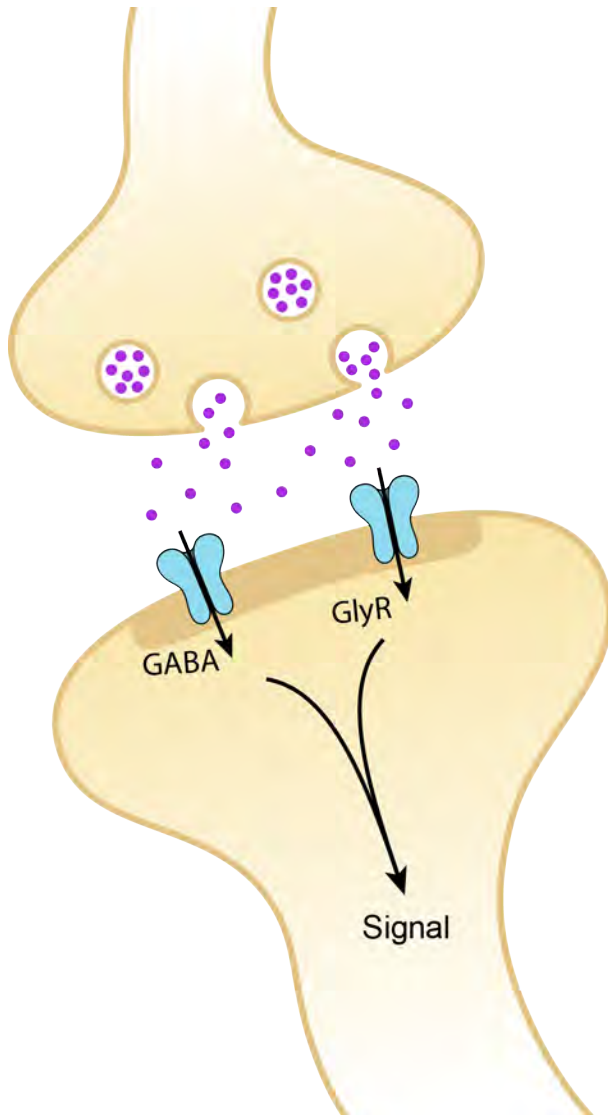


Mechanism of gating and partial agonist action in the glycine receptor

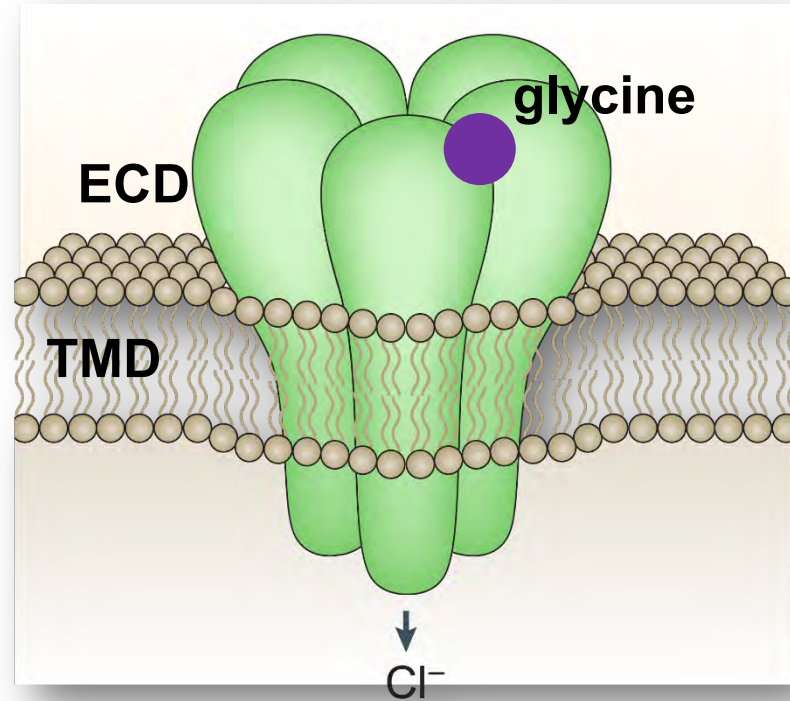
Jie Yu
Gouaux Lab
2020-03-20

Oregon Health & Science University
Vollum Institute

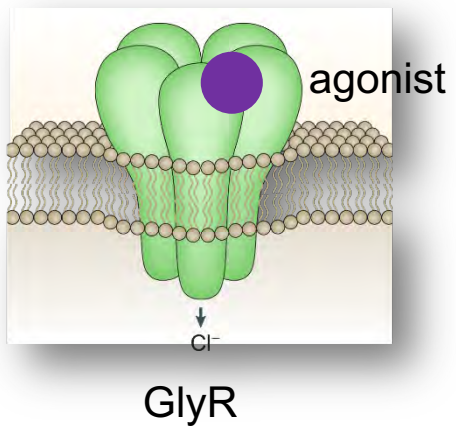
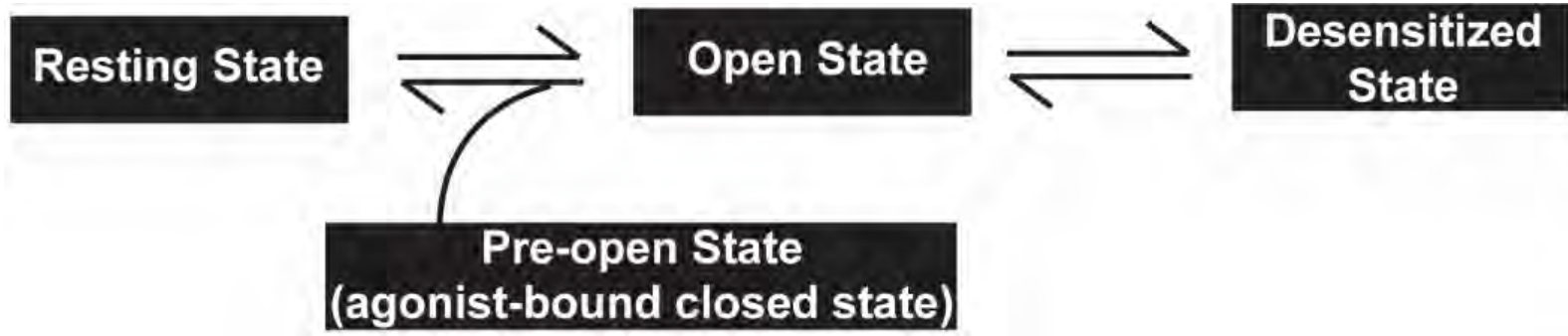
Inhibitory Synapse



Glycine Receptor

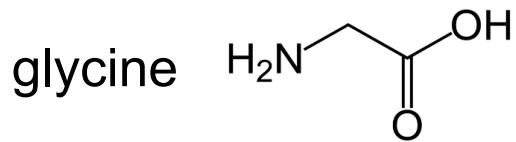


Hyperekplexia (startle disease)



