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Mesostructure of polymer collapse and fractal smoothing

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We investigate the internal structure of a polymer during collapse from an expanded coil to a compact globule. Collapse is more probable in local regions of high curvature, so a smoothing of the fractal polymer structure occurs that proceeds systematically from the shortest to the longest length scales. A proposed universal scaling relationship is tested by comparison with Monte Carlo simulations. We speculate that the universal form applies to various fractal systems with local processes that promote smoothness over time. The results complement earlier work showing that on the macroscale polymer collapse proceeds by driven diffusion of the polymer ends. [S1063-651X(99)01209-X]

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Understanding the collapse of homopolymers from a flexible coil to a compact globule is a first step towards modeling the kinetics of molecular self-organization. It may be relevant to a description of DNA aggregation and the initial collapse of proteins from an expanded state to a molten globule from which the final ordered structure is formed [1,2]. We have performed scaling analysis and simulation of this transition to investigate kinetic effects during collapse [3,4]. The results suggest that the motion of the polymer ends plays an important role in kinetics because their motion is constrained only by a single bond. Along the contour, monomers have two bonds, their motion is more constrained, and aggregation is more difficult. Thus, collapse for a long polymer occurs almost as a one-dimensional process where the polymer ends accumulate mass by moving along the contour of the polymer while accreting monomers and small aggregates. Encounters between monomers far apart along the contour to form rings are rare so they play no role in the collapse. As a result of the faster aggregation at the polymer ends, the collapsing polymer on a macroscopic scale takes on a dumbbell-like appearance. The few DNA fluorescence measurements that follow a single polymer collapse and its metastable states also indicate the special role of polymer ends [5–7]. However, a description of the internal structure of the polymer away from the polymer ends has not, thus far, been obtained.

In this paper we consider the internal structure of the polymer during collapse, not including the ends. Our objective is to understand the local contour structure that consists of small aggregates and polymer segments between them. Our arguments generalize the consideration of the freedom of motion of monomers, because monomers found in straight segments are much more constrained in their motion than monomers in curved segments. This results in faster collapse in regions of high polymer curvature.

We will focus on intermediate length scales between the size of the expanded polymer and the size of the collapsed aggregate. The length scales to which this analysis is relevant are between the size of the initial coil, which scales as N^{ν}, where N is the number of monomers and $\nu=0.6$ is the Flory exponent, and the size of the final aggregate, which scales as $N^{1/3}$ (assuming a compact aggregate). For long polymers these scales are well separated. During collapse, at these intermediate length scales, the internal structure of the final aggregate as well as of intermediate clusters that are formed should not be relevant. When convenient we can treat clusters as point objects, though this is not always necessary. In particular, it is not necessary for treatment of their dynamic properties. The dynamic properties of cluster movement follow Stokes' law—the diffusion constant of clusters decreases slowly with cluster size, $D\sim R^{-1}$, where R is the radius of a cluster. This implies that the dynamics of clusters varies smoothly from that of the original monomers, and a universal scaling behavior of the polymer during collapse should be found. By focusing on intermediate length scales, our results should be widely relevant to polymers with varied properties. While the eventual structure of the collapsed polymer depends in detail on monomer-monomer interactions, the separation of lengths scales implies that for a long enough polymer with a compact final aggregate, the details of these interactions should not be relevant to the kinetics of the collapse at early times.

To characterize the collapse it is useful to compare the distance between two monomers with the contour length of the polymer connecting them. In conventional scaling the polymer end-to-end distance R is expressed as a function of the number of monomers N, or the number of links in the chain $L=N-1$. When aggregation occurs, the small aggregates that form, appearing like beads on a chain, decrease the effective contour length of the polymer. We can define the effective contour length by counting the minimum number of

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monomer-monomer bonds that one must cross in order to travel the polymer from one end to the other. Bonds formed by aggregation allow us to bypass parts of the usual polymer contour. Because we are not interested in the structure of aggregates, we can neglect the difference between different kinds of bonds. In this way the effective number of links in the chain decreases over time. Thus, in order to study the internal polymer structure during collapse, we investigate, via scaling arguments and simulations, the scaling of the end-to-end distance $r(l,t)$ of internal polymer segments as a function of their effective contour length l.

