

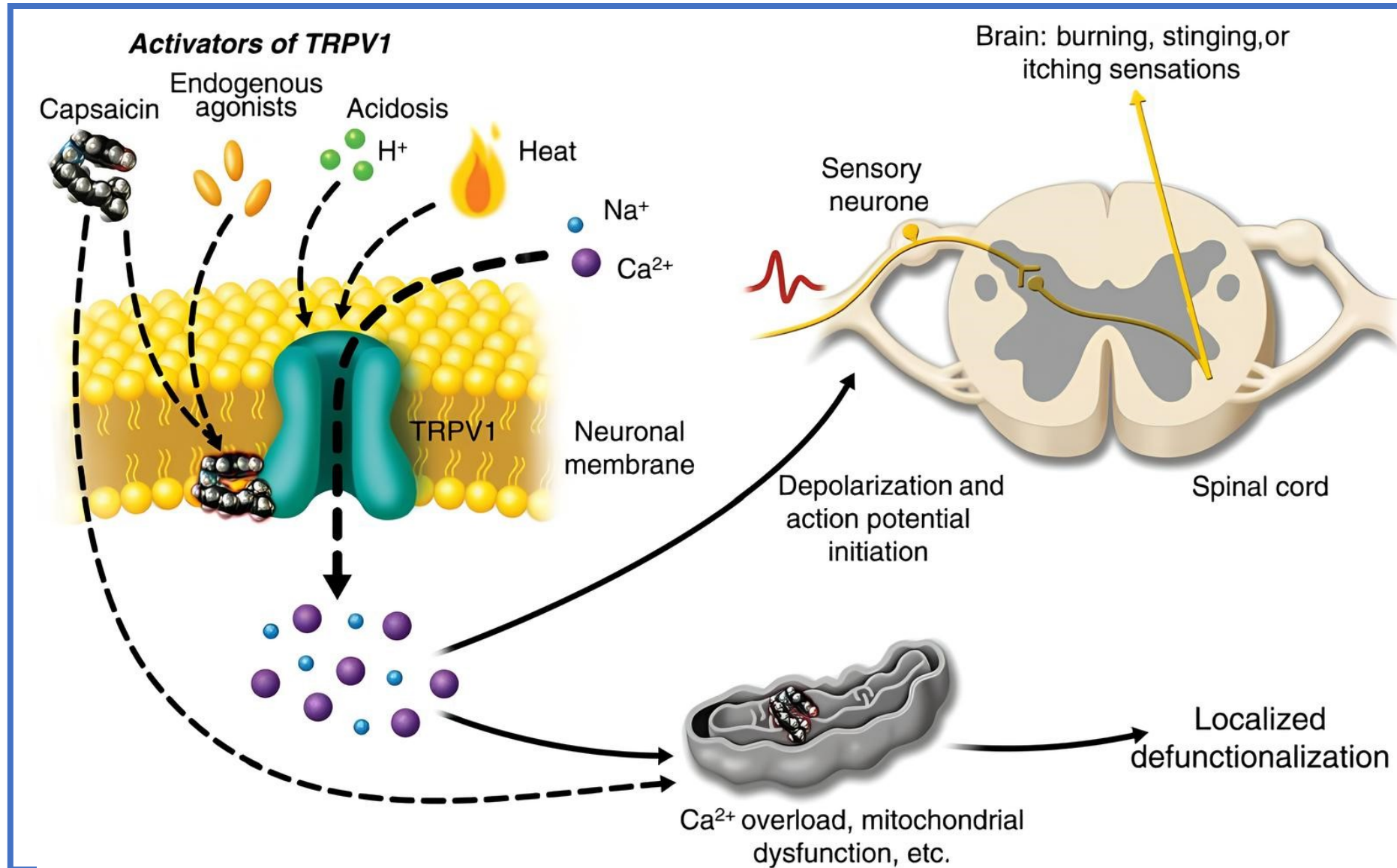


Polar patch in the hydrophobic gate of TRPV1 channel and its functional role

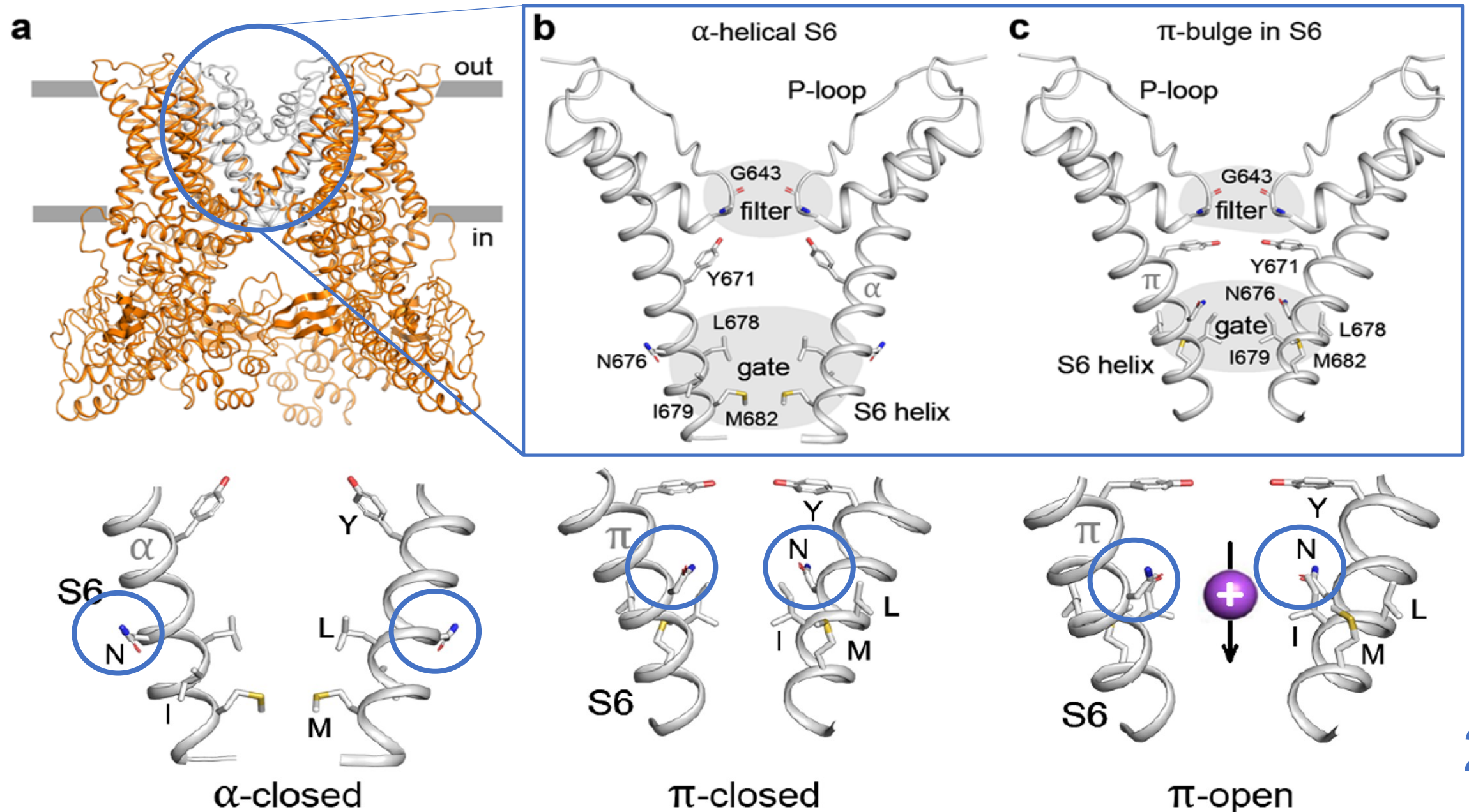
**Lazarev I.V. ,
Trofimov Y. A.,
Efremov R.G.**

Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, RAS, Moscow, Russia

Introduction



Structure of TRPV1

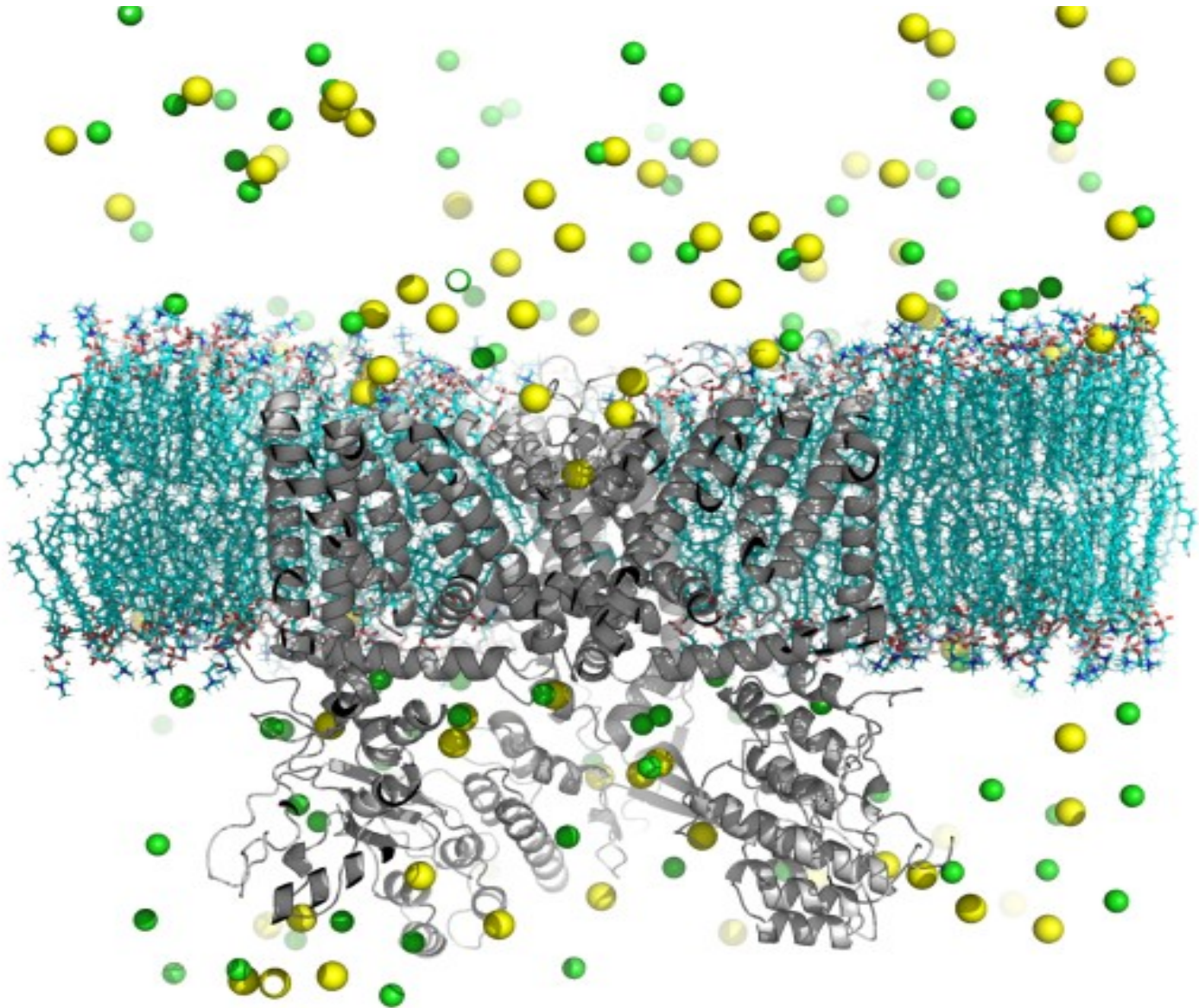


MD protocol

Amber99sb-id1n **force field**
200 ns

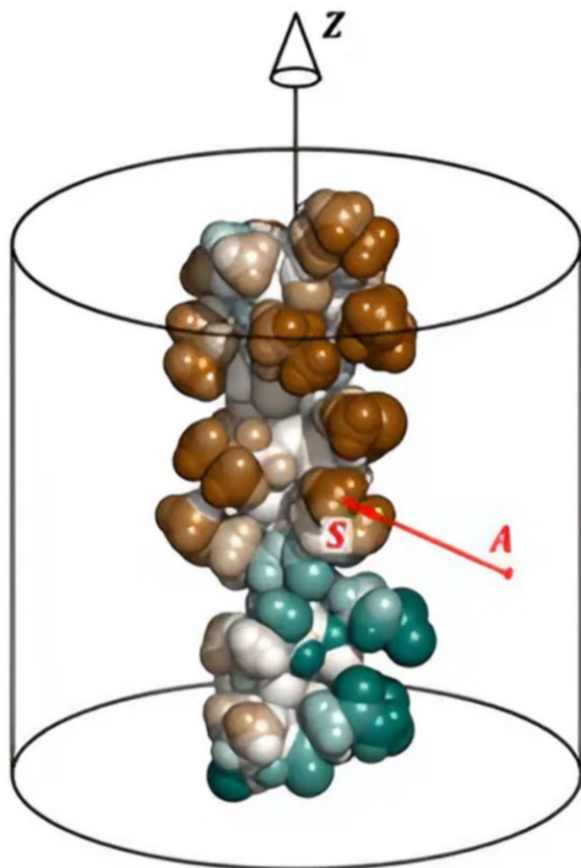
25% POPE
25% CHL
50%POPC

