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Dynamics of DNA tumbling in shear to rotational mixed flows: Pathways and periods

Joo Sung Lee,[1] Eric S. G. Shaqfeh,[2] and Susan J. Muller[1]
[1]*Department of Chemical Engineering, University of California, Berkeley, California 94720, USA*
[2]*Departments of Chemical and Mechanical Engineering, Stanford University, Stanford, California 94305, USA*
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The tumbling dynamics of DNA have been examined via experiments and Brownian dynamics (BD) simulations in mixed flows that vary from pure shear to pure rotation. In shear, tumbling pathways and periods agree well with earlier studies; in rotation-dominated flows, a new tumbling pathway is identified and experimentally observed. Based on these results, we have developed robust scaling laws for DNA tumbling in both shear and rotational flows and have found a critical flow-type parameter for transition from the shearlike flow regime to the rotation-dominated one.

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Recent developments in direct visualization methods, coupled with Brownian dynamics simulations, have allowed the dynamics of single DNA molecules in flow to be studied with unprecedented detail [1,2]. These studies have shed light on the dynamics of long chain molecules relevant to a spectrum of applications from the manipulation of single DNA molecules in lab-on-a-chip devices to the processing of synthetic polymers in complex industrial flows. To date, single molecule studies have focused primarily on pure shear flow and on extensional flow [1–5].

When DNA molecules are subjected to hydrodynamic forces in a flow field, their conformational response depends on flow strength, parametrized by the Weissenberg number Wi and the flow-type parameter α [6,7]. Considering planar mixed flows, the dimensionless velocity gradient is given by

$$\frac{\partial u_i^{\infty}}{\partial x_j} = \dot{\gamma}\begin{bmatrix} 0 & 1 & 0 \\ \alpha & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \tag{1}$$

where $\dot{\gamma}$ is the strain rate. The Weissenberg number is defined as $\mathrm{Wi}=\dot{\gamma}\tau_0$, where τ_0 is the longest relaxation time of the molecule. Motivated by de Gennes' prediction of shear flow as a critical point with respect to the coil-stretch transition [8], Shaqfeh, Chu, and co-workers have investigated DNA tumbling dynamics in pure shear flow ($\alpha=0$) [5,9] and *near* shear flows [6]; a few results are also available for mixed flows with $\alpha>0$ [7]. While rotational flow is important in many complex geometries (converging, diverging, and bending channels), there is little research on DNA dynamics in rotation-dominated flows. Indeed, many microfluidic geometries, including grooved or curved channels and cavity flows, have been designed specifically to generate vorticity to enhance mixing and accelerate hybridization [10–12]. Here, we examine the tumbling dynamics of single DNA molecules across the spectrum of flow type from pure shear to pure rotational ($\alpha=-1$) flows over a wide range of flow strength Wi. Brownian dynamics (BD) simulations were carried out for free-draining, wormlike bead-spring models [13] using a numerical scheme described elsewhere [14]. Except where noted, calculations were made for a number of springs $N_s=9$, with 17 Kuhn steps per spring, which corresponds to λ DNA at high salt concentration [13]. Direct visualization experiments on fluorescent λ DNA were performed in a microfluidic four-roll mill [15] that allowed control of the flow type over $-1<\alpha<0$ for varying Wi.

Due to vorticity, polymer molecules in all flows considered undergo end-over-end tumbling resulting in fluctuations in the fractional molecular extension x/L, where L is the polymer contour length, and in the polymer orientation angle θ. As noted by others, evaluation of the tumbling period using the power spectral density (PSD) of the molecular extension is difficult because the PSD does not exhibit distinct peaks in shear or weak flow [2,5,9,16]. We use molecular angle (θ), defined by the ratio of molecular lengths between flow gradient (δ_2) and flow directions [$\theta=\tan^{-1}(\delta_2/x)$], to directly count the molecular tumbling as suggested by Schroeder *et al.* [5]. By examining θ of molecules alternately passing the tumbling axis ($\theta=\pi/2$ or $-\pi/2$), and directly recording molecular conformations, the tumbling dynamics of DNA molecules have been captured.

