Giant Nonmonotonic Stretching Response of a Self-Associating Polymer in Shear Flow

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Giant non-monotonic stretching response of a self-associating polymer in shear flow

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Self-associating polymers are ubiquitous in synthetic and biological systems. Here, we **use a combination of simulation and theory to** show that these polymers exhibit a counterintuitive strong non-monotonic stretching response in shear flow. Furthermore, we demonstrate that this behavior can be tuned by controlling the barrier for dissociation of the bonds and develop a quantitative and predictive theory based on conformational transitions to explain the observed behavior. Our results can be important in understanding previous experimental and theoretical observations and further aid in the development of novel smart materials.

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One important and ubiquitous aspect of biological molecules is their wide variety of binding and association behaviors. A great deal of effort has gone into characterizing the kinetics and force response of these biological bindings, which often display counterintuitive and complex behavior. [1–3] Experimental and theoretical investigations have incorporated some of these ideas into novel material systems, especially gels, that demonstrate responses to external stimuli on the time scales governed by the kinetics of associating groups.[4–12] On the single chain level, it has been demonstrated that these polymers display both a collapse transition upon increasing the binding energy and a polymer dynamic regime governed by binding kinetics.[13]. However, most of the promising properties of these biologically inspired systems will occur in situations far away from equilibrium, when subjected to external forces such as fluid flows.

In this letter, we investigate the conformational response of a single self-associating polymer in simple shear flow. Understanding the response of a single polymer chain to an applied flow field has been an active area of research for the past few decades, yielding insight into the dynamics of polymers in dilute solution.[14–27] This has had ramifications in a wide variety of situations, including disparate fields such as protein conformational behavior,[17, 20, 28, 29] macroscopic fluid rheology,[27] and molecular-level single chain manipulation[16, 19, 21, 23]. Contrary to previous studies, we find for the present situation that the inclusion of self-associations and the consequent introduction of an additional time scale manifests itself in a counterintuitive non-monotonic stretching response with increasing shear rate. This effect was first observed recently using self-avoiding polymers that exhibited a rather weak non-monotonicity, an effect amplified when (non-physical) phantom chains were considered.[18] For real chains, however, it was neither clear how large this effect could be nor how one could modulate or tune it. Here we explicitly show the origin of this effect and how one can manipulate it. Under some conditions, in fact, we obtain a very large reduction in the average chain size for moderate to high shear rates. Our results can also be potentially important for understanding previous experimental observations on the response of DNA conformations in microchannels to oscillatory electric fields.[30] In these experiments, similar non-monotonic frequency behaviors arise, an effect attributed to the natural system relaxation time.[30] Furthermore, our results have strong implications in the study of biological polymers where interaction time scales may result in complex dynamic behavior, and in the development of novel material systems where the use of supramolecular chemistry concepts may provide opportunities for engineering dynamic properties on the molecular level. For example, there is much newfound interest in the possibility of using fluid flows to exert control over the molecular details of polymer solutions, in much the same way that molecules such as DNA and proteins are manipulated in biological systems to display function at the molecular level.[17, 23, 31]

We develop a picture of the shear response of a single polymer based on understanding the kinetic behavior as the polymer proceeds through the relevant trajectory in conformational space. This is similar in spirit to approaches by DeGennes and Peterlin in deriving the dumbbell equation,[14, 15] only we consider a coarse-grained representation of conformational space that is generalized to two situations: a stuck globule that cannot be stretched due to constraints, and an unstuck chain that can be freely stretched. The basic idea behind this model is that the globule needs to relax internal constraints (or bonds) in order to be able to stretch under shear. The original conceptual picture is an alternation between the coil (or globule) and the stretched conformation (a process known as tumbling). In this process, the shear flow can stretch out the polymer from the coiled state if it overcomes the entropic polymer relaxation, but will also drive the polymer back into the coil (globule) state due to a flow instability. This behavior prevents full and continuous elongation of the polymer, and has been directly observed in both simulation and experiment.[15, 21, 23] We postulate that, in the case of self-associating polymers, one must include apart from the coil and the stretched conformations another constrained state that we denote as the "stuck globule". Our approach thus considers associations as these constraints, however other effects (hydrodynamic shielding and counterion mobilities, for example) may also serve this role. Furthermore, we assume that the stuck globule state is attained immediately following the stretched conformation after a tumbling event**, likely due to the**

