

Coarsening Model of Chromosomal Crossover Placement

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Chromosomal crossovers play a crucial role in meiotic cell division, as they ensure proper chromosome segregation and increase genetic variability. Experiments have consistently revealed two key observations across species: (i) the number of crossovers per chromosome is typically small, but at least one, and (ii) crossovers on the same chromosome are subject to interference, i.e., they are more separated than expected by chance. These observations can be explained by a recently proposed coarsening model, where the dynamics of droplets associated with chromosomes designate crossovers. We here introduce an extended coarsening model, which includes material exchanges between droplets, the synaptonemal complex, and the nucleoplasm. Using a comprehensive analysis, including scaling laws for the crossover count, allows us to analyze data across species. Moreover, our model provides a coherent explanation of experimental data across mutants, including the wild type and *zyp1* mutant of *Arabidopsis thaliana*. Consequently, the extended coarsening model provides a solid framework for investigating the underlying mechanisms of crossover placement.

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I. INTRODUCTION

Chromosomal crossovers (COs) are crucial for successful meiosis and thus sexual reproduction. COs promote reciprocal genetic exchange, increasing genetic variability, and they create a physical connection between homologous chromosomes ensuring correct segregation [1–7]. The latter aspect is established by *CO assurance*, which describes the observation that essentially all chromosomes contain at least one CO [8–12]. However, the number of COs rarely exceeds a few per chromosome [13–15], and their placement is subject to *CO interference*, implying COs on the same chromosome are more separated than expected by chance [10–12,16–19].

CO formation is an evolutionarily conserved process: During prophase I of meiosis I, compacted homologous chromosomes pair up and are connected along their axes by the synaptonemal complex (SC) [20–23], which is highly ordered but permits lateral diffusion [24,25], akin to a liquid crystal [25]. Class I COs, which are subject to CO interference, form from precursors known as recombination nodules (RNs) that associate with the SC [1,20,22] via the ZMM pathway [6,12,26], whereas less prevalent class II COs result from a different pathway and appear to be noninterfering [6,11,12]. In early pachytene, many RNs form, typically around DNA double-strand breaks (DSBs), but the RN count decreases over

time [1], so that eventually only a few late RNs remain, which typically lead to COs [10,20,21,27–30]. Despite significant progress in the past decades, the mechanisms designating which RNs become COs remains highly debated [4–7,10–12]. In particular, there is no comprehensive model that explains CO placement across species and mutants.

Models of CO placement can be broadly classified as mechanical models and diffusion-based models: In mechanical models, such as the beam-film model [30,31], COs are designated by physical constraints on chromosomes. In contrast, diffusion-based models use the localization of signaling molecules to promote COs [10,32,33]. In particular, the recently proposed coarsening model [34–36] can explain key features of class I CO placement in wild-type *Arabidopsis thaliana* [12,34,35] and *Caenorhabditis elegans* [36]. The model describes RNs as droplets that exchange material by diffusion along the SC, so droplets compete for material. Although different proteins are involved (particularly HEI10 in plants [35,37] and ZHP-3/4 in *C. elegans* [33]), it is suggested that coarsening provides a general mechanism for CO interference that is conserved across species [12].

The simplest version of the coarsening model treats pairs of homologous chromosomes separately, although material exchange via the nucleoplasm generally couples the dynamics. Such material exchange is particularly relevant in mutants lacking SCs, like the *zyp1* mutant of *A. thaliana*, which still exhibit COs but lack interference [23,34,38,39]. To address exchange via nucleoplasm, Fozard *et al.* [39] proposed coarsening models for the wild type and the *zyp1* mutant, which are consistent with experimental data on CO counts, CO positioning, and CO interference. However, they only allowed for exchange between droplets and nucleoplasm, while a possible exchange between SC and nucleoplasm is also likely and would affect CO placement. Moreover, Fozard *et al.* [39] assumed smaller exchange rates between droplets and

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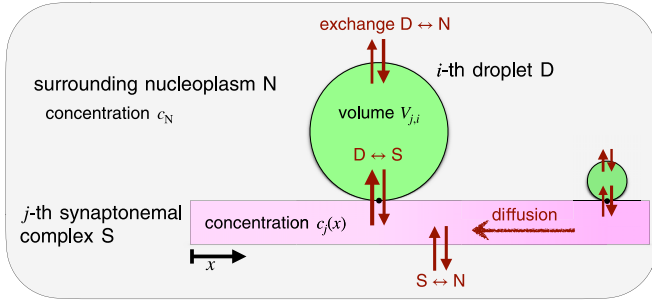


FIG. 1. Schematic of the extended coarsening model of CO placement showing CO precursor droplets (green) associated with a synaptonemal complex (SC, pink) embedded in nucleoplasm. All compartments exchange material (red arrows) and the key droplet component diffuses along the SC. The system is characterized by the average concentration $c_N(t)$ in nucleoplasm, the concentrations $c_j(x, t)$ along the SCs, and droplet volumes $V_{j,i}(t)$.

nucleoplasm in the wild-type model than in the model of the *zyp1* mutant. Consequently, a comprehensive, quantitative coarsening model that explains data across sexes, mutants, and species is still lacking.

We here present a thermodynamically consistent version of the coarsening model that includes nucleoplasmic exchange and coherently explains experimental data across mutants. We use *A. thaliana* as an example to develop the model, but generalize results to other species later. In particular, we discuss CO assurance and CO interference quantitatively and we derive asymptotic scaling relations for CO counts, which allow us to constrain model parameters and investigate data across species. We also study details of CO placement, like CO homeostasis (wherein the changing number of DSBs hardly affects the CO count [1,4,13,40]) and heterochiasmy in the wild type (male and female exhibit different CO counts [12,34,39]). The extended coarsening model thus enables a quantitative analysis of CO placement, and the role of nucleoplasmic exchange, across species and mutants.

II. COARSENING MODEL OF CROSSOVER PLACEMENT

A. Thermodynamically consistent coarsening model including nucleoplasm

We aim to derive a minimal model of the placement of class I COs, which form from recombination nodules (RNs) enriched in HEI10 in *A. thaliana*. Motivated by the observation that HEI10 can phase separate *in vitro* [41], we describe RNs as droplets that grow and compete for material. For simplicity, we assume that all RNs existing after a fixed time T_{final} become COs, so we are essentially asking which droplets survive. To do this, we model the coupled systems of nucleoplasm (N), synaptonemal complex (S) linking homologous chromosomes, and droplets (D) (Fig. 1). We consider a nucleoplasm with constant volume V_N , and assume that diffusive transport of HEI10 in the nucleoplasm is fast compared to diffusion along the SC. Consequently, we assume that spatial variations of the HEI10 concentration are negligible in the nucleoplasm, and we characterize it by an average concentration $c_N(t)$. The N_S SCs in the nucleoplasm have physical lengths L_j for $j = 1, \dots, N_S$, and a constant effective cross

section a^2 , which defines our fundamental length scale a . We parametrize the HEI10 concentration along the j th SC by $c_j(x, t)$, where $x \in [0, L_j]$ parametrizes the corresponding arclength. The j th SC possesses N_j HEI10 droplets, placed along the arc at positions $x_{j,i}$ for $i = 1, \dots, N_j$. For simplicity, we assume constant HEI10 concentration c_D in droplets, so they are fully described by their volume $V_{j,i}$. The system's state is thus characterized by the nuclear concentration $c_N(t)$, the concentrations $c_j(x, t)$ on the SCs, and the droplet volumes $V_{j,i}(t)$.

We next derive a simple dynamical description based on the idea that the system relaxes toward equilibrium. Even though active processes, like post-translational modifications, might play a role in reality [42,43], we find that they are not necessary to explain the data. Instead, such active processes might be used to initiate the process, control its termination, or modify passive parameters, like affinities. The advantage of using a passive description is that it prohibits spurious circular fluxes between nucleoplasm, SCs, and droplets, which could lead to many unwanted effects, including suppression of coarsening and size control [44–48]. To avoid such fluxes, we need to ensure that our model is thermodynamically consistent.