Experiments in pure shear flow report two tumbling pathways: via coiled and folded states [5,17]. It is known that the probability of tumbling via the folded shape increases with flow strength, while the coiled state is dominant at low Wi. Both tumbling pathways are observed in our simulations. Figure 1(a) shows the probability of the molecular length in the flow-gradient plane for a λ DNA for a series of molecular trajectories for varying flow strength and type from our simulations. In weak shear flow, the molecular trajectory is practically symmetric about the orientation angle. In this regime, molecules generally tumble in the coiled state, so the end position is smoothly reduced by the spring force. As Wi increases, a tail in the molecular trajectory appears caused by folded DNA conformations. Here, the molecular angle is more closely aligned with the flow axis, and a Brownian fluctuation can kick a segment away from the flow axis, so that the end position suddenly decreases by the reverse flow. Thus, the probability below the orientation angle is asymmetrically increased. For $\alpha<0$, this trajectory is changed to an ellipsoid whose major and minor axes lie on the flow and flow-gradient axes, respectively. This ellipsoid becomes a circle for purely rotational flow independent of Wi. The tumbling motion of λ DNA molecules was measured directly in the rotation-dominated regime using a microfluidic four-roll mill device [15]. While the tumbling pathways are well

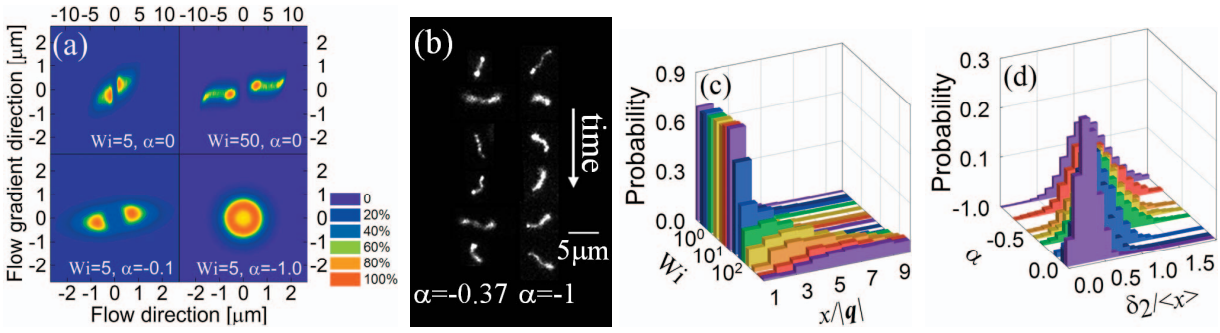

FIG. 1. (Color) Change of tumbling pathway with the flow strength (Wi) and flow type (α). (a) Molecular trajectories for varying Wi and α obtained from probabilities of the molecular length of λ-DNA molecules relative to the center of mass, located at the origin. (b) Experimentally observed images of λ DNA in partially (Wi=4.65, $\alpha=-0.37$) and purely (Wi=2.95, $\alpha=-1.0$) rotational flow during a period. (c) Changes in characteristic length ratio ($x/|\mathbf{q}|$) during tumbling versus Wi to distinguish coiled from folded shapes in shear flow. (d) Molecular thickness in flow-gradient direction during tumbling compared with average molecular extension ($\delta_2/\langle x\rangle$) versus α at Wi=50.

known in near shear flow [5,17], Fig. 1(b) represents the transition of the tumbling pathway from an ellipsoidal orbit to circular shape as the flow-type parameter goes to −1, consistent with the simulations in Fig. 1(a).