Na⁺ Cl⁻ Membrane



“Dynamic molecular portrait” approach

$$C_{PP/PW} = MHP_{self} \times MHP_{ind} \times S^2 \times I$$

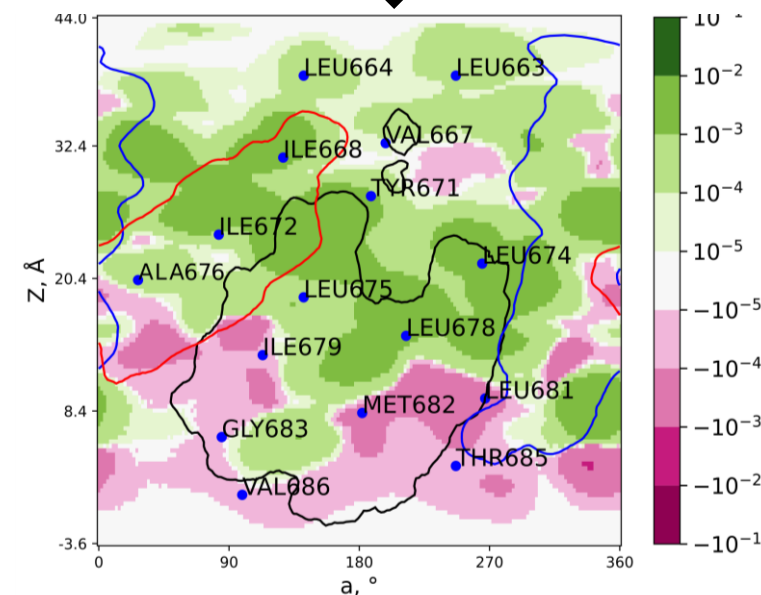
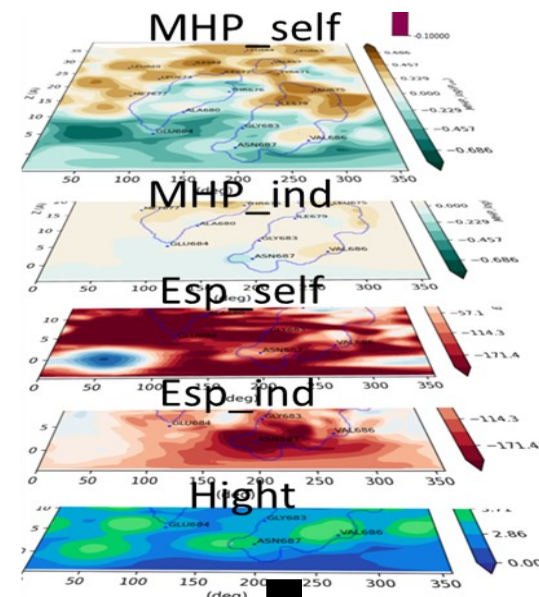
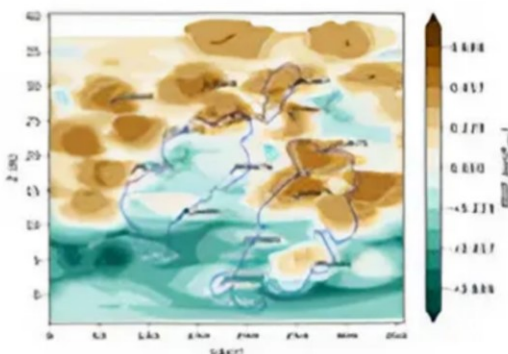
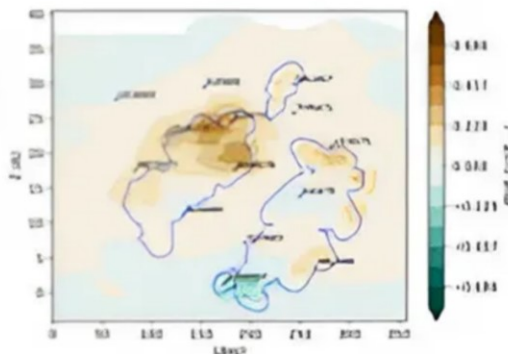


