Confinement-induced glassy dynamics distinguishes chromosome organization across organisms

Supplemental Material

Hongsuk Kang,[1] Young-Gui Yoon,[2] D. Thirumalai,[1] and Changbong Hyeon[3]

[1]*Institute for Physical Sciences and Technology, University of Maryland, College Park, MD 20742*

[2]*Department of Physics, Chung-Ang University, Seoul 156-756*

[3]*Korea Institute for Advanced Study, Seoul 130-722*

Model. In order to assess the conditions describing the onset of glassy dynamics of a confined flexible polymer we introduce a model in which the potential energy is given by

$$\begin{aligned} U(\vec{r}_1,...,\vec{r}_N) &= \sum_{i=1}^{N-1} U_i^{\rm bond} + \sum_{i=1}^{N-1}\sum_{j=i+1}^{N} U_{i,j}^{\rm ex} + \sum_{i=1}^{N} U_i^{\rm surf} \\ &= \frac{k}{2}\sum_{i=1}^{N-1}\frac{(|\vec{r}_{i+1}-\vec{r}_i|-a)^2}{a^2} \\ &+ \sum_{i=1}^{N-1}\sum_{j=i+1}^{N}\epsilon\left(\frac{a}{|\vec{r}_i-\vec{r}_j|}\right)^{12} \\ &+ \sum_{i=1}^{N} 4\epsilon\left(\frac{a}{R_s-|\vec{r}_i|}\right)^{12}, \end{aligned} \tag{1}$$

where a is a bond length, $k = 80\,k_{\rm B}T$, $\epsilon = 2\,k_{\rm B}T$, $\vec{r}_i$ is the position of the i^{th} monomer. To model the effect of confinement we placed the polymer chain in a sphere surface of radius R_s. The interaction between the monomers and the sphere surface is repulsive, given by the last term in Eq.(1).

We performed Brownian dynamics simulations of a self-avoiding polymer under spherical confinement with N = 50, 75, 100, 125, 150, 200, 250, and 300 by integrating the following equations of motion,

$$\zeta\frac{d\vec{r}_i}{dt} = -\nabla_{\vec{r}_i}U(\vec{r}_1,\cdots,\vec{r}_N) + \vec{\Gamma}_i(t), \tag{2}$$

where $\vec{\Gamma}_i(t)$ is the Gaussian random force satisfying the fluctuation-dissipation theorem, $\langle\vec{\Gamma}_i(t)\cdot\vec{\Gamma}_j(t')\rangle = 6k_{\rm B}T\zeta\delta(t-t')\delta_{ij}$. With the Brownian time defined as $\tau = a^2/D$ where $D = k_BT/\zeta$, we chose the integration time step $\delta t = 8.6\times10^{-6}\ \tau$ as a compromise between accuracy and computational cost.

For eukaryotic genome, $D = \frac{k_BT}{6\pi\eta(a/2)} = \frac{4.14pN\cdot nm}{6\pi\times(0.89\times10^{-3}N/m^2\cdot sec)\times10nm} \approx 250\ \mu m^2/s$ with $\eta = 0.89\times10^{-3}Pa\cdot s$ and $a\approx20$ nm; and hence we set $\tau = a^2/D \approx 1.6\ \mu s$ and $\delta t \approx 13.7$ ps.

We gradually reduced R_s from $4R_g$ to the value at which τ_α or $\chi_4^{\rm max}$ (see Eqs. (2) and (3) in the main text) starts to diverge. Although the detailed procedure of reducing the confinement size R_s varies with N, the rate of R_s reduction $r = \Delta R_s/\Delta t \sim 0.15\ (R_s/a)/(2\times10^8\times\delta t)$ is almost identical for all N when R_s approaches to the point of dynamical arrest. The R_s values varied in the simulations are listed in Table I, and the time-dependent protocol of reducing R_s is plotted in Fig. S1. At each $R_s^{(i)}$, we simulated for $2\times10^8\ \delta t$ and took the last conformation from the previous simulation at $R_s^{(i-1)}$ as the initial conformation for simulation in $R_s^{(i)}$. We reduced R_s from $R_s^{(i-1)}$ to $R_s^{(i)}$ linearly for $2\times10^4\delta t$, allocated the next $2\times10^6\ \delta t$ for an equilibration, and used the rest of 2×10^8 steps to calculate $F_{q_{\rm max}}(t)$ and $\chi_4^{\rm max}$. We generated 10 independent trajectories for $N \le 150$ and 25 for $N \ge 200$ to improve the quality of statistics.

It is worth emphasizing that the critical volume fraction ϕ_c is robust and insensitive to the range of confining speed. To show this, we used two different confining speeds for a polymer with $N = 150$: one is $r_f = -0.30(R_s/a)$/step, 2 times faster than r and the other is $-0.10(R_s/a)$/step, 1.5 times slower than r. Both from τ_α using $F_q(t)$ and $\chi_4^{\rm max}$, we obtained $\phi_c = 0.383$ for both quenched and annealed cases, which is in full agreement with the regular case (see Fig.S2).

