The Ultrasensitivity of Living Polymers

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Synthetic and biological living polymers are self-assembling chains whose chain length distributions (CLDs) are dynamic. We show these dynamics are ultrasensitive: Even a small perturbation (e.g., temperature jump) nonlinearly distorts the CLD, eliminating or massively augmenting short chains. The origin is fast relaxation of mass variables (mean chain length, monomer concentration) which perturbs CLD shape variables before these can relax via slow chain growth rate fluctuations. Viscosity relaxation predictions agree with experiments on the best-studied synthetic system, α-methylstyrene.

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The term "living polymers" labels a remarkable and diverse family of self-assembling systems in which molecules or other microscopic units spontaneously aggregate into long chains by continuously adding to chain ends. Their technological and biological importance and their unusual properties as examples of soft condensed matter have driven a large body of experimental and theoretical research [1–12]. The classic synthetic example is ionic living polymerization [1–7], where monomers assemble into flexible polymer chains by adding to charged chain ends which remain "alive" even after the monomer is consumed, a property widely exploited commercially to synthesize high performance block copolymers and other novel materials [2]. A recent variant on this theme with immense technological potential is living free radical polymerization [8], where ingenious capping-decapping schemes prevent termination and yet permit chain propagation. In the biological world, actin and microtubule filaments, rapidly assembled from the proteins actin and tubulin, are essential to the motility and structural integrity of living cells [9].

As polymeric or filamentous materials, the novel and distinguishing feature of these systems is that unlike inert polymers the chains are *dynamic* or "living" objects whose lengths constantly fluctuate. The polymerization processes are alive: When external conditions change, chain length distributions can respond dynamically and relax to a new equilibrium. This adaptability is the crucial property exploited in both synthetic and natural applications. For example, it enables living cells to rapidly initiate motion or shape changes by altering cellular conditions in response to extracellular signals.

In this Letter, we study this dynamical responsiveness theoretically. While a rather clear picture of equilibrium properties [1,3] has been established, living polymer dynamics are far less well understood [4–7]. We focus on the synthetic system which has received most experimental attention [1,5–7], the anionic living polymer poly-α-methylstyrene (PAMS), and we compare our predictions to PAMS viscosity relaxation measurements at the end of this Letter. Aside from its intrinsic importance, PAMS is a model system for more complex cases such as biological living polymers, and most of our results are completely general. We use the term living polymers in the traditional sense [1,2] to denote systems where (i) the concentration of living chains, ρ_{chains}, is fixed for all time by the number of initiators, and (ii) chains grow at their ends only. Related classes include systems where surfactants aggregate into spherical [11] or elongated ("wormlike") micelles [12] whose number is not fixed, and whose dynamics [11,12] are very different.

The principal conclusion of this work is that living polymers are *ultrasensitive*, i.e., highly dynamically susceptible to small perturbations. Thus, a small change in external conditions, inducing a small change in the equilibrium state well described by a linear susceptibility, has nonetheless a large dynamical effect: Intermediate states deviate strongly from equilibrium in that some observables are perturbed in a highly nonlinear manner. To quantify this, consider PAMS whose equilibrium chain length distribution (CLD) is close to the broad exponential [1,5] predicted by theory, $\phi_{eq}(N) \sim e^{-N/\bar{N}_{eq}}$ (see Fig. 1), with typical mean number of monomer units per chain $\bar{N}_{eq}$ in the range [7] of a few 100 to several 1000. A standard experimental procedure is the "T-jump" where temperature is suddenly changed by an amount ΔT. Consider a PAMS system with $\bar{N}_{eq} = 1000$ subjected to a small decrease $\Delta T = -5\,^\circ\mathrm{C}$ as measured by the small parameter $\epsilon \equiv -\Delta T/T_0 \approx 0.1$, where $T_0 \equiv \partial T/\partial \ln m_{eq} \approx 50\,^\circ\mathrm{C}$ for typical PAMS studies and m_{eq} is the equilibrium monomer concentration. The theory presented here predicts the onset after $\sim$3 h of a drastic depletion of short chains. By 10 h, a hole has appeared in the CLD in the region $0 < N \lesssim 400$ (see Fig. 1) and lengths $N \lesssim 100$ have virtually disappeared. This is despite the fact that the change in the equilibrium CLD $\phi_{eq}(N)$, which is recovered after $\sim 10^3$ h, is destined to be small, $\delta\phi_{eq}(N)/\phi_{eq}(N) = \mathcal{O}(\epsilon)$ for all N. This hole completely invalidates perturbation theory: *there are no small perturbations* (other than those so tiny as to be beyond typical experimental resolution). This is the essence of ultrasensitivity.

