Supplementary Material: Sequence dependent lipid-mediated effects modulate the dimerization of ErbB2 and its associative mutants †

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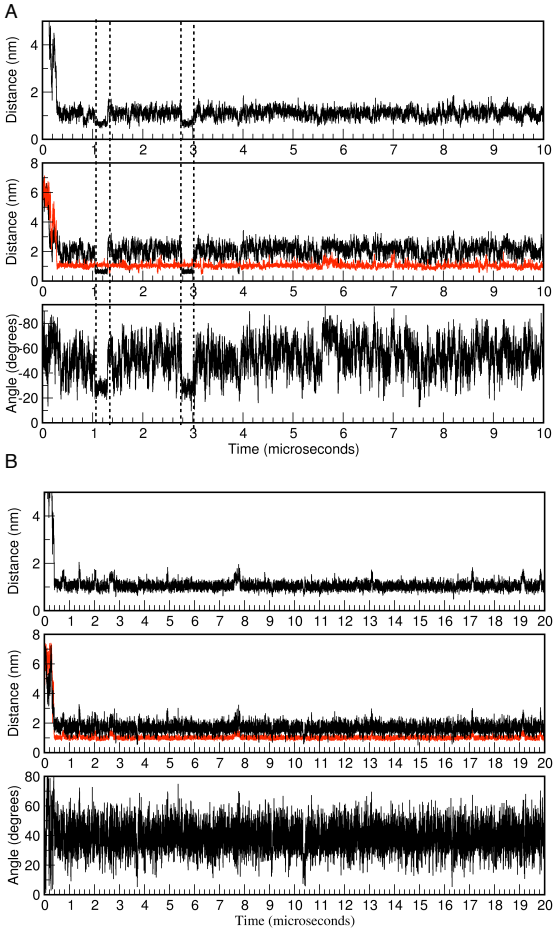
Received Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
First published on the web Xth XXXXXXXXXX 20XX
DOI: 10.1039/b000000x



Supplementary Fig. 1 Dimer characteristics of the transmembrane helix dimer of A: the V664E and B: V659EV664E mutant of ErbB2, as a function of time. The top panel (in both sub-figures) shows the inter-helical distance, the middle panel shows the distance between N- and C-terminal residues in black and red respectively and the bottom panel shows the inter-helical angle. For further details see Methods section.