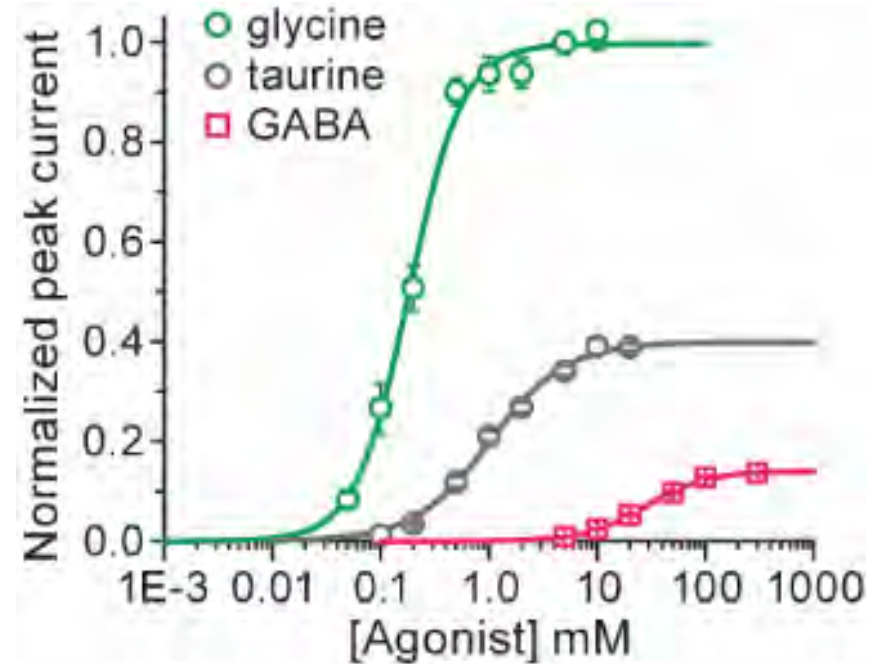
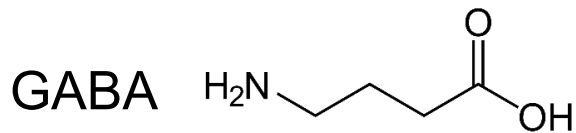
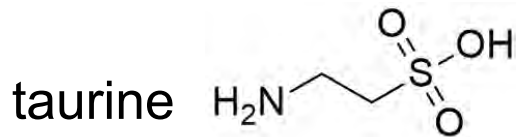
High efficacy

Full agonist



Low efficacy

Partial agonist



Therapeutics

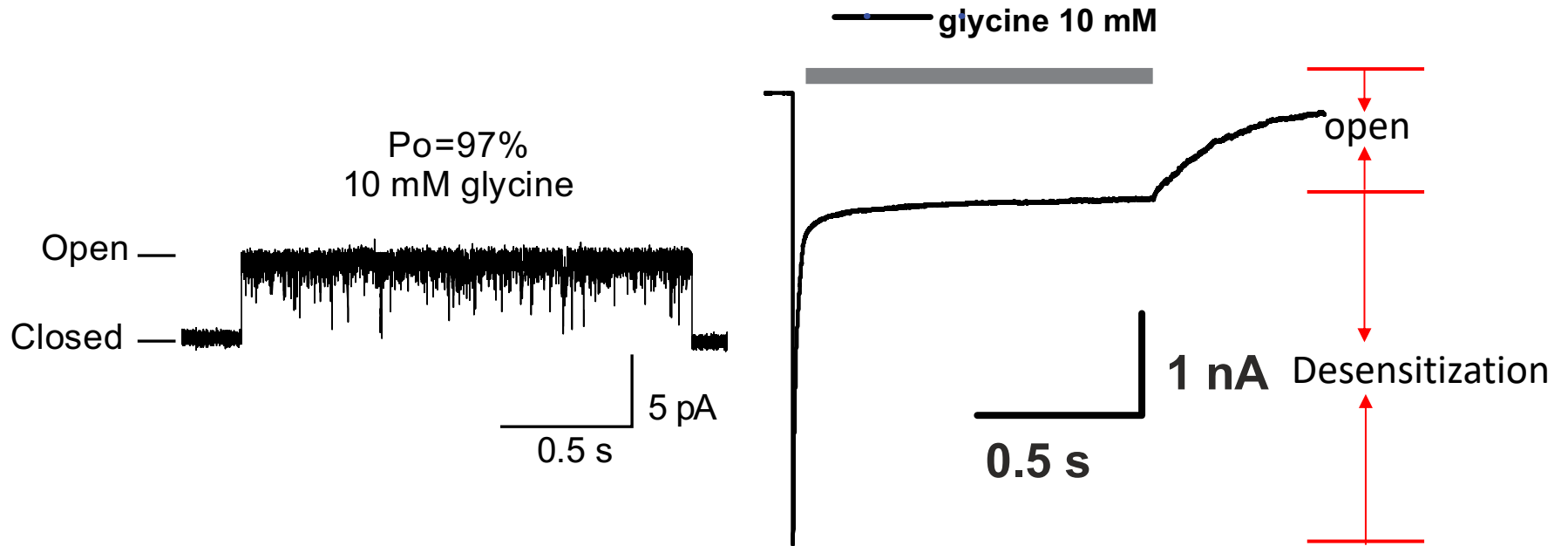


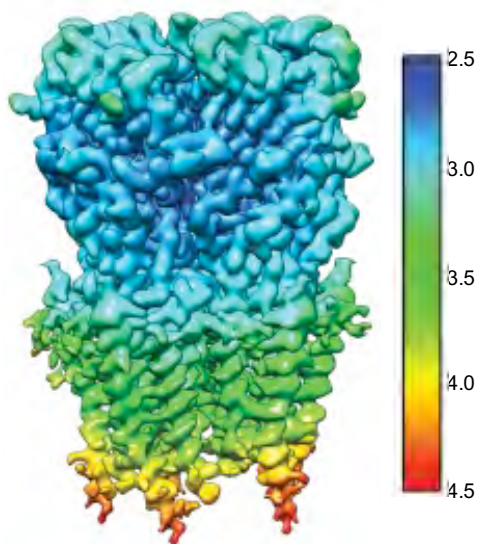
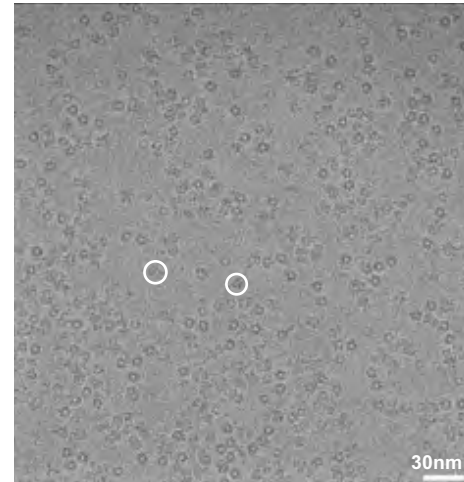
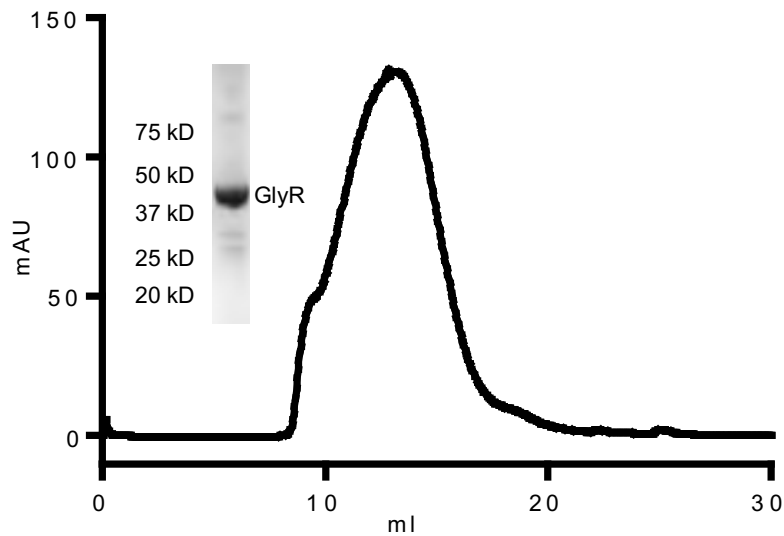
Partial agonist

- Structures of full length GlyR with agonists in the native lipids environment
- Partial agonists action mechanism
- Gating mechanism

