

Supporting Materials

Solving an Old Puzzle: Elucidation and Evaluation of the Binding Mode of Salvinorin A at the Kappa Opioid Receptor

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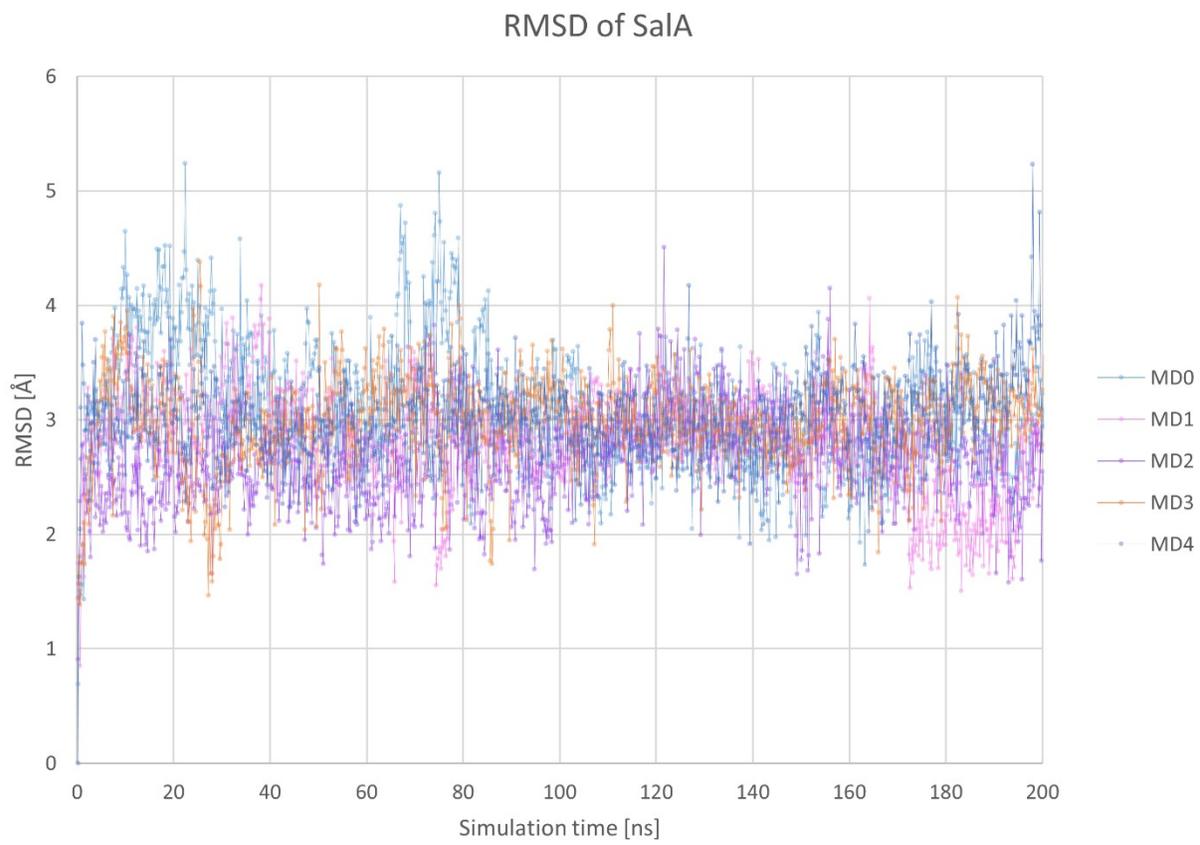


Figure S1. Root mean square deviation of SalA (1) in complex with the KOR over the simulation time.

