SMC Condensin: The Motor behind Bacterial Chromosome Organization?

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Abstract

The bacterial chromosome is highly structured. A prominent structural feature was revealed by recent Hi-C experiments on various species, providing evidence for anomalously high contacts between opposite pairs of DNA loci on the left and right chromosome arms. These long-range contacts in Hi-C maps have been attributed to various nucleoid-associated proteins, including the highly conserved ATPase SMC condensin. Although the molecular structure of these ATPases has been mapped in detail, it still remains unclear how they collectively generate long-range chromosomal contacts. To resolve this puzzle, we develop a computational model for the dynamic organization of circular DNA by condensins as active slip-links. We first consider a scenario in which the ATPase activity of slip-links regulates their DNA-recruitment near the origin of replication, while the slip-link dynamics is assumed to be diffusive. We find that such diffusive slip-links can organize the entire chromosome into a state with aligned arms, but not within physiological constraints. However, slip-links that include motor activity are far more effective at organizing the entire chromosome over all length-scales. The persistence of motor slip-links at physiological densities can generate large, nested loops and drive them into the bulk of the DNA. Finally, our model with motor slip-links can quantitatively account for the rapid arm–arm alignment of chromosomal arms observed in vivo.

1 Introduction

The bacterial chromosome is highly structured over a wide range of length-scales [1, 2, 3, 4]. Indeed, microscopy experiments have revealed a remarkable degree of sub-cellular organization of the chromosome across many species, including Bacillus subtilis, Caulobacter crescentus and Escherichia coli [5, 6, 7, 8, 9]. The structural organization of chromosomes was further exposed by recent Hi-C experiments measuring the contact probability between pairs of loci on the chromosome [10, 11, 12, 6, 13]. On small length-scales, the chromosome appears to be organized in so-called Chromosome Interaction Domains: genomic domains with above-average contact probabilities between pairs of loci. On large length-scales, the most prominent feature is the emergence of a cross-diagonal in Hi-C maps spanning the whole length of the genome, indicating anomalously high contact probabilities between opposing pairs of DNA-loci positioned on the left and right chromosomal arms. Such a cross-diagonal is observed in B. Subtilis and C. crescentus [11, 12, 10, 14], but not in E. Coli [15].

The measured cross-diagonal indicates a robust juxtaposition of the left and right arms of the chromosome [10, 12, 11, 14], an organizational feature that is important for faithful chromosome segregation [16, 6, 17, 9, 18]. Indeed, this juxtaposed organization depends on the ParABS partitioning system, and is largely controlled by the highly conserved ATPase SMC condensin [11, 12, 6]. While much is known about condensin at the molecular level [10, 20, 21, 22, 23, 24], it is unclear how small numbers of condensins (3–30 per chromosome [25]) are capable of collectively organizing the chromosome over such a range of length-scales. Thus, the physical principles underlying the juxtaposed organization of the chromosome remain elusive.
The functional capability of SMC condensins to organize the chromosome into a juxtaposed state crucially depends on two factors: (i) the presence of a specific loading site on the chromosome close to the origin of replication (ori) [11, 25], and (ii) the ability of condensin to bind and hydrolyze ATP [26, 25]. In *B. subtilis*, the loading site near ori is established by a large nucleoprotein complex composed of ParB proteins bound around parS [27, 28, 29, 30]. ChIP-seq data shows that condensins are recruited to this ParBS region, and from there propagate deep into the bulk of the DNA polymer [20, 25]. Suppressing condensin recruitment to ori in ParB or parS deletion mutants (ΔParB/S) results in a loss of the cross-diagonal in Hi-C maps [11, 12]. Moreover, the translocation of condensins away from the loading site near ori depends on their ATPase activity; condensin mutants that cannot bind ATP only weakly associate with DNA, and mutants that do not hydrolyze ATP do not efficiently propagate away from the ParBS loading site (SI 2.2 and 20, 25).

The SMC condensin complex consists of two main subunits: Smc coiled coils that emanate from a hinge domain and end in two head-domains, which are connected to establish a ring-like topology [19, 23, 24, 31, 20]. Interestingly, condensin is rod-shaped in solution [23], but undergoes a conformational transition into an open configuration upon ATP-induced DNA-binding [19, 21]. With a typical size of 25 – 50 nm, the ATP-bound condensin ring is large enough to trap a DNA loop by threading a DNA duplex through it [23, 31, 19]. It has been proposed that the possibility of condensins to trap DNA-loops would enable them to align the chromosomal arms by progressively extruding DNA-loops from the origin to the terminus region [11, 12, 6].

Important clues on the role of ATPase activity in SMC condensin come from *in vitro* single-molecule experiments. These experiments revealed that *Saccharomyces cerevisiae* condensin is a molecular motor, and performs active translocation over DNA duplexes [32]. Kymographs showed that the direction of movement of yeast condensin is *a priori* random, and switches direction after a typical time-scale; in other words, yeast condensin performs persistent random motion over DNA. In fact, recent single-molecule experiments have revealed that such yeast condensin performs active loop extrusion [33]. Similar experiments have not yet observed such motor activity for bacterial condensin [34]. Nevertheless, it has been widely speculated that the ATPase activity of bacterial condensin is also directed towards motor activity [35, 31, 25, 22]. In this picture, condensin would actively extrude DNA-loops, possibly by feeding DNA duplexes through its ring-like structure [36, 37, 38, 39]. In contrast, other models have been proposed in which the ATPase activity of condensin is directed towards regulating its association with DNA [25, 20, 38, 40]. Thus, it remains an open question whether bacterial condensin also acts as a loop extruding enzyme, or whether the ATPase activity primarily regulates the DNA-recruitment of condensins.

To elucidate the role of condensin ATPase activity on bacterial chromosome organization, we develop two minimal models for condensin–DNA interactions, where we describe SMC condensin as a slip-link that non-topologically traps a DNA-loop (Fig. 1). In the most basic model, condensin activity is assumed to be directed towards regulating its DNA-recruitment, while the dynamics of condensin slip-links on the DNA is diffusive. Interestingly, we find that such diffusive slip-links can organize the chromosome into a juxtaposed state, but not within physiological constraints. Next, we expand the model to include motor slip-links that perform persistent random motion on DNA. We find that these motor slip-links are much more effective in organizing the entire chromosome. In particular, our motor slip-link model requires at least 2–3 orders of magnitude fewer condensins to organize the chromosome than in the diffusive slip-link model. In addition, the development of the juxtaposed state exhibits sub-diffusive dynamics in the diffusive slip-link model, in contradiction with the rapid re-organization observed *in vivo* [12]. We show that such a fast re-organization of the chromosome is achieved by motor activity in the form of active loop extrusion. More generally, the computational model we develop here offers a framework to study how the ATPase-activity of nucleoid-associated proteins impacts chromosome organization.

## 2 Model

Our model of condensin–DNA interactions (Fig. 1) contains two ingredients: (i) a circular DNA polymer, and (ii) multiple SMC condensins that interact with the DNA. We employ a lattice polymer with a lattice constant set by the persistence length of DNA (SI 1). Condensins are modeled as slip-links: elastic rings that trap a DNA-loop (Fig. 1). In the most basic model, condensin activity is assumed to be directed towards regulating its DNA-recruitment, while the dynamics of condensin slip-links on the DNA is diffusive. Interestingly, we find that such diffusive slip-links can organize the chromosome into a juxtaposed state, but not within physiological constraints. Next, we expand the model to include motor slip-links that perform persistent random motion on DNA. We find that these motor slip-links are much more effective in organizing the entire chromosome. In particular, our motor slip-link model requires at least 2–3 orders of magnitude fewer condensins to organize the chromosome than in the diffusive slip-link model. In addition, the development of the juxtaposed state exhibits sub-diffusive dynamics in the diffusive slip-link model, in contradiction with the rapid re-organization observed *in vivo* [12]. We show that such a fast re-organization of the chromosome is achieved by motor activity in the form of active loop extrusion. More generally, the computational model we develop here offers a framework to study how the ATPase-activity of nucleoid-associated proteins impacts chromosome organization.
slip-links to actively extrude DNA loops.