hydrophilic hydrophobic

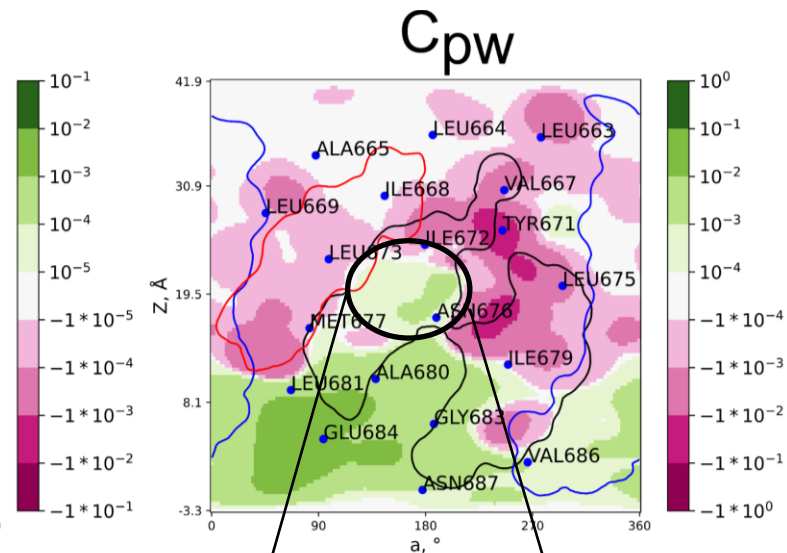
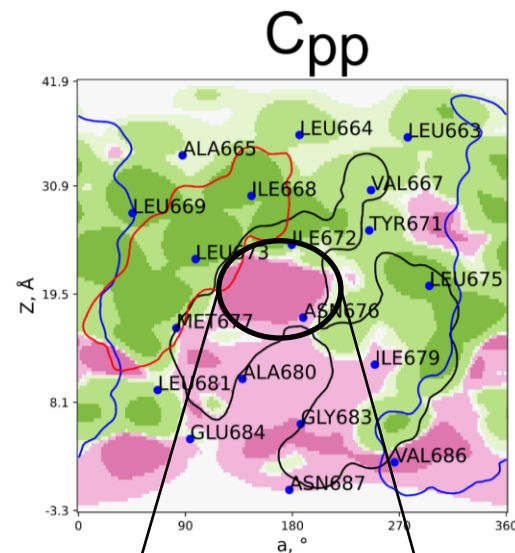
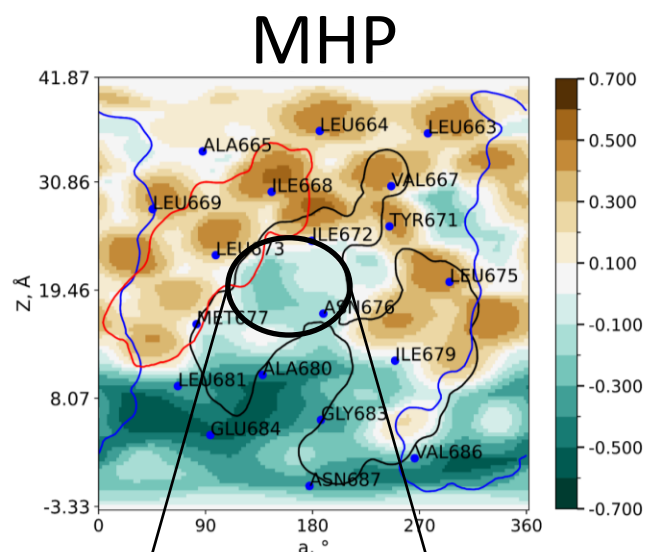
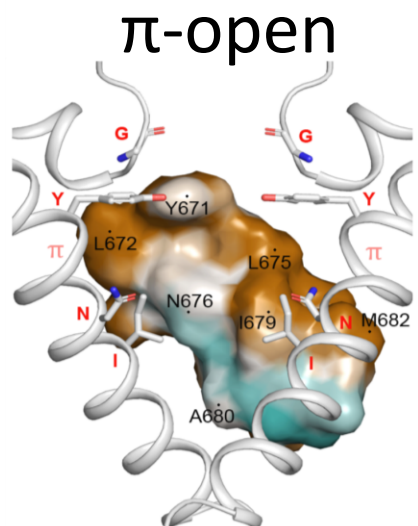
Induced MHP



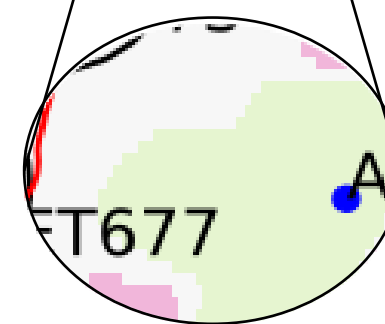
