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) non-linearly 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, \alpha-methylstyrene.

PACS numbers: 82.35.-x,05.40.-a,87.15.Rn

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\textsuperscript{[12,13]}. The classic synthetic example is ionic living polymerization\textsuperscript{[13]} where monomers assemble into flexible polymer chains by adding to charged chain ends which remain “alive” even after monomer is consumed, a property widely exploited commercially to synthesize high performance block copolymers and other novel materials\textsuperscript{2}. A recent variant on this theme with immense technological potential is living free radical polymerization\textsuperscript{[13]} where ingenious capping-decapping schemes prevent termination and yet permit chain propagation. In the biological world, actin and microtubule filaments, rapidly assemble into long chains by continuously adding to chain ends. Their technological and biological importance 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 are ingenuous capping-decapping schemes prevent termination and yet permit chain propagation.

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 responsensiveness theoretically. Whilst a rather clear picture of equilibrium properties\textsuperscript{[4,6]} has been established, living polymer dynamics are far less well understood\textsuperscript{[5,8,9,10,11,12,13]}. We focus on the synthetic system which has received most experimental attention\textsuperscript{[4,6,8,9,10,11,12,13]}, the anionic living polymer poly \alpha-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\textsuperscript{1,2} to denote systems where (i) the concentration of living chains, \rho_{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\textsuperscript{[11]} or elongated (“wormlike”) micelles\textsuperscript{[12]} whose number is not fixed, and whose dynamics\textsuperscript{[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 non-linear manner. To quantify this, consider PAMS whose equilibrium chain length distribution (CLD) is close to the broad exponential\textsuperscript{[4,6]} predicted by theory, \phi_{eq}(N) \sim e^{-N/N_{eq}} (see fig. \textsuperscript{11}), with typical mean number of monomer units per chain \bar{N}_{eq} in the range\textsuperscript{[6]} of a few 100 to several 1000. A standard experimental procedure is the “T-jump” where temperature is suddenly changed by an amount \Delta T. Consider a PAMS system with \bar{N}_{eq} = 1000 subjected to a small decrease \Delta T = -50^\circ C as measured by the small parameter \epsilon \equiv -\Delta T/T_0 \approx 0.1, where \textcolor{red}{T_0 \equiv \partial T/\partial \ln m_{eq} \approx 50^\circ C for typical PAMS studies and m_{eq} is the equilibrium monomer concentration. The theory presented here predicts the onset after \sim 3 hours of a drastic depletion of short chains. By 10 hours a hole has appeared in the CLD in the region 0 < N \lesssim 400 (see fig. \textsuperscript{11}) 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 hours, is destined to be small, \delta \phi_{eq}(N)/\phi_{eq}(N) = O(\epsilon) for all N. This hole completely invalidates perturbation theory: \textit{there are no small perturbations} (other than those so tiny as to be beyond typical experimental resolution).
The diffusivity is $D_{eq} \approx v^-$ and the velocity has a small negative value relative to the characteristic scale $v^-$

$$v_{eq} = -v^-/N_{eq}.$$  

This is just sufficient to negate diffusive broadening which would otherwise smear out the equilibrium MWD of width $N_{eq}$ after time $\tau_{slow} = N_{eq}^2/D_{eq}$; i.e., $v_{eq}\tau_{slow} = -N_{eq}$. 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.

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 $\Delta T$, after which the current monomer concentration $m$ exceeds its equilibrium value for the new temperature by $\delta m \approx -(\Delta T/T_0)m_{eq} \equiv \epsilon m_{eq}$ ($\delta X$ 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 $1/N_{eq}$, we have

$$\delta v \approx \epsilon v^-.$$  

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 $\delta v$ greatly exceeds the equilibrium velocity $v_{eq}$. This holds for any $\epsilon$ above a tiny threshold $1/N_{eq}$. Immediately after the perturbation, diffusive broadening $\sim (D_{eq}t)^{1/2}$ is still stronger than coherent chain growth $\sim v^+ t$. But for times larger than $t^* \approx D_{eq}/\epsilon^2 v^-$ chains grow coherently, i.e. $\dot{N}$ will increase until the excess mass $\delta m$ 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 $-\delta N$ determined by conservation of total concentration of monomers $m_{total}$:

$$m + \rho_{chains} \dot{N} = m_{total}, \quad \delta N/N_{eq} = -\epsilon \theta^{-1}.$$  