To simulate the dynamics of both the DNA polymer and the slip-links, we developed a Kinetic Monte-Carlo (KMC) algorithm (SI 1). Our KMC algorithm simulates the Rouse dynamics of DNA [41, 42], the associated stochastic motion of slip-links on the DNA, as well as the microscopic reactions in which slip-links bind to (rate $k_+$) or unbind from (rate $k_-$) the DNA. For simplicity, we assume instantaneous slip-link binding $k_+ \to \infty$, justified by the relatively fast cytosolic diffusion of condensin [43]. Additionally, we fix a maximum number of slip-links $N_p$ that can bind to the DNA.

Results

2.1 Diffusive slip-links with a specific loading site can organize the chromosome

In the simplest implementation of our model, there is no specific loading site: diffusive slip-links can bind and unbind anywhere on the DNA (Fig. 2a, $\Delta$ParB/S). This assumption results in a homogeneous binding probability $p_p(i)$ (Fig. 2a, bottom). Importantly, in the $\Delta$ParB/S scenario, all microscopic reactions are fully reversible, implying that the system relaxes into thermodynamic equilibrium. In equilibrium, small loops are strongly favored, owing to the increasing entropic cost of loop formation with larger loop size. This tendency to form small loops is reflected in the loop diagrams (Fig. 2a, top). Indeed, the loop sizes trapped by the slip-links are consistent with the equilibrium loop-size distribution (SI 9.1). Furthermore, in this scenario the contact maps are structureless and only exhibit a single main diagonal (Fig. 2a, middle), as for a random polymer. These results demonstrate that our KMC model with reversible microscopic reactions evolves towards thermodynamic equilibrium. Thus, although the slip-links can easily bind over the full extent of the polymer, they do not organize the chromosome. We next investigate how the presence of a slip-link loading site [26, 25, 11, 12, 16] impacts steady-state chromosome organization. Note, while recruitment of slip-links in our model is exclusive to ori, unbinding can occur anywhere on the DNA. This implies that the reactions involving slip-link binding/unbinding are partially irreversible. Hence, detailed balance is broken [44], and the system may no longer evolve towards thermodynamic equilibrium. Nevertheless, for slow dissociation kinetics (small $k_-$), we observe an unstructured contact map (Fig. 2b; SI 9.1), similar to the equilibrium system lacking a specific loading site (Fig. 2b; SI 9.1). Moreover, the loop diagrams again show that the slip-links mostly encircle small loops (Fig. 2b, top). In sum, we see that, although detailed balance is broken on the level of slip-link binding/unbinding, the diffusive slip-links with slow dissociation kinetics do not appear to organize the DNA polymer.

Interestingly, increasing the dissociation kinetics of slip-links results in dramatically different contact map. We observe the emergence of a prominent cross-diagonal, which either disperses away from the loading site (Fig. 2c) or remains clearly resolved over the whole polymer (Fig. 2d), depending on the density of slip-links. Interestingly, the loop diagrams for these systems exhibit a topology distinct from the equilibrium configuration; slip-links trap DNA-loops in a cooperative, nested manner. Movies of the loop diagrams and contact maps clearly demonstrate that these nested loops propagate away from the loading site, dynamically driving a juxtaposition of the two polymer arms (SI movies 3a–b; SI 10). This dynamical arm–arm alignment is a distinct out-of-equilibrium phenomenon, and thus requires the exclusive binding of slip-links to the loading site. Thus, our observations show that diffusive slip-links with fast dissociation kinetics in conjunction with a loading site can, in principle, generate a non-equilibrium
Figure 2: Steady-state organization of a circular chromosome by diffusive and motor slip-links. For all sub-figures (a)–(h): top panels show a loop diagram that illustrates the loop structure induced by slip-links, middle panels the contact map $p_c(i, j)$, and bottom panels the binding profile $p_p(i)$ of slip-links along the DNA. 

**Diffusive slip-links, (a)–(d):** (a) lacks a specific loading site ($\triangle ParB/S$), (b) slow slip-link dissociation ($k_\text{slow} = 10^{-6} k_0$), (c)–(d) high dissociation rate ($k_\text{fast} = k_0$) with $N_p = 5$ in (c) and $N_p = 25$ in (d). 

**Motor slip-links, (e)–(g):** (e) lacks a specific loading site ($\triangle ParB/S$), (f) low switching rate ($k_{\text{switch}} = 10^{-6} k_{\text{motor}}$), (g) high switching rate ($k_{\text{switch}} = 10^{-1} k_{\text{motor}}$). All simulations were performed with a circular polymer polymer of length $N_m = 80$. Maximum number of polymer-bound slip-links from (a)–(g) are respectively $N_p = 16, 20, 5, 25, 2, 2$.

**Legend, (h):** We use the fraction of nested loops ($\theta$, see SI 3.1), cross-diagonal length ($X_c$, see SI 3.2) and the slip-link propagation distance ($X_p = \sqrt{\text{var} \ p_p(i)}$) to quantify polymer organization. Contact probabilities are scaled logarithmically and shown over a range $p_c(i, j) = 10^{-3} ... 1$.

To investigate the role of slip-link kinetics on loop topology more quantitatively, we employ a metric that captures essential topological differences between the loop network of random and juxtaposed polymers (compare Fig. 2 to Figs. 2–d). To this end, we define the order parameter $\theta \in [0, 1]$ as the fraction of nested loops (Fig. 2h and SI 3.1). We observe a sigmoidal relation between $\theta$ and the dissociation rate $k_-$ for diffusive slip-links, with $\theta$ transitioning from low to high values with increasing $k_-$ (Fig. 3, blue; SI 9.2). The increase in $\theta$ at higher $k_-$ stems from the increased lifetime of nested loops, and can be estimated using a simple mean-field model (solid curve in Fig. 3, SI 9.2). Furthermore, we find that the characteristic dissociation rate at the inflection point of $\theta$ coincides with the transition from a random polymer to a juxtaposed organization with a cross-diagonal in contact maps ($d_1$ vs. $d_2$ in Fig. 3). In addition, we observe that the equilibrium implementation of diffusive slip-links that bind non-specifically to the DNA ($\Delta ParB/S$) yields $\theta \approx 0$ ($d_4$ in Fig. 3), confirming our previous observation that the loading site is necessary for creating large, nested loops (SI 9). Thus, in the presence of a loading site, diffusive slip-links appear to drive a dynamical transition between phases of weak and strong nesting of DNA-loops, and this transition is crucial to establish the juxtaposed state of the chromosome.

Importantly, in our model with diffusive slip-links, we find that having many nested loops is a necessary, but not sufficient condition to organize the polymer into a juxtaposed state (SI 8). These loops also need to propagate into the bulk of the polymer. Indeed, we find that the propagation of diffusive slip-links is a density-driven process: the nested loops only propagate over the full length of the polymer for very high slip-link densities (SI 3). This can be clearly seen in the binding profiles $p_p(i)$: at low slip-link densities, the binding profile is sharply peaked around the loading site (Fig. 2, bottom), whereas this peak broadens as we increase the slip-link density (Fig. 2, bottom).
2.2 Motor slip-links are highly effective in organizing the chromosome, even at low densities

Motivated by recent observations of motor activity of yeast condensin in single-molecule experiments [32, 33], we next explore how such activity impacts the ability of slip-links to organize the chromosome. In our model, motor slip-links are assumed to perform persistent random motion (Fig. 1, inset). Such persistent slip-links actively extrude loops [34, 35, 36, 37, 38, 39]. The active dynamics of motor slip-links is characterized by the switching rate \( k_{\text{switch}} \) (in units of the slip-link translocation rate \( k_{\text{motor}} \)). Error bars represent the standard deviation \( \sqrt{\text{var}} \). A mean-field model yields an estimate for \( \theta \) of diffusive slip-links (blue curve, see SI 9.2 for details). Representative loop diagrams and contact maps are indicated for different parameter choices, labeled \( d_1-d_3 \) for diffusive links and \( m_1-m_3 \) for motor slip-links. Also shown are \( \theta \) for diffusive \( (d_3) \) and motor \( (m_3) \) slip-links with non-specific slip-link binding \( (\Delta \text{ParB}/S) \). Polymer lengths \( N_m \) and slip-link numbers \( N_p \) are \( N_m = 40, N_p = 10 \) (diffusive slip-links) and \( N_m = 80, N_p = 2 \) (motor slip-links).