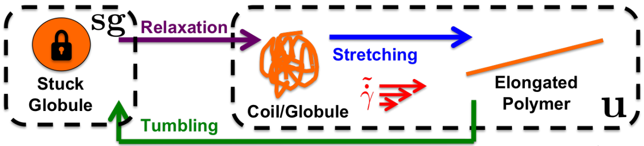

FIG. 1. Relevant transitions in conformational space. A coil or globule will be stretched by a shear flow $\tilde{\dot{\gamma}}$. The concurrent tumbling instability will drive the polymer back into the coil or globule, however due to either hydrodynamic effects or association constraints the polymer may be at first resistant to stretching for some subsequent amount of time. We dub this state the "stuck globule" (sg) state, and the traditional coil-elongational description represents the "coil-stretch" (cs) state. The arrows show the conformational trajectory of a self-associating polymer in shear flow.

compressive portion of the tumbling cycle that has recently been experimentally shown to significantly affect chain conformations.[32] Once this stuck globule state is reached, these constraints largely prevent the subsequent elongation of the polymer until it can relax into the coil state. We indicate this tumbling trajectory in Figure 1.

With this conceptual picture, we consider the kinetic equations of the form $\partial n_i/\partial t = \dot{n}_i = \sum_j \nu_{ji} n_j$ where n_i is the fraction of polymers in an ensemble with conformation i and ν_{ji} is the frequency that state j proceeds to state i. This, combined with the steady-state assumption $\dot{n}_i = 0$ and a normalization condition $\sum_i n_i = 1$, represent a discrete analogue to the DeGennes and Peterlin dumbbell theory.[14, 15] Conveniently, we can draw the boundaries of these conformations i in any way we like, and as per Figure 1a we consider only two states, a stuck-globule state and an unstuck state. These are represented with subscripts sg and u respectively. For our purposes, the unstuck globule/coil-stretch state is analogous to the traditional stretching response of a non-associating polymer with an equivalent equilibrium state.

Since we are considering a two-state model, there are only two transitions: the stuck globule relaxation (represented by the subscript $sg-u$), and the tumbling process (represented by the subscript $u-sg$). The relaxation from the $sg \rightarrow u$ occurs with a frequency governed by the inverse of its characteristic relaxation time, τ_L, i.e. $\nu_{sg-u} \sim \tau_L^{-1}$ **(where a $\sim$ indicates proportionality of order unity)**. The form for τ_L is reliant on the origin of the globule's "stickiness", and is thus situation dependent. For the particular case we study here, the relaxation timescale can be tuned by changing the binding constants, as will be shown below. On the reverse pathway, the frequency of tumbling and sticking is governed by the time scale of the fluid flow. "Attempts" to the stretching process occur twice during a single rotation of the coil due to the two directions along the stretching axis of the elongational portion of the flow, and the coil rotates at a frequency of half the shear rate $\tilde{\dot{\gamma}}/2$.[33] Since tumbling (and therefore sticking) immediately follows stretching, we can write the the frequency of the coil-globule sticking as proportional to the frequency of stretching $\nu_{u-sg} \sim \tilde{\dot{\gamma}}/4$.[34]

By considering only two states we obtain the straightforward result:

$$n_{sg} = \frac{\nu_{sg-u}}{\nu_{u-sg} + \nu_{sg-u}} = \left[1 + \frac{C4}{\tilde{\dot{\gamma}}\tau_L}\right]^{-1} \tag{1}$$

where C absorbs the proportionality constants from the values related by a $\sim$ (since both are of order unity, we assume $C \approx 1$ throughout the rest of this letter). This equation represents the transition from a globule-deficient regime at low $\tilde{\dot{\gamma}}$ to a coil-deficient regime at high $\tilde{\dot{\gamma}}$, with a transition between the two regimes that occurs at a critical shear rate $\tilde{\dot{\gamma}}^* \sim 4/\tau_L$. To place this in the context of the observable variables of the shear transition, namely the average extension of the polymer chain $\langle L\rangle$, we calculate the weighted average based on the number of states:

