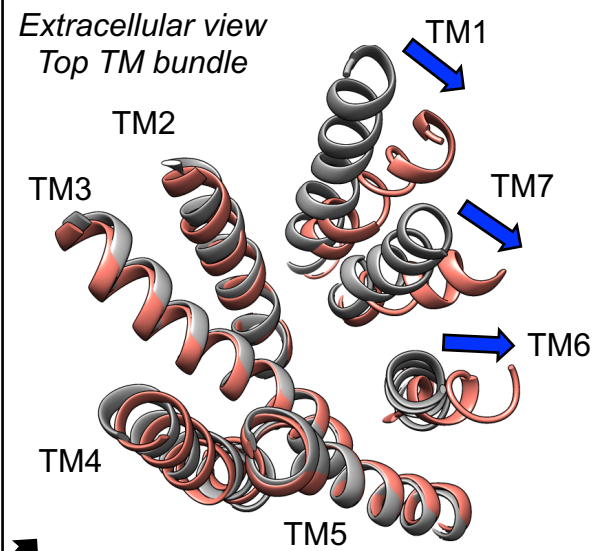
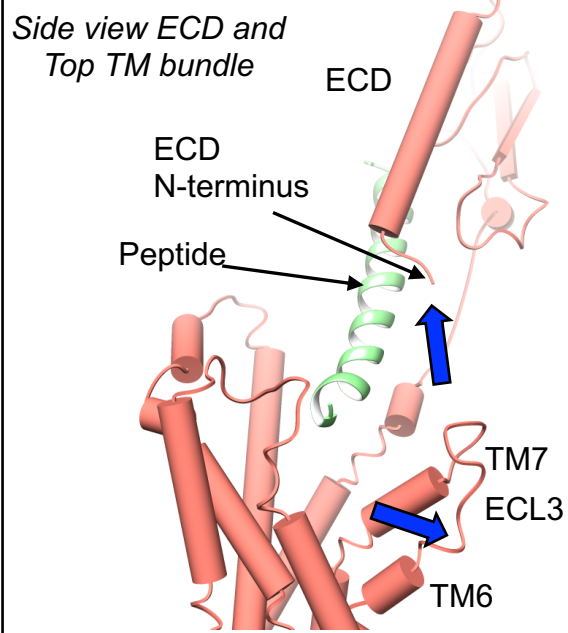


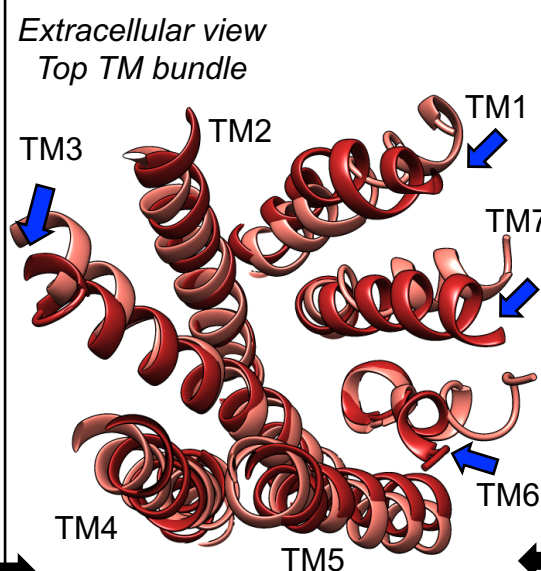
Peptide C-terminus interaction with ECD releases ECD constraints on TM1, TM6 and TM7



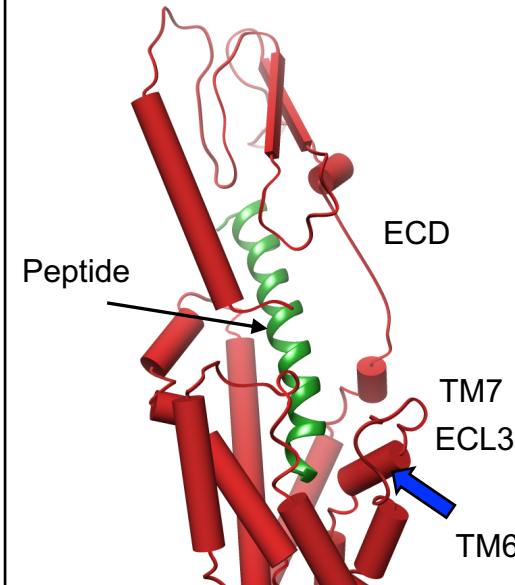
Inactive
Peptide-bound ECD
(intermediate conformation)