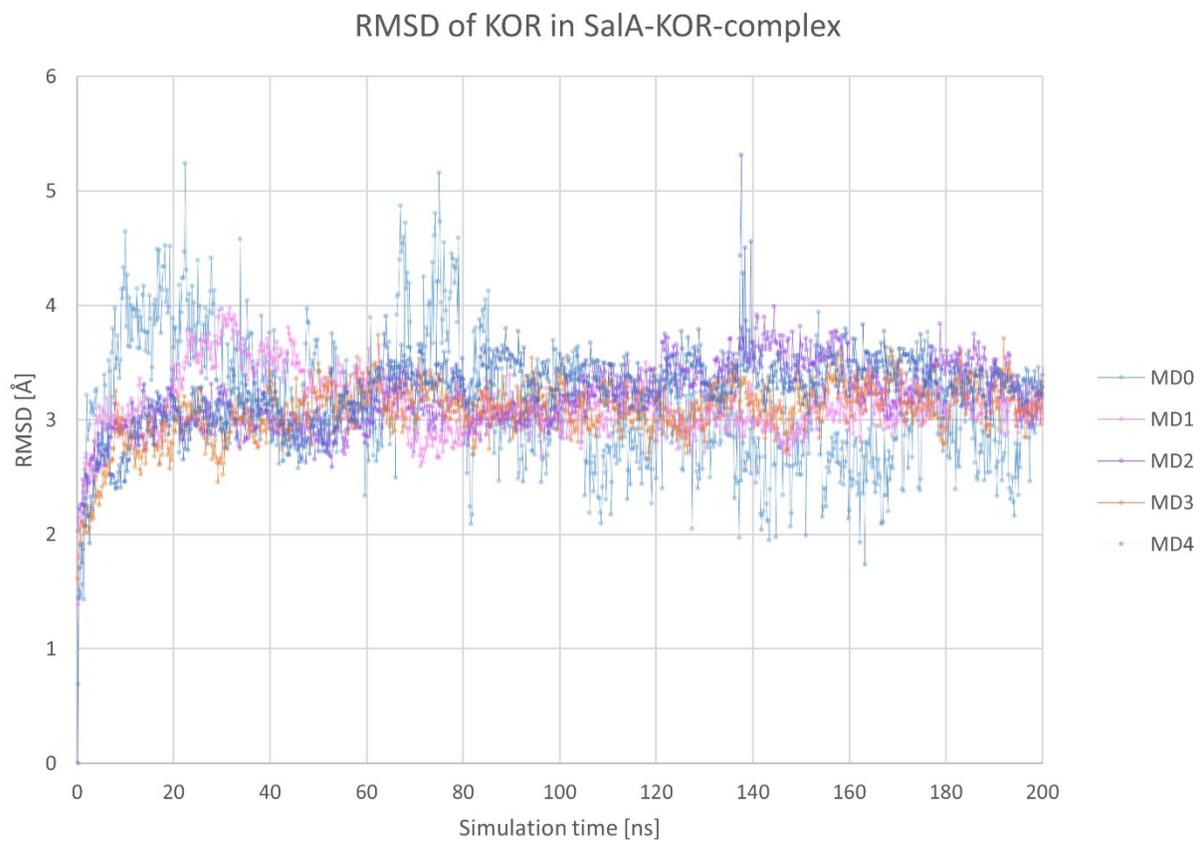


Figure S2. Root mean square deviation of the KOR backbone atoms in complex with SaIA (**1**) over the simulation time.

	Identity				Similarity			
	1.	2.	3.	4.	1.	2.	3.	4.
1. hKOR		53.5	57.4	50.3		67.0	69.6	64.3
2. hMOR	56.3		60.5	50.3	70.5		70.7	63.8
3. hDOR	56.3	56.2		50.0	68.2	65.8		62.4
4. hNOP	48.9	46.5	49.7		62.6	59.0	62.1	

Figure S3. Sequence identity and similarity of the full sequence of KOR, MOR, DOR, and NOP.