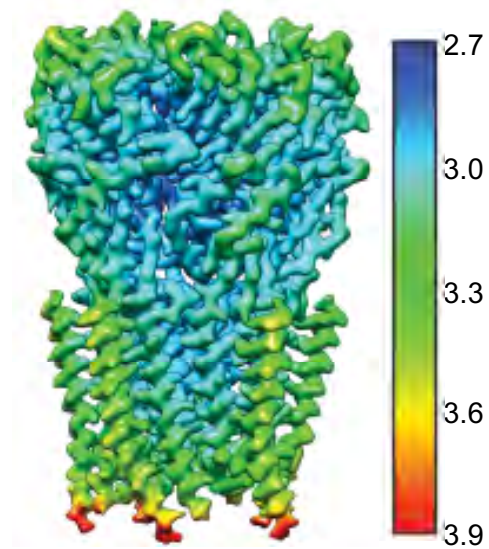
- Structures of full length GlyR with agonists in the native lipids environment
- Partial agonists action mechanism
- Gating mechanism

Full agonist-glycine





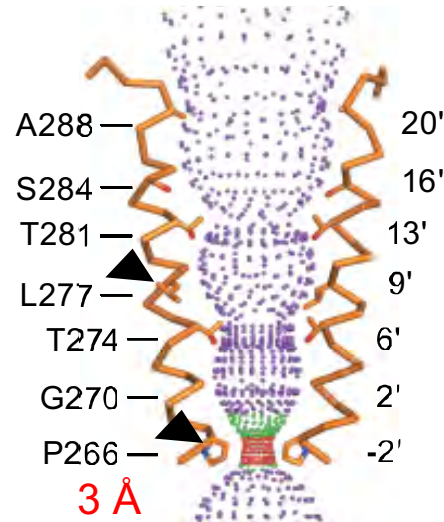
Desensitized State



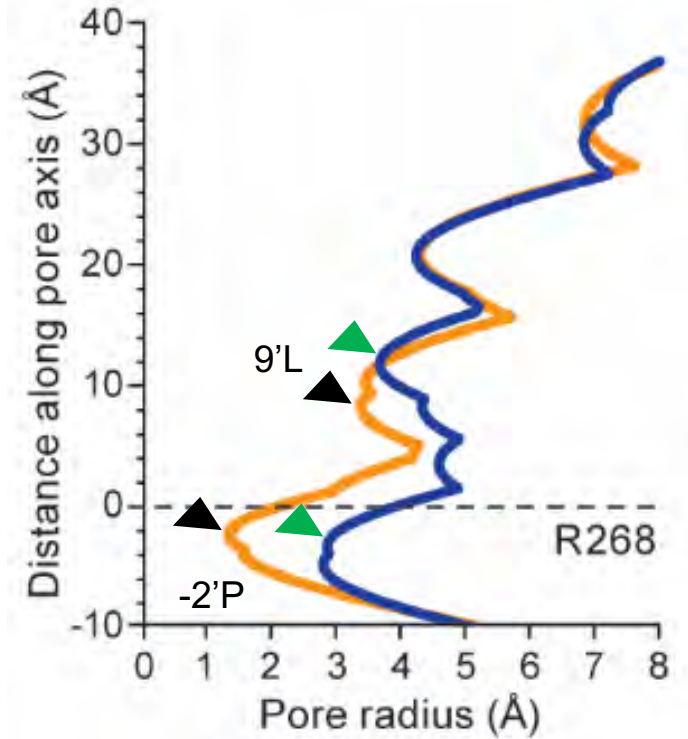
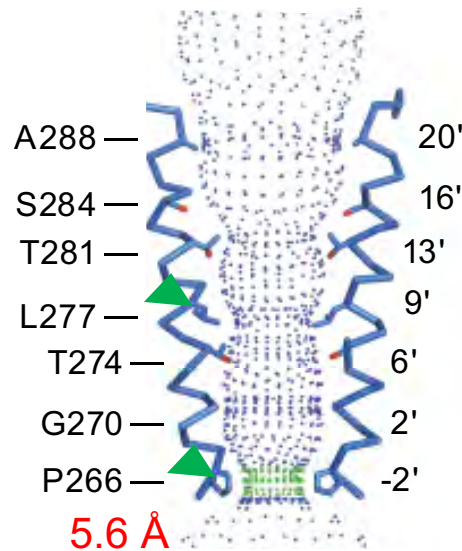
Open State

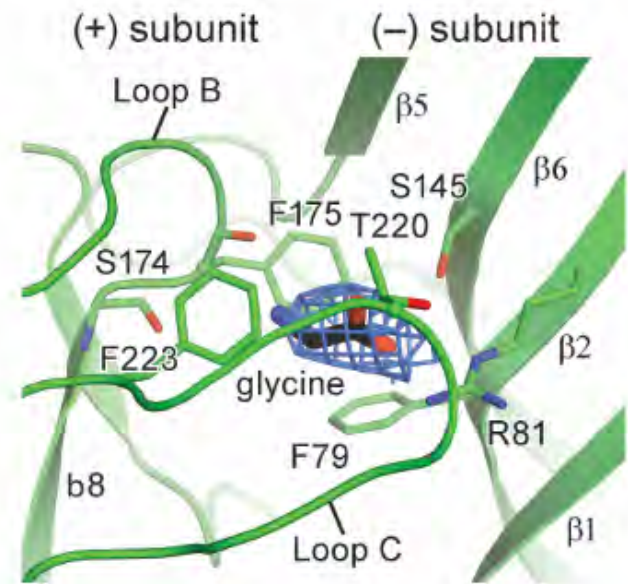
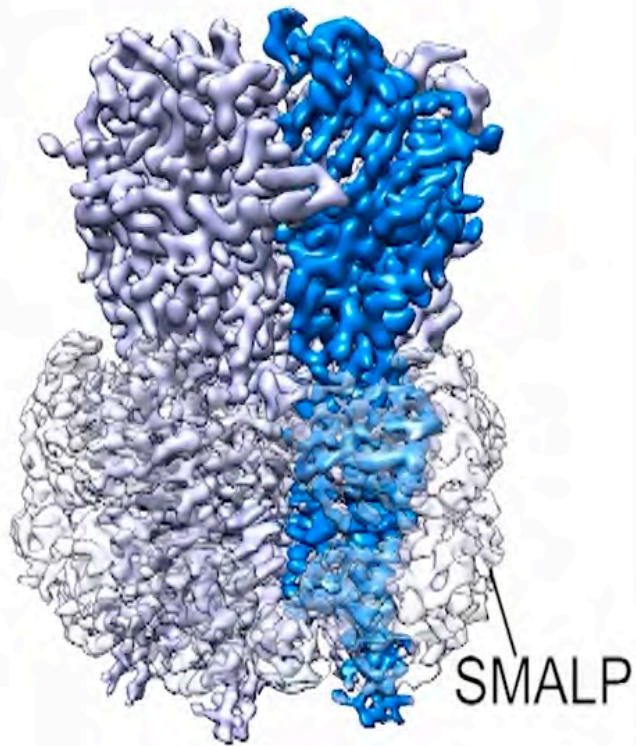
GlyR with glycine in the SMA