To derive a thermodynamically consistent coarsening model, we base our description on the chemical potentials of HEI10, $\mu_\alpha = k_B T \ln(\gamma_\alpha c_\alpha / c_D)$, in the three compartments $\alpha = N, S, D$, where $k_B T$ is the energy scale, we use c_D as a reference concentration, and γ_α are activity coefficients accounting for interactions. For simplicity, we describe HEI10 as an ideal solution in the nucleoplasm and SC, implying that both activity coefficients are constant. In contrast, we assume that larger droplets have a higher affinity for HEI10 to ensure that they grow at the expense of smaller droplets, which we capture by a phenomenological expression of γ_D . Taken together,

$$\gamma_N = 1, \quad (1a)$$

$$\gamma_S = \exp(-\omega_S / k_B T), \quad (1b)$$

$$\gamma_D(V_{j,i}) = \gamma_0 \left(\frac{V_{j,i}}{a^3} \right)^{-\nu}, \quad (1c)$$

where we choose the nucleoplasm as reference, ω_S accounts for the affinity of HEI10 molecules toward the SC, and γ_0 is related to the affinity of HEI10 to a droplet of reference volume a^3 . The size dependence of the HEI10 affinity toward droplets is captured by the exponent $\nu > 0$. The particular choice $\nu = \frac{1}{3}$ corresponds to typical surface tension effects [45,49], which will allow us to compare our results to the classical coarsening process of Ostwald ripening [50]. The affinities given by Eqs. (1) govern the long-term behavior of the system when it tends toward thermodynamic equilibrium. At that point, all chemical potentials are balanced, implying

$$c_N^* = \gamma_S c_j^* = \gamma_0 c_D \left(\frac{V_{j,i}^*}{a^3} \right)^{-\nu}. \quad (2)$$

In particular, the form of Eq. (1c) implies that at most a single droplet will remain in the system after a very long time, but to understand droplet placement at finite times, we need to study the dynamics.

The dynamics of the system comprise diffusion of HEI10 along the SC and its exchange between all compartments (Fig. 1). While we assume simple diffusion, describing the exchange dynamics requires more care to ensure thermodynamic consistency to avoid spurious circular fluxes between the compartments. In particular, the forward flux $S^{\alpha \rightarrow \beta}$ and the backward flux $S^{\beta \rightarrow \alpha}$ between compartments $\alpha, \beta = N, S, D$ need to satisfy the local detail balance condition [49,51]

$$\frac{S^{\alpha \rightarrow \beta}}{S^{\beta \rightarrow \alpha}} = \exp\left(\frac{\mu_\alpha - \mu_\beta}{k_B T}\right). \quad (3)$$

This general condition constrains the ratio of the fluxes in the two directions. However, to obtain an expression for the net flux, $S^{\alpha\beta} = S^{\beta \rightarrow \alpha} - S^{\alpha \rightarrow \beta}$, from β to α , we require a detailed kinetic model. For simplicity, we use a model inspired by transition-state theory [52–54] with a fast-decaying transition state and constant energy barrier [45,47,55–57], resulting in

$$S^{\alpha\beta} = \tilde{\Lambda}_{\alpha\beta} \left[\exp\left(\frac{\mu_\beta}{k_B T}\right) - \exp\left(\frac{\mu_\alpha}{k_B T}\right) \right], \quad (4)$$

where the square bracket ensures that Eq. (3) is obeyed, whereas $\tilde{\Lambda}_{\alpha\beta}$ sets the overall kinetic rate of the particular exchange. Using Eqs. (1), the exchange between nucleoplasm and SC then reads

$$s_j^{\text{SN}} = \frac{\Lambda_{\text{SN}}}{a^3} [c_N - \gamma_S c_j(x)], \quad (5a)$$

where $\Lambda_{\text{SN}} = \tilde{\Lambda}_{\text{SN}} a^3$ denotes the kinetic rate. In contrast, the exchange between droplets and the surroundings generally depends on droplet volume $V_{j,i}$, e.g., because the exchange is limited by diffusion, by conversion at their interface [58–60], or by other kinetic processes. We capture such size dependence by generic power laws, implying

$$S_{j,i}^{\text{DS}} = \Lambda_{\text{DS}} \left(\frac{V_{j,i}}{a^3}\right)^{\nu_S} \left[\gamma_S c_j - \gamma_D c_D \left(\frac{V_{j,i}}{a^3}\right)^{-\nu_D} \right], \quad (5b)$$

$$S_{j,i}^{\text{DN}} = \Lambda_{\text{DN}} \left(\frac{V_{j,i}}{a^3}\right)^{\nu_N} \left[c_N - \gamma_D c_D \left(\frac{V_{j,i}}{a^3}\right)^{-\nu_D} \right], \quad (5c)$$

where $\Lambda_{\text{D}\beta}$ are base kinetic rates, whereas $0 \leq \nu_\beta \leq 1$ denotes size sensitivities, for $\beta = S, N$. Particular cases include size-independent exchange ($\nu_\beta = 0$), diffusion-limited exchange ($\nu_\beta = \frac{1}{3}$ [58,61]), conversion-limited exchange ($\nu_\beta = \frac{2}{3}$ [58–60]), and volume-limited exchange ($\nu_\beta = 1$). Taken together, the dynamics are described by

$$c_D \frac{dV_{j,i}}{dt} = S_{j,i}^{\text{DS}} + S_{j,i}^{\text{DN}}, \quad (6a)$$

$$\frac{\partial c_j}{\partial t} = D \partial_x^2 c_j + s_j^{\text{SN}} - \frac{1}{a^2} \sum_{i=1}^{N_j} S_{j,i}^{\text{DS}} \delta(x - x_{j,i}), \quad (6b)$$

$$V_N \frac{dc_N}{dt} = - \sum_{j=1}^{N_S} \left[\sum_{i=1}^{N_j} S_{j,i}^{\text{DN}} + a^2 \int_0^{L_j} s_j^{\text{SN}} dx \right], \quad (6c)$$

where D is the diffusivity of HEI10 along the SC, and we impose no-flux boundary conditions at both ends. These

equations conserve the total amount M of HEI10,

$$M = V_N c_N + a^2 \sum_{j=1}^{N_S} \int_0^{L_j} c_j dx + c_D \sum_{i=1}^{N_j} V_{j,i}. \quad (7)$$

Consequently, the system's state is fully specified by $c_j(x)$ and $V_{j,i}$, whereas c_N can be obtained from Eq. (7). Given an initial condition, the dynamics of the system follow from Eqs. (6a) and (6b). Since the model obeys thermodynamic constraints, the dynamics will reach thermodynamic equilibrium with at most one droplet as described by Eq. (2) in the long-time limit. However, since droplets are designated as COs after a finite time T_{final} , we below analyze the positions of the remaining droplets as a proxy for CO placement. In particular, we discuss four relevant cases of the model: (i) initial loading of HEI10 onto the SC without considering droplets, (ii) coarsening of droplets along a single SC without nucleoplasm, (iii) growth and coarsening of droplets without SC, and (iv) the combined case.

B. Exchange rate determines SC loading rate and accelerates diffusion along the SC

To study the initial loading of HEI10 onto already-assembled SCs before droplets form, we consider the exchange of material with nucleoplasm. A mode analysis (Supplemental Material (SM), Sec. S2 B [62]) shows that the overall dynamics relax toward equilibrium with rate

$$k_{\text{load}} = \frac{\Lambda_{\text{SN}}}{a^3} \left(\gamma_S + \frac{V_S}{V_N} \right), \quad (8)$$

where $V_S = a^2 L$ denotes the volume of all SCs with total length $L = \sum_j L_j$. This expression shows that loading onto SCs is faster for larger exchange rates Λ_{SN} and if SCs contains fewer molecules, e.g., for small cross sections a^2 or lower affinity (higher γ_S). The second factor in Eq. (8) accounts for the depletion of the nucleoplasm, which accelerates the relaxation.

We next study the dynamics of heterogeneous HEI10 profiles by investigating diffusive relaxation along the SC. A mode analysis (SM, Sec. S2 B [62]) shows that deviations of wavelength ℓ relax with rate

$$k_{\text{diff}}(\ell) = \frac{4\pi^2 D}{\ell^2} + \frac{\gamma_S \Lambda_{\text{SN}}}{a^3}. \quad (9)$$

This expression emphasizes two contributions to spatial transport: The first term describes diffusive transport along the SC, which is slower for longer distances ℓ . The second term describes alternative transport by unbinding, fast diffusion through nucleoplasm, and rebinding, which additionally facilitates transport between different SCs. This term becomes more important for larger exchange rate Λ_{SN} , but it does not depend on ℓ since we assumed fast diffusion in nucleoplasm. In particular, the rate of transport via nucleoplasm is similar to Eq. (8) in the typical situation where γ_S is comparable to or larger than V_S/V_N . This second nucleoplasmic contribution can also be characterized as a nonlocal fast transport that effectively increases the diffusion along the SC. Consequently, faster loading of the SC implies stronger transport via nucleoplasm and between SCs, which will affect droplet coarsening.

