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Interconvertible Lac Repressor–DNA Loops Revealed by Single-Molecule Experiments

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At many promoters, transcription is regulated by simultaneous binding of a protein to multiple sites on DNA, but the structures and dynamics of such transcription factor-mediated DNA loops are poorly understood. We directly examined in vitro loop formation mediated by E. coli lactose repressor using single-molecule structural and kinetics methods. Small (150 bp) loops form quickly and stably, even with out-of-phase operator spacings. Unexpectedly, repeated spontaneous transitions between two distinct loop structures were observed in individual protein–DNA complexes. The results imply a dynamic equilibrium between a novel loop structure with the repressor in its crystallographic "V" conformation and a second structure with a more extended linear repressor conformation that substantially lessens the DNA bending strain. The ability to switch between different loop structures may help to explain how robust transcription regulation is maintained even though the mechanical work required to form a loop may change substantially with metabolic conditions.