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Entropy in DNA Double-Strand Break, Detection and Signaling YANG ZHANG, CHRISTINA SCHINDLER, DIETER HEERMANN, Heidelberg University, Institute for Theoretical Physics, Heidelberg, Germany — In biology, the term entropy is often understood as a measure of disorder - a restrictive interpretation that can even be misleading. Recently it has become clearer and clearer that entropy, contrary to conventional wisdom, can help to order and guide biological processes in living cells. DNA double-strand breaks (DSBs) are among the most dangerous lesions and efficient damage detection and repair is essential for organism viability. However, what remains unknown is the precise mechanism of targeting the site of damage within billions of intact nucleotides and a crowded nuclear environment, a process which is often referred to as recruitment or signaling. Here we show that the change in entropy associated with inflicting a DSB facilitates the recruitment of damage sensor proteins. By means of computational modeling we found that higher mobility and local chromatin structure accelerate protein association at DSB ends. We compared the effect of different chromatin architectures on protein dynamics and concentrations in the vicinity of DSBs, and related these results to experiments on repair in heterochromatin. Our results demonstrate how entropy contributes to a more efficient damage detection. We identify entropy as the physical basis for DNA double-strand break signaling.

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