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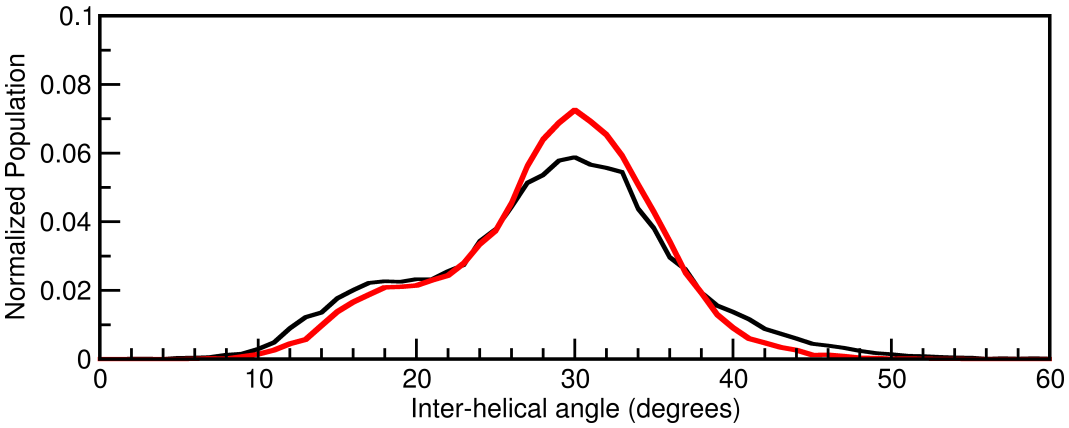
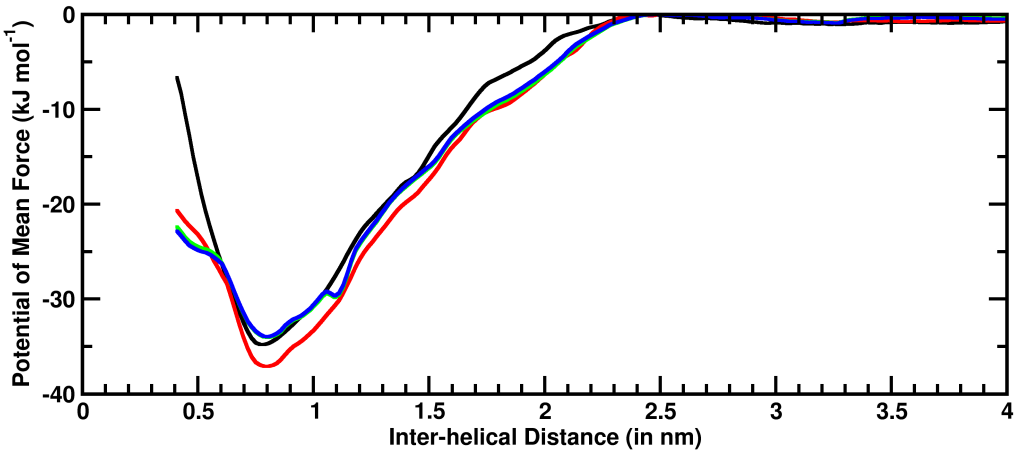
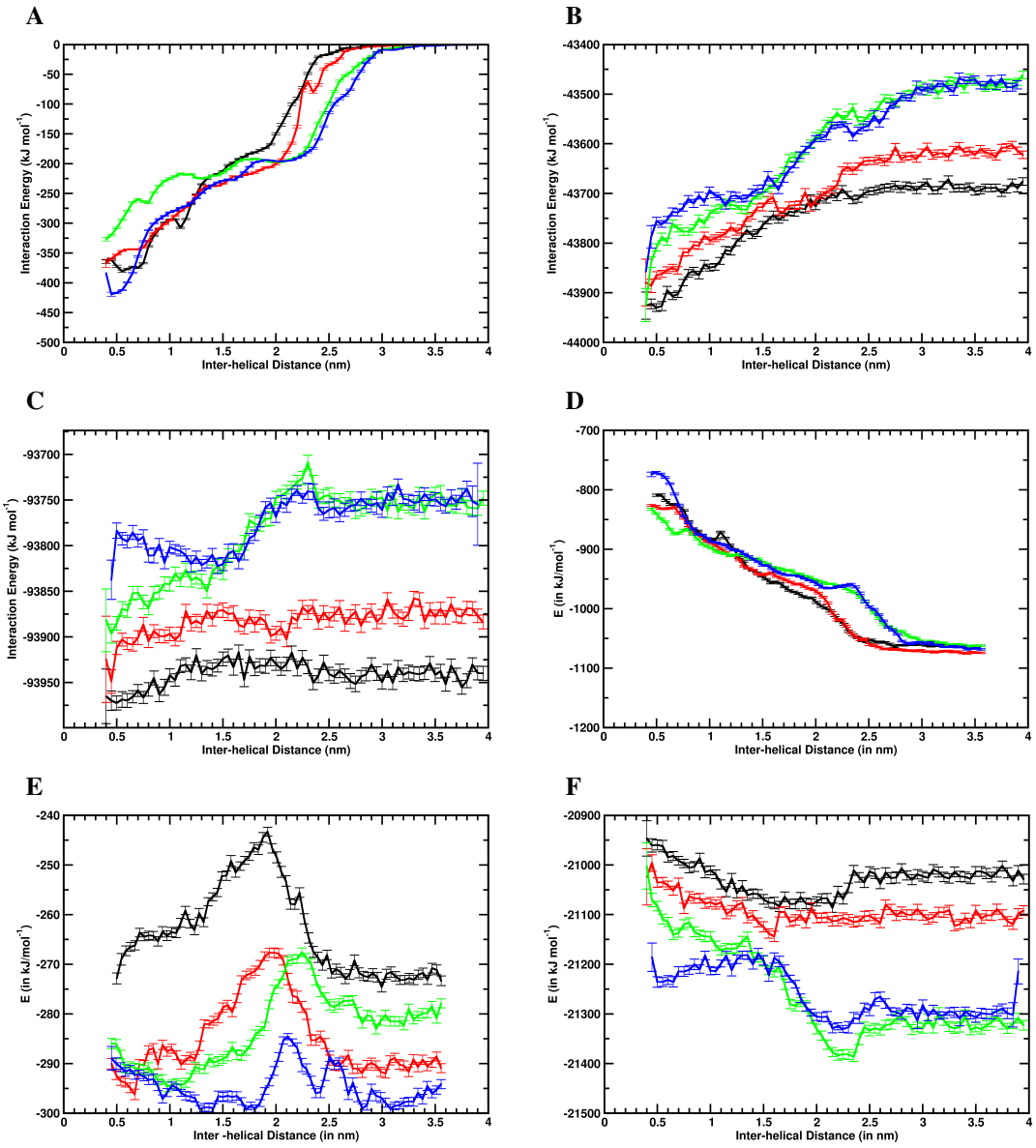
Keyword: MARTINI force field; transmembrane helix association; solvophobic



