Z-DNA-forming TG repeats are dynamic mechanical switches sensitive to tension and torsion.

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Although Z-DNA, the left-handed DNA, is an unstable state in comparison with B-DNA, Z-DNA exists stably under certain conditions such as high salt concentrations or negative supercoiling. In biological systems, potential Z-DNA-forming sequences are located near the promoter region of many genes and are thought to play a role in transcription initiation. Recently we studied the B-Z transition in a short d(GC/GC)n repeats in the presence of controlled tension and superhelicity via a hybrid technique of single-molecule FRET and magnetic tweezers[1]. In fact, another Z-DNA-forming sequence, d(CA/TG)n, is more frequently and widely found in eukaryotic genome and believed to have more important biological functions although the B-Z transition in that sequence is much less studied.

Here, we examined the B-Z transition of the TG repeat sequence using the hybrid method from the mechanistic viewpoints. We found that negative supercoiling is more effective in inducing the Z-conformation than high salt concentrations. Even at room temperature, the sequence undergoes dynamic inter-conversion between the two states permitting direct determination of kinetic constants and implying smaller energy barrier between the states. Compared to the GC repeat, TG repeats required more torsional energy to trigger the transition and the repeat length dependence of the critical superhelicity provides quantitative information about the transition. In summary, this study provides the biophysical details of the transition and also demonstrates that physical factors such as tension and torsion play critical roles in biological phenomena