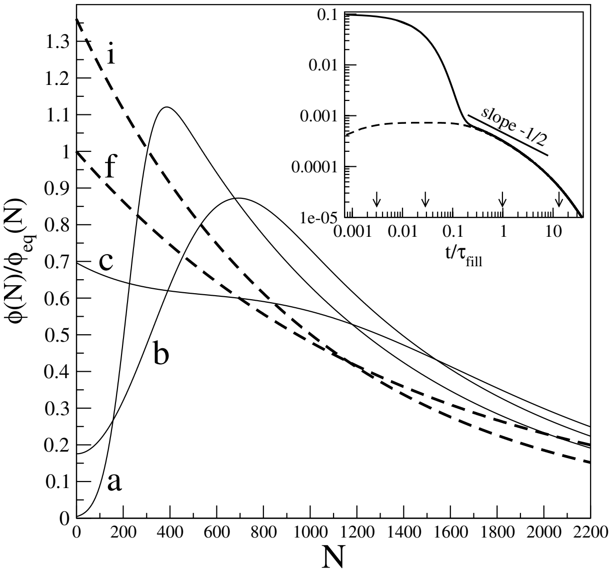

FIG. 1. Numerical results for response of CLD to a small T-jump perturbation of amplitude $\epsilon = 0.1$ perturbing T-dependent parameters v^- and k^+ in Eq. (1). Final equilibrium exponential (curve f, $\bar{N}_{eq} = 1366$, $\theta = 0.37$) is close to the initial equilibrium exponential (curve i). Along its path $i \to f$, the CLD deviates nonlinearly from both. Times in units of v^- (for PAMS [1], $v^- \approx 0.1$ s). Time scales: $t^* \approx 400$, $\tau_{\text{fast}} \approx 3640$, $\tau_{\text{fill}} \approx 1.32 \times 10^5$, $\tau_{\text{slow}} \approx 1.86 \times 10^6$. Curve a, $t = 3640$: A hole has appeared at small N. Curve b, $t = 3 \times 10^4$: hole filling. Curve c, $t = 2.3 \times 10^5$: final shape relaxation towards equilibrium, curve f. Inset: Relaxation of fast and slow variables. Arrows from left to right indicate t^* τ_{fast}, τ_{fill}, and τ_{slow}. Fast variables $\delta m_t/m_{eq} = -\theta\, \delta\bar{N}_t/\bar{N}_{eq}$ (solid line) decay exponentially after τ_{fast}, and are then enslaved to the slow variable $-\delta\phi_t(0)$ (dashed line). Note initial nonlinear increase of $-\delta\phi_t(0)$ after t^*. Theory predicts $\delta\phi_t(0) \sim t^{-1/2}$ during $\tau_{\text{fill}} < t < \tau_{\text{slow}}$ and $\delta\phi_t(0) \sim e^{-t/\tau_{\text{slow}}}$ for $t > \tau_{\text{slow}}$.

We consider living polymers, such as the PAMS systems studied by Greer and co-workers [1,5–7], where monomers spontaneously polymerize below a ceiling temperature T_p (see Fig. 2). The dynamics of $\phi_{t,N}$, the number of chains of length N, are $\dot{\phi}_{t,N} = v^+ \phi_{t,N-1} - (v^+ + v^-)\phi_{t,N} + v^- \phi_{t,N+1}$, where $v^+ = k^+ m$ and v^- are monomer addition and dissociation rates from chain ends [13] (k^+ is the addition rate constant). Rearranging terms and taking the continuous limit immediately gives