The equilibrium structure of the polymer before collapse—in good solvent conditions—is a self-avoiding random walk, where $r \sim l^{\nu}$ and $\nu = 0.6$ in three dimensions. The contour length is proportional to the number of monomers. During collapse, monomers are constrained from aggregating with other monomers by their already existing bonds. A completely straight segment of polymer does not allow aggregation because no monomer can move to bond with another monomer. In contrast, highly curved regions are more flexible and monomers in these regions may aggregate. Aggregation in a curved region reduces the contour length and the polymer becomes straighter, smoothing the rough fractal polymer structure. We therefore expect that the scaling exponent will increase over time. At long enough times the scaling will approach that of a straight line $(r \sim l)$. However, this smoothing occurs first at the shortest length scales. In effect the polymer structure becomes consistent with a progressively longer persistence length. Assuming scaling, we anticipate that the polymer end-to-end distance for a polymer segment away from the ends of contour length l will follow the dynamic scaling formula:

$$r = l f(t/l^{z}). \tag{1}$$

The universal function $f(x)$ is a constant for large values of its argument so that $r \sim l$ (long times), and scales as $x^{(1-\nu)/z}$ for small values of its argument, so that $r \sim l^{\nu}$ (short times). The short time regime described by Eq. (1) starts after an initial transient (a very short time regime) in which no new bonding has taken place. During the very short time regime the time dependence of the universal scaling function does not apply. The usual scaling of the contour length and end-to-end distance persists until just after the very short time regime because the bonds that are formed initially do not form large rings and thus do not affect the large scale polymer structure. The short time regime begins with the first formation of individual bonds and lasts until the characteristic relaxation time of the contour of length l. This time—the relaxation time of the contour of length l—is the crossover time between the short and long time regimes which follows a scaling law $\tau \sim l^{z}$. The dynamic exponent z is assumed to be consistent with conventional Zimm relaxation, $z = 3\nu$. Finally, we can also rewrite this scaling relation in terms of the number of monomers n in a polymer segment. Since the average mass along the contour is $M \sim n/l$ and M follows power-law scaling [3] $M \sim t^{s}$—we substitute $l \sim n t^{-s}$ in Eq. (1) to obtain $r(n,t)$.

We emphasize that kinetic effects become important for collapse of polymers in poor solvent, after equilibration in good solvent—the result of a quench in solvent affinity or temperature below the thermodynamic transition at Θ solvent conditions. Close to the Θ point a mean-field argument where kinetics do not play a significant role is likely to apply [8,3]. In contrast, we will approximate the collapse by a completely irreversible model where no disaggregation occurs. Because the scaling variable that determines the effective distance from the Θ point is $N^{1/2}\Delta T$, long lengths are equivalent to small temperatures, and microscopic reversibility becomes irrelevant at long enough length scales. We are thus consistently adopting a description that is valid for lengths longer than the microscopic regime. We further restrict our study to diffusive monomer motion and short-range interactions.

The scaling relationship, Eq. (1), was tested by Monte Carlo simulations. These simulations in part include the effects of hydrodynamics during collapse by scaling the diffusion constant of aggregates according to Stokes' law. The simulations are based on the two-space lattice Monte Carlo algorithm [3,4,9,10] developed for simulating high-molecular-weight polymers, and shown to be significantly faster than previous state-of-the-art techniques [9,10]. In the two-space algorithm, odd monomers and even monomers of a polymer are distinct and may most easily be described as residing in two separate spaces. Each monomer occupies one cell of a square lattice. Both connectivity of the polymer and excluded volume are imposed by requiring that, in the opposite space, only the nearest neighbors along the contour reside in the $3\times3\times3$ neighborhood of cells around each monomer. Motion of monomers is performed by Monte Carlo steps that satisfy the polymer constraints. Since adjacent monomers (and only adjacent monomers) may lie on top of each other, the local motion of the polymer is flexible. Despite the unusual local polymer properties, the behavior of long polymers is found to agree with conventional scaling results.

