SUPPLEMENTAL INFORMATION

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ANALYSIS OF AGONIST AND ANTAGONIST EFFECTS ON THYROID RECEPTOR CONFORMATION BY HYDROGEN/DEUTERIUM-EXCHANGE

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Configuration files: Atomic coordinates and configuration files for molecular dynamics simulations are available upon request to authors.

Figure 1 - Figure S1 Deuterium (D_2O) incorporation for each peptide from peptic cleavage of Apo-TR, TR+NH3 and TR+T3, in all incubation time (1min, 3min, 8min, 15min, 1h, 3h and 5h).

Figure 2: Further comparison between holo and apo structures obtained from the 298 K annealed simulations. **A.** Details of the dimerization surface shows significant changes in the H7, H8, and especially in H11, when compared to the annealed structures (I, red, II / III blue) with the structure of holo-TR (gray). The H11 is broken in two, with its C-terminal part occupying part of the empty LBP, which increases the contact of hydrophobic residues. The region N-terminal H11 breaks with the displacement of the C-terminal, also changing the dimerization region. Helices H9 and H10 are unchanged. **B.** In the absence of the ligand, the LBP reduces volume, with the polar residues that make interactions with the ligand being exposed to solvent. As an example, this picture shows the changes observed in H435, the most buried polar residue in the LBP. In the holo structure, H435 interacts directly with the ligand. In the transition structure I, the volume of hydrophobic cavity is smaller but still contains H435. In structures II/III, where H12 is already in the inactive position, the side chain of H435 leaves the the hydrophobic region to make full contact with the solvent. **C.** Number of water molecules in the first solvation shell around the C-terminal part of H3 (N_W - H3). The MD simulations clearly show a lower hydration of H3 in the annealed apo structures (I and II/III), consistent with that observed experimentally.

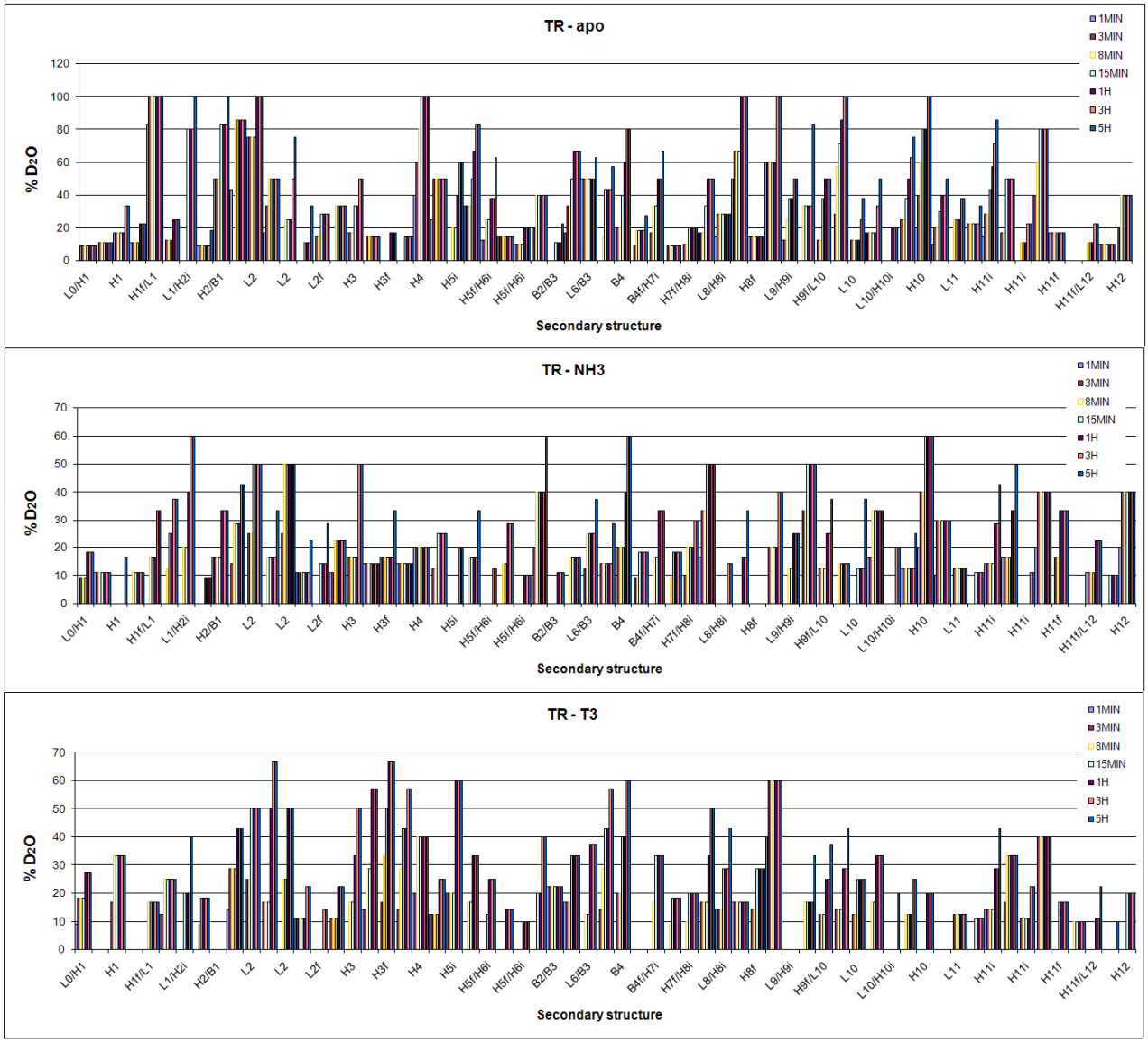
TR - apo
% D2O
Secondary structure
1MIN
3MIN
8MIN
15MIN
1H
3H
5H
L0/H1
H1
H11/L1
L1/H2i
H2/B1
L2
L2
L2f
H3
H3f
H4
H5i
H5f/H6i
H5f/H6i
B2/B3
L6/B3
B4
B4f/H7i
H7f/H8i
L8/H8i
H8f
L9/H9i
H9f/L10
L10
L10/H10i
H10
L11
H11i
H11i
H11f
H11f/L12
H12
TR - NH3
% D2O
Secondary structure
TR - T3
% D2O
Secondary structure

