Fig. 10. Beam/film model and application to modeling of meiotic crossover/chiasma patterns.

Crack interaction model: Film on a substrate

Thin films bonded to thick substrates often support a tensile stress σ_0 acting parallel to the film (*A*; ref. 1). The stress can arise during deposition of the film, or it can occur after deposition, when temperature changes are imposed on the system due to thermal expansion differences between the materials comprising the film and the substrate. If the film is brittle, but well bonded, cracks penetrating to the substrate will propagate across the film in a direction perpendicular to the tensile stress. The cracks are nucleated at small stress-sensitive defects in the film that are inevitably present.

Locally, on either side of any crack, the stress in the film will be relieved (*B*). When subsequent cracks form, they are most likely to be nucleated outside the stress-relieved zones near existing cracks (*B*). With increasing overall stress (driven, for example, by further temperature change), this process leads to a crack pattern that is relatively uniformly spaced, even though the defects are distributed randomly in the film. The characteristic length quantity in the process is the distance ℓ over which stress relief occurs:

$$\ell = \sqrt{Et/k} \qquad [\mathbf{1}]$$

where E is the Young's modulus of the film, t is the film thickness, and k scales with the effective elastic shear stiffness of the substrate in units of stress/length.

The crack interaction is modeled as a one-dimensional problem with x as the distance along the film and $u(x)$ as the change resulting from the cracks of the displacement component tangent to the film/substrate interface. Well away from the ends of the film, which will also be modeled, the stress in the film in the absence of any cracks is uniform and denoted by σ_0, which can be regarded as the unrelieved reference stress. The equation governing the displacement change due to cracking is

$$\frac{d^2u}{dx^2} - \frac{1}{\ell^2}u = 0 \qquad \textbf{[2]}$$

resulting in a new stress distribution, $\sigma(x)$, given by

$$\sigma = \sigma_0 + E\frac{du}{dx} \qquad \textbf{[3]}$$

Suppose a crack forms at x_1 well away from any other cracks, and assume the ends of the film are at infinity. The stress in the film is reduced to zero at the crack. The solution to Eqs. **2** and **3** displays stress build-up to σ_0 away from the crack according to

$$\sigma = \sigma_0\left[1 - e^{-|x-x_1|/\ell}\right] \qquad \textbf{[4]}$$

If two cracks happen to form with communicating distance of one another, say at x_1 and x_2, then the solution is (with the ends still at infinity)

$$\begin{aligned} &\sigma = \sigma_0\left[1 - e^{(x-x_1)/\ell}\right] \quad x < x_1 \\ &\sigma = \sigma_0\left[1 - \frac{cosh\left[\left(x-(x_2+x_1)/2\right)/\ell\right]}{cosh\left[(x_2-x_1)/(2\ell)\right]}\right], \quad x_1 < x < x_2 \\ &\sigma = \sigma_0\left[1 - e^{-(x-x_2)/\ell}\right] \quad x > x_2 \end{aligned} \qquad \textbf{[5]}$$

where $cosh\,\xi = (e^{\xi} + e^{-\xi})/2$ is the hyperbolic cosine. This distribution is sketched in *B*, where it is seen that the maximum stress between the cracks occurs at their midpoint. If the crack spacing, $x_2 - x_1$, is large compared to ℓ, there will be a central region with the stress at σ_0. However, if the spacing is comparable to ℓ, crack interaction reduces the stress below σ_0 everywhere between the two cracks, as depicted.

Conditions at the ends of a finite-length film depend on details of the film/substrate geometry. A range of end conditions will be modeled lying between two limiting conditions: stress-free and clamped (*C*). If the film ends abruptly on the substrate, the stress at that end will be zero. In this case, the end has the same effect as a preexisting crack at that location. At the other extreme, a film can be wrapped around the corner of a substrate at its end such that it can support stress there. Generally, there will be some relaxation at such an end configuration, but a useful model is to make the limiting assumption that the end is clamped with $u = 0$. With the left end of the film at $x = 0$ and the right end at $x = L$, the end conditions imposed on Eqs. **2** and **3** are

$$(1-\lambda_L)u - \lambda_L\left(\frac{du}{dx} + \frac{\sigma_0}{E}\right) = 0 \quad at \;\; x = 0$$
$$(1-\lambda_R)u + \lambda_R\left(\frac{du}{dx} + \frac{\sigma_0}{E}\right) = 0 \quad at \;\; x = L \qquad [\mathbf{6}]$$

where $\lambda = 0$ corresponds to completely clamped and $\lambda = 1$ to stress-free, with $0 < \lambda < 1$ corresponding to intermediate conditions. A film with a stress-free end will have an end zone of reduced stress, as if a preexisting crack had been introduced there. The stress distribution near a clamped end has the uniform reference value σ_0 prior to any crack formation. A representative stress distribution is sketched in *B* for a film with a stress-free left end, a clamped right end, and cracks at $x_1, x_2, x_3, \ldots.$.

