Supplementary Information

Multivalent binding proteins can drive collapse and reswelling of chromatin in confinement

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Chromatin volume fraction

The human nuclear size varies in between $D_{nucleus} = 6 - 11\mu m$ in diameter[1]. The human genome is known to consist 6×10^6 kilobasepairs (kbp)[1] while 30 nm fibre bead is assumed to have 3 kbp[2]. Therefore the chromatin polymer corresponding to human genome would have $N = 2 \times 10^6$ beads of diameter $d = 30$ nm. Hence the chromatin volume fraction is given by,

$$\phi = N \times \frac{\frac{4}{3}\pi \left(\frac{d}{2}\right)^3}{\frac{4}{3}\pi \left(\frac{D_{nucleus}}{2}\right)^3} \approx 0.04 - 0.25 \tag{1}$$

The chromatin volume fraction in our simulation can be calculated as $\phi = 256 \times \frac{\left(\frac{\sigma}{2}\right)^3}{R^3}$. Therefore the chromatin volume fraction in our simulation corresponding to confinement radii $R = 15\sigma$, $R = 9\sigma$ and $R = 6.5\sigma$ are given by 0.01, 0.044 and 0.11 respectively.

Chromatin bead size

DNA of length 3kbp is assumed to be coiled into a 30 nm bead[2]. Therefore if a bead size of σ corresponds to 40 kbp of chromatin, then

$$\frac{40}{\frac{4}{3}\pi \left(\frac{\sigma}{2}\right)^3} = \frac{3}{\frac{4}{3}\pi \left(\frac{30}{2}\right)^3} \quad \Rightarrow \quad \sigma \approx 70 \ nm \tag{2}$$

Binder number density

The CTCF abundance is 10^5 per nucleus[3]. Hence the mean CTCF number density inside nucleus is in the range

$$c_r = \frac{10^5}{\frac{4}{3}\pi \left(\frac{D_{nucleus}}{2}\right)^3} \approx (1.44 \times 10^{-7} - 8.84 \times 10^{-7}) \ /nm^3 \tag{3}$$

Therefore in terms of σ scale, the CTCF number density can be written as

$$c = c_r \times \left(\frac{70nm}{\sigma}\right)^3 = (0.05 - 0.3) \ /\sigma^3 \tag{4}$$

Simulation details

In our simulation, the timescale is scaled with the usual LJ time $\tau_{LJ} = \sigma\sqrt{m/\epsilon}$ [4]. The Brownian timescale is given by $\tau_B = \sigma/D$ where $D = k_B T/\gamma$ is the diffusion constant and γ is the friction constant. As per usual custom[4], we set $\tau_{LJ} = \tau_B = \tau = m/\gamma$ and the mass of the particles are chosen to be unit, $m = 1$. The temperature of the system is maintained at $T = \epsilon/k_B$. We performed under-damped Langevin dynamics simulation using Velocity-Verlet algorithm[5] with time step $\delta t = 0.002\tau$ and $\gamma = 1$. It is easy to gain an intuition of the physical timescale corresponding to our simulation time scale (τ). The friction coefficient for spherical beads of diameter σ is given by $\gamma = 3\pi\eta\sigma$ where η is the nucleoplasm viscosity which is typically of the range of 10-100 cP[6]. Hence for typical

value of $T = 300$ K, the timescale ranges in between $\tau = \tau_{LJ} = \tau_B = 3\pi\eta\sigma^3/\epsilon \simeq 6 - 60$ ms.

Binder valency

To enforce the binder valency limited to six, we first check the number of monomers bound to each binder at every time step. If the binder is bound to less than 6 monomers then we make a 'probable binding list' of monomers (that are not bound to that binder) inside the interaction range. If the number of monomers in the list is less than the free bonds of the binder then the binder binds to all the possible monomers at once. In case the number of monomers in the list is larger than the number of free bonds then the binder exhausts its valency by binding to the monomers randomly chosen from the 'probable binding list'.