Desensitized State



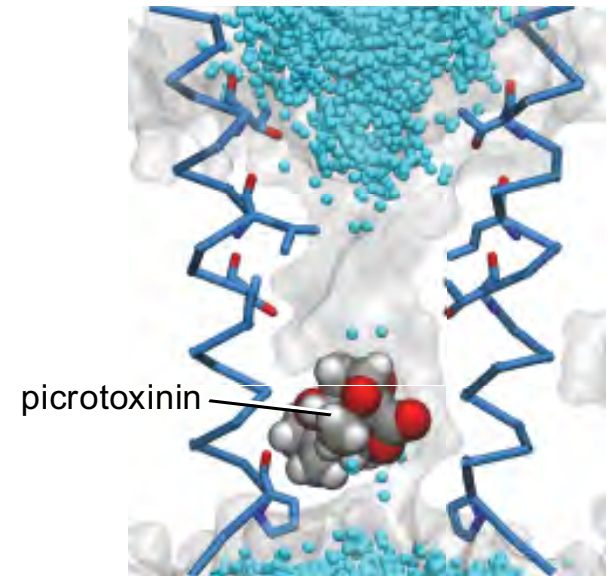
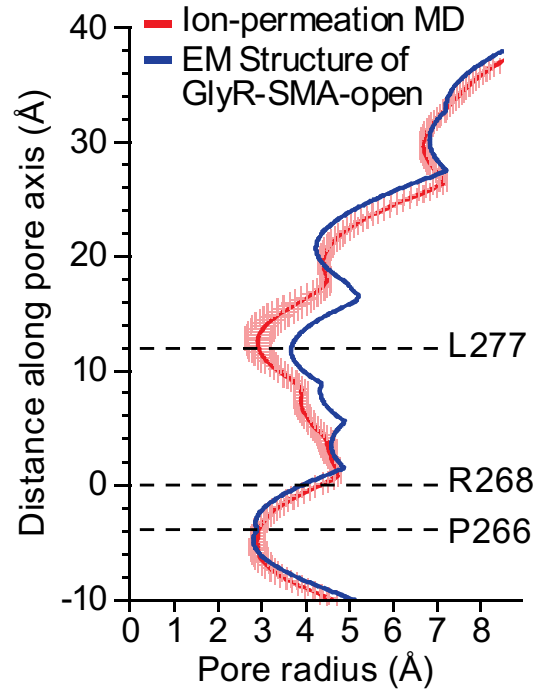
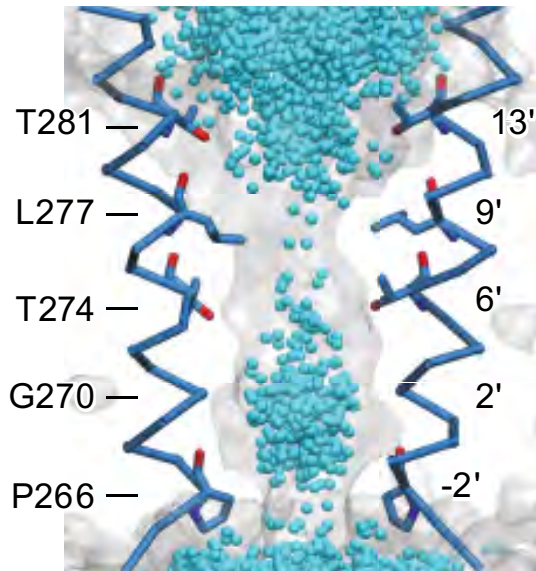
Open State