![Diagram showing diffusive and motor slip-links](image)

**Figure 3:** Loop network topology controls polymer organization. The fraction of nested loops \( \theta \) of diffusive slip-links (blue) is shown as a function of the dissociation rate \( k_1 \) (in units of the slip-link diffusion rate \( k_0 \)), and for motor slip-links (red) as a function of the switching rate \( k_{\text{switch}} \) (in units of the slip-link translocation rate \( k_{\text{motor}} \)). Error bars represent the standard deviation \( \sqrt{\text{var}} \). A mean-field model yields an estimate for \( \theta \) of diffusive slip-links (blue curve, see SI 9.2 for details). Representative loop diagrams and contact maps are indicated for different parameter choices, labeled \( d_1-d_3 \) for diffusive links and \( m_1-m_3 \) for motor slip-links. Also shown are \( \theta \) for diffusive \( (d_3) \) and motor \( (m_3) \) slip-links with non-specific slip-link binding \( (\Delta \text{ParB}/S) \). Polymer lengths \( N_m \) and slip-link numbers \( N_p \) are \( N_m = 40, N_p = 10 \) (diffusive slip-links) and \( N_m = 80, N_p = 2 \) (motor slip-links).

2.3 Condensins need motorized movement to efficiently propagate into the bulk of the chromosome

*In vivo* experiments have demonstrated that condensins propagate far from their loading site [26, 27]. To quantify the distribution of condensins on the chromosome in our model, we measure the extent \( \bar{X}_p \) of slip-link propagation as the standard deviation of the binding profile \( p_p(i) \) (Fig. 3). We eliminate the system-size dependence by considering the scaled propagation length \( \bar{x}_p = \bar{X}_p/\frac{1}{2}N_m \) (SI 1) as a function of slip-link density \( \varphi_p = 2N_p/N_m \).

The scaled propagation length of diffusive slip-links only approaches the *in vivo* value, \( \bar{x}_p \approx 0.5 \) (26, 27) and...
Figure 4: Propagation length of slip-links and associated arm–arm juxtaposition

(a) Scaled propagation length $\hat{x}_p \equiv \bar{X}_p / \frac{1}{2} N_m$ as a function of slip-link density $\phi_p$ for diffusive (blue) and motor (red) slip-links. Indicated are also experimental measurements from [20] for wild-type cells (“WT”, red star) and mutants whose SMC condensins have suppressed ATPase activity (“ATP-mutant”, blue star) (SI 2.2). (b): State diagram of scaled cross-diagonal length $\hat{x}_c = X_c / \frac{1}{2} N_m$ for diffusive slip-links as a function of dissociation rate $k_-$ (in units of $k_0$) and slip-link density $\phi_p$. (c): State diagram of scaled cross-diagonal length $\hat{x}_c$ for motor slip-links as a function of the switching rate $k_{\text{switch}}$ (in units of $k_{\text{motor}}$) and slip-link density $\phi_p$. Both (b–c) have $N_m = 100$. Marker “exp.”: is an estimate of WT behavior, using the values $\phi_p = 10^{-4} \ldots 10^{-3}$ as in B. Subtilis [25], $k_{\text{switch}}^{-1} = 222 \text{ min (SI 2.1)}$ and $k_{\text{motor}}^{-1} = 0.12 \text{ s (SI 1.3.3)}$. Markers $m_1$ (SI movie 10a) and $m_2$ (SI movie 10b) are respectively at low and high switching rates. Hatched area indicates values of $\phi_p$ that we did not reach computationally. For both panels (b) and (c), we define $\hat{x}_c$ as the 75th percentile of the cross-diagonal contacts (SI 3.2).

SI 2.2, when we use slip-link densities $\gtrsim 10\%$ in our simulations (Fig. 4, blue). Importantly, this slip-link density would correspond to thousands of condensins on the chromosome, 2–3 orders of magnitude more than reported in vivo [25]. This further illustrates that diffusive slip-links are not efficient at forcing the nested loops into the bulk of the polymer at low densities. In contrast, motor slip-links propagate over the full length of the polymer at all slip-link densities we considered (red data in Fig. 4), as observed experimentally in cells ([20, 25] and SI 2.2).

Our results are summarized in a “state diagram” (Figs. 4b–c), indicating the scaled extent $\hat{x}_c = X_c / \frac{1}{2} N_m$ of the cross-diagonal in contact maps. Diffusive slip-links require both fast dissociation kinetics as well as a high slip-link density to bring the polymer into the juxtaposed state (Fig. 4b). For high densities of motor slip-links $\phi_p \gtrsim 10\%$ and low $k_{\text{switch}}$, the slip-links readily juxtapose the DNA polymer (e.g. $m_1$ in Fig. 4). Contrarily, for increasing $k_{\text{switch}}$, motor slip-links antagonize each other’s translocation (e.g. $m_2$ in Fig. 4), impeding the collective propagation of slip-links away from the loading site, thereby resulting in a reduced $\hat{x}_c$ (compare $m_1$, $m_2$ in Fig. 4; SI movies 10a–b). In the limit $k_{\text{switch}} \gg k_{\text{motor}}$, motor slip-links effectively behave as diffusive slip-links with enhanced unbinding kinetics, placing them in the fast dissociation regime (data for $k_{\text{switch}} \gtrsim 10 k_{\text{motor}}$ in Fig. 4). In contrast, for $\phi_p \lesssim 10\%$, motor slip-links only require $k_{\text{switch}}$ to be sufficiently low. We estimate that
wild-type condensin is indeed in this slow switching regime (“exp.” in Fig. 4c). In sum, our simulations indicate that condensins at physiological densities can drive nested loops into the bulk of the polymer, crucial for establishing arm–arm alignment, only if they perform motorized, persistent motion.

2.4 SMC condensin requires motor activity to rapidly re-organize the chromosome

SMC induction experiments revealed that condensin can propagate from the loading site into the bulk of the DNA, thereby organizing an entire bacterial chromosome in a timespan of only $T_{\text{WT}} \approx 24 \text{ min}$ (SI 2.3 and [12]). Based on these experiments, we estimate that condensins translocate away from their loading site with a velocity of $\approx 300 \text{ nm/s}$. To understand the origin of these remarkably fast dynamics, we compute time-traces $X_p(t)$ of the width of the slip-link binding profile for our minimal models. From these traces, we extract a typical propagation time $T$ for slip-links to establish a steady-state binding profile on a DNA polymer of physical length $L = aN_m$ (Fig. 5, inset), where $a \approx 50 \text{ nm}$ is the size of one monomer (SI 1.3).

The propagation time of diffusive slip-links scales strongly with DNA length: $T \sim L^x$, with $x \approx 2.5$ (Fig. 5 blue). This scaling differs from simple diffusive motion ($x = 2$, black in Fig. 5), which we attribute to the loop-entropic forces that impede slip-link movement away from their loading site. Based on this observed scaling of $T$, we estimate that diffusive slip-links propagate several orders of magnitude slower over the DNA than observed in live cells (Fig. 5 “WT”). In contrast, the propagation time of motor slip-links exhibits ballistic scaling, $T = L/v$ (Fig. 5 red), where the translocation velocity $v$ depends on the motor activity and DNA relaxation dynamics, but not on the system size employed (SI 5). Interestingly, our model prediction of motor slip-links, $T = vL$, is remarkably close to the observed propagation time in vivo (Fig. 5 “WT”). Indeed, recent single-molecule experiments have revealed that yeast condensin can extrude DNA loops with a velocity of up to $425 \text{ nm/s}$ [33]. These data combined with our simulations, strongly indicate that rapid re-organization of the chromosome by SMC condensin requires fast and active loop extrusion.

3 Discussion

Our computational framework reveals the basic physical requirements for condensins to collectively organize the bacterial chromosome as observed in live cells [11, 12, 6, 10]. In the presence of a specific loading site and with physiologically relevant numbers of condensins, we find that motor activity is required to robustly and rapidly generate a system-size spanning juxtaposition of the chromosomal arms. In contrast, purely diffusive condensins would require more kinetic fine-tuning and unphysiologically high copy numbers to organize the chromosome.