$$\partial\phi_t/\partial t = -v_t \partial\phi_t/\partial N + D_t \partial^2\phi_t/\partial N^2,$$
$$0 = v_t\phi_t(0) - D_t[\partial\phi_t/\partial N]_{N=0}, \qquad (1)$$

where a zero current boundary condition applies at $N = 0$. Note a second derivative term naturally emerges, with a "diffusivity" coefficient $D_t \equiv (v^+ + v^-)/2$, representing fluctuations about the average growth rate or "velocity" $v_t \equiv v^+ - v^-$. Both v_t and D_t depend on ϕ_t [see Eq. (7) and following remarks]. Setting $\partial\phi_t/\partial t = 0$ gives the equilibrium exponential CLD with $\bar{N}_{eq} = -D_{eq}/v_{eq}$. Since $\bar{N}_{eq} \gg 1$, it follows that in equilibrium $v^+ \approx v^-$, the diffusivity is $D_{eq} \approx v^-$, and the velocity has a small negative value relative to the characteristic scale v^-:

$$v_{eq} = -v^-/\bar{N}_{eq}. \qquad (2)$$

This is just sufficient to negate diffusive broadening which would otherwise smear out the equilibrium CLD of width $\bar{N}_{eq}$ after time $\tau_{\text{slow}} = \bar{N}_{eq}^2/D_{eq}$; i.e., $v_{eq}\tau_{\text{slow}} = -\bar{N}_{eq}$. Note that since the average velocity over all chains must vanish in equilibrium (there can be no net dissociation to the monomer pool), the $N > 0$ chains must have a small negative velocity to balance the unique $N = 0$ chains (consisting of an initiator only, Fig. 2) which cannot depolymerize and so have a *positive* velocity.

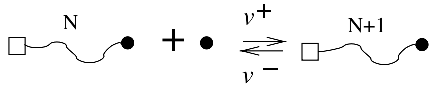

FIG. 2. A living polymer is an initiator (square) plus N monomers. Monomers can add (subtract) from its live end (filled circle) at rates v^+ (v^-). The initiators of Refs. [5,7] are bifunctional (one interior initiator plus two live ends).

A clue as to the origin of ultrasensitivity is already apparent in this equilibrium situation. The significance of Eq. (2) is that equilibrium is an extremely delicate balance sustained by a tiny negative velocity easily overwhelmed by even a very small perturbation. Consider an equilibrium system suddenly subjected to a small negative T-jump ΔT, after which the current monomer concentration m exceeds its equilibrium value for the new temperature by $\delta m \approx -(\Delta T/T_0)m_{eq} \equiv \epsilon m_{eq}$ (δX denotes the deviation of any property X from its equilibrium value, X_{eq}, which will eventually be attained after relaxation). This generates a velocity boost $\delta v = k^+ \delta m$. Since $k^+ m_{eq} \approx v^-$ to order $1/\bar{N}_{eq}$, we have

$$\delta v \approx \epsilon v^-. \qquad (3)$$

Comparing Eqs. (2) and (3), one sees that despite the smallness of the perturbation, $\epsilon \ll 1$, the delicate balance of velocity and diffusion which characterizes equilibrium is destroyed since the boost δv greatly exceeds the equilibrium velocity v_{eq}. This holds for any ϵ above a tiny threshold $1/\bar{N}_{eq}$. Immediately after the perturbation, diffusive broadening $\sim(D_{eq}t)^{1/2}$ is still stronger than coherent chain growth $\sim\epsilon v^- t$. But for times larger than $t^* \approx D_{eq}/\epsilon^2 v^-$ chains grow coherently, i.e., $\bar{N}$ will increase until the excess mass δm held by the monomer reservoir has been transferred to the polymer system and the velocity boost has decayed. In the process, the mean chain length increases by an amount $-\delta\bar{N}$ determined by conservation of total concentration of monomers m_{total}:

$$m + \rho_{\text{chains}}\bar{N} = m_{\text{total}}, \qquad \delta\bar{N}/\bar{N}_{eq} = -\epsilon\theta^{-1}. \qquad (4)$$

The parameter $\theta \equiv (m_{\text{total}} - m_{eq})/m_{eq} \approx (T_p - T)/T_0$ measures distance into the polymerization regime, and will be taken as order unity here. Thus, the entire CLD translates uniformly by $\approx \epsilon\bar{N}_{eq}$ (Fig. 1) in time

$$\tau_{\text{fast}} = \delta\bar{N}/(\epsilon v^-) = \bar{N}_{eq}/(\theta v^-). \tag{5}$$

This leaves behind a hole in the CLD: Chains with lengths less than $\epsilon\bar{N}_{eq}$ have disappeared.