The polymer is initially relaxed into an equilibrium configuration using a fast nonlocal ''reptation'' Monte Carlo algorithm. Monomers are randomly moved from one end of the polymer to the other, which, for equilibrium geometries, provides equivalent results to the local two-space dynamics.

Collapse of the polymer is then simulated using local diffusive Monte Carlo dynamics, but without the excluded volume constraint. Simulations of a variety of models indicate that excluded volume does not significantly affect the kinetics of collapse [4]. Monomers are no longer stopped from entering the neighborhoods of other monomers; they continue to be required not to leave any neighbors behind. This allows monomers in the same space (odd or even) to move on top of each other, and thus aggregate. Aggregates of any mass occupy only a single lattice site, and are moved as a unit by the same dynamics used for monomers. The mass of an aggregate is set equal to the number of monomers located at that site. The probability of moving an aggregate is adjusted to be consistent with a diffusion constant that scales by Stokes' law for spherical bodies in three dimensions, $D \sim M^{-1/3}$. This represents the effects of hydrodynamics on individual aggregates, but does not include coupling of motion of different aggregates. One time interval consists of attempting a number of aggregate moves equal to the number of remaining aggregates.

The end-to-end distances of polymer segments, r, were measured as a function of the effective contour length, l. The

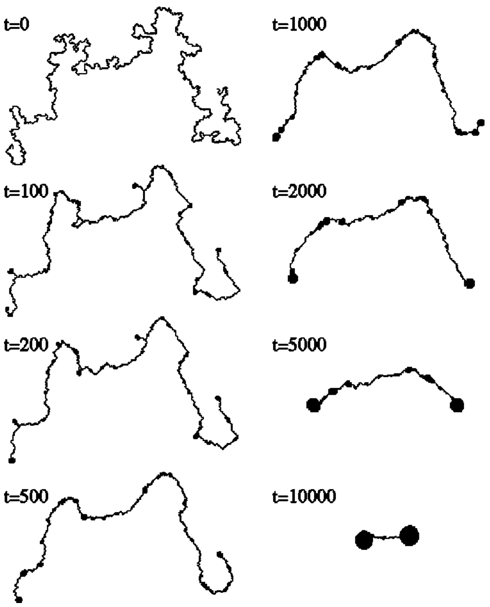

FIG. 1. ‘‘Snapshots’’ of the collapse of a single homopolymer of length $N=500$ monomers in $2D$ using the two-space algorithm. The plot is constructed by placing dots of area $M^{1/2}$ for an aggregate of mass M. This does not reflect the excluded volume of the aggregates, which is zero during this collapse simulation. The frames demonstrate the process of local smoothing that occurs progressively from short to long length scales. The behavior of the ends is discussed in Refs. [3] and [4]. The primary effects of hydrodynamics are included in the simulations by applying Stokes’ law to the diffusion of aggregates.

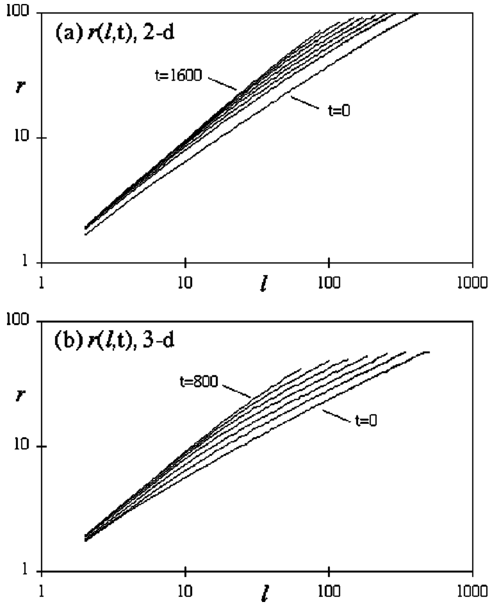

FIG. 2. Plot of the internal polymer segment end-to-end distance r, as a function of segment contour length l, and collapse time, t, in both (a) two dimensions $(2D)$, for $t=0$, 25, 50, 100, 200, 400, 800, 1600 and (b) three dimensions $(3D)$, with $t=0$, 25, 50, 100, 200, 400, 800. In both cases the polymer contained 500 monomers and results were averaged over 200 collapses.