Our minimal model for the action of SMC condensin as a motor slip-link accounts for several key observations, including the rapid development of the juxtaposed state [12] and the crucial role of the ParBS nucleoprotein complex as a specific loading site [11, 12, 16, 6]. Without a well-defined loading site ($\Delta \text{ParB/S}$), motor slip-links still transiently organize the polymer into a juxtaposed state. However, the chromosomal fold diffuses along the chromosome, resulting in a structureless time-averaged contact map with enhanced long-range contacts (Fig. 2).
and SI 10). This may account for observations in E. coli, where the action of the SMC complex MukBEF does not seem to involve an exclusive loading site [15]. Indeed, Hi-C maps of E. coli do not display a cross-diagonal, but rather an elevated contact probability at large length-scales [15], in line with our simulations (Fig. 2 and SI 10).

Experiments of SMC condensin propagation in B. subtilis suggest that two condensin complexes might link together in a hand-cuff topology, with each of the two condensins in the dimer actively extruding a separate DNA duplex [12, 13]. In our model, motor slip-links extrude DNA in a symmetrical fashion, as expected for condensins in a hand-cuff configuration: both sides of a slip-link move over a separate DNA duplex with the same translocation rate. However, in recent in vitro assays, single yeast condensin complexes actively extrude DNA loops asymmetrically: one end of the complex appears anchored at a DNA locus, while the opposite end actively translocates over DNA [33]. Interestingly, contact maps of such asymmetric motor slip-links contain a star-shaped pattern around the loading site (SI 11), a feature that is also visible in Hi-C maps of B. subtilis [11, 6]. This suggests that there is at least some fraction of condensins performing asymmetric translocation. An equally tantalizing explanation is that the movement of one of the condensins in a dimer is impeded by other DNA-bound factors, thereby forcing a condensin-dimer to propagate asymmetrically. Indeed, there is growing evidence that the movement of SMC complexes can be antagonized by oncoming transcription factors [11, 13, 12].

It has also been suggested that the cylindrical geometry of many bacteria, combined with DNA–cell-pole tethering, facilitates chromosome organization [15, 46]. However, our simulations indicate that the effect of confinement alone on chromosome organization is weak, and hence cannot be solely responsible for the juxtaposed organization observed in live cells (SI 7). This is in line with the observation that mutants lacking SMC condensin, but with the ori-proximal loci still tethered to a cell-pole, also lack the cross-diagonal [12].

Our simulations further indicate that even purely diffusive slip-links with fast dissociation kinetics can induce arm-arm alignment, but at low slip-link densities this organized state remains localized near the loading site (SI 6). For a given number of condensins (3–30 per chromosome [25]), however, the slip-link density depends on DNA length. Therefore, we expect that a physiological number of non-motorized condensins can organize a mini-chromosome or plasmid of tens of microns in length. Indeed, plasmids are known to bind SMCs [47] and contain ParBS nucleoprotein complexes that could act as a condensin loading site [48].

Finally, our computational model can be used to unravel the function of juxtaposed organization in faithful chromosome segregation [49, 11, 50, 10, 17, 6, 51]. More broadly, we provide a framework to elucidate the role of loop-extruding enzymes and ATPases [40, 38, 50, 2, 15] on chromosome organization.

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Supplementary Information

1 Kinetic Monte-Carlo algorithm

Our lattice Kinetic Monte-Carlo (KMC) framework employs a Gillespie-type algorithm \[52\]. This KMC algorithm is schematically illustrated in Fig. S1 and consists of the following steps:

1. Construct initial configuration of the DNA polymer \{r_i\}

2. Build a rate catalog \(\Omega = \{(T_i, k_i)\}\) of all possible transitions \(T_i\) and their associated rates \(k_i\), with all transitions \(T_i\) assumed to be Poissonian. Next, enter the loop consisting of steps (a)–(e):

   (a) Randomly select one of the transitions \(T_j\) in \(\Omega\). The probability to perform transition \(T_i\) is \(k_i/\sum_i k_i\), which we implemented using tower sampling \[53\].

   (b) Update the KMC time \(t \rightarrow t + \Delta t, \Delta t = -\log r / K\), where \(r\) is a uniformly sampled random number \(r \in [0, 1]\) and \(K = \sum_i k_i\) is the total rate of the system \[52\].

   (c) Perform transition \(T_j\) that was selected in (a), which can affect the DNA polymer or the particles interacting with the polymer.

   (d) Update the entire rate catalog of possible transitions \(\Omega\) based on the transition \(T_j\) that was just performed. For more details, see section 1.1.

   (e) Return to step (a).

\[
\begin{align*}
\Omega = \{(T_i, k_i)\} & \quad \text{start with initial configuration} \\
r_1, r_2 \in [0, 1] & \quad \text{build a catalog of all possible transitions} \\
& \quad \text{select two random numbers} \\
& \quad \text{select process based on tower-sampling} \\
t \rightarrow t - K^{-1} \log(r_1) & \quad \text{update time} \\
& \quad \text{update lattice configuration} \\
& \quad \text{update catalog of transitions} \\
\Omega_{\text{old}} \rightarrow \Omega_{\text{new}} & \quad \text{perform } T_j \\
& \quad \text{perform } N \text{ times}
\end{align*}
\]

Fig. S1. Schematic illustration of KMC algorithm More details are found in section 1.1
1.1 Updating the KMC rate catalog

Every iteration of the KMC loop (see Fig. S1) requires an update of the rate catalog Ω. For computational efficiency we only update the part of the rate catalog \( \delta \Omega_j \in \Omega \) that is possibly affected by the previous transition \( T_j \). Let \( \Theta_j \) be the set of coordinates of monomers that are displaced by the transition \( T_j \). We update all coordinates \( q \) in the rate catalog that satisfy \( |p - q| \leq m \), \( p \in \Theta_j \), since our move set displaces particles by at most \( m = 2 \) lattice points (Fig. S2, "crankshaft").

1.2 Lattice KMC moves

The lattice KMC moves that we employ are illustrated in Fig. S2. Importantly, this move-set with local moves for the polymer dynamics is guaranteed to give rise to Rouse dynamics [42].

1.3 Justification of simulation units

Because cytosolic diffusion of condensin is fast compared to diffusion of condensin over dsDNA [43], we assume a regime in which the condensin binding rate is much higher than the slip-link movement attempt rate, \( k_+ \gg k_0 \). We implemented loading to the ParBS region [20] by binding slip-links only to a predetermined loading site (ori) on the polymer. Slip-links can, however, unbind anywhere on the DNA, as long as the slip-link encircles a loop of only one lattice width (Fig. S2).
1.3.1 Length of *B. subtilis* genome in simulation units

Each monomer size (i.e. the lattice constant $\ell_0$) in our lattice simulation is set equal to the persistence length of dsDNA, approximately 50 nm \[54\]. This is a convenient choice since the size of SMC condensin is also $\sim 25-50$ nm \[23, 31\], which we thus also take to be one lattice size. In these units, the *B. subtilis* genome of 4 Mbp (1.4 mm) \[26\] corresponds to $28 \times 10^3$ monomers.

1.3.2 Monomer relaxation time

The monomer relaxation time $\tau_{\text{monomer}}$ for a cylindrically shaped polymer bond, according to the Rouse model is \[55, 56\]

$$\tau_{\text{monomer}} = \frac{2 \pi a^2 b \eta}{k_B T} \approx 0.8 \mu s,$$

where $a \approx 50$ nm is the length of one monomer (SI 1.3.1), $b \approx 2$ nm is the radius of dsDNA \[57\], $k_B T \approx 4.2$ pN nm \[57\] and $\eta \approx 1$ mPa/s is the cytosolic viscosity \[58, 59, 60\].

