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A quantitative model of nucleosome dynamics ROBERT FORTIES, JUSTIN NORTH, SARAH JAVAID, OMAR TABBAA, RICHARD FISHEL, MICHAEL POIRIER, RALF BUNDSCHUH, The Ohio State University — The expression, replication and repair of eukaryotic genomes require the fundamental organizing unit of chromatin, the nucleosome, to be unwrapped and/or disassembled. We have developed a quantitative model of nucleosome dynamics which provides a fundamental understanding of these DNA processes. We calibrated this model using results from high precision single molecule nucleosome unzipping experiments, and then tested its predictions for experiments in which nucleosomes are disassembled by the DNA mismatch recognition complex hMSH2-hMSH6. We found that this calibrated model quantitatively describes hMSH2-hMSH6 induced disassembly rates of nucleosomes with two separate DNA sequences and four distinct histone modification states. In addition, this model provides mechanistic insight into nucleosome disassembly by hMSH2-hMSH6 and the influence of histone modifications on this disassembly reaction. This model's precise agreement with current experiments suggests that it can be applied more generally to provide important mechanistic understanding of the numerous nucleosome alterations that occur during DNA processing.

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