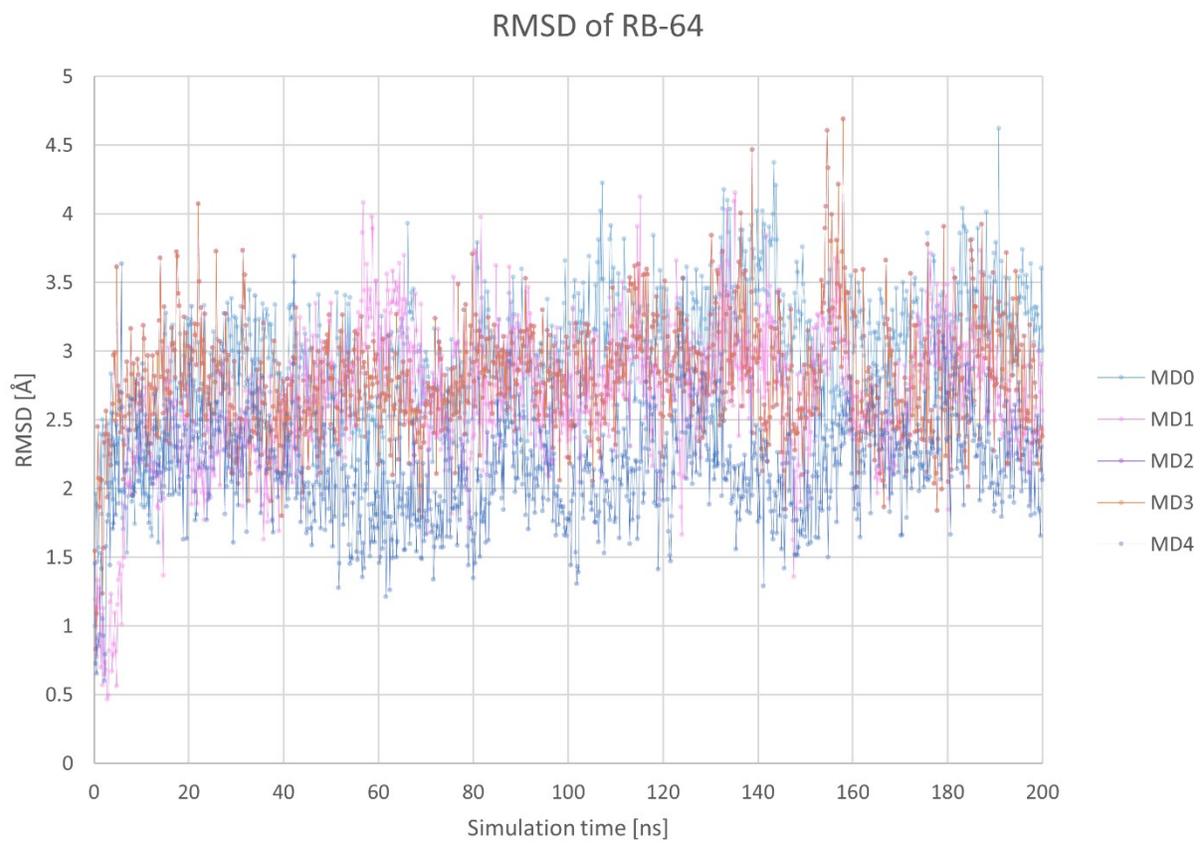


Figure S4. Root mean square deviation of RB-64 (7) in complex with the KOR over the simulation time.

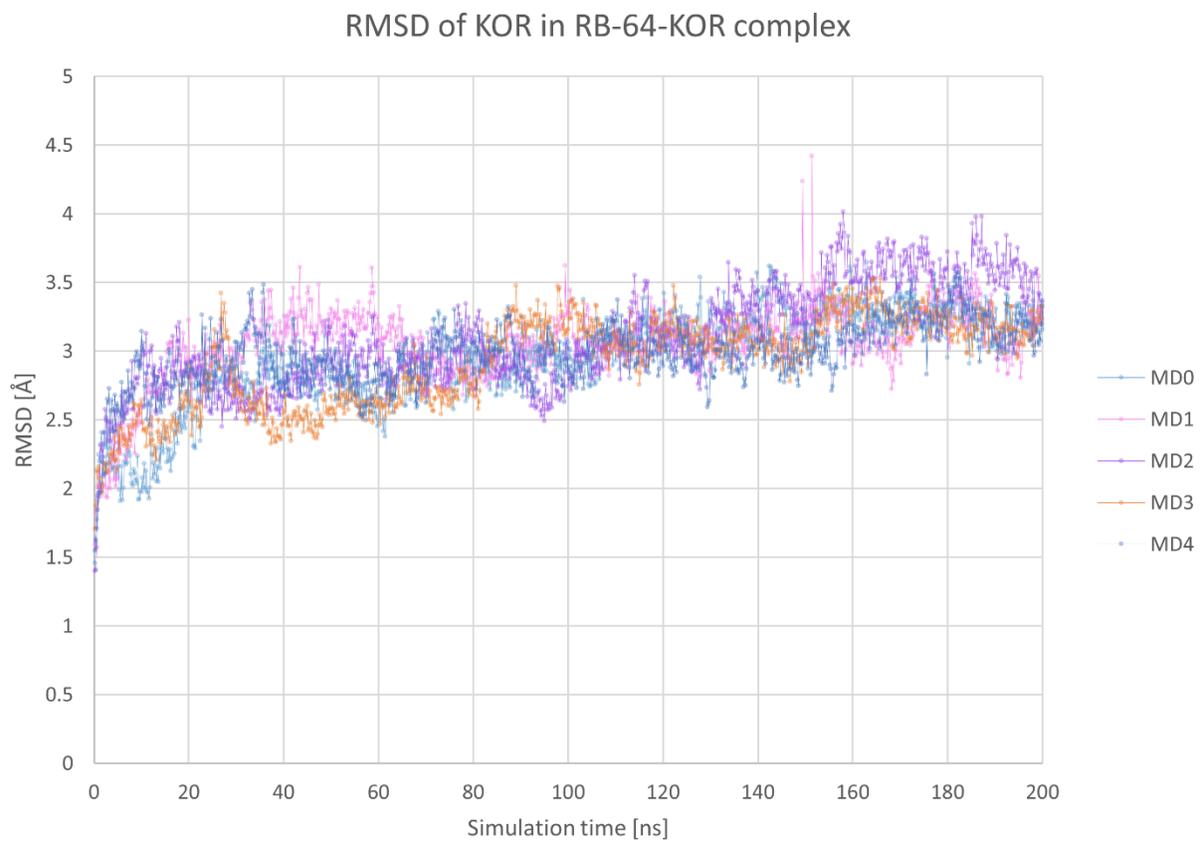


Figure S5. Root mean square deviation of the KOR backbone atoms in complex with RB-64 (7) over the simulation time.