For times beyond τ_{fast}, mass transfer is essentially complete and m, v, and $\bar{N}$ are very nearly relaxed. These are the fast variables. The process of CLD *shape* relaxation needs much more time. It relies on the far slower diffusive process of incoherent reshuffling of monomers between chains. The time τ_{fill} needed to fill the hole is simply the diffusion time corresponding to the hole width,

$$\tau_{\text{fill}} = \epsilon^2\tau_{\text{slow}}/\theta^2. \tag{6}$$

The last process is global CLD shape relaxation on the scale $\bar{N}_{eq}$, requiring a diffusion time $\tau_{\text{slow}} = \bar{N}_{eq}^2/D_{eq}$. These events are depicted in Fig. 1.

In summary, relaxation to the new equilibrium state involves three distinct episodes: (i) coherent chain growth for $0 < t < \tau_{\text{fast}}$ during which fast mass variables relax, (ii) hole filling, i.e., recovery of short chains, during $\tau_{\text{fast}} < t < \tau_{\text{fill}}$, and (iii) global diffusive relaxation for $t > \tau_{\text{fill}}$ during which slow shape variables relax on a time scale τ_{slow}. It is this conflict of time scales which is the origin of the nonlinear hole produced by (i): Slow diffusive shape equilibration simply cannot keep pace with the rapid deformation produced by mass transfer.

It is interesting to compare this with spherical micelle aggregation which involves two distinct relaxation processes [11]. The first entails fast mass exchange between monomers and nearly monodisperse micelles whose number remains essentially fixed due to large aggregate nucleation/dissociation barriers. This is similar to process (i) above. However, a crucial difference is that the number of aggregates can ultimately change and the time scale for this process in consequence depends inversely on total monomer concentration (whereas τ_{fast} is independent of m_{total}). During a second, much slower process, the number of micelles reequilibrates. This process has no analogue for the living polymers we study.

Let us now briefly outline formal calculations justifying these arguments, starting from Eq. (1). Its steady state solution is the equilibrium Flory-Schultz [1] CLD, $\phi_{eq}(N) = e^{-N/\bar{N}_{eq}}/\bar{N}_{eq}$ with $\bar{N}_{eq} \approx m_{\text{total}}\theta/[\rho_{\text{chains}}(1+\theta)]$. Multiplying Eq. (1) by N and integrating, one has

$$\dot{v}_t = -v_t/\tau_{\text{fast}} - D_t\phi_t(0)/\tau_{\text{fast}}, \tag{7}$$

after using Eqs. (4) and (5). Given the CLD ϕ_t, this relationship determines the time-dependent velocity v_t and, thence, diffusivity $D_t = v_t/2 + v^-$. The technical difficulty is that both v_t and D_t depend nonlocally on ϕ_t, i.e., Eq. (1) is a nonlinear and nonlocal system.

Consider a negative T-jump perturbation inducing, as discussed, a velocity $v_0 \approx \epsilon v^-$ at $t = 0$. Now, to order ϵ, $D_t \approx v^- \approx D_{eq}$. Thus, in the velocity kinetics, Eq. (7), the v_t term is initially much greater than the D_t term (provided $\epsilon > 1/\bar{N}_{eq}$). Hence, $v_t \approx \epsilon v^- e^{-t/\tau_{\text{fast}}}$ in the CLD evolution kinetics Eq. (1) in which, for $t > t^*$, the coherent term wins and the CLD translates along the N axis, $\phi_t(N) \approx \phi_0(N - \int_0^t v_t)$. Its displacement converges for $t \gg \tau_{\text{fast}}$ to $\epsilon\bar{N}_{eq}/\theta$. In other words, the CLD translates and then halts on a time scale τ_{fast}, leaving a hole of size $\approx \epsilon\bar{N}$ in its wake (see Fig. 1). More precisely, the trailing edge broadens by $(D_{eq}t)^{1/2}$ and produces an exponentially small amplitude at the origin, $\phi_t(0) \sim e^{-t/t^*}$.