1.3.3 Diffusion and translocation times of SMC complexes

The one-dimensional diffusion coefficient of dsDNA-bound cohesin (an SMC complex related to condensin \[61\]) at physiologically relevant salinity is $D \approx 1 \mu m^2/s$ \[43\], so that the diffusion time over one polymer bond of $a \approx 50$ nm \[54\] is approximately

$$\tau_{\text{diff.slip-link}} \approx \frac{a^2}{2D} \approx 1250 \mu s.$$

The average velocity of persistent motion of yeast condensin without the application of force is approximately $v \approx 1.25$ kbp/s $\approx 425$ nm/s \[33\]. This means that the average time to traverse one polymer bond by active translocation is

$$\tau_{\text{motor.slip-link}} \approx \frac{a}{v} \approx 0.12 \text{ s}.$$

2 Measurement of metrics from empirical data

2.1 Motor direction switching time in yeast condensin

*In vitro* DNA curtain experiments have shown that a fraction of condensins can reverse their active motion within a time $\tau_r$ \[32\]. In these experiments, the condensins can only be monitored over a maximum distance $L_{\text{assay}} = 16.49 \mu m$. The time a condensin can be observed to move with a constant velocity $v \approx 20$ nm/s is, therefore $t^* = L_{\text{assay}}/v \approx 825$ s \[32\]. In \[32\], the probability for the motor to be reversed at least once within this time $t^*$ has been measured to be $p_r(t^*) \approx 6\%$. Assuming Poissonian statistics, the probability of the condensin having reversed within a time $t^*$ is

$$p_r(t^*) = 1 - \exp(-t^*/\tau_r),$$

from which we estimate a typical switching time for yeast condensin $\tau_r \approx 222$ min. Based on a typical velocity of $v \approx 20$ nm/s \[33\], we estimate that a yeast condensin travels on average a distance $L_{\text{max}} = v \tau_r \approx 266 \mu m \approx 785$ kbp before switching direction. Crowding on the DNA by other proteins *in vivo* could affect these estimates.

2.2 Measuring propagation length of condensin in *B. subtilis*

We analyzed ChIP-seq data from \[26\] of the strains “WT” (wild-type), “ATP_−” (mutant with strongly suppressed ATP hydrolysis) and ΔParB (mutant without ParB). As a baseline for the SMC signal, we used the ΔParB data for both the WT and ATP_− strains and computed the difference in their SMC ChIP-Seq signals $c_{\text{SMC}}(i)$ (Fig. S3).

$$\Delta c_{\text{SMC,WT}}(i) = c_{\text{SMC,WT}}(i) - c_{\text{SMC,ΔParB}}(i)$$

$$\Delta c_{\text{SMC,ATP}_-}(i) = c_{\text{SMC,ATP}_-}(i) - c_{\text{SMC,ΔParB}}(i).$$
We then smoothed the data with a Savitzky-Golay-filter of window 21 and order 2 and extracted typical widths $\hat{X}_{SMC}$, defined as the standard deviation of the smoothed ChIP profiles. We computed the typical widths $\hat{X}_{SMC,WT} \approx 7000\ell_0, \hat{X}_{SMC,ATP_-} \approx 2000\ell_0$—or, when scaled by the system size $\hat{x}_{SMC,WT} \approx 13\%, \hat{x}_{SMC,ATP_-} \approx 45\%$.

2.3 Measuring condensin propagation timescale

Recent *in vivo* experiments have been performed in which ChIP-seq data was measured at various time-points after induction of SMC condensin [12]. From these ChIP-seq data, the typical width $\hat{X}_p(t)$ of condensin propagation was measured as a function of time. Since the curve of $\hat{X}_p(t)$ was well approximated by an exponential curve, we extracted a typical timescale of $\approx 24$ min from these curves (Fig. S4).

3 Measurement of metrics from simulation data

3.1 Measuring the loop network topology

We quantify the loop network topology using an order parameter $\theta \in [0,1]$ that measures the fraction of nested loops. This order parameter is defined for a slip-link–polymer network, so that we can measure $\theta$ for each time-point $t$, i.e. $\theta(t)$ is well-defined. Variances ($\text{var} \theta$) were computed as the variance of the time-sequence $\{\theta(t_1), \theta(t_2), \ldots\}$. Whenever we refer to $\theta$ in the main manuscript without explicit reference to the time-dependence, we imply $\theta = \langle \theta(t) \rangle$ where we used a time average for $\langle \cdot \rangle$. Below we have reproduced a pseudocode to measure $\theta$:

3.2 Determination of typical length of cross-diagonal

We first extract an ‘unprocessed’ cross-diagonal probability $p_{c,\text{unprocessed}}(k) \in [0,1]$ as illustrated in Fig. S5. Neither the moments $\langle k^n \rangle$ nor the $p-$th percentile of the ‘unprocessed’ distribution $p_{c,\text{unprocessed}}(k)$ correlated well with the

![Fig. S3. Determination of typical SMC propagation width from SMC ChIP-seq data.](#)

Top: Raw relative ChIP-seq data $c_{SMC}(i) - c_{SMC}(i/2N_m)$ (i.e. we subtracted the ChIP-signal at $ter$) of three strains from [26]: “WT” (wild-type, red), “ATP_” (mutant with strongly suppressed ATP hydrolysis, blue) and $\Delta$ParB (mutant lacking ParB, green). Bottom: We use the $\Delta$ParB signal as a baseline for the SMC ChIP-signal. The WT and ATP_ signals with the $\Delta$ParB signal subtracted (thin curves) and with an additional smoothing using a Savitzky-Golay filter (window: 21, order: 2) (thick curves). The typical width of these graphs was then defined as $\sqrt{\text{var}[c_{SMC}(i)]}$ (dotted vertical lines). Lengths are in units of polymer bond lengths $\ell_0 = 50$ nm (see section 1.3.1). ChIP-seq data were taken from the ArrayExpress database at EMBL-EBI (www.ebi.ac.uk/arrayexpress) under accession number E-GEOD-76949.
**Fig. S4.** The ChIP-seq data of the SMC condensin propagation width has a typical timescale of \( \approx 24 \) min. Fit parameters \( \tau \approx 24 \) min, amplitude \( \approx 1368 \) kbp were found by fitting the data from [12] with an exponential.

**Fig. S5.** Illustration of our procedure to extract the cross diagonal from a contact map. (a): A single contact map. (b): Make a \( 2 \times 2 \) tiling of contact maps. (c): Extract the 10 most central cross-diagonal rows (similar to the procedure published in [12] [10]). (d): Average the data from step (c) over the 10 rows, returning a cross-diagonal probability \( p_c(k) \) where \( k = -\frac{1}{2}N_m, \ldots, +\frac{1}{2}N_m \) is the distance from ori. In order to isolate the cross-diagonal from the rest of the contact map, we select the 10 most central rows from the contact map (i.e. \( |k| \leq 5 \)).

The cross-diagonal width based on visual inspection. The reason for this is that \( p_{c, \text{unprocessed}}(k) \) contains large flanks at \( |k| \approx N_m/2 \gg 1 \) (Fig. 5b) that were found to significantly impact estimates of \( X_c \).

The flanks in \( p_{c, \text{unprocessed}}(k) \) (Fig. 5b) arise due to the circular topology of the polymer, with an increasing contact probability for \( |k| \approx N_m/2 \gg 1 \). A naive estimate of the flanks is a power-law with Flory-scaling \( p_{c, \text{naive}} \sim (\frac{1}{2}N_m - |k|)^{d\nu}, d = 3, \nu \approx 3/5 \) [62]. Subtracting this naive estimate from \( p_{c, \text{unprocessed}}(k) \), was found to sometimes lead to negative probabilities. To avoid this, we instead subtracted an underestimate of the flanks, namely a power-
Input: slip-link sites \{(i, j)_n\}, \(n = 1, \ldots, N_p\) (with \(N_p\) the number of slip-links).

