



Fig. S5 Cryo-EM density maps of the inactive mGlu2–mGlu3 heterodimers. a, b The mGlu2–mGlu3 heterodimer in the presence of LY341495 in dimerization modes I (a) and II (b). **c, d** The mGlu2–mGlu3 heterodimer in the presence of LY341495 and NAM563 in dimerization modes I (c) and II (d). **e, f** The mGlu2–mGlu3 heterodimer in the presence of

LY341495, NAM563, and LY2389575 in dimerization modes I (**e**) and III (**f**). **g** The mGlu2–mGlu3 heterodimer in the presence of NAM563. Maps and models are shown for all transmembrane helices, B and C helices in the VFTs, antagonist (in **a–f**), agonist (in **g**), NAM (in **g**), lipid (cholesterol, CLR; in **c**, **e** and **g**) and some non-conserved residues in the two subunits that aided modelling. The models are shown as cartoon and sticks, and colored blue (mGlu2) and purple (mGlu3). The density maps are colored grey.