The parameter $\theta \equiv (m_{total} - m_{eq})/m_{eq} \approx (T_p - T)/T_0$ 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
\[ \tau_{fast} = \delta \bar{N}/(\epsilon v^-) = \bar{N}_{eq}/(\theta v^-) . \] (5)

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

For times beyond $\tau_{fast}$, 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 $\tau_{fill}$ needed to fill the hole is simply the diffusion time corresponding to the hole width,
\[ \tau_{fill} = \epsilon^2 \tau_{slow}/\theta^2 . \] (6)

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

In summary, relaxation to the new equilibrium state involves 3 distinct episodes: (i) coherent chain growth for $0 < t < \tau_{fast}$, during which fast mass variables relax, (ii) hole-filling, i.e. recovery of short chains, during $\tau_{fast} < t < \tau_{fill}$ and (iii) global diffusive relaxation for $t > \tau_{fill}$ during which slow shape variables relax on a timescale $\tau_{slow}$. It is this conflict of timescales which is the origin of the non-linear 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. 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 timescale for this process in consequence depends inversely on total monomer concentration (whereas $\tau_{fast}$ is independent of $m_{total}$). During a second, much slower process, the number of micelles re-equilibrates. This process has no analogue for the living polymers we study.

Let us now briefly outline formal calculations justifying these arguments, starting from eq. 11. Its steady state solution is the equilibrium Flory-Schultz CLD, $\phi_{eq}(N) = e^{-N/\bar{N}_{eq}}/\bar{N}_{eq}$ with $\bar{N}_{eq} \approx m_{total}/[\rho_{chains}(1 + \theta)]$. Multiplying eq. 11 by $N$ and integrating one has
\[ \dot{\phi}_t = -\dot{v}_t/\tau_{fast} = -D_t \phi_t(0)/\tau_{fast} , \] (7)

after using eqs. 11 and 6. Given the CLD $\phi_t$, this relationship determines the time-dependent velocity $\dot{v}_t$ and thence diffusivity $D_t = \dot{v}_t^2/2 + v^-$. The technical difficulty is that both $\dot{v}_t$ and $D_t$ depend non-locally on $\phi_t$, i.e. eq. 11 is a non-linear and non-local system.

Consider a negative T-jump perturbation inducing, as discussed, a velocity $\dot{v}_0 \approx \epsilon v^-$ at $t = 0$. Now, to order $\epsilon$, $D_t \approx v^- \approx D_{eq}$. Thus in the velocity kinetics, eq. 7, the $\dot{v}_t$ term is initially much greater than the $D_t$ term (provided $\epsilon > 1/\bar{N}_{eq}$). Hence $\dot{v}_t \approx \epsilon v^- e^{-t/\epsilon \tau_{fast}}$ in the CLD evolution kinetics eq. 11, in which, for $t > t^*$, the coherent term wins and the CLD translates along the $N$ axis, $\phi_t(N) \approx \phi_0(N - \int_0^t \dot{v}_t)$. Its displacement converges for $t \gg \tau_{fast}$ to $\epsilon \bar{N}_{eq}/\theta_2$. In other words the CLD translates and then halts on a timescale $\tau_{fast}$, 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, $\phi_t(0) \sim e^{-t/\epsilon \tau^*}$.