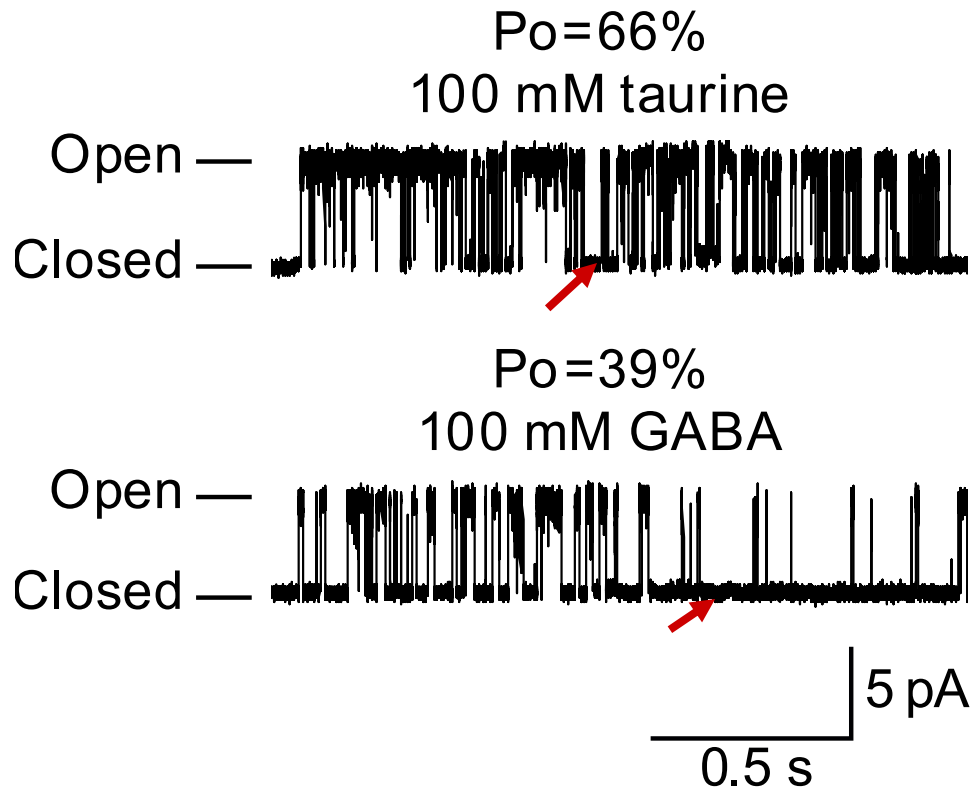
Open State

Molecular Dynamic Simulation



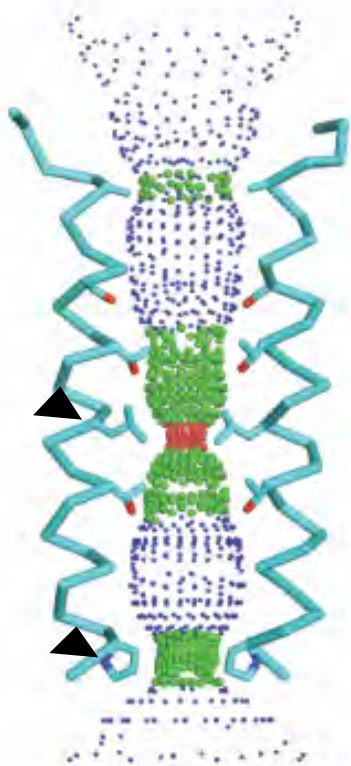
GlyR-gly-SMA-open

Partial agonists- taurine/GABA

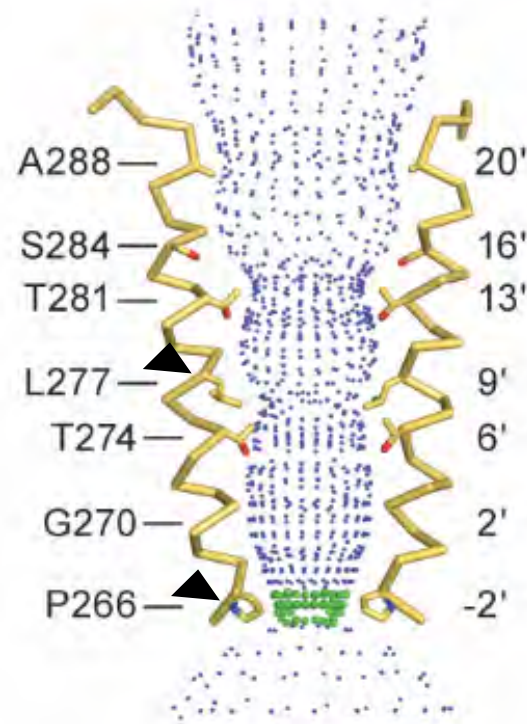


GlyR with taurine in the SMA

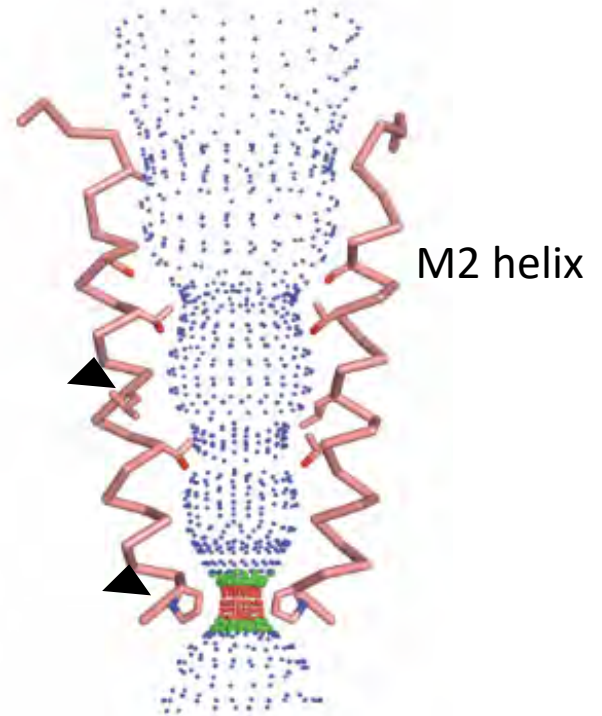
Closed State

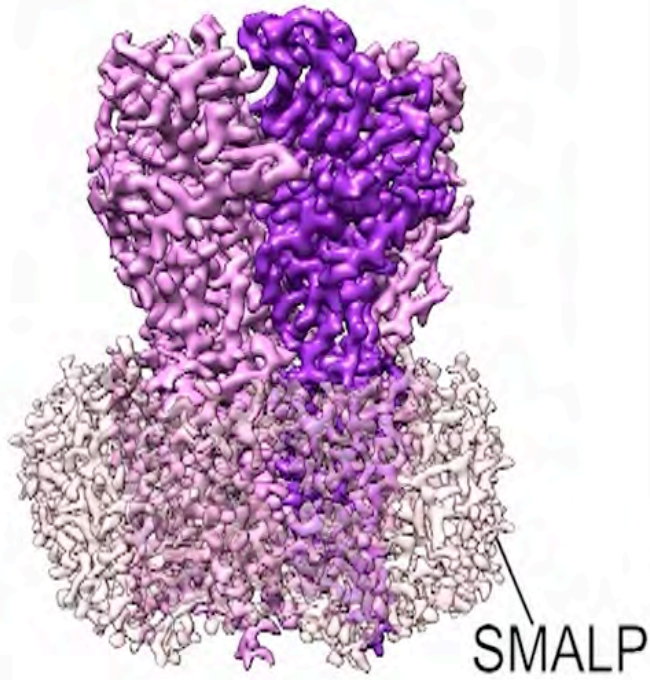


Open State

