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Title:	Spatially coordinated replication and minimization of expression noise constrain three-dimensional organization of yeast genome
Authors:	Singh, Arashdeep (/jspui/browse?type=author&value=Singh%2C+Arashdeep) Bagadia, Meenakshi (/jspui/browse?type=author&value=Bagadia%2C+Meenakshi) Sandhu, K.S. (/jspui/browse?type=author&value=Sandhu%2C+K.S.)
Keywords:	3D genome organization Long-range chromatin interactions Expression noise Evolutionary constraints
Issue Date:	2016
Publisher:	Oxford University Press
Citation:	DNA Research, 23(2), pp. 155-169
Abstract:	Despite recent advances, the underlying functional constraints that shape the three-dimensional organization of eukaryotic genome are not entirely clear. Through comprehensive multivariate analyses of genome-wide datasets, we show that cis and trans interactions in yeast genome have significantly distinct functional associations. In particular, (i) the trans interactions are constrained by coordinated replication and co-varying mutation rates of early replicating domains through interactions among early origins, while cis interactions are constrained by coordination of late replication through interactions among late origins; (ii) cis and trans interactions exhibit differential preference for nucleosome occupancy; (iii) cis interactions are also constrained by the essentiality and co-fitness of interacting genes. Essential gene clusters associate with high average interaction frequency, relatively short-range interactions of low variance, and exhibit less fluctuations in chromatin conformation, marking a physically restrained state of engaged loci that, we suggest, is important to mitigate the epigenetic errors by restricting the spatial mobility of loci. Indeed, the genes with lower expression noise associate with relatively short-range interactions of lower variance and exhibit relatively higher average interaction frequency, a property that is conserved across Escherichia coli, yeast, and mESCs. Altogether, our observations highlight the coordination of replication and the minimization of expression noise, not necessarily co-expression of genes, as potent evolutionary constraints shaping the spatial organization of yeast genome.
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