To quantitatively confirm the tumbling pathway, we introduce a characteristic length ratio defined as the ratio of molecular extension (x) to magnitude of the end-to-end vector ($|\mathbf{q}|$) of a DNA molecule when it tumbles. If the molecule tumbles via the coiled state, this characteristic length ratio remains near unity, whereas it has a value greater than unity for the folded state. For shear flow [Fig. 1(c)], the probability that $x/|\mathbf{q}|\sim 1$ was almost unity at $\mathrm{Wi}<20$, but decreased dramatically when $\mathrm{Wi}>20$, in agreement with experiments [5,17]. Simulations reveal a new tumbling pathway for rotational flows. With decreasing α, the characteristic length ratio became unity, however, not because the molecule was tumbling via a coiled state. Unlike in shear flow (where the molecule stretches, aligns, flips, and collapses), the molecular length during tumbling in a rotational flow is almost constant in time: the molecule tumbles via a vanelike motion. The length ratio between molecular thickness (δ_2) and average molecular length ($\langle x\rangle$) during tumbling shows a normal distribution, centered around 1 in pure rotational flow ($\alpha=-1$), because the DNA molecule rotates with the flow field, and the molecular length only fluctuates by thermal motion [Figs. 1(b) and 1(d)]. The transition to this vane pathway in mixed flow will occur in the vicinity of shear flow [cf. Fig. 1(d)], thus the tumbling dynamics will shift from shearlike to the rotation-dominated regime at α near 0.

The transition of the tumbling dynamics from the shearlike to the rotational regime has also been substantiated using the tumbling period (Fig. 2). The tumbling periods T are classified into three modes depending on the flow strength and type. First, in the low Wi regime T_{BM} was almost constant since in very weak flows tumbling is due mainly to Brownian motion and is independent of the flow field or type. Second, in the shearlike regime $T_{shear}\sim \mathrm{Wi}^{-0.62}$, identical to earlier results for pure shear [5,17]. Third, in the rotationlike regime, $T_{rotation}\sim \mathrm{Wi}^{-1}$. We also note that for $\alpha\sim 0$, before the transition from the Brownian-dominated to the shearlike region, T shows a slight overshoot near Wi=1.

To elucidate the change of tumbling period with Wi and α and establish scaling laws, we have examined the ratio of mean fractional extension to mean fractional thickness ($\langle x\rangle/\langle\delta_2\rangle$) in shear and rotational flows. As shown by others [5,17], in shear flow this quantity determines the time scales of the advection-driven phases of the tumbling process (molecular stretching, alignment, and collapsing); i.e., $t_{\mathrm{adv}}\sim\langle x\rangle/\mathrm{Wi}\langle\delta_2\rangle$, while the time scale for the diffusive, flipping phase of tumbling goes as $t_{\mathrm{diff}}\sim\langle\delta_2\rangle^{8/3}$. In shear at high Wi, our simulations show $\langle x\rangle/\langle\delta_2\rangle\sim\mathrm{Wi}^{0.38}$, consistent with previous experiments and simulations. However, $\langle x\rangle/\langle\delta_2\rangle$ deviates from this asymptotic line ($\sim\mathrm{Wi}^{0.38}$) at lower Wi and ultimately reaches a constant value at $\mathrm{Wi}\ll 1$ where the flow cannot extend the molecule from the coiled state [Fig. 3(a)]. Due to the reduction of this length ratio from $\sim\mathrm{Wi}^{0.38}$ at moderate Wi, the tumbling period decreases from the general scaling law $\sim\mathrm{Wi}^{0.62}$ and estimated T_{shear}. At $\mathrm{Wi}<1$, there is no advection phase, and the tumbling period approaches the duration time for the diffusive, flip phase only. Therefore, the tumbling period in the weak flow regime has a constant value (T_{BM}) since $\langle\delta_2\rangle/\langle\delta_{2,0}\rangle\sim 1$.

For rotation-dominated flows, there is a smooth transition from T_{BM} to $T_{rotation}$ with increasing Wi. Moreover, the overshoot in T near $\mathrm{Wi}\sim 1$ was not observed in rotational flow because $\langle x\rangle/\langle\delta_2\rangle$ is independent of Wi [Fig. 3(a)]. Our simulations show that as α approaches −1, the ratio ($\langle x\rangle/\langle\delta_2\rangle$) $\sim 1/|\alpha|^{0.5}$ [Fig. 3(b)]. Since the advection time scales as

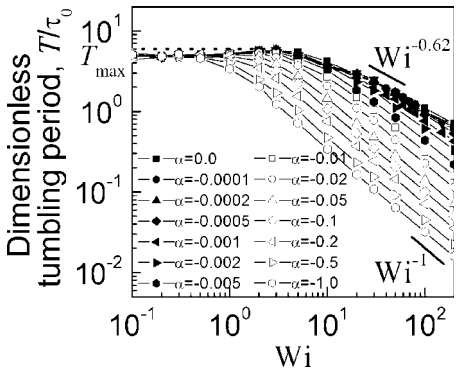

FIG. 2. Dimensionless tumbling periods (T/τ_0) of λ DNA in mixed flow; τ_0 is the relaxation time.