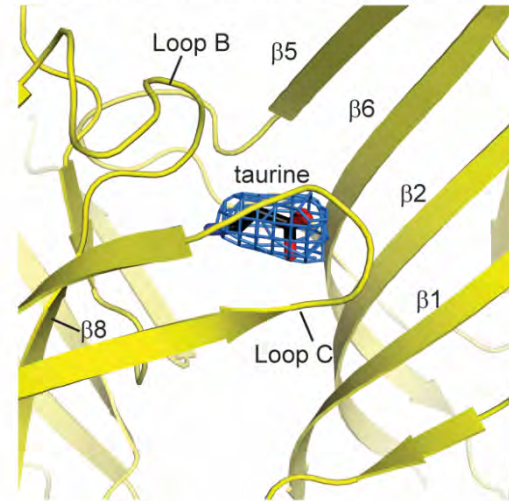


Desensitized State

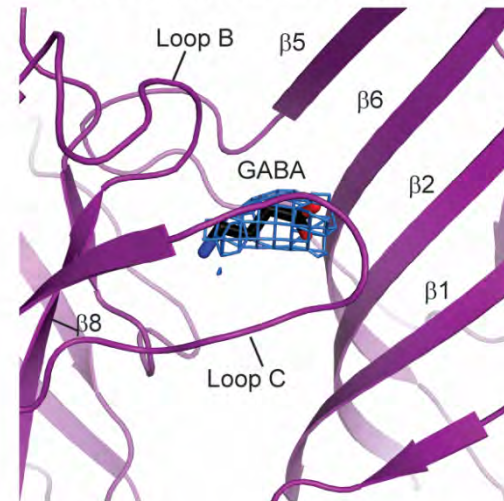




Taurine-closed state

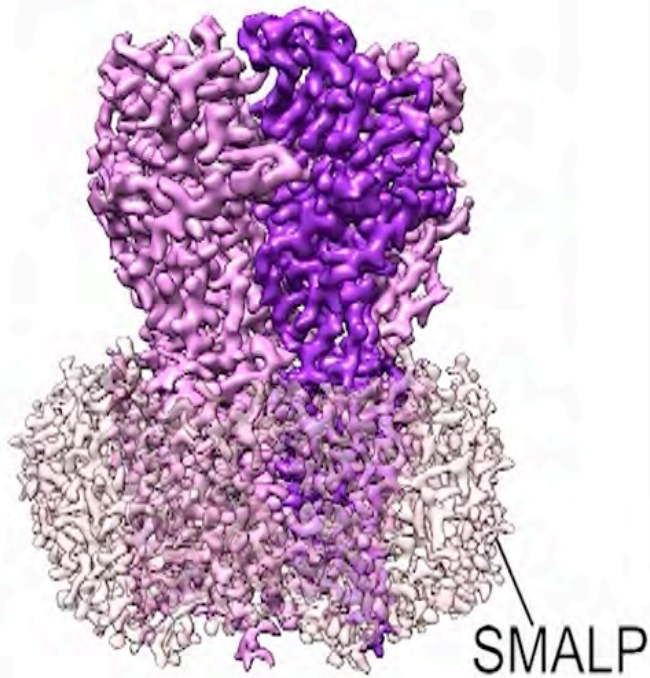


GABA-closed state

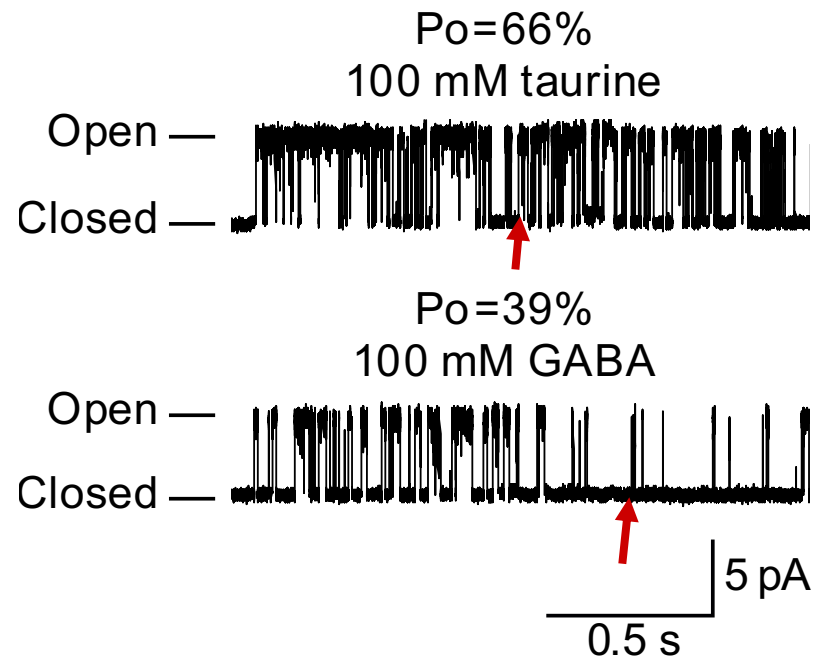


GABA-closed state





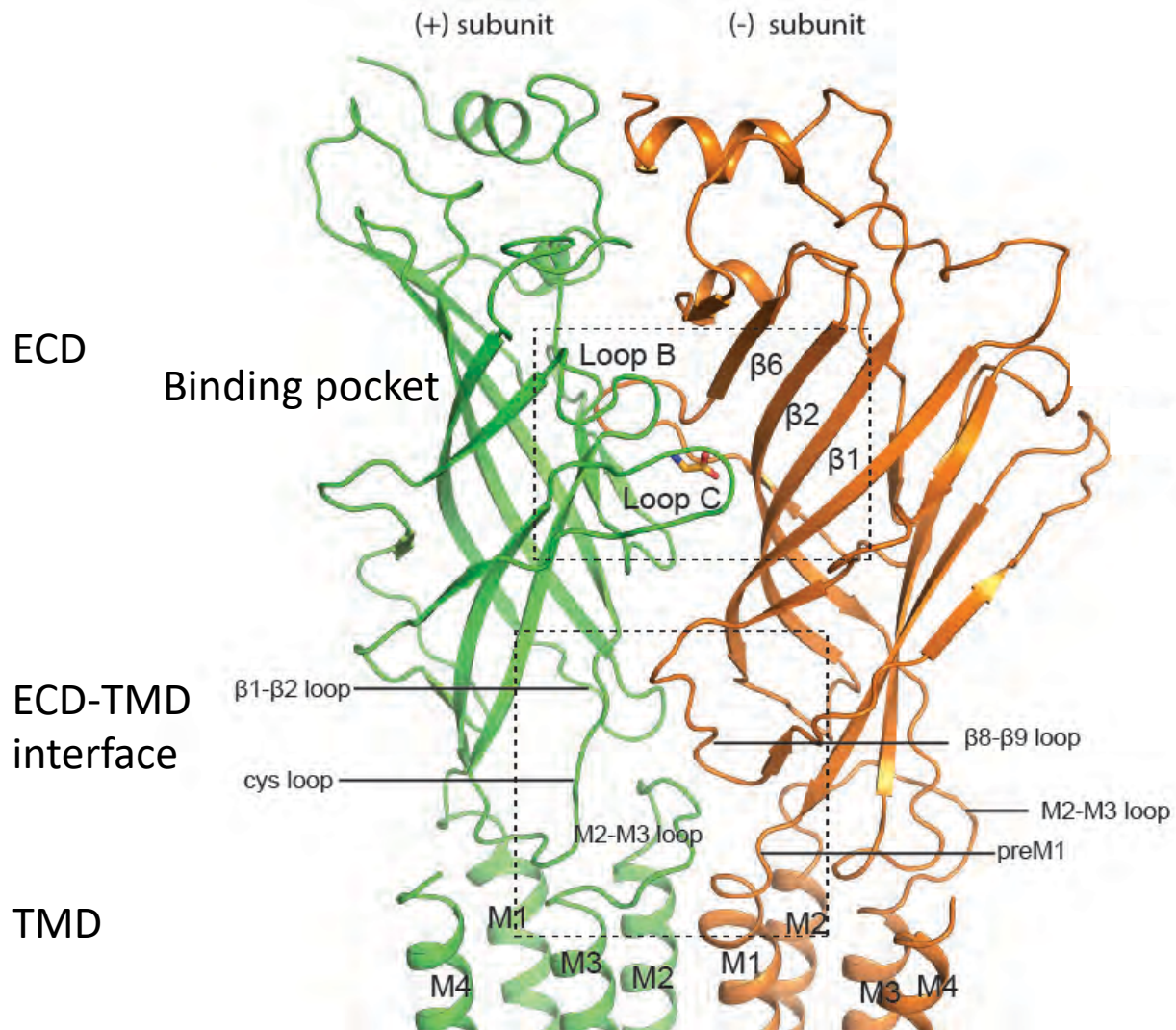
GABA-closed state

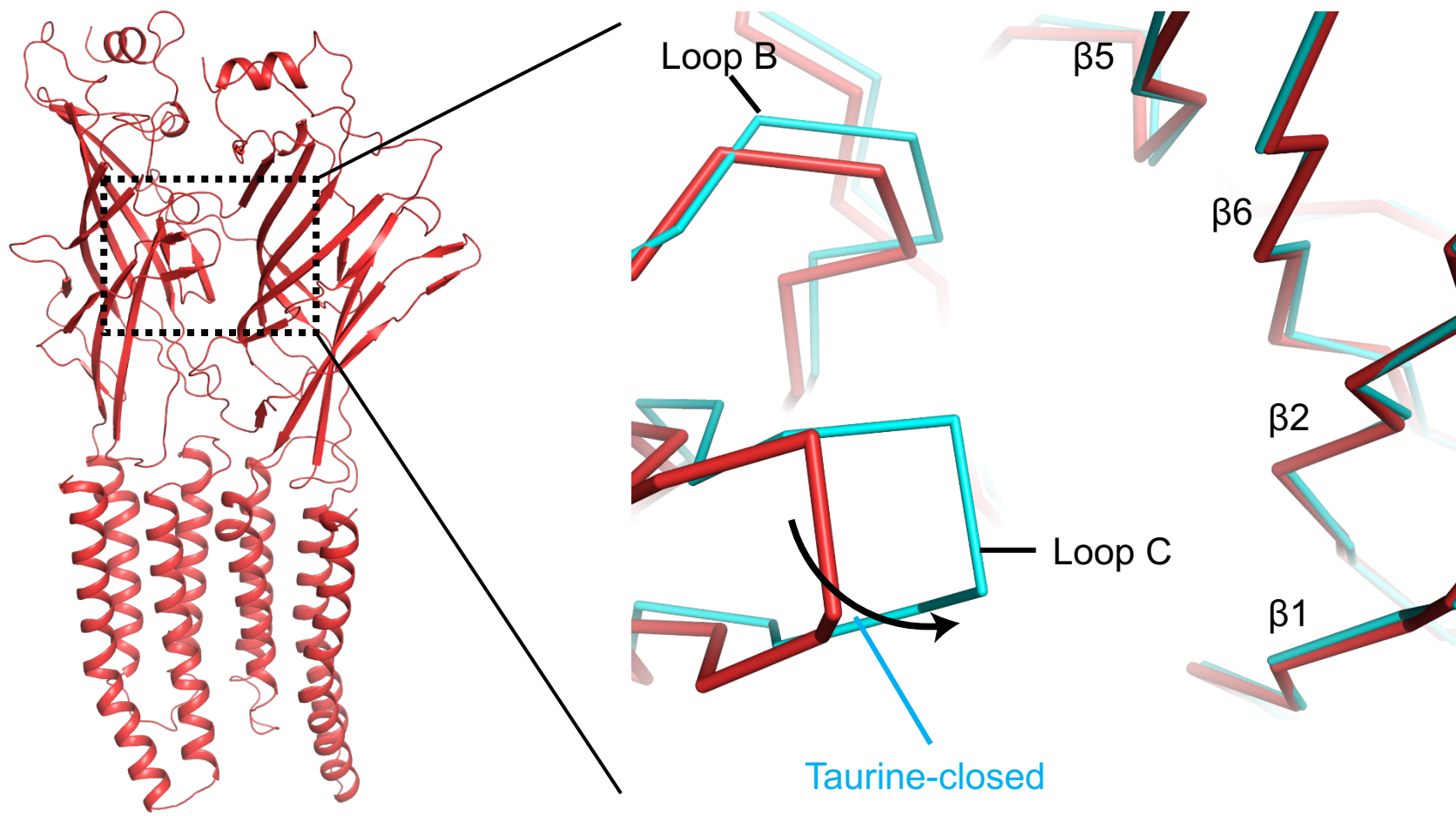


