



Fig. S6 Cryo-EM density maps of the agonist-bound mGlu hetero- and homodimers. a, b

The mGlu2–mGlu3 heterodimer in the presence of glutamate, JNJ-40411813, and CaCl₂ in the Rco (a) and Acc (b) conformational states. **c** The G₁₁-bound mGlu2–mGlu3 heterodimer. **d** The mGlu2–mGlu4 heterodimer in the presence of glutamate, JNJ-40411813, and ADX88178. **e** The G₁₁-bound mGlu2–mGlu4 heterodimer. **f** The G₁₃-bound mGlu4 homodimer. Maps and

models are shown for all transmembrane helices, B and C helices in the VFTs, agonists, PAMs (in **c**, **e** and **f**), lipids (CLR and DPPE (1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine); in **a**, **c** and **d**) and some non-conserved residues in the two subunits that aided modelling. The models are shown as cartoon and sticks, and colored blue (mGlu2), purple (mGlu3), and orange (mGlu4). The density maps are colored grey.