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Dynamic investigation of DNA bending and wrapping by type II topoisomerases QING SHAO, LAURA FINZI, Physics Department, Emory University, DAVID DUNLAP, Cell Biology Department, Emory University — Type II topoisomerases catalyze DNA decatenation and unwinding which is crucial for cell division, and therefore type II topoisomerases are some of the main targets of anti-cancer drugs. A recent crystal structure shows that, during the catalytic cycle, a yeast type II topoimerase can bend a 10 base pair DNA segment by up to 150 degrees. Bacterial gyrase, another type II topoisomerase, can wrap DNA into a tight 180 degree turn. Bending a stiff polymer like DNA requires considerable energy and could represent the rate limiting step in the catalytic (topological) cycle. Using modified deoxyribonucleotides in PCR reactions, stiffer DNA fragments have been produced and used as substrates for topoisomerase II-mediated relaxation of plectonemes introduced in single molecules using magnetic tweezers. The wrapping ability of gyrase decreases for diamino-purine-substituted DNA in which every base pair has three hydrogen-bonds. The overall rate of relaxation of plectonemes by recombinant human topoisomerase II alpha also decreases. These results reveal the dynamic properties of DNA bending and wrapping by type II topisomerases and suggest that A:T base pair melting is a rate determining step for bending and wrapping.

Qing Shao
Physics Department, Emory University

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