This concludes episode (i). The linearly related fast variables v, m, and $\bar{N}$ have the same decay kinetics and for $t \gg \tau_{\text{fast}}$ have all relaxed. Since the velocity is exponentially small, the CLD kinetics Eq. (1) now describe essentially pure diffusion with reflecting boundary conditions. This is episode (ii): On the time scale τ_{fill}, diffusion fills the hole (see Fig. 1) and replenishes the amplitude at the origin, $\phi_t(0) \approx (t/\tau_{\text{fill}})^{1/2}e^{-4\tau_{\text{fill}}/t}/\bar{N}_{eq}$. This recovery of $\phi_t(0)$ and the decay of v_t imply that at time $\tau_{qs} \approx (\tau_{\text{fast}}\tau_{\text{fill}})^{1/2}$ the two right-hand side terms in the velocity dynamics Eq. (7) become equal. Self-consistently, one finds that thereafter they remain matched, i.e., $\dot{v}_t$ is much smaller than either of these terms. Thus, from this time on, the fast velocity variable (intrinsic time scale τ_{fast}) evolves *quasistatically*, enslaved to the slow variable $\phi_t(0)$ (intrinsic time scale τ_{slow}) according to

$$v_t \approx -v^-\phi_t(0) \qquad (t > \tau_{\text{qs}}). \tag{8}$$

It follows that the velocity now undergoes a recovery as the hole fills up. By τ_{fill} its magnitude is of the order of the equilibrium value and can thus compete with diffusion. This heralds the onset of episode (iii): We return to the basic dynamics, Eq. (1), with velocity and diffusion terms now of equal importance. For the first time, relative perturbations of all quantities are now small, and we can apply standard perturbation theory. We find the $N = 0$ chains recover as $\delta\phi_t(0) \sim t^{-1/2}$ up to τ_{slow} and $\sim e^{-t/\tau_{\text{slow}}}$ for $t > \tau_{\text{slow}}$. During these very late stages the fast variables, which long ago decayed close to equilibrium, are fine-tuned to their true equilibrium values, following $\phi_t(0)$ quasistatically according to Eq. (8).

Note we implicitly assumed sufficient time for the hole to develop before mass transfer is complete, i.e., $\tau_{\text{fast}} > t^*$. This is true provided $\epsilon > \epsilon_c = 1/\bar{N}_{eq}^{1/2}$. For very small perturbations $\epsilon < \epsilon_c$, the relative depth of the hole though much greater than ϵ is less than unity. Finally, we have studied $\Delta T < 0$. The response to a *positive* T-jump is similar, but instead of a hole a large peak $\sim\bar{N}_{eq}\epsilon^2$ develops for small N, decaying after τ_{fill}.

We tested our theory by numerical integration of coupled differential equations describing the monomer-polymer dynamics. Figure 1 shows the predicted deep hole developing after a small negative T-jump. Long time enslavement of fast variables to slow ones is clearly demonstrated (inset).

We conclude by discussing our results and comparing to experiment. We found that, following a perturbation,

