I. MATERIALS AND METHODS

A. Details about the optimization of the linear charge density

In order to establish a reliable estimate of the linear charge density $\lambda$ we need an experimental quantity which can be related to the fine details of the interactions. One possibility, widely explored in the past, is to determine the potential interaction parameters from the experimental measurement of the second virial coefficient, $B_2$, which parametrizes the expansion of the osmotic pressure at the second order in the chain concentration. For molecular systems $B_2$ admits a simple integral definition of the form

$$B_2 = \frac{1}{2} \int dR \langle e^{-\sum_{ij} \beta_{\text{inter}}(r_{ij})} - 1 \rangle_{R_{\text{cm,1}}=0, R_{\text{cm,2}}=R},$$

where $\langle \cdot \rangle_{R_{\text{cm,1}}=0, R_{\text{cm,2}}=R}$ denotes the average over all the configurations of two polymers whose centers of mass are held fixed in the origin and in $R$ respectively, and $\sum_{ij} \beta_{\text{inter}}$ represents the total intermolecular potential energy between the two chains which depends on the specific choice of $\lambda$.

One of the most common ways to access to this quantity is by means of static light scattering (SLS) experiments in which the following combination $A_2 = N_A/M_w^2 B_2$ is usually measured, $N_A$ and $M_w$ being the Avogadro number and chain molecular weight respectively. In what follows we will consider the SLS measurements of $A_2$ for short fragments of dsDNA of contour length 56.4nm and molecular weight $M_w = 1.1 \times 10^5$ g mol$^{-1}$ in an aqueous solution at various concentrations of NaCl ranging from 0.5 to 0.002 mol l$^{-1}$, see Ref. 3.

![Graph](http://example.com/graph.png)

**FIG. S1:** Main Panel: Second virial combination $A_2$ from experiments and from MC simulations of the interacting chain model introduced in the main manuscript. The dashed line represents the virial coefficient for a linear tangent hard spheres chain (LTHS) of 23 sites of diameter $\sigma = 2.5$nm. In the inset we report the relative square error as a function of the effective linear charge density at a fixed ionic strength equal to $0.1$ mol l$^{-1}$.

From the theoretical side, the estimate of $B_2$ was obtained considering a model chain of 23 interaction sites, fixing the potential parameters as discussed in the manuscript. Monte-Carlo (MC) simulations, employing standard pivot and crankshaft moves, and the efficient algorithm for the calculation of $B_2$ described in Ref. 6 were used. The optimal
linear charge density was finally obtained by minimizing the least squares relative error

$$\chi^2_{rel}(\lambda) = \frac{1}{N_d} \sum_{\alpha=1}^{N_d} \frac{(A_{2,\text{sim}}(\lambda, I_\alpha) - A_{2,\text{exp}}(I_\alpha))^2}{A_{2,\text{exp}}(I_\alpha)} ,$$

(2)

where the summation runs over all the data available for the different ionic strengths, $A_{2,\text{exp}}(I_\alpha)$ is the experimental value for $A_2$ at the generic ionic strength $I_\alpha$ and $A_{2,\text{sim}}(\lambda, I_\alpha)$ is the corresponding value obtained from Monte Carlo (MC) simulations for a given choice of $\lambda$. In Fig. S1 we display the predictions for $A_2$ by using the optimal value of $\lambda$ at various ionic strengths and also $\chi^2_{rel}(\lambda)$ as a function of $\lambda$ at $I = 0.1 \text{mol} \text{l}^{-1}$.

Finally, it is also interesting to notice how, for the highest ionic strength considered, the second virial coefficient can be well approximated by the analogous quantity for a rigid chain of $m$ tangent spheres of diameter $d = 2.5 \text{nm}$ without electrostatics, for which an analytical prediction is known

$$A_2 = \frac{N_A \pi \sigma^3}{6 \left( 1.38784(m - 1)^2 + \frac{11m - 3}{2} \right)} .$$

(3)

Indeed, considering $m = 23$ and $\sigma = 2.5$ as before, we find $A_2 = 0.324 \times 10^{-6} \text{mol l}^{-1}$ in good agreement with both the simulation results, obtained considering a semi flexible fragment at $I = 0.5 \text{mol} \text{l}^{-1}$, and the corresponding experimental value, see Fig S1. This evidence provides a posteriori a further independent justification of our choice of taking $\sigma = 2.5 \text{nm}$.

II. ADDITIONAL RESULTS

A. Monte Carlo results for the chain compaction and the knotting probability for the interacting chain model

In this section we collect the explicit MC results for the chain size and the knotting probability as computed for the interacting chain model in the presence of hard spheres of various size at volume fraction $\phi_c = 0.3$.

TABLE I: Monte Carlo results for the root mean square gyration radius $R_g = \sqrt{\langle R^2_g \rangle}$ and the knotting probability $P_k\%$ for colloids of various size at $\phi_c = 0.3$. We also report the results for the reference isolated chain case.

<table>
<thead>
<tr>
<th>$d_c$[nm]</th>
<th>$R_g$[nm]</th>
<th>$R_g/R_0^c$</th>
<th>$P_k%$</th>
<th>$P_k/P_k^c$</th>
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Isolated Chain 236.02(6) 1 1.73(1) 1
TABLE II: Monte Carlo results for the root mean square gyration radius $R_{g,\text{knotted}}$ of the knotted chains for colloids of various size at $\phi_c = 0.3$. As a term of comparison, we also report the data for the reference isolated chain case.

