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Micromechanical study of mitotic chromosome structure[1]

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Our group has developed micromanipulation techniques for study of the highly compacted mitotic form of chromosome found in eukaryote cells during cell division. Each metaphase chromosome contains two duplicate centimeter-long DNA molecules, folded up by proteins into cylindrical structures several microns in length. Native chromosomes display linear and reversible stretching behavior over a wide range of extensions (up to 5x native length for amphibian chromosomes), described by a Young modulus of about 300 Pa. Studies using DNA-cutting and protein-cutting enzymes have revealed that metaphase chromosomes behave as a network of chromatin fibers held together by protein-based isolated crosslinks. Our results are not consistent with the more classical model of loops of chromatin attached to a protein-based structural organizer or "scaffold". In short, our experiments indicate that metaphase chromosomes can be considered to be "gels" of chromatin; the stretching modulus of a whole chromosome is consistent with stretching of the chromatin fibers contained within it. Experiments using topoisomerases suggest that topological constraints may play an appreciable role in confining chromatin in the metaphase chromosome. Finally, recent experiments on human chromosomes will be reviewed, including results of experiments where chromosome-folding proteins are specifically depleted using siRNA methods.

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