$$\langle L\rangle = n_{sg}\langle L\rangle_{sg} + n_u\langle L\rangle_u \tag{2}$$

where $\langle L\rangle_i$ is the average extension of a polymer in state i. Generally, the average extension can be a function of $\tilde{\dot{\gamma}}$ for a given state depending on the details within the state itself. Since the u-state contains both the coiled polymer and the stretched polymer, the balance between the two will demonstrate a response similar to the non-sticky polymer of the same geometry (the equilibrium structure for the non-sticky and self-associating polymers should be equivalent). This condition is requisite due to the highly conformation-dependent dynamics of a polymer chain in solution, since HI become highly screened as the polymer collapses more and more. For the sg-state, $\langle L\rangle$ depends weakly on $\tilde{\dot{\gamma}}$, and is roughly constant except when $\tilde{\dot{\gamma}}$ is large enough to elicit small responses similar to traditional droplet stretching.

To corroborate our results we perform Brownian Dynamics simulations with hydrodynamic interactions to investigate the behavior of a self-associating single polymers in flow. The model is based on a coarse-grained representation of a polymer. The interactions between the different monomers are given as follows: the connectivity along the backbone is ensured by using stiff harmonic springs between neighboring monomers along the contour, self-avoidance is assured by employing a Lennard-Jones potential between all monomers with an attractive well depth of 0.41 k_BT that ensures a non-associating polymer will be in the θ-state, and finally, we include binding between monomers that are within a reaction radius. The last interaction is the self-associating interaction and the one that allows us to tune the relaxation timescale of the polymer without changing its equilibrium conformation. For the last interaction we use the classical binding model of Bell (see Fig. 2).[2] Details of the implementation of the model can be found in the supplementary material (SM) or in Ref. [13].

We carried out the aforementioned simulations with a reaction radius of $r_{rxn} = 2.1$, which has been previously shown to work well in this type of simulation,[13] and use $1/\tau_0 = 1/(0.0025\tau)$ as our attempt rate. We mainly

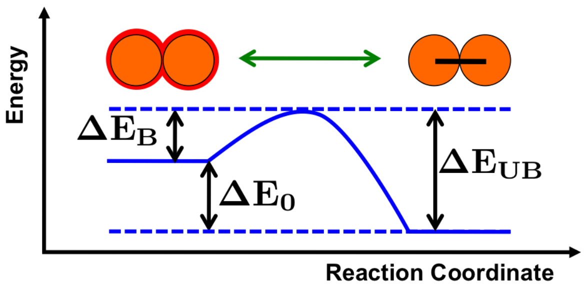

FIG. 2. The energy landscape for a single associating pair of binding monomers. If two spatially adjacent monomers are within the reaction radius, there is a possibility that these monomers will bind and a spring between the two will form. The energy barrier to form this bond is given by ΔE_B, and the barrier to unbind from this bond is given by ΔE_{UB}.

measure the extension distance $\langle \tilde{L} \rangle$ as a function of the shear rate $\tilde{\dot{\gamma}}$ since this value is a standard measurement in the previous literature to describe the geometry of the polymer chain.[15, 19, 20, 23] Other measures could be used, however we expect them to demonstrate essentially the same behavior. We plot in Figure 3a the fractional extension $\langle L \rangle/(2Na)$ as a function of shear rate $\tilde{\dot{\gamma}}$ for a number of different binding energy landscapes (parameterized by ΔE_{UB}, $\Delta E_0 = \Delta E_B - \Delta E_{UB}$) for chain length $N = 80$. We expect that, in the limit $\tilde{\dot{\gamma}} \to 0$, the equilibrium value of $\langle L \rangle$ should approach the same value for the same value of ΔE_0 regardless of ΔE_{UB}. This is indeed the case, and as ΔE_0 decreases we also observe the anticipated decrease in the size of the coil in this limit. The behavior at finite and positive values are dependent, however, on ΔE_{UB}. As the shear rate $\tilde{\dot{\gamma}}$ increases, the shear response follows the expected elongation behavior for the coil-stretch state. At some point, however, there is a sudden and marked decrease in the elongation with an increase in shear rate. This non-monotonic behavior subsequently reverses at even larger values of $\tilde{\dot{\gamma}}$, to once again exhibit an increase in elongation with increasing shear rate. This can be attributed to the globule stretching response to the fluid flow, which occurs at large shear rates relative to the typical stretch transition for the coil or lightly-collapsed globule. At low enough values of $\Delta E_0 \approx -4$, the stretching behavior is fully arrested as the binding energy becomes too much for the flow to overcome regardless of ΔE_{UB}.