➤ Structures of full length GlyR with agonists in the native lipids environment

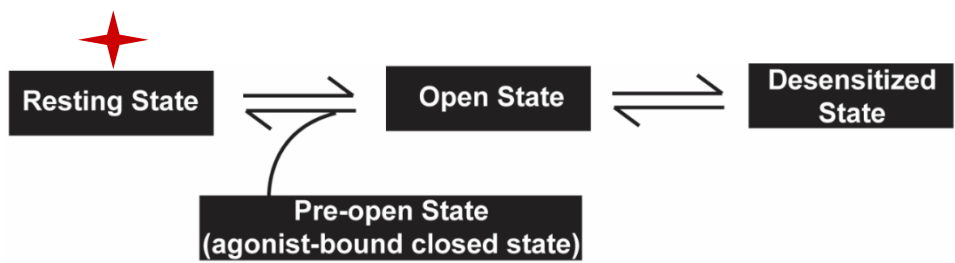
➤ **Partial agonists action mechanism**

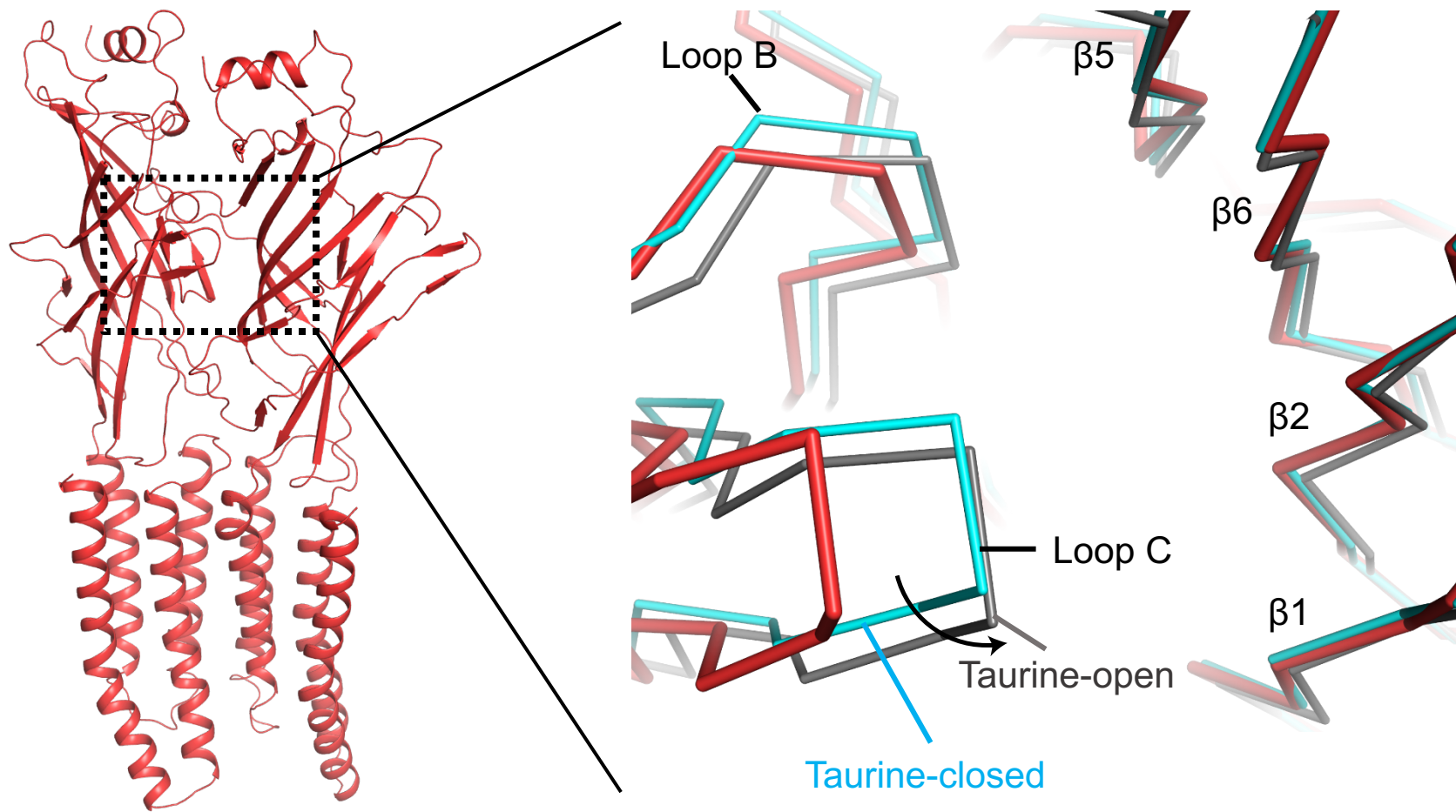
➤ Gating mechanism





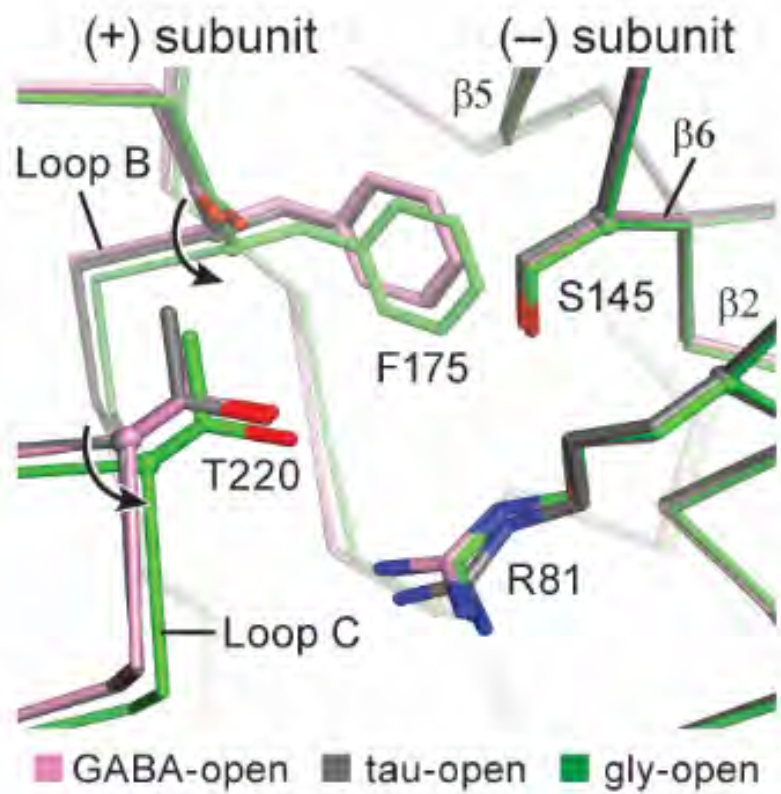
Apo state

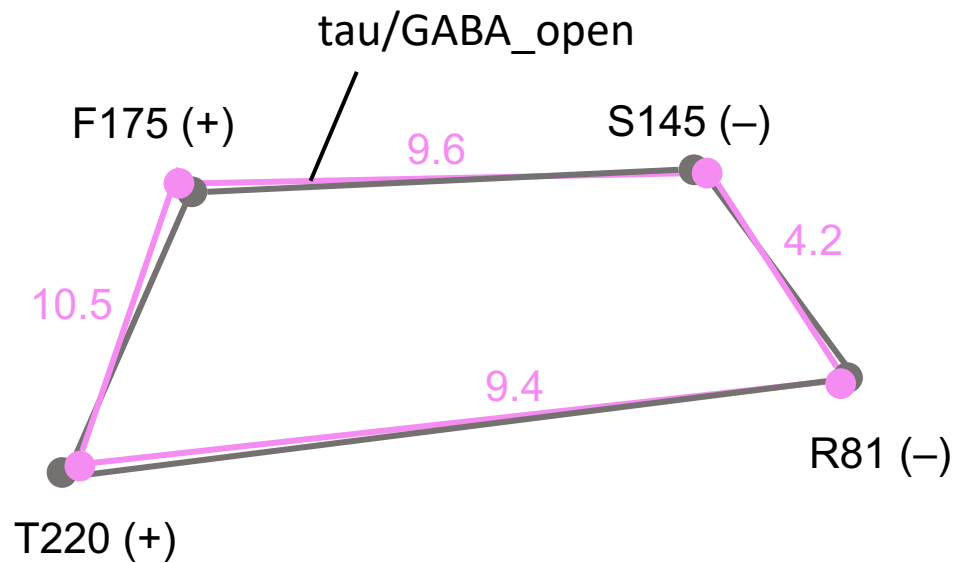
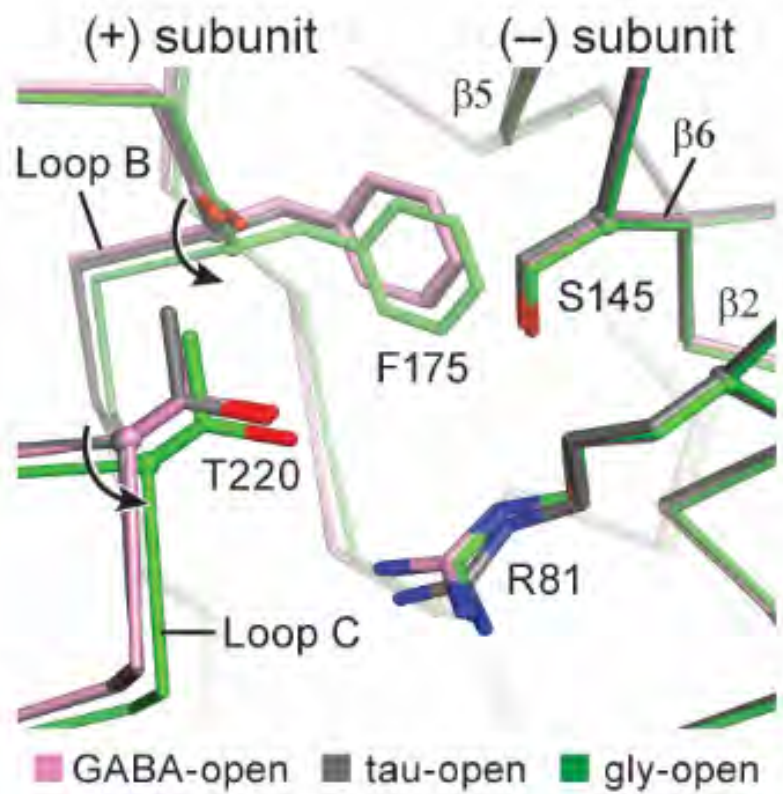


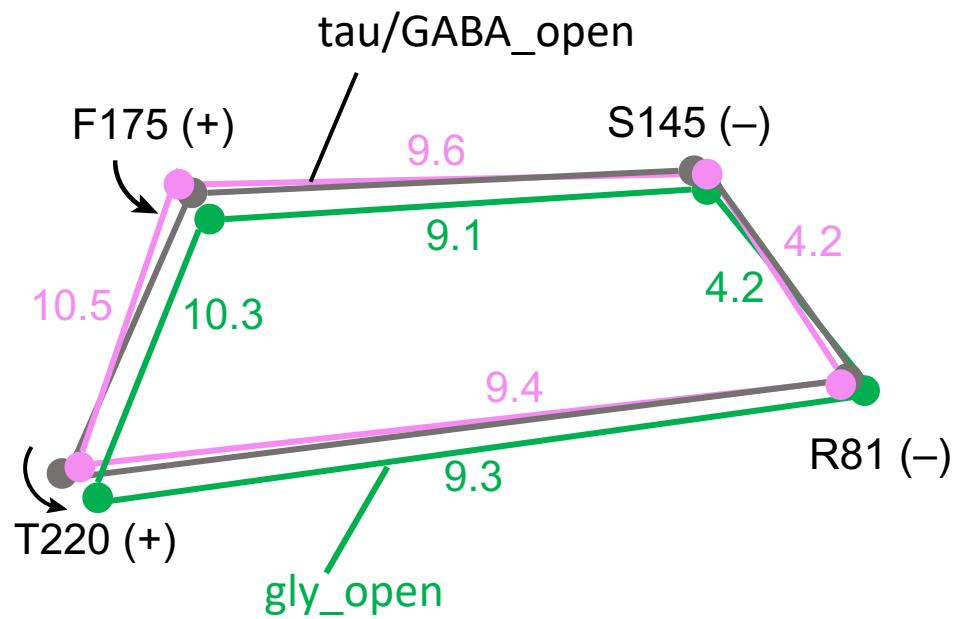