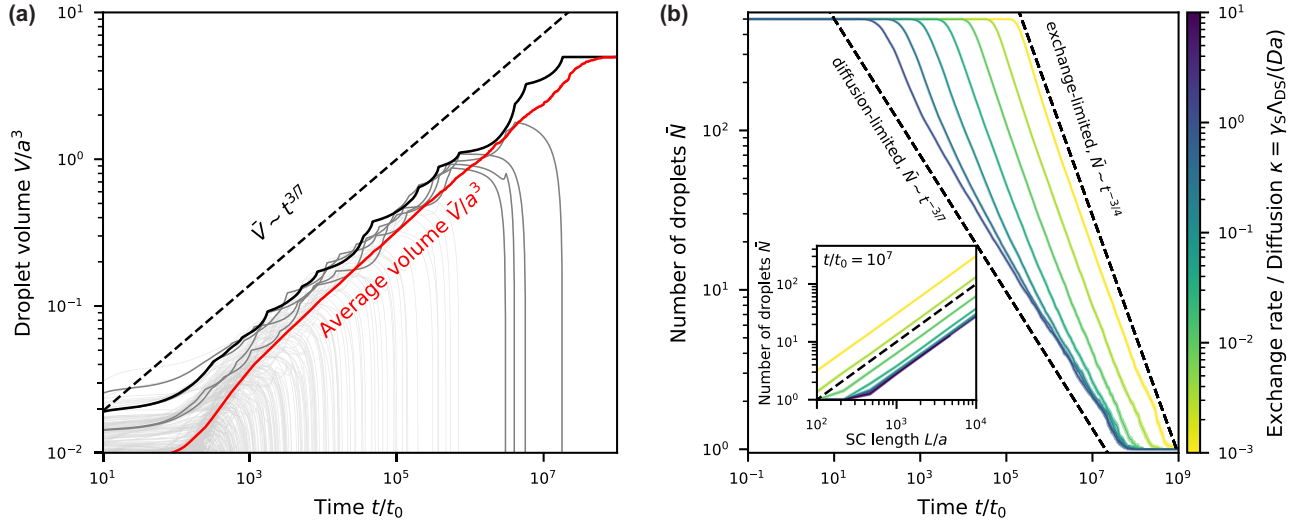


FIG. 2. Droplet coarsening without nucleoplasmic exchange. (a) Droplet volumes V as a function of time t for an exemplary system with $\kappa = 1$ without nucleoplasm. Shown are individual droplets (thin gray lines), the five largest droplets (thick gray lines), the droplet that remains until the end (black line), the average volume $\bar{V}(t/t_0)$ of the remaining droplets (red line), and the theoretical scaling for the diffusion-limited scenario for large $\kappa = \gamma_S \Lambda_{DS}/(Da)$ (dashed line). (b) Average number of all remaining droplets, $\bar{N}$, as a function of t for various κ . The inset shows $\bar{N}$ as a function of SC length L for various κ with $\Delta x_{\text{grid}} = 0.25a$ and sample size $n \geq 160$. Additional model parameters are $\nu = \frac{1}{3}$, $\nu_S = 0$, $\gamma_0/\gamma_S = 10^{-4}$, $L = 500a$, $N_{\text{init}} = L/a$, $M = 10^{-2} c_D L a^2$, $t_0 = a^2/D$, $\bar{V}_{\text{init}} = 10^{-3} a^3$, $\sigma_V^{\text{init}} = 10^{-1} \bar{V}_{\text{init}}$, $\Delta x_{\text{grid}} = 0.5a$, and sample size $n = 100$.

To study coarsening, we first focus on the simpler case without nucleoplasmic exchange before considering it again in Sec. II E.

C. Droplet coarsening via the SC implies linear scaling of droplet count with SC length

To study the simplest case of droplet coarsening, we focus on the dynamics of droplets on a single SC, neglecting nucleoplasm. For simplicity, we consider the case where the SC has been loaded homogeneously with HEI10, implying $c(x, 0) = \bar{c}$, and that multiple small HEI10 droplets already exist. We distribute the droplets uniformly along the SC and draw their volumes from a Gaussian distribution around a mean volume that is large enough to ensure that droplets initially grow until they reach local equilibrium with the SC instead of dissolving spontaneously. We then simulate Eqs. (6) to obtain droplet volumes as a function of time. Figure 2(a) shows that most droplets vanish in a short time, while some survive longer. This coarsening process is characterized by a growing average droplet volume $\bar{V}(t)$ (red line), and it ceases when only a single droplet remains, which then obeys Eq. (2). We quantify the coarsening dynamics by measuring the average droplet volume $\bar{V}(t)$, which exhibits a power-law scaling of $\bar{V}(t) \propto t^{3/7}$ [Fig. 2(a)]. This power-law scaling deviates from the seminal Lifshitz-Slyozov-Wagner scaling of t^1 [58,61], even though we choose the corresponding volume sensitivity $\nu = \frac{1}{3}$. This observation suggests that restriction to one-dimensional diffusion along the SC slows down coarsening, even though droplets are still three dimensional.

Additional simulations [Fig. 2(b)] show that coarsening depends on the ratio of the exchange rate Λ_{DS} to the diffusivity D , which we quantify by the nondimensional ratio $\kappa = \gamma_S \Lambda_{DS}/(Da)$. In particular, we find less steep slopes when

the exchange between SC and droplets is fast compared to diffusion of HEI10 along the SC ($\kappa \rightarrow \infty$). In that scenario, HEI10 concentrations on the SC at positions x_i of droplets are dictated by local equilibrium, $\gamma_S c(x_i) = c_D \gamma_0 (V_i/a^3)^{-\nu}$, which depends on the droplet volume V_i . Since droplets of different size result in different concentration on the SC, the dynamics are governed by relatively slow diffusion between neighboring droplets. An asymptotic analysis inspired by Lifshitz, Slyozov, and Wagner [58,61] predicts the number N of droplets remaining on the SC (SM, Sec. S2 C 2 [62]),

$$\bar{N}(t) \approx K_0(\nu) \frac{L}{a} \left(\frac{\lambda}{c_D a^2} \right)^{\frac{1+\nu}{2+\nu}} \left(\frac{\gamma_S a^2}{\gamma_0 D t} \right)^{\frac{1}{2+\nu}}, \quad (10)$$

where $K_0(\nu) \approx 1$ collects constants that only depend on ν (SM, Sec. S2 C 2 [62]), and λ quantifies the initial line density of HEI10 along the SC including HEI10 contained in initial droplets, which sets the total amount $M = \lambda L$.

In the opposing case of fast diffusion ($\kappa \rightarrow 0$), concentrations are equilibrated along the entire SC, so slow exchange determines the dynamics of individual droplets. The corresponding asymptotic analysis predicts (SM, Sec. S1 C 3 [62])

$$\bar{N}(t) \approx K_1(\nu, \nu_S) \frac{\lambda L}{c_D a^3} \left(\frac{1}{\gamma_0 \Lambda_{DS} t} \right)^{\frac{1}{1+\nu-\nu_S}} \quad (11)$$

for $0 < \nu, \nu_S < 1$, where $K_1(\nu, \nu_S)$ again collects the constants and only depends on ν and ν_S (SM, Sec. S2 C 3 [62]). Figure 2(b) shows that both scaling laws are consistent with numerical data in respective limiting cases. Our predictions also capture the corresponding distribution of droplet volumes in both limits (Figs. S2 and S4 in the SM [62]). Taken together, these scaling laws allow us to make quantitative predictions for large and small κ , and intermediate values interpolate between the extremes.