Semiflexible polymer

We model the semiflexible polymer by introducing a bending energy to the Hamiltonian of the polymer chain. The bending energy of the semiflexible polymer is given by,

$$U_{BEND} = \kappa \sum_{i=1}^{N-1} \left[1 - \frac{\vec{d_i} \cdot \vec{d}_{i+1}}{|\vec{d_i}||\vec{d}_{i+1}|} \right] \tag{5}$$

where κ is the bending rigidity, $\vec{d_i} = \vec{r}_{i+1} - \vec{r_i}$ and $\vec{r_i}$ is the position vector of i-th monomer.
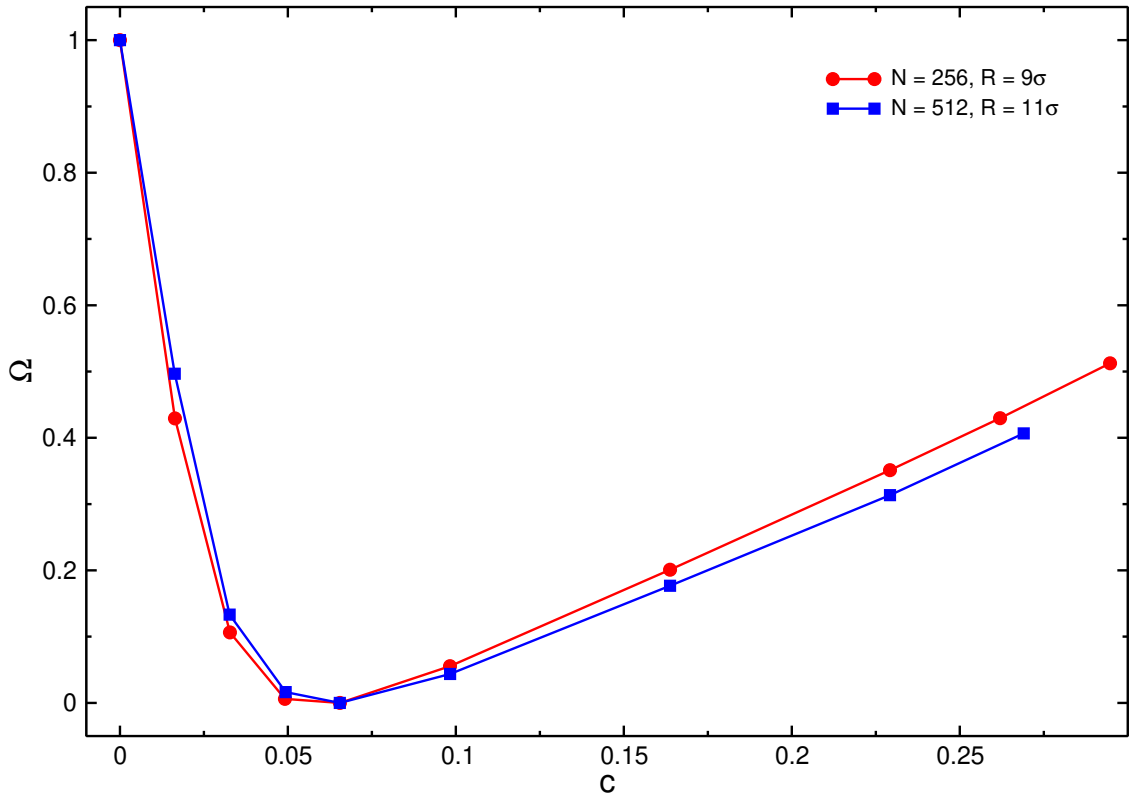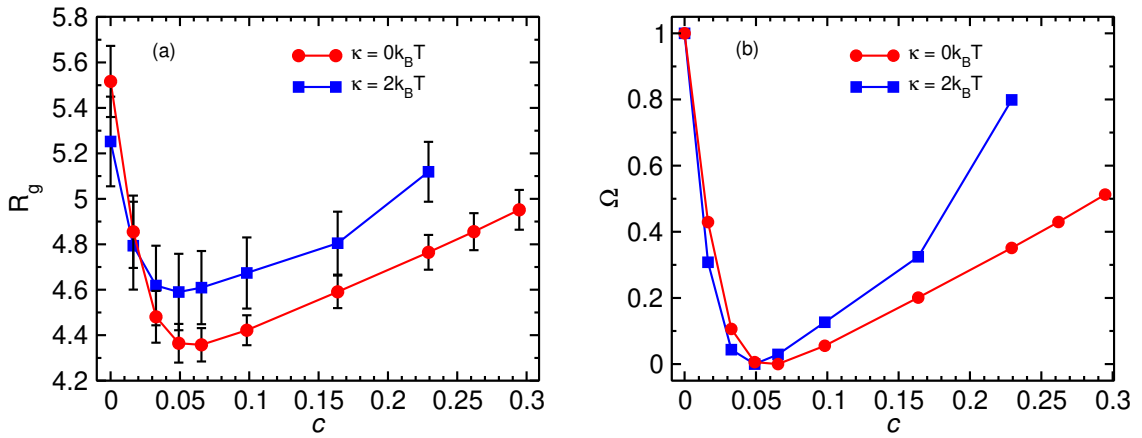
Suppl. Fig. 1: Comparison of compaction parameter (Ω) as a function of binder density for two different sizes of polymer chain. The confinement radii in two cases are adjusted to maintain the same chromatin volume fraction.
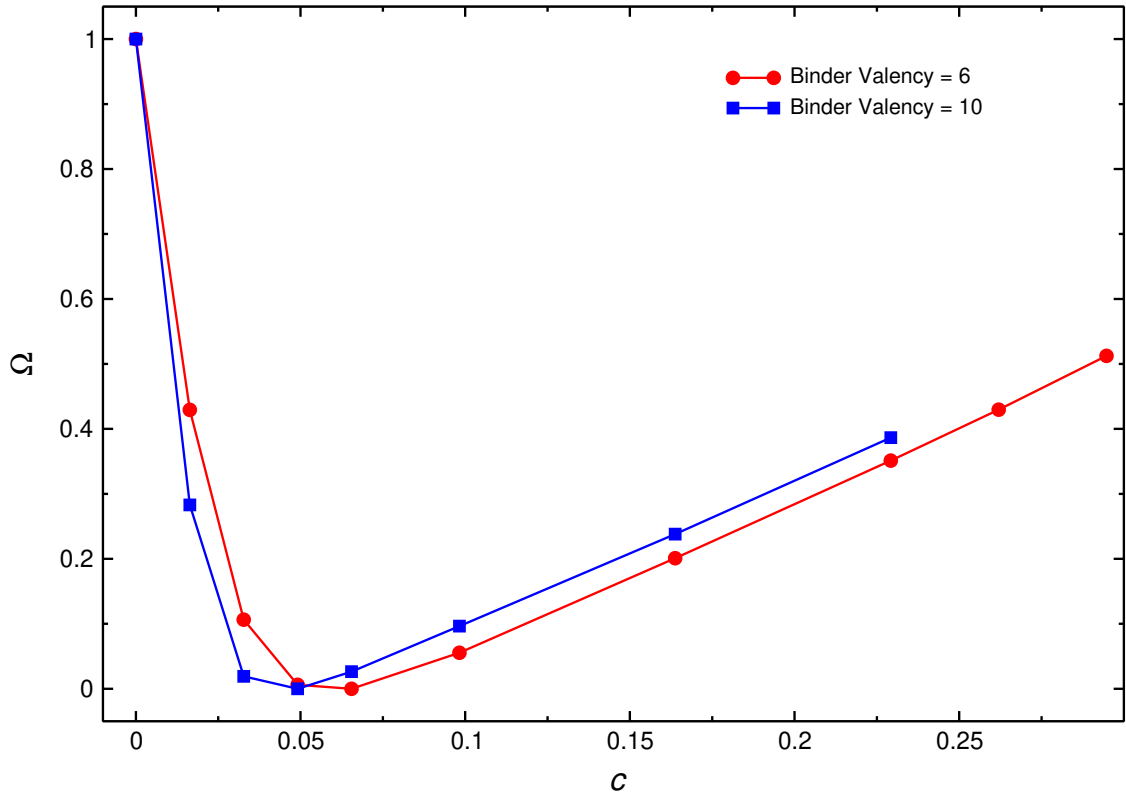