Volume fraction of a confined polymer. When a polymer is confined to a sphere with radius R_s, the size of the polymer R_g^c can be related to the radius of gyration for polymer in free space (R_g^o) via the following scaling relation with $x = R_g^o/R_s$:

$$R_g^c = R_g^o f(x). \tag{3}$$

(i) Under weak confinement ($x \ll 1$), corresponding to large R_s, the chain statistics will be unaltered $R_g^c \sim R_g^o \sim N^\nu$ with $\nu = 3/5$, and thus $f(x) \sim$ constant. (ii) In contrast, a strong confinement ($x \gg 1$) induces polymer collapse, so that $R_g^c \sim N^{1/d}$ and $f(x) \sim x^p$. From $N^{1/d} \sim N^\nu(N^\nu/R_s)^p$, the exponent p ought to be $p = (d\nu)^{-1} - 1$. Therefore, substituting $R_g^o = aN^\nu$ where a is the Kuhn length, one gets $R_g^c = R_s(a/R_s)^{1/d\nu}N^{1/d}$.

A definition of polymer volume fraction (ϕ) using the ratio between R_g^c and R_s, $\phi = (R_g^c/R_s)^d$ gives distinct

N	50	75	100	125	150	200	250	300
$i=1$	$R_s = 10a$	$10a$	$10a$	$10a$	$10.8a$	$13.3a$	$13.3a$	$13.3a$
2	$9.2a$	$9.2a$	$9.2a$	$9.2a$	$9.2a$	$11.7a$	$11.7a$	$11.7a$
3	$8.3a$	$8.3a$	$8.3a$	$8.3a$	$8.3a$	$10.8a$	$10.8a$	$10.8a$
4	$7.5a$	$7.5a$	$7.5a$	$7.5a$	$7.5a$	$9.2a$	$9.2a$	$9.2a$
5	$6.7a$	$6.7a$	$6.7a$	$6.7a$	$6.7a$	$8.3a$	$8.3a$	$8.3a$
6	$5.8a$	$5.8a$	$6.2a$	$6.2a$	$6.2a$	$7.5a$	$7.5a$	$7.5a$
7	$4.3a$	$4.3a$	$5.8a$	$5.8a$	$5.8a$	$6.7a$	$6.7a$	$6.7a$
8	$4a$	$4a$	$5.5a$	$5.5a$	$5.5a$	$6.3a$	$6.3a$	$6.3a$
9	$3.7a$	$3.7a$	$5a$	$5a$	$5a$	$6a$	$6a$	$6a$
10	$3.3a$	$3.3a$	$4.7a$	$4.7a$	$4.7a$	$5.7a$	$5.7a$	$5.7a$
11	$3a$	$3a$	$4.3a$	$4.3a$	$4.3a$	$5.3a$	$5.3a$	$5.3a$
12	2.7a	2.7a	$4a$	$4a$	$4.2a$	$5a$	$5a$	$5a$
13	2.5a	2.5a	$3.7a$	$3.7a$	$3.8a$	$4.7a$	$4.7a$	$4.7a$
14	2.3a	2.3a	$3.3a$	$3.3a$	$3.3a$	$4.3a$	$4.3a$	$4.3a$
15	2.2a	-	$3a$	3a	$3.2a$	$4.2a$	$4.2a$	$4.2a$
16	2a	-	$2.7a$	2.8a	$3a$	$4a$	$4a$	$4a$
17	-	-	-	2.5a	-	$3.7a$	$3.7a$	$3.8a$
18	-	-	-	-	-	-	-	$3.7a$

TABLE I: R_s values used for the simulations with various N. In the table, a is the monomer-monomer distance. R_s was sequentially reduced from $i = 1$ to $i = i_{\max}$ according to the procedure described in the SI text. The initial conformation was taken from the last conformation of the previous run except $i = 1$ where we generated unconstrained chain conformation. We set $R_s^{(0)}$ to four times the R_g of the unconstrained chain, and slowly decreased $R_s^{(0)}$ to $R_s^{(1)}$.

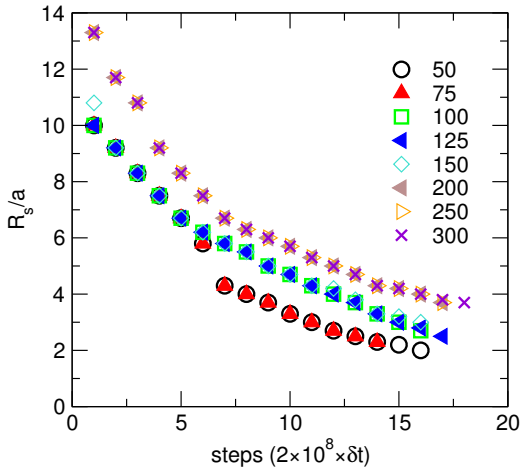

FIG. S1: The protocol used to reduce the confinement size (R_s) for different N. The reduction rate of confinement size near the dynamical arrest point is similar for all N as $r \sim -0.15(R_s/a)$/step.