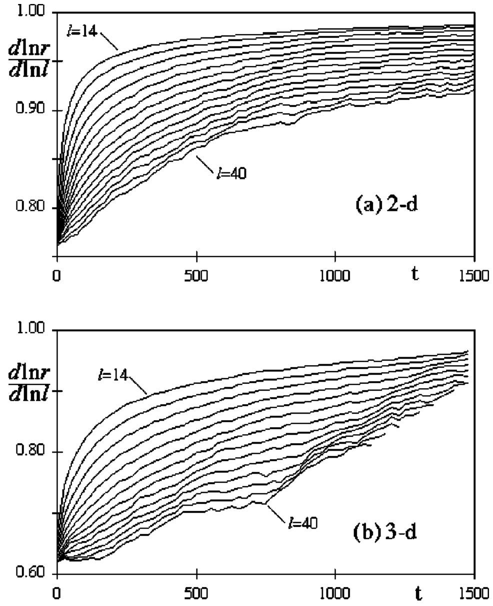

FIG. 3. Plot of the scaling exponent $d\ln r/d\ln l$ as a function of time for different segment contour lengths l. This figure was obtained from Fig. 2 by calculating average slopes over a segment length of 20.

effective contour length is the minimum number of links along the polymer that connect a monomer at one end of the segment with the other end of the segment. Since an aggregate occupies only a single lattice site, interior bonds of the aggregate need not be counted, and it can be treated like a single monomer. The end-to-end distance is not exactly the Euclidean distance between the ends. Instead it is correctly defined as the minimum number of links needed to connect the two ends by any curve in space. Due to the underlying lattice in our algorithm, a Manhattan metric, with the inclusion of diagonals, is appropriate.

In addition to simulations of polymer collapse in three dimensions, we also performed simulations of polymers whose motion is confined to two dimensions, which are convenient for pictorial illustration (Fig. 1). These are not conventional two-dimensional simulations because of the well known problems with hydrodynamics in two dimensions [11]. Instead, they represent the dynamics of a polymer confined at an interface (e.g., between two fluids). Thus the polymer is confined to two dimensions while the hydrodynamics is three dimensional. In this case we have $\nu=0.75$, $z=3\nu$, and $D\sim M^{-1/2}$. The frames in Fig. 1 illustrate contour smoothing. Starting with short length scales, the polymer becomes progressively smoother and approaches a straight line.

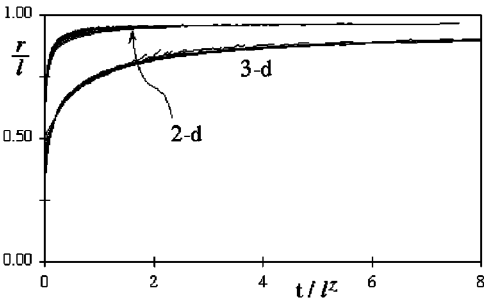

FIG. 4. Plot of the rescaled end-to-end polymer segment distance, r/l, as a function of the rescaled time, t/l^z. Data for both $2D$ and $3D$ are shown. The coincidence of the curves is consistent with validity of the universal scaling relationship, Eq. (1).

In Fig. 2 we show log-log plots of contour length (l) versus end-to-end distance (r) for both $2D$ and $3D$ simulations. Initially the results are consistent with $r \sim l^{\nu}$ for a self-avoiding random walk. As time progresses the polymer becomes smooth, resulting in a slope that approaches 1. The asymptotic behavior can be seen to occur earlier at the shortest length scales.

Figure 3 shows the derivative, obtained from finite differences, as a function of time for different segment contour lengths. For all segment lengths the derivative starts at approximately ν and approaches 1 as the collapse proceeds. The rate of collapse becomes progressively slower as l increases. The scaling relation, Eq. (1), predicts that the relaxation time will scale with l as l^z. Figure 4 shows the data following rescaling. r/l is plotted against the rescaled time, t/l^z. The generally good coincidence of the different curves confirms that the simulation obeys Eq. (1) [12]. An attempt to use an asymptotic scaling exponent, $r \sim l^u$, with $u = 0.95$, led to a visibly poorer fit, as did small variations in the exponent z.