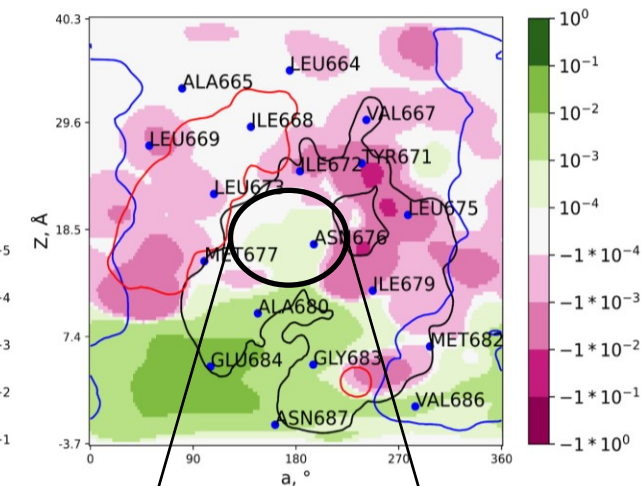
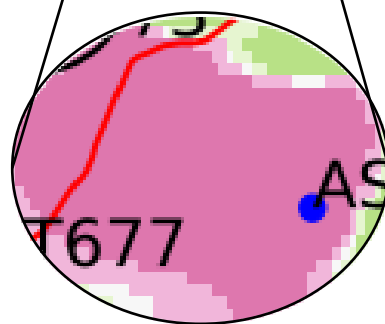
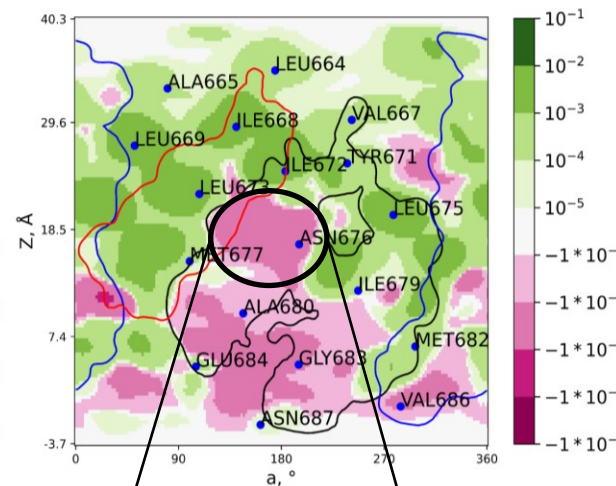
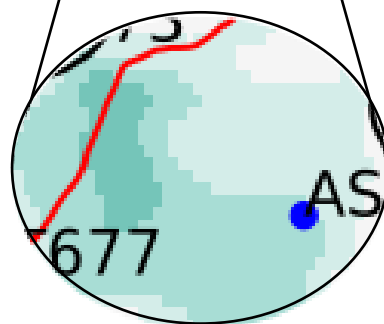
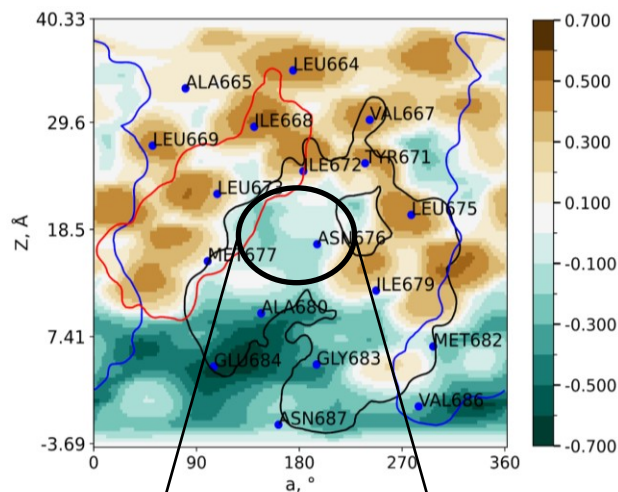
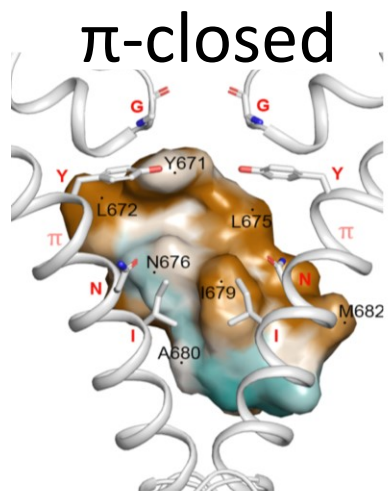
Self MHP