Output: loop network topology order parameter \(\theta \in [0, 1]\)

\[n_{\text{nested}} \leftarrow 0;\]

\textbf{for } \(n \leftarrow 1 \text{ to } N_p\) \textbf{do}

\begin{enumerate}
    \item get slip-link sites \((i_n, j_n)\) of slip-link \(n\);
    \item compute self-loop-size of slip-link \(n\): \(\Delta_{\text{self}} \leftarrow |i - j|\);
    \item get sites \((i, j)_{n-1, n+1}\) of neighboring slip-links \(n-1, n+1\);
    \item compute nested-loop-size between slip-link \(n\) and \(n-1, n+1\):
        \[\Delta_{(n,n-1)} = |i_n - i_{n-1}| + |j_n - j_{n-1}|,\]
        \[\Delta_{(n,n+1)} = |i_n - i_{n+1}| + |j_n - j_{n+1}|;\]
    \item \(\Delta_{\text{nested}} \leftarrow \min(\Delta_{(n,n-1)}, \Delta_{(n,n+1)})\);
    \item \textbf{if } \(\Delta_{\text{nested}} < \Delta_{\text{self}}\) \textbf{then}
        \[n_{\text{nested}} \leftarrow n_{\text{nested}} + 1;\]
    \end{enumerate}

\textbf{end}

\[\theta \leftarrow n_{\text{nested}}/N_p;\]

\textbf{return } \theta

\textbf{Algorithm 1:} Pseudocode for computing the loop-network order parameter \(\theta\). In this algorithm, we use the convention \(|\Delta| = \min(\Delta, N_m - \Delta)|.

law with 50% stronger scaling than the naive estimate: \(p_{c,\text{underest.}}(k) \sim \left(\frac{1}{2}N_m - |k|\right)^{-1.5d - \nu} \leq p_{c,\text{naive}}\) (Fig. S6, compare black and blue histograms). By visual inspection on a variety of representative test-cases, we found that this method indeed suppressed the flanks of \(p_{c,\text{unprocessed}}(k)\), but left the cross-diagonal itself intact (Fig. S6, blue histogram).

After subtracting the flanks from \(p_c(k)\) (Fig. S6 blue histogram), we calculate the typical length \(X_{c,p} = \frac{1}{2}n_p^k\) with parameter \(p\) as the \(p\)-th percentile of the distribution \(p_c(k)\). We computed various percentiles \(\{m_{50\%}, m_{75\%}, m_{90\%}, m_{95\%}\}\) on a representative collection of contact maps and empirically found by visual inspection that \(m_{75\%}\) was a good measure for the typical length of the cross diagonal in contact maps.

4 Universal scaling of slip-link propagation length for diffusive slip-links

The propagation length \(\hat{X}_p\) and the number of slip-links \(\hat{N}_p\) depend on \(N_m\) (Fig. S7 left). For diffusive slip-links in the regime of fast dissociation kinetics, the relation between their scaled intensive counterparts \(\hat{X}_p = \hat{X}_p/N_m, \hat{\phi}_p = 2\hat{N}_p/N_m\) appear to be described by a single master curve (Fig. S7 right).

5 Universal scaling of the translocation rate of motor slip-links

What is the relationship between the slip-link translocation attempt rate \(k_{\text{motor}}\), the monomer diffusion attempt rate \(k_0\), the polymer size \(N_m\), and the effective motorized slip-link translocation velocity \(v_{\text{motor}}\)? To answer this question, we distinguish two regimes: a fast relaxation regime \(k_{\text{motor}} \ll k_0\) and a slow relaxation regime \(k_{\text{motor}} \gg k_0\). In both regimes, for a stiff slip-link to make a step, the two polymer bonds in the direction of movement need to be parallel (Fig. S8). If we denote the prior probability of observing these two polymer bonds to be parallel by \(C \approx 3/16\) (Fig. S8), then the effective rate of bond–bond alignment is \(k_0^{\text{eff}} \approx Ck_0\). Hence, the characteristic rate \(k_{\text{motor}}^*\) that sets the transition from the fast relaxation to the slow relaxation regime occurs at \(k_{\text{motor}}^* = k_0^{\text{eff}}\). Consistent with
the prediction that $k_{\text{motor}}$ only depends on local kinetics, our data shows that $k_{\text{motor}}$ is independent of the system size (Fig. S10).

In the fast relaxation regime, the rate-limiting factor is $k_{\text{motor}}$. In this case, the velocity of slip-links is approximated by $v_{\text{motor}} \approx C\ell k_{\text{motor}}$. As already stated, the fast relaxation regime transitions into the slow relaxation regime at $k_{\text{motor}}^* = k_{\text{eff}}^0$, where the movement of motor slip-links becomes limited by polymer relaxation so that $v_{\text{max}} = C(k_{\text{motor}}^* = C^2\ell k_0)$.

This heuristic argument suggests that the scaling form of dimensionless variables $\tilde{v} \equiv v/(\ell k_0)$, $\tilde{k} \equiv k_{\text{motor}}/k_0$ will collapse the data of $k_{\text{motor}}, v, k_0$ onto a universal curve $\tilde{v} = C\tilde{k}$ for $\tilde{k} < C$ and $\tilde{v} = C^2$ for $\tilde{k} \geq C$. Indeed, our numerical data is well-described by this scaling (Fig. S9–c). By combining in vitro with in vivo empirical data, we estimate that SMC condensin in B. subtilis is well within the fast relaxation regime $k_{\text{motor}} < 10^{-5}k_0 \ll k_0$ (Fig. S9c, “WT”).

6 Stability of juxtaposed organization by diffusive slip-links

To investigate the stability of the juxtaposed state with diffusive slip-links, we prepared a polymer in a juxtaposed organization. This was achieved by positioning immobilized slip-links at regular intervals along the polymer but nevertheless allowing for polymer relaxation (Fig. S10). After we turned on slip-link movement, we recorded kymographs of the cross-diagonal.

Kymographs clearly reveal that the cross-diagonal in the regime of slow dissociation propagates away from the loading site (Fig. S10b). The region around ori in the contact maps slowly loses the anomalously high contact probabilities over time, meaning that the cross-diagonal disappears for diffusive slip-links in the slow dissociation regime. For slip-links in the fast dissociation regime, however, the cross-diagonal persists and remains stable over time for $N_p$ above a critical value (Fig. S10c). Ensemble averaged movies of contact maps for $N_p = 1, 2, 4, 8, 16, 32$ confirm that the cross-diagonal only persists in the fast dissociation regime (SI movies 4[a-f] for fast dissociation and 5[a-f] for slow dissociation).

Fig. S6. Computation of the length of the cross-diagonal using the $p$–th percentile. We first measured the ‘unprocessed’ cross-diagonal contact probability $p_{c,\text{unprocessed}}(k)$ from contact maps (black, see Fig. S5 for the procedure). Then, we subtract an estimate for the left and right flanks (blue, see section 3.2) and computed the $p$–th percentile $m_p$ of $p_c(k)$. The half-width of the $p$–th percentile $\frac{1}{2}m_p$ is shown for $p = 50, 75, 90, 95\%$ (blue vertical lines, from left to right), and the typical width of the curve is defined as $X_c \equiv \frac{1}{2}m_p$. 

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maximum number of slip-links  $\hat{N}_p$

slip-link propagation length  $\hat{X}_p$

maximum slip-link density  $\hat{\phi}_p$

rescaled slip-link propagation length $\hat{x}_p$

7 Cell anisotropy and confinement does not explain juxtaposed organization

To investigate the role of an anisotropic confinement on the cross-diagonal, we use an ellipsoidal harmonic potential,

$$V_{\text{conf.}}(x, y, z) = \frac{1}{2} \left( k_x x^2 + k_y y^2 + k_z z^2 \right),$$

where the $k_{x,y,z}$ specify the ‘spring-constants’ of the confinement for monomers with positions $x, y, z$. The ellipsoidal potential simulates the combined action of the cell membrane and crowding agents. We assume cylindrical symmetry $x^2 = y^2 = r^2$ where $r$ is the radius of the cylindrical confinement. We use a length-to-width ratio of 4, slightly larger than the typical length-to-width ratio $\approx 3$ of many bacteria [37].