The crack interaction model is completed with the specification of an initial defect population and a criterion for a defect to become critical, thereby nucleating a crack. For a film of length L, let N be the number of defects and let the locations of these defects be $x_i^d, i = 1, N$. For a chosen value of N, the defects locations may either be randomly or evenly distributed over $[0, L]$. Let σ_i^d be the local stress needed to nucleate a crack at the ith defect. That is, assume a crack forms at the ith defect when the local stress there attains the critical condition: $\sigma(x_i^d) = \sigma_i^d$. In the model, it is assumed that this stress is inversely proportional to the square root of the amplitude of the *i*th defect. Specifically, the critical stresses of the defects are generated by

$$\sigma_i^d = \sigma_{crit} / \sqrt{a_i^d}\,, \quad i = 1, N \qquad [\mathbf{7}]$$

where the defect amplitude, a_i^d, is modeled as a uniform random variable on [0,1]. Thus, the critical stress quantity, σ_{crit}, represents the lowest value of stress at which a crack can form (at an defect with amplitude unity) and thereby sets the scale of the sequential cracking process.

A numerical simulation for a specific set of end conditions and a given realization of the defect population, $(x_i^d, \sigma_i^d)\ \ i = 1, N$, proceeds as follows. At the start, the film is crack-free. The initial stress distribution is determined from Eqs. **2** and **3** in terms of reference stress, σ_0, which is increased monotonically from zero. If the film is clamped at both ends, $\sigma(x) = \sigma_0$. If the conditions are relaxed from the clamped condition at one or more of the ends, the initial distribution will reflect the stress reduction near the ends. As σ_0 is increased, the defect at which the cracking condition is first attained will become critical nucleating a crack at that location. The stress redistribution is then resolved from Eqs. **2**, **3**, and **6**, accounting for the presence of the first crack; σ_0 is increased again until the second crack becomes critical. The procedure repeats with a new crack added in each step. A new solution for $\sigma(x)$ is generated after each new crack is formed, accounting for all the cracks at each stage. The procedure continues until σ_0 reaches a prescribed limit, $(\sigma_0)_{max}$.

Simulations are repeated many times (10,000 runs for the results reported in the paper), with new sets of defect locations and defect amplitudes generated in each simulation. For the purpose of statistical analysis, the beam is divided into M equally spaced intervals. The number of cracks lying within each interval is tallied, and the coefficients of coincidence are computed for the full set of simulations. The calculations are performed by scaling the distance along the film and the locations of the defects by L, such that the film length is unity The stress relief length ℓ is also scaled by L (i.e., ℓ is replaced by ℓ / L). All the stress quantities are normalized by σ_{crit}, and, in particular, σ_0 is replaced by σ_0 / σ_{crit}. The results presented in the paper used these normalizations.

Using the beam/film system to model experimentally observed crossover/chiasma distributions

Note: Relevant computer program and detailed description of its use are available from the Kleckner laboratory.

Applications of beam/film model

Parameter values. To predict the number and distribution of cracks (crossovers/chiasmata), values were assigned for the following parameters (above):

N = total number of flaws (equivalent to total number of meiotic recombination initiations/double-strand breaks)

σ_{max} = maximal stress level reached

l = distance over which stress relief is effective

λ = end conditions: each end of the beam may either be fully clamped ($\lambda = 0$); completely unclamped (stress-free) ($\lambda = 1$); or partially clamped ($0 > \lambda > 1$.

Illustration of basic effects. The following behaviors are of special relevance to pattern formation along a chromosome, e.g., crossovers/chiasmata. The basic effect is that, as the stress level rises, one flaw goes critical and becomes a crack, resulting in a surrounding zone of stress relief in the immediate vicinity, which in turn inhibits formation of cracks nearby. As a result, ensuing cracks occur at more distant positions and, overall, in the regions between previously formed cracks. These effects are further modulated by "end effects" (clamping).

1. At fixed values of other parameters, the number of cracks (crossovers/chiasmata) increases with increasing stress level (σ_{max}) (*D*).

2. For a particular maximal stress level, the final total number of cracks varies inversely with the distance over which stress relief redistributes (l): the longer the distance over which stress relief operates, the fewer the number of cracks (*E*).