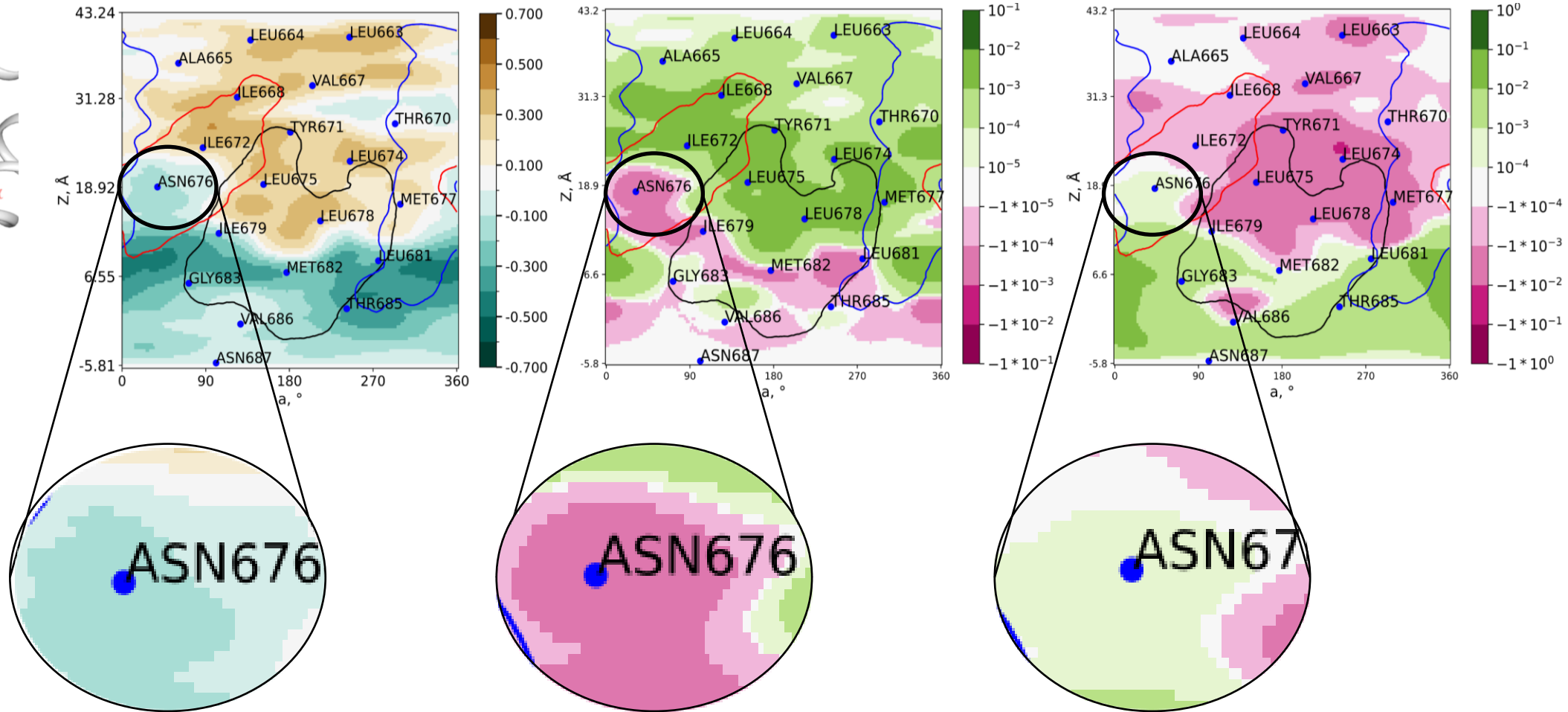
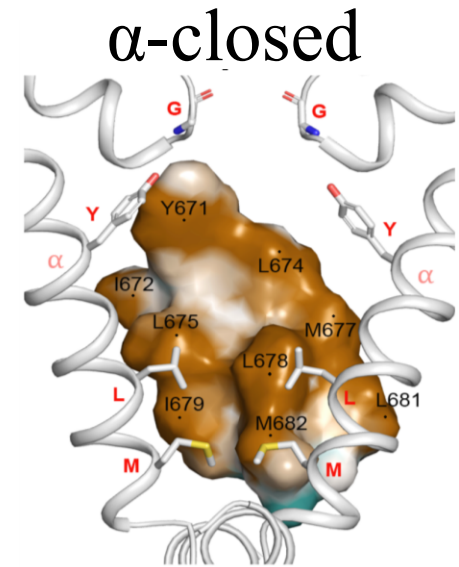
Mapping for TRPV1 in the π -open state



