Computational analysis of homologous chromosome pairing in fission yeast

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1 Introduction

Homologous chromomes pairing is an important event during meiosis, which is followed by recombination and proper segregation. How the search for the partner chromosomes is attained has long been a crucial question in cell biology. During meiotic prophase, telomeres form a cluster beneath nuclear envelope with a polarized chromosome arrangement. The arrangement is highly conserved among eukaryotes, and often referred to as "bouquet" [1]. In addition, in fission yeast *Schizosaccharomyces pombe*, a telomere-led dynamic nuclear oscillation is observed [2]. Various mutant analyses demonstrated that inhibition of the bouquet or the nuclear movement shows marked reduction of recombination frequency. The results indicate that both the bouquet and the nuclear movement facilitate pairing, yet their direct contributions is not resolved. In this study, therefore, we examined the direct contributions and mechanisms of the bouquet and nuclear oscillation by making series of computer simulations.

2 Results

A chromosomes is modeled as a set of beads connected by springs (Fig. 1A). The model consists of a set of Langevin equations, each of which represents the dynamics of a bead on the chromosome. Each bead on the string corresponds to a pairing site on a chromosome in our model.

Based on the model, parameter values were initially estimated. The values related to the springs were estimated using image data in which chromosomes are visualized by histone-GFP. The values related to random motion were estimated using image data of thiabendazole-treated chromosomes in which *ade3*/*lys1* loci were stained. Other values were estimated from references.

In order to test the validity of the model, we simulated the pairing process. We measured the time until when all pairing sites on chromosomes undergo pairing, which we call "pairing time." As the results, the mean pairing time was 83 min, which was within the observed time of nuclear movement to continue *in vivo* (146 min).

To determine the roles of the bouquet and nuclear oscillation against pairing, we simulated the pairing process under three conditions (Fig. 2A–C): (i) with neither bouquet nor nuclear oscillation; (ii) with bouquet but no nuclear oscillation; and (iii) with both bouquet

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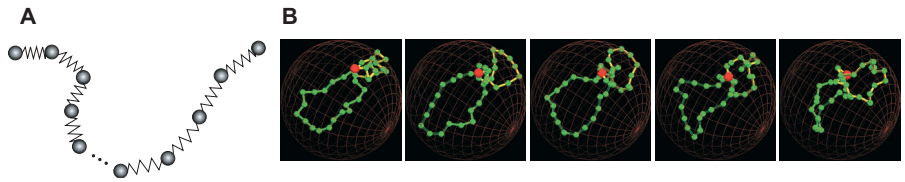

Figure 1: Chromosome model and simulations of pairing process. **A**. Schematic view of the chromosome model. **B**. Snapshots of simulations under condition of telomere clustering.

and nuclear oscillation. The time needed for all the pairing sites to attain pairing is defined as "the pairing time", and is used as a criterion to measure pairing performance. As expected, we found that the pairing time with condition (ii) was 77% shorter than that with condition (i), and the pairing time with (iii) was 94% shorter than that with condition (i) (Fig. 2D). Furthermore, the variation of the pairing time was reduced in both cases. These results indicate that the bouquet directly shortens the pairing time and also reduces its scatter, which is further augmented by nuclear oscillation.

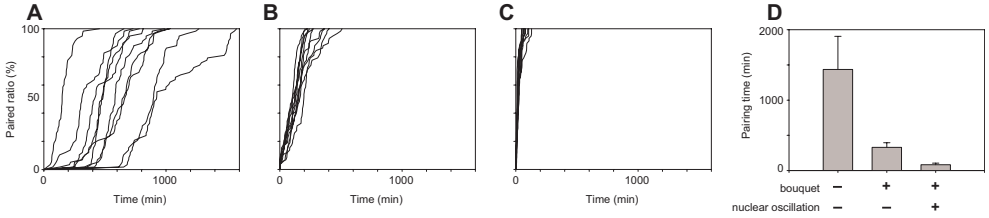

Figure 2: Simulated pairing time under various conditions. **A-C**. Ratio of paired sites as a function of time. The superimposed 10 tracks are illustrated under 3 conditions. **D**. Mean pairing time and its variance. The error bars represent standard deviations.

Further analyses suggest that the bouquet formation contributes to pairing by (a) spatially constraining the chromosomes in the proximity, and (b) disposing the chromosomes in a way that all pairing loci lie within closed-end regions. The nuclear oscillation contributes to pairing probably by aiding the spatial constraint of the chromosomes.

3 Concluding Remarks

In this study, we have examined direct roles and mechanisms of the bouquet and nuclear oscillation upon pairing by computer simulations. In conjunction with cytological and molecular biology approach, our approach will make a significant contribution to our understanding of chromosome dynamics.

References

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