Rabl Organization of Chromosomes in the Yeast Nucleus

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The spatial organization of genomes plays an important role in cell biology as it influences chromosome functions such as recombination and repair of broken DNA. The Rabl model proposed in the late 1800's describes the organization of budding yeast chromosomes during interphase, with the centromeres tethered at the spindle pole body (SPB) and the telomeres tethered to the nuclear periphery. Here we address the question, to what extent does the Rabl organization of chromosomes whose conformations are described by a simple polymer model, quantitatively account for the positioning of genetic loci within the interphase nucleus? To investigate this question we performed a combined experimental and theoretical study of the organization of yeast chromosome III. By imaging two fluorescent markers, one at the SPB and the other proximal to the HML locus that is involved in DNA recombination during mating type switching, we measured the distribution of distances. In addition to wild type cells, yku70Δ and esc1Δ mutants with disrupted telomere tethering and mutants that have a proximal HML marker tethered to the nuclear periphery were also considered. We compared our experimental results with a random-walk polymer model that takes into account different tethering scenarios and confinement of chromosomes in the nucleus, and found that the model recapitulates the observed spatial organization of chromosome III in yeast in quantitative detail. The Rabl model makes specific predictions for chromosome organization in yeast, and suggests new experiments to test them.