Figure 1

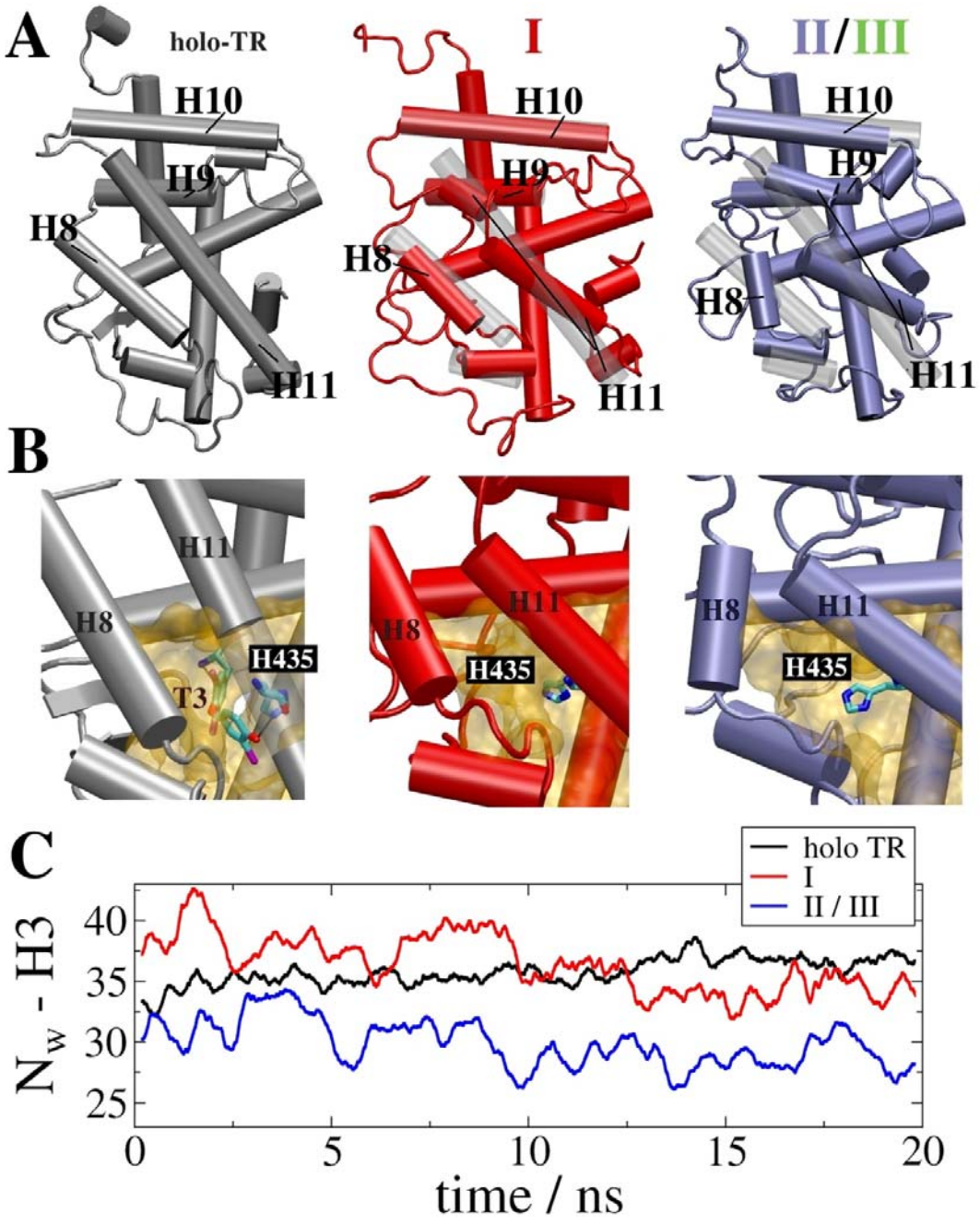
A
holo-TR
H10
H9
H8
H11
I
H10
H9
H8
H11
II/III
H10
H9
H8
H11
B
H11
H8
H435
T3
H11
H8
H435
H8
H11
H435
C
holo TR
I
II / III
N_w - H3
40
35
30
25
0
5
10
15
20
time / ns

Figure 2