This concludes episode (i). The linearly related fast variables $v, m$ and $\bar{N}$ have the same decay kinetics and for $t \gg \tau_{fast}$ have all relaxed. Since the velocity is exponentially small, the CLD kinetics eq. 11 now describe essentially pure diffusion with reflecting boundary conditions. This is episode (ii): on the timescale $\tau_{fill}$, diffusion fills the hole (see fig. 1) and replenishes the amplitude at the origin, $\phi_t(0) \approx (t/\tau_{fill})^{1/2}e^{-4t/\tau_{fill}}/\bar{N}_{eq}$. This recovery of $\phi_t(0)$ and the decay of $\dot{v}_t$ imply that at time $\tau_{qs} \approx (\tau_{fast} \tau_{fill})^{1/2}$ the two RHS terms in the velocity dynamics eq. 11 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 onwards, the fast velocity variable (intrinsic timescale $\tau_{fast}$) evolves quasi-statically, enslaved to the slow variable $\phi_t(0)$ (intrinsic timescale $\tau_{slow}$) according to
\[ \dot{v}_t \approx -v^- \phi_t(0) \quad (t > \tau_{qs}) \] (8)

It follows that the velocity now undergoes a recovery as the hole fills up. By $\tau_{fill}$ its magnitude is of order the equilibrium value and can thus compete with diffusion. This heralds the onset of episode (iii): we return to the basic dynamics, eq. 11, 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 $\tau_{slow}$ and $\sim e^{-t/\tau_{slow}}$ for $t > \tau_{slow}$. During these very late stages the fast variables, which long ago decayed close to equilibrium, are fine-tuned to their true equilibrium values, following $\phi_t(0)$ quasi-statically according to eq. 8.

Note we implicitly assumed sufficient time for the hole to develop before mass transfer is complete, i.e. $\tau_{fast} > t^*$. 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 $\epsilon$ 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 $\dot{N}_{eq} \epsilon^2$ develops for small $N$, decaying after $\tau_{fill}$.

We tested our theory by numerical integration of coupled ODEs describing the monomer-polymer dynamics. Fig. 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, 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 diffusion-like fluctuations in chain growth rates (relaxation time $\tau_{\text{slow}} \sim \bar{N}^2$.) These timescales 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 6 different temperatures. Now generally we expect viscosity $\eta \sim c_{\phi} \bar{N}^\gamma$ where $\gamma$ is a characteristic exponent and $c_\phi$ depends on the entire CLD, $\phi(N)$, including shape properties. Our theory thus predicts a fast initial relaxation of $\eta$ in a time $\tau_{\text{fast}}$ followed by a slow relaxation in $\tau_{\text{slow}}$. Now $\rho_{\text{chains}} \approx 2.7 \times 10^{-4}$ gm/cm$^3$ while $k^+ \approx 0.2 M^{-1} \text{sec}^{-1}$ was measured to vary by $\pm 10\%$ over this temperature range. Thus, rewriting $\tau_{\text{fast}} = 1/\rho_{\text{chains}} k^+$, we predict a constant relaxation time ($\pm 10\%$) for all 12 measurements, $\tau_{\text{fast}} \approx 2000$ seconds. 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 $\tau_{\text{slow}} = \tau_{\text{fast}}^{-1} \bar{v}^{-1} \theta \approx 1$ week-1 month, after estimating $\bar{v}^{-1} \approx 0.1 \text{sec}^{-1}$. The second shape-derived relaxation of $\eta$ is therefore unobservably long for this experiment.

Very large temperature quenches were studied in ref. [6] following small $T$-jumps ($|\Delta T| \approx 1^\circ K$) on PAMS in tetrahydrofuran initiated by sodium naphthalide. Reproduced from fig. 1. of ref. [6]. Circles (triangles) refer to positive (negative) $\Delta T$. $\eta_{\text{total}} = 0.29$ gm/cm$^2$, $\rho_{\text{chains}} \approx 2.7 \times 10^{-4}$ gm/cm$^3$ (semi-dilute conditions).

In this letter we showed that even a small perturbation leads to a non-linear 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 $\bar{N}$. Of all slow variables, the most sensitive is $\phi_0(0)$, 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 $\phi_0(0)$ 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.

This work was supported by the Petroleum Research Fund under grant no. 33944-AC7.

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