<table>
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<tr>
<th>$d_c$ [nm]</th>
<th>$R_{g,\text{knotted}}$ [nm]</th>
<th>$R_{g,\text{knotted}}/R_0$</th>
<th>$R_{g,\text{knotted}}/R_g$</th>
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Isolated Chain 197.45(38) 1 0.837(2)
B. Dependence of the abundance of the dominant topologies on the crowder size

FIG. S2: Abundance of trefoil knots ($3_1$) as a function of the crowder diameter.

FIG. S3: Abundance of figure eight knots ($4_1$) as a function of the crowder diameter.
C. Long wavelength limit of the polymer structure factor

In this section we show the long wavelength limit of the polymer structure factor. Specifically, we focus on the range of wavevectors $kR_0 g \lesssim 1$ where $\tilde{F}(k) = (kR_0 g)^2/\sum L^2 e^{i k \cdot r_{ij}}$ can be approximated as

$$\tilde{F}(k) = (kR_0 g)^2 [1 - (kR_0 g)^2/3 + ...]$$

where $\alpha_g = (R_g/R_0 g)^2$. Results for the isolated chain ($\alpha_g = 1$), the optimal crowder case ($\alpha_g \approx 0.721$) and the confined chain case with the same degree of chain compaction are reported in Fig. II E.

\[\text{FIG. S4: Kratky Form of the polymer scattering function in the long wavelength limit. All the cases considered approaches to the expected analytical behavior of Eq. 4.}\]

D. Knotting probability as a function of the distance between the crowders

\[\text{FIG. S5: Relative enhancement of the knotting probability, } P_k/P_0 k - 1, \text{ as a function of the dimensionless combination } x = R_0 g / D, \text{ D being the average crowders separation. Data points for various size of the colloids are reported together with best-fits of the form } \propto x^\beta \text{ displayed as dashed lines. We numerically found } \beta \text{ to vary in the interval } [1.6:2.3].\]
E. Monte Carlo results for the chain compaction and the knotting probability for the ideal chain model

In this section we collect the explicit MC results for the chain size and the knotting probability as computed for the phantom chain model in the presence of hard spheres of various size and volume fraction.

TABLE III: Monte Carlo results for the root mean square gyration radius $R_g = \sqrt{\langle R_g^2 \rangle}$ and the knotting probability $P_k\%$ for colloids of various size at volume fractions in the interval $\phi_c = [0.05, 0.3]$. For the chain in the absence of colloids we measured $R_g^0 = 224.11(5)$nm and $P_k^0 = 5.10(2)\%$.

<table>
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<th>$\phi_c$</th>
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F. Structural and thermodynamic properties of the colloidal particles

In this section we show some structural and thermodynamic results for the various colloidal systems considered in the main manuscript. Specifically, in the right panel of Fig. S6 we report the colloidal radial distribution function $g(r)_{cc}$, obtained by MC simulations of the interacting chain model at fixed colloid volume fraction, $\phi_c = 0.3$, and various colloids’ size. The results for the different colloids’ size are perfectly superimposed witnessing how the system size has been properly chosen so that the colloids retain their bulk behavior over a wide range of length scales. As a term of comparison, we also displayed the results for $g(r)_{cc}$ for a pure colloidal system obtained from integral equations using the accurate Verlet-Weis correction to the Percus-Yevick solution⁹. For colloidal systems in the presence of the phantom chain we extrapolated the zero-momentum value of the colloid structure factor $S_{cc}(k)$ which is directly
related to the isothermal compressibility of the system through the compressibility relation
\[
\lim_{k \to 0} S_{cc}(k) = \rho_c k_B T \chi_T,
\]
where \(\rho_c\) is the colloids number density, \(\chi_T = 1/\phi_c (\partial \phi_c / \partial P)_T\) and \(P\) is the (osmotic) pressure of the dispersion. The \(k \to 0\) extrapolation was performed numerically assuming for \(S_{cc}(k)\) the following expansion
\[
S_{cc}(k) = S_{cc}(0) + a_1 k^2 + a_2 k^4 + o(k^6),
\]
then considering the three smallest wave-vectors available for a finite box of volume \(V = M^3\), i.e. \(k_1 = 2\pi/M, k_2 = 2k_1\) and \(k_3 = 3k_1\), and the approximant
\[
S_{cc}(0) = \frac{3}{2} S_{cc}(k_1) - \frac{3}{5} S_{cc}(k_2) + \frac{1}{10} S_{cc}(k_3) + O(M^{-6}).
\]
Results are displayed in the left panel of Fig. S6 together with the accurate predictions obtained from the Carnahan-Starling equation of state of the hard sphere model. 

![Graph](image)

**FIG. S6**: On the left: Radial distribution function between the crowders at \(\phi_c = 0.3\) as obtained from the simulations of the interacting chain model. Results for different colloidal size are reported together with the results from integral equations. On the right: Zero-momentum extrapolated value of \(S_{cc}(k)\), for colloids of various size and densities. We also reported the predictions based on the compressibility equation using the Carnahan-Starling equation of state for the hard spheres.
1 D. Stigter, Biopolymers 16, 1435 (1977).