1139-92-543 **Jonathan M. Fogg**, Houston, TX 77030, **Qian Wang**, Galveston, TX, **Rossitza N. Irobalieva**, Houston, TX 77030, **Muyuan Chen**, Houston, TX 77030, **Steven J. Ludtke**, Houston, TX 77030, and **Sarah A. Harris** and **Wah Chiu**, Houston, TX 77030, and **B. Montgomery Pettitt** and **E. Lynn Zechiedrich*** (elz@bcm.edu), One Baylor Plaza, Mail-Stop: BCM-280, Baylor College of Medicine, Houston, TX 77030. *Beyond the static DNA models of Watson and Crick.*

Despite its importance, much about supercoiled DNA (positively supercoiled DNA, in particular) remains unknown. We utilized electron cryo-tomography to investigate the 3D structures of individual 336 bp (32 exact turns of the helix) DNA minicircles with defined supercoiling. Minicircles in each supercoiling state adopt a unique and wide distribution of 3D conformations (Irobalieva 2015 Nat Comm 6, 8440). Increased mono- or divalent cations increased minicircle compaction, and thus mobility, of (-) supercoiled minicircles but had no effect on (+) supercoiled topoisomers. Assays revealed increased exposed DNA bases with increased (-) supercoiling. Our data support the "cooperative kinking model" of Lionberger 2011 Nuc Acids Res 39, 9820), in which an apical bend on one side of the supercoiled minicircle renders a site 180 degrees away susceptible to nuclease. Modeling these bending sites, we simulated minicircles with new supercoiling-dependent shapes (Wang 2017 Nuc Acids Res 45, 7633). Beyond a sharp supercoiling threshold, we detected exposed bases in (+) supercoiled DNA. These experiments reveal unexpected and dynamic supercoiling-dependent structural alterations in DNA and represent a step toward creating designer gene therapy vectors for use in treating human diseases. (Received February 19, 2018)