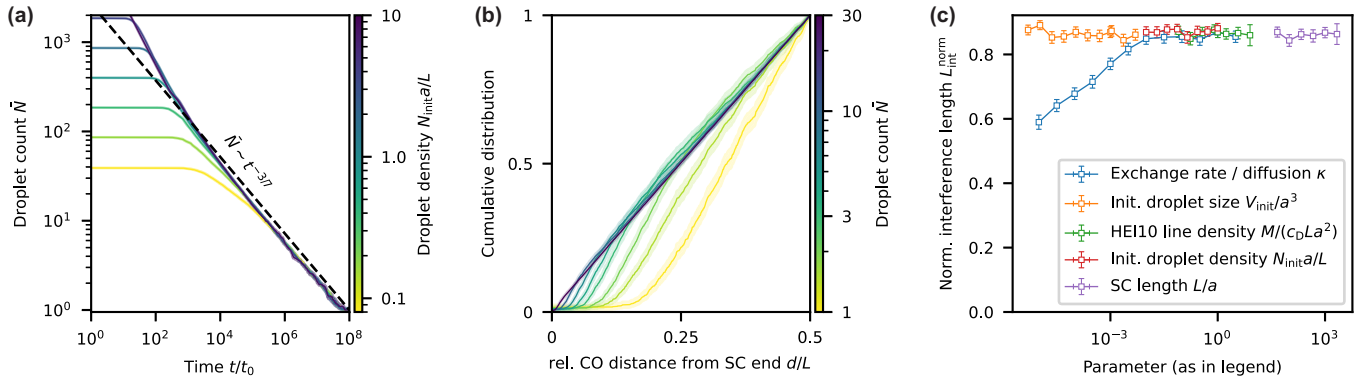


FIG. 3. Details of initial conditions do not affect CO patterning. (a) Average number of droplets, $\bar{N}$, as a function of time t for various initial droplet density $N_{\text{init}}a/L$ [shaded area indicates standard error of the mean (SEM)] and constant overall HEI10 line density $M/(c_D a^2)$ per unit length along the SC. The dashed line marks the theoretical asymptotic scaling for the diffusion-limited scenario, $\bar{N} \sim t^{-1/2}$. (b) Cumulative distribution of relative distance d/L of droplets from SC ends at fixed times corresponding to a given average droplet count $\bar{N}$ (color), averaged over $n = 5000$ samples using $\Delta x_{\text{grid}} = a$ (shaded area indicates SEM). (c) Normalized interference length $L_{\text{int}}^{\text{norm}}$ as a function of initial droplet density $N_{\text{init}}a/L$, SC length L/a , initial droplet volume V_{init}/a^3 , HEI10 line density $M/(c_D a^2 L)$, and ratio $\kappa = \gamma_S \Delta_{\text{DS}} / (D a)$ of exchange rate and diffusion. Each parameter is varied individually while the others are kept fixed. Data are shown for a fixed time at which the average droplet count over all samples is $\bar{N} = 4$. Additional parameters are $\kappa = 1$ and those given in Fig. 2.

The analytical predictions for small and large κ both imply that the number of droplets, N , scales linearly with SC length L . Numerical simulations show that this linear scaling is preserved for all values of κ [inset in Fig. 2(b)]. Consequently, doubling L also doubles the droplet count, independent of whether coarsening is limited by exchange or diffusion. In contrast, κ affects the coarsening dynamics [Fig. 2(b)]. In the exchange-limited case ($\kappa \rightarrow 0$), we obtain the seminal Lifshitz-Slyozov scaling $N \sim t^{-1}$ for $\nu = \nu_S = \frac{1}{3}$ [58,61], whereas the diffusion-limited case ($\kappa \rightarrow \infty$) leads to $N \sim t^{-3/7}$. This suggests that coarsening is slowed because the diffusive flux is restricted to one dimension and the distances between remaining droplets increase over time (SM, Sec. S2 C 3 [62]). Both scaling laws also predict that only the initial line density λ is relevant for the late-stage dynamics, whereas other details of the initial condition are negligible. This suggests that droplet patterning is insensitive to details of the initial conditions.

D. Details of initial conditions do not affect droplet patterning

To study droplet patterning, we return to detailed numerical simulations. We first vary the number N_{init} of initial droplets while reducing the concentration $\bar{c}$ on the SC to keep the total amount M constant. Figure 3(a) shows that N_{init} affects the average CO count $\bar{N}$ only early, whereas $\bar{N}$ is independent of N_{init} in late stages and instead follows scaling relation (10). Similarly, we find that changing SC length L , the volume of initial droplets V_{init} , or the HEI10 line density $\lambda = M/L$ does not affect the asymptotic behavior when accounting for the scaling relation (Fig. S3 in the SM, Sec. S2 C [62]).

We next investigate droplet positions in detail. When few droplets remain, our model predicts they are less likely to be near the ends of the SC [Fig. 3(b)], even though we start with a homogeneous distribution of initial droplets. This behavior follows from the competition of droplets for material: Droplets toward the end can only receive material from one side, so they tend to grow less and get outcompeted by more

centrally located droplets. This boundary effect becomes more severe for smaller droplet count $\bar{N}$ [Fig. 3(b)] since coarsening has progressed more.

Our numerical simulations also exhibit CO interference; i.e., small inter-CO distances are inhibited (Fig. S4(b)B in the SM [62]). To quantify CO interference, we use the interference length L_{int} , which estimates the size of the region around a droplet where interference takes place [63]. This region increases during coarsening, and theoretical models predict that L_{int} scales with $\bar{N}^{-1}$ [63]. We thus consider the normalized interference length, $L_{\text{int}}^{\text{norm}} = \bar{N} L_{\text{int}} / L$, where L is the length of the single SC we consider. Figure 3(c) shows that CO interference, as measured by $L_{\text{int}}^{\text{norm}}$, is not affected by details of the initial condition (i.e., initial droplet density N_{init}/L , initial droplet volume V_{init} , HEI10 line density $\lambda = M/L$, SC length L), as long as we compare data for the same average droplet count $\bar{N}$. In contrast, decreasing κ , i.e., decreasing the exchange rate Δ_{DS} relative to diffusion D along the SC, reduces $L_{\text{int}}^{\text{norm}}$, suggesting weaker CO interference. Note that $L_{\text{int}}^{\text{norm}}$ does not vanish, even for arbitrarily small κ , because coarsening leads to a narrow distribution of CO counts. This distribution differs from a Poisson distribution, which is expected for the null hypothesis that COs are placed independently along all SCs, implying finite $L_{\text{int}}^{\text{norm}}$ (SM, Sec. S1 F [62]). However, CO positions are still uncorrelated, consistent with the asymptotic limit of fast diffusion ($\kappa \rightarrow 0$), where the SC is homogeneous and CO positions become irrelevant for material exchange. A similar behavior emerges when the SC is completely absent.

E. Droplets in mutants without SC first grow and then coarsen

We next consider the case without the SC, but we assume that chromosome pairing still works properly, and droplets are arranged along the axes of the chromosomes, consistent with experiments in *A. thaliana* [34]. In this case, HEI10 droplets are still associated with chromosomes, but they can exchange material only with the nucleoplasm. Since we

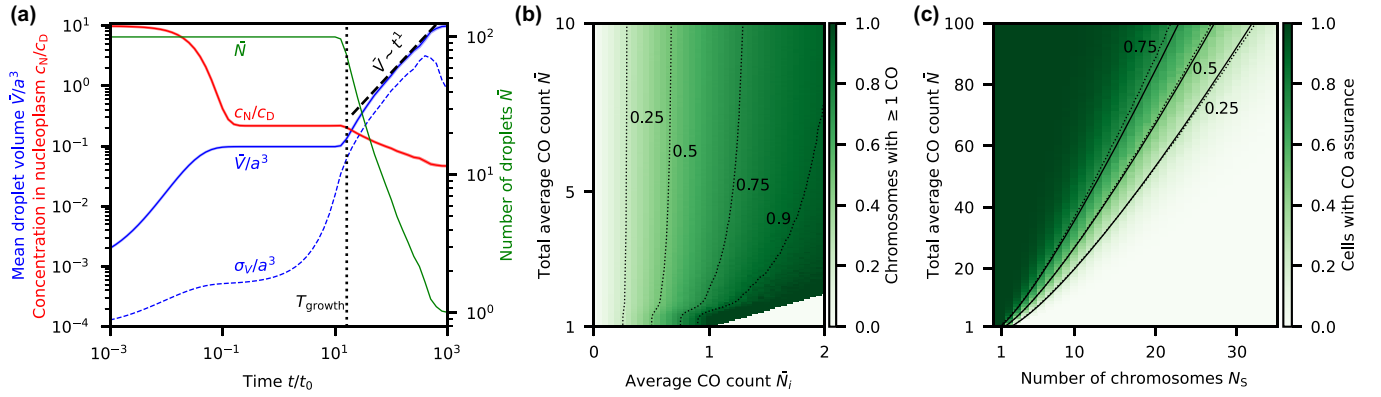


FIG. 4. Coarsening model without SC exhibits growth and coarsening regime. (a) Average droplet volume $\bar{V}/a^3$, average variance of droplet volumes, σ_V/a^3 , and HEI10 concentration in nucleoplasm, c_N/c_D , as a function of time t . The coarsening regime with $\bar{V} \propto t^1$ (dashed black line) starts beyond T_{growth} [vertical dotted line, Eq. (12)]. Model parameters are $\gamma_0 V_N = 0.1a^3$, $\nu = \nu_N = \frac{1}{3}$, $N_{\text{init}} = 100$, $M = 10 c_D a^3$, $V_{\text{init}} = 10^{-3} a^3$, $\sigma_V^{\text{init}} = 10^{-1} V_{\text{init}}$, and sample size $n = 100$. (b) Probability $P(N_i \geq 1)$ of having at least one CO on a chromosome as a function of its average CO count $\bar{N}_i$ and the average total CO count $\bar{N}$ in the cell (N is drawn randomly from Gaussian distribution with mean $\bar{N}$ and standard deviation $0.2\bar{N}$). Dotted lines highlight isolines of constant probability. (c) Probability $P(\min(N_i) \geq 1)$ that all chromosomes have at least one CO (see SM Eq. (S50a), SM S1 E [62]) as a function of the number N_S of chromosomes (of equal average CO count) and $\bar{N}$ [analogously to panel (b)]. The theoretical approximation given by Eq. (15) (solid lines) agrees with numerical isocontours (dotted lines).

assume fast diffusion in nucleoplasm, the kinetics are limited by the exchange rate Λ_{DN} between droplets and nucleoplasm. The resulting growth dynamics exhibit two qualitatively different regimes, which we now discuss before considering CO interference and assurance.