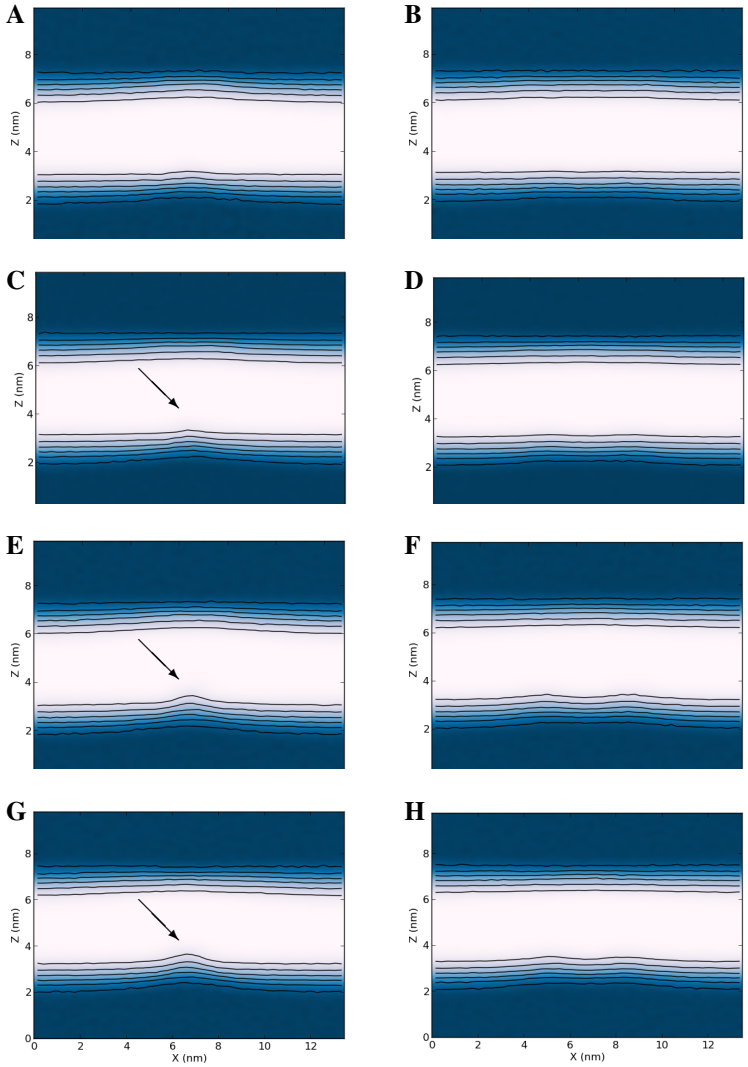
Supplementary Fig. 2 Population analysis of the inter-helical angles sampled during the self-assembly simulations (black) and umbrella sampling simulations (red). Only the dimer regime is analysed for the self assembly simulations and only the windows close to the main minima (0.7-0.9 nm) are analyzed for the umbrella sampling simulations. Two distinct populations are observed: the N-terminal dimer with an inter-helical angle around 20^o and a C-terminal dimer with an inter-helical angle of 30^o. When the helices are further away the average inter-helical angle is zero.



