

A Reaction-Diffusion Model for Genetic Interference

Youhei Fujitani¹

youhei@appi.keio.ac.jp

Shintaro Mori²

mori@jet.sci.kitasato-u.ac.jp

Ichizo Kobayashi³

ikobaya@ims.u-tokyo.ac.jp

¹ Department of Applied Physics and Physico-Informatics, Keio University,
3-14-1 Hiyoshi, Kouhoku-ku, Yokohama 223-8522, Japan

² Kitasato University, 1-15-1 Kitasato, Sagamihara 228-8555, Japan

³ Department of Molecular Biology, Institute of Medical Science, University of Tokyo,
4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan

Keywords: meiotic recombination, chiasma interference, diffusion-annihilation model

1 Introduction

As was found early in this century, chiasmata are not distributed randomly along a chromosome; occurrence of one chiasma apparently tends to suppress another in the neighborhood, which is called genetic interference, or more specifically chiasma interference [2]. Assuming no chromatid interference and no intersister chiasmata [3], we here propose a simple model with two fitting parameters; we show that numerically obtained correlation length between chiasmata remains consistent with experimental data *over a wide range of parameter values*.

2 Model

It was suggested recently that a premeiotic contact point between a pair of homologous regions primes homologous recombination in meiosis [1]. This contact point, probably accompanied with subcellular machinery, is thought to be unstable and to induce a second contact point at a nearby homologous region. We simply assume that this contact point is a one-dimensional random-walker (an A -particle) along a pair of homologous chromosomes; a pair of homologous regions would form a lattice-site. A contact point would disappear by encounter with another contact points ($A + A \rightarrow \emptyset$), considering their instability and possible steric hindrance between involved machines. Once homologous recombination is initiated, the contact point would become more stable and immobile. Calling this immobile point a B -particle, we express this transition by $A \rightarrow B$. We simply assume that a B -particle is doomed to be a chiasma between one of four possible pairs of nonsister chromatids. An A -particle would also disappear by encounter with a stable B -particle, which is expressed by $A + B \rightarrow B$. We study numerically this one-dimensional reaction-diffusion model, imposing the periodic boundary condition and assuming that A -particles are initially distributed at random.

Our model has two parameters α and h ; the former denotes the initial average number of A -particles per lattice-site, and the latter denotes a transition-rate of $A \rightarrow B$. The final average number of B -particles at a site j , $\langle n_j^{(B)} \rangle$, does not depend on j because of homogeneity of the system. Similarly, the final correlation function of B -particles, $\langle n_j^{(B)} n_{j+l}^{(B)} \rangle$, depends not on the site j but on the interval (or the physical distance) l . A normalized correlation function:

$$S_l \equiv \langle n_j^{(B)} n_{j+l}^{(B)} \rangle / (\langle n_j^{(B)} \rangle)^2 \quad (1)$$

is referred to as coincidence and has been used as a measure of interference [3]. An interval along one chromatid is usually measured by the genetic distance, which is defined as the average number of

physical exchanges within the interval (see e.g. [3]). Assumption of no chromatid interference leads to a relationship between the physical distance, l , and the genetic distance, g_l :

$$g_l \equiv l \langle n_j^{(B)} \rangle / 2 . \quad (2)$$

3 Results

Studying our model numerically, we plot the values of S_l against the genetic distance g_l in Fig. 1 ($\alpha = 0.1$; $h = 0.001(\triangle), 0.01(*), 0.1(+)$). Results converge on a curve. From other results not shown here, we find that results converge on the limit curve as h decreases and as α increases. We plot

$$F_l \equiv -\ln(1 - S_l) \quad (3)$$

against g_l in Fig. 2. Using coincidence values on the limit curve as S_l -values, we obtain triangles in Fig. 2, which are approximately on a line. This means that the limit curve can be approximately expressed by $S_l = 1 - \exp[-g_l/\xi]$. Curve-fitting yields $\xi = (1.18 \pm 0.01) \times 10^{-1}$ (a solid line). Using the experimental data of coincidence, which come from Ref.[3]'s replot of Ref.[2]'s data, as S_l -values, we obtain symbols \times in Fig. 2. They are also approximately on a line when $g_l \gtrsim 0.15$. This means that the experimental data can be approximately expressed by $S_l = 1 - \exp[-(g_l - g^{(0)})/\xi]$ for $g_l \gtrsim 0.15$. Curve-fitting yields $\xi = (0.9 \pm 0.2) \times 10^{-1}$ and $g^{(0)} = (1.5 \pm 0.1) \times 10^{-1}$ (a dashed line). The ξ -value represents correlation length of chiasmata measured by the genetic distance; that of the limit curve and that of the experimental data agree well. We guess that the $g^{(0)}$ -value probably reflects a size of machinery involved with a contact point, that of a chisma, and details of interactions between a contact point and a chiasma, which are not considered in our simple model.

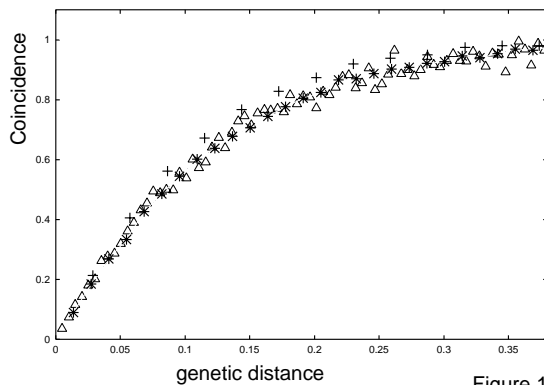


Figure 1

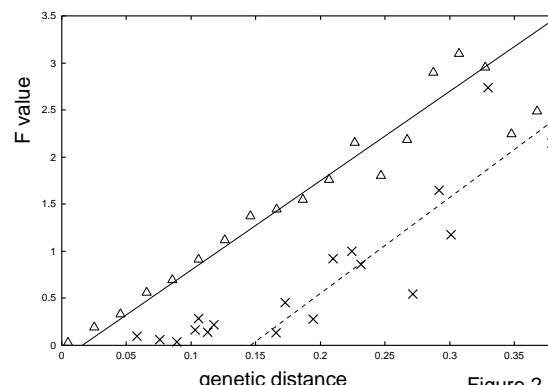


Figure 2

References

- [1] Kleckner, N., Interactions between and along chromosomes during meiosis, *The Harvey Lectures* 91, Wiley-Liss, 21–45, 1997.
- [2] Morgan, T. H., Bridges C. B., and Schultz, J., Constitution of the germinal material in relation to heredity, *Carnegie Instit. Washington* 34: 284–291, 1935.
- [3] McPeck, M.S. and Speed, T.P., Modeling interference in genetic recombination, *Genetics*, 139(2):1031–1044, 1995.