Suppl. Fig. 2: The plot depicts the variation of compaction parameter (Ω) as a function of binder number density (c) for two different binder valencies. The confinement radius is taken to be $R = 9\sigma$.
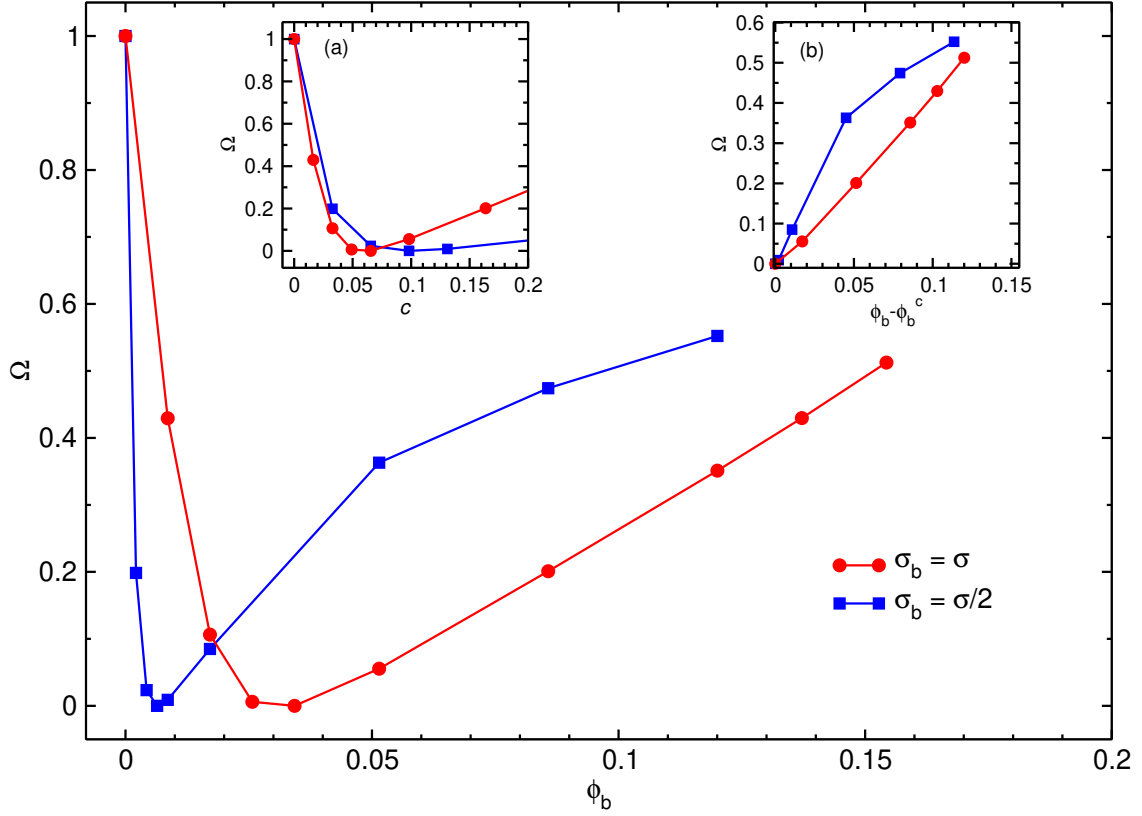
Suppl. Fig. 3: The plot compares the variation of compaction parameter (Ω) of chromatin polymer as a function of binder volume density (ϕ_b) for two different binder sizes. Inset (a) demonstrates that, for a given confinement, the collapse of the polymer chain is determined by binder number density (c) whereas inset (b) shows that the reswelling is driven by the volume fraction of the binder (or precisely on the difference between binder volume fraction (ϕ_b) and critical binder volume fraction (ϕ_b^c) required for polymer collapse. The confinement radius is chosen to be $R = 9\sigma$.