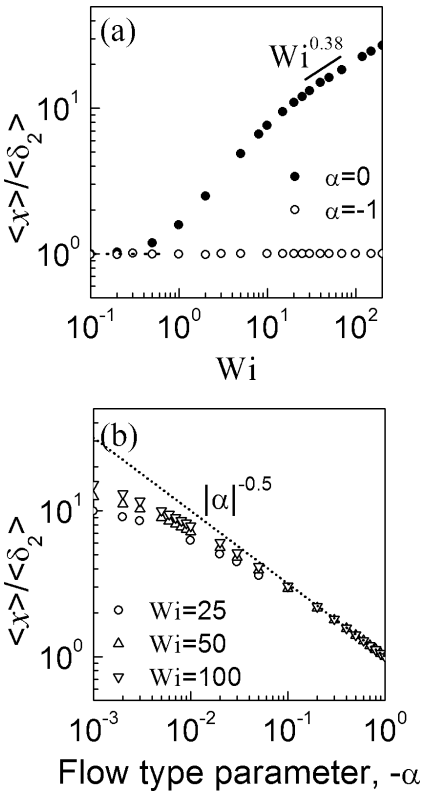

FIG. 3. Molecular length ratio between flow and flow-gradient direction ($\langle x\rangle/\langle\delta_2\rangle$) as a function of (a) Wi in shear and rotational flow and (b) α for λ DNA.

$\langle x\rangle/\mathrm{Wi}\langle\delta_2\rangle$, the scaling law for the tumbling period in mixed flow—except for $\alpha\sim 0$—can be represented as a function of effective Wi ($\mathrm{Wi}_{\mathrm{eff}}=\mathrm{Wi}|\alpha|^{0.5}$), as previously introduced in extensional-dominated flow [7,18]. We note that for rotational flow, the duration time for the flipping phase scales as $\sim\langle\delta_2\rangle/\mathrm{Wi}|\alpha|\langle x\rangle$ since the flip occurs due to the rotational component of the flow field rather than Brownian motion. Thus, $T\sim\mathrm{Wi}_{\mathrm{eff}}^{-1}$ for all but "near-shear" mixed flows at high Wi. Figure 4(a) demonstrates that the tumbling period obeys a universal scaling law with $\mathrm{Wi}_{\mathrm{eff}}$ over a very broad range of α and Wi; all simulation results collapse without any fitting parameter. We verified that the tumbling period determined by direct counting is identical to that from the PSD of x/L at $\mathrm{Wi}_{\mathrm{eff}}=30$ [inset, Fig. 4(a)]. This tumbling frequency also coincides with the analytical solution for a Hookean dumbbell model in the high $\mathrm{Wi}_{\mathrm{eff}}$ limit [[7], Eq. (4)]. Moreover, experimentally observed tumbling periods, measured for $1.1<\mathrm{Wi}<18.7$ and $-1<\alpha<-0.3$ and plotted in Fig. 4(a), agree quantitatively with the scaling law.

On the other hand, very near pure shear (i.e., $\alpha\sim 0$), the tumbling period departs from the universal behavior in Fig. 4(a) due to the increasingly strong effects of Brownian motion relative to rotational flow on the time for the flipping phase. As noted by Woo and Shaqfeh [6], this transition in tumbling behavior occurs in a very narrow α range; our simulations show shearlike tumbling only at $\alpha>-0.01$ for λ DNA. For the shearlike regime, Brownian motion flips the molecule faster than the flow field; in the rotation-dominant regime, Brownian motion loses the competition with flow.