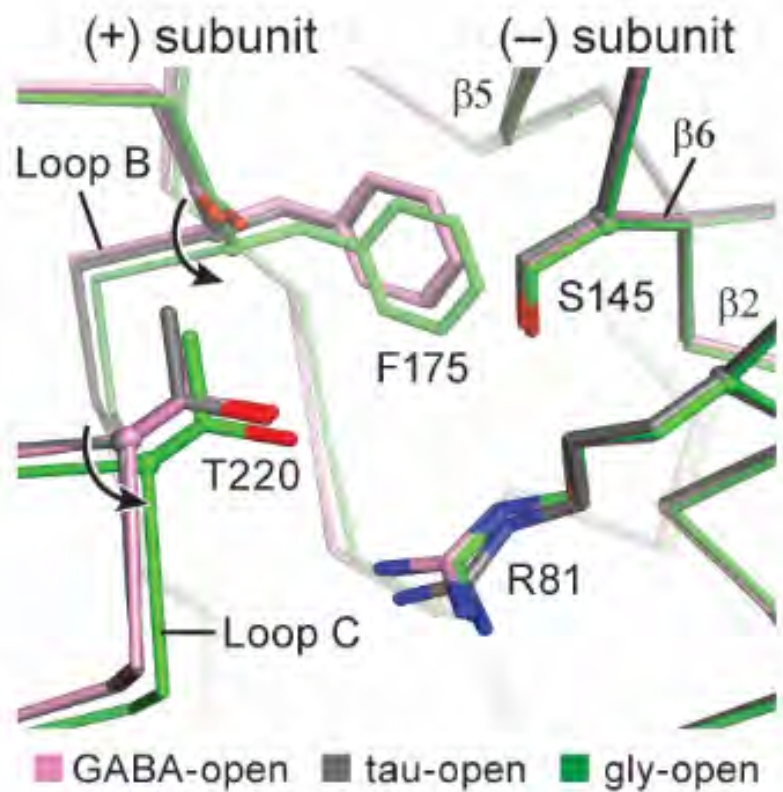


Apo state









- Structures of full length GlyR with agonists in the native lipids environment
- Partial agonists action mechanism
- **Gating mechanism**

Closed State

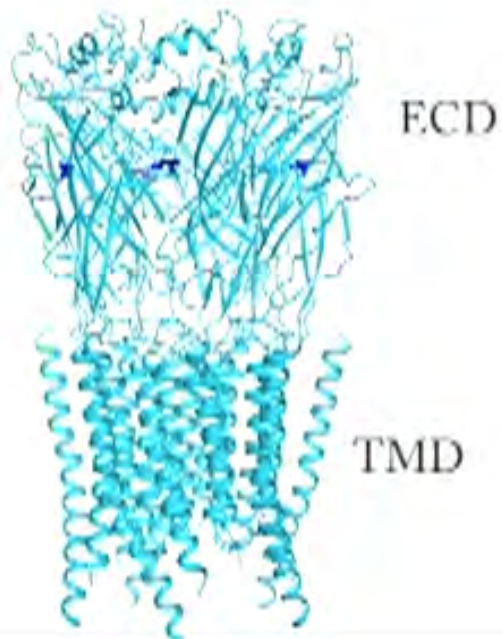


Open State



Desensitized State

Closed State



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