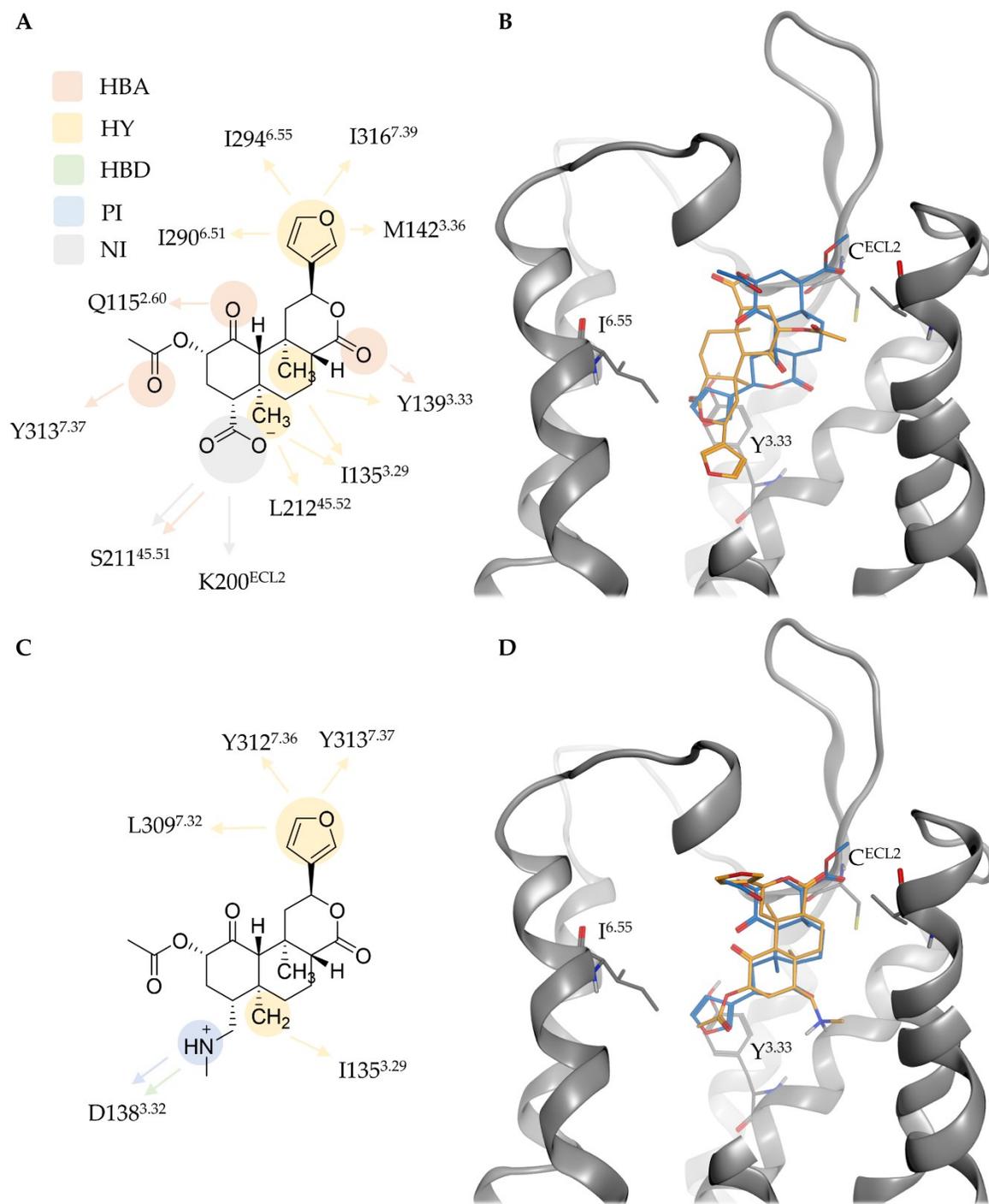


Figure S6. Protein-ligand interactions and binding mode of **8** (A, B, orange) and **9** (C, D, orange) at the KOR in comparison to SalA (blue). **8** is shifted in the binding side and shows an alternative scaffold orientation while **9** shows a reversed orientation compared to SalA. Y^{3.33} denotes to Y139^{3.33}, C^{ECL2} to C210^{ECL2}, and I^{6.55} to I294^{6.55}. Interactions types are abbreviated with HBA for hydrogen bond acceptor, HY for hydrophobic contact, HBD for hydrogen bond donor, NI for negative charged interaction, and PI for positive charged interaction.