We additionally include a spring-like tether capturing the effect of proteins, such as DivIVA in $B. subtilis$ and PopZ in $C. crescentus$, that localize ori to one of the cell poles [1]. We use equilibrium Monte-Carlo simulations [27] to investigate the organization of DNA in the presence of a confinement potential and tether. We find that the contact maps do not exhibit a cross-diagonal. The confinement potential does result in a slight asymmetry in the contact maps that increases weakly with the number of slip-links $N_p$ (Fig. S11a–b). This slight asymmetry resembles a cross-diagonal under conditions of large $N_p$ and small polymer-length $N_m$, but only becomes visually apparent in
Fig. S9. (a): The average motor velocity (error bars: standard deviation) for various translocation attempt rates (turquoise to dark blue, \( k_{\text{motor}} = 100 \ldots 0.01 \)) and various system sizes \( N_m \). We shifted the datapoints for decreasing \( k_{\text{motor}} \) to increase clarity of the data; the value of \( N_m \) used is always the datapoint corresponding to \( k_{\text{motor}} = 100 \) (turquoise). There is a clear dependency of \( v \) on \( k_{\text{motor}} \), but not on \( N_m \). (b): Unscaled data of the motor velocity versus the translocation attempt rate \( k_{\text{motor}} \) and versus the monomer diffusion attempt rate \( k_0 \) (inset). For these data, we used a range of system sizes \((N_m = 20 \ldots 200)\) and monomer diffusion attempt rates \((k_0 = 0.02 \ldots 5)\). (c): Expressing dynamics of the motor slip-links as dimensionless variables collapses the data onto a single master-curve (error bars: twice the standard deviation). Estimate of master curve (solid black line, see text) is indicated in the graph, where the critical motor movement attempt rate \( \tilde{k} = C \) \((C = 3/16, \) dashed vertical, see Fig. S8) separates the “fast relaxation” and “slow relaxation” regimes. Propagation of wild-type condensins (“WT” marker, inset) is within the “fast relaxation” regime. Data for “WT” was calculated using \( k_{\text{motor}} = 425 \text{ nm/s/}\ell \) \([33]\) where \( \ell = 50 \text{ nm}\) \([54]\), \( k_0 = 1.25 \mu s^{-1} \) \((\text{section 1.3.2})\) and \( \tilde{v} = v/\ell k_0 \) with \( v = 46 \text{ kbp/min} \) \([12]\) so that \( \tilde{k} = 6.8 \times 10^{-6}, \tilde{v} = 4 \times 10^{-6} \).

Fig. S10. The juxtaposed organization is only stable for fast dissociation kinetics. (a): Illustration of our simulation to text the stability of the juxtaposed organization. We first initialize a polymer in the juxtaposed organization with immobilized diffusive slip-links, but allow for polymer relaxation. We then turn on slip-link diffusion along the polymer, and recorded kymographs of the cross-diagonal from contact maps. (b): Kymograph of the cross-diagonal for slow dissociation kinetics. The cross-diagonal disappears over time (see also SI movies 5[a–f]). (c): Kymograph of the cross-diagonal for fast dissociation kinetics. The cross-diagonal persists (see also SI movies 4[a–f]). For both kymographs (b-c) we used \( N_m = 200, N_p = 32 \).

our contact maps when the density of slip-links is 10%, 100 times higher than the SMC condensin density in vivo \([25]\). Even so, even at this unphysiologically high concentration of slip-links, the asymmetry in the contact maps is very diffuse compared to that of the in vivo Hi-C maps (Fig. S11[b–c]). The width of the off-diagonal structure broadens as we increase \( N_m \). Indeed, the cross-diagonal for \( N_m = 200 \) is only clearly resolved when we increase the asymmetry of the confinement potential to unrealistically high values \( \sqrt{z^2/r^2} > 30 \) (Fig. S11[c–d]). In sum, our simulations indicate that ellipsoidal confinement and tethering alone cannot be responsible for a cross-diagonal.
Fig. S11. Physiologically relevant confinement potentials do not result in a cross-diagonal. (a–b): contact maps from polymers with $N_p = 0$ (a) and $N_p = 100$ (b) equilibrium slip-links with a confinement potential of widths $(\sqrt{x^2}, \sqrt{y^2}, \sqrt{z^2}) = (5\ell_0, 5\ell_0, 20\ell_0)$, where $\ell_0$ is the monomer length. Polymer length $N_m = 2000$. (c–d): Simulation with a confinement potential of anisotropy ratio $\sqrt{100} \approx 31.6$. Polymer length $N_m = 200$. See SI movie 6 for a movie of the polymer for various other anisotropies.

8 Relationship between $\theta$, $\hat{X}_p$ and $\hat{X}_c$

Our simulations reveal that the cross-diagonal length $\hat{x}_c$ is well approximated by an ‘and-gate’ of $\theta$ and $\hat{x}_p$ (Fig. S12). This shows that one needs cooperative loops (high $\theta$) that also propagate deep into the bulk of the polymer (high $\hat{x}_p$).

Fig. S12. The relative cross-diagonal width is $\approx \text{const.} \theta \hat{x}_p$ with const. = 1.3. Error bars: standard deviation $\sqrt{\text{var} \hat{x}_c}$. 
9 Loop topology of polymers with diffusive slip-links

9.1 Non-specific binding (ΔParB/S) and exclusive binding in the slow dissociation regime

We implemented a system with diffusive slip-links that can bind and unbind anywhere (ΔParB/S), so that this system obeys detailed balance and hence relaxes into thermodynamic equilibrium. The scaling we observe for the ΔParB/S scenario \( p \sim \Delta^{1.7} \) (Fig. S13a, left) is nearly identical to that of a random polymer \( p \sim \Delta^{\nu}, \nu \approx 1.8 \) [62].

The distribution of \( \theta \) is highly peaked at \( \theta = 0 \), showing that the diffusive slip-links almost always enclose self-loops and almost never enclose nested loops (Fig. S13a, right). The system with diffusive slip-links that can only bind to the loading site breaks detailed-balance, but we find that for slow dissociation kinetics, the resulting distribution of loop-sizes \( p \sim \Delta^{1.8} \) is nevertheless consistent with that of a random polymer (Fig. S13b).

Fig. S13. Left panels: Contact distribution \( p(\Delta) \) for loop-size \( \Delta \). Right panels: Distributions \( p(\theta) \) of loop nesting parameter \( \theta \). (a): Diffusive slip-links that bind non-specifically to the polymer (ΔParB/S). (b): Diffusive slip-links that bind exclusively to the loading site, but with slow dissociation kinetics (\( k_- = 10^{-6}k_0 \)).

9.2 Exclusive loading site, arbitrary dissociation kinetics

When increasing the dissociation kinetics, we observe a sigmoidal increase of \( \langle \theta \rangle \) to a \( \theta_{\text{max}} \) at \( k_- \to \infty \). \( \theta_{\text{max}} \) tends to 1 as we increase the system size (Fig. S14).

Fig. S14. There is a sigmoidal relation between \( \theta \) and \( k_- \) and \( \theta_{\text{max}} \to 1 \) as \( N_m \to \infty \). We define \( \theta_{\text{max}} \) as the the saturating value of \( \theta \) as \( k_- \to \infty \) (inset). As the system size \( N_m \to \infty \), we observe \( \theta_{\text{max}} \to 1 \) (main plot).

We can understand the relationship between \( \theta \) and \( k_- \) by constructing a simple mean-field model. In particular, we model the loop topology of the slip-links as \( N_p \) uncorrelated two-state systems: (i) self-loops (S) with a lifetime
\( \tau_S \); (ii) nested loops (NS) with a lifetime \( \tau_{NS} \). The fraction of nested loops \( \langle \theta \rangle \) is simply the weighted lifetime of a nested loop:

\[
\langle \theta \rangle = \frac{p_{0,NS}\tau_{NS}}{p_{0,NS}\tau_{NS} + p_{0,S}\tau_S},
\]

where the \( p_{0,S}, p_{0,NS} \) are the probability for a diffusive slip-link to enclose a self, nested loop after loading to ori. The lifetime of a self-loop is \( \tau_S = k_0^{-1} \).

We estimate the lifetime of a nested loop by

\[
\tau_{NS} \approx \frac{1}{2}N_m \langle v \rangle + k_0^{-1},
\]

where \( \langle v \rangle \) is the mean velocity of a slip-link moving through the bulk of the polymer. Since the nested loops propagate ballistically in the high density phase (Fig. S15, inset; SI movie 3b), there exists a well-defined velocity, but this velocity \( \langle v \rangle \) does depend on the system size. In particular, we empirically find for \( \phi_p = 0.4 \) that \( \langle v \rangle \approx c k_0/N_m^2 \) where \( k_0 \) is the slip-link movement attempt rate and \( c \approx 9 \) (Fig. S13). This \( 1/N_m^2 \) scaling is distinct from the \( 1/N_m \) scaling observed in the Simple Symmetric Exclusion Process [63], likely due to the presence of polymer loop entropy that impedes the movement of slip-links away from the loading site.