Suppl. Fig. 4: The plot depicts (a) the variation of R_g and (b) compaction parameter (Ω) as a function of binder number density c for semi-flexible polymer chain with bending rigidity $\kappa = 2k_BT$. In panel (b), we also compare the compaction results with the flexible chain ($\kappa = 0k_BT$). The chosen confinement radius is $R = 9\sigma$.
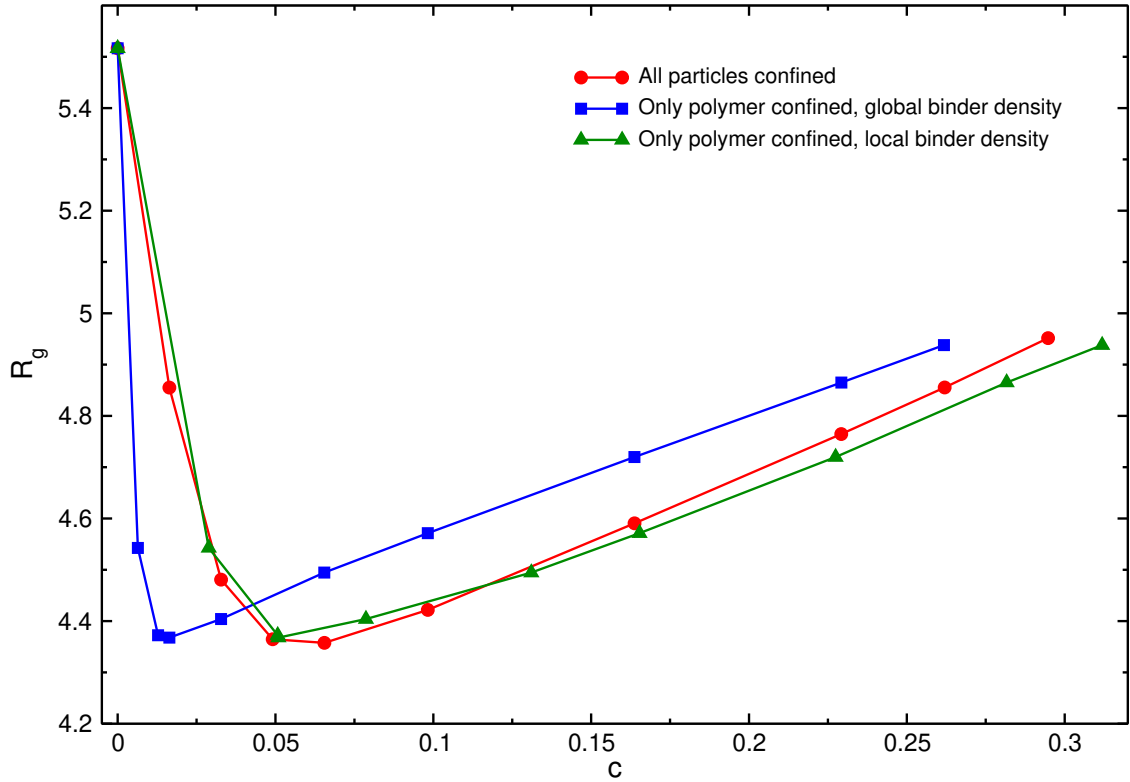
Suppl. Fig. 5: Comparison between cases when both polymer and binders are confined within the sphere (red circle) and when only polymer is confined and binders are in a larger periodic box (blue square). In the later case binders can freely penetrate through confinement wall . The green (triangle) curve shows the R_g variation as a function the mean local binder density inside the confinement sphere in case of periodic boundary.The confinement radius is same as before ($R = 9\sigma$)

References

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