Action at a Distance in the Yeast Nucleus

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Various functions performed by chromosomes, such as transcription regulation and DNA recombination involve long-range communication between DNA sequences that are hundreds of thousands of bases apart along the chromatin, and microns apart in the nucleus. I will discuss two modes of long-range communication in the nucleus, chromosome looping, which brings distant DNA sequences in close spatial proximity, and protein-sliding between distant sequences along the chromosome, both in the context of DNA-break repair in yeast.

Yeast is an excellent model system for studies that link chromosome shape to its function as there is ample experimental evidence that yeast chromosome conformations are described by a simple polymer model. Using a combination of polymer theory and cell experiments, I will show that loss of polymer entropy due to chromosome looping serves as the driving force for homology search during repair of broken DNA. I will also discuss the spread of histone modifications away from the DNA break point in the context of simple physics models based on chromosome looping and protein sliding, and show how combining physics theory and cell-biology experiment can be used to dissect the molecular mechanism of the spreading process. The key goal is to show how combined theoretical and experimental studies reveal physical principles of long-range communication in the nucleus.