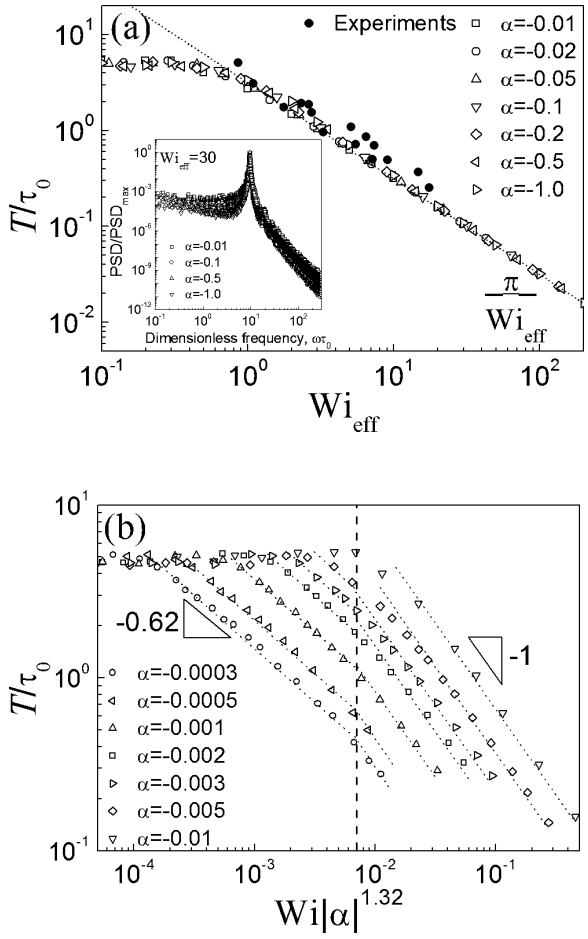

FIG. 4. (a) Master curves of dimensionless tumbling period (T/τ_0) in rotational flow regime using $\mathrm{Wi}_{\mathrm{eff}}$. The peak frequency in the inset coincides with the direct counting method by BD simulation (open symbols) and experimental observations (closed circles) for $1.1<\mathrm{Wi}<18.7$ and $-1<\alpha<-0.3$. (b) Critical value for transition from shearlike ($\sim\mathrm{Wi}^{-0.62}$) to rotational-dominant region ($\sim\mathrm{Wi}^{-1}$).

Hence, in the shearlike regime, as Wi is increased from $\mathrm{Wi}\ll 1$, there is at least some window in which the tumbling period follows the shear ($\mathrm{Wi}^{-0.62}$) scaling before switching to the Wi^{-1} dependence seen in rotation-dominated flows. Thus, no master curve for the near-shear simulations was possible using $\mathrm{Wi}_{\mathrm{eff}}$. However, we have derived a critical value for the transition from the shearlike ($\sim\mathrm{Wi}^{-0.62}$) to rotational ($\mathrm{Wi}_{\mathrm{eff}}^{-1}$) regime based on the tumbling period of each phase ($T_{shear}=T_{rotation}$). From this relation, the critical value was determined by plotting the tumbling period against $\mathrm{Wi}|\alpha|^{1.32}$. As shown in Fig. 4(b), the slope changes drastically at the critical value of $(\mathrm{Wi}|\alpha|^{1.32})_c\approx 0.007$.

The very different effects of molecular contour length L on the tumbling period in shear and rotational flow can also be rationalized in terms of $\langle x\rangle/\langle\delta_2\rangle$. In pure shear, both Graetz-Levecque dispersion layer arguments [9] and BD simulations [6] yield a time scale for the advective phase $t_{\mathrm{adv}}\sim\mathrm{Wi}^{-0.62}L^{0.35}$. For the overall tumbling time T, the length exponent is less than 0.35, because the flipping time by Brownian motion has no length dependency [17]. Our

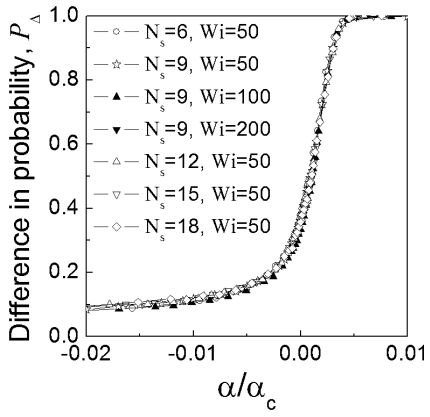

FIG. 5. Master curve for difference in probability using critical flow-type parameter scaling law.

