

# A continuous complete RNA translocation cycle by the DEAH-box helicase Prp43 in atomic detail

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Understanding conformational cycles of complex macromolecular machines in atomic detail remains a central goal of molecular biophysics. Here, we focus on helicases that are crucial for every living organism to carry out functions such as DNA/RNA transcription, translation, DNA/RNA repair, recombination and splicing. The largest group among helicases is the Superfamily 2 (SF2), which includes the DEAD- and DEAH-box helicases as key players in the splicing pathway. Despite the wide interest in understanding the detailed mechanism of ssRNA translocation during splicing, the exact movements are still unknown. Using molecular dynamics simulations and enhanced sampling techniques, we observed a complete RNA translocation cycle of the DEAH-box helicase Prp43 in atomic detail. The simulations reveal the collective behaviour of the three main domains RecA1, RecA2 and CTD, like the detachment and the formation of the interface of the RecA domains or the rotation of the CTD. Additionally, the simulations give detailed insight in the essential and atomistic processes during the large domain motions, e.g. a movement cascade induced by an arginine finger in the ATP binding side, the conformational change of a serine loop to a helical state, the cleavage and formation of various hydrogen bonds, including the so called Hook-loop and Hookturn, the behaviour of the ssRNA during the process and more.