The excellent agreement with the expected universal scaling relationship using the hydrodynamic exponent, $z = 3\nu$, may be fortuitous because the simulations do not contain the full effects of hydrodynamics. Specifically they contain only the effect of hydrodynamics on individual aggregates and not the coupling between aggregate motion.

In summary, we have found that polymer collapse displays a process of fractal smoothing that occurs first at the shortest length scales. Our simulations were found to be in good agreement with a universal scaling relationship. It is interesting to speculate that this may also apply to other fractal systems where local smoothing processes occur. Several groups have attempted to measure the self-affine scaling of horizontal transects of mountain ranges [13,14]. They found that a unique fractal dimension, D_H, cannot be assigned, but that the effective fractal dimension decreases with length scale. For example, Dietler and Zhang [13] have performed calculations for Switzerland, an area of 7×10^4 km^2, with a resolution of 100 m. They obtained $D_H \approx 1.43$ at length scales below approximately 5 km, and $D_H \approx 1.73$ for larger length scales. The data points could also lie on a continuous curve rather than two distinct scaling regimes. Thus the landscape appears smoother at shorter length scales. Short-range smoothing may arise from processes, such as weathering, that also give rise to short-range correlations. Various fractal biological systems formed as a result of an initial developmental process may also suffer smoothing as part of aging.

Since this work [15] was completed, a number of other works have explored the kinetics of collapse using simulations, analytic treatments, and scaling arguments. Timoshenko, Kuznetsov, and Dawson [16] studied the kinetics of collapse using Monte Carlo simulations and a mean-field ‘‘Gaussian self-consistent’’ approach. Their Monte Carlo simulations are based upon an underlying lattice model which is similar to ours, however they do not move aggregates as a unit. Since they only move individual monomers, Monte Carlo rejection of moves causes the diffusion constant of aggregates to decrease very rapidly with aggregate size (naively, it decreases exponentially [17]). By contrast, in a fluid, collective motion results in Stokes' law diffusion, which we have included in our simulations. The slow diffusion of aggregates in their simulations causes their results to be distinct from ours. From their figures it appears clear that aggregates tend to pin the polymer contour. Their Gaussian self-consistent approach is analytically elaborate, however it is not clear from their analysis whether it treats correctly the diffusion of clusters. Moreover, since some equilibrium scaling laws are not correct in this method, it is hard to evaluate whether the kinetic properties are correct and their analysis does not clarify this point aside from the claim that the analytic results are in agreement with their Monte Carlo simulations.

Buguin, Brochard-Wyart, and de Gennes [18] have presented scaling arguments based on a model of local cluster ‘‘pearls’’ forming during collapse close to the Θ point in the mean field regime where surface tension is the driving force of collapse. Pitard [19] has further considered the dynamics of collapse in this mean-field regime by discussing the effect of tension along a polymer contour between two clusters (pearls) and extended the arguments to considerations of a string of clusters. These papers refer to a different regime (i.e., the mean-field regime) than our analysis. Within this regime they provide complementary insights about the structure of clusters or pearls during collapse and the formation of a globule, which is important both to the kinetics of collapse and to the eventual structure of the aggregate that is formed at the end. It is worth noting that our simulations do not allow monomers, by motion along the polymer contour, to leave and join aggregates. The distribution of cluster sizes may be affected by such motion. We note, however, that the essential results of this paper should not be changed by redistribution of monomers along the contour, and resulting change in the distribution of the sizes of clusters, because they only affect the distribution of diffusion constants which vary only weakly with aggregate size. Moreover, the scaling law Eq. (1) does not refer to aggregate size and should not be affected.

Finally, Kantor and Kardar [20] have investigated the properties of charged polymers and find their compact form exhibits a necklace shape with end aggregates and intermediate aggregates forming as a function of the charge density. These results also display some interesting similarities to collapse behavior and further research may reveal a connection between their results and the studies of collapse.

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