The observed non-monotonicity is not unique to this particular scenario, since a similar feature has been reported previously for non-associating Θ-coils in shear and a dynamically-induced collapse transition was seen experimentally in DNA under oscillating electric fields.[18, 30] In our case, we can however, show that by changing the time scale of the binding kinetics a sticky globule state is indeed the relevant pathway. In Figure 3b, we again plot $\langle L \rangle$ versus $\tilde{\dot{\gamma}}$ for the case of $\Delta E_0 = 0$ for a number of different values of ΔE_{UB}. The parameter ΔE_{UB} directly changes the relaxation time of the polymer through the relationship $\tilde{\tau}_L \approx 1 + \tilde{\tau}_0 e^{\Delta E_{UB} - \langle \tilde{F}_B \rangle \tilde{r}^*}$.[13] We also plot for reference the shear response of a non-associating coil with $\tilde{u} = 0.55$, which has the same equilibrium size as a polymer with $\Delta E_0 = 0$. The non-associating polymer with $\tilde{u} = 0.55$ is useful as an input to our theory data, since it serves as an approximation of $\langle L \rangle_u$. We use a function of $\langle \tilde{L} \rangle_{sg}/(2N)$ that is ≈ 0.15 for $\tilde{\dot{\gamma}} \lesssim 1$ and increases in the same fashion as the $\Delta E_{UB} = 11$ data for $\tilde{\dot{\gamma}} \gtrsim 1$, which is suggested by the simulation data in Figure 3c. This is somewhat larger than the equilibrium value for the rest state, because of the shear-induced bias of the globule state towards a slightly elongated structure. In the SM, we provide a small analysis of our simulation determination for the $\langle \tilde{F}_B \rangle \tilde{r}^*$ term, but even at shear rates on the high end of what we consider ($\tilde{\dot{\gamma}} = 10.0$) $\langle \tilde{F}_B \rangle \tilde{r}^*$ is well below ca. $1 k_B T$. With these parameters, we can demonstrate quantitative matching between simulated shear responses and equations 1 and 2, which are shown as solid lines in Figure 3b. This model provides an excellent fit to the data over the entire simulation range of $\tilde{\dot{\gamma}}$, indicating that we correctly capture the physics present in the simulations. Deviations begin to appear at high ΔE_{UB}, which we attribute to tumbling events that do not lead to sticking. **While such non-sticking events are rare in our simulations since associations occur between all non-nearest-neighbor beads, we expect specific interactions like those found in proteins would necessitate modifications to our theory to accommodate this effect and would display behaviors similar to work by Szymczak and Cieplak.[29]**

To reinforce the idea that such a coarse view of the polymer conformation space is indeed valid, we provide in Figure 3c a number of time plots of the elongation $\langle L \rangle$ for a number of shear rates for a polymer that displays non-monotonicity (in this case, $\Delta E_{UB} = \Delta E_B = 5.0$). These time plots display the features that we expect for our postulated situation; at $\tilde{\dot{\gamma}} = 0.025$, there is little elongation. At $\tilde{\dot{\gamma}} = 0.25$ there are large tumbling fluctuations in $\tilde{L}$ characteristic of a typical polymer coil-stretch transition. At even larger $\tilde{\dot{\gamma}} = 2.5$, elongation becomes significantly suppressed due to slow response of the "stuck" polymer. Occasional extension occurs, but quickly reverts to the sticky globule state upon tumbling. Finally, at the highest simulated $\tilde{\dot{\gamma}} = 10.0$ the stuck globule state begins to elongate due to the influence of shear. In the SM we also present a spectral analysis of these time plots that demonstrates features characteristic of this "sticky globule" behavior.