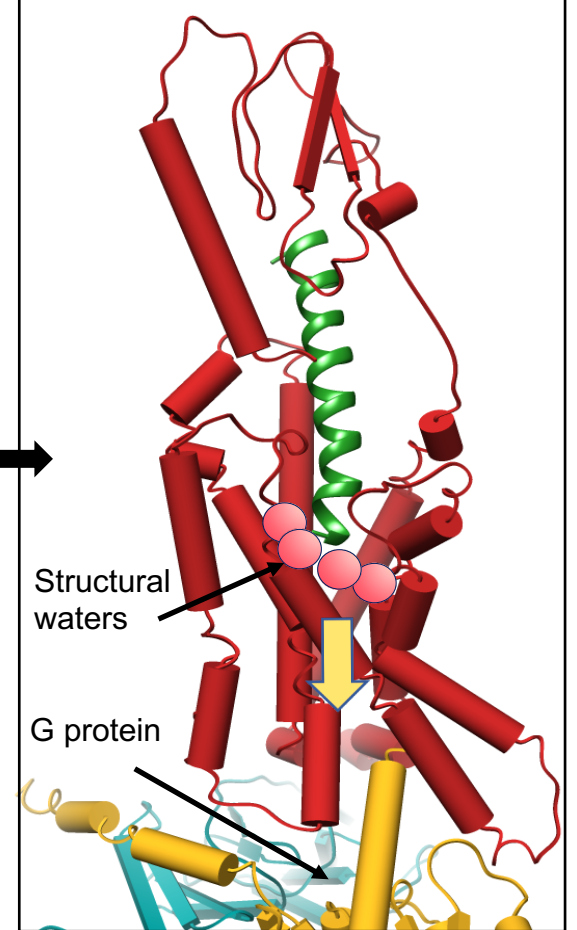
Peptide N-terminus engages TM6/TM7 and deep within the TM bundle closing up the TM binding site



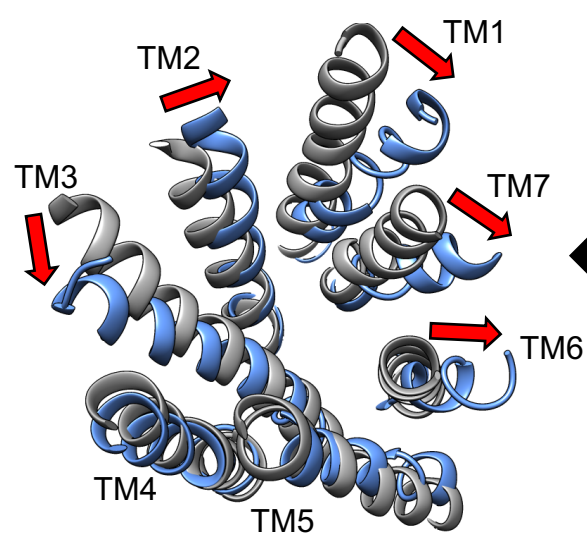
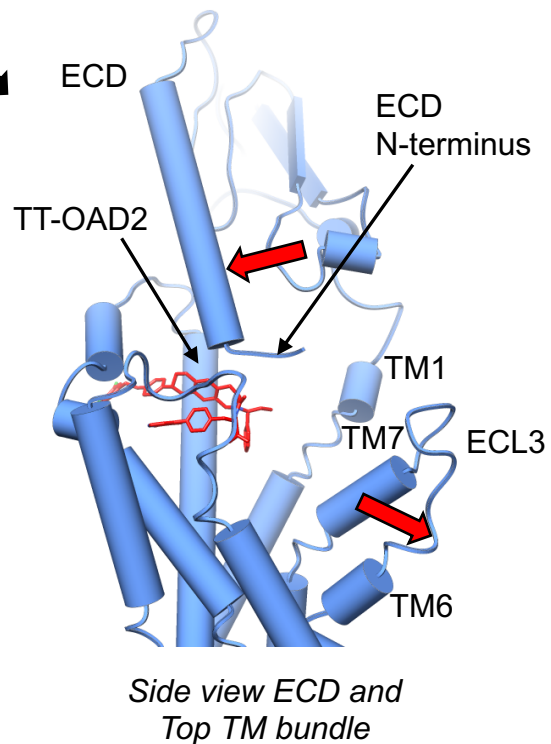
Peptide-bound ECD
(intermediate conformation)
Peptide fully engaged
(ECD & TM bundle)



Peptide full agonists directly interact with central polar network to promote a fully active receptor conformation



Binding to the top of the bundle releases ECD constraints on TM1, TM6 and TM7. No engagement with TM5-TM7 promotes open helical bundle.



Inactive
TT-OAD2 bound conformation

TT-OAD2 allosterically communicates with central polar network to promote a fully active receptor conformation

