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Action at a Distance in the Cell's Nucleus[1]

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Various functions performed by chromosomes involve long-range communication between DNA sequences that are tens of thousands of bases apart along the genome, and microns apart in the nucleus. In this talk I will discuss experiments and theory relating to two distinct modes of long-range communication in the nucleus, chromosome looping and protein hopping along the chromosome, both in the context of DNA-break repair in yeast. Yeast is an excellent model system for studies that link chromosome conformations to their function as there is ample experimental evidence that yeast chromosome conformations are well described by a simple, random-walk polymer model. Using a combination of polymer physics theory and experiments on yeast cells, I will demonstrate that loss of polymer entropy due to chromosome looping is the driving force for homology search during repair of broken DNA by homologous recombination. I will also discuss the spread of histone modifications along the chromosome and away from the DNA break point in the context of simple physics models based on chromosome looping and kinase hopping, and show how combining physics theory and cell-biology experiment can be used to dissect the molecular mechanism of the spreading process. These examples demonstrate how combined theoretical and experimental studies can reveal physical principles of long-range communication in the nucleus, which play important roles in regulation of gene expression, DNA recombination, and chromatin modification.

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