Assuming N_{init} initial small droplets form, our model predicts that all droplets grow by depleting the nucleoplasm until their average volume obeys equilibrium relation (2). During this growth phase, the mean droplet volume $\bar{V}$ and the corresponding standard deviation σ_V grow [Fig. 4(a)]. However, in our model, the coefficient of variation, $\sigma_V/\bar{V}$, decreases for $\nu_N < 1$, indicating that the size distribution becomes narrower. After this growth phase, larger droplets grow at the expense of smaller droplets, leading to an increase of $\sigma_V/\bar{V}$ until the first droplet vanishes. The duration without coarsening is approximately given by (SM, Sec. S1 D 2 [62])

$$T_{\text{growth}} \approx \frac{a^3}{\nu \gamma_0 \Lambda_{\text{DN}}} \log \left(\frac{\sigma_V^{\text{init}}}{V_{\text{init}}} \right) \left(\frac{M}{c_D a^3 N_{\text{init}}} \right)^{1+\nu-\nu_N}, \quad (12)$$

assuming that most HEI10 ends up in droplets. This expression reveals that the growth duration T_{growth} increases with total amount of HEI10, M , for $\nu_N < 1$, since $\nu > 0$. In any case, the droplet count N remains roughly constant initially and coarsening sets in only after T_{growth} , consistent with simulations [Fig. 4(a)].

During droplet coarsening, the average droplet volume increases, whereas the droplet count N gradually decreases. After an initial transient, the system approaches an asymptotic behavior [Fig. 4(a)], which we describe using a scaling analysis similar to the one in Sec. II C for $0 < \nu, \nu_N < 1$,

$$\bar{N}(t) = K_1(\nu, \nu_N) \frac{M}{c_D a^3} \left(\frac{1}{\gamma_0 \Lambda_{\text{DN}} t} \right)^{\frac{1}{1+\nu-\nu_N}}, \quad (13)$$

where $K_1(\nu, \nu_N)$ collects the constant (SM, Sec. S2 D 1 [62]). This scaling law is equivalent to Eq. (11), essentially since both processes are limited by material exchange between droplets and their surroundings, while transport in the

surroundings is fast. In particular, we recover the typical Lifshitz-Slyozov-Wagner scaling, $\bar{N} \sim t^{-1}$, for $\nu = \nu_N$.

The absence of the SC also has profound consequences for CO interference and assurance. Since the spatial positioning of droplets is irrelevant for their dynamics, CO interference is governed by the patterning of initial droplets, if only the growth regime is relevant. Even if coarsening takes place, CO interference will be hardly affected since coarsening corresponds to removal of a random subset of droplets. Similar considerations hold for CO assurance, which we quantify by the probability of retaining at least one CO per chromosome. To derive an analytic estimate, we consider a cell with exactly N COs, which are randomly allocated to multiple chromosomes. The probability that a single chromosome with average CO count $\bar{N}_i \leq N$ has at least one CO is

$$P(N_i \geq 1) = 1 - \left(1 - \frac{\bar{N}_i}{N} \right)^N \stackrel{\bar{N}_i \ll N}{\approx} 1 - e^{-\bar{N}_i}. \quad (14)$$

Consequently, CO assurance increases with larger $\bar{N}_i$, whereas the influence of CO count N is weak and variations have only minor effects (compare Fig. 4(b) and Fig. S6 in the SM, Sec. S2 E [62]). The fact that any chromosome might lack COs lowers CO assurance of the entire cell, i.e., the probability that all chromosomes in the cell have at least one CO. To estimate this probability, we consider N_S chromosomes with the same average droplet count $\bar{N}_i = N/N_S$, leading to

$$P(\min(N_i) \geq 1) \approx \exp(-N_S e^{-N/N_S}), \quad (15)$$

which corresponds to the classical occupancy problem [64–66] (SM, Sec. S1 E [62]). Equation (15) shows that CO assurance approaches 1 for $N \gg N_S$, whereas we necessarily have chromosomes with missing COs when $N < N_S$. Figure 4(c) shows that these limits are obeyed over a large parameter regime, whereas intermediate values are rare. This observation implies that COs are virtually assured for $\bar{N}/N_S > 5$, but CO assurance can be strongly suppressed even if the average CO count per chromosome is larger than 1. Moreover, CO

assurance is reduced when the average CO count $\bar{N}_i$ differs between chromosomes (SM, Sec. S1 E [62]). In contrast, variations in total CO count N have only a minor effects (compare Fig. 4(c) and Fig. S5 in the SM [62]). Taken together, the absence of SC implies vanishing CO interference and reduced CO assurance because droplet dynamics are insensitive to the allocation of droplets to chromosome and the associated position along the arc.

In summary, we find two qualitatively different regimes for the dynamics of droplets without SC (Fig. 4). First, all initiated droplets grow, implying that the total droplet count N is controlled by details of droplet initiation. After a duration T_{growth} , coarsening sets in and $\bar{N}$ decreases according to Eq. (13). In the scaling regime, $\bar{N}$ is then independent of the initial condition, and instead depends on the total amount of material, M . Our analysis of droplet dynamics without SC resembles the *zyp1* mutant in *A. thaliana* [34,39]. It explains the absence of CO interference and the reduced CO assurance, but we currently cannot decide which of the two regimes is relevant, since we lack time-resolved experimental data.

F. Exchange via nucleoplasm reduces crossover interference and assurance

We finally consider the case where HEI10 can exchange between droplets, SC, and nucleoplasm to describe wild-type behavior. If exchange via nucleoplasm is negligible, we expect the full model to converge to the simpler case discussed in Sec. II C, which exhibited strong CO interference and assurance. The exchange between a droplet and the SC, together with diffusion along the SC, limits competition to droplets in its neighborhood on the same SC, whereas exchange with the nucleoplasm leads to global competition, as well as nonlocal competition along the same SC. Since both exchanges might be relevant, we now ask how much exchange can take place via the nucleoplasm so that the predicted behavior is still compatible with wild-type measurements.

We start by investigating the exchange between droplets and nucleoplasm, proportional to Λ_{DN} , while neglecting the exchange between SC and nucleoplasm ($\Lambda_{\text{SN}} = 0$), similar to the work of Fozard *et al.* [39]. Numerical simulations of a nucleoplasm containing multiple SCs of the same length indicate that droplets coarsen faster for larger Λ_{DN} [Fig. 5(a)]. This is because droplets can now exchange material via an additional pathway. Note that we recover the scalings derived in Secs. II C and II E when either pathway dominates. If competition along the same SC dominates, the system first plateaus when every SC has exactly one droplet. If nucleoplasmic exchange is nonzero, the system then exhibits further coarsening and approaches the regime with $\bar{N} \sim t^{-1}$ derived in Sec. II E. Since the additional exchange via nucleoplasm accelerates coarsening, a comparison of data at the same time is not informative, and we thus compare at the same mean total droplet count $\bar{N}$ in the following.

We next ask how exchange between SC and nucleoplasm affects droplet coarsening, thus going beyond the model by Fozard *et al.* [39]. Figure 5(b) shows that increasing Λ_{DN} or Λ_{SN} leads to faster coarsening; i.e., the system reaches the same ensemble-averaged droplet count $\bar{N}$ in shorter times T_c . However, the two processes differ in the limit of fast

exchange: For large Λ_{DN} , droplets predominately coarsen via direct exchange through nucleoplasm, approaching the behavior we discuss in Sec. II E, so the coarsening time T_c required for the system to reach the ensemble-averaged droplet count $\bar{N}$ scales inversely with the exchange rate, i.e., $T_c \propto \Lambda_{\text{DN}}^{-1}$. In contrast, increasing Λ_{SN} does not decrease T_c arbitrarily, since this pathway is still limited by exchange between droplets and SC. In any case, Fig. 5(c) shows that CO interference, quantified by the normalized interference length $L_{\text{int}}^{\text{norm}}$, tends to decrease if Λ_{SN} or Λ_{DN} is increased. Taken together, more exchange via nucleoplasm thus tends to accelerate coarsening and decrease CO interference.

