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**Rest Assured: Programmed Translational Stalling Studied by Means of Md Simulations.**

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Gene regulation can occur in bacteria through programmed translational stalling. The SecM arrest peptide, e.g., up-regulates secretion of proteins through the cell membrane by inducing stalling. Stalling is released by a mechanical pulling force acting on the N-terminus. Recently, novel arrest peptides like ApdP have been discovered which share with SecM a conserved Arg-Ala-Pro-Pro motif. Cryo-EM structures of the stalled E. coli ribosome containing the peptide-Arg-Ala-Pro-tRNA in the ribosomal P site and a Pro-tRNA in the A site, suggest that peptide bond formation is affected during translation of ApdP and SecM. In all current models of peptide bond formation, the nucleophilic attack of the aminoacyl-tRNA α-amino group to the carbonyl-carbon of the peptidyl-tRNA is facilitated by the extraction of a proton from the attacking α-amino group. Using molecular dynamics (MD) simulations of the E. Coli ribosome in complex with wt ApdP and non-stalling variants, we found that specific hydrogen bonds between the Arg-Ala-Pro peptide and the A-site Pro prevent the efficient adoption of conformations that allow the proton extraction as well as the subsequent nucleophilic attack. Additionally, we investigated how pulling of the N-terminus of SecM relieves stalling, identifying the sequence of events that leads to the disruption of the stalling conformation of the Arg-Ala-Pro-Pro motif.