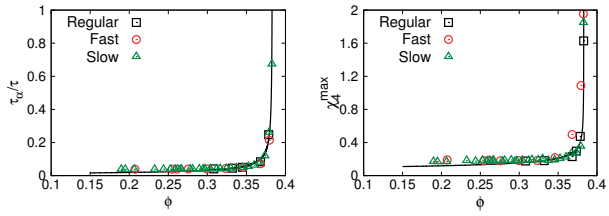

FIG. S2: Robustness of ϕ_c value for different reduction rate of confinement size. In the legend, "Fast" denotes the faster confining speed; "Slow" is for the slower one; and "Regular" is the speed used in Table 1. Black lines are the fits for the values obtained at the regular speed. In all cases, we obtained $\phi_c = 0.383$ for $N = 150$.

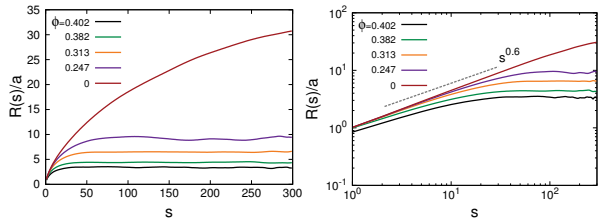

FIG. S3: Mean spatial distance of polymer with $N = 300$ as a function of intersegmental separation s for varying volume fraction ϕ. Log-log plot is shown on the right panel with the dotted line expected for the scaling of SAW ($R(s) \sim s^{0.6}$). Note that the condition of confinement ($R_g^o > R_s$) trivially gives rise to the plateauing of $R(s)$ [1, 2].

scaling of ϕ with N, depending on the strength of confinement:

$$\phi = \left(\frac{R_g^c}{R_s}\right)^d = \begin{cases} \left(\frac{a}{R_s}\right)^d N^{\nu d} : (\text{weak, } R_g^o \ll R_s) \\ \left(\frac{a}{R_s}\right)^{1/\nu} N : (\text{strong, } R_g^o \gg R_s) \end{cases} \quad (4)$$

where $1/\nu = d$ for the case of strong confinement. Note that this definition of ϕ is invariant under coarse-graining.

Radial distribution function. We used

$$g(r) = \frac{2}{N(N-1)} \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \delta(|\vec{r}_i - \vec{r}_j| - r) \quad (5)$$

to capture the extent of packing between monomers in Fig.1c.

Contact probability. Contact probability as a function of genomic separation $|i - j| = s$ in Fig.1d is given

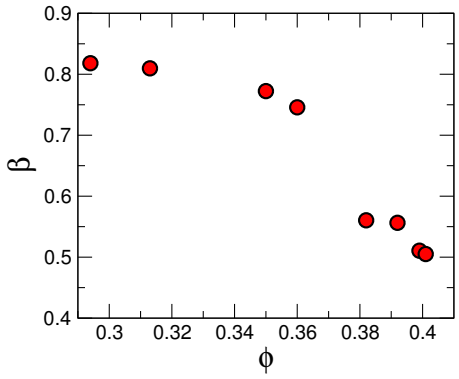

FIG. S4: β value from the fit of $F_{q_{\max}}(t) \sim e^{-(t/\tau_\alpha)^\beta}$ for the confined polymer ($N = 300$) as a function of ϕ. It is noteworthy that the decrease of β, the phenomenological stretching exponent that characterizes the extent of glassiness, is consistent with our observation that the polymer dynamics becomes more glassy with increasing ϕ.

by,

$$P(s) = \frac{\sum_{i=1}^{N-1}\sum_{j=i+1}^{N}\delta(|i-j|-s)\Theta(a-|\vec{r}_i-\vec{r}_j|)}{\sum_{i=1}^{N-1}\sum_{j=i+1}^{N}\delta(|i-j|-s)} \tag{6}$$

where $\Theta(\ldots)$ is the Heaviside step function. $\Theta(x) = 1$ for $x \geq 0$; otherwise $\Theta(x) = 0$.