simulations in shear flow for $6<N_s<18$ show $T_{shear} \sim \mathrm{Wi}^{-0.62}L^{0.3}$. However, $\langle x\rangle/\langle \delta_2\rangle$ is only a function of α in the rotational flow regime; in rotation, both the advection time and the flipping time are independent of L. Based on the expressions for tumbling periods of shearlike and rotational flow dominant regimes ($\alpha<0$), we can derive the scaling for the critical flow-type parameter $|\alpha_c| \sim \mathrm{Wi}^{-0.76}L^{-0.6}$. This expression for α_c, which indicates that both flow strength and molecular length reduce the shearlike regime, is qualitatively similar to the scaling law of Woo and Shaqfeh [6] derived from physical arguments based on the principal axis of the flow. To test the effectiveness of our scaling law for α_c, we calculated the difference in probability (P_Δ) representing conformational phase transitions for different Wi and molecular length [cf. [6], Eq. (11)]. Even though α_c was derived for $\alpha<0$, the difference in probability for varying L, α, and Wi is effectively collapsed over the range shown onto a reference state (λ DNA at Wi=50) using our α_c scaling (Fig. 5).

In summary, we have investigated the dynamics of DNA tumbling by experiment and direct simulation in flows of varying flow strength and type. For rotation-dominated flows, both experiments and simulations reveal that DNA molecules tumble with the flow field via a vanelike motion, and the tumbling period follows a universal law. A transition from shearlike to rotational flow dominant regimes has been observed and the critical flow-type parameter for this transition α_c has been derived. This critical flow-type parameter qualitatively coincides with values and scaling laws proposed earlier [6], and quantitatively collapses simulation data.

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[1] E. S. G. Shaqfeh, J. Non-Newtonian Fluid Mech. **130**, 1 (2005).
[2] R. G. Larson, J. Rheol. **49**, 1 (2005).
[3] P. S. Doyle, B. Ladoux, and J.-L. Viovy, Phys. Rev. Lett. **84**, 4769 (2000).
[4] D. E. Smith, H. P. Babcock, and S. Chu, Science **283**, 1724 (1999).
[5] C. M. Schroeder, R. E. Teixeira, E. S. G. Shaqfeh, and S. Chu, Phys. Rev. Lett. **95**, 018301 (2005).
[6] N. J. Woo and E. S. G. Shaqfeh, J. Chem. Phys. **119**, 2908 (2003).
[7] J. S. Hur, E. S. G. Shaqfeh, H. P. Babcock, and S. Chu, Phys. Rev. E **66**, 011915 (2002).
[8] P. G. de Gennes, J. Chem. Phys. **60**, 5030 (1974).
[9] J. S. Hur, E. S. G. Shaqfeh, and R. G. Larson, J. Rheol. **44**, 713 (2000).
[10] T. M. Squires, and S. R. Quake, Rev. Mod. Phys. **77**, 977 (2005).
[11] H. Song, D. L. Chen, and R. F. Ismagilov, Angew. Chem., Int. Ed. **45**, 7336 (2006).
[12] H. H. Lee *et al.*, Lab Chip **6**, 1163 (2006).
[13] J. F. Marko and E. D. Siggia, Macromolecules **28**, 8759 (1995).
[14] M. Somasi *et al.*, J. Non-Newtonian Fluid Mech. **108**, 227 (2002).
[15] J. S. Lee, R. Dylla-Spears, N. P. Teclemariam, and S. J. Muller, Appl. Phys. Lett. **90**, 074103 (2007).
[16] R. Delgado-Buscalioni, Phys. Rev. Lett. **96**, 088303 (2006).
[17] R. E. Teixeira *et al.*, Macromolecules **38**, 581 (2005).
[18] G. G. Fuller and L. G. Leal, Rheol. Acta **19**, 580 (1980).