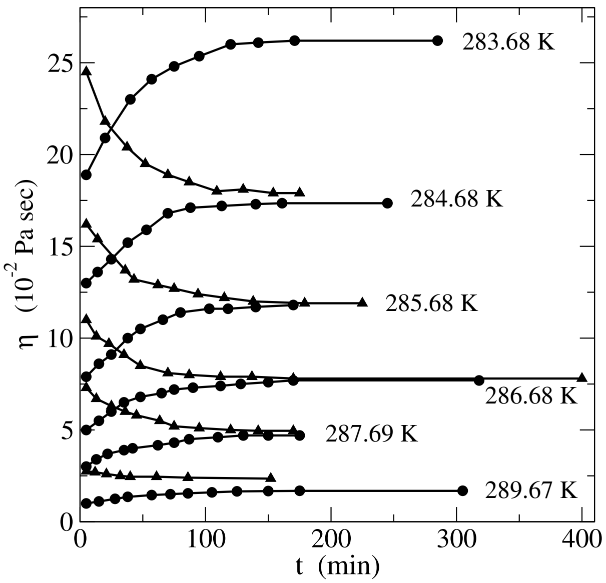

FIG. 3. Viscosity relaxation measurements by Ruiz-Garcia and Greer [7] following small T-jumps ($|\Delta T| \approx 1°$ K) on PAMS in tetrahydrofuran initiated by sodium naphthalide. Reproduced from Fig. 1 of Ref. [7]. Circles (triangles) refer to positive (negative) ΔT. $m_{\text{total}} = 0.29$ gm/cm^3, $\rho_{\text{chains}} \approx 2.7 \times 10^{-4}$ gm/cm^3 (semidilute conditions).

living polymers relax by adjusting (a) their total *mass*, proportional to first moment $\bar{N}$ and (b) the *shape* of their CLD. Mass variables are fast (relaxation time $\tau_{\text{fast}} \sim \bar{N}$) because monomer-polymer mass transfer is a coherent process. Coherent chain growth, however, cannot affect CLD shape whose relaxation therefore relies on slow diffusionlike fluctuations in chain growth rates (relaxation time $\tau_{\text{slow}} \sim \bar{N}^2$). These time scales are typically separated by 2 or 3 orders of magnitude. In Fig. 3, we reproduce viscosity relaxation measurements by Ruiz-Garcia and Greer [7] after small positive and negative temperature jump perturbations of the living polymer PAMS at six different temperatures. Now generally we expect viscosity $\eta \sim c_\phi \bar{N}^\gamma$, where γ is a characteristic exponent [7] and c_ϕ depends on the entire CLD, $\phi(N)$, including shape properties. Our theory thus predicts a fast initial relaxation of η in a time τ_{fast} followed by a very slow relaxation in τ_{slow}. Now [7] $\rho_{\text{chains}} \approx 2.7 \times 10^{-4}$ gm/cm^3 while [6] $k^+ \approx 0.2M^{-1}$ sec^{-1} was measured to vary by $\approx 10\%$ over this temperature range. Thus, rewriting $\tau_{\text{fast}} = 1/\rho_{\text{chains}} k^+$, we predict a *constant* relaxation time (± 10%) for all 12 measurements, $\tau_{\text{fast}} \approx$ 2000 sec. This agrees very closely with experiment (see Fig. 3) despite the fact that the observed viscosities varied by an order of magnitude and the mean chain lengths are estimated to vary from almost zero up to several thousand units at the lowest temperature. Note $\tau_{\text{slow}} = \tau_{\text{fast}}^2 v^- \theta \approx$ 1 week–1 month, after estimating [1] $\theta \approx 0.5$ and using $v^- = 0.1$ sec^{-1}. The second shape-derived relaxation of η is therefore unobservably long for this experiment.

Very large temperature quenches were studied in Ref. [5]. $\bar{N}$ relaxed faster than the second moment, though it was unclear if m and $\bar{N}$ were coupled as required by mass conservation, possibly due to ionic aggregation [10]. The authors of Ref. [4] studied large perturbations theoretically, identifying the time scales τ_{fast} and τ_{slow}. Their analytical results were valid for short times and very small θ.

In this Letter, we showed that even a small perturbation leads to a nonlinear dynamical response. This ultrasensitivity is due to the inability of slow CLD shape variables to keep pace with the fast relaxation of $\bar{N}$ which entails simple translation of the CLD leaving a hole or peak at small N. Of all slow variables, the most sensitive is $\phi_t(0)$, the number of $N = 0$ chains, which becomes exponentially small or massively enhanced. These free initiators also govern the very late fine-tuning of the fast variables $\bar{N}$ and m, the free monomer concentration. Physically, this is because monomers add to chain ends only. But all ends are identical except for the $N = 0$ chains which cannot shed monomers. Thus, $\phi_t(0)$ is the only dynamic polymer property featuring in the kinetics of m. Given its central role, we propose measurement of the number of free initiators by spectroscopic or other methods as a revealing probe of ultrasensitivity.

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