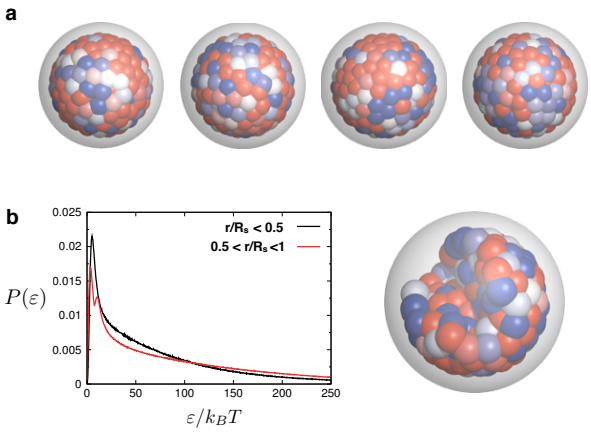

FIG. S5: (a) Snapshots of polymer under strong confinement ($\phi = 0.402$). Monomers, colored based on the energy value, underscore the spatial heterogeneity of stress in the organization of the polymer. (b) Monomer energy distribution, $P(\varepsilon)$, at $\phi = 0.402$ for different range of r: $r/R_s < 0.5$ for core and $0.5 < r/R_s < 1$ for the surface. Together with the snapshot displaying the interior of the globule on the right, $P(\varepsilon)$ for the different range of r highlights that the spatial heterogeneity of the monomer energy is present in the interior as well as on the surface of globule.

Scaling relationship of contact probability for SAW. In the absence of confinement, the chain statistics should obey that of self-avoiding walk. Given the distance distribution $P_s(r)$ between two interior points separated by s along the contour, the contact probability is defined as $P(s)(\approx P_s(r = 0))$. From $P_s(r) \sim (1/s^\nu)^d f(r/s^\nu) \sim (1/s^\nu)^d (r/s^\nu)^g$ for $r \ll s$, where g is the correlation hole exponent and $g = \theta_2$ for two interior points [3]. The scaling exponent should be similar to the probability of two interior points of a SAW chain to be in contact, $P(s) \sim s^{-(d+\theta_2)\nu} \approx s^{-2.18}$ with $d = 3$, $\theta_2 = 0.71$, $\nu = 0.588$ [3–5]. In accord with this expectation, our simulation shows $\alpha = 2.18$ in the absence of confinement ($R_s/a \to \infty$). Note that for Gaussian chain (or polymer melt) $g = 0$, $\nu = 1/2$, and $d = 3$, so that we retrieve the scaling relation for an equilibrium globule $P(s) \sim s^{-1.5}$ in the above.

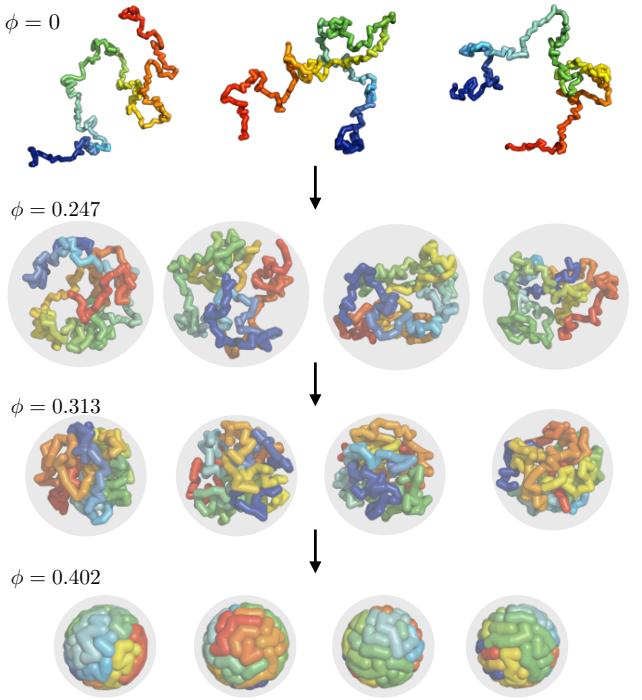

FIG. S6: Formation of fractal-like globules from self-avoiding chain with increasing extent of confinement ($\phi = 0 \to 0.402$). At $\phi = 0.402$, the globules display segregated domains with ultra-slow mobility.

[1] J. Mateos-Langerak, M. Bohn, W. de Leeuw, O. Giromus, E. M. Manders, P. J. Verschure, M. H. Indemans, H. J. Gierman, D. W. Heermann, R. Van Driel, et al., Proc. Natl. Acad. Sci. U. S. A. **106**, 3812 (2009).

[2] M. Barbieri, M. Chotalia, J. Fraser, L.-M. Lavitas, J. Dostie, A. Pombo, and M. Nicodemi, Proc. Natl. Acad. Sci. U. S. A. **109**, 16173 (2012).
[3] J. des Cloizeaux, J. Phys. **41**, 223 (1980).
[4] S. Redner, J. Phys. A: Math. Gen. **13**, 3525 (1980).
[5] N. Toan, P. Greg Morrison, C. Hyeon, and D. Thirumalai, J. Phys. Chem. B **112**, 6094 (2008).