Since the two pathways of exchange with nucleoplasm have qualitatively similar effects, we next discuss them together by choosing $\Lambda_{\text{DN}} = 10\Lambda_{\text{SN}}$ to compare to the exchange between droplets and SC, which is quantified by Λ_{DS} . Figure 5(d) shows that CO interference is strongest when exchange is limited by diffusion along a SC (large Λ_{DS} ; compare to Sec. II C) while exchange via nucleoplasm is limited [small Λ_{DN} , Λ_{SN} ; compare to Fig. 5(c)]. However, we find a complex behavior in the remaining parameter regime, where interference is weaker. In particular, our model shows highly reduced, and even negative, CO interference for $\Lambda_{\text{DN}} \approx 10\Lambda_{\text{DS}}$. For these parameters, droplets tend to cluster on SCs, which is a consequence of initial conditions: If a particular region on a SC starts with relatively few droplets, these droplets have less local competition and can thus grow larger than droplets in denser regions. This initial bias in size gets amplified by global competition via the nucleoplasm, so that droplets in less dense regions have a higher chance of surviving, leading to clustered distributions, resulting in negative $L_{\text{int}}^{\text{norm}}$. To understand why this effect requires that direct exchange via SC is balanced with exchange via nucleoplasm, we next consider various values of Λ_{DS} : If Λ_{DS} is too large, competition along the individual SC dominates, and CO interference is strong. In contrast, if Λ_{DS} is too small, material uptake from the SC, and thus the initial size bias, is negligible. Taken together, we find a large parameter regime with similarly strong CO interference, although other quantities, particularly the coarsening time T_c (Fig. S7(B) in the SM [62]), still vary.

The exchange via nucleoplasm also affects CO assurance. To quantify this statement, we next measure how often we observe a SC without any droplets. Figure 5(e) shows that virtually all SCs carry droplets when exchange is limited by diffusion along the SC (large Λ_{DS}), while exchange via nucleoplasm is limited (small Λ_{DN} , Λ_{SN}). In contrast, significant exchange via nucleoplasm leads to a high chance of SCs without droplets (compare Sec. II E), and we observe signatures of droplet clusters analogous to Fig. 5(d). Taken together, we expect CO assurance precisely in the parameter regime where CO interference is strong.

In summary, we have shown that exchange of HEI10 via nucleoplasm limits CO interference and assurance. To obtain an intuitive picture of how much exchange via nucleoplasm is tolerable, we need to quantify the exchange. This is challenging because the exchange between SC and nucleoplasm is not directly linked to droplet dynamics, so we cannot directly determine how much nuclear exchange contributes to droplet growth. To still enable a fair comparison, we instead quantify the coarsening time T_c , relative to the time

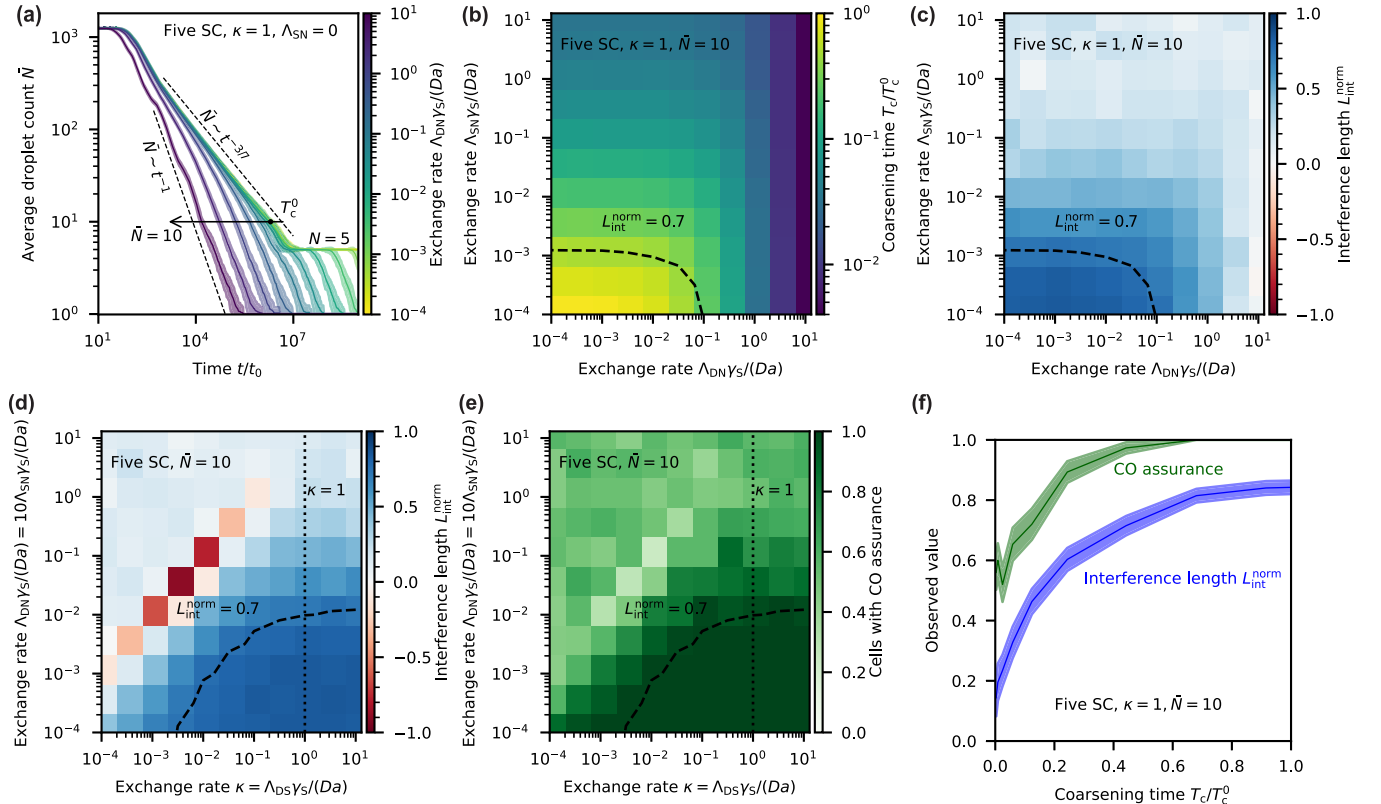


FIG. 5. Nucleoplasmic exchange accelerates coarsening while reducing CO interference and CO assurance. (a) Average total droplet count $\bar{N}$ as a function of time t for a system of five SCs with the same length in a nucleoplasm (shaded area indicates SEM). Colors correspond to various exchange rates Λ_{DN} of droplets with nucleoplasm, increasing from negligible exchange (yellow) with a slope of $\bar{N} \sim t^{-3/7}$ to strong nucleoplasmic exchange (blue) with a slope of $\bar{N} \sim t^{-1}$. Increasing Λ_{DN} decreases the coarsening time T_c , which corresponds to the time required for the system to reach the ensemble-averaged droplet count $\bar{N} = 10$ (black arrow), compared to the scenario without nucleoplasmic exchange, T_c^0 (black dot). The exchange rate $\kappa = \gamma_S \Lambda_{DS}/(Da) = 1$ of HEI10 between droplets and SC and the diffusion along the SC, D , is fixed and the exchange between SC and nucleoplasm is zero ($\Lambda_{SN} = 0$). (b) Relative coarsening time T_c/T_c^0 as a function of Λ_{DN} and Λ_{SN} for fixed diffusion rate D , exchange rate $\kappa = 1$, and $\bar{N} = 10$. (c) Normalized interference length L_{int}^{norm} corresponding to panel (b). (d) L_{int}^{norm} as a function of Λ_{DS} and $\Lambda_{DN} = 10\Lambda_{SN}$. Note that we observe $L_{int}^{norm} \approx 0.11 \pm 0.02$ for $\Lambda_{DS} = 0$, consistent with a narrower CO count distribution (SM, Sec. S1 F [62]). (e) Probability $P(\min(N_i) \geq 1)$ that all chromosomes have at least one CO as a function of Λ_{DS} and $\Lambda_{DN} = 10\Lambda_{SN}$. For large Λ_{DN} , we expect $P(\min(N_i) \geq 1) \approx 0.52$ for $\bar{N} = 10$ (SM, Sec. S1 E [62]). [(b)–(e)] Isolines mark parameters that exhibit a normalized interference length of $L_{int}^{norm} = 0.7$. (f) Fraction of cells that preserve CO assurance and normalized interference length L_{int}^{norm} (shaded area indicates SEM) as a function of the relative coarsening time T_c/T_c^0 for a fixed exchange rate $\kappa = 1$ [compare vertical dotted lines in (d) and (e)]. Model parameters are $\nu = \nu_N = \frac{1}{3}$, $\nu_S = 0$, $\frac{\gamma_0}{\gamma_S} = 10^{-4}$, $\frac{1}{\gamma_S} \frac{V_0}{V_N} = 0.1$, $M = 10 c_D a^3$, $L = 250a$, $N_{init}a/L = 1$, $V_{init} = 10^{-3}a^3$, $\sigma_V = 10^{-1}V_{init}$, $\Delta x_{grid} = 0.5a$, and sample size $n = 50$.

