

Description of Additional Supplementary Files

Supplementary Data 1: Forward and reverse primers used to generate NBCn1 mutant constructs.

Supplementary Data 2: Initial OF and IF NBCn1 + 2Na⁺ + CO₃²⁻ and NBCn1 + Na⁺ + CO₃²⁻ structures for calculations of free energy of ion binding.

Supplementary Data 3: Structures (beads) produced by the Climber simulations of the OF to IF transition in apo-NBCn1.

Supplementary Data 4: First and last step of the 200 ns unrestrained MD trajectories of OF and IF NBCn1 + 2Na⁺ + CO₃²⁻ (3 replicas per system).

Supplementary Data 5: First and last step of the 100 ns MD simulation with applied position restraints (movement along z restrained and movement in the xy plane allowed) of the OF and IF NBCn1 + 2Na⁺ + CO₃²⁻ (71 simulation windows per system).

Supplementary Data 6: First and last step of the 1 μs unrestrained MD simulations, starting from intermediate structures along the OF to IF transition in apo-NBCn1 (2 sets, 16 replicas per set).

Supplementary Data 7: First and last step of the 1 μs unrestrained MD Anton2 trajectories of OF and IF apo NBCn1 (3 replicas per system).

Supplementary Movie 1: Elevator-type core domain (orange) motion relative to gait domain (purple) during the OF to IF transition in human NBCn1. The overall downward shift of the core is ~ 5 Å combined with a small lateral movement in the xy plane. Significant motion of IL5 (cyan) can be seen.