**Fig. S15.** Tracer slip-links propagate over a polymer in the juxtaposed state with a velocity \( \langle v \rangle \sim 1/N_m^2 \). Main panel: Averaged velocities of tracer slip-links \( \langle v \rangle \) (markers) for different system sizes \( N_m \) as indicated (error bars: twice the standard error in the mean). A power-law \( \langle v \rangle \approx 9 k_0/N_m^2 \) agrees well with the data (dashed). The data in this graph were computed in the high-density and fast-dissociation regime \( \phi_p = 0.4, k_- = k_0 \). Inset: Individual trajectories of diffusive slip-links \( l(t) \) were collected (thin, gray), where \( l(t) \) is the distance traversed by a tracer slip-link at time \( t \) after it was loaded onto the polymer. The ensemble-averaged trajectory \( \langle l(t) \rangle \) (thick, blue; shaded region is the standard deviation) was computed by binning the trajectories. The average velocity is defined as \( \langle v \rangle = \langle l(t_{\max}) \rangle/t_{\max} \) (blue, dashed).

In sum, our estimate for \( \langle \theta \rangle \) is

\[
\langle \theta \rangle \approx \frac{1}{2}\frac{C}{3} \left( \frac{1}{2}C N_m^3 k_0^{-1} + k_-^{-1} \right) + \left( 1 - \frac{1}{2}C \right) k_-^{-1}.
\]

(1)

Given an estimate of \( c \) from a measurement of \( \langle v \rangle \) (Fig. S15), this form for \( \langle \theta \rangle \) does not contain any free fit-parameters, and collapses data for various \( N_m, k_- \) onto a single master curve (Fig. S16).

10 Diffusing cross-diagonal for motor slip-links without a loading site

Time-averaged contact maps of a polymer with motor slip-links but no loading site (\( \Delta ParB/S \)) are, apart from the main diagonal, homogeneous. Upon closer inspection, however, movies of the contact maps (SI movie 7a) suggest
Fig. S16. A single master curve approximately describes the fraction of loops. Main panel: Loop parameter $\langle \theta \rangle$ (markers) for different system sizes $N_m$ as indicated (error bars: standard deviation $\sqrt{\text{var} \theta}$). All data were measured in the high-density regime ($\phi_p = 0.4$ for $N_m = 20, 40, 200$ and $\phi_p = 0.38$ for $N_m = 100$). A mean-field-theoretical estimate (equation (S1)) describes these data well (solid curves). Inset: The mean-field-theoretical estimate for $\theta$ (equation (S1)) collapses the data onto a single master-curve $x/(1+x)$. The reduced parameters in this graph are: $\bar{\theta} = (\theta - \theta_{\text{min}})/(\theta_{\text{max}} - \theta_{\text{min}}), \theta_{\text{max}} = 1, \theta_{\text{min}} = 1/3C$ and $x = \frac{C}{3-C}(\frac{1}{2}CN^3 \tilde{k} - k_0 + 1)$ that scales as $x \sim N^3_m k_0$ for $N_m \gg 1$.

Fig. S17. Left panels: Representative contact map at a time $t$ averaged over a time-interval $\Delta t$. Right panels: The Hough transform of the contact map. (a): Simulation was performed with $\hat{N}_p = 1$ with persistence time $\tau_{\text{switch}} = 10^{-3}$. (b): Simulation was performed with $\hat{N}_p = 2$ with persistence time $\tau_{\text{switch}} = 10^{-3}$. The Hough transforms in (b) displays an additional locus in the area $\theta = 40^\circ \cdots 50^\circ, r = 14 \cdots 42\text{ px}$. This locus diffuses randomly over time (inset).
11 The impact of asymmetrical translocation on chromosome organization

We implemented asymmetric active translocation or loop extrusion as detailed below (see SI movie 9 for the dynamics of a loop diagram and the contact map in Fig. S18):

1. A slip-link is added to the loading site
2. One of the two sides of the slip-link is immobilized
3. The side of the slip-link that is not immobilized is assigned a random translocation direction (i.e. positive or negative).

Fig. S18. Asymmetric loop extrusion results in a star-shaped pattern in contact maps. For these data, we bound one asymmetric highly persistent motorized slip-link to the loading site. Note, in this simulation, none of the slip-links perform symmetric loop extrusion, which is the type of motor activity discussed in the main text.

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## Supplementary Movies

All movies can be found at [https://syncandshare.lrz.de/filestable/MiNmZTluQ2pDc0RkYWNhQ2NrQ3JH](https://syncandshare.lrz.de/filestable/MiNmZTluQ2pDc0RkYWNhQ2NrQ3JH)

| Movie No. | Filename | Description |
|-----------|----------|-------------|
| 1 | SI_movie_1_random.mov | Rotating a polymer with diffusive slip-links and slow dissociation. The resulting 3d configuration looks like that of a random polymer. |
| 2 | SI_movie_2_juxtaposed.mov | Rotating a polymer with diffusive slip-links and fast dissociation. The resulting 3d configuration has a juxtaposed organization. |
| 3a | SI_movie_3a_contact_map_dynamics_diffusive_SLs.mov | A high density of diffusive slip-links with fast dissociation with an origin (ParBS) structure contact maps in our simulations, effecting a robust cross-diagonal. |
| 3b | SI_movie_3b_chord_diagram_dynamics_diffusive_SLs.mov | Same simulations and data as SI movie 3a, but now we visualize the loop diagram dynamics. Timescale of this movie is the same as in SI movie 3a. |
| 4[a–f] | SI_movie_4[a–f].mov | We first immobilized the diffusive slip-links and positioned them at sites with regular intervals. After the polymer relaxed into an equilibrium configuration, we turned on fast slip-link diffusion with \( k_- = k_0 = 1 \) and made movies of the contact maps. Movies 4a,b,c,d,e,f have a number of slip-links respectively \( N_p = 1, 2, 4, 6, 16, 32 \). |
| 5[a–f] | SI_movie_5[a–f].mov | We first immobilized the diffusive slip-links and positioned them at sites with regular intervals. After the polymer relaxed into an equilibrium configuration, we turned on slow slip-link diffusion with \( k_- = 10^{-6} k_0 \) and made movies of the contact maps. Movies 5a,b,c,d,e,f have a number of slip-links respectively \( N_p = 1, 2, 4, 6, 16, 32 \). |
| 6 | SI_movie_6.mov | Equilibrium Monte-Carlo simulations of a polymer of length 200 in potential of increasing anisotropy as simulation time progresses. Length to radius anisotropy is \( 1, \sqrt{8}, 8, \sqrt{1000} \). |
| 7a | SI_movie_7a.mov | Movies of contact maps of two motor slip-links with a switching rate of \( 10^{-3} \) times the motor stepping rate, i.e. \( k_{\text{switch}} = 10^{-3} k_{\text{motor}} \). |
| 7b | SI_movie_7b.mov | Same data as movie 7a, but now the dynamics of the loop diagram. |
| 8 | SI_movie_8.mov | Same data as from movie 7. We visualized the Hough transform over time. The stationary and prominent locus around \( -45^\circ \) measured the strength of the main diagonal, whereas the locus around \( +45^\circ \) quantifies the cross-diagonal. The dynamics of the Hough transform shows that the cross-diagonal diffuses over a variety of positions. |
| 9 | SI_movie_9.mov | Loop diagram of asymmetric loop extrusion was implemented as a persistent random walker with one of the two sides of the slip-link immobilized. Both the side and the direction of movement were chosen randomly. |
| 10a | SI_movie_10a.mov | Movies of contact maps of 10 motor slip-links on a polymer of length \( N_m = 80 \) for a motor switching rate of \( k_{\text{switch}} = 0.0001 k_{\text{motor}} \). |
| 10ab | SI_movie_10b.mov | Movies of contact maps of 10 motor slip-links on a polymer of length \( N_m = 80 \) for a motor switching rate of \( k_{\text{switch}} = k_{\text{motor}} \). |