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Resolution-exchanged structural modeling and simulations jointly unravel that subunit rolling underlies the mechanism of programmed ribosomal frameshifting

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Biological regulation is a manifestation of binding-triggered force controls at the molecular levels. Existing theoretical tools can hardly describe such a control at atomistic details for huge molecular machineries that orchestrate a repertoire of functional motions over long time periods. Here, we leverage linear response theories and resolution-exchanged simulations to study the pseudoknot (PK)-induced force control over programmed ribosomal frameshifting (PRF). Connecting and rationalizing existing structural, single-molecule and mutagenesis data by first principles, we demonstrated how steric hindrance of a stable mRNA structure transiently modifies the conformational dynamics of the ribosome, and subsequently allows tRNA to shift one nucleotide backwards during -1 PRF. Our study provides a temporal and spatial description of PRF with unprecedented mechanistic details to conclude that 30S subunit rolling is the motion that mediates the delicate force control of cis-element unwinding over -1 PRF. The introduced method is also instrumental in studying force-induced controls over other supramolecular machineries.

Introductory videos about ribosome:
https://youtu.be/1PSwhTGFMxs; https://youtu.be/kmrUzDYAmEI
Our publication & frameshift related info:
https://viralzone.expasy.org/860
our recent publication
https://academic.oup.com/bioinformatics/advance-article/doi/10.1093/bioinformatics/bty762/5086394?guestAccessKey=3484e180-0783-4552-aa80-2bcea3e406e8