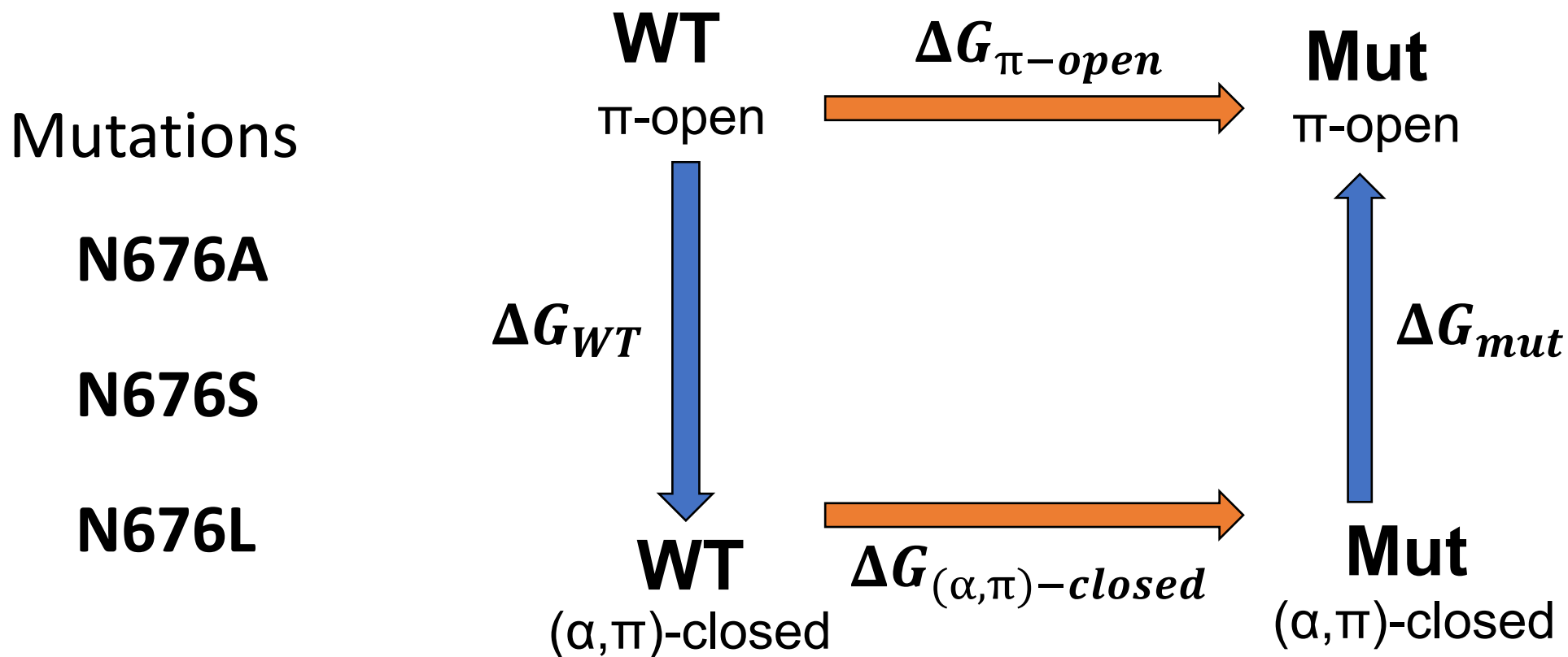
Mapping for TRPV1 in the π -closed state



