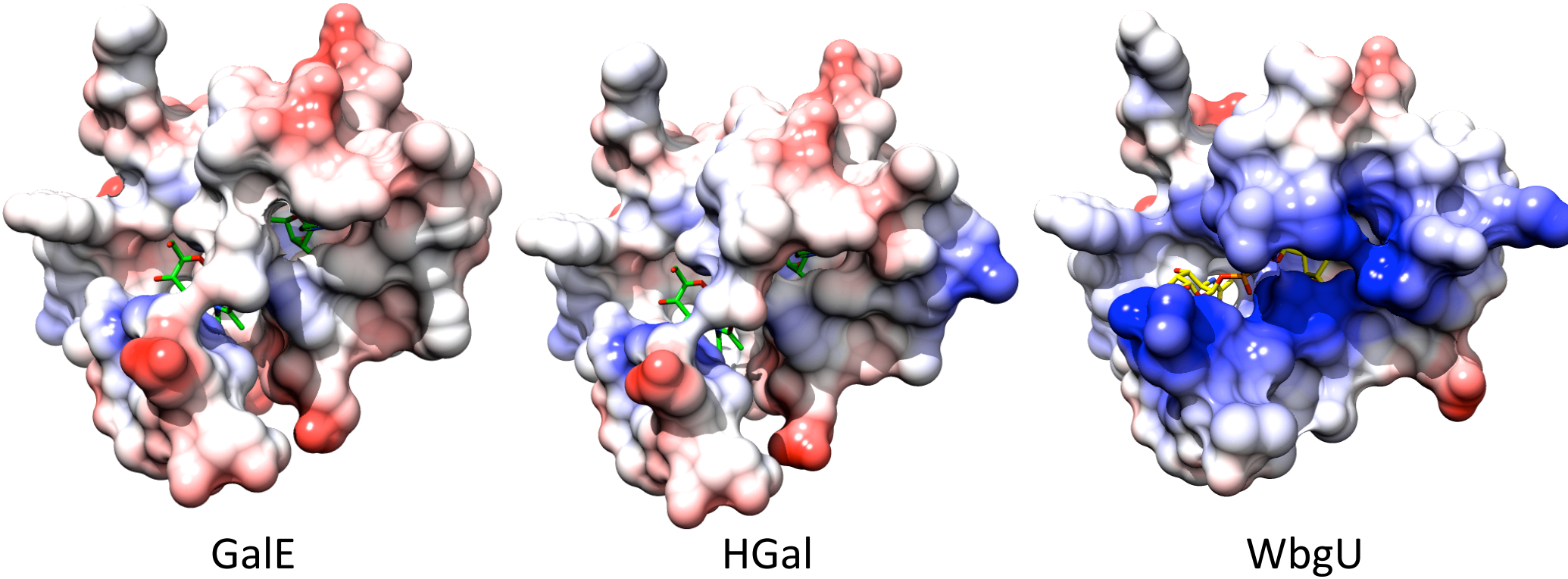




Supplementary Fig. 1. A 2-fold symmetry axis relates two (dark red and dark blue) of the four subunits present in the asymmetric unit of the WbgU/NAD(H)/UDP-GlcNAc crystal structure.



Supplementary Fig. 2. Overall superposition of the 5 structures of UDP-hexose 4-epimerases, each representing one of the 3 groups. The C-terminal substrate binding domain of the group 3 epimerases (WbgU: grey and WbpP: cyan) is significantly different from the corresponding domain of the group 1 epimerases (GalE: pink) and the group 2 epimerases (CGne: green and HGal: purple). The structural deviations are maximal in the region labeled as '297-308' belt. This also happens to be the substrate binding region. The C-terminal domain in this region of the group 3 epimerases is closer to the carboxy edge of the β sheet of N-terminal domain than the group 1 and the group 2 epimerases. The axes represent an angle of ~10° and were computed from the C-terminal α helix to the middle of 297-308 belt. In contrast to the C-terminal domain, the N-terminal domain exhibits a higher degree of structural conservation across all the 3 groups. The superposition also highlights the conservation of active site architecture among both of the group 3 epimerases, namely, WbgU and WbpP and among the group 1 and the group 2 epimerases.



Supplementary Fig. 3. Surface topology and charge distribution at the active sites of each of the 3 groups. Electrostatic surface rendition of the substrate binding region of GalE (left), HGal (center) and WbgU (right) shows that the substrate binding region has very similar overall charge distribution and surface curvature in case of GalE and HGal, whereas being markedly different in WbgU.