T_c^0 without exchange via nucleoplasm. Larger exchange via nucleoplasm reduces T_c/T_c^0 [Fig. 5(b)], so that this quantity serves as a proxy for that exchange. Figure 5(f) shows that CO interference and assurance increase with T_c/T_c^0 , as expected. However, both quantities are still close to their maximal value even when $T_c = \frac{1}{2}T_c^0$, suggesting that the material exchange via nucleoplasm can be almost as strong as the direct exchange via the SC without impacting CO interference and CO assurance significantly.

III. COMPARISON WITH EXPERIMENTAL DATA

Our theoretical model of crossover placement makes detailed predictions that we next compare to published experimental data.

A. Linear scaling with SC length explains CO count across species

We start by comparing the average number $\bar{N}$ of COs as a function of chromosome length L across various species, using the dataset published by Fernandes *et al.* [15]. Our theory predicts CO assurance ($\bar{N} \geq 1$) when material exchange along the SC dominates. Beyond that, the theory predicts a linear scaling of the number of class I COs with chromosome length ($\bar{N} \propto L$), independent of whether coarsening is limited by exchange or diffusion, assuming a linear mapping between SC length and chromosomes length, i.e., homogeneous chromatin compaction. Most species contained in Ref. [15] follow this general trend (see Fig. 6 and Fig. S8 in the SM [62]), although interesting details are apparent: First, some species (e.g., *plasmodium* and honey bee) exhibit almost perfect linear scaling, consistent with our theory. Second, most species (e.g.,

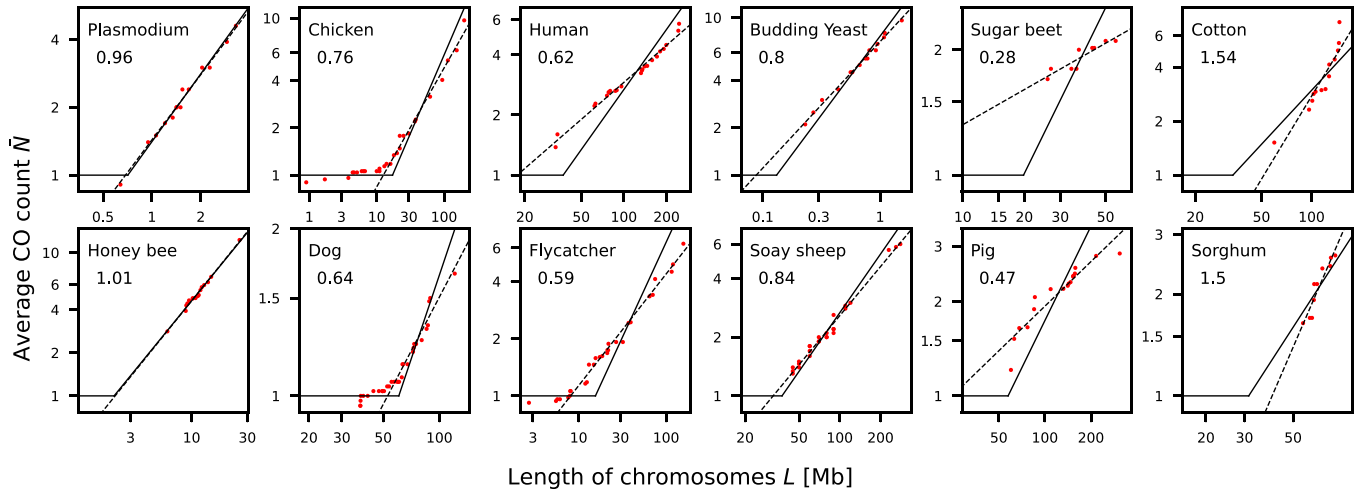


FIG. 6. Theoretical scalings explain data for various species. Average CO count $\bar{N}$ as a function of chromosome length L (measured in mega-base pairs [Mb]) for several species given by Fernandes *et al.* [15]. CO count was estimated by rescaling genetic data given in centiMorgans (cM) by 50, using that only half of chromosomes remain in genetic data. Theoretical predictions (black lines) are compared to optimal power-law fit (dashed lines, fitted slope indicated) for all chromosomes with $N \geq 1.2$ COs. Section S2 E in the SM [62] contains additional plots.

chicken, dog, human, flycatcher, and budding yeast) exhibit slight sublinear scaling (with slopes between 0.5 and 0.8), and some (e.g., sugar beet and pig) have a much smaller exponent, indicating that long chromosomes have fewer COs than we expect. Third, some species (e.g., cotton and sorghum) exhibit superlinear scaling, suggesting long chromosomes have more COs than predicted by theory. The observed deviations from linear scaling could generally originate when HEI10 line densities or chromatin compaction differs between chromosomes of different length. Moreover, the deviations could also be caused by special chromosome regions like centromeres and telomeres, which tend to occupy a larger fraction in shorter chromosomes and could affect HEI10 availability. Taken together, the experimental data are consistent with CO assurance and a roughly linear scaling beyond this regime for most species, while deviations point toward additional processes that affect CO count.

B. Model parameters determined from *A. thaliana* wild type and *zyp1* mutant

We next determine parameters of our model that are consistent with empirical data of wild-type and *zyp1*-mutant *A. thaliana*. We estimate the diffusion constant as $D \approx 1 \mu\text{m}^2 \text{s}^{-1}$, based on the measured diffusion of ZHP-3/4 along the SC in *C. elegans* [24]; the SC diameter is $a \approx 100 \text{ nm}$ [23]. We then choose the volume sensitivities as $\nu = \nu_N = \frac{1}{3}$. To have significant CO interference and assurance in wild type we require $\gamma_S \Lambda_{DS}/(Da) > 10^{-1}$ [Figs. 5(d) and 5(e)], and we choose $\nu_S = 0$ for simplicity. The total amount M of HEI10 is limited by the total volume of droplets, assuming that most HEI10 ends up in N droplets of volume a^3 in wild type, $M \approx c_D a^3 N$ [67]. We get $\gamma_0/\gamma_S \approx 10^{-4}$ by applying analytical scaling relation (10) to wild-type CO counts [34], assuming coarsening approximately lasts for the duration of pachytene, $T_{\text{pach}} \approx 10 \text{ h}$ [68]. We next estimate the exchange rate $\gamma_S \Lambda_{SN}/a$ between SC and nucleoplasm by

assuming that HEI10 loads onto SCs within at most several hours [68], implying $\gamma_S \Lambda_{SN}/(Da) > 10^{-6}$ using Eq. (8) (SM, Sec. S2 E 2 [62]). However, if $\gamma_S \Lambda_{SN}$ is too large, CO interference would be impaired [Fig. 5(c)], suggesting the upper bound $\gamma_S \Lambda_{SN}/(Da) < 10^{-3}$. Finally, we estimate $\gamma_S \Lambda_{DN}$ based on the *zyp1*-mutant data [34], where we consider both scenarios discussed in Sec. II E: If droplets only grow, and do not coarsen, we must have $T_{\text{pach}} < T_{\text{growth}}$, implying $\gamma_S \Lambda_{DN}/(Da) < 3 \times 10^{-2}$ using Eq. (12). In contrast, if droplets coarsen, we get $\gamma_S \Lambda_{DN}/(Da) \approx 10^{-1}$ based on CO counts in *zyp1* mutants compared to scaling relation (13). Note that we do not have any experimental measurements to estimate γ_S or γ_0 directly, so we choose $\gamma_S = 10 a^3/V_N$, which produces reasonable results and ensures that most HEI10 ends up in droplets.