Mapping for TRPV1 in the α -closed state

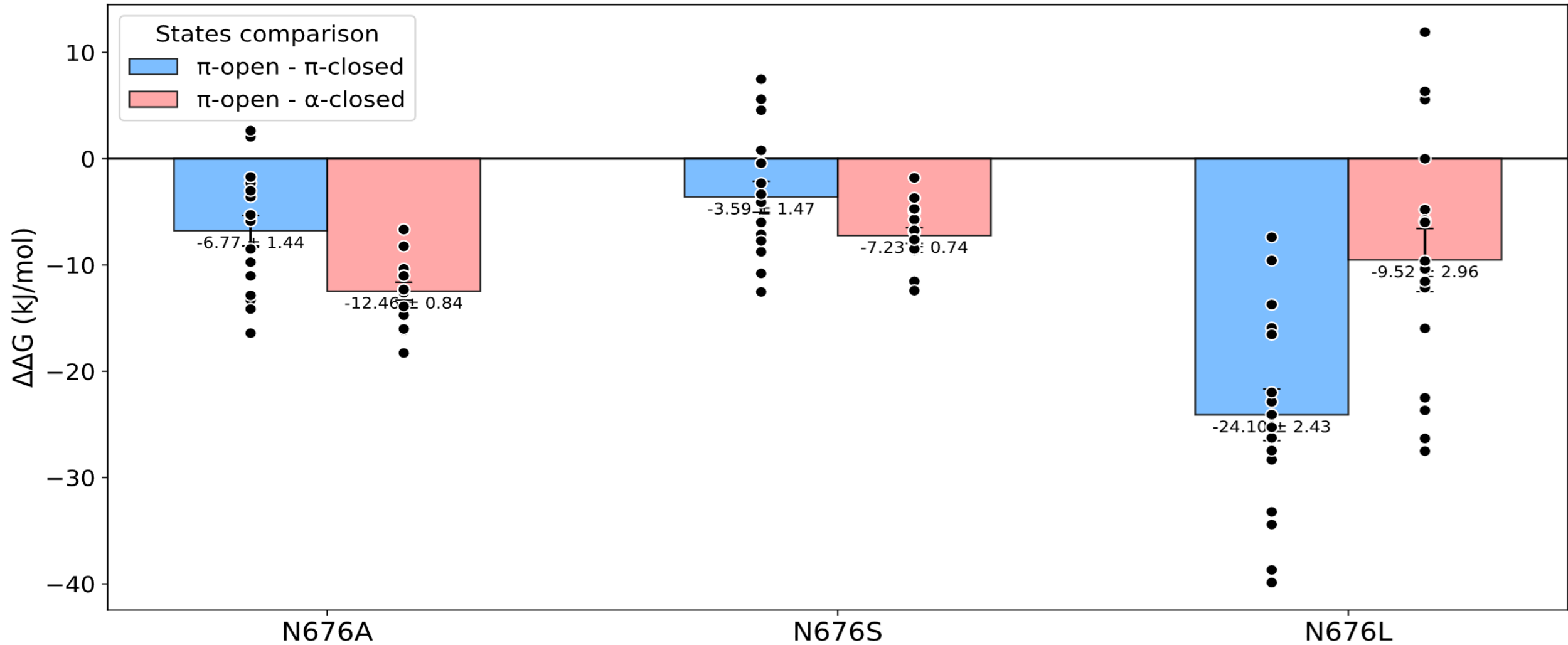


Alchemical transformation method



$$\Delta\Delta G = \Delta G_{WT} - \Delta G_{mut} = \Delta G_{(\alpha, \pi)-closed} - \Delta G_{\pi-open}$$

$\Delta\Delta G$ values for mutations N676A, N676S, N676L



Conclusion

1. In the **π -open state**, the **asparagine residue** ensures **complementary contacts with water** within the hydrophobic gates, promoting their **hydration**.
In the **α -closed state**, strong **hydrophobic contacts** form in the pore, preventing ion conduction.
2. Substitutions **N676A, N676S, and N676L** shift the equilibrium toward the **closed states**.
N676A and **N676S** primarily favor the **α -closed state**, whereas **N676L** favors the **π -closed state**.
3. Overall, **N676 stabilizes the π -open state** of TRPV channels.

Thank you for listening!



More detailed information is presented in E-poster