In summary, we have shown that the inclusion of self-associating binders based on Bell model kinetics[2] has a profound affect on the dynamics of polymers responding to an applied shear flow. Due to the competition between the relaxation time of the polymer, the relaxation time of the binders, and the deformation time scale of the fluid flow, a strong non-monotonic shear response is observed. Our coarse-grained theoretical approach is sufficient to capture the underlying physics that govern the response observed **in the simulations**, which can

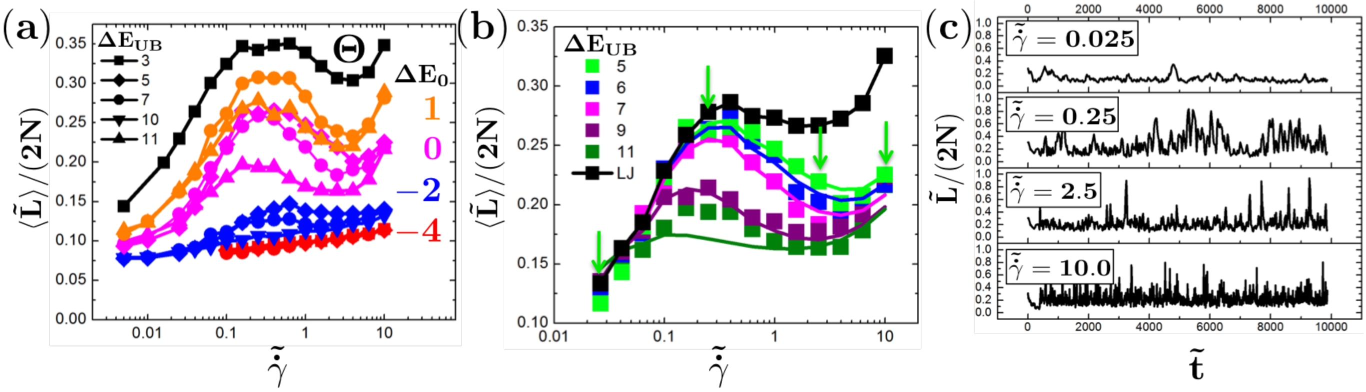

FIG. 3. (a) Polymer elongation $\langle L\rangle/(2N)$ as a function of the shear rate $\tilde{\dot{\gamma}}$ for different values of ΔE_0 and ΔE_{UB}. As expected, decrease in ΔE_0 results in the collapse of the polymer at all values of $\tilde{\dot{\gamma}}$. Increasing values of ΔE_{UB} demonstrate the presence of a marked decrease in the ability of the polymer to elongate under the influence of shear for all values of ΔE_0. The response for a Θ-polymer is also shown, and also demonstrates non-monotonicity due to the same effect as that seen for the binders, only solely due to hydrodynamic effects. (b) $\langle L\rangle/(2N)$ vs. $\tilde{\dot{\gamma}}$ for different values of ΔE_{UB} at $\Delta E_0 = 0$. Simulation data (points) matches well with the theoretical prediction (lines). The LJ response for a polymer of similar level of collapse $\tilde{u} = 0.55$ is also shown (connected points), and serves as an input for the theory. Green arrows correspond to time sequences shown in (c). For (a) and (b), error bars are smaller than symbol size. (c) Polymer elongation $\tilde{L}/(2N)$ as a function of time at a number of shear rates with $\Delta E_0 = 0$ and $\Delta E_{UB} = 5.0$. Notice the suppresion of stretching events as shear rate is increased.

be readily tuned by changing the kinetic characteristics of the binders. The non-monotonic behavior shown and manipulated here is an example of concepts that may prove useful in describing a number of similar behaviors, such as those seen in Θ-polymers in shear[18] and DNA responding to AC electric fields.[30]

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[33] Tildes indicate that a value was rendered dimensionless by a combination of the single-bead diffusion time τ_0, thermal energy k_BT, and the bead radius a as discussed in the SM.

[34] Tumbling of Θ-polymers typically follows the scaling $\nu_{tumble} \sim \dot{\tilde{\gamma}}^m$, where $m < 1$. Since we are dealing with collapsed polymers, however, stretching attempts are associated with globule rotation and $\nu_{u-sg} \sim \dot{\tilde{\gamma}}^1$ (see for example peak f_1 in fig. 8 of [29]).