3. If the stress level is high enough, every beam will acquire at least one crack. Because resulting stress relief reduces the possibility of further cracks, it is possible to ensure that each beam acquires at least one crack, whereas the average number of cracks per beam is quite low. This is illustrated for suitable parameter values in *F*: the fraction of beams having 0 cracks (i.e., the fraction having one or more) falls rapidly to 0 at relatively low stress levels, ≈1.1 (*Left*), at which point no beam has more than one or two cracks (*Right*). In the extreme case that the stress relief distance is close to the total length of the beam (and assuming a sufficient level of stress), every beam will acquire exactly one and only one crack (*E*). This situation mimics cases in which a meiotic chromosome always acquires one and only one bivalent.

4. Occurrence of a crack at one position "interferes" with occurrence of cracks at nearby positions, with a tendency for even spacing. These effects are seen in appropriate plots (see text; Fig 1 *C* and *D*; Fig. 10 *B* and *G*). Additionally, the extent of interference can be modulated by the level of stress: as the stress level increases, interference remains present but is exerted over shorter and shorter distances, as cracks are "forced" to occur in regions of lower remaining stress (*G*).

5. To the extent that a particular end of a beam is "unclamped," it is as if there is a preexisting crack at that end (*C*). As a result, there will be a differential deficit of cracks near the end. Oppositely, if an end is fully clamped, stress relief will emanate across that end only from one direction (the internal part of the beam) rather than from both directions, as for internal portions of the beam. As a result, there will tend to be an excess of near-terminal cracks.

Matching experimentally observed crossover/chiasma numbers and distributions

Chorthippus L3 bivalent. Given the relatively large genome size of this organism, predictions were explored using relatively high values of *N*, ≈15 times the number of chiasmata; this value is intermediate between that of mammals (≈10) and higher plants (≈30), which have somewhat smaller and somewhat larger genome sizes, respectively. Predicted chiasma numbers and distributions were obtained within the three-dimensional space defined by $10 < N < 20$; $0.1 < l < 1$; and $1 < \sigma_{max} < 10$. Both ends were considered fully clamped ($\lambda = 0$). For the simulation shown in Fig. 1 *C* and *D*, $N = 14$, $l = 0.2$, and $\sigma_{max} = 1.6$.

Drosophila X chromosome. Experimental observations suggest that each *Drosophila* X chromosome acquires an average of ≈7 initiations (2); thus, *N* was set at 7. Predicted crack (crossover) numbers and distributions were then determined for all reasonable values of σ_{max} (0.1-3) and l (0.1-1). Both ends were considered clamped for the simulation shown. For the simulation shown in Fig. 1 *C* and *D*, $N = 7$, $l = 0.4$ and $\sigma_{max} = 2.86$.

The distribution of crossovers along the *Drosophila* X chromosome is asymmetric, with a deficit at the "centromeric" end (2). This effect could be modeled by reducing the clamping specifically at this end. In fact, the X chromosome is "acrocentric," meaning that the centromere is at one end, rather than in the middle, as is more typically seen. Further, during meiosis in this organism, the centromeric end is located in the middle of the nucleus, whereas the other end is attached to the inner surface of the nuclear envelope, thus providing a potential physical basis for "unclamping" and "clamping," respectively.

Mathematical analyses of crossover distributions along the *Drosophila* X chromosome also suggest that adjacent crossovers are separated by an essentially fixed number of initial interactions that are matured in another way (to "noncrossovers") (2). This in turn has been interpreted to mean that the interference process "counts" recombinational interactions (2). This interpretation can be restated in another way, as a suggestion that recombinational interactions are the metric of interference. The beam/film model described above could be modified to incorporate a role for recombinational interactions by assuming that flaws have a tendency to stretch prior to cracking. In this situation, each recombinational interaction would represent a local "sink" for absorption of stress relief. In any given case, then, the distance of stress redistribution would reflect the combined effects of uniform absorption of stress relief along the length of the beam and differential absorption of stress relief at each encountered flaw. Correspondingly, stress relief would return to its resting level "discontinuously," with a discrete jump at the position of each encountered flaw, rather than smoothly as in *B*. For chromosomes, this would imply contributions both from overall physical distance (e.g., along the chromosome axes) and from encountered local recombination ensembles. Relative contributions of the two features might vary from one region of a chromosome to another and/or from one organism to another.

Interestingly, also, in mathematical modeling of crossover distributions, it was assumed that "counting" began at the centromere end (2). This is equivalent to assuming the presence of a preexisting crossover at that end and thus is equivalent to having that end "unclamped," which is the predicted situation (above).

1. Xia, Z. C. & Hutchinson, J. W. (2000) *J. Mech. Phys. Solids* **48,** 1107-1131.

2. Lande, R. & Stahl, F. (1993) *Cold Spring Harbor Symp. Quant. Biol.* **58**, 543-552.