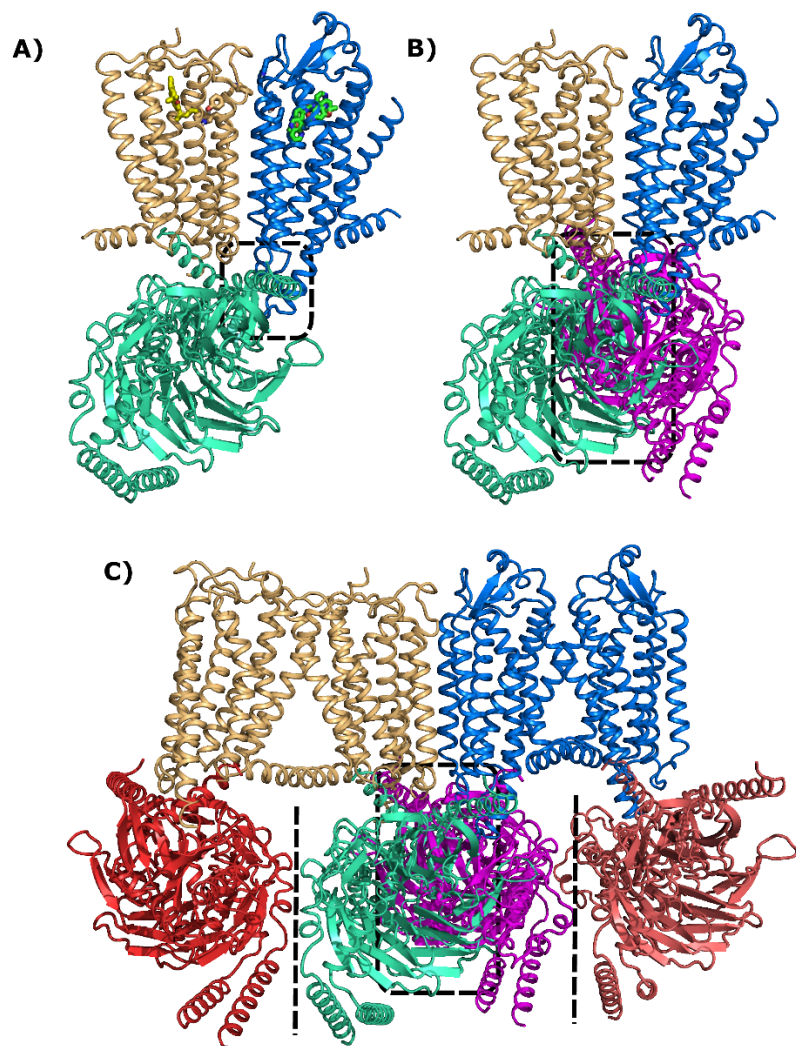




Supplementary Figure S1. How many proteins can fit a CB₂R-OX₁R heteromer? Computational model of the heteromeric TM4/5 CB₂R/JWH133.OX₁R/SB334867 complex viewed from the membrane. A) CB₂R receptor is shown in gold, OX₁R receptor in blue and a superposed G-protein in green. The heteromer would fit one G protein with only minor changes in the loop connecting TMs 3 and 4, and the end of TM6, or a small rotation of the G protein. B) An additional G-protein (in purple) would clash sterically with the first G-protein if bound simultaneously. C) In a tetramer it is possible to bind additional proteins. As an example the panel displays homodimers modeled using symmetric TM1 interfaces taken from the κ -opioid receptor (PDB id 4DJH) that could bind two additional G-proteins.