We next check whether our estimate of the magnitude of nucleoplasmic exchange is still compatible with the observed CO interference of $L_{\text{int}}^{\text{norm}} \approx 0.7$ [34,35,63] in wild type, which is smaller than the prediction without exchange via nucleoplasm [Fig. 3(c)]. One reason for this reduction in genetic data could be noninterfering class II COs. However, a similar reduction is also observed in cytological data [35], suggesting additional effects. We thus hypothesize that the observed reduction could be a consequence of nucleoplasmic exchange, and Figs. 5(c) and 5(d) suggest that $\gamma_S \Lambda_{DN}/(Da) \approx 10^{-2}$ and $\gamma_S \Lambda_{SN}/(Da) \approx 10^{-3}$ would explain the observations. We next test whether these parameters are consistent with observed CO assurance. For wild-type data [35], CO assurance is still close to 1 and thus consistent with our model [Fig. 5(e)]. The *zyp1* mutant exhibits reduced CO assurance [Eq. (15) in Sec. II E], which is consistent with the observation that 3 of 14 cells have at least one chromosome that does not carry COs ($p = 0.23$) [39]. Taken together, we find that the coarsening model tolerates substantial exchange via nucleoplasm, essentially because small differences in droplet volume suffice to select final droplets. This implies that there are a range of model parameters that are consistent with observed CO

counts, CO assurance, and CO interference in wild-type and *zyp1*-mutant *A. thaliana*.

C. Scaling laws help to interpret observed heterochiasmy in *A. thaliana*

We next apply our analytical scaling relations to heterochiasmy, which refers to differences in CO count between sexes. For example, *A. thaliana* males exhibit 50 % more COs than females in wild type [34,39]. Since SCs are roughly 50 % longer in males [34], scaling relation (10) in the diffusion-limited scenario directly implies the observed heterochiasmy if the average HEI10 line density λ and the time T_{final} when droplets are designated to become COs is the same between both sexes in wild type. However, pachytene is typically longer in females [69], which could imply larger T_{final} , too. If this was true, the observed heterochiasmy would imply higher average HEI10 line density in females. While these details are currently unclear, the scaling relation (10) generally allows connecting the observed heterochiasmy to measured differences between male and female in wild type.

The observed heterochiasmy vanishes in *A. thaliana zyp1* mutants [34,39]. Similar to wild type, sex differences in the mutant are currently unclear, but we can use the scaling relations to discuss various scenarios. In particular, and in contrast to wild type, it is currently unclear whether droplets in the *zyp1* mutant actually exhibit coarsening or whether they merely grow [23]. If droplets only grow, essentially all droplets will become COs, so the absence of heterochiasmy must follow from a separate mechanism that ensures an equal number of initial droplets in both sexes. In contrast, if coarsening is relevant, the droplet count reduces through competition for HEI10. Assuming that physical parameters (like exchange rates and affinities) are identical across sexes, Eq. (13) implies

$$\frac{N_{\text{male}}}{N_{\text{female}}} \approx \frac{M_{\text{male}}}{M_{\text{female}}} \left(\frac{T_{\text{female}}}{T_{\text{male}}} \right)^{\frac{1}{1+\nu-\bar{N}}} \approx 1, \quad (16)$$

where N_{α} is the average CO count, M_{α} the total amount of HEI10, and T_{α} the final designation time for both sexes ($\alpha = \text{male, female}$). If designation times are similar ($T_{\text{female}} \approx T_{\text{male}}$), a lack of heterochiasmy implies similar amounts M of HEI10 in both sexes ($M_{\text{male}} \approx M_{\text{female}}$). In contrast, plausible differences in designation times would require a corresponding difference in total amounts. We thus conclude that droplets in the *zyp1* mutant either only grow or that designation times and total amounts are balanced such that heterochiasmy is absent.

Heterochiasmy in *A. thaliana* is also affected by the overall levels of HEI10. For instance, the overexpression mutant HEI10^{oe} does increase the CO count in both sexes [34]. This is consistent with predicted scaling relation (10), which predicts a sublinear scaling with total HEI10 line density λ , $\bar{N} \propto \lambda^{4/7}$ for $\nu = \frac{1}{3}$. Moreover, heterochiasmy is still present in HEI10^{oe} [34], as expected. The CO count increases further when additionally the SC is removed (in the *zyp1* HEI10^{oe} mutant), but heterochiasmy is completely absent [34]. The lack of heterochiasmy would be easy to explain if droplets again only grew without the SC, although we again cannot exclude a balance of designation times and total amounts. If droplets only grew without coarsening, the number of initial droplets,

N_{init} , would need to depend on the HEI10 level, consistent with known nucleation mechanisms [70]. Taken together, our scaling laws constrain possible scenarios explaining heterochiasmy, but we cannot identify a most plausible hypothesis since too many details are currently unknown. In particular, clear evidence whether droplets coarsen or only grow in the *zyp1* mutant would constrain possible explanations.

D. Coarsening model may explain homeostasis

We next compare our model to experimentally observed CO homeostasis [10,13,35,40,71,72], i.e., the fact that the observed CO count $\bar{N}$ depends only weakly on the number $\bar{N}_{\text{DSB}}$ of double-strand breaks (DSBs). In particular, a 46% decrease in DSB count in *A. thaliana* results in only a 17% CO count decrease [72], which corresponds to a sublinear scaling of $\bar{N} \sim \bar{N}_{\text{DSB}}^{0.3}$. Since DSBs are typically associated with early droplets [3], the simplest interpretation would be that $\bar{N}_{\text{DSB}}$ controls the number N_{init} of initial droplets in our coarsening model. We show in Sec. IID that N_{init} does not affect the CO count in the coarsening regime, provided the total amount of HEI10 is unaffected. The observed weak dependency thus suggests that increasing $\bar{N}_{\text{DSB}}$ increases the HEI10 line density λ , which would affect the CO count sublinearly, e.g., $\bar{N} \propto \lambda^{4/7}$ for $\nu = \frac{1}{3}$ [Eq. (10)]. Taken together, our model predicts that altered DSB count affects the CO count not by changing the number of initial droplets, but by increasing the HEI10 line density.

IV. DISCUSSION AND CONCLUSION

We derive a thermodynamically consistent coarsening model with material exchange between nucleoplasm, synaptonemal complex, and HEI10 droplets. Our model explains key experimental observations, such as CO counts, CO assurance, and CO interference. The asymptotic scaling relations we derive enable a simple and quantitative discussion of parameter dependence; for instance, CO count scales linearly with SC length. More generally, these relations allow us to derive a consistent set of model parameters for describing CO placement in *A. thaliana* wild type and mutants, as well as HEI10 overexpression [34].

Our extended coarsening model enables a detailed analysis of the material exchange via nucleoplasm. Data from the *A. thaliana zyp1* mutant suggest that nucleoplasmic exchange is substantial, so it likely cannot be neglected in wild type. This is consistent with reduced CO interference in wild type compared to a model without nucleoplasmic exchange [63]. In particular, the observed CO assurance and reduction of CO interference in wild type is consistent with an acceleration of coarsening due to nucleoplasmic exchange of up to a factor of 2, suggesting that up to half of the HEI10 exchange could be mediated by the nucleoplasm. However, in contrast to wild type, where experimental data suggest that coarsening occurs, it remains unclear whether coarsening takes place in the *A. thaliana zyp1* mutant (cf. Refs. [12,34,39]). Alternatively, droplets could simply grow, and the lack of heterochiasmy would then be a consequence of details of droplet formation. Taken together, more detailed cytological observations of *A.*

thaliana zyp1 mutants could help to answer this question and refine our model.

Our model suggests that CO patterning is insensitive to details of initial conditions, provided the total initial HEI10 density is uniform along the SC. This is a direct consequence of the rapid initial coarsening of small droplets in close vicinity. If the initial HEI10 density is uniform along the SC, our model predicts that chromosome end regions (telomeres) exhibit fewer COs [Fig. 3(b)]. In contrast, some experiments register elevated CO frequencies at telomeres [34,35,39,73], which points at one or more heterogeneities along the SC:

(i) Initial HEI10 loading could be heterogeneous [35,39], e.g., because SC might assemble from telomeres, enabling more loading of HEI10.

(ii) Earlier SC formation might induce earlier droplet growth and coarsening, allowing these droplets to outcompete others.

(iii) A heterogeneous density of DSBs, e.g., DSB hotspots [10,74], could affect HEI10 loading [11].

(iv) HEI10 affinity, captured by ω_S in our model, might depend on position along the SC.

Such heterogeneities, or combinations, could promote COs at telomeres, but they also explain why centromeric regions typically contain no crossovers [1,7]. An extreme form of heterogeneity is the partial SC mutant, where chromosome

zipping is not complete, and multiple intact SC fragments exist along the same chromosome pair. To understand such heterogeneities in more detail, a better understanding of SC assembly, initial HEI10 loading onto the SC, and dynamics of early HEI10 droplets is needed. Our current model does not describe the initial formation of droplets, it includes neither fluctuations nor active modifications (e.g., via post-translational modifications) of the involved proteins [42,43], and it currently does not capture the physical interaction between droplets and SCs, e.g., due to wetting [45]. However, the model provides a solid framework and can be extended to study these details in the future.

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DATA AVAILABILITY

The data that support the findings of this article are openly available [75].

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