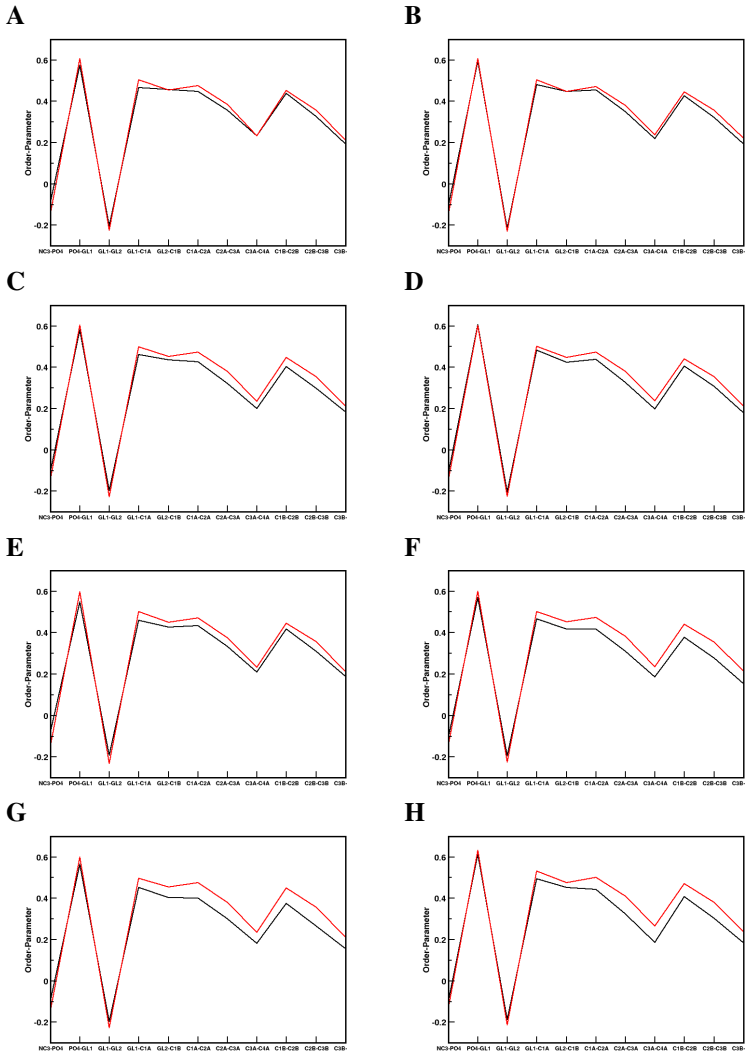
Supplementary Fig. 3 The potential of mean force of dimerization of wildtype ErbB2 transmembrane helices, calculated by umbrella sampling calculations by considering a trajectory of 0-2μs (black), 2-4μs (red), 4-6μs (blue) and 4-16μs (green) sampling per window. The profiles for the 4-6μs (blue) and 4-16μs (green) lie on top of each other and are difficult to distinguish.



Supplementary Fig. 4 The protein-protein (A), lipid-lipid (B), water-water (C), protein-lipid (D), protein-water (E) and lipid-water (F) interaction energies as a function of inter-helical distance, for wildtype ErbB2 (black) and its V659E (red), V664E (green) and V659EV664E (blue) mutants.



Supplementary Fig. 5 Water partial densities calculated along the membrane normal and one of the membrane lateral axis and averaging over the lateral axis. The two columns show the partial densities of water for the dimerized state (left column) and monomer regimes (right column) of of the wildtype ErbB2 (A, B), V659E (C, D), V664E (E, F) and V659EV664E (G, H) mutants, respectively. The arrows represent the bulge in the water densities seen near the glutamate residue.



Supplementary Fig. 6 The membrane order parameters, P_2 of the annular (black) and bulk (red) lipids around the dimerized state (left panel) and monomeric regime (right) of the wildtype ErbB2 (A, B) and the V659E